| Modern Management of

ABNORMAL UTERINE BLEEDING



Edited by

Peter Joseph O'Donovan Charles Miller



MODERN MANAGEMENT OF ABNORMAL UTERINE BLEEDING

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Composition by Exeter Premedia Services Private Ltd., Chennai, India Printed and bound in India by Replika Press Pvt. Ltd I would like to dedicate this book to my parents, Patrick and Sheila and also my loving wife Carmel and children, James, Olivia, Charles and Niamh, who have always been a constant source of encouragement to me.

Peter Joseph O'Donovan

I would like to dedicate this book to the women in my life – my mother, Muriel, my daughter, Abagayle and my loving wife Laura.

Charles E Miller

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Preface

Our original concept was to construct the authoritative reference on the current management of abnormal uterine bleeding. Divided into subsections to make resourcing easier, it would be carefully crafted to provide a complete up-to-date overview of this common concern. Chapters were to be designed to discuss pathophysiology, diagnosis, the myriad of treatment options, as well as future research. Contributing authors selection was to be rigorous, as it would be based on an international reputation, recognized expertise in the field, and their appreciation for the clinical arena. Their task at hand was to incorporate current medical practice, with evidence in literature, and the latest research to create a relevant discourse.

The resultant *Modern Management of Abnormal Uterine Bleeding* is a unique and valuable resource for medical students, housestaff undergoing training in gynecology, as well as physicians currently in practice. Ultimately, it is our desire that this treatise will challenge all those involved in the treatment of the female with abnormal uterine bleeding to provide a holistic, state-of-the-art, evidence based approach to her care.

Peter Joseph O'Donovan Charles E Miller

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Charles E Miller

Menstruation: historical perspective

1

James Drife

INTRODUCTION

The history of menstruation is a story of change. Over the centuries, society's attitude to women has altered, and so have women's attitudes to doctors and to their own bodies. This process seems to be accelerating. Only a few years ago, reviews of the history of menstruation made relaxing reading, with little relevance to current practice.1 They covered predictable ground - primitive superstition, medical ignorance, and societal taboos - and made modern doctors feel superior to their predecessors. In recent years, however, universities have established departments of feminist studies, and a new wave of academics, mainly but not exclusively women, has begun in-depth examination of historical attitudes to menstruation. Their work includes critical examination of doctors' assumptions, and some of their conclusions make disturbing reading for gynecologists. Our belief that we are motivated mainly by sympathy for women and women's troubles is now being subjected to hostile scrutiny.

This chapter will look at menstruation from a historical perspective under three headings familiar to medical educators. The first section, on 'knowledge', will outline how medical science's understanding of menstruation has progressed over the centuries. The second section, on 'skills', will briefly review the development of medical methods for investigating and treating menstrual disorders. The third section, on 'attitudes', will focus on how society in general and women in particular view this aspect of human physiology.

KNOWLEDGE

Compared to subjects such as astronomy and architecture, knowledge about human physiology developed late in human history. For many centuries, philosophy, science, and religion were closely interlinked, making it difficult for us in retrospect to separate knowledge from attitudes. For example, Aristotle (384–322 BC) believed that the ideal human form was male and the female body

was a distortion of the ideal. He taught that women have fewer teeth than men. He believed that semen and menstrual fluid were both products of the blood, which in the male is fermented to form sperm but in the female is not fully fermented and leaves the body with less force because women have less energy than men.²

Aristotle's father was a physician and a near-contemporary of Hippocrates, who lived from 460 to 370 BC). Greek physicians were forbidden to dissect corpses and had to make their observations on material that had left the body. The writings of Hippocrates (actually written by several doctors) include a detailed description of menstrual flow and its abnormalities in the presence of disease. The menses were examined to determine which of the four humors – phlegm, blood, bile, and water – predominated, and this would form the basis for diagnosis. Chinese medicine in the 7th century AD also relied heavily on a woman's description of her periods, and medicines were used to try to achieve 'menstrual balancing'.³

In medieval Europe, menstruation was seen, not as a function of the uterus, but as a purification of the whole body. This concept persisted until the 18th century, as shown by the 1st edition of the *Encyclopaedia Britannica*, published in 1771:

MENSES, Flours, Courses, *catamenia*: in medicine, the monthly evacuations from the uterus of women not with child and not giving suck. ... As soon as a healthy female arrives at her full growth, she generates more blood than can be conveniently contained in the vessels; wherefore the superfluity is evacuated by the uterine arteries, and is call the Menses. Boerhaave observes, that in a suppression of the menses there is a plethora, with a listlessness to motion; a heaviness, a paleness, a pain in the loins and of the groin; all the functions, whether natural, vital, or animal, are depraved. Sometimes the menses will force a way thro' the eyes, ears, nostrils, gums, the salival ducts, bladder, breasts, skin, wounds or ulcers.⁴

Objective scientific observation had begun, however, during the 17th century, helped by the invention of

the microscope. Regnier de Graaf had described the ovarian follicle in 1672, but although he thought it must contain an oocyte he never saw one. The human oocyte was finally identified in 1778 by William Cruikshank, a Scottish-born anatomist and partner of William Hunter. In 1775, another contemporary, Percival Pott, linked oophorectomy with cessation of menstruation.

In the 19th century menstruation was recognized to be linked to ovulation. In 1866, J Marion Sims, the 'father of American gynecology' wrote in his textbook Clinical Notes on Uterine Surgery:

Menstruation is the sign of ovulation; it is preparatory to the reception of the ovum ... the ovum reaches the cavity of the uterus two to ten days after menstruation ... the uterus itself is the normal seat of conception.

The mechanism of uterine bleeding, however, was still a mystery. In the 1860s Pflüger developed the 'German theory' that increasing pressure in the Graafian follicle caused reflex irritation of the ovarian nerves, leading to pelvic congestion and menstruation. This theory was still predominant at the start of the 20th century, but, by then, animal experiments had begun to clarify endometrial physiology. An overview in the first issue of the *British Journal of Obstetrics and Gynaecology* (then the *Journal of Obstetrics and Gynaecology of the British Empire*) in 1902 commented:

On Menstruation we have fairly clear ideas. Opinion has rather swung round to Pfluger's views as to the causal relation between ovulation and menstruation. Heape's researches on the changes in the uteri of monkeys have supported markedly those who held that during menstruation a superficial denudation of the mucous membrane goes on. The exact nature of menstruation and its significance is still a matter for speculation ...⁵

In 1908 Hitschmann and Adler published detailed histologic pictures of the human endometrial cycle and around this time knowledge of physiology began to catch up with knowledge of anatomy. In the early 1900s the word 'hormone' was coined by a colleague of Ernest Starling, Professor of Physiology at University College, London,⁶ but it was some time before the sex hormones were identified. Trying to understand menstruation before this must have been tantalizing. In 1909, Willey summarized knowledge thus:

The monthly cycle should probably be regarded as a vasomotor change (produced by a stimulus whose source is uncertain, but dependant on the integrity of the ovaries) by means of which the uterine wall is richly supplied with blood in preparation for the normal function of hypertrophy in presence of an impregnated ovum. At all events, we know that the uterus does become enlarged at the monthly cycle through over-filling of its capillary system with blood, and when no pregnancy occurs, the increased blood supply escapes by rupture of capillaries and diapedesis of corpuscles, with possibly some slight destruction of the surface epithelium.⁷

Animal experiments during the 1920s and 1930s clarified the nature of estrogen and progesterone^{8,9} and it became accepted that menstruation was caused by withdrawal of ovarian hormones, although in 1935 this was still being disputed.¹⁰ In 1937, it was suggested that estrin (estrogen), but not progestin, was in some way related to a chemical substance causing the necrosis of the endometrium.¹¹ Prostaglandins were discovered in 1936 by Ulf von Euler, Professor of Physiology at the Karolinska Institute in Stockholm, who later discovered norepinephrine and received the 1970 Nobel Prize for Physiology or Medicine. (His father and his godfather had also been Nobel prizewinners.) Follicle-stimulating hormone and luteinizing hormone were identified in 1939.

The effects of the cycle on the endometrium were described by Markee in 1940 after classic experiments on explants in the eyes of Rhesus monkeys. The human endometrial cycle was described in 1950 by Noyes et al. In the late 1950s, estrogens and progestogens were synthesized through the work of chemists such as Carl Djerassi, ushering in the era of hormonal contraception and giving women control of menstruation for the first time.

SKILLS

During the last two centuries, treatment of menstrual disorders moved from ineffectual drugs, through major surgery, to more effective medication and minimal access surgery. The debate about when menstruation becomes a 'menstrual disorder' will be discussed later but some cases are clearly pathologic. The *Lancet* of 1828 reported a case hemorrhagic shock due to a bleeding fibroid polyp weighing nearly two pounds (just under 1 kg). It was removed from the vagina by progressively tightening a ligature around its base and the woman survived. At the other extreme, the *Lancet* of 1850 described women with no uterine or vaginal disease, who were regularly treated by caustic applied through a vaginal speculum and who had 'the most revolting attachment ... to the practice and to the practitioner'. 15

In 1857, Henry Savage, senior physician to the Samaritan Hospital, London, described the treatments then available for heavy periods:

Menorrhagias (or rather metrorhagias) are said to be active, passive, functional, or symptomatic, according as they are considered to depend on general vascular derangement, on diathesis, or on morbid states of the womb itself. The remedies most useful, are such as correspond with these views. Thus cooling purgatives, drastics, antimonials, bleeding, astringents, have each had their advocates. The same may be said of the series of special antimenorrhagics – bitartrate of potash, oxide of silver, Indian hemp, digitalis, Cayenne pepper, cinnamon &c, and of the removal from the womb itself of some tangible exciting cause, as polypus in one or other of its innumerable varieties. The majority of menorrhagias yield to one or other of the above remedies; but some do not.¹⁶

Savage described the successful treatment of two cases of 'obstinate menorrhagia' in which the cervix was dilated by sponge tents over 3 days. One woman was then treated by curettage (which she did not find painful), and the other by injections of iodine into the uterus (which she did, but which were nevertheless continued every 3 days for a fortnight). The uterine curette had been invented in 1843 by a French surgeon, JCA Recamier, at the Hôtel-Dieu in Paris.

Hysterectomy

Major surgery was initially limited to cases of prolapse or massive abdominal tumor. In 1809, the first ovariotomy was performed by Ephraim McDowell in Kentucky, on a woman with a huge ovarian cyst. The first planned and successful vaginal hysterectomy was carried out in 1813, by Conrad Langenbeck of Göttingen. The first abdominal hysterectomy in England was performed in 1843 in Manchester by Charles Clay, who had expected to remove an ovarian cyst but instead discovered a huge fibroid – a diagnostic pitfall that remained common until the advent of ultrasound. He removed the uterus and the patient died shortly afterwards.¹⁷

Ether anesthesia was discovered in 1846 by William Morton in Massachusetts and chloroform anesthesia by James Young (JY) Simpson in Edinburgh in 1847. (The word 'anesthesia' was coined by poet and physician Oliver Wendell Holmes in a letter to Morton.) The first successful abdominal hysterectomy was carried out in 1853 in Massachusetts by Walter Burnham, using chloroform anesthesia. Burnham (who, like Charles Clay, had expected to find an ovarian cyst) commented that 'he would not easily be induced to make another attempt to extirpate the uterus.' Others were more enthusiastic, however. The first successful abdominal hysterectomy with bilateral salpingo-oophorectomy was carried out in 1856 in Knoxville, Tennessee, by William J Baker of Kentucky. Europe's first successful hysterectomy was performed by

Charles Clay in 1863 and the specimen, a large fibroid, was taken to Edinburgh by JY Simpson, who happened to visit Manchester after the operation.

Surgery became less dangerous after Lister introduced antisepsis in 1865¹⁹ and the indications quickly extended. Bilateral oophorectomy for intractable menorrhagia was first performed in 1872 in Birmingham, England, by Robert Lawson Tait (who also introduced salpingectomy for ectopic pregnancy). In 1881, Thomas Savage of Birmingham reported carrying out 28 bilateral oophorectomies, with recovery of the patient in each case, 20 and the Lancet reported a 33-year-old woman with ovarian dysmenorrhoea treated by bilateral oophorectomy in the North Staffordshire Infirmary: 'The patient was evidently of an hysterical disposition, and the constant pain had increased this tendency.' The consultant commented that 'the question of the propriety of removing the ovaries whole in an incipient state of disease' was an open one, but felt justified in doing so because the woman, having been unfit for work for 2 years, seemed cured by the operation.²¹ Two cases of oophorectomy for dysmenorrhea were reported from Bradford in 1884: both women, aged 26 and 28 years old, had been keen for surgery and both were delighted at being cured.²²

At this time it was taught that hysterectomy should not be performed 'until oophorectomy had been already tried and had failed'. ²³ Lawson Tait was said to believe that menstrual function depended on the fallopian tubes, not the ovaries, but this was questioned and hysterectomy became more common. In 1897 the British Gynaecological Society discussed cases of hysterectomy for menorrhagia in young women, and debated the wisdom of removing the uterus in all cases of protracted bleeding because of concern that some might be due to cancer. Doubts were expressed about the reliability of histopathologic reports. ²⁴

Minimal access surgery

The picture is one of rapid acceptance of surgical treatment, both major and minor. In 1888, a correspondent wrote in the *British Medical Journal*: 'My present practice is to curette in every case of disease affecting the uterine mucous membrane'. The era of offering curettage as a treatment for all forms of uterine bleeding lasted for almost a century and is remembered without fondness by today's senior gynecologists. It is only relatively recently that blind curettage has been replaced by visualization of the uterine cavity, either by ultrasound or hysteroscopy.

The story of hysteroscopy, however, also began at the start of the 19th century. A 'light conductor', consisting of a wax candle, mirrors, and metal conducting tubes, was developed by Philipp Bozzini, a German doctor who died in 1809 aged 35 years old. Antonin Jean Desormeaux, at

the Hôpital Necker in Paris, then developed an endoscope to study the urethra and bladder. In 1865, Francis Cruise of Dublin improved the illumination with a paraffin-lamp light source. Its use in investigating the uterus was first reported by D Commander Pantaleoni, who graciously thanked Dr Cruise in his first and only paper on the subject in 1869.¹⁷

Endoscopy was taken up by urologists, but the uterus, unlike the bladder, was difficult to distend and bled easily on contact. In France, JM David described uterine endoscopy in 1907 and in America in 1925 IC Rubin described the use of carbon dioxide as a distention medium. Complications were reported, however, and it was not until the second half of the 20th century that the combination of cold light sources, better lenses, and modern fiberoptics brought in the era of modern hysteroscopy. 25

Laparoscopy was first reported in humans in 1910 by HC Jacobaeus in Sweden. 'Celioscopy' was further developed in 1943 by Raoul Palmer at the Broca Hospital in Paris, and in 1958 he was visited by Patrick Steptoe, who introduced the technique into Britain and wrote a monograph on the subject in 1967. At first, gynecological laparoscopy was limited to minor procedures such as sterilization, but innovators such as the late Kurt Semm of Kiel, Germany, pioneered techniques that led to modern minimal access surgery.

ATTITUDES

Attitudes to menstruation are affected by a society's culture, in particular its attitude to women. Culture is influenced by religion and, nowadays, by the media and advertising. Attitudes are also affected by gender. Male and female commentators have different views on how our ancestors viewed menstruation, and on the evolution of menstruation.

Evolution

The menstrual cycle occurs only in humans, apes, and some monkeys. ²⁶ In many species the reproductive cycle is controlled by the sun. How ovulation became linked with the lunar cycle is unknown. A male chronobiologist suggested that primitive humans were nocturnal, so that selection pressure favored women who ovulated at the time of the new moon when it was too dark for hunting. A female biologist suggested that the menstrual cycle is economical in terms of energy consumption, a woman's metabolic rate being at least 7% lower during the follicular phase than during the luteal phase of the cycle. ²⁷ Rosalind Miles, in *The Women's History of the World*, commented that the change from an estrus to a menstrual cycle made humans much more fertile than other primates, and thus

the main reason why our species has been so successful may have been a female, not a male, evolutionary adaptation.²⁸ Desmond Morris, in *The Naked Ape*, pointed out that when humans adopted the upright posture, male genital display – an unusual activity among animal species – became inevitable but the vulva became hidden, and he suggested that this may have been a factor in initiating the menstrual taboo.²⁹

The menstrual taboo

The Polynesian word 'taboo' means 'forbidden' or 'sacred': it is said that it also means 'menstruation', but evidence is lacking for this. ³⁰ Nevertheless, as Rosalind Miles points out, 'of all human substances, blood is the most highly charged with power and danger'. The early Native Americans of Dakota believed that the *wakan* (sacredness or power) of a menstrual woman could weaken the *wakan* of all masculine objects of power, both of war and peace. Miles also cites 'the dietary prohibition against eating blood in force from Jews to Sioux to Hindus'.

In many societies menstruation was regarded as unclean. In ancient China, menstrual blood was not allowed to touch the ground for fear of offending the Earth spirit. In ancient Egypt, ritual cleansing baths were mandatory at the end of menstruation. Hindu teaching, according to the Parsi sage Zoroaster was: 'A menstruous woman is the work of Uhremaun, the Devil. A woman in her courses is not to gaze upon the sacred fire, sit in water, behold the sun or hold conversation with a man.' Nowadays, in Britain, Hindu women may ask for tablets to delay their period so that they may take part in religious festivals.

Paula Weideger quotes numerous examples of how some primitive peoples segregate women during menstruation: 'Special huts are built for menstruating women by the Baikairi of Brazil, the Shuswap of British Columbia, the Guari of Northern India, the Veddas of Ceylon, and the Algonquin of the North American forest.' In some cultures, segregation goes further: 'In Uganda, pots which a woman touches while the impurity of menstruation is upon her have to be destroyed; spears and shields defiled by her touch are, however, merely purified. Among the Bribri indians of Costa Rica the only plates she may use for her food are banana leaves, which, when she has done with them, she throws away in some sequestered spot; for if a cow were to find them, and eat them, it would waste away. And she drinks out of a special vessel for the same reason: if any one drank out of the same cup after her, he would surely die.' Among the Dogan of East Africa, a menstruating woman brings misfortune to everything she touches: not only is she segregated in an isolated hut and provided with special eating utensils but also if she is seen passing through the village a general purification must take place.³¹

In the Middle East, women during menstruation sometimes must leave the home and live in a menstruation hut or tent. If the woman is allowed to live in the home, she must not prepare any food or touch her husband. Nor may she enter a house in which there is an ill person.

Menstrual myths were described by the Roman historian Pliny the Elder in AD 77 in his *Natural History*, which was arguably the first encyclopedia. Its oft-quoted description of menstruation is reproduced from O'Dowd and Philip's *History of Obstetrics and Gynaecology*:

A fatal poison corrupting and decomposing urine, depriving seeds of their fecundity, blasting garden flowers and grasses, causing fruits to fall from branches, dulling razors. ... If the menstrual discharge coincides with an eclipse of the moon or sun, the evils resulting from it are irremediable. ... Congress with a woman at such time being noxious and attended with fatal effects to man. ... Contact with [menstrual blood] turns new wine sour, crops touched by it become barren, grafts die, seeds in gardens are dried up, the fruit of trees fall off, the edge of steel and the gleam of ivory are dulled, hives of bees die, even bronze and iron are at once seized by rust and a horrible smell fills the air; to taste it drives dogs mad and infects their bites with an incurable poison. ... Even that very tiny creature the ant is said to be sensitive to it, and throws away grains of corn that taste of it and does not touch them again. ... Over and above there is no limit to woman's power. First of all, they say that hail storms and whirl winds are driven away if menstrual fluid is exposed to the very flashes of lightning; that stormy weather too is thus kept away. It makes a liniment for gout and by her touch a woman in this state relieves scrofula, parotid tumours, superficial abscesses, boils and eye fluxes.³²

As recently as 1937 in the *Journal of Obstetrics and Gynaecology of the British Empire*, Beatty, arguing for the existence of a menstrual toxin, pointed out that:

Folklore on the Continent forbids the handling of fruit or flowers then, and declares that dough kneaded by a menstruating woman will not rise properly. It is also a common belief in some parts of the country that if a woman cures hams while she is menstruating the hams may be spoilt.¹¹

Menarche

In some cultures, even those which observe menstrual taboos, menarche is an event to be celebrated by the

whole tribe.³¹ In New Guinea, Margaret Mead observed that at the first menstruation of a young girl who is already married, her brothers build her a menstrual hut and her female relatives rub her with stinging nettles: after 3 days her mother's brother makes decorative cuts on her shoulders and buttocks. In South India, members of the Brahmin community perform the ritual of Samati Sadang: the girl is given a milk bath by a married male relative and then joins a family feast. Rosalind Miles quotes a ritual among the Kafe of Papua New Guinea:

When a girl began to menstruate she was shut in a darkened hut for a week, deprived of food, and taught that she was dangerous to herself and to others if she failed to abide by the ritual restrictions: her body and blood would make a man vomit, turn his blood black, corrupt his flesh, addle his wits and waste him to death.

Such rituals seem strange to us now, but Paula Weideger wrote:

In some families a vestige of more elaborate ritual remains. Among Jewish families, for example, it is customary to slap a young woman's face on the day that menstruation begins. The women I have met who have had this experience say they hadn't the vaguest notion of why their mothers slapped them. Many believed that it was a unique experience and the product of an aberration or a disturbed mother.

Nevertheless, in Western culture, the menarche is generally a secret and unwelcome development. Simone de Beauvoir wrote about puberty in her classic book *The Second Sex*:

She is proud of becoming a woman and watches the maturing of her bosom with satisfaction, padding her dress with handkerchiefs and taking pride in it before her elders; she does not yet grasp the significance of what is taking place in her. Her first menstruation reveals this meaning, and her feelings of shame appear. ... All the evidence agrees in showing that whether the child has been forewarned or not, the event always seems to her repugnant and humiliating.³³

Havelock Ellis reported that in 1896 about half of American schoolgirls had either no advance knowledge or only vague knowledge at the time of their first menses. De Beauvoir suggested that things were much the same in 1946. The Reverend Chad Varah founded the charity, The Samaritans, in 1953, having been deeply affected by his first funeral as a vicar: a 14-year-old girl had killed herself after her periods started, thinking it was venereal disease.

Germaine Greer, in *The Female Eunuch*, gave a frank description of her own menarche:³⁴

The arrival of menarche is more significant than any birthday, but in the Anglo-Saxon households it is ignored and carefully concealed from general awareness. For six months while I was waiting for my first menstruation I toted a paper bag with diapers and pins in my school satchel. When it finally came, I suffered agonies lest anyone should guess or smell it or anything. My diapers were made of harsh towelling, and I used to creep into the laundry and crouch over a bucket of foul clouts, hoping that my brother would not catch me at my revolting labours. It is not surprising that well-bred, dainty little girls find it difficult to adapt to menstruation, when our society does no more than explain it and leave them to get on with it. Among the aborigines who lived along the Pennefather river in Queensland the little girl used to be buried up to her waist in warm sand to aid the first contractions, and fed and cared for by her mother in a sacred place, to be led in triumph to the camp where she joined a feast to celebrate her entry into the company of marriageable maidens, it seems likely that menstruation was much less traumatic.

Religion

Early religions involved worshipping goddesses and, in some religions, menstruating goddesses were considered more powerful.³⁵ The ancient Egyptians, Greeks, and Romans had a mixture of gods and goddesses but the modern monotheistic religions – Judaism, Bhuddism, Christianity, and Islam – all perceive God as male. His prophets were male and his priests, even today, are almost all male. This gender imbalance has had profound effects on attitudes to menstruation.

In the Book of Leviticus, generally dated at the 7th century BC, Chapter 15 begins with rules of hygiene relating to a discharge from a man's body – perhaps an infected wound or an abscess. It then applies them to semen and to both regular and irregular 'discharge of blood' from a woman's body. After emission of semen, a man is unclean until the evening, but the rules for women are more rigorous:

When a woman has a discharge of blood which is her regular discharge from her body, she shall be in her impurity for seven days, and whoever touches her shall be unclean until the evening. And everything upon which she lies during her impurity shall be unclean; everything also upon which she sits shall be unclean. And whoever touches her bed shall wash his clothes, and bathe himself in water, and be unclean until the evening. And whoever touches anything upon which she sits shall wash his clothes, and bathe himself in water, and be unclean until the evening; whether it is the bed or anything upon which she sits, when he touches it he shall be unclean until the evening. And if any man lies with her, and her impurity is on him, he shall be unclean seven days; and every bed on which he lies shall be unclean. [verses 19–24]

If a woman's cycle is abnormal, the strictures are more severe:

And if a woman has a discharge of blood for many days, not at the time of her impurity, or if she has a discharge beyond the time of her impurity, all the days of the discharge she shall continue in uncleanness. ... But if she is cleansed of her discharge, she shall count herself seven days, and after that she shall be clean. And on the eighth day she shall take two turtledoves or two young pigeons, and bring them to the priest, to the door of the tent of meeting. And the priest shall offer one for a sin offering and the other for a burnt offering; and the priest shall make atonement for her before the Lord for her unclean discharge. [verses 25–30]

Early Christian practices forbade menstruating or postpartum women from entering church or taking communion. In the late 6th century, Pope Gregory the Great challenged this, arguing that menstruation was an involuntary 'infirmity', but his views were not universally endorsed. Exclusionary practices were ended in the 12th century by Pope Innocent III, who decided that a menstruating woman could not be prohibited from entering church, although if she wanted to stay out she should not be discouraged from doing so.³⁶ The Church continued to prohibit sexual intercourse during menstruation. Its negative attitudes were not confined to its male priests. Hildegard of Bingen, a 12th century abbess, agreed with the view that menstruation was a punishment for the fall of Eve in the Garden of Eden.

The Koran does not forbid prayer or worship during menstruation and does not require any 'cleansing' rituals, although verse 2:222 states that sexual intercourse must be avoided during the menses.

Medical attitudes

Unlike the church, the medical profession in the distant past was not exclusively male. In the 11th century, Trotula was a physician and gynecologist, and wrote a book called *The Diseases of Women*. Between 1389 and 1497 in

Frankfurt, there were 15 licensed women doctors in practice, and in the 15th century German women were presenting theses at medical schools. Women were, however, not generally welcomed. By 1220, the University of Paris had introduced statutes to debar women from admission to its medical school and, in 1485, the King of France issued a decree withdrawing women's right to work as surgeons. In Italy, some universities disbarred women from attending, although the University of Bologna had a female professor of medicine in the 14th century, as well as a female professor of mathematics and a woman pathologist.

In Britain in the 19th century the rising medical profession fiercely excluded women. Apart from James Miranda Barry, who pretended to be a man and qualified in Edinburgh in 1812, and Elizabeth Blackwell, who graduated in New York in 1849, Britain's first woman medical graduate was Elizabeth Garrett in 1865. For the next 100 years, British medical schools imposed strict limits on the number of female entrants into medicine. It was only in 1979 that the British Medical Association had a female president, Dame Josephine Barnes, who had experienced prejudice before being appointed in 1954 as an obstetrician and gynecologist in Charing Cross Hospital, London, where she was the first female member of the consultant staff.

Nineteenth century doctors clearly saw women as 'the weaker sex'. In 1888 the *Lancet*, commenting on a paper on 'hysteria' wrote: 'It cannot, of course, be denied that women have nerves strung to finer issues and more multiplied sensations than are those of men, and that pain, *qua* pain, is not necessarily such a serious or significant thing in women as in men.'³⁷ In both Britain and America, women (at least those of the middle and upper classes) were regarded as delicate. The American medical historian Harold Speert quotes *Harper's* magazine:

'The fact is certain, that the American girl is a very delicate plant ... not generally strong in nerve and muscle, and too ready to fade before her true midsummer has come' and Edward Clarke, in a popular book published in 1874: 'A girl cannot spend more than four, or, in occasional instances, five hours of force daily upon her duties, and leave sufficient margin for the general physical growth that she must make. ... If she puts as much force into her brain education as a boy, the brain or the special apparatus will suffer.'³⁸

This attitude towards women underlay the advice given about menstruation itself. Speert quotes William Robinson, from a book which was first published in the late 19th century but went through many editions until 1928:

'Rest is just as important during menstruation as cleanliness, if not more so. ... It is an outrage that

many delicate, weak girls and women must stay on their feet all day or work on a machine when they should be at home in bed or lying down on a couch. ... there should be as much rest as possible. For delicate and sensitive girls it is always best to stay away from school during the first and second days. ... It is best that dancing, bicycle riding, horseback riding, rowing, and other athletic exercises be given up altogether during the means. Automobile riding and railroad and carriage travel prove injurious in some instances.'

This attitude was challenged by Mary Putnam Jacobi, one of the first women to graduate in medicine in the USA. In 1876 she published a report, *The Question of Rest for Women during Menstruation*, noting how many women work for a living, including 467 261 women employed in the textile industry in Great Britain. She performed experiments showing that muscular strength did not change during the monthly cycle, and circulated a questionnaire to 1000 women, of whom 268 responded. The results of showed that 35% did not suffer pain, discomfort, or weakness during menstruation. Dr Jacobi concluded:

Purely spasmodic pain of moderate intensity, may be, and certainly is, tolerated in an immense majority of cases, far better while the ordinary occupations are continued. ... The only cases where rest really cures or prevents menstrual pain, are those where general debility is so marked that the loss of blood at menstruation is sufficient to lower the nutrition of the nerve centres below the level to which they are capable of generating force with ease. ... There is nothing in the nature of menstruation to imply the necessity, or even the desirability, of rest, for women whose nutrition is really normal. ... The menstrual flow is the least important part of the menstrual process, and the arguments for rest drawn from the complexity of the physiological phenomena involved in this, should logically demand rest for women during at least twenty days of the twenty-eight or thirty. In other words, should consign them to the inactivity of a Turkish harem.

Nevertheless, doctors continued to perceive and describe menstruation in terms of illness. In the 19th century, the menstrual cycle was linked with insanity and 'hysteria' and dysmenorrhea was considered normal. In the 20th century, the Medical Women's Federation attempted to change this perception, and in 1925 the Federation issued *The Hygiene of Menstruation: An Authoritative Statement*, which was distributed to doctors

and schools and attempted to introduce positive terminology: 'Menstruation is a natural function; it is not an illness, and girls should continue their ordinary work and play during the period. It should not be and is not normally accompanied by pain and malaise.'³⁹

Nevertheless, even today, many women find normal periods burdensome and turn to a doctor for help. At the end of the 20th century in Britain, over 20% of women underwent hysterectomy before the menopause. Gynecologists were bitterly criticized because of this⁴⁰ and the rate has now fallen, mainly because of the introduction of new methods of abolishing or reducing menstruation without the need for major surgery. Our specialty is caught between the wishes of individual patients and the political force of feminism.

Feminism

Modern feminism began in the late 18th century. In prerevolutionary France, philosophers wrote in favour of female emancipation. In England, Mary Wollstonecraft, arguably the first major feminist, published *A Vindication* of the Rights of Women in 1792, proposing that women should receive the same treatment as men in education, work, and politics and should be judged by the same moral standards. In the USA, the Women's Rights Convention in 1848 promoted a bill of rights demanding a redress of the wrongs done to women. In 1869, the British philosopher John Stuart Mill (influenced by his essayist wife, Harriet Taylor Mill) wrote *The Subjection of Women*, asking why one-half of the human race should be subjected to the other.

In 1949, Simone de Beauvoir's *The Second Sex* argued that liberation for women meant liberation for men too. In the USA, Betty Friedan published *The Feminine Mystique* in 1963 and founded the National Women's Movement in 1966, attacking the conditioning of women to accept passive roles and depend on male dominance. Women's movements proliferated in many countries and the United Nations declared 1975 International Women's Year. The aims of feminism vary hugely from country to country. In some the goals are basic, such as abolishing the custom of buying a bride, and in others they go beyond equal opportunity and place feminist concerns at the center of the political agenda.⁴¹

Feminists have divided opinions about menstruation. Some celebrate it as an essential part of womanhood⁴² and would disagree with what Germaine Greer wrote in 1960: 'Menstruation does not turn us into raving maniacs or complete invalids; it is just that we would rather do without it.' Feminist comedians enjoy breaking the menstrual taboo, as Dr Greer did:

Women still buy sanitary towels with enormous discretion, and carry their handbags to the loo

when they only need to carry a napkin. They still recoil at the idea of intercourse during menstruation, and feel that the blood they shed is of a special kind, although perhaps not so special as was thought when it was the liquid presented to the devil in witches' loving cups. If you think you are emancipated, you might consider the idea of tasting your menstrual blood – if it makes you sick, you've a long way to go, baby.

Also in *The Female Eunuch*, Dr Greer commented on the language of menstruation:

The contradiction in the attitude that regards menstruation as divinely ordained and yet unmentionable leads to the intensification of the female revolt against it, which can be traced in all the common words for it, like the *curse*, and male disgust expressed in terms like *having the rags on*. We have only the choice of three kinds of expression: the vulgar resentful, the genteel ('I've got my period', 'I am indisposed'), and the scientific jargon of the *menses*. Girls are irrepressible though: in one Sydney girls' school napkins are affectionately referred to as *daisies*; Italian girls call their periods *il marchese* and German girls *der rote Konig*.

The word 'curse', however, may come from 'courses', and 'rags' is an allusion to sanitary protection before the invention of the disposable napkin. Until well into the 20th century women used rags or pieces of linen which they washed after use. Modern disposable sanitary towels were first marketed in the USA in 1921 under the brand name 'Kotex' (a contraction of 'cotton-like texture'). The idea of internal tampons was patented in the USA in 1937 when the Tampax Company was founded, but their use did not spread around the world until after World War II.

Advertising these products created difficulties. Early advertisements for Kotex referred to 'woman's greatest hygienic handicap', reinforcing negative views of menstruation. Some feminists are uneasy that menstruation has been taken over by big business and that advertising reinforces the idea that it is shameful. Shail and Howie begin their recent book *Menstruation: A Cultural History* with a description of a cinema advertisement showing a crowded cinema auditorium:

A warning sign and voiceover follows, indicating that 'the following manoeuvre must only be undertaken with the proper protective gear'. A woman is then shown moving along a crowded row to her seat, the camera following her bottom and hips closely. She sits down and the safety gear is revealed to be the Tampax Compak tampon.⁴⁴

Advertising sanitary protection on British television was banned entirely until 1979, when a limited range of advertisements was allowed for an experimental period, and was finally allowed in the 1980s, after research showed increasing public acceptance. Some feminists felt that the decision to allow advertising owed more to commercial pressure than to a wish for equality of the sexes. Sophie Laws, in *Issues of Blood: The Politics of Menstruation*, quoted the guidelines to advertisers: 'No commercial may contain anything likely to cause embarrassment or to undermine an individual's confidence in her own personal hygiene standards', 'No advertisement may feature an unwrapped towel or tampon', and 'The use of potentially offensive words like "odour" is not acceptable.' On screen, blue fluid is used to illustrate absorbency.

Feminists in the UK also campaigned against value added tax (VAT) being charged on sanitary protection, unlike other necessities of life which are exempt. In the early 1990s this tax brought the Treasury at least £30 million a year. Although mainstream political parties and even medical organizations apparently felt too embarrassed to protest, the tax was quietly reduced from 17.5% to 5% in 2001.

Women can now do without periods completely if they so wish. The oral contraceptive pill was originally formulated to give women a monthly withdrawal bleed for marketing reasons because monthly bleeds seemed 'normal'. This pattern is a major reason for the Pill's failure rate and it has been known for 30 years that is unnecessary. Nevertheless, most women do not want to take the pill continuously or in a 'tri-cycle' pattern. Long-acting progestogens also offer freedom from menstruation

and are proving popular in the form of subcutaneous implants for contraception among young women or an intrauterine progestogen-containing system among older women.

Some feminists, however, feel strongly that this represents needless medical interference with the female reproductive system and argue that women can do without the help of doctors. *Menstruation: A Cultural History* includes a scathing onslaught on the idea, promoted mainly by men,²⁶ that menstruation is an unfortunate by-product of evolution which we can now reverse. Zahra Meghani writes:

They do not recommend that men's reproductive physiology be aligned with the evolutionary norm for non-human primates. ... Bipedalism, for instance, is not categorised as a pathological evolutionary aberration although it is both unique to humans and causes some percentage of the population to experience various physical ailments such as fallen arches and back pain...⁴⁹

Most men would not like to menstruate and male gynecologists have generally been sympathetic to women who complain about their periods. The gender balance in our specialty is rapidly changing now, at least in the UK, but feminist thinkers are likely to continue to regard female and male doctors with equal suspicion. Whether their views about menstruation will be influential remains to be seen, but the current debate exemplifies the mixed feelings with which individual women view their periods. The sympathetic gynecologist needs to understand the background to this ambivalence.

References

- Drife JO. Menstruation: a cultural and historical perspective. In: Cameron IT, Fraser IS, Smith SK, eds. Clinical Disorders of the Endometrium and Menstrual Cycle. Oxford: Oxford University Press, 1998: 3–12.
- Hiltman G. Menstruation in Aristotle's concept of the person.
 In: Shail A, Howie G, eds. Menstruation: A Cultural History.
 Basingstoke: Palgrave Macmillan, 2005: 25–37.
- Arata L. Menses in the corpus Hippocraticum. In: Shail A, Howie G, eds. Menstruation: A Cultural History. Basingstoke: Palgrave Macmillan, 2005: 13–24.
- 4. Encyclopaedia Britannica. Edinburgh, 1771.
- Hart DB. Obstetrics at the beginning of the twentieth century: an attempt at an appreciation. J Obstet Gynaecol Br Emp 1902; 1: 51–60.
- 6. Starling EH. The Croonian Lectures on the chemical correlation of the functions of the body. Lancet 1905; 166: 299–41.

- 7. Willey FE. Menstruation and menorrhagia. J Obstet Gynaecol Br Emp 1909; 15: 236–40.
- 8. Corner GW. Our knowledge of the menstrual cycle 1910–1950. Lancet 1951; i: 919–23.
- 9. Allen WM, Meyer RK. The quantitative separation of progestin from oestrin in extracts of the corpus luteum. Am J Physiol 1933; 106: 55–63.
- Cannon DJ. Menstruation and menstrual disorders. J Obstet Gynaecol Br Emp 1935; 42: 88–106.
- 11. Beatty J. The immediate cause of menstruation. J Obstet Gynaecol Br Emp 1937; 44: 1080–8.
- Markee JE. Menstruation in intraocular endometrial explants in the rhesus monkey. Contrib Embryol Carnegie Inst 1940; 28: 219–308.
- 13. Noyes RW, Hertig AT, Rock J. Dating the endometrial biopsy. Fertil Steril 1950; 1: 3–25.

- Smith C. Large polypus uteri successfully treated by ligatures. Lancet 1828; 10: 827–8.
- Hall M. On a new and lamentable form of hysteria. Lancet 1850; 55: 660–1.
- 16. Savage H. On obstinate menorrhagia. Lancet 1857; 70: 570-1.
- 17. Baskett TF. On the Shoulders of Giants: Eponyms and Names in Obstetrics and Gynaecology. London: RCOG Press, 1996.
- Hall JJ, Hall DJ. The forgotten hysterectomy. The first successful abdominal hysterectomy and bilateral salpingo-oophorectomy in the United States. Obstet Gynecol 2006; 107: 541–3.
- 19. Lister J. On the antiseptic principle in the practice of surgery. Lancet 1867; 90: 353–6.
- 20. Savage T. Oophorectomy. Lancet 1881; 117: 805.
- Anonymous. North Staffordshire Infirmary. Case of oophorectomy for ovarian dysmenorrhoea; recovery. Lancet 1881; 118: 750–1.
- Spence WJ. Bradford Infirmary. Two cases of double oophorectomy. Lancet 1884; 124: 1091–2.
- Bantock GG. Clinical remarks on a case of hysterectomy. Lancet 1883; 121: 627–8.
- Anonymous. British Gynaecological Society. Lancet 1897; 150: 1650–1.
- Sutton C. Hysteroscopic surgery. Best Pract Res Clin Obstet Gynaecol 2006; 20: 105–37.
- Short RV. The evolution of human reproduction. Proc Roy Soc B 1976; 195: 3–24.
- 27. Strassmann BI. The evolution of endometrial cycles and menstruation. Q Rev Biol 1996; 71: 181–22.
- 28. Miles S. The Women's History of the World. London: Michael Joseph, 1988.
- 29. Morris D. The Naked Ape. London: Jonathan Cape, 1967.
- 30. Buckley T, Gottlieb A. A critical appraisal of theories of menstrual symbolism. In: Buckley T, Gottlieb A, eds. Blood Magic: The Anthropology of Menstruation. Berkeley: University of California Press, 1988: 3–50.
- 31. Weideger P. Female Cycles. London: The Women's Press, 1978.
- 32. O'Dowd M, Philip E. History of Obstetrics and Gynaecology. London: Parthenon, 1994.
- 33. De Beauvoir S. The Second Sex. London: Jonathan Cape, 1953.
- 34. Greer G. The Female Eunuch. London: MacGibbon & Kee,

- Jenett DE. Menstruating women/menstruating goddesses: sites
 of sacred power in South India. In: Shail A, Howie G, eds.
 Menstruation: A Cultural History. Basingstoke: Palgrave Macmillan, 2005: 176–87.
- Green MH. Flowers, poisons and men: menstruation in mediaeval Western Europe. In: Shail A, Howie G, eds. Menstruation:
 A Cultural History. Basingstoke: Palgrave Macmillan, 2005: 51–64.
- 37. Anonymous. "Hysteria". Lancet 1888; 131: 236.
- Speert H. Obstetric and Gynaecologic Milestones. London: Parthenon, 1996.
- 39. Strange JM. "I believe it to be a case depending on menstruation": madness and menstrual taboo in British medical practice c 1840–1930. In: Shail A, Howie G, eds. Menstruation: A Cultural History. Basingstoke: Palgrave Macmillan, 2005: 102–16.
- 40. Greer G. The Whole Woman. London: Doubleday, 1999.
- Eisenstein H. Contemporary Feminist Thought. London: Unwin, 1984.
- Meador BdeS. Thesmophoria: a woman's fertility ritual. In: Zweig C, ed. To Be a Woman: The Birth of the Conscious Feminine. London: Mandala, 1991.
- Vostral SL. Masking menstruation: the emergence of menstrual hygiene products in the United States. In: Shail A, Howie G, eds. Menstruation: A Cultural History. Basingstoke: Palgrave Macmillan, 2005: 243–58.
- 44. Shail A, Howie G. "Talking your body's language": the menstrual materializations of sexed ontology. In: Shail A, Howie G, eds. Menstruation: A Cultural History. Basingstoke: Palgrave Macmillan, 2005: 1–10.
- Laws S. Issues of Blood: The Politics of Menstruation. Basingstoke: Macmillan, 1990.
- 46. Drife JO. Rags to riches. BMJ 1992; 304: 646.
- 47. Dillon J. Parties have women on their mind. Independent Online Edition: published March 26, 2000.
- Loudon NB, Foxwell M, Potts DM, Guild AL, Short RV. Acceptability of an oral contraceptive that reduces the frequency of menstruation: the tri-cycle pill regimen. BMJ 1977; ii: 487–90.
- Meghani Z. Of sex, nationalities and populations. The construction of menstruation as patho-physiology. In: Shail A, Howie G, eds. Menstruation: A Cultural History. Basingstoke: Palgrave Macmillan, 2005: 130–45.

Michael Zinger

HYPOTHALAMIC CONTRIBUTION

Gonadotropin-releasing hormone (GnRH) plays a vital, permissive role throughout the phases of the menstrual cycle. It is released from the arcuate nuclei of the hypothalamus and then travels to the pituitary through the portal circulation. GnRH is always secreted in a pulsatile fashion, and this pulsing pattern is a prerequisite for gonadotropin production and release from the pituitary gland. Gonadotropins, in turn, stimulate ovarian function. The complex feedback loop between ovarian steroids and gonadotropins then brings about the normal cyclic nature of menstruation. However, without the constant, underlying pulsation of GnRH, no activity can occur within the reproductive axis.

The pulsation of GnRH release is intrinsic to the neurons that produce it. There are, however, factors that exert influence over the rate and the amplitude of the pulsations. Gamma-aminobutyric acid (GABA) and the endorphins are intermediaries for the effects of the ovarian steroids, as described below. Additionally, although its specific role is not well understood, leptin is integrally involved in the suppression of GnRH that can occur when energy expenditure exceeds caloric intake.

Pulsatile GnRH is both permissive and regulatory of pituitary production of the gonadotropins, follicle-stimulating hormone (FSH) and luteinizing hormone (LH). Lower frequency of GnRH pulsations favors greater FSH production, while higher frequency favors LH. Pituitary concentrations of follistatin increase with greater GnRH pulse frequency. Indeed, follistatin appears to be the local pituitary intermediary of the selective FSH suppression caused by increasing GnRH frequencies. Follistatin acts by binding and neutralizing activin, an autocrine/paracrine promoter of pituitary FSH production. As opposed to its important local function, circulating activin appears to be entirely neutralized by follistatin binding, thus preventing any endocrine activity.¹

In contrast to the gonadotropin-promoting effect of pulsatile GnRH, exposure to constantly elevated levels of GnRH inhibits FSH production. This counterintuitive

effect occurs due to either receptor saturation, preventing further stimulation, or to internalization of the GnRH receptors. Exposure to long-acting GnRH agonists causes suppression of the pituitary—ovarian axis within approximately 3 weeks. The resulting condition is a temporary menopausal state. This response has been exploited for the purposes of treating problems such as fibroids and dysfunctional uterine bleeding.

MENSTRUAL CYCLE

The start of menses heralds the beginning of the follicular phase. By definition, the first day of menstrual bleeding is considered day 1 of the cycle. The length of the cycle is considered to be the number of days from the start of menstrual bleeding in one cycle until the start of bleeding with the next cycle. Definitions of the normal length vary. Depending on the source, the minimum normal length ranges from 21 to 24 days while the maximum ranges from 35 to 40 days. More typically, the length will consistently be close to 28 days.

Physiologic menstruation occurs due to the failure of an oocyte to fertilize and establish a pregnancy. There are three components to this cyclic process that must precede each physiologic menstruation:

- the follicular phase in the ovary, which induces a simultaneous proliferative phase in the endometrium
- ovulation
- the luteal phase in the ovary, which induces a simultaneous secretory phase in the endometrium.

Follicular phase

At the start of the menstrual cycle, there are normally more than seven early antral follicles, amongst both ovaries, that may be visualized by ultrasound as being 4–10 mm in size (Figure 2.1).² These early antral follicles have developed from primordial follicles over a number of months in a process that appears to be mostly independent of



Figure 2.1 Early antral follicles as seen on day 1 of the menstrual cycle.

FSH. However, at the early antral stage they have become dependent on FSH for their growth and survival.³ In fact, a rise in FSH at the start of the follicular phase is critical to rescue these follicles from atresia. Combination oral contraceptives, for example, prevent development of a follicle by preventing a rise in FSH, thus leading to atresia of these follicles.

As the ovarian follicle develops further, it produces increasing amounts of estradiol through cooperation of its two distinct cell types: theca cells produce androgens in response to LH stimulation; granulosa cells aromatize these androgens into estradiol in response to FSH stimulation. Estradiol is secreted into the bloodstream, resulting in increasing serum levels, which guide endometrial development.

Activin is produced by the granulosa cells during the early part of the follicular phase. As an autocrine factor, it drives aromatization and FSH and LH receptor production within the granulosa cell. As a paracrine factor, activin suppresses excess androgen production within the theca cells.

In response to FSH stimulation, the granulosa cells produce increasing amounts of inhibin B, which acts in both endocrine and paracrine roles. Circulating inhibin B is necessary to suppress pituitary FSH production, leading to a plateau in FSH levels in the mid-follicular phase. Local inhibin acts on the theca cells in a paracrine fasion to augment LH-induced androgen production during the late follicular phase.

Estradiol further suppresses FSH production at both the hypothalamic and pituitary levels, bringing about a decline in FSH levels as the follicular phase progresses. In the hypothalamus, (GABA) probably functions as an intermediary, resulting in decreases of GnRH pulse amplitude without change in the pulse frequency. In the pituitary, estradiol appears to have a direct inhibitory effect on gonadotrophs, further decreasing FSH production.¹

Around the end of the first week of the follicular phase, one follicle amongst the two ovaries gains advantage, allowing it to outgrow and suppress its peers. As the serum FSH level dwindles, it is not adequate to maintain the non-dominant follicles; thus, they undergo atresia. Their death is hastened by the increasingly androgenic environment. The dominant follicle, however, has the advantages of developing adequate aromatase capacity which can continue, even with decreasing FSH levels, to enrich the follicle's local estrogen/androgen ratio.

The insulin-like growth factors (IGFs) are peptides, structurally similar to insulin, that exert ovarian paracrine and autocrine activity. FSH and estradiol may stimulate IGF-I production by the granulosa cells. IGF-I acts on the theca and granulosa cells to augment steroidogenesis, aromatase activity, LH receptor synthesis, and inhibin secretion. However, IGF-II is the dominant ovarian IGF. IGF-II is expressed both by granulosa and by theca cells and appears in greater concentrations in follicular fluid than does IGF-I. IGF-II stimulates granulosa cell mitosis as well as steroidogenesis and aromatase activity. It produces many of the same actions as IGF-I, as it is able to bind both the IGF-I and the IGF-II receptor. IGF-I can only bind the IGF-I receptor.

Growth hormone (GH) augments the gonadotropininduced follicular steroid production. Indeed, increasing GH serum levels are mirrored by increases in estradiol levels throughout the follicular phase. The ovarian effects of GH are mediated by IGF-I.⁵

Proliferative phase

The successive changes in the endometrium during the follicular phase are directly guided by steroid hormone secretion from the developing oocyte follicle in its goal to prepare an ideal environment for implantation. Estrogen is the necessary stimulant of endometrial proliferation. This growth appears to be triggered by a threshold estrogen concentration of 50–100 pg/ml.⁶

As the cycle begins, most of the endometrial surface has been lost during menstruation. All that remains is the basalis, a thin covering of the myometrium. The basalis is a non-functional layer that ultimately gives rise to reformation of a functional endometrium. The remaining epithelium is in the area of the tubal ostia and at the isthmus, i.e. the junction between the cervix and the uterine cornua. In the presence of estrogen, this epithelium spreads from these remnants and, in a matter of 2–3 days, grows to cover the entire uterine cavity.⁷ Rather than a direct effect on the endometrial epithelium, estrogen acts on the underlying stroma, which in turn produces a mediator that carries this message to the epithelium.⁸ This local mediator of estrogen action is very likely to be IGF-1.

As the follicular phase progresses, estrogen leads to thickening of the endometrium from less than 1 mm up to 3.5-6 mm. Endometrial lining thickness can easily be measured by transvaginal ultrasound, with distinctive changes seen through the cycle. Near the completion of menses, the two basalis layers are directly opposed without intervening functionalis, appearing as a thin echogenic stripe (Figure 2.2). The developing functionalis appears as a non-echogenic area between the two echogenic basalis stripes. The potential space that is the endometrial cavity represents a third, middle stripe creating the trilaminar appearance that is characteristic of the follicular phase (Figure 2.3). This is the only stage at which the two endometrial linings are seen separately. By convention, the standard format for reporting endometrial thickness at any point during the cycle is a single measurement across both sides of the endometrial lining.

The progressive thickening of the endometrium is due to estrogen-driven growth in the functionalis, composed of the spongiosa and superficial compact layers. As opposed to the basalis, the functionalis is the more superficial portion of the endometrium that is entirely lost during each normal menstruation. It is also the portion of the endometrium that prepares for blastocyst implantation. The

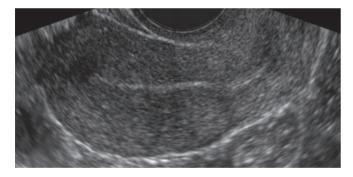


Figure 2.2 Thin endometrial canal at start of proliferative phase.



Figure 2.3 Thickening trilaminar endometrium near the end of the proliferative phase.

tremendous growth is probably fueled by estrogenactivated oncogenes.

The basal arteries, which flow toward the cavity through the basal layer, extend to become spiral arteries in the functionalis as it grows. Near the epithelial surface of the functionalis, a plexus of capillaries develops, which is fed by the spiral arteries. This impressive degree of angiogenesis stems from migration and mitosis of endothelial cells with critical structural support by pericytes and extracellular matrix. Regulation is achieved by a multitude of growth factors and cytokines which are ultimately driven by the ovarian steroids. A central role for vascular endothelial growth factor (VEGF) has been promulgated; however, its concentration within the endometrium does not vary during the menstrual cycle. 10

Ovulation

By creating increasing serum levels of estrogen, the maturing dominant follicle induces the pituitary gland to trigger the follicle's own ovulation. This trigger occurs in the form of an enormous spike in serum LH levels. The steadily increasing levels of estradiol have acted directly on the pituitary gland by heightening its sensitivity to GnRH. Thus, the ever-present GnRH pulsations now elicit a greatly enhanced response of LH secretion from the pituitary gland. Interestingly, progesterone production by the ovarian follicle begins to occur prior to the start of the LH surge, leading to speculation that progesterone may facilitate the surge.

Surging serum levels of LH act directly on the mature follicle to bring about release of the oocyte 34–36 hours after the beginning of the surge. 11 Prostaglandins are crucial intrafollicular mediators of ovulation, so that the process may be disrupted by non-steroidal anti-inflammatories. 12

Luteal phase

Directly following ovulation, the follicle transforms into a corpus luteum. The granulosa cells within the follicle luteinize, gaining the ability to make progesterone, as well as VEGF. In response to VEGF, vascular invasion into the new corpus luteum occurs quickly, creating an extensive capillary network.¹³ This blood supply is critical to delivering adequate cholesterol substrate, in the form of low-density lipoprotein (LDL), to allow a tremendous rate of progesterone production. Adequate progesterone is essential for inducing the secretory phase in the endometrial lining and preventing premature breakdown of the lining.

Progesterone acts on the hypothalamus through endorphin intermediaries. The result is a slowing of GnRH pulse frequency and thus also the frequency of FSH as well as LH pulsations. However, the amplitude of LH pulses is increased even as their frequency declines.

Typically, the luteal phase, and the progesterone production that it entails, lasts 14 days, with a normal range of 12–16 days. During this time, increased amplitude of pituitary LH pulses maintains sufficient progesterone production in the corpus luteum. At the end of the luteal phase, however, the responsiveness of the corpus luteum to LH diminishes greatly, leading to plunging progesterone levels. Declining LH responsiveness and the scheduled disruption of the corpus luteum, i.e. luteolysis, appears to be triggered by invading leukocytes producing tumor necrosis factor alpha (TNF- α) and hydrogen peroxide. Another potential mediator of declining LH responsiveness is prostaglandin F2 α (PGF2 α), although its origin is unclear. ¹⁴

If fertilization occurs and the resulting embryo implants successfully in the endometrium, it will, prior to luteolysis, secrete human chorionic gonadotropin (hCG) into the serum. The embryonic hCG prevents luteolysis and, by cross-reacting with the LH receptor, provides continuing stimulation for progesterone production. Persisting serum progesterone levels prevent endometrial shedding, thus precluding menses and allowing the pregnancy to develop.

Decreased LH stimulation prematurely depletes corpus luteum function, i.e. causes luteal phase deficiency. This can occur in a number of conditions, including thyroid disease, hyperprolactinemia, opioid use, or stress, although commonly it is an idiopathic occurrence. It can also occur sporadically in only one cycle. Regardless of the cause, it presents as either a shortened cycle, spotting near the end of the cycle, or inadequate secretory transformation of the endometrium leading to infertility.

With the end of the luteal phase, GnRH and therefore FSH pulse frequency is released from progesterone suppression. Accelerated FSH pulsatility sets the stage for stimulation of another cohort of follicles with the start of the next cycle.

Secretory phase

With exposure to adequate progesterone, growth of endometrial thickness ceases. This sudden halt appears to be related to progesterone suppression of estrogen-induced oncogenes. Indeed, adequate progesterone exposure on a regular basis is necessary to prevent endometrial hyperplasia and the risk of carcinoma.

The rapid development of a functionalis vascular system that occurred in the proliferative phase also ceases during the secretory phase. The change is due to progesterone promotion of angiogenesis inhibitors. Abnormally prolonged progestin influence over these mediators may

lead to structural changes in the endometrial surface vasculature, leading to the 'break-through' bleeding often seen with long-term progestin administration.¹⁵

Secretory endometrial cells also prepare the means for shedding the functionalis should pregnancy not occur. During the early secretory phase, the Golgi apparatus of epithelial, stromal, and endothelial cells within the endometrial functionalis produce lysosomes containing powerful lytic enzymes. These enzymes, if released, are capable of completely disrupting the cells of the functionalis layers. Adequate progesterone levels maintain the lysosomal integrity, preventing the autodigestion that their contents would cause.¹⁵

The hallmark of the secretory phase is increasing function of the endometrial glands. As their surrounding endometrial structure is no longer expanding, the lengthening glands become increasingly tortuous. Furthermore, they become filled with secretions of glycoproteins, peptides, and plasma transudate.⁴

The effects of progesterone can be identified by ultrasound, even early in the secretory phase, as an increased echogenicity of the functionalis. The trilaminar appearance that is noted during the proliferative phase disappears as the middle line, which represents the uterine cavity, is obscured by the increasing echogenicity (Figure 2.4). The two sides of the endometrial lining can no longer be separated on a standard ultrasound image.

Histologically, the secretory endometrium progresses through multiple changes, including pseudostratification, basal vacuolation, and stromal edema. Because of the orderly development of these findings, it is possible, by histologic examination of the endometrium, to determine the presence, length, and adequacy of progesterone exposure. This has been the gold-standard diagnostic measure of luteal phase deficiency. However, there are



Figure 2.4 Secretory endometrium.

concerns about the accuracy of this method due to significant intra-observer and cycle-to-cycle variations.¹⁷

MENSTRUATION

Physiologic menstruation results from self-destruction of the endometrial functionalis and the shedding of its remains. Throughout the luteal phase, progesterone suppresses release and production of enzymes that can bring about the autodigestion of the fuctionalis. In the absence of pregnancy, at the end of the luteal phase, progesterone levels drop and its endometrium-protecting effects are lost.

During the preceding luteal phase, progesterone suppresses expression of matrix metalloproteinases (MMPs), an action mediated by transforming growth factor beta (TGF-B). ¹⁹ The MMPs are a large family of enzymes that, in the absence of progesterone, digest the components of the extracellular matrix, leading to a structural breakdown of the endometrial functionalis. Additionally, with the loss of progesterone support, intracellular lysosomes rupture, releasing their destructive enzyme contents. These enzymes digest all cellular contents as well as surface membranes. ¹⁵

Contributing further to the degradation of the endometrium, is an inflammatory reaction that results from leukocyte-attracting chemokines released by the endometrial cells. Analogous to the regulation of MMPs, progesterone suppresses chemokine formation until the progesterone levels dwindle with the end of the luteal phase. Indeed, leukocyte infiltration is the final histologic change noted just prior to menses. The invading leukocytes further contribute to the supply of proteolytic enzymes that degrade the extracellular matrix, as well as signaling apoptosis within the cells of the functionalis. 20,21

With the destruction of the overlying layers that they were supplying, the basilar arteries instead lead to blood loss directly into the endometrial cavity. Blood loss continues until the epithelium reforms over the basalis. This occurs during the first few days of the proliferative phase of the subsequent cycle (see Proliferative phase section above). In the meantime, arterial vasoconstriction, mediated by endothelins and prostaglandins, helps to limit blood loss.²²

Based on monkey models, it was initially thought that vasoconstriction played a central role in bringing about sloughing of the functionalis through ischemia. This has since been disproven in humans in favor of the current autodigestion process described above. Thus, vasoconstriction has been relegated to a later role, assisting in hemostasis rather than initiating menstruation.

Clotting of blood at the basilar surface also helps to decrease blood loss. However, this clotting is partially prevented by plasminogen activators that are released from the endometrial tissue during its destruction. They increase the conversion of plasminogen to plasmin, which disrupts the formation of clots. This accounts for the non-coagulability of menstrual blood. In addition, plasmin functions to cleave and activate MMP proenzymes.²⁵

The endometrium's significant prostaglandin content is released during the destruction of the functionalis layers. In addition to arterial vasoconstriction, prostaglandins cause myometrial contractions. These contractions seem to contribute little if at all to decreasing blood loss but can lead to significant dysmenorrhea.

PERIMENARCHE

In the early reproductive years, the pituitary LH surge response to increasing estrogen levels is not reliable. As a result, the LH surge can be delayed, leading to a prolonged follicular phase. ²⁶ However, in the majority of perimenarchal months, the LH surge does not occur at all. Up to 82% of cycles during the first 2 years after menarche are anovulatory. ²⁷ As the hypothalamic–pituitary–ovarian axis matures, ovulation becomes consistent.

PERIMENOPAUSE

The average length of the menstrual cycle undergoes a slight, progressive decrease, especially in the late 30s and early 40s due to accelerated follicle selection. As this continues, the limited supply of follicles diminishes greatly, a phenomenon that is notable by a decrease in antral follicle count in baseline ultrasound evaluation.² Later, as the supply of follicles nears exhaustion, the frequency of ovulation becomes erratic. This leads to an increase in variability as well as in the average length of the menstrual cycle in the 2–8 years before menopause.²⁸ Additionally, decreasing follicle supply elicits a compensatory increase in FSH, possibly leading to elevated estradiol levels.²⁹

Because of the risks of increasing estrogen production and inconsistent ovulation, the physiologic menopausal transition is often associated with irregular bleeding. Ovulation may frequently fail; thus, unopposed estrogen can lead to heavy and unpredictable estrogen-withdrawal bleeding. Endometrial hyperplasia can also occur, with a concomitant increase in risk of carcinoma.³⁰

References

- Hall JE. Neuroendocrine control of the menstrual cycle. In: Strauss JF, Barbieri RL, eds. Yen and Jaffe's Reproductive Endocrinology, 5th edn. Philadelpia: Elsevier Saunders, 2004: 195–211.
- Frattarelli JL, Lauria-Costab DF, Miller BT, Bergh PA, Scott RT. Basal antral follicle number and mean ovarian diameter predict cycle cancellation and ovarian responsiveness in assisted reproductive technology cycles. Fertil Steril 2000; 74(3): 512–17.
- Strauss JF, Williams CJ. The ovarian life cycle. In: Strauss JF, Barbieri RL, eds. Yen and Jaffe's Reproductive Endocrinology, 5th edn. Philadelpia: Elsevier Saunders 2004: 213–53.
- Speroff L, Fritz M. Clinical Gynecologic Endocrinology and Infertilty, 7th edn. Philidelphia: Lippincott Williams & Wilkins, 2005.
- Rebar RW, Hodgen GD, Zinger M. The normal menstrual cycle and the control of ovulation. In: Becker KL, ed. Principles and Practices of Endocrinology and Metabolism. 3rd edn. Philadelphia: Lippincott Williams & Wilkins; 2001: 935–46.
- Key TJ, Pike MC. The dose–effect relationship between 'unopposed' oestrogens and endometrial mitotic rate: its central role in explaining and predicting endometrial cancer risk. Br J Cancer 1988; 57(2): 205–12.
- Ferenczy A, Bergeron C. Histology of the human endometrium: from birth to senescence. Ann NY Acad Sci 1991; 622: 6–27.
- Cooke PS, Buchanan DL, Young P, et al. Stromal estrogen receptors mediate mitogenic effects of estradiol on uterine epithelium. Proc Natl Acad Sci USA 1997; 94(12): 6535–40.
- Folkman J, Klagsbrun M. Angiogenic factors. Science 1987; 235(4787): 442–7.
- 10. Lau TM, Affandi B, Rogers PA. The effects of levonorgestrel implants on vascular endothelial growth factor expression in the endometrium. Mol Hum Reprod 1999; 5(1): 57–63.
- Hoff JD, Quigley ME, Yen SS. Hormonal dynamics at midcycle: a reevaluation. J Clin Endocrinol Metab 1983; 57(4): 792–6.
- Norman RJ. Reproductive consequences of COX-2 inhibition. Lancet 2001; 358(9290): 1287–8.
- Geva E, Jaffe RB. Role of vascular endothelial growth factor in ovarian physiology and pathology. Fertil Steril 2000; 74(3): 429–38.
- Davis JS, Rueda BR. The corpus luteum: an ovarian structure with maternal instincts and suicidal tendencies. Front Biosci 2002; 7: d1949–78.
- Ferenczy A. Pathophysiology of endometrial bleeding. Maturitas 2003; 45(1): 1–14.

- Noyes RW, Hertig AT, Rock J. Dating the endometrial biopsy. Fertil Steril 1950; 1(1): 3–25.
- Li TC, Dockery P, Rogers AW, Cooke ID. How precise is histologic dating of endometrium using the standard dating criteria? Fertil Steril 1989; 51(5): 759–63.
- 8. Salamonsen LA. Tissue injury and repair in the female human reproductive tract. Reproduction 2003; 125(3): 301–11.
- Bruner KL, Rodgers WH, Gold LI, et al. Transforming growth factor beta mediates the progesterone suppression of an epithelial metalloproteinase by adjacent stroma in the human endometrium. Proc Natl Acad Sci USA 1995; 92(16): 7362–6.
- Kokawa K, Shikone T, Nakano R. Apoptosis in the human uterine endometrium during the menstrual cycle. J Clin Endocrinol Metab 1996; 81(11): 4144–7.
- Salamonsen LA, Zhang J, Brasted M. Leukocyte networks and human endometrial remodelling. J Reprod Immunol 2002; 57(1–2): 95–108.
- Christiaens GC, Sixma JJ, Haspels AA. Morphology of haemostasis in menstrual endometrium. Br J Obstet Gynaecol 1980; 87(5): 425–39.
- Markee J. Menstruation in intraocular endometrial transplants in the Rhesus monkey. Contrib Embryol 1940; 177: 220–230.
- Gannon B, Carati C, Verco C. Endometrial perfusion across the normal human menstrual cycle assessed by laser Doppler fluxmetry. Hum Reprod 1997; 12(1): 132–9.
- Casslen B, Andersson A, Nilsson IM, Astedt B. Hormonal regulation of the release of plasminogen activators and of a specific activator inhibitor from endometrial tissue in culture. Proc Soc Exp Biol Med 1986; 182(4): 419–24.
- 26. Adams Hillard PJ. Menstruation in young girls: a clinical perspective. Obstet Gynecol 2002; 99(4): 655–62.
- 27. Gidwani GP. Vaginal bleeding in adolescents. J Reprod Med 1984; 29(6): 417–20.
- 28. Treloar AE, Boynton RE, Behn BG, Brown BW. Variation of the human menstrual cycle through reproductive life. Int J Fertil 1967; 12(1 Pt 2): 77–126.
- 29. Rannevik G, Jeppsson S, Johnell O, et al. A longitudinal study of the perimenopausal transition: altered profiles of steroid and pituitary hormones, SHBG and bone mineral density. Maturitas 1995; 21(2): 103–13.
- Buckler HM, Anderson DC. The perimenopausal state and incipient ovarian failure. In: Lobo RA, ed. Treatment of the Postmenopausal Woman. Philadelphia: Lippincott-Raven, 1996: 11–23.

Terminologies and definitions around abnormal uterine bleeding

3

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INTRODUCTION

The world has suddenly woken up to the realization that terminologies concerning disturbances of menstrual bleeding are used in very different ways in different countries and different cultures. These variations have impact on the words which are used, the definitions of those words, and the classifications of symptoms and underlying causes. They have the potential to cause confusion concerning the interpretation of data from clinical trials and in the interpretation of scientific studies of the mechanisms of different types of abnormal uterine bleeding (AUB).

Furthermore, until agreement on terminologies in well-designed prospective multicenter trials is reached, evaluating therapeutic interventions will be problematic, owing to likely confusion and inconsistency surrounding inclusion and exclusion criteria. The need for international agreement on terminology and definitions is increasingly important for routine clinical management and training purposes.

A HISTORICAL PERSPECTIVE

Disturbances of menstruation have been a prominent part of the workload of physicians throughout recorded history, and the early literature is filled with a range of simple, descriptive terms used to characterize the symptoms of heavy and irregular menstrual bleeding. Hippocrates made the basic observation 'menstruation, if too abundant, produces disease', in his Aphorisms, Section V, LVII.³

Perusal of the early literature makes it clear that most of these physicians were dealing primarily with excessively heavy bleeding, of a degree which was a major threat to health and even to survival – the type of bleeding which nowadays we might call acute and severe.⁴

Hippocrates is quoted by Aristotle⁵ as saying: 'In quantity, bleeding is excessive, when they flow about eighteen ounces, and in time when they flow heavily about 3 days'.

He further comments, 'but it is inordinate flowing when the faculties of the body are thereby weakened'. Eighteen ounces is a considerable volume to lose each month, when a modern ounce is approximately 30 ml. Even if this 540 ml includes the 50% of endometrial transudate,⁶ a regular monthly blood loss of 270 ml for someone of limited nutrition in ancient times must have been debilitating. Thomas Sydenham⁷ clearly states that 'when menstrual flow is inordinate, there is difficulty, weakness, anorexia, cachexia, cadaverous complexion and swelling of the feet'

The ancient and medieval literature typically used terms such as:

- the overflowing of the courses
- this immoderate flux
- menstruation is profuse
- excessive flooding
- menses in too great abundance
- uterine hemorrhage.

This sense of an acute event was reflected in contemporary writings in other languages, such as the French 'L'eruption des regles'.⁸

Many authors reflected a broader understanding of the variation in bleeding symptoms, with terms such as 'immoderate, long continued and frequent menstruation' or 'the flux is immoderate either when the periods return too often, when they continue too long, or when too much blood is discharged at one time'. None of these publications uses terms like menorrhagia or metrorrhagia, even though many of them were written in Latin.

Terms like menorrhagia and metrorrhagia seem to have been coined in Edinburgh in the late 1700s by William Cullen, Professor of the Practice of Physic at the University of Edinburgh. ^{9,10} Cullen originally wrote in Latin, but was also writing in English later in his career. 'Menorrhagia' is derived from the Greek word 'mene' meaning moon, and the verb 'regnumi' meaning to burst forth, to let loose, or to break asunder. He only considered menorrhagia

as a disease with 'those deviations which are excessive in degree, which are permanent and which induce a manifest state of disability'. ¹⁰ He goes on to state that 'the flow of the menses is considered immoderate when it recurs more frequently, when it continues longer, or when during the ordinary continuance it is more abundant than is usual with the same person at other times'. This suggests that he was using the term 'menorrhagia' to cover any type of excessive bleeding – heavy, prolonged, frequent.

The term 'menorrhagia' was taken up with enthusiasm by subsequent writers but was usually not defined. The sense in which it is used usually implies that the reader is expected to understand that it refers in some way to the symptom of heavy 'menstrual' or uterine bleeding.

It is likely that the term 'metrorrhagia', to describe irregular bleeding, came into usage at about the same time, since Cullen certainly used the term 'maetrorrhagia' in his lectures.¹⁰ However, this seems to have been less popular than 'menorrhagia'. Other authors were also using the terms 'amenorrhea' and 'dysmenorrhea' at this time.

An understanding of the causes of AUB really only began around the late 1800s with the development of major surgery allowing exploration of the pelvic organs. Gradually it became clear that malignant and benign tumors and infections were major causes of abnormal bleeding, but more precise definition had to await modern pathologic examination of excised tissues and progressively more effective imaging, through X-rays, ultrasound, and endoscopy.

The major clinical and pathologic correlations of uterine fibroids, adenomyosis, endometriosis, endometrial hyperplasia, and endometritis were made in the first couple of decades of the 1900s. 11-16 These seminal papers provided some remarkable clinical and pathologic detail, although attempts at classification of these conditions still leads to some controversy.

CURRENT USAGE OF TERMINOLOGIES

Acknowledging the worldwide confusion in terminologies and definitions around abnormalities of menstrual and uterine bleeding, a recent review has explored origins and current usages of the terms for symptoms, signs, and causes of abnormal uterine bleeding, and thereby highlighted the international lack of uniformity in usage of such terms (Table 3.1).¹⁷ This lack of uniformity has resulted in inevitable inconsistencies in clinical management and in the interpretation of research on basic mechanisms and clinical trials.^{1,2}

The most frequently used terms such as menorrhagia, metrorrhagia, and dysfunctional uterine bleeding (DUB)

Table 3.1 Analysis of the apparent meaning of usage of the term *menorrhagia* in 100 publications between 2000 and 2006, where the term *menorrhagia* appeared in the title of the publication

1 (a)	Defined	56	
(b) Undefined	44	n = 100
2 (a)	Used as <i>symptom</i> of heavy uterine bleeding, irregular or regular, with or without pathology	34	
(b)	Used as <i>symptom</i> of heavy uterine bleeding, regular, with or without pathology	28	
(c)	Used as a <i>symptom</i> of heavy uterine bleeding, regular with no detectable pathology	16	n = 78
3 (a)	Primarily reflecting patient complaint	59	
(b)	Primarily reflecting the doctor's definition	19	n = 78
4 (a)	Used as a diagnosis	5	
(b)	Used as a <i>diagnosis</i> when combined with another term (e.g. 'idiopathic')	17	n = 22

Adapted from Woolcock et al.¹⁷

have different meanings in different countries, and textbooks often fail to define such terms or provide conflicting descriptions and definitions. By way of examples, use of the term 'DUB' may indicate either the presence of ovular or anovular cycles, depending on which side of the Atlantic the patient is seen. Furthermore, clinicians may use a variety of terms to describe disorders of menstrual bleeding. These include descriptive and diagnostic terms and phrases, with terms used in varied ways by different gynecologists within a single practice setting.¹

The term 'abnormal uterine bleeding' has received greater acceptance and encompasses a wide range of uterine bleeding symptoms.^{2,4} In this context, a recent exercise that incorporated widespread consultation with relevant international and national organizations, journal editors, and individuals, enabled a modified Delphi process to be developed to assess current use of contemporary terminologies.¹⁸ This was followed by a structured face-to-face international meeting of 35 clinicians (mostly gynecologists) and scientists. The outcome, recently published simultaneously in the European and North American medical press,² reported almost universal agreement that poorly defined terms of classical origin used in differing ways in the English medical language should be discarded.

There was agreement that these should be replaced by simple, descriptive terms with clear definitions. These should be easily understood by health professional and patient alike, and translatable into most languages. The major recommendations were to abolish and replace terms such as menorrhagia, metrorrhagia, hypermenorrhea, and dysfunctional uterine bleeding.

A simple terminology was recommended for the description and definition of symptoms and signs of abnormal uterine bleeding. Emphasis was placed on the fact that the manuscript reporting the deliberations of the international agreement meeting should be a 'living document' and thus part of an ongoing process with international medical and community debate. Necessarily, also, the classification of causes, investigations, cultural, and quality of life issues were identified as crucial components of this iterative and ongoing process.

There does, however, remain the issue within the context of employment of simple terminology for describing symptoms and signs of abnormal uterine bleeding, whether heavy uterine or heavy menstrual bleeding best reflects the subjective complaint of unacceptable heavy blood loss either at the time of menstruation or as an unscheduled event. Clinicians involved with the care of women with menstrual bleeding complaints may use 'heavy menstrual bleeding' or 'heavy uterine bleeding' as a reflection of the impact of the patient's complaint of heavy bleeding on their quality of life.

The first authoritative use of the term 'heavy menstrual bleeding' appears to have been in the New Zealand Guidelines on Heavy Menstrual Bleeding. ¹⁹ Clear definitions in such guidelines doubtless dispenses with confusion about who to treat. Following the introduction of the guidelines, practice preferences and the attitudes of New Zealand gynecologists, general practitioners, and family planning doctors were evaluated by a postal survey and provided data on demographics, practice preferences, knowledge of, usage of, and attitudes toward the New Zealand Guidelines for the Management of Heavy Menstrual Bleeding. ²⁰

A modification of prescribing patterns among specialist and general practitioners and family planning doctors in New Zealand in accordance with these guidelines was recorded.

In the UK, a Guideline for the Management of Heavy Menstrual Bleeding was launched in 2007 by the National Institute for Health and Clinical Excellence (NICE).²¹ This guideline states that it was not within its remit to include conditions where heavy menstrual bleeding (HMB) was not the main presenting symptom (e.g. endometriosis and gynecologic bleeding symptoms other than HMB). Moreover, recommendations for research are identified within the guideline, such as epidemiology of

women presenting with HMB; hence, the need for clear definitions and terminology is endorsed.

The guideline²¹ provides a definition of heavy menstrual bleeding that takes into account the evidence available on normal menstrual patterns, including length of cycle and duration of bleeding. Typical duration in the reported four observational studies, all graded as evidence level (EL) 3, spanned a 3–8-day experience and included the classic work of Treloar et al.²² Within the NICE guideline,²¹ three observational studies (all EL = 3) are identified that report attempts at research assessment of menstrual blood loss.

Just over 20 years ago Snowden and Christian²³ reported a comprehensive study sponsored by the World Health Organization (WHO) on patterns and perception of menstruation. This large cross-cultural study included findings on over 5000 women in 14 sociocultural groups in 10 countries. In each country, the sample size was experience from 500 women. Inclusion required women to be parous, non-pregnant, non-menopausal, and not lactating at the time of interview. Women who recorded their menstrual experience had not recently been pregnant and were not using a contraceptive method known or believed to affect the duration, amount, or frequency of menstrual blood loss. The six major areas of enquiry were:

- (1) The significant characteristics women associate with menstrual bleeding.
- (2) The perceived physiologic and/or psychologic sequelae of menstrual bleeding.
- (3) The behavior associated with menstrual bleeding.
- (4) Women's beliefs concerning the norms for behavior associated with menstrual bleeding.
- (5) Social and cultural meaning of menstruation.
- (6) Women's reaction to changes in their pattern of menstrual bleeding.

Women's perceptions may now of course be different in the 21st century; however, the experience of the pattern of menstruation will probably be unchanged. Perceptions on certain patterns of menstruation, e.g. amenorrhea, have changed. By way of an example, in the WHO-sponsored study involving 14 cultural groups (1973–1979), women's attitude to menses demonstrated preference for methods of contraception that did not result in amenorrhea or change in blood loss and definitely preferred predictable bleeding.²⁴ In contrast, in the 1990s, a re-evaluation of the characteristics of menstrual patterns in relation to reproductive status and contraception in a study of 1300 women in the Netherlands was performed by telephone interview.²⁵ Over 80% of menstruating

women preferred shorter, lighter, and/or less-frequent periods and, interestingly, the desire for amenorrhea increased with age. A quarter of subjects preferred amenorrhea in adolescence, half in their 40s, and as many as three-quarters of women, if they were still menstruating, in their 50s.²⁵

A more recent study, which specifically sought opinion about amenorrhea in association with contraception, was an international study on acceptability performed between study centers in Edinburgh, Cape Town, Hong Kong, Shanghai, and Sagamu, Nigeria.²⁶ In this more contemporary study, amenorrhea was highly acceptable to the majority of women in each of these different geographical locations. This was a questionnaire study of both providers and users. There were 200 clients in each center and 50 providers.

This latter study provided a very important observation that it was the providers who overestimated the importance of regular menses to their clients. Indeed, many women were quite prepared to try a contraceptive associated with amenorrhea. These attitudes to amenorrhea reflect a change over the last two decades. Potential health benefits of amenorrhea include the abolition of problematic bleeding, the abolition of dysmenorrhea, and maintained iron status, as well as possible protection against future gynecologic disease.

The cross-cultural study on menstruation conducted in the late 1970s, referred to earlier,²³ acknowledged that the social significance of menstruation was learned and that strong cultural influences impact on the perception of this pivotal physiologic reproductive event.

Historically, society has acknowledged the occurrence of menstruation in a context which is important for those around the menstruating woman, and has often imposed social conventions such as restrictions on behavior. The principal endeavors of the WHO cross-cultural study²³ were first to ascertain the degree of women's awareness of their menstrual pattern by self-reports and prospective daily records and, secondly, to determine how menstrual bleeding influenced activity and emotions and perception. Although determination of menstrual predictability was a major objective of this study, the prospective recording of bleeding experience was without doubt a methodologic challenge for the study.

Key observations from this study, published over 20 years ago, include the fact that menstruation was deemed an event of such significance that the majority of women (82–95%) found no difficulty in recall when enquiry was made about features of their last menstrual period. Interestingly, women in each of the cultural groups concentrated on the bleeding experience itself rather than bleed-free aspects of their menstrual cycles. The majority of women in each culture studied described physical discomfort in association with their menstrual period. Such discomfort

tended to be in the immediate premenstrual days and during bleeding itself. Discomfort was reported less commonly after menstruation. The report did not indicate that country of residence influenced the experience of discomfort.

In each culture, women were aware of an experience of negative mood in the context of menstruation, but the study commented that fewer women perceived mood changes than perceived physical discomfort. These negative mood experiences occurred premenstrually and during menstruation, with relief experienced on completion of menstruation. A not-surprising observation was that women in the developing countries felt a greater degree of lethargy during menstruation.23 Taboos and behavior restrictions associated with the menstrual period were commonly recounted. Such influences on daily behavior are documented elsewhere.²⁷ A particular aim of this detailed cross-cultural study was to determine the degree to which women were aware of timing of menstrual events. A subgroup of 10% of the study respondents were asked to prospectively keep a menstrual diary. The diary card data provided documentation that the bleeding experience was remarkably similar across the whole group, despite the wide cultural and environmental differences in the populations.

The WHO cross-cultural study provided support that, for an accurate and useful definition of menstruation, it was necessary to determine separate components of the menstrual experience: i.e. amount, duration, regularity, frequency, and associated body changes.²³ Differentiation was made between the bleeding episode itself and the bleed-free interval: notably, when a bleed-free interval was important in the context of the absence of social restrictions and personal discomfort. The study identified the need to examine further the importance of the bleeding episode and the bleed-free experience in different cultures. Such information was deemed important for the development of methods of fertility control.

The conclusion of this study is most cogent: 'menstruation is not simply a physiological process but is linked with the psychological, social and cultural variables'. The study also identified the fact that women perceived bleeding in two ways: – from their own experience and from their position as a member in society – and therein lie the meanings given to menstruation. The study concluded that the interactions of these two perceptions influenced attitudes of women.²³

BREAKTHROUGH BLEEDING WITH HORMONAL THERAPIES

Hormonal therapies with various steroid formulations and combinations are notorious for the unpredictable

bleeding patterns which they cause. Continuous exposure to progestogens or to estrogen—progestogen combinations tends to produce the least predictable patterns, varying from complete amenorrhea, through infrequent, light bleeding, to frequent or prolonged episodes. Heavy bleeding tends to be unusual.

These unusual patterns of bleeding demanded new ways of accurately defining and describing women's experiences, and the Population Council²⁸ and the WHO²⁹ invested considerable effort into the development and testing of new approaches. These methods require the use of prospective, detailed menstrual charting²³ and an analysis based on 90-day reference periods (the approximate equivalent of three menstrual cycles).^{30,31} There was also a requirement to develop new terminologies and definitions, which have permitted a more accurate description of these highly variable patterns (Table 3.2), and this system has been widely accepted for this specific situation of menstrual diary data analysis.

Table 3.2 Definitions of bleeding patterns which can be used in reference period analysis

Bleeding

Any bloody vaginal discharge that requires the use of such protection as pads or tampons

Spotting

Any bloody vaginal discharge that is not large enough to require sanitary protection (or where women may use a modern 'mini-pad')

Bleeding/spotting episode

One or more consecutive days on which bleeding or spotting has been entered on the diary card

Bleeding/spotting-free interval

One or more consecutive days on which no bleeding or spotting has been entered on the diary card

Bleeding/spotting segment

One bleeding/spotting episode and the immediately following bleeding/spotting-free interval

Reference period

The number of consecutive days upon which the analysis is based (this is usually standardized to 90 days)

Menstrual diary cards

These are designed for simple prospective recording of daily experience of 'bleeding' (B) or 'spotting' (S)

Since 'breakthrough' or 'unscheduled' bleeding with long-acting hormonal contraceptives is rarely heavy, there was limited need to tackle the thorny problem of assessment of the heaviness of uterine bleeding in these women, apart from defining the very light 'spotting' or 'staining' that is not uncommon with these methods (see Table 3.2). Perhaps some variation of this menstrual diary analysis approach could be adapted for a more quantitative clinical assessment of spontaneous episodes of abnormal bleeding.

RECOMMENDATIONS ON TERMINOLOGIES FOR SYMPTOMS AND SIGNS OF SPONTANEOUS ABNORMAL UTERINE BLEEDING

The recently published international meeting on terminologies for the symptoms and signs of spontaneous AUB has been described above.² There was agreement that AUB is not a diagnosis, but, instead, should be considered a symptom and a sign, and women with this sign should be regarded as a subset of the group of clinical problems encompassed by 'abnormal reproductive tract bleeding', recognizing that such bleeding may sometimes come from other parts of the reproductive tract. Furthermore, using a validated process, we have learned that this group of experts determined that the terms *DUB*, *menorrhagia*, *metrorrhagia*, and *meno-metrorrhagia* are used in such an inconsistent manner that they should be discarded, but that the term 'intermenstrual bleeding' should remain as a description of a symptom.

Defining terminologies for the description of AUB in the reproductive years requires that the parameters of normal menstruation be determined, including cycle length, cycle predictability, and the duration and volume of blood flow. Menses occurring more or less often than the 95th and 5th percentiles can be classified as abnormal, and duration of flow outside these same centile limits should also be considered to be pathologic (Table 3.3). Using these parameters, the range of normal cycle length has been estimated to be from 22 to 35 days in the mid reproductive years.²³ Predictability and consistency in cycle length are also considered important normal parameters, and, consequently, a change in the menstrual pattern for a particular woman can be abnormal even if the interval or duration of flow remains within the 5th-95th percentile. However, at this time, there is no evidence to provide a threshold for determining an unacceptable level of change. It is also important to note that a number of additional parameters may impact the determination of 'normal', including age and the population being considered.^{22,23}

Table 3.3 Suggested 'normal' limits for menstrual parameters in the mid reproductive years

Clinical dimensions of menstruation and menstrual cycle	Descriptive terms	Normal limits (5th–95th centiles)
Frequency of menses (days)	Frequent	<24
	Normal	24–38
	Infrequent	>38
Regularity of menses (cycle-to-cycle variation over 12 months; in days)	Absent	_
	Regular	Variation ±2 to 20 days
	Irregular	Variation greater than 20 days
Duration of flow (days)	Prolonged	>8.0
	Normal	4.5–8.0
	Shortened	<4.5
Volume of monthly blood loss (ml)	Heavy	>80
	Normal	5–80
	Light	<5

Based primarily on references 22, 23, 33, and 34.

The participants in the agreement process agreed strongly that it was important to describe AUB symptoms using a limited set of four dimensions and only three choices of descriptive words for each dimension that depict 'normal', 'above normal', and 'below normal', as previously defined (see Table 3.3). Consequently, for a given individual, each of the four key menstrual dimensions should be described using one of the following terms: cycle regularity, frequency of menstruation, duration of menstrual flow, and volume of menstrual flow:

- regularity of menstruation: irregular, regular, or absent
- frequency of menstruation: frequent, normal, or infrequent
- duration of menstrual flow: prolonged, normal, or shortened
- volume of menstrual flow: heavy, normal, or light.

Any additional abnormality should be specified (e.g. change in the menstrual pattern, intermenstrual bleeding, premenstrual spotting). The concept of menstrual 'shape' was also discussed, where the patient's perception of the pattern of changes in volume from day to day is recorded.²³ It was felt that there are so few data available about this concept that it cannot currently be incorporated into a menstrual assessment scheme, although research on the topic is clearly needed

TERMINOLOGY OF CAUSES

The commonest causes of AUB have now been relatively precisely defined with the use of modern imaging and biopsy techniques. These technologies have permitted the development of simple broad classifications of causes, but significant gaps and controversies remain (Table 3.4). It is a matter of fairly general agreement that many cases of AUB will fit within the two clearly recognizable categories of pelvic pathology and systemic medical disease. The third category is currently a diagnosis of exclusion, which many people label as 'dysfunctional uterine bleeding' (see Table 3.4).

Dysfunctional uterine bleeding was first used by Graves³² to describe regular or irregular cases of 'menor-rhagia or metrorrhagia' caused by 'impairment of the endocrine factors' that normally control menstrual function. These usages suggest that he was applying the term 'dysfunctional uterine bleeding' to unexplained causes of a wide range of menstrual symptoms, whether or not they were related to ovulation or anovulation.

Since the first usage of the term 'dysfunctional uterine bleeding', it has been used very variably in different parts of the world, usually as an undefined (or vaguely defined) diagnosis of exclusion, but sometimes as a symptom without being specific about the volume or pattern of menstrual flow.^{2,17} It is now strongly recommended that this term be discarded. Consideration should be given to use

 Table 3.4
 The main currently recognized causes of abnormal uterine bleeding

Pelvic pathology

(a) Surface lesions of the genital tract

- Uterine leiomyomata
 Uterine adenomyomata or diffuse adenomyosis
- 2. Endometrial polyps
- 3. Endometrial hyperplasia (often a consequence of anovulation)
- 4. Endometrial adenocarcinoma; rare sarcomas
- 5. Uterine or cervical infection
- 6. Endometrial or cervical infections
- 7. Benign cervical disease
- Cervical squamous and adenocarcinoma (complications of unrecognized early pregnancy)

(b) Deeper lesions of the uterus

- 1. Uterine leiomyomata
- 2. Uterine adenomyomata or diffuse adenomyosis
- 3. Endometriosis
- 4. Myometrial hypertrophy
- 5. Uterine arteriovenous malformations

Systemic medical disease

- Disorders of hemostasis (typically von Willebrand's disease and platelet disorders; excessive anticoagulation)
- Hypothyroidism
- Other rarities, such as systemic lupus erythematosus and chronic liver failure

Abnormal uterine bleeding of mechanisms currently unexplained (MCU) – previously controversially termed 'dysfunctional uterine bleeding' (DUB) and subdivided as below:

- Ovulatory DUB a primary endometrial disorder of the molecular mechanisms controlling the volume of blood lost during menstruation
- Anovulatory DUB a primary disorder of the hypothalamic–pituitary–ovarian axis, resulting in excessive unopposed ovarian estrogen secretion and a secondary endometrial disturbance

of a term such as 'AUB – mechanisms currently unexplained' (MCU). Ovulatory MCU would then be a primary endometrial disorder of the molecular mechanisms controlling the volume of blood loss during menstruation. Anovulatory MCU would be a primary disorder of the hypothalamic–pituitary–ovarian axis, resulting in excessive unopposed ovarian estrogen secretion and a secondary disturbance of endometrial function and breakdown.

These terminologies and definitions require much further international debate to allow development of a strong measure of agreement.

THE FUTURE

It is clear that there is great worldwide confusion in the way that terminologies are used to describe most aspects of abnormal uterine bleeding, and that few authors provide precise definitions for the terminologies they use. The terminologies that are most widely abused are menorrhagia, metrorrhagia, hypermenorrhea, and dysfunctional uterine bleeding. The international group which met in Washington in February 2005² has strongly recommended that these terminologies be abolished and be replaced by something much simpler (see above).

These recommendations will need widespread discussion because of the entrenched usage of many of these descriptive terms in most countries. The International Federation of Gynecology and Obstetrics (FIGO) has agreed to endorse a study group to ensure that the initial manuscript from the Washington meeting² is a 'living document' that will be debated widely. This study group has been charged with responsibility for bringing together a range of individuals from widely differing backgrounds to explore the several areas of terminology confusion that remain, to develop clinically meaningful and research-relevant classifications of underlying causes of AUB, to identify ways of involving family practitioners and community representatives, and to explore the importance of quality of life and cultural issues.

The ultimate aim of these initiatives is to ensure that we are all talking the same 'language', which will not only allow better communication between doctors and with patients but will also ensure that multinational clinical trials are possible and that we can clearly interpret the meaning of basic research studies on specific subgroups of patients.

- Fraser IS, Inceboz US. Defining disturbances of the menstrual cycle. In: O'Brien PMS, Cameron IT, MacLean AB, eds. Disorders of the Menstrual Cycle. London: RCOG Press, 2000: 141–52.
- Fraser IS, Critchley HOD, Munro MG, Broder MG. Can we achieve international agreement on terminologies and definitions used to describe abnormalities of menstrual bleeding? Hum Reprod 2007; 22: 635–43. Fraser IS, Critchley HOD, Munro MG, Broder M. A process designed to lead to international agreement on terminologies and definitions used to describe abnormalities of menstrual bleeding. Fertil Steril 2007; 87: 466–76. [simultaneous publication]
- Hippocrates (around 400 BC). The Aphorisms of Hippocrates: translated into English by Thomas Coar. London: Longman & Co, 1822: 314.
- 4. Munro MG. Abnormal uterine bleeding in the reproductive years. Part 1 pathogenesis and clinical investigation. J Am Assoc Gynecol Laparosc 1999; 6: 393–416.
- Aristotle's Masterpieces. Of the overflowing of the menses. Directions for Midwives, Counsel and Advice for Childbearing Women. London: printed for the booksellers. (translated and revised 1817.) Chap VIII: 49–52.
- Fraser IS, McCarron G, Markham R. Blood and total fluid content of the menstrual discharge. Obstet Gynecol 1985; 65: 194–8.
- Sydenham T (1666). Medical observations concerning the history and the cure of acute diseases. In: The Works of Thomas Sydenham. London: The Sydenham Society, 1868: 395.
- 8. Emett R. Theorie Nouvelle du Flux Menstrual et Traite des Maladies de la Tête. Paris: Chez Vincent, 1757.
- Perroneau R. Disputatio Medica, Inauguralis, de Menstruorum Profluvio Immodico. Edinburgh: Balfour & Smellie, 1775.
- 10. Cullen W. First Lines of the Practice of Physic. Edinburgh: Bell and Bradfute, 1816.
- Cullen TS. Adenoma of the Uterus. Philadelphia: WB Saunders, 1908.
- 12. Kelly H, Cullen TS. Myomata of the Uterus. Philadelphia: WB Saunders, 1909: 723.
- Schroder R. Endometrial hyperplasia in relation to genital function. Am J Obstet Gynecol 1954; 68: 294–309.
- 14. Sampson JA. Perforating hemorrhagic (chocolate) cysts of the ovary. Arch Surg 1921; 3: 245–323.
- Sampson JA. Peritoneal endometriosis due to the menstrual dissemination of endometrial tissue into the peritoneal cavity. Am J Obstet Gynecol 1927; 14: 411–69.
- Frankl O. Adenomyosis uteri. Am J Obstet Gynecol 1925; 10: 680–4.
- Woolcock J, Critchley HOD, Munro MG, et al. A review of the confusion in current and historical usage of terminologies a nd definitions for disturbances of menstrual bleeding. 2007, submitted.
- Brook RH, Chassin MR, Fink A et al. A method for the detailed assessment of the appropriateness of medical technologies. Int J Technol Assess Health Care 1986; 2: 53–63.
- New Zealand Working Party for Guidelines for the Management of Heavy Menstrual Bleeding. An evidence-based guideline for

- the management of heavy menstrual bleeding. NZ Med J 1999; 112: 174–7.
- Park S, Farquhar CM. A survey of practice preferences and attitudes to the New Zealand Guidelines for the Management of Heavy Menstrual Bleeding. Aust NZJ Obstet Gynaecol 2002; 42: 374–8.
- NICE Clinical Guideline 44. Heavy Menstrual Bleeding. UK: National Institute for Health and Clinical Excellence, 2007.
- Treloar AE, Boynton RE, Behn BG, Brown BW. Variation of the human menstrual cycle through reproductive life. Int J Fertil. 1967; 12: 77–126.
- Snowden R, Christian B, eds. Patterns and Perceptions of Menstruction. A World Health Organization International Collaborative Study. London: Croom Helm, 1983.
- 24. World Health Organization. A cross-cultural study of menstruation: implications for contraceptive development and use. World Health Organization Task Force on Psychosocial Research in Family Planning, Special Programme of Research, Development and Research, Training in Human Reproduction. Stud Fam Plann 1981; 12: 3–15.
- 25. Tonkelaar I, Oddens BJ. Preferred frequency and characteristics of menstrual bleeding in relation to reproductive status, oral contraceptive use, and hormone replacement therapy use. Contraception 1999; 59: 35–62.
- 26. Glasier A, Smith KB, van der Spuy ZM, Ho PC, et al. Amenorrhea associated with contraception an international study on acceptability. Contraception 2003; 67: 1–8.
- Fraser IS, McCarron G, Markham R. A preliminary study of factors influencing perception of menstrual blood loss volume. Am J Obstet Gynecol 1984; 149: 788–93.
- 28. Rodriguez G, Faundes-Latham A, Atkinson L. An approach to the analysis of menstrual patterns in the clinical evaluation of contraceptives. Stud Fam Plann 1976; 7: 42–51.
- Belsey EM, Machin D, d'Arcangues C. The analysis of vaginal bleeding patterns induced by fertility-regulating methods. Contraception 1986; 34: 253–60.
- D'Arcangues C, Odlind V, Fraser IS. Dysfunctional uterine bleeding induced by exogenous hormones. In: Alexander NJ, d'Arcangues C, eds. Steroid Hormones and Uterine Bleeding. Washington: American Association for the Advancement of Science, 1992: 81–105.
- Fraser IS. Bleeding arising from the use of exogenous steroids.
 In: Smith SK, ed. Dysfunctional Uterine Bleeding. Baillière's Clin Obstet Gynaecol 1999; 13: 203–22.
- 32. Graves WP. Some observations on etiology of dysfunctional uterine bleeding. Am J Obstet Gynecol 1930; 20: 500–18.
- Hallberg L, Hogdahl A-M, Nilsson L, Rybo G. Menstrual blood loss – a population study. Acta Obstet Gynecol Scand 1966; 45: 320–51.
- 34. Belsey EM, Pinol AP. World Health Organization Task Force on Long-Acting Systemic Agents for Fertility Regulation. Menstrual bleeding patterns in untreated women. Contraception 1997; 55: 57–65.

Epidemiology of abnormal uterine bleeding

4

Michael Zinger

INTRODUCTION

Abnormal uterine bleeding is a widespread complaint among menstruating women in industrialized countries. One-quarter report menorrhagia, while 21% complain of shortened cycles, 17% complain of intermenstrual bleeding, and 6% complain of postcoital bleeding. These issues have significant personal, medical, and economic impacts.

From a personal standpoint, menorrhagia is the menstrual symptom most often noted to interfere with daily life. As many as 30% of menstruating women feel that their menses are heavy, while 5% characterize them as very heavy. Perhaps most importantly, 22% describe their menses as a marked or severe problem.²

From a medical standpoint, abnormal uterine bleeding can be a sign of underlying disease. Information regarding endometrial pathology is only available for women in whom bleeding was alarming enough to indicate dilatation and curretage. Within this group, 20% have endometrial hyperplasia, a potentially precancerous state.³

From an economic standpoint, enormous costs have been associated with uterine bleeding. Women with self-described heavy bleeding are 28% less likely to work.⁴ However, confounding social and psychological factors may affect both perception of heavy bleeding and employment.

One of the greatest challenges in epidemiologic studies of abnormal uterine bleeding is quantification of menstrual flow. Unfortunately, subjective patient evaluation of volume is largely inaccurate. Less than half of patients with a convincing complaint of menorrhagia actually fit the technical definition of greater than 80 ml of blood loss.

Numerous techniques have been used to quantify menstrual blood loss. Unfortunately, there is no correlation between the number of pads or tampons used and the amount of blood loss. Objective approaches, such as alkaline hematin extraction, are the gold standard.⁵ Of the subjective approaches, pictorial blood loss assessment charts are the most promising, with 88% sensitivity, although the false-positive rate is 59%.⁶

It has also been argued that the common, objective definition of menorrhagia may actually have little relevance. Women whose menstrual blood loss is measurably greater than 80 ml have a similar rate of menstrual complaints and of anemia as women with less than 80 ml.⁷ Thus, the 80 ml cutoff, which was derived from a statistical definition of normal, is a poor predictor of clinical endpoints. Evidence suggests that a cutoff of 120 ml would be significantly more predictive of anemia; however, such a high cutoff has not been widely used in studies.⁸

Despite these caveats in defining abnormal uterine bleeding, much valuable information has been compiled on various epidemiologic factors that are related to this condition.

PREDISPOSING CHARACTERICS

Adolescence

Abnormal uterine bleeding is experienced by almost three-quarters of women in their early teenage years. ⁹ It is the most common cause of hospital admission for young women. In 46–95% of these cases, anovulation is identified as the main etiology. ¹⁰ In up to one-third of cases the menorrhagia has been attributed to coagulopathy. ¹¹

Anovulation in teenage girls is typically related to inadequacy of the ovulation trigger due to an immature hypothalamic–pituitary–ovarian axis. ¹⁰ The resulting greater length of estrogen stimulation unopposed by ovulatory progesterone predisposes to menorrhagia. This primarily endocrinologic problem responds to medical management in over 90% of cases. ¹² Despite the high rate of abnormal uterine bleeding in adolescent girls, rarely does surgical intervention become necessary. ¹³

Anovulation is more likely if menarche occurs late. When menarche is prior to age twelve then half of cycles are ovulatory, while menarche after age twelve portends less frequent ovulation in the first year following menarche. Within three years postmenarche three-quarters of cycles are ovulatory. The woman's normal cycle length is established by the sixth year postmenarche.¹⁴

Previously undiagnosed coagulopathy is another leading finding in adolescents with menorrhagia. Whereas most other causes of menorrhagia are acquired later in life, coagulopathy causes menorrhagia starting at menarche. At least 65% of women with menorrhagia related to coagulopathy will report menorrhagia dating back to menarche, while only 9% of women with menorrhagia not caused by coagulopathy will give this history (p = 0.001). ¹⁵

With increasing physician awareness, coagulopathy is unlikely to remain undiagnosed in women beyond their adolescent years. Thus, the prevalence of undiagnosed coagulopathy is greatest (45%) in girls who present with heavy bleeding with their first period. In girls presenting in the years just after menarche, coagulopathy explains 20% of cases. Additionally, the prevalence of coagulopathy in this group is inversely related to hemoglobin levels.¹⁶

The most common coagulopathies are von Willebrand's disease and factor XI deficiency, occurring in 13% and 4%, respectively, of women presenting with unexplained menorrhagia. ^{17,18} Factor X deficiency and heterozygosity for hemophilia were each found in less then 1%. ¹⁵

Among 15–19-year-old girls in the USA, the pregnancy rate is 4.1%. Pregnancy must be kept in mind as a possible cause of abnormal bleeding in this age group.

Perimenopause

The perimenopausal transition is associated with a greater occurrence of abnormal uterine bleeding. The incidence of menorrhagia is significantly increased over the age of 40 years.²⁰

A typical finding is menorrhagia in conjunction with oligomenorrhea. This is most commonly due to anovulation paired with increased estradiol levels.²¹ The abnormal bleeding in this group is associated with an increase in endometrial hyperplasia and its associated risks of endometrial cancer.²²

Menopause

Uterine bleeding of any amount in menopausal women not receiving hormone replacement should be considered abnormal. When this occurs, endometrial cancer must be suspected. In a study of 245 women undergoing dilatation and curretage for postmenopausal bleeding, one-quarter had either endometrial carcinoma or hyperplasia with atypia. Obesity, nulliparity, and age over 60 years old each increased the risk.²³

Fibroids

The presence of fibroids has long been associated with menorrhagia.²⁴ The cause of this relationship has been

conjectured to involve an overall enlargement of the uterine cavity, changes in venous blood flow, and disruption of normal prostaglandin function.²⁵

Surprisingly, fibroid size is not predictive of menor-rhagia. However, a submucosal location of fibroid does have a strong association with the presence of menorrhagia.²⁶

Obesity

Body weight has been linked with anovulation, a causative factor in abnormal bleeding. A body mass index (BMI) of >27 kg/m2 more than triples the risk.²⁷ This link is, at least in part, due to the tendencies toward both obesity and anovulation that are seen with polycystic ovarian syndrome.

Although abnormal bleeding in any woman may cause concern regarding the possibility of endometrial cancer, this is a heightened concern when the woman is also overweight. Obesity is known to significantly increase the risk of endometrial cancer.²⁸

In contrast, low body weight predisposes to cessation of menstrual flow. Athletes have secondary amenorrhea rates as high as 21%. The likelihood is directly related to decreasing body weight.²⁹

Tubal sterilization

There is a large body of evidence that the incidence of hysterectomy is greater following surgical tubal ligation. This has been attributed to changes in utero-ovarian circulation that lead to an increase in menstrual abnormalities, which in turn lead to hysterectomy. However, numerous confounding factors may be present. Tubal sterilization implies completion of family, a situation that would greatly increase the likelihood for selecting hysterectomy. Additionally, since these women have chosen a surgical approach to contraception, they may have a more favorable attitude toward surgery in general. Furthermore, most controls are presumably utilizing another form of contraception, which, in the case of oral contraceptives or injectable progestin, have an ameliorating affect on menorrhagia.

The greatest association between tubal ligation and menstrual disorders was in women who underwent tubal ligation prior to 30 years old.³⁰ In contrast, a more recent study of almost 10 000 women was able to correct for the confounding effect of oral contraceptives by utilizing controls whose male partners have been sterilized. Interestingly, it was found that tubal sterilization decreased the amount and length of menstrual blood loss as well as its associated pain. However, the risk of cycle irregularity did increase with tubal ligation.³¹

Coagulopathy

The prevalence of coagulopathy as a cause of abnormal bleeding is discussed in relation to adolescence earlier in this chapter. The converse – i.e. the prevalence of abnormal uterine bleeding in women with known coagulopathy – is addressed here.

Menorrhagia is over twice as likely to occur in women who carry an inherited coagulopathy. The highest prevalence of menorrhagia (78%) is among women with von Willebrand's disease. Menorrhagia is less common in women with factor XI deficiency and carriers of hemophilia; under 60% can be objectively demonstrated to have menorrhagia.³²

EPIDEMIOLOGIC FACTORS IN TREATMENT CHOICES

Interestingly, multiple unrelated factors play a role in determining treatment of abnormal uterine bleeding.

Women with severe symptoms, those who had not received higher education, those who had completed their family, those who have menstrual pain, and those who are unemployed are more likely to prefer surgical treatment.^{33,34} Interestingly, psychiatric issues do not play a role.³⁴ Women with menstrual disorders seeing male physicians are more likely to have surgery. Additionally, they were found to be less likely to participate in treatment decisions but more likely to be satisfied with their care.³⁵

In a study of British women seeking help for menstrual disorders, there was found to be a strong bias towards stating the diagnosis as a bleeding problem rather than a pain problem. Unfortunately, this appears to affect treatment, as surgical treatment is correlated to the physician's diagnosis of bleeding and not to the woman's characterization of her complaint as bleeding.³⁶

- Shapley M, Jordan K, Croft PR. An epidemiological survey of symptoms of menstrual loss in the community. Br J Gen Pract 2004; 54(502): 359–63.
- Santer M, Warner P, Wyke S. A Scottish postal survey suggested that the prevailing clinical preoccupation with heavy periods does not reflect the epidemiology of reported symptoms and problems. J Clin Epidemiol 2005; 58(11): 1206–10.
- Anastasiadis PG, Skaphida PG, Koutlaki NG, et al. Descriptive epidemiology of endometrial hyperplasia in patients with abnormal uterine bleeding. Eur J Gynaecol Oncol 2000; 21(2): 131–4.
- 4. Cote I, Jacobs P, Cumming D. Work loss associated with increased menstrual loss in the United States. Obstet Gynecol 2002; 100(4): 683–7.
- Fraser IS, McCarron G, Markham R. A preliminary study of factors influencing perception of menstrual blood loss volume. Am J Obstet Gynecol 1984; 149(7): 788–93.
- 6. Deeny M, Davis JA. Assessment of menstrual blood loss in women referred for endometrial ablation. Eur J Obstet Gynecol Reprod Biol 1994; 57(3): 179–80.
- Warner PE, Critchley HO, Lumsden MA, et al. Menorrhagia II: is the 80-mL blood loss criterion useful in management of complaint of menorrhagia? Am J Obstet Gynecol 2004; 190(5): 1224–9.
- Janssen CA, Scholten PC, Heintz AP. Reconsidering menorrhagia in gynecological practice. Is a 30-year-old definition still valid? Eur J Obstet Gynecol Reprod Biol 1998; 78(1): 69–72.
- Friberg B, Orno AK, Lindgren A, Lethagen S. Bleeding disorders among young women: a population-based prevalence study. Acta Obstet Gynecol Scand 2006; 85(2): 200–6.
- Deligeoroglou E. Dysfunctional uterine bleeding. Ann NY Acad Sci 1997; 816: 158–64.

- Smith YR, Quint EH, Hertzberg RB. Menorrhagia in adolescents requiring hospitalization. J Pediatr Adolesc Gynecol 1998; 11(1): 13–15.
- 12. Falcone T, Desjardins C, Bourque J et al. Dysfunctional uterine bleeding in adolescents. J Reprod Med 1994; 39(10): 761–4.
- 13. Gidwani GP. Vaginal bleeding in adolescents. J Reprod Med 1984; 29(6): 417–20.
- Diaz A, Laufer MR, Breech LL. Menstruation in girls and adolescents: using the menstrual cycle as a vital sign. Pediatrics 2006; 118(5): 2245–50.
- Kadir RA, Economides DL, Sabin CA, Owens D, Lee CA. Frequency of inherited bleeding disorders in women with menorrhagia. Lancet 1998; 351(9101): 485–9.
- Claessens EA, Cowell CA. Acute adolescent menorrhagia. Am J Obstet Gynecol 1981; 139(3): 277–80.
- Lukes AS, Kadir RA, Peyvandi F, Kouides PA. Disorders of hemostasis and excessive menstrual bleeding: prevalence and clinical impact. Fertil Steril 2005; 84(5): 1338–44.
- Kujovich JL. von Willebrand's disease and menorrhagia: prevalence, diagnosis, and management. Am J Hematol 2005; 79(3): 220–8.
- Martin JA, Hamilton BE, Sutton PD, et al. Births: final data for 2004. Natl Vital Stat Rep 2006; 55(1): 1–101.
- Janssen CA, Scholten PC, Heintz AP. Menorrhagia a search for epidemiological risk markers. Maturitas 1997; 28(1): 19–25.
- Speroff L, Fritz M. Clinical Gynecologic Endocrinology and Infertility, 7th edn. Philadelphia: Lippincott Williams & Wilkins, 2005.
- 22. Buckler HM, Anderson DC. The perimenopausal state and incipient ovarian failure. In: Lobo RA, ed. Treatment of the Postmenopausal Woman. Philadelphia: Lippincott-Raven, 1996: 11–23.

- Alberico S, Conoscenti G, Veglio P, et al. A clinical and epidemiological study of 245 postmenopausal metrorrhagia patients. Clin Exp Obstet Gynecol 1989; 16(4): 113–21.
- 24. Stewart EA. Uterine fibroids. Lancet 2001; 357(9252): 293-8.
- West CP, Lumsden MA. Fibroids and menorrhagia. Baillières Clin Obstet Gynaecol 1989; 3(2): 357–74.
- Sulaiman S, Khaund A, McMillan N, Moss J, Lumsden MA. Uterine fibroids – do size and location determine menstrual blood loss? Eur J Obstet Gynecol Reprod Biol 2004; 115(1): 85–9.
- Grodstein F, Goldman MB, Cramer DW. Body mass index and ovulatory infertility. Epidemiology 1994; 5(2): 247–50.
- Strauss JF, Lessey BA. The structure, function, and evaluation of the female reproductive tract. In: Strauss JF, Barbieri RL, eds. Yen and Jaffe's Reproductive Endocrinology, 5th edn. Philadelphia: Elsevier Saunders, 2004: 213–53.
- Toriola AL, Mathur DN. Menstrual dysfunction in Nigerian athletes. Br J Obstet Gynaecol 1986; 93(9): 979–85.
- 30. Gentile GP, Kaufman SC, Helbig DW. Is there any evidence for a post-tubal sterilization syndrome? Fertil Steril 1998; 69(2): 179–86.

- Peterson HB, Jeng G, Folger SG, et al. The risk of menstrual abnormalities after tubal sterilization. U.S. Collaborative Review of Sterilization Working Group. N Engl J Med 2000; 343(23): 1681–7
- 32. Kadir RA, Economides DL, Sabin CA, Pollard D, Lee CA. Assessment of menstrual blood loss and gynaecological problems in patients with inherited bleeding disorders. Haemophilia 1999; 5(1): 40–8.
- Coulter A, Peto V, Doll H. Patients' preferences and general practitioners' decisions in the treatment of menstrual disorders. Fam Pract 1994; 11(1): 67–74.
- Vuorma S, Teperi J, Hurskainen R, et al. Correlates of women's preferences for treatment of heavy menstrual bleeding. Patient Educ Couns 2003; 49(2): 125–32.
- Coulter A, Peto V, Doll H. Influence of sex of general practitioner on management of menorrhagia. Br J Gen Pract 1995; 45(398): 471–5.
- Warner P, Critchley HO, Lumsden MA, et al. Referral for menstrual problems: cross sectional survey of symptoms, reasons for referral, and management. BMJ 2001; 323(7303): 24–8.

5

Practical assessment and measurement of abnormal uterine bleeding

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BACKGROUND

Abnormal uterine bleeding (AUB) is one of the commonest presenting symptoms and signs in gynecology, and has been recognized as such since ancient times. In centuries past, medical writings make it clear that the majority of women presenting to a physician with a menstrual bleeding problem did so with acute and severe uterine bleeding.¹ This symptom is variously described by medieval and ancient writers as excessive flooding, an overflowing of the courses, inordinate flowing, the immoderate flux, and so on. These physicians were dealing with a problem which was not only a serious social disturbance, but one which frequently led to the medical consequences of severe iron deficiency, anemia, and rarely, even death by exsanguinations.²

It is only within the past half century or so that surgical and medical management have become so effective and safe that lesser degrees of severity of abnormal uterine bleeding have gained much greater importance. In the 1960s and 1970s hysterectomy for benign gynecologic disease became very common in countries like the USA and Australia, and many of these women had presented with a complaint of heavy menstrual bleeding. Yet it soon became clear that individual women found it very difficult to assess the volume of their menstrual loss, and had no absolute yardstick against which to make comparisons. 3,4 These women sometimes even had difficulty in assessing changes in volume of menstrual blood loss from one day to the next.4 Nevertheless, when well counseled, many women were able to give a fairly accurate overall picture of their loss.5

As the social status of women in westernized society has changed, and many young women compete with men for demanding professional jobs, there is decreasing occupational flexibility for the woman with severe, recurrent menstrual symptoms, whether they be heavy bleeding, prolonged bleeding, frequent bleeding, or menstrual pain. The associated symptom complex accompanying heavy

bleeding, comprising headaches, extreme lethargy, dragging pelvic ache, backache, diarrhea, abdominal bloating, etc., compounds the social and occupational interference. These symptoms still constitute the commonest cause of days lost from the female workforce, and young women are necessarily becoming much less tolerant of these phenomena. There is an increasing demand in many countries for a 'bleed-free' existence from young women until such time as they start to plan for a family.

In these times of changing importance and tolerance of menstrual symptoms, there is still a real need for an understanding of the actual menstrual experience of each woman, which may lead to the initial menstrual complaint. This should be put in social and medical context against a background of increasing precision in pelvic imaging and other investigations, ^{8,9} for detection of underlying causes, and an increasing range of options for medical and surgical management. In order to make good choices, a modern woman needs to have good information about what her menstrual experience means and what sequelae she may encounter if the symptoms progress.

OTHER FEATURES OF MENSTRUAL COMPLAINT

In some women the flow is lost from the uterus in a variable continuous discharge through the cervix, but in the majority it is lost in 'gushes' of varying volume. It seems that the uterine cavity tends to fill with blood, fluid, and cell debris while the myometrium is relaxed, and then when a contraction occurs, the contents are expelled into the vagina. Transvaginal ultrasound can give a valuable picture of the changes in blood in the uterine cavity, if timed appropriately. Mostly, these little gushes are of a volume around 0.5–1 ml, but in women with excessive bleeding we have measured, on ultrasound scan, a uterine cavity volume of up to 28.5 ml immediately before a uterine contraction, and a 'large gush' around the vaginal

ultrasound probe. These gushes are presumably mainly responsible for the 'accidents' and 'floodings' which women with excessive bleeding commonly report. A sudden uterine contraction expelling a volume of around 30 ml will be a substantial test of the absorbent quality of the best and largest menstrual pads and tampons! This phenomenon is the assumed cause of what the menstrual hygiene product manufacturers rather quaintly call 'product failure'! Repeated 'accidents' and 'floodings' of this type appear to be significant contributors to a woman's perception of her menstrual loss as heavy, or exceedingly heavy.

These 'patterns of loss' may be very important for the individual woman and her perception of the problem. The 'menstrual shape', where the variation in heaviness of flow from day to day is recorded, is very poorly researched. It is not known how this affects individual women. Variation in menstrual flow from one period to the next may sometimes be considerable in women with heavy periods, 11,12 and variable menstrual patterns are more common than regular. 13

Perception and tolerance may be important facets of the likelihood of clinical presentation. A minority of women with excessively heavy bleeding may be highly tolerant of the clinical problem, and may even record their loss as 'light'. They have no 'yardstick'! In Hallberg's landmark study, 11% of women who perceived their loss as 'light' actually had measured blood loss greater than 80 ml, while 27% of those with a complaint of heavy menstrual loss had a measured blood loss in the lower part of the normal range.

Women with a tendency to depression appear more likely to complain if the periods are difficult to manage, and in the past a high proportion of these women came to hysterectomy. Fastidiousness with personal hygiene may influence complaint. We have seen a woman who gave a convincing history of heavy menstrual bleeding with many 'saturated' tampons, and on testing of the 52 tampons which she used in one period, the total volume of contained blood was 9 ml! Perceived change in the pattern of menstrual flow is important, and may be associated with a fear of cancer.

The use of modern highly absorbent gel pads appears to greatly influence women's awareness of the heaviness of their periods, and this may be an important aspect of future complaint, or lack of complaint.

ALTERNATIVE MEASUREMENT TECHNIQUES

It is clear from some of the earlier discussion that objective assessment of the menstrual loss of an individual

patient is very difficult, yet 'complaint' of heavy bleeding is very common. Many of these women will admit, on close questioning, that they perceive their bleeding as heavy, but not excessively heavy, but they still perceive it as a problem.¹² Many of these women have perceived a change in their pattern of flow.

Memory of menstrual events is highly fallible and a simple prospective daily diary recording of bleeding patterns^{16,17} often provides a very different perspective from the original case history. We generally recommend a simple calendar with the possibility to record the patient's perception of her daily variations in flow. This gives an instant assessment of regularity and pattern of flow with changes over time.

STRUCTURED AND UNSTRUCTURED HISTORY

History taking as a component of assessment of menstrual bleeding complaint has been addressed in the UK National Institute for Health and Clinical Excellence (NICE) Guideline for management of heavy menstrual bleeding.¹⁸ In that document history taking aims to 'define the presenting condition as one of heavy menstrual bleeding, determine the problems that it is causing the woman and detect symptoms that may indicate significant pathology'. The Guideline Development Group were unable to identify an evidence base relating to history taking from women with menstrual bleeding complaint and thus commentary was limited to discussion within the Guideline Development Group.¹⁸ They considered there to be three main areas of inquiry: the nature of bleeding, symptoms indicative of possible pathology (pain and pressure effects), and features that may direct treatment strategies (concerns, expectations, and needs). Importantly, the Guideline Development Group flagged 'non-menstrual bleeding' as an important feature to elicit. For example, intermenstrual bleeding and postcoital bleeding may be symptoms indicative of female reproductive tract cancer and thus necessitate specific targeted investigation.¹⁹ The concept of taking a structured menstrual history is not discussed, although recommended areas of inquiry during history taking for heavy menstrual bleeding are provided.18

The routine clinical assessment of volume of menstrual flow is particularly difficult, but precision from clinical assessment can be improved by consideration of structured questioning. These potentially valuable elements of a structured history were developed from an expert international working group (gynecologists, endocrinologists, and other scientists) who met in Washington in 2005 to review the inconsistencies and confusion of

terminologies around abnormal uterine bleeding,^{20,21} but also to consider a range of important approaches to introducing consistency of assessment (Table 5.1).

Semi-quantitative assessment scales

A pictorial blood loss assessment chart (PBAC) provides an indirect method of evaluation of menstrual bleeding experience, but recording with such tools is highly variable. The format that has received most attention is that originally described over 15 years ago by Higham et al.²² This study compared measurement of menstrual blood loss (MBL) by the alkaline hematin method³ with PBAC scores. A PBAC score of >100 compared with MBL >80 ml,

Table 5.1 Potentially important elements of a structured menstrual history needing to be broadly quantified (or otherwise assessed) in women presenting, in specialist clinical practice, with a complaint of abnormal uterine bleeding, as considered by a group of experienced clinicians meeting in Washington in 2005^{20,21}

Duration of flow

Frequency of bleeding

Regularity of bleeding

Intermenstrual bleeding

Postcoital bleeding

Overall volume assessment and specific questioning:

- number of sanitary towels per period
- use of two towels simultaneously
- use of incontinence pads or 'nappies'
- frequency of changing during full flow
- size and number of 'clots'
- soaking of clothing
- · frequency of changing at night

Recent changes in menstrual pattern

Possibility of hemostatic disorder:

- · bleeding during dental work
- postpartum bleeding
- excessive bleeding since menarche
- history of very easy bruising

History of anemia or iron supplementation

Influence of bleeding on personal daily activities, working capacity, physical activities, leisure activities, sex life

Influence of co-morbidities (e.g. pelvic pain, premenstrual symptomatology); medications

with a good correlation (r = 0.847), sensitivity (86%), and specificity (89%). The recent UK NICE Guideline on Heavy Menstrual Bleeding¹⁸ pointed out that, despite there being data available from six diagnostic and observational studies, meta-analysis was not possible due to the heterogeneity of the various study populations. The guideline has usefully summarized the evidence available on use of pictorial PABCs. 18 The clinical recommendation was that measurements of MBL, either directly by the alkaline hematin method or indirectly with PBAC, were not endorsed.¹⁸ An informed history from the women herself was considered essential. Janssen et al.²³ have also described a potentially useful visual assessment which they have indicated is a reasonable discriminator between women with heavy bleeding over 120 ml per month and those with 'normal' loss.

Objective measurement of menstrual blood loss

Attempts have been made to measure actual volumes of MBL per month by individual women since the 1930s.²⁴ Most of these techniques have relied upon the meticulous collection of all sanitary towels and of the 'clots' and fluid which might have been lost in the shower and toilet, and then application of some specific laboratory technique to measure the amount of hemoglobin present. The gold standard of these methods rapidly became the alkaline hematin technique of Hallberg and Nilsson,²⁵ and this allowed the first large-scale population studies of monthly blood loss in normal menstruating women.^{3,26}

The only serious attempt to measure blood loss using a totally different principle utilized an intravenous injection of an accurately known quantity of radioactive chromium-labeled red cells.²⁷ Whole body radioactivity counting was carried out before and after the menstrual period. The principle appeared sound, but significant difficulties arose in interpretation, and routine use of radioactively labeled red cells would nowadays be ethically difficult.

The alkaline hematin technique has been applied to a large number of subsequent research studies, although most investigators have been aware of the potential for bias through loss of some blood and clots down the toilet. An important basis for the accuracy of this technique has been the thorough counseling of subjects in ways to minimize the extraneous loss. Wyatt et al. have demonstrated that this may sometimes be substantial, and does not usually correlate with the absolute measured loss in that period. Overall, their menstrual pictogram correlated reasonably well with the alkaline hematin method.

It has been suggested by others²⁹ that the failure to assess total blood loss could systematically underestimate the proportion of women with heavy bleeding. This does

not seem to be the case in practice, but there does seem to be a small group of women who will sometimes lose significant amounts of blood in the toilet. The original population studies did not take extraneous blood loss into account^{3,26} and upper limits of normality were based on these volumes as they related to declining hematologic parameters. Hence, the absolute upper limit of measured blood loss might have to be redrawn if a reliable means of estimating extraneous blood loss is devised. In the meantime, in research studies it is critical to counsel volunteers in ways of minimizing blood loss in the shower and toilet.

RESEARCH COMPARISONS

There is a need for doctors to define what they want to measure when assessing menstruation or AUB, whether it be regularity, unexpected episodes, cycle frequency and duration, menstrual flow duration, menstrual 'shape', blood loss volume, or total menstrual fluid volume.

Most of the parameters of regularity, frequency, and duration can be accurately measured by daily diary recording, provided that the woman is motivated to undertake prospective daily recording. However, the diary approach has limited value in determining volume of blood or fluid loss, or menstrual 'shape'.²⁹ If the doctor wishes to study volume, a decision needs to be made whether this should be total fluid, total blood, or daily changes in volume ('shape') of loss. Assessment in routine clinical practice will have different requirements from research assessment.

The alkaline hematin technique, first described by Hallberg and Nilsson,²⁵ is generally taken to be the gold standard for research assessment of the volume of MBL although there are a number of criticisms of this technique, as discussed above. First, the accuracy of the method is dependent on the ability of the woman to meticulously collect all the menstrual flow, including clots and fluid which may be lost down the toilet and in the shower.²⁸ Secondly, it only measures the blood component of the menstrual loss, which may constitute much less than 50% of the total loss, the remainder comprising an endometrial transudate and other genital tract

secretions.^{11,30} The total fluid loss may be much more meaningful to the woman herself.³¹ These collection requirements are demanding and embarrassing for the woman, but simpler techniques with similar accuracy have not yet been devised.

There is a real need for a comprehensive comparison of a selection of the most promising techniques in the same patients at the same time, allowing an assessment of the practicality and clinical validity of simpler techniques, including weighing techniques¹¹ against the alkaline hematin method.

A PRACTICAL CLINICAL APPROACH TO THE ASSESSMENT OF FLOW

It is clear from some of the earlier discussion that objective assessment of menstrual loss by an individual patient is very difficult, yet complaint of heavy bleeding is very common. Many of these women will admit, on close questioning, that they perceive their bleeding as heavy, but not necessarily excessively heavy, but they still perceive it as a problem. Many of these women have perceived a change in their pattern of flow.

The routine clinical assessment of volume of menstrual flow is particularly difficult, but precision from clinical assessment can be improved by consideration of the structured questioning discussed above, which can be very valuable in the minority of cases where there are uncertainties in the initial history.

Memory of menstrual events is highly fallible, and simple prospective daily diary recording of bleeding patterns often provides a very different perspective from the original case history. ^{16,17} We recommend a simple calendar, with the possibility for the patient to record, with symbols, her perception of her daily variations in flow (heavy, moderate, light). This gives an instant assessment of regularity and pattern of flow with changes over time, but collected on a prospective basis. It is surprising how often these prospective charts differ from the original history! Many versions of such diaries are available, tailored to different requirements.

- Fraser IS, Critchley HOD, Munro MG. Abnormal uterine bleeding – getting our terminology straight. Curr Opin Obstet Gynecol 2007; in press.
- Woolcock J, Critchley HOD, Munro MG, Broder M, Fraser IS. A comprehensive review of the worldwide confusion on menstrual terminologies and definitions. Fertil Steril 2007; in press.
- Hallberg L, Hogdahl A, Nilsson L, Rybo G. Menstrual blood loss – a population study. Acta Obstet Gynecol Scand 1966; 45: 320–51.
- 4. Fraser IS, McCarron G, Markham R. A preliminary study of factors influencing perception of menstrual blood loss volume. Am J Obstet Gynecol 1984; 149: 788–93.

- Warner PE, Critchley HOD, Lumsden MA, et al. Menorrhagia
 I: measured blood loss, clinical features, and outcome in women
 with heavy periods: a survey with follow-up data. Am J Obstet
 Gynecol 2004; 190: 1216–23.
- Warner PE, Critchley HOD, Lumsden MA, et al. Referral for menstrual problems: cross-sectional survey of symptoms, reasons for referral and management. BMJ 2001; 323: 24–8.
- Thomas S, Ellertson C. Nuisance or natural and healthy: should monthly menstruation be optional for women? Lancet 2000; 355: 922-4.
- 8. Fraser IS. Menorrhagia a pragmatic approach to the understanding of causes and the need for investigations. Br J Obstet Gynaecol 1994; 101(Suppl 11): 3–7.
- Ramsay P. How can imaging techniques assist in the assessment and management of abnormal uterine bleeding. Gynaecol Forum 2007; 12: 27–9.
- Snowden R, Christian B. Patterns and Perceptions of Menstruation. London: Croom Helm, 1983.
- 11. Fraser IS, Warner P, Marantos PA. Estimating menstrual blood loss in women with normal and excessive menstrual fluid loss volume. Obstet Gynecol 2001; 98: 806–14.
- Warner PE, Critchley HOD, Lumsden MA, et al. Menorrhagia II: is the 80 ml bloodloss criterion useful in management of complaint of menorrhagia? Am J Obstet Gynecol 2004; 190: 1224–9.
- Gorrindo T, Lu Y, Pincus S, et al. Lifelong menstrual histories are typically erratic and trending: a taxonomy. Menopause 2007; 14: 74–88.
- Greenberg M. The meaning of menorrhagia. An investigation into the association between the complaint of menorrhagia and depression. J Psychosom Res 1983; 27: 209–14.
- Fraser IS, Pearse C, Shearman RP, Elliott PM, Markham R. The efficacy of mefenamic acid in patients with a complaint of menorrhagia. Obstet Gynecol 1981; 58: 543–51.
- Rodriguez G, Faundes-Latham A, Atkinson LE. An approach to the analysis of menstrual patterns in the critical evaluation of contraceptives. Stud Fam Plann 1976; 7: 42–51.
- Belsey EM, Machin D, D'Arcangues C. The analysis of vaginal bleeding patterns induced by fertility regulating methods. Contraception 1986; 34: 253–60.

- National Institute for Health and Clinical Excellence. Heavy Menstrual Bleeding. Guideline 44. London: NICE, 2007.
- National Institute for Health and Clinical Excellence. Referral Guidelines for Suspected Cancer. London: NICE, 2005.
- 20. Fraser IS, Critchley HOD, Munro MG, Broder M. Can we achieve international agreement on terminologies and definitions used to describe abnormalities of menstrual bleeding? Hum Reprod 2007; 22: 635–43.
- 21. Fraser IS, Critchley HOD, Munro MG, Broder M. A process designed to lead to international agreement on terminologies and definitions used to describe abnormalities of uterine bleeding. Fertil Steril 2007; 87: 466–76.
- Higham JM, O'Brien PM, Shaw RW. Assessment of menstrual blood loss using a pictorial chart. Br J Obstet Gynaecol 1990; 97: 734–9.
- Janssen CA, Scholten PC, Heintz AP. A simple visual assessment technique to discriminate between menorrhagia and normal menstrual blood loss. Obstet Gynecol 1995; 85: 977–82.
- 24. Barer AP, Fowler WM. The blood loss during normal menstruation. Am J Obstet Gynecol 1934; 31: 979–86.
- Hallberg L, Nilsson L. Determination of menstrual blood loss. Scand J Clin Lab Invest 1964; 16: 244–8.
- Cole SK, Billewicz WZ, Thomson AM. Sources of variation in menstrual blood loss. J Obstet Gynaecol Br Commonw 1971; 78: 933–9.
- Callender ST, Warner GT, Cope E. Treatment of menorrhagia with tranexamic acid. A double-blind trial. Brit Med J 1970; 4 (5729): 214–16.
- Wyatt KM, Dimmock PW, Walker TJ, O'Brien PMS. Determination of total menstrual blood loss. Fertil Steril 2001; 76: 125–31.
- 29. Hurskainen R, Teperi J, Turpeinen U, et al. Combined laboratory and diary method for subjective assessment of menstrual blood loss. Acta Obstet Gynecol Scand 1998; 77: 201–4.
- 30. Fraser IS, McCarron G, Markham R, Resta T. Blood and total fluid content of menstrual discharge. Obstet Gynecol 1985; 65: 194–8.
- Reid PC. Assessment of menorrhagia by total menstrual fluid loss. J Obstet Gynaecol 2006; 26: 438–41.

Pathogenesis of abnormal uterine bleeding

6

Malcolm G Munro and Ian S Fraser

DEFINITION OF ABNORMAL UTERINE BLEEDING

The diagnosis of abnormal uterine bleeding (AUB) implies that a visual examination of the lower reproductive tract has determined that bleeding is emanating from the uterus itself and/or that there are no lower tract, perianal, or periurethral lesions that may be responsible for the patient's complaint. The definition of AUB varies with the reproductive status of the individual; for premenarcheal girls and postmenopausal women, any spontaneous uterine bleeding is abnormal, while for women of reproductive age, when cyclical bleeding is the norm, abnormal variations in frequency, cycle length, and duration and rate of menstrual flow are individually or collectively the features that define AUB. Finally, AUB may occur in the context of the use of local or systemically administered gonadal steroids or other pharmacologically active agents that impact the endometrium directly, or, in reproductive-aged women, as the result of their interaction with the hypothalamic-pituitary-ovarian axis.

The nomenclature relating to AUB has been thoroughly discussed in Chapter 3. To reiterate, clinicians and investigators use a variety of terms to describe disorders of menstrual bleeding, often commingling a variety of descriptive and diagnostic terms and phrases. The fact that similar terms are used in different ways in different countries and even by different gynecologists within a single practice setting has confounded both the design and interpretation of clinical investigation in this arena. As a result, the simplified nomenclature discussed previously will be used to facilitate discussion about the definitions and symptoms of AUB. These definitions generally use the 5th and 95th centiles to discriminate between normal and abnormal menstrual function.

In the reproductive years, following menarche, cyclic ovulation results in the onset of menstrual periods every 24–38 days.^{2–5} While there is variation between women, this cycle length in a given individual should remain reasonably constant. As a result, an individual who has variable onset between 22 and 35 days, for example, would

be considered to have AUB based on irregular timing of the onset of menses.⁶ Women who have cycle lengths less than 24 days have menses that are too frequent, a type of AUB that has, in the past, been termed 'polymenorrhea'. At the other end of the spectrum is 'oligomenorrhea', which describes women who bleed but for whom the interval between onsets of menses is greater than 38 days. The upper limit for this interval is 6 months, after which the woman is deemed to have amenorrhea. The 5th and 95th centiles for menstrual duration of menses are 4.5 and 8.0 days, respectively. Consequently, women who bleed fewer than 4.5 days or more than 8.0 days may be said to have shortened or prolonged menses, respectively – another parameter that defines AUB.

Finally, perhaps the most controversial defining parameter of AUB is the volume of bleeding, which has been investigated rather extensively on a research basis, ^{3,7} but which also has the least applicability to the clinician 'in-the-field' who is without the means to quantify this variable. The normal range is 5–80 ml; less than 5 ml per month could be defined as 'light' bleeding, while volumes over 80 ml are called 'heavy menstrual bleeding' and are associated with depletion of iron stores.^{7,8}

For three of the four variables described above – cycle length (frequency), predictability, and duration - AUB may be primarily considered to be a symptom, provided the clinician determines that the bleeding indeed emanates from the endometrial cavity, including the endocervical canal. The fourth variable, is, in essence a laboratory finding that distinguishes among women who have less than normal, normal, or greater than normal menstrual volume. Collectively, this group of women could be said to have AUB secondary to abnormalities of the normal menstrual process.⁶ This process has been called ovulatory dysfunctional uterine bleeding (DUB), and even though the term is not always satisfactorily defined,1 it will be used in this chapter to denote the group of women with AUB who have 'excessive bleeding of uterine origin (excessively heavy, excessively frequent or excessively prolonged) which is not due to complications of pregnancy or to recognizable pelvic or systemic disease'. 9,10

Another group of women with AUB are those who have bleeding between their menses. Such women may be said to have intermenstrual bleeding, which may occur either spontaneously or following contact such as occurs with sexual intercourse or the placement of pessaries or vaginal contraceptive devices.

The final group of women with AUB are those who bleed in association with the use of gonadal steroids, usually for contraception, but often for other reasons such as treatment of disorders that manifest as AUB. In most instances this bleeding is called 'breakthrough bleeding'.

PATHOGENESIS OF ABNORMAL UTERINE BLEEDING

Composition of the menstrual flow

The menstrual flow has only been studied in a limited manner and only to a minimal extent using modern laboratory research technologies. It clearly contains some of the elements of whole blood, with red cells and leukocytes (especially polymorphonuclear leukocytes), but virtually no platelets. Assessment of the hemoglobin content makes it clear that it is composed of very dilute blood, and the 'whole blood' content appears generally to vary between 30 and 40%, with the remainder probably being made up of an endometrial transudate. In women with heavy menstrual bleeding, the mean whole blood component increases to around 50%.

The menstrual flow is greatly deficient in platelets and clotting factors,11 but fibrin monomer fibers can be recognized under the electron microscope even if a true blood clot with mature fibrin does not form. The apparent blood 'clots' which many women observe in their menstrual flow are aggregations of red cells held together loosely by mucinous proteins.¹⁴ These tend to become more prominent when the bleeding is heavier. Endometrial tissue fragments are usually recognizable in the flow, although their composition varies greatly from clumps of histologically typical endometrial glandular and stromal tissue through viable single cells to non-viable and unrecognizable tissue fragments and cellular material.¹¹ The larger tissue fragments tend to start appearing in the menstrual flow around 12 hours after the onset of bleeding. The cellular content of the flow has not been well studied, and there is limited information on the day-to-day changes in composition.

Various other substances, such as enzymes, protein degradation products, and reproductive hormones, 11,14,15 have been measured in menstrual blood by a limited number of investigators, but these data have shed little light on aspects of AUB.

Mechanisms of abnormal uterine bleeding

Abormal uterine bleeding secondary to disorders of hemostasis

Disorders of hemostasis seem to be far more common that generally recognized. Von Willebrand's disease was found in 10.7% of women with 'menorrhagia' in a case-control study by the Centers for Disease Control and Prevention in the United States, ²⁸ a number much lower than the 17% and 34% with disorders of hemostasis recently reported from the UK and Sweden, respectively, but nonetheless higher than previously perceived. ^{29,30} In each instance, the vast majority of cases were von Willebrand's disease, a diagnosis that may be increasing, at least in part, because of a greater understanding of the requirements for diagnosis of different variants of this condition.

Three variants of von Willebrand's disease are now recognized; the majority (60–80%) are a mild form (type 1), which is commonly overlooked and can only be diagnosed with certainty with repeated specialized testing for von Willebrand's factor levels.^{31,32} Type 2 disease is a quantitative defect that way not manifest with clotting impairment; but may solely manifest with bruising or heavy menstrual bleeding. These individuals typically have vWF levels that are 10–45% of normal. The severe form (type 3), with major deficiency of von Willebrand's factor, usually leads to serious bleeding with mild injury, first noted in childhood, and excessively heavy menstrual bleeding from the menarche onwards. The three different types of von Willebrand's disease are probably determined by different genes.

Excessively heavy menstrual bleeding is also a common feature of other disorders of hemostasis such as thrombocytopenia, the thrombocytopathies (such as Glanzmann disease), and rarer deficiencies of factors II, V, VII, VIII, IX, X, XI, and XII.³³ Heavy bleeding also occurs in some women on anticoagulant drugs, and occasionally this may be severe.

Abnormal uterine bleeding with demonstrable local pelvic pathology or disturbed endometrial function

Leiomyomas The cause of bleeding associated with leiomyomas remains an enigma. It is clear that the majority of myomas are asymptomatic, 34,35 and it is generally accepted, but not proven, that those myomas that cause bleeding are those situated near or adjacent to the endometrium or those that otherwise distort the endometrial surface area. There is evidence that the endometrium overlying myomas is noticeably thinner and more vascular than in parts of the uterus where there is no underlying myoma³⁶ but the significance of this finding is unclear.

Although a leiomyoma-induced increase in endometrial surface area has been reported in the past, it is apparent that abnormal bleeding may also accompany the presence of relatively small leiomyomas or those that do not distort the endometrial cavity.³⁷

In some women, dilated thin-walled and rather fragile blood vessels are visible on the surface of submucous myomas. The search for biochemical mechanisms of leiomyoma-associated uterine bleeding has demonstrated the capacity of myoma smooth muscle cells to release angiogenic and growth factors, such as vascular endothelial growth factor (VEGF), basic fibroblast growth factor (bFGF), and transforming growth factor beta (TGF- β), ³⁸ as well as plasminogen activators and inhibitors. Leiomyoma MMP-11 activity has been demonstrated to be two-fold greater than that of normal myometrium, but MMP-1 and MMP-3 remain unchanged. The relationship of these findings to myoma-related AUB remains unclear. ³⁹

Endometrial polyps These polyps are common but rather mysterious lesions whose origins are very poorly understood. 40 It is generally assumed that they arise because a limited portion of endometrium fails to be shed at menstruation, and that this tissue continues to proliferate each month. On the other hand, some polyps may arise because of abnormal proliferation of a group of cells in the basal layer of endometrium – tissue which is not susceptible to menstrual breakdown and shedding. Endometrial polyps usually have a single artery as blood supply, and this can often be clearly demonstrated on ultrasound scan.

Many polyps are symptomless, but others may be associated with a history of increased volume of bleeding, or of irregular light bleeding (which may be intermenstrual or premenstrual). Symptoms usually improve following surgical excision of the polyps, but the actual mechanisms of polyp-associated AUB are unclear. Some polyps undergo patchy surface necrosis, and others can be seen to have prominent thin-walled surface vessels, which may result in erratic light bleeding, but mechanisms of heavy bleeding are unknown.

Adenomyosis This condition is typically said to cause heavy menstrual bleeding, perimenstrual pain, and pelvic tenderness (such as deep dyspareunia), but many cases are asymptomatic and others are associated with endometriosis, uterine myomas, or endometrial hyperplasia.⁴¹ Hence, the actual association of symptoms with the adenomyosis is uncertain, which makes the study of the mechanisms of symptom generation very difficult.

Adenomyosis is an estrogen-dependent disease,⁴² like many benign and malignant gynecologic pathologies, and polymorphisms have been detected in the estrogen

receptor alpha gene in adenomyosis. Additionally, adenomyosis tissue has been shown to contain progesterone receptors, as well as the capacity to synthesize its own aromatase and sulfatase enzymes. This combination of functions almost certainly contributes to the growth and function of the abnormal tissue.

Magnetic resonance imaging has demonstrated that disruption of the endometrial–myometrial interface and disorganization of the uterine junctional zone may play an integral role in the pathogenesis of adenomyosis. Disruption of the normal cycle-dependent contraction waves of the junctional zone have been linked to dysmenorrhea and heavy menstrual bleeding.⁴³

Arteriovenous malformations These lesions have typically been associated with episodes of acute and excessively heavy bleeding, sometimes but not always coinciding with menstruation. In the past, hysterectomy was the usual treatment, demonstrating coils of distended and thin-walled vessels in the myometrium and endometrium. Bleeding is assumed to have occurred from the superficial, thin-walled and possibly fragile vessels. Nowadays, these lesions are diagnosed on a regular basis in women with acute episodes of bleeding through the use of transvaginal ultrasound scanning incorporating a Doppler facility. Many of these lesions occur following curettage for retained placental tissue, and resolve spontaneously with time; their mechanisms are unknown.

Infection Chronic low-grade infection of the ectocervix or endocervical infection with chlamydia or gonorrhea typically lead to unpredictable episodes of light intermenstrual or postcoital bleeding, presumably from abnormal, fragile surface vessels on these surface lesions in the lower genital tract. Chronic endometrial infection may be associated with similar symptoms, but sometimes may cause recurrent and excessively heavy menstrual bleeding. Mechanisms of such bleeding are uncertain, but again, may be associated with the distended thin-walled, fragile vessels caused by inflammation and abnormal angiogenesis.

Abnormal uterine bleeding without a demonstrable mechanism (dysfunctional uterine bleeding)

Dysfunctional uterine bleeding may occur either in the context of ovulatory cycles (ovulatory DUB) or in association with an anovulatory or mostly anovulatory state (anovulatory DUB), each of which is unrelated to structural abnormalities of the genital tract but which may exist in the presence of asymptomatic structural anomalies such as small endometrial polyps or subserous leiomyomas.¹⁸

Ovulatory

Ovulatory DUB appears to occur when there is loss of local control of the mechanisms which normally limit the volume of blood lost during menstrual tissue shedding, primarily the processes of vasoconstriction and hemostasis. This could be termed a primary endometrial disorder of bleeding. There is now extensive evidence for disturbances of a range of endometrial molecular mechanisms in women with a convincing complaint of heavy menstrual bleeding. 18,19 These include endothelin expression, prostaglandin secretion and binding, fibrinolytic activity, platelet function, heparin-like activity, lysosomal enzymes, VEGF, and MMPs. There are significant, but subtle, disturbance of vascular morphology with ovulatory DUB, such as increased endometrial endothelial cell proliferation, and reduced proliferation and differentiation of vascular smooth muscle cells around spiral arterioles¹⁹ with minor abnormalities of the morphology of endometrial and myometrial veins.44

Several disturbances of prostaglandin metabolism and binding have been demonstrated, ^{18,19} including an increase in total prostaglandin synthesis and release with a disproportionate rise in PGE₂ compared with PGF₂ α . ^{45,46} The synthetic capacity for PGI₂ is increased, ⁴⁷ and the binding sites for PGE₂ and PGI₂ are increased. PGE₂ and PGI₂ are vasodilatory PGs in the endometrium, and PGI₂

is the most potent natural inhibitor of platelet aggregation. Reduced levels of endometrial endothelins may also lead to less vasoconstrictive activity in menstrual endometrium of women with heavy menstrual bleeding, 48 and increased synthesis of heparin-like activity may contribute. 49 Recent demonstration of reduced levels of VEGF-A and the matrix metalloproteinases MMP-2 and MMP-9, and elevated TNF- α in the menstrual endometrium and the discharge from the uterus in women with heavy menstrual bleeding, is an indication that a range of endometrial regulatory molecules may be involved in abnormal bleeding. 50

Enhanced fibrinolysis, through increased endometrial levels of tissue plasminogen activator, may greatly impede the attainment of local hemostasis and has been demonstrated in women with ovulatory DUB, ^{20,51} who revert to normal menstrual volumes when antifibrinolytic agents are employed.⁵²

Recent research has begun to focus on the activation of specific genes that may be associated with AUB. A novel gene called 'endometrial bleeding-associated factor' (ebaf, also known as LEFTY-A) is transiently expressed in normal endometrium at menstruation and much more strongly expressed in AUB. 53 This gene is located on chromosome 1 and codes for a member of the TGF- β super-family. The concept of multigene activation patterns is now being explored as a possible explanation

Table 6.1 Suggested normal limits for menstrual parameters in the mid reproductive years

Clinical dimensions of menstruation and menstrual cycle	Descriptive terms	Normal limits (5th–95th percentiles)
Frequency of menses (days)	Frequent	<24,
	Normal	24–38
	Infrequent	>38
Regularity of menses (cycle-to-cycle variation over 12 months; in days)	Absent	-
·	Regular	Variation ±2 to 20 days
	Irregular	Variation greater than 20 days
Duration of flow (days)	Prolonged	>8.0
	Normal	4.5-8.0
	Shortened	<4.5
Volume of monthly blood loss (ml)	Heavy	>80
	Normal	5–80
	Light	<5

for complex functional disturbances of the type exemplified by ovulatory DUB.

Anovulatory

The mechanisms involved in anovulatory DUB are systemic in nature, although local hemostatic mechanisms may be rendered deficient secondary to the absence of cyclical production of progesterone and the related biosynthesis of prostaglandins and other regulatory substances necessary to control blood loss. In addition, the absence of ovulation makes the bleeding unpredictable, a circumstance that can negatively affect the woman's lifestyle due to the constant concern about unexpected bleeding. Finally, anovulatory DUB creates an endocrinologic endometrial milieu of unopposed estrogen, known to facilitate the development of endometrial hyperplasia and endometrial adenocarcinoma, with their thin-walled, tortuous, fragile and superficial endometrial vessels.54-56 The etiology of anovulation in any given woman may range from immaturity of the hypothalamic-pituitary-ovarian axis, frequently seen in perimenarcheal girls with failure of maturation of the positive feedback response to estradiol,⁵⁷ through a number of entities that are known or suspected of impacting on the normal function of the hypothalamic-pituitary-ovarian axis. The secondary endometrial mechanisms leading to abnormal bleeding probably include effects of unopposed estrogen on uterine vascular tone,⁵⁸ increased VEGF expression with disturbed angiogenesis,⁵⁹ disturbed prostaglandin synthesis60 and increased NO production.²³ Polycystic ovarian syndrome is perhaps the most common entity and may sometimes result in anovulatory DUB. Hyperprolactinemia and hypothyroidism are endocrinopathies that typically result in anovulation. Untreated hypothyroidism causes anovulation that is typically manifest as amenorrhea, but may occasionally, and especially in older women, be associated with heavy, prolonged and unpredictable bleeding.61

Hyperprolactinemia also commonly causes anovulation, but this virtually always results in amenorrhea.

Manifestations of abnormal uterine bleeding

It is recognized that the available literature has not formally distinguished between acute and chronic AUB in non-pregnant women. It is recommended that chronic AUB be defined as bleeding from the uterine corpus that is abnormal in volume, regularity, and/or timing and which has been present for at least 3 months. Chronic AUB would not require urgent or emergent intervention. Acute AUB, on the other hand, is AUB that, in the opinion of the clinician, is of sufficient volume to require urgent or emergent intervention. Acute AUB may present as a sudden and excessive episode in the context of existing chronic AUB or might occur without a recent history of chronic abnormal uterine bleeding. Women in the reproductive years with acute AUB require unique interventions, but their follow-up care may largely be dependent upon whether or not they require investigation and ongoing care for an underlying chronic condition.

Relatively little attention has been given to study of the natural history of different types of AUB, because active treatment is usually requested and many women end up with various types of surgical intervention. In the past, many women underwent hysterectomy for a range of benign causes of AUB, but these major surgical procedures are declining substantially in many countries. 62-64 Nowadays, many women will use long-term combined oral contraceptives or the levonorgestrel intrauterine system for many years. Consequently data on the likelihood of natural 'cure', the likelihood of gradual progression, or the likelihood of recurrence after treatment are mainly anecdotal for most different types or causes of AUB. There is, nevertheless, strong belief that most types of AUB will persist or progress if not treated or will recur after short-term medical treatment.

- Fraser IS, Inceboz US. Defining disturbances of the menstrual cycle. In: O'Brien PMS, Cameron IT, MacLean AB, eds. Disorders of the Menstrual Cycle. London: RCOG Press, 2000: 141–52.
- Treloar SA, Martin NG, Heath AC. Longitudinal genetic analysis of menstrual flow, pain and limitation in a sample of Australian twins. Behav Genet 1998; 28: 107–16.
- 3. Snowden R, Christian B. Patterns and Perceptions of Menstruation. London: Croom Helm, 1983.
- Chiazze L, Brayer FT, Macisco J. The length and variability of the human menstrual cycle. JAMA 1968; 203: 377–85.
- Belsey EM, Pinol A, Task Force on Long-Acting Systemic Agents for Fertility Regulation. Menstrual bleeding patterns in untreated women. Contraception 1997; 55: 57–65.
- 6. Fraser IS, Critchley HOD, Munro MG, Broder M. Can we achieve international agreement on terminologies and definitions used to describe abnormalities of menstrual bleeding? Hum Reprod 2007; 22: 635–43. Fraser IS, Critchley HOD, Munro MG, Broder M. A process designed to lead to international agreement on terminologies and definitions used to describe abnormalities of menstrual bleeding. Fertil Steril 2007; 87: 466–76 [Simultaneous Publication].

- Hallberg L, Hogdahl AM, Nilsson L, Rybo G. Menstrual blood loss – a population study. Acta Obstet Gynecol Scand 1966; 45: 320–51.
- Cole SK, Billewicz WZ, Thomson AM. Sources of variation in menstrual blood loss. J Obstet Gynaecol Br Commonw 1971; 78: 933–9.
- Fraser IS. The dysfunctional uterus: dysmenorrhoea and dysfunctional uterine bleeding. In: Shearman RP, ed. Clinical Reproductive Endocrinology. Edinburgh: Churchill Livingstone, 1985: 579–98.
- Crosignani PG, Rubin B. Review and guidelines on dysfunctional uterine bleeding. Study Group of the European Society for Human Reproduction and Embryology Hum Reprod 1990; 5: 637–8
- Hahn L. Composition of menstrual blood. In: Diczfalusy E, Fraser IS, Webb FTG, eds. Endometrial Bleeding and Steroidal Contraception. Bath: Pitman Press, 1980: 107–37.
- Fraser IS, McCarron G, Markham R, Resta T. Blood and fluid content of menstrual discharge. Obstet Gynecol 1985; 65: 194–8.
- Fraser IS, Warner P, Marantos PA. Estimating menstrual blood loss from the total menstrual fluid volume in women with normal and excessive menstrual bleeding. Obstet Gynecol 2001; 98: 806–14.
- Beller FK. Observations on the clotting of menstrual blood and clot formation. Am J Obstet Gynecol 1971; 111: 535–43.
- 15. Zhou JP, Fraser IS, Caterson I et al. Reproductive hormones in menstrual blood. J Clin Endocrinol Metab 1989; 69: 338–42.
- Corner GW. The Hormones in Human Reproduction. Princeton: Princeton: Princeton University Press, 1942: 279.
- Markee J. Menstruation in intraocular endometrial transplants in the rhesus monkey. Contrib Embryol Carnegie Inst 1940; 28: 219–308.
- Livingstone M, Fraser IS. Mechanisms of abnormal uterine bleeding. Hum Reprod Update 2002; 8: 60–7.
- Jabbour HN, Kelly RW, Fraser HM, Critchley HOD. Endocrine regulation of menstruation. Endocrinol Rev 2006; 27: 17–46.
- Gleeson N, Devitt M, Sheppard BL, Bonnar J. Endometrial fibrinolytic enzymes in women with normal menstruation and dysfunctional uterine bleeding. Br J Obstet Gynaecol 1993; 100: 768–71.
- Christiaens GCML, Sixma JJ, Haspels AA. Hemostasis in menstrual endometrium – a review. Am J Reprod Immunol 1982; 5: 78–83.
- Cameron IT, Campbell S. Nitric oxide in the endometrium. Hum Reprod Update 1998; 4: 565–9.
- Chwalisz K, Garfield RE. Role of nitric oxide in implantation and menstruation. Hum Reprod 2000; 15(Suppl 3): 96–111.
- Zhang J, Nie G, Jian W, Woolley DE, Salamonsen LA. Mast cell regulation of human endometrial matrix metalloproteinases: a mechanism underlying menstruation. Biol Reprod 1998; 59: 693–703.
- Lockwood CJ, Krikun G, Hausknecht VA, Papp C, Schatz F. Matrix metalloproteinase and matrix metalloproteinase inhibitor expression in endometrial stromal cells during progestininitiated decidualization and menstruation-related progestin withdrawal. Endocrinology 1998; 139: 4607–13.
- Marbaix E, Vekemans M, Galant C et al. Circulating sex hormones and endometrial stromelysin-1 (matrix metalloproteinase-3) at the start of bleeding episodes in levonorgestrel-implant users. Hum Reprod 2000; 15 (Suppl 3): 120–34.

- 27. Salamonsen LA. Tissue injury and repair in the female genital tract. Reproduction 2003; 125: 301–11.
- 28. Dilley A, Drews C, Miller C et al. von Willebrand disease and other inherited bleeding disorders in women with diagnosed menorrhagia. Obstet Gynecol 2001; 97: 630–6.
- Kadir RA, Lee CA, Sabin CA, Pollard D, Economides DL. Pregnancy in women with von Willebrand's disease or factor XI deficiency. Br J Obstet Gynaecol 1998; 105: 314–321.
- Edlund M, Blomback M, von Schoultz B, Andersson O. On the value of menorrhagia as a predictor for coagulation disorders. Am J Hematol 1996; 53: 234–8.
- 31. Kouides PA, Conard J, Peyvandi F, Lukes A, Kadir R. Hemostasis and menstruation: appropriate investigation for underlying disorders of hemostasis in women with excessive menstrual bleeding. Fertil Steril 2005; 84: 1345–51
- 32. Lukes AS, Kadir RA, Peyvandi F, Kouides PA. Disorders of hemostasis and excessive menstrual bleeding: prevalence and clinical impact. Fertil Steril 2005; 84: 1338–44.
- 33. Peyvandi F, Duga S, Akhavan S, Mannucci PM. Rare coagulation deficiencies. Haemophilia 2002; 8: 308–21.
- 34. Day Baird D, Dunson DB, Hill MC, Cousins D, Schectman JM. High cumulative incidence of uterine leiomyoma in black and white women: ultrasound evidence. Am J Obstet Gynecol 2003; 188: 100–7.
- 35. Fraser IS, Peric H. Clinical presentation and symptoms associated with uterine fibroids. In: Brosens I, ed. Uterine Fibroids: Pathogenesis and Management. London: Taylor & Francis, 2006: 95–106.
- Patterson-Keels LM, Selvaggi SM, Haefner HK, Randolph JF Jr. Morphologic assessment of endometrium overlying submucosal leiomyomas. J Reprod Med 1994; 39: 579–84.
- 37. Sehgal N, Haskins AL. The mechanism of uterine bleeding in the presence of fibromyomas. Am J Surg 1960; 26: 21–3.
- Stewart EA, Nowak RA. Leiomyoma-related bleeding: a classic hypothesis updated for the molecular era. Hum Reprod Update 1996; 2: 295–306.
- Palmer SS, Haynes-Johnson D, Diehl T, Nowak RA. Increased expression of stromelysin 3 mRNA in leiomyomas (uterine fibroids) compared with myometrium. J Soc Gynecol Invest 1998; 5: 203–9.
- 40. Van Bogaert LJ. Clinico-pathologic findings in endometrial polyps. Obstet Gynecol 1988; 71: 771–3.
- 41. Peric H, Fraser IS. The symptomatology of adenomyosis. Best Pract Res Clin Obstet Gynaecol 2006; 20: 547–56.
- Kitawaki J. Adenomyosis: the pathophysiology of an oestrogendependent disease. Best Pract Res Clin Obstet Gynaecol 2006; 20: 493–502.
- 43. Fusi L, Cloke B, Brosens JJ. The uterine junctional zone. Best Pract Res Clin Obstet Gynaecol 2006; 20: 479–91.
- Hourihan H, Sheppard BL, Bonnar J. The morphologic characteristics of menstrual hemostasis in patients with unexplained menorrhagia. Int J Gynecol Pathol 1989; 8: 221–9.
- 45. Smith SK, Abel MH, Kelly RW, Baird DT. Prostaglandin synthesis in the endometrium of women with ovular dysfunctional uterine bleeding. Br J Obstet Gynaecol 1981; 88: 434–42.
- Makarainen L, Ylikorkala O. Primary and myoma-associated menorrhagia: role of prostaglandins and effects of ibuprofen. Br J Obstet Gynaecol 1986; 93: 974–8.
- 47. Smith SK, Abel MH, Kelly RW, et al. A role for prostacyclin (PGI₂) in excessive menstrual bleeding. Lancet 1981; i: 522–4.
- 48. Marsh MM, Butt AR, Riley SC et al. Immunolocalisation of endothelin and neutral endopeptidase in the endometrium of

- users of subdermally implanted levonorgestrel (Norplant). Hum Reprod 1996; 10: 2584–9.
- Paton RC, Tindall H, Zuzel M, McNicoll GP. Haemostatic mechanisms in the normal endometrium and endometrium exposed to contraceptive steroids. In: Diczfalusy E, Fraser IS, Webb FTG, eds. Endometrial Bleeding and Steroidal Contraception. Bath: Pitman Press, 1980: 325–41.
- Malik S, Day K, Perralut I et al. Reduced levels of VEGF-A and MMP-2 and MMP-9 activity and increased TNF-alpha in menstrual endometrium and effluent in women with menorrhagia. Hum Reprod 2006; 21: 2158–66.
- Gleeson NC, Buggy F, Sheppard BL, Bonnar J. The effect of tranexamic acid on measured menstrual loss and endometrial fibrinolytic enzymes in dysfunctional uterine bleeding. Acta Obstet Gynecol Scand 1994; 73: 274

 –7.
- Rybo G. Plasminogen activators in the endometrium. II. Clinical aspects. Variation in the concentration of plasminogen activators during the menstrual cycle and its relation to menstrual blood loss. Acta Obstet Gynecol Scand 1966; 45: 429–50.
- Kothapalli R, Buyuksal I, Wu S, Tabibzadeh S. Detection of ebaf, a novel human gene of the transforming growth factor beta superfamily: association of gene expression with endometrial bleeding. J Clin Invest 1997; 99: 2342–50.
- Brown JB, Kellar RJ, Matthew GD. Urinary oestrogen excretion in certain gynaecological disorders. J Obstet Gynaecol Br Emp 1959; 66: 177–211.
- Schroder R. Endometrial hyperplasia in relation to genital function. Am J Obstet Gynecol 1954; 68: 294–309.
- Hamou J. Hysteroscopy and Microhysteroscopy. Norwalk, Connecticut: Appleton Lange, 1985.

- 57. Fraser IS, Michie EA, Baird DT, Wide L. Pituitary gonadotropins and ovarian function in adolescent dysfunctional uterine bleeding. J Clin Endocrinol Metab 1973; 37: 407–14.
- Fraser IS, McCarron G, Hutton B, et al. Endometrial blood flow measured by xenon-133 clearance in women with normal menstrual cycles and dysfunctional uterine bleeding. Am J Obstet Gynecol 1987; 156: 158–66.
- Smith SK. Angiogenesis, vascular endothelial growth factor and the endometrium. Hum Reprod Update 1998; 4: 509–19.
- 50. Smith SK, Abel MH, Kelly RW et al. The synthesis of prostaglandins from persistent proliferative endometrium. J Clin Endocrinol Metab 1982; 55: 284–9.
- Krassas GE, Pontikides N, Kaltsas T, et al. Disturbances of menstruation in hypothyroidism. Clin Endocrinol (Oxf) 1999; 50: 655–9.
- 62. Reid PC, Mukri F. Trends in number of hysterectomies performed in England for menorrhagia: examination of health episode statistics 1989 to 2002-3. Br Med J 2005; 330: 938-9.
- Mansour D. Overview of contraception methods: a provider's perspective. In: Glasier A, Wellings K, Critchley H, eds. Contraception and Contraceptive Use. London: RCOG Press, 2005; 44–77.
- Babalola EO, Bharucha AE, Schleck CD, et al. Decreased utilisation of hysterectomy: a population-based study in Olmsted County, Minnesota 1965–2002. Am J Obstet Gynecol 2007; 196: 214.e1–7.
- 65. Treloar AE, Boynton RE, Behn BG, Brown BW. Variation of the human menstrual cycle through reproductive life. Int J Fertil 1967; 12: 77–126.

Menstrual problems in adolescence

7

D Keith Edmonds

INTRODUCTION

The transition from childhood to adulthood for women is fortunately a smooth one for the majority. The process of puberty involves the development of secondary sexual characteristics that include menarche and subsequent menstruation. However, the transition is much more than a physical one, and the evolution psychologically from childhood to adulthood is a slower process than the physical changes that occur and, whereas the majority of physical processes have been completed by the age of 15 years old, psychological maturation is not complete until between the ages of 18 and 20 years old.

It is therefore imperative that the clinician understands the difference between normality and abnormality when it comes to menstrual dysfunction, as the definitions of menstrual change are different in adolescents, and adults.

NORMAL MENSTRUATION DURING ADOLESCENCE

Menarche, the onset of menstruation, varies by nationality (Table 7.1). The age of onset of breast growth (Breast Stage 2) and its relationship to menarche seems reasonably constant throughout the world and ranges from 2 to 3 years. There have been several suggestions that the age of menarche has been significantly falling. However, in a recent study by Whincup et al.,1 comparison between the 1950s, the 1960s, and British girls born between 1982 and 1986 show very little change, with a mean age of menarche around 13 years. A similar study published in the USA² shows that in the USA there has been no decrease in the age of menarche since 1973. Whereas these two studies address populations where socioeconomic status is high, changes in the age of onset of menarche have fallen in those countries where socioeconomic status has changed during this 50-year period. However, in looking at Table 7.1, it is apparent that throughout the world there is very little difference in the mean age of menarche for teenage girls.

Once menstrual cycles begin, the pattern of bleeding may take some years to become established in a regular menstrual cycle. In the first postmenarcheal year, although 50% of cycles are anovulatory, 80% are irregular and the range of the menstrual cycle is from 21 to 45 days, with 2–7 days of bleeding. Ninety-five percent of cycles will fall into this range by the third postmenarchel year and by the sixth postmenarcheal year, menstrual patterns will have stabilized.³ It is of interest to note that girls who begin their menarche earlier tend to have regular ovulatory cycles more rapidly than those who have a later menarche.⁴

It is against this background that clinical histories of alleged menstrual disturbance need to be taken. It is very important that the clinician understands that a teenager reporting irregular cycles is normal and it is therefore beholden on the clinician to explain to the mother and the teenager that a pattern of irregular bleeding is to be expected. It is this type of reassurance which will be all that is required for the vast majority of teenage girls who present to a clinician with menstrual problems. Only a minority will have true menstrual dysfunction that requires medical intervention.

AMENORRHEA

The absence of menstrual periods is classified in one of two ways: it is either primary in which menstruation has never occurred, or secondary, when menstruation has occurred and subsequently there is a cessation of periods. There is considerable debate as to how long absence of menstruation needs to occur before an adolescent is defined as having secondary amenorrhea. In the light of the irregularity of periods in postmenarcheal life, it is most useful to use 6 months without periods as the time frame. It goes without saying that in all adolescents who have undergone pubertal change, pregnancy must always be considered a cause of amenorrhea in either primary or secondary situations.

The investigation of girls with amenorrhea should always be taken seriously. Any mother who brings her

Table 7.1 Age of puberty by nationality

	Breast stage 2	Menarche
USA 1973	10.9	12.8
USA 2001	9.7	12.5
USA (Black) 1997	8.9	12.2
Europe	10.6 – 11.2	12 – 13.3
UK	11.2	13.0
Asia	9.8	12.5
Africa	10.4	13.2
South America	10.4	12.6

daughter to a clinician to raise concern about the fact that menarche has not occurred should have the matter investigated fully. There has been a trend in the past to delay investigation until the girl is aged 15 or 16 years old, but this is completely unreasonable, as the mother and her daughter have requested clinical intervention because of their concern and therefore their complaint should be taken seriously and fully investigated at the time of presentation.

Primary amenorrhea management

In managing primary amenorrhea, the clinician needs to take a detailed history and examine the patient. It is essential to record body mass index and pubertal stage, and it is usual to use the Tanner system of staging breast and pubic hair development in order to compare development against normal.⁵ In referring to management (Figure 7.1), the patients will then fall into two groups: girls with delayed puberty, where secondary sexual development has not occurred or is minimal, and girls with normal puberty.

Delayed puberty

In patients with delayed puberty, the simplest investigation is to perform a serum follicle-stimulating hormone (FSH) test. If the FSH level is high, then the differential diagnosis is either Turner's syndrome, XY female, or primary ovarian failure. If the FSH level is low, then the differential diagnosis is constitutional delay, anorexia nervosa, systemic illness, or Kallmann's syndrome.

Turner's syndrome is characterized by a karyotype of 45,XO with a normal female phenotype without secondary sexual characteristics. The classical features of Turner's syndrome include streak ovaries but with an intact uterus and vagina, short stature, web neck, broad chest, widely

spaced nipples, and pectus excavatum. However, there are some individuals who will have a genetic mosaic 46,XO:46,XX in whom the physical examination may vary widely from the classical situation. If these features are present, it is therefore mandatory that the karyotype should be performed.

This will also be required if androgen insensitivity is suspected, and here the features are of normal growth but scanty pubic hair, no axillary hair, and some small breast growth may have occurred. The karyotype will be reported as 46,XY and, in these circumstances, circulating testosterone levels tend to be in the male range. The testes are functional but there are no androgen receptors and therefore masculinization is not possible. The testes, which are usually intra-abdominal or may be found in the inguinal canals, should be removed due to the risk of malignancy.

Primary ovarian failure may occur as a result of either childhood chemotherapy, irradiation, or infection, which damages the ovaries. If chemotherapy and radiotherapy have been administered, the diagnosis is usually easy to make, but previous infection that might damage the ovaries is often speculative.

In those individuals who have a low FSH, constitutional delay is by far the commonest cause of primary amenorrhea and here, when all other causes of delayed puberty have been excluded, reassurance is all that is required. Eventually, puberty will occur and normal development will be concluded. In some individuals where development is seriously delayed, the induction of puberty may be necessary and is always available as an option. If the individual patient finds the situation intolerable, this is a perfectly reasonable strategy to follow.

Normal puberty

When the patient is found to have normal secondary sexual characteristics, the most useful investigation is a pelvic ultrasound. An abnormal ultrasound will identify either outflow tract obstruction or Müllerian agenesis, which will make the diagnosis obvious. If the ultrasound is normal, the investigations proceed as outlined under the Secondary Amenorrhoea section (see below).

Outflow tract obstruction may occur at the level of the hymen or it may occur at three different levels in the vagina. Obstruction by an imperforate hymen presents with cyclical abdominal pain, and examination of the vulva will reveal a bulging, blue membrane through which the menstrual blood can be seen because it cannot escape. Management is straightforward, with an incision in the hymen that will release the menstrual flow, and no further treatment is necessary. Obstruction of the vagina may occur at the lower third, middle third, or upper third levels, and here surgical intervention is much more complex.

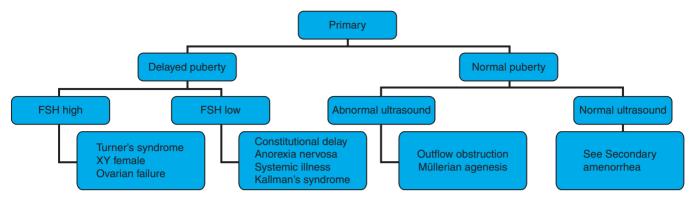


Figure 7.1 Management of primary amenorrhea. FSH, follicle-stimulating hormone.

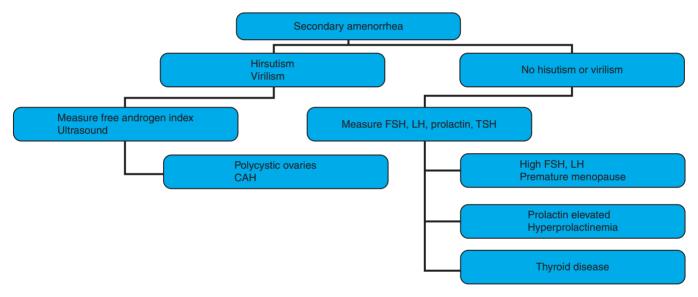


Figure 7.2 Management of secondary amenorrhea. FSH, follicle-stimulating hormone; LH, luteinizing hormone; TSH, thyroid-stimulating hormone; CAH, congenital adrenal hyperplasia.

Examination of the vulva will reveal a swelling on occasions, but this is pink because the transverse vaginal septum obstructs menstrual flow. Removal of the septum requires considerable surgical expertise, as vaginal reconstruction will need to follow. In these circumstances, patients should be referred to specialist centers where the appropriate surgical expertise is available.

Müllerian agenesis is the second most common cause of primary amenorrhea, second only to Turner's syndrome. It is classically known as Mayer–Rokitansky–Hauser (MRKH) syndrome, and here failure of the development of the Müllerian ducts leads to absence of the upper vagina and uterus. There is no surgical treatment for this condition, but creation of a neovagina at some time in the girl's life is more than possible. The management of this condition is outside the scope of this chapter and authors are referred to the work of Edmonds.⁶

SECONDARY AMENORRHEA

As mentioned above, an episode of 6 months without periods in the adolescent would constitute secondary amenorrhea that requires further investigation. Again, a detailed history and examination needs to be carried out in order to assess the patient clinically. Figure 7.2 shows the management algorithm for secondary amenorrhea. The presence of hirsutism and/or virulism would prompt the clinician to measure the free androgen index and perform a pelvic ultrasound specifically looking at ovarian structure. The differential diagnosis here is either polycystic ovarian syndrome (PCOS) or congenital adrenal hyperplasia.

Polycystic ovarian syndrome is being increasingly diagnosed in adolescent girls, as an increasing number are presenting with either oligomenorrhea, secondary

amenorrhea, or hirsutism. Timely diagnosis is important, because PCOS contains the component of insulin resistance which increases the risk of type 2 diabetes, hyperlipidemia, and cardiovascular disease in later life. The reason why this diagnosis is so important is that lifestyle intervention is critical in these individual patients, as the tendency to develop obesity, hypertension, and diabetes needs to be controlled. Therapeutic interventions remain controversial, and there are no long-term follow-up studies of the efficacy of any of them at the present time. The options of using the oral contraceptive pill, insulin sensitizers, antiandrogens, or a combination of these therapies have been addressed only in the short term. Many studies have demonstrated that the benefits of any of these therapies disappear upon discontinuation of treatment. The most concerning aspect of this in adolescents is the unknown sequelae that may result on the developing brain; the impact of PCOS on the skeleton is also important. In adult women with PCOS, bone density is preserved, if not elevated, and it is suggested that this might be attributeable to elevated levels of insulin or androgen. Any of the therapies suggested above may have an impact on bone mineral density, and long-term studies are still awaited. It is therefore extremely important to take a conservative view before introducing therapeutics into the management of these patients, and the lifestyle approach should be the first line of treatment.7

In those individuals who do not have hirsutism or virulism, measurements of FSH, luteinizing hormone (LH), prolactin, and thyroid-stimulating hormone are useful. Patients with an elevated level of FSH and LH, they may have undergone premature menopause and require hormone replacement therapy. If prolactin is elevated, the diagnosis of hyperprolactinemia and a pituitary adenoma need to be excluded, and appropriate investigations done to evaluate this. Finally, an abnormal thyroid function profile would prompt the clinician to investigate the possibility of a thyroid disorder.

DYSMENORRHOEA

Dysmenorrhea, or painful periods, is responsible for teenagers losing more time from school and work than any other single cause. Dysmenorrhea increases in frequency during the adolescent years, with increasing frequency of ovulatory cycles. At age 12 years old, approximately 40% of teenagers have dysmenorrhea, but by 17 years old this has risen to 70%. Fifteen percent of all teenagers who have dysmenorrhea are incapacitated for between 1 and 3 days, but 30–50% describe the pain as mild. Dysmenorrhea is divided into primary and secondary: primary dysmenorrhea is defined as dysmenorrhoea in the presence of

normal uterine anatomy and the absence of disease, whereas secondary dysmenorrhea is identified as being in conjunction with pelvic pathology.

Primary dysmenorrhea

Dysmenorrhea in these circumstances is due to the release of prostaglandins at the time of menstruation. These prostaglandins stimulate local vasoconstriction and myometrial contractility and the combination of ischemia of the endometrial lining and myometrial contraction leads to crampy, lower abdominal pain. The side effects of prostaglandin excess include nausea, vomiting, fatigue, irritability, diarrhea, backache, or headache, and a number of studies have shown that the degree of dysmenorrhea relates to the quantity of prostaglandin released. 9,10

The management of primary dysmenorrhea begins with an explanation as to the reasons why dysmenorrhea occurs. Frequently, this will be sufficient to allay the fears that may have arisen in both the mother and the teenager, and simple analgesics such as aspirin or acetaminophen are to be encouraged as the analgesics of first choice. When these are ineffective, non-steroidal anti-inflammatory drugs (NSAIDS) can be considered, e.g. ibuprofen, naproxen, and mefenamic acid. All of those analgesics, including aspirin, work by decreasing the amount of prostaglandin release. The NSAIDs are highly effective so long as therapeutic doses are administered, and will be sufficient for the majority of teenagers. If these approaches are unsuccessful, then the oral contraceptive pill should be considered, and here a 90% cure can be expected. There are considerable anxieties in mothers agreeing to their daughters taking the oral contraceptive pill under the age of 16 years old, where the maternal consent is desirable. Most of these anxieties are around unsubstantiated fears that it will either lead to promiscuity or interfere with development, (neither of which are true), and reassurance for the mother will be important. In the small proportion of patients who fail to respond to analgesics or the oral contraceptive pill, an ultrasound scan should be performed to exclude a uterine anomaly.

Secondary dysmenorrhea

Secondary dysmenorrhea is much less common in adolescents. It tends to give pain not in conjunction with the onset of menstruation, but pain that begins some days before the onset of menstruation, and usually the pain is relieved by menstrual flow. The differential diagnosis includes pelvic inflammatory disease, endometriosis, or an ovarian cyst. The management depends on the diagnosis. Chronic pelvic inflammatory disease requires an aggressive approach with antibiotics over a prolonged period of time.

However, a delay in the diagnosis and institution of treatment may result in pelvic damage, leading to chronic pelvic pain. Endometriosis occurs in teenagers and is being increasingly diagnosed in this age group. ¹¹ It is not important in this age group to make a diagnosis by laparoscopy, as this does not affect the decisions to treat; neither does it affect the choice of treatments available. Abolition of menstruation is the therapeutic goal, and may be achieved by the continuous use of the oral contraceptive pill or by the use of gonadotropin-releasing hormone (GnRH) analogues plus addback therapy. This long-term therapy is complex to administer and the side effects of this type of approach remain unproven.

In both primary and secondary dysmenorrhea, an approach using the levonorgestrel intrauterine system (IUS) is being increasingly tried in this age group. The first of these follow-up studies, published by Suhonen et al., 12 consisted of a population of 18–25 year olds who were themselves seeking contraception as well as control of dysmenorrhea. The levonorgestrel IUS had equally effective control of their dysmenorrhea as the oral contraceptive group. Studies on girls between 12 and 18 years old are still awaited, and will require the introduction of a smaller device; however, the therapeutic benefits of are obvious, and it is likely that the levonorgestrel will become part of the therapeutic armamentarium in the next few years.

Dysfunctional uterine bleeding

Establishing whether or not menstrual loss in a teenager is abnormal or not is very difficult from the history. In fact, it is always a very difficult assessment to make in all women during their menstrual life, as they have really very little with which to compare. So, although a history is important in which increased frequency of menstruation and the presence of clots or flooding are elicited, an objective measurement of menstrual loss is difficult to ascertain. It is therefore prudent to use hemoglobin as a surrogate for blood loss, which allows therapeutic strategies to be instituted.

The majority of teenagers with dysfunctional uterine bleeding have anovulation as the underlying etiology. The lack of ovulation means that the release of estradiol from the ovary promotes proliferative endometrium which is never opposed by progestogen. There is, therefore, a thicker endometrium than would develop in an ovulatory cycle and the lack of progesterone means that local prostaglandin release is impaired and therefore vasoconstriction and myometrial contraction fail to occur. Thus, dysfunctional uterine bleeding is associated with less dysmenorrhea and heavier uterine bleeding. In these circumstances, menstrual loss can be extremely heavy or may at least be perceived as this. As shown in Figure 7.3, if the hemoglobin level is greater than 12 g/dl, the teenage girl is coping with whatever blood flow she is experiencing. In these circumstances, reassurance is essential. A menstrual calendar can be given, and if the flow is considered to be such as to be interfering with normal activity, tranexamic acid 500 mg 6-hourly can be prescribed. This is extremely effective in reducing flow in these circumstances; as tranexamic acid is not hormonal, and need only be taken at the time of menstruation, it is an extremely useful therapy. Patients should be given a menstrual calendar because, as time goes by, menstrual cycles will become

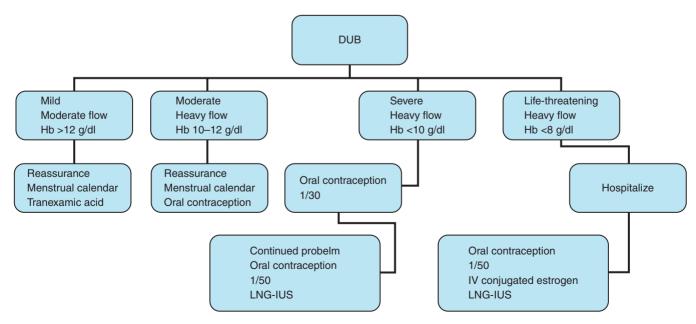


Figure 7.3 Dysfunctional uterine bleeding (DUB). Hb, hemoglobin; LNG-IUS, levonorgestrel intrauterine system.

increasingly regular and more episodes of ovulation will occur and it is then pictorially demonstrable that their menstrual flow and cycle length is improving. Repeated visits to the gynecologist are important, as reassurance during these difficult times is very useful.

If the hemoglobin level is between 10 and 12 g/dl, there is some degree of compromise in the patient and, in this case, while reassurance from a menstrual calendar is equally important, oral contraception is probably the best strategy. It is unlikely that tranexamic acid or progestogens would be effective in controlling blood loss sufficiently to correct the mild anemia, whereas the oral contraceptive pill would be extremely effective at doing this. Any patient who is started on such a therapy needs to continue for at least 1 year and then the oral contraceptive pill can be withdrawn to see whether cycle maturation has occurred sufficiently to correct the menstrual flow problem. If it has not, the heavy periods would recommence and reinstitution of the oral contraceptive pill for a further year should be carried out. Annual withdrawal of the pill should be carried out until such times as menstrual maturation has occurred.

In patients who present with heavy menstruation and hemoglobin of less than 10 g/ld, again the oral contraceptive pill can be used. However, a 30 µg pill may be inadequate to correct this problem and, if this is the case, a 50 µg pill should be introduced. This is almost certainly sufficient to control almost all patients with heavy menstrual loss in these circumstances. However, in exceptional circumstances, the levonorgestrel IUS can be considered and thereby create amenorrhea. Until such times as menstrual maturation will have occurred, those few individuals who have embarked on this treatment have found it extremely effective and, of course, it acts as a contraceptive, as does the oral contraceptive pill in these circumstances.

Finally, in a life-threatening situation where menstrual flow is continuous and hemoglobin levels are less than 8 g/dl, hospitalization is mandatory. The oral contraceptive pill should be commenced and a 50 µg pill should be used. If menstrual flow is not controlled after 24 hours, it may be necessary to use intravenous (IV) conjugated oestrogen at a dose of 25 mg 6-hourly until menstrual flow

ceases. The etiology of this life-threatening situation is somewhat different to the previous three types of presentations. A lack of production of estrogen to promote endometrial cell growth, and thereby close the capillary bed in the basalis layer of the endometrium, is the cause of the problem, and hence the use of estrogen to promote endometrial cell growth is the strategy of choice. Again, in patients intolerant of the oral contraceptive pill, or in whom control of bleeding continues to be difficult, the levonorgestrel IUS can be used. In all teenagers who have very heavy bleeding an ultrasound scan should be carried out to exclude uterine pathology. Although these pathologies are rare, it is obviously imperative that they should be screened for.

MENSTRUAL PROBLEMS AND BLEEDING DISORDERS

Hematologic abnormalities in association with adolescent menorrhagia are rare. However, in those individuals who have very heavy bleeding which results in anemia, it is pertinent and appropriate to perform a coagulation screen. In adults who have been screened for menorrhagia, some 7% of women who have very severe bleeding may be found to have a bleeding disorder, of which von Willebrand's disease is the most common. 13 However, it is also pertinent to note that a recent study¹⁴ looking at bleeding disorders in teenagers presenting with menorrhagia did not find that menstrual loss was a predictor of the bleeding disorder. Although it seems prudent to screen for these disorders in this rare group of teenagers who have severe menstrual loss, it does not seem to be a useful investigation in those who do not. For adolescents with menorrhagia secondary to systemic bleeding disorders, the therapeutic management depends on the disorder itself, and they should be managed by a hematologist in conjunction with a gynecologist. From a gynecologic management strategy, the oral contraceptive pill can be used, as can Depo progestogen, GnRH analogues, or the levonorgestrel IUS, all of which can be used to control menstrual loss in these circumstances.

- 1. Whincup PH, Gilg JA, Odoki K, Taylor SJC, Cook DC. Age of menarche in contemporary British teenagers: survey of girls born between 1982 and 1986. BMJ 2001; 322:1095–6.
- Chumlea WC, Schubert CM, Roche AF, et al. Age at menarche and racial comparison in US girls. Pediatrics 2003; 111: 110–13.
- 3. Hillard P. Menstruation in young girls: a clinical perspective. Obstet Gynecol 2002; 99: 655–62.
- 4. Vihko R, Apter D. Endocrine characteristics of adolescent menstrual cycles. J Steroid Chem 1984; 20: 231–36.
- Tanner JM. Growth and maturation during adolescence. Nutr Rev 1981; 39: 43–55.

- Edmonds DK. Congenital malformations of the genital tract and their management. Best Pract Res Clin Obstet Gynaecol 2003; 17: 19–40.
- Warren-Vlanel J. Treatment of PCOS in adolescence. Best Pract Res Clin Endo Metab 2006; 20: 311–30.
- 8. Braverman PK, Neinstein LS. Dysmenorrhoea and premenstrual tension. In: Neinstein LS, (ed). Adolescent Health Care: A Practical Guide. 4th edn. Baltimore: Lippincott, Williams & Wilkins, 2002; 952–65.
- 9. Tzafettas J. Painful menstruation. Pediatr Endocrinol Rev 2006; 3(Suppl 1):160–3.
- Jabbour HN, Sales K, Smith OP, Battersby S, Boddy SC. Prostaglandin receptors are mediators of vascular function in endometrial pathologies. Mol Cell Endocrinol 2006; 252: 191–200.

- 11. Attaran M, Gidwani GP. Adolescent endometriosis. Obstet Gynecol Clin North Am 2003; 30: 379–90.
- 12. Suhonen S, Haukkamaa M, Jaobsson T, Rauramo I. Clinical performance of a levonorgestrel releasing intrauterine system and oral contraceptives in nulliparous young women. Contraception 2004; 69: 407–12.
- 13. Kadir RA, Economides DL, Sabin CA, Owens D, Lee CA. Frequency of inherited bleeding disorders in women with menorrhagia. Lancet 1998; 351: 485–9.
- 14. Jayasinghe Y, Moore P, Donoth S et al. Bleeding disorders in teenagers presenting with menorrhagia. Aust NZ J Obstet Gynaecol 2005; 45: 439–43.

Menstrual dysfunction secondary to medical diseases

8

Tharani Balasubramaniam and LA Parapia

INTRODUCTION

Abnormal uterine bleeding (AUB), in women of childbearing age, is associated with any change in menstrual frequency, duration, quantity of blood loss, and intermenstrual bleeding. Awareness of potential medical causes will guide investigations to offer appropriate treatment for this common condition.

Menorrhagia is one of the four most common reasons for referral to a gynecologist, and 12% of all gynecology referrals are for this complaint. This is of concern, because referral for menorrhagia is associated with a 60% probability of hysterectomy in the ensuing 5 years.

Perception of menorrhagia is influenced by cultural, social, and demographic factors, making diagnosis difficult. The objective definition of menorrhagia is menstrual blood loss exceeding 80 ml per menstruation.⁴ However, in clinical practice, the diagnosis is subjective and relies on the women's description of her blood loss, which is often inaccurate. In a population study, 4% of women with actual menstrual loss of >80 ml considered their periods to be moderate or scanty, and 14% of women with actual loss <20 ml considered their period to be heavy.4 Most laboratory techniques used to measure menstrual blood loss are specialized, time-consuming, expensive, and involve collection and saving of sanitary material; therefore, they have never been established as part of routine practice. Instead, the pictorial blood assessment chart (PBAC) is often used as a semi-objective assessment of menstrual blood loss, and is based on the number and saturation of sanitary pads and tampons. A score of >100 has been shown to have a reasonable accuracy for identifying menorrhagia, with a reported sensitivity of 86% and specificity of 89%.5

Table 8.1 outlines the causes of AUB; however, for about 50% of women with menorrhagia, an underlying cause is not found,⁶ and many of these are treated surgically. In the period 2002–2003, the National Health Service (NHS) in England performed 8332 hysterectomies and 4921 endometrial ablations for menorrhagia.⁷

The following sections discuss some of the medical diseases associated with AUB, concentrating in particular on underlying bleeding disorders. Increasing clinical awareness of these conditions may avoid unnecessary operations, and their associated morbidity and mortality.

PATHOPHYSIOLOGY OF HEMOSTASIS AND MENORRHAGIA

Menstruation is a remarkable example of controlled tissue remodeling, where, over a period of 3–5 days, the old lining is removed and a new lining regenerated without scarring. It requires a regulated hemostatic and fibrinolytic system, and an intact hypothalamic–pituitary–ovarian axis.

Hemostasis in the menstruating uterus is a delicate balance between platelet aggregation, fibrin formation, vasoconstriction, and tissue regeneration on the one hand, and prostaglandin-induced platelet inhibition, vasodilatation, and fibrinolysis on the other. Disturbance of this intricate balance will result in hemorrhagic or thrombotic disorders.

The endothelial cells of blood vessels not only maintain the integrity of the vessel wall but also secrete various hemostatic factors, including tissue factor, thrombixane A₂ (TXA₂), von Willebrand's factor (VWF), and cytokines (procoagulants), as well as antithrombotic agents prostacyclin, nitric oxide, and tissue plasminogen activator.8 Injury to a vessel wall results in exposure of the subendothelial connective tissue, activating platelet adhesion and aggregation, and causing vasoconstriction. VWF released from endothelial cells and platelets binds to glycoprotein Ib and IIb/IIIa receptors on platelets, and to the subendothelium, facilitating platelet adhesion and aggregation. VWF is also important in carrying blood coagulation factor VIII:C (FVIII:C), preventing its premature enzymatic degradation and localizing FVIII to the sites of vessel injury.9 This, and the release of other procoagulant factors, promote accumulation of white blood cells, and form the platelet plug. Exposed collagen

Table 8.1 Medical causes of abnormal uterine bleeding

Organic	Endocrinologic	Anatomic	Iatrogenic
Genitourinary infections	Hypothyroid	Benign pelvic pathology:	IUD
		polyps	
		 fibroids 	
Coagulation disorders:	Hyperthyroid	Malignant lesions:	Steroid hormones
• von Willebrand's disease		• endometrium	
• factors II, V, VII, VIII, IX, XIII		 cervical 	
• prothrombin deficiency		• ovarian	
Thrombocytopenia	Adrenal gland dysfunction	Endometrial hyperplasia, endometriosis	Chemotherapy
Platelet disorders	Pituitary disorders	Pregnancy	Anticoagulants
Hepatic failure	Hypothalamic disorders	Pregnancy-related issues	Other medications
Renal failure	PCOS	Trauma	

IUD, intrauterine device; PCOS, polycystic ovarian syndrome.

and platelet phospholipids also activate the coagulation cascade, involving clotting factors I–XIII. The final step of the process is stabilization of the platelet plug to a solid mass of cross-linked fibrin.

The initiation of menstruation is linked to the associated dip in progesterone levels. Progesterone has been found to increase tissue factor (a hemostatic agent), and levels of type 1 plasminogen activator inhibitor (inhibits the cleavage of plasminogen to plasmin, which is required for fibrinolysis). Thus, withdrawal of progesterone results in a shift in the endometrial balance from the hemostatic phase to the hemorrhagic stage. It is therefore not surprising that patients with defects in the coagulation system suffer with menorrhagia.

VON WILLEBRAND'S DISEASE

Von Willebrand's disease (VWD) is one of the most common inherited bleeding disorders, affecting 0.8–1.3% of women. Despite this high prevalence, women referred for menorrhagia are not routinely screened for this coagulation disorder. In a recent UK survey, only 13% of gynecologists would request a standard clotting screen and 2% would test for VWD in a 35-year-old woman with menorrhagia and no pelvic pathology.

Dr Erik von Willebrand first reported the disease in 1926. He described a family of 66 members, of which 23 were bleeders including 16 female; five of these women died from bleeding, including a 13-year-old girl who died of uncontrollable menstrual loss. ¹⁴ This female-to-male imbalance has been reported by others ¹² and is of no surprise, considering women will always experience a greater frequency and degree of hemostatic challenges throughout their life.

VWD is characterized by a quantitative deficiency as in types 1 and 3 VMF, or a qualitative deficiency as in the type 2 variant of which there are numerous subvariants (Table 8.2). Type 1 is the most common form of VWD and the mildest; thus, affected women may not discover problems until faced with a hemostatic challenge such as occurs in menstruation, childbirth, surgery, and dental work.

Menorrhagia is a common symptom of VWD, and may be the only symptom in some. In a recent study using the PBAC score >100 for menorrhagia, the diagnosis was confirmed in 74% of women with VWD, 59% with factor XI deficiency, and 57% of carriers of hemophilia. There has been recent interest in the association between menorrhagia and inherited bleeding disorders, and studies from England and the USA suggest a prevalence between 6.6% and 24% of VWD in women with menorrhagia. When compared to the prevalence in the general population of 1–2%, 11,12 this seems significant. However, establishing a diagnosis of VWD is also difficult and complex, and in the absence of a genetic test, it requires laboratory and clinical assessment. The VWF gene is located on the short arm of chromosome 12, but it is large and

Type of VWD	Clinical features	Mode of inheritance	Laboratory findings
1	Mild–moderate bleeding (70% of all VWD)	Autosomal dominant	Partial quantitative deficiency of normal VWF
2A	Moderate/variable bleeding	Autosomal dominant	Abnormal VWF, ↓ HMWM, ↓ platelet association
2B	Moderate/variable bleeding	Autosomal dominant	Abnormal VWF, ↑ affinity for platelets → platelet aggregation → thrombocytopenia
2M	Moderate/variable bleeding	Autosomal dominant	Abnormal VWF, ↓ platelet association
2N	Moderate/variable bleeding	Autosomal dominant	Abnormal VWF, \downarrow affinity for FVIII
3	Severe bleeding	Autosomal recessive	Virtually complete deficiency of VWF, \downarrow FVIII

Table 8.2 Summary of the main differences between the various subtypes of VWD

VWD, von Willebrand's disease; VWF, von Willebrand's factor; FVIII, factor VIII; HMWM, high molecular weight multimers.

difficult to analyze,¹⁹ and there is some evidence to suggest that some cases of VWD are linked to other gene loci.²⁰

Plasma VWF concentrations are influenced by several genetic and environmental factors; thus, laboratory tests may fluctuate with time in a given individual.²¹ Factors affecting VWF levels include ABO blood group, ethnicity, age, hormones, and stress. People with blood group O have a lower VWF level than people with other blood groups, but whether or not ABO group has any effect on the specific activity of VWF is unresolved.²¹ A study by Dilley et al. in North America showed that black women have a lower prevalence of VWD than white women (1.4% vs 15.9%, respectively), 16 despite the fact that black women have higher levels of VWF antigen activity than white women.²² Reasons for the low prevalence in black women may be because of cultural differences in the perception of menorrhagia or the genetic defect(s) causing VWD may be less common in women of African descent. Further studies using objective methods of assessing menorrhagia and race-specific threshold levels for diagnosis are required.

There are conflicting data regarding changes in VWF during the menstrual cycle. The UK Haemophilia Centre Doctors' Organization (UKHCDO) suggests there is insufficient data to recommend testing for VWD during a specific point of the menstrual cycle.²¹ However, the timing of testing in relation to the menstrual cycle should be noted, and, if the results are borderline, the test should be repeated during days 1–4 of the menstrual cycle.²³

Usage of the oral contraceptive pill (OCP) results in a small rise in the level of VWF:Ag and VWF:RCo, thus possibly masking the diagnosis of VWD, but this has not been assessed in women with VWD. The effect of estrogen on

clotting factors appears to be dose dependent (>50 μg of ethyinyl estradiol), but the doses commonly used today are much smaller and less likely to be significant.²⁴ The recommendation is women on the OCP with borderline VWF levels should be retested if the opportunity arises when off the OCP.²³

Menstrual stress and strenuous exercise is also associated with significant increase in VWF:Ag. However, this is unlikely to be the case for the 'moderate' exercise related to attending hospital.²¹ VWF is an acute-phase reactant; therefore inflammatory, malignant, infective, and vasculitic diseases can cause a raised level.²⁵

When requesting a VWD screen, most laboratories check VWF antigen (VWF:Ag), factor VIII assay, and the ability of VWF to bind platelets as determined by the riscocetin cofactor agglutination activity assay (VWF:RCo), and some laboratories use the VWF collagen-binding assay (VWF:CB). The bleeding time and activated partial thromboplastin time (APTT) may be normal in patients with mild VWD, and therefore are not sensitive enough to be used for screening and diagnosis. ^{17,21} Factors VIII, IX, XI, and XII influence APTT levels, and if these factors are more than 30% of normal, the APTT will not be prolonged. ²⁶

Some centers suggest the use of a platelet function analyzer (PFA-100) as an alternative to bleeding time for screening. It is quoted as having a sensitivity >95%.²⁷ It can reliably detect moderate or severe disease, but it is subjective to the natural fluctuations that make assessment of VWD so difficult.²¹

A key part of the assessment is eliciting a history of bruising, epistaxis, oral cavity bleeding, and menorrhagia in women. A knowledge of response to hemostatic challenges – e.g. operations, trauma, dental extractions, and postpartum hemorrhage (PPH) – is also helpful, bearing in mind many young women have yet to face such challenges. Bleeding histories are subjective, but by ascertaining the requirements for a blood transfusion as a result of bleeding, medical intervention to stop the bleeding or the development of anemia adds weight to the history. ²¹ A scoring system for a positive bleeding history has been suggested: ²³

- (1) excessive menstrual bleeding since menarche
- (2) history of PPH, surgery-related bleeding, or bleeding associated with dental work
- (3) history of bruising >5 cm one or two times per month, epistaxis one or two times per month, frequent gum bleeding, or family history of bleeding symptoms.

A positive screen entails any one from category 1 or 2, or two or more from category 3.

Menorrhagia in adolescent girls is likely to be secondary to an immature hypothalamic–pituitary–ovarian axis causing anovulatory cycles; however, an underlying bleeding disorder may be identified in a significant proportion of cases. In one study, 11 out of 106 adolescents with menorrhagia had an underlying bleeding disorder. Positive predictors include a positive family history and menorrhagia requiring hospital admission.²⁸

The management of women with menorrhagia and bleeding disorders depends on the age of the woman, childbearing status, and individual preference.

Oral therapies such as the antifibrinolytic drug tranexamic acid and the OCP are usually the first-line treatments for menorrhagia in patients with VWD. In patients with underlying bleeding disorders, non-steroidal anti-inflammatory drugs (NSAIDs) are ineffective and may increase menstrual blood loss. Tranexamic acid is an antifibrinolytic agent; it inhibits the binding of plasminogen to fibrin, and several studies have demonstrated increased fibrinolysis in the uterus of women with menorrhagia.²⁹ Taken at a dose of 1 g four times a day on days 1-5 of the menstrual cycle, it has been shown to reduce menstrual blood loss by 54%.30 The OCP is a valuable treatment for menorrhagia, especially secondary to anovulation. In a study of 30 women with VWD and menorrhagia, 73% had a good response to the OCP; the estrogen acts on the VWF stored in the endothelial cells and increases FVIII levels.³¹ Increased risk of thrombosis is the main concern associated with OCP use, but the risk of thrombosis is low in women with bleeding disorders. Progesterone-only preparations have been found to be less effective reducing blood loss than the methods discussed already. They are also inferior to the levonorgesterol-releasing

intrauterine device (LNG-IUD), which has been shown to reduce menstrual blood loss by 74% at 3 months and 97% at 12 months in women with menorrhagia and normal coagulation. A recent study looked at the effects of LNG-IUD on menorrhagia in 16 women with inherited bleeding disorders: all 16 women reported improvements in their periods, both subjectively and objectively (using the PBAC chart), and they all had higher hemoglobin concentrations. The main side effects are expulsion of the device and irregular bleeding, but, if tolerated, the device is beneficial in those women who want to preserve fertility and it can be inserted in the outpatient department.

If menorrhagia persists, desmopressin (DDAVP) has been found to be effective treatment in VWD. It is a very valuable drug, as when effective it means avoidance of blood products and the potential for blood-borne virus transmission. DDAVP is a synthetic vasopressin analogue, and it increases plasma concentrations of FVIII and VWF from endogenous storage sites. It can be administered intravenously, subcutaneously (dose of 0.3 µg/kg for both), or intranasally (300 µg for adults). 29,34 It is effective in type 1 VWD, but not in type 3, and has variable response in type 2 patients.²⁹ Therefore, patients should have a trial of DDAVP to observe its effectiveness. Intranasal DDAVP allows patients to self-treat at home, and hence presents as an attractive treatment. A study of intranasal DDAVP in type 1 VWD reported excellent or good response from 92% of patients,35 and subcutaneous DDAVP was found to be effective in 86% of patients.³⁶ The main adverse effects are hypotension, tachycardia, facial flushing, and fluid overload resulting in hyponatremia, but on the whole it is well tolerated. The risk of hyponatremia is avoided with advice to restrict fluid intake on the days of administrating DDAVP, which is also an effective treatment for bleeding episodes in patients with mild hemophilia A and platelet disorders.³⁷

A small proportion of patients require factor concentrates containing VWF. These products are usually of intermediate purity and plasma derived, and although they are virally inactivated, there is still a small risk of transmission of infections.²⁹ At this stage, patients should be under joint management with gynecologists and hematologists.

CLOTTING FACTORS

Hemophilia A and B

Hemophilia A and B are sex-linked recessive disorders, with a deficiency of FVIII and FIX, respectively. The prevalence is of 1 in 10000 (hemophilia A) and 1 in 10000 (hemophilia B) in the UK; however, the prevalence of

carrier women is unknown. Most carriers have FVIII or FIX levels within the normal range, although a wide range of values have been reported.³⁶ This is probably secondary to lyonization of the X chromosome. It has been shown that carriers are more at risk of bruising, prolonged bleeding from wounds, and following delivery.³⁸ A study looking at menstrual blood loss in patients with inherited bleeding disorders found that 57% of hemophilia A carriers have objectively (using PBAC) verified menorrhagia; such a high result may be secondary to a low response rate.¹⁵

Obtaining a history of bruising when faced with hemostatic challenges, and inquiring about family history, especially bleeding amongst male members, is important to help guide investigations towards identifying hemophilia carriers. Carriers of hemophilia A with bleeding symptoms may benefit from treatment with DDAVP, which increases the release of FVIII from intracellular stores.³⁷

Factor XI deficiency

Factor XI deficiency is a rare autosomal disorder, also known as hemophilia C. It predominantly affects Ashkenazi Jews, with low FXI levels found in up to 8% of the population.³⁹ FXI deficiency has been found in 4% of women suffering with menorrhagia in a study by Kadir et al.¹⁷ (the catchment area included a large Jewish population). In another study, 59% of women with FXI deficiency were shown to have objectively verified menorrhagia.¹⁵ Bleeding usually occurs after a hemostatic challenge (surgery or trauma), but as the correlation between FXI concentration and bleeding symptoms is poor,⁴⁰ it makes management difficult. An FXI concentrate exists, but may cause arterial and venous thromboembolism.⁴⁰

Factor II, V, VII, XIII deficiencies

Rarer clotting factor deficiencies such as FXIII, FVII, FV, and FII have also been identified in studies of women with menorrhagia, but at much lower frequencies than VWD. These deficiencies are more common in populations where consanguineous marriages occur.

Platelet disorders

Menorrhagia can be caused by thrombocytopenia (secondary to drugs, bone marrow disorders, autoimmune or inherited), or functional platelet disorders. These include rare disorders such as Bernard–Soulier Syndrome (absent or reduced expression of glycoprotein Ib), Glanzmann's thrombasthenia (defective glycoprotein IIb/IIIa receptor), or platelet storage diseases. The result is defective platelet–vessel wall interaction and platelet–platelet

aggregation. The prevalence of platelet functional disorders in the general population is unknown. Most studies of menorrhagia and bleeding disorders do not systematically include evaluations for platelet disorders. However, two studies have found platelet dysfunction to be common in women with otherwise unexplained menorrhagia, 41,42 one of which found 47% of women had abnormal platelet aggregation. 42

Desmopressin can be effective in Bernard–Soulier syndrome (if thrombocytopenia is not too severe) and in patients with drug-induced platelet dysfunction, and can temporarily correct platelet dysfunction caused by systemic diseases, e.g. uremia and liver cirrhosis.³⁷

OTHER CAUSES OF ABNORMAL UTERINE BLEEDING

When investigating a woman for AUB, the main differential diagnosis will depend on the age of the woman.

In women of childbearing age, pregnancy and pregnancy-related issues should first be ruled out. It is also important to investigate for any genitourinary infections, especially atypical presentations of sexually transmitted diseases. Eliciting a history of abnormal Papanicolaou (Pap) smears, gynecologic surgery, trauma, or sexual abuse is essential, as genital tract pathology is associated with intermenstrual, postcoital, and heavy menstrual bleeding. Benign pelvic pathology, including cervical and endometrial polyps, fibroids, and endometriosis, can also present with AUB, and should be excluded.

In the peri- and postmenopausal woman, AUB should be considered the result of malignancy of the reproductive tract until proven otherwise. Cancer is not the most frequent cause of AUB in this age group, but it is the most important.

Early menarche is often associated with AUB, mainly amenorrhea secondary to an immature hypothalamic—pituitary—ovarian axis. It is still important to bear in mind other causes such as trauma, sexual abuse, and bleeding disorders.

Iatrogenic causes include drugs such as anticoagulants, selective serotonin reuptake inhibitors (SSRIs), antipsychotics, corticosteroids, hormonal treatments, tamoxifen, and intrauterine coil devices. Herbal substances, including ginseng, ginkgo, and soy supplements, interfere with estrogen levels or clotting parameters and cause menstrual irregularities.⁴²

Hypothalamic dysfunction, hyperprolactinemia, androgen excess, and chronic illness are all conditions that can cause chronic anovulation. This may present as secondary amenorrhea, infrequent uterine bleeding, or irregular episodes of excessive uterine bleeding.

Hypothalamic disorders

Release of follicle-stimulating hormone (FSH) and luteinizing hormone (LH) from the pituitary is controlled by the secretion of luteinizing hormone-releasing hormone (LHRH) from the hypothalamus in a pulsatile fashion. This, in turn, is controlled by negative feedback from gonadal steroid hormones and local neuromodulaters in the brain, including norepinephrine, dopamine, and β -endorphins. Any central nervous system (CNS) disorder that interferes with this process can cause anovulation (Table 8.3).

Functional hypothalamic anovulation is the most common form of hypothalamic anovulation, and is asso-

Table 8.3 Disorders of the hypothalamic–pituitary axis causing abnormal uterine bleeding

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Neoplastic	Functional
Craniopharyngioma	Stress
Glioma	Excessive exercise
Metastasis	Anorexia nervosa
Pituitary tumors:	Chronic illness:
• prolactinoma	• liver failure
• growth hormone-secreting adenoma	• renal failure
• Cushing's disease	
Drugs	Infiltrative
Dopamine antagonists	Sarcoidosis
Opiates	Histiocytosis X
	Tuberculosis
Anatomic	Infection
Pituitary stalk section	Meningitis
Pituitary apoplexy	Encephalitis
Pituitary aneurysm	Syphilis
Empty sella syndrome	
Trauma	Other
Basal skull fracture	Radiation
Surgery	Fibrosis
	Chemotherapy
	Congenital Kallmann's syndrome (isolated gonadotropin deficiency)

ciated with excessive exercise, abrupt weight loss and psychological stress.⁴³

Amenorrhea associated with abrupt weight loss usually occurs when the body mass index (BMI) falls below 19 kg/m². ⁴³ It is thought that reduced secretion of leptin results in impaired secretion of gonadotropins, especially LH, resulting in alteration in the pulsatile secretion of LHRH. ⁴⁴ This is a basic survival mechanism, as it avoids reproduction occurring in adverse circumstances.

Normally, changes in lifestyle to reverse the primary cause result in the return of normal cycles. One of the concerns of persistent anovulation is the effect of long-term hypoestrogenemia on bone metabolism. If reversal of the primary cause is not practical (e.g. professional athletes, ballerinas) or the patient is unable to put on weight, estrogen replacement should be considered, such as a low-dose combined oral contraceptive pill (COCP).⁴³

Pituitary causes

The commonest pituitary cause of AUB is hypersecretion of prolactin from a prolactinoma. Signs and symptoms include galactorrhea, anovulatory bleeding, amenorrhea, headaches, and bitemporal hemianopia. Shrinkage of tumor is achieved in most cases with bromocriptine, a dopamine agonist. Whereas dopamine is an inhibitor of prolactin secretion, thyrotropin-releasing hormone (TRH) and estrogen stimulate the release of prolactin. A large number of medications are dopamine antagonists and therefore impair the inhibitory action of prolactin; these include phenothiazines, metoclopramide, reserpine, and methyldopa. 43

Androgen excess

Hyperandrogenization in women is associated with hirsutism, virilization, and amenorrhea. This may be due to defects in adrenal steroid biosynthesis (congenital adrenal hyperplasia, Cushing's syndrome) or excess production of androgens. Rapidly progressing symptoms of androgen excess suggest the presence of an androgen-secreting tumor, the majority of which arise from the ovary and produce large quantities of testosterone. In comparison, testosterone-secreting tumors of the adrenal gland are extremely rare: most secrete large amounts of dehydroepiandrosterone sulfate (DHEAS), dehydroepiandrosterone (DHEA), and androstenedione (androgen precursors).⁴³

Cushing's syndrome is a result of excess glucocorticoid secretion. Excess androgen secretion in this syndrome may be secondary to concomitant release of androgens with glucocorticoids as in Cushing's syndrome caused by adrenal tumors, or may be as a result of adrenocorticotropic hormone (ACTH)-mediated adrenal androgen

secretion (as in pituitary-dependent Cushing's disease, ectopic ACTH syndrome, adrenal hyperplasia). Contributing to reproductive dysfunction is hypogonadism as a result of the inhibitory effects of cortisol upon gonadotropin-releasing hormone (GnRH) pulsatility, and LH and FSH secretion.

The most common cause of hyperadrogenization-causing chronic anovulation is polycystic ovarian syndrome (PCOS), which occurs in approximately 5–10% of reproductive-aged women.⁴⁵ This is a heterogeneous disorder composed of anovulation, irregular menses, obesity, hirsutism, and insulin resistance. There is failure of the polycystic ovaries to convert androgens made in excessive amounts to estrogens. The increased levels of testosterone inhibit secretion of FSH and stimulate secretion of LH. The result is anovulation and reduced progesterone, and the increased level of LH encourages the ovarian cells to oversecrete androgens.

Thyroid disease

Most medical textbooks associate hypothyroidism with menorrhagia and hyperthyroidism with oligomenorrhea, with little evidence for either. There still remains controversy over whether thyroid function should be tested in women with AUB. The physiology to support these claims has been documented.

In hypothyroidism, sex hormone-binding globulin (SHBG) levels are reduced, causing reduced total estradiol levels and increased free estradiol and testosterone in the serum. 46,47 Estradiol is preferentially metabolized to estriol, which may have a lesser feedback effect on the pituitary than estradiol. 46

Elevated TRH in hypothyroidism not only stimulates the release of thyroid-stimulating hormone (TSH) but also induces prolactin release, which also causes menstrual dysfunction. The changes on the pituitary–ovarian axis result in oligomenorrhea, or amenorrhea and menorrhagia, reflecting probable estrogen breakthrough bleeding because of anovulation.⁴⁸

Thyroid hormones may also act directly on the ovary. Thyroxine (T_4) enhances the action of gonadotropins on luteinization and progestin secretion by granulosa cells of the ovary where TSH and thyroid receptor cells have also been found. Thus, inadequate thyroid hormones at the level of the ovary may contribute significantly to gonadal dysfunction.⁴⁷

In hyperthyroidism, SHBG is increased, resulting in raised total estradiol and testosterone levels, whereas free estradiol levels decrease. Raised LH levels have been found to be higher possibly because of loss of negative feedback from decreased estradiol levels. This, and blunting of the mid-cycle LH peak, probably interferes with ovulation. 46,47

Of interest is the fact that TSH, LH, and FSH are structurally very similar. Such homology raises the possibility of cross-reactivity at the receptors. Thus, theoretically low TSH levels in hyperthyroidism may cause an increase in LH levels as a result of reduction in binding of TSH to LH receptors as well as its own.⁴⁶

The prevalence of menstrual disturbances in thyroid disease has been quoted as being up to 60% in hyperthyroidism and up to 70% in hypothyroidism. 46 These are from studies dating from the 1950s and 1960s. More recent studies have reported a much lower prevalence of 21.5% 49 and 23.4% 48 for hyperthyroidism and hypothyroidism, respectively. However, none of these studies measured menstrual loss objectively and, considering that both menorrhagia and thyroid disease are relatively common in the general population, it may not be surprising that there is a proportion of women with both conditions.

Guidelines from the Royal College of Obstetricians and Gynaecologists (RCOG) on the initial management of menorrhagia do not advocate routine thyroid function tests (TFTs) unless the woman has symptoms or signs of hypothyroidism.⁵⁰ This is in agreement with the UKH-CDO guidelines which suggest TFTs should be considered if the patient is symptomatic, implying other symptoms associated with thyroid disease.²³

Renal failure

Owing to changes in the hypothalamic–gonadal axis in dialyzed women, amenorrhea is the most common menstrual abnormality. Of those women that do menstruate, a proportion suffer from hypermenorrhea, menorrhagia, and oligomenorrhea. There is abnormality of the pulsatile release of LH and the high preovulatory peak of LHRH and, consequently, the LH required for ovulation. As a result, the increase in progesterone that normally occurs is absent. The progesterone deficiency results in incomplete maturation of the endometrium, followed by hypermenorrhea and dysfunctional bleeding. Hyperprolactinemia is common in dialysis patients, and this contributes to the menstrual abnormalities.

For patients with amenorrhea and oligomenorrhea who desire menstruation, a low-dose COCP is suggested, or progesterone alone during the final days of the monthly cycle. For women with hypermenorrhea, which can contribute significantly to anemia, high doses of progesterone throughout the month will suppress menstrual bleeding.⁵¹ Hysterectomy remains the final option for refractory uterine bleeding.

Uremia, per se, is associated with increased risk of bleeding and, consequently, will encourage the problem of menorrhagia in those women affected by it. The pathogenesis of uremic bleeding is multifactorial. Main abnormalities

involve platelet–platelet and platelet–vessel wall interactions. ^{53,54} However, the platelet count is usually normal in uremia. It is thought that substances accumulate in uremic plasma that are involved in the genesis of uremic platelet dysfunction. ^{53,55} The introduction of dialysis has improved the hemostatic abnormalities associated with uremia, but not eliminated the risk of bleeding.

Bleeding can be controlled with conjugated estrogens and desmopressin either intravenously, subcutaneously or intranasally.^{53,54,56}

Liver disease

Liver cirrhosis is associated with a significant risk of bleeding. The liver parenchymal cells produce most of the factors and inhibitors of clotting and fibrinolysis. In cirrhosis, there are both quantitative and qualitative platelet abnormalities, manifesting as a prolongation of the bleeding time. Thrombocytopenia is secondary to pooling of platelets in the spleen caused by portal hypertension and splenomegaly, and immunologic destruction of platelets.⁵⁷

The liver is responsible for detoxification, metabolism, and excretion of sex hormones; therefore, cirrhosis will alter the hypothalamic–pituitary–endocrine gland axis. The effect this has on men, feminization and hypogonadism, is well documented; however, there have been few studies looking at the effects on women.

In men, there is a reduction in the level of serum testosterone and a relative increase in circulating estrogen levels due to peripheral conversion of weak androgens. Reduced testosterone is secondary to primary gonadal failure and central hypothalamic–pituitary defect in GnRH secretion.⁵⁷ Similar findings were found in a study of 111 amenorrheic females with associated liver disease, where the hypothalamus rather than the pituitary was the primary site of disturbance.⁵⁸ In a separate study, postmenopausal women were found to have raised estradiol levels, reduced testosterone, LH, and FSH, and these

seem to correlate with severity of liver disease.⁵⁹ In younger women, this would imply amenorrhea. However, women who drink heavily have reported more painful, heavy, and irregular menses compared to other women,⁶⁰ but the degree of liver dysfunction was not noted. There is scope for more research on the effects and extent of liver damage on menstrual cycles in women.

Menstruation is an inconvenience for women in general, but for those with AUB, especially menorrhagia, it has a significant negative effect on the quality of life. In one study, which looked at the quality of life in women with inherited bleeding disorders and menorrhagia, 39% of the women had to cut down the time they spent at work or other activities, 47% felt they had accomplished less than they would have liked to during this period, and 38% felt they were limited to the kind of work they could do. 61 Menorrhagia is the commonest bleeding symptom in women with inherited bleeding disorder, but the cause may be multifactorial. In a survey of women with VWD, half the women undergoing hysterectomy for menorrhagia had additional pelvic pathology such as fibroids or endometriosis.⁶² Thus, gynecologic evaluation should be performed on all women with AUB with an awareness of other potential medical causes. The UKHCDO guidelines for the management of women with inherited bleeding disorders and menorrhagia²³ suggest that:

- (1) A focused personal and family history of bleeding symptoms should be taken, and if there is a positive bleeding history or surgical intervention is planned, then laboratory testing should be carried out.
- (2) Laboratory testing should be undertaken in settings where necessary expertise and resources are available.
- (3) The management of women with inherited bleeding disorders should be provided by a multidisciplinary team including both hematologist and gynecologist: ideally, a multidisciplinary clinic.

- Royal College of General Practitioners: Office of Population Censuses and Surveys. Department of Health 1981–1982. Morbidity statistics from general practice. third national study: socio-economic analysis, Series 5. London: HMSO, 1990.
- Bradlow J, Coulter A, Brooks P. Patterns of Referral. Oxford: Health Services Research Unit, 1992.
- 3. Coulter A, Bradlow J, Agass M, Martin-Bates C, Tulloch A. Outcomes of referrals to gynaecology outpatient clinics for menstrual problems: an audit of general practice. Br J Obstet Gynaecol 1991; 98: 789–96.
- 4. Hallberg L, Hogdahl H, Nislon L, Rybo G. Menstrual blood loss a population study. Variation at different ages and attempts to define normality. Acta Obstet Gynaecol Scand 1966; 45: 320–51.
- Higham JM, O'Brien PM, Shaw RW. Assessment of menstrual blood loss using a pictorial chart. Br J Obstet Gynaecol 1990; 97: 734–9.
- 6. Rees M. Menorrhagia. BMJ 1987; 294: 759-62.
- 7. Reid PC, Mukri G. Trends in number of hysterectomies performed in England for menorrhagia: examination of health episode statistics, 1989 to 2002–3. BMJ 2005; 330: 938–9.

- 8. Hoffbrand AV, Pettit JE, Moss PAH, et al. Essential Haematology, 4th edn. Oxford: Blackwell Science, 2001: 236–47.
- Ruggerri ZM. Mechanisms initiating thrombus formation. Thromb Haemost 1997; 78: 611–16.
- Salamonsen LA, Kovacs GT, Findlay JK. Current concepts of the mechanisms of menstruation. Baillière's Clin Obstet Gynaecol 1999; 13(2): 161–79.
- Rodeghiero F, Castaman G, Dini E. Epidemiological investigation of the prevalence of Von Willebrands disease. Blood 1987; 69: 454–9.
- Werner EJ, Broxon EH, Tucker EL, Giroux DS. Prevalence of von Willebrand disease in children: a multiethnic study. J Paediatr 1993; 123: 893–8.
- Chi C, Shiltagh N, Kingman CEC, Economides DL. Identification and management of women with inherited bleeding disorders: a survey of obstetricians and gynaecologists in the United Kingdom. Haemophilia 2006; 12: 405–12.
- Von Willebrand EA. Hereditare pseudohaemophilic. Finnska Iaekaellsk Handl 1926; 68: 87–112.
- Kadir RA, Economides DL, Sabin CA, Pollard D, Lee CA. Assessment of menstrual blood loss and gynaecological problems in patients with inherited bleeding disorders. Haemophilia 1999; 5: 40–8.
- 16. Dilley A, Drews C, Miller C, et al. von Willebrand disease and other inherited bleeding disorders in women with diagnosed menorrhagia. Obstet Gynecol 2001; 97(4): 630–6.
- Kadir RA, Economides DL, Sabin CA, Owens D, Lee CA. Frequency of inherited bleeding disorders in women with menorrhagia. Lancet 1998; 351: 485–9.
- Krause M, Aygoren-Pursen E, Ehrenforth S, Ludwig G. Coagulation disorders in women with menorrhagia. Haemophilia 2000; 6: 240–7.
- Mancuso DJ, Tuley EA, Westfield LA. Human von Willebrand factor gene and pseudogene: structural analysis and differentiation by polymerase chain reaction. Biochemistry 1991; 30: 253–69.
- Castaman G, Eikenboom JC, Bertina RM, Rodeghiero F. Inconsistency of association between type 1 Von Willebrand disease phenotype and genotype in families identified in an epidemiological investigation. Thromb Haemost 1999; 82: 1065–70.
- 21. Laffan M, Brown SA, Collins PW, Cumming AM. The diagnosis of Von Willebrand disease: a guideline from the UK Haemophilia Centre Doctors' Organization. Haemophilia 2004; 10: 199–217.
- Kadir RA, Economides DL, Sabin CA, Owens D, Lee CA. Variations of coagulation factors in women; effects of age, ethnicity, menstrual cycle and combined oral contraceptives. Thromb Haemost 1993; 70: 380–5.
- Lee CA, Chi C, Pavord SR, Bolton-Maggs PHB. The Obstetric and Gynaecological Management of women with inherited bleeding disorders – review with guidelines produced by a taskforce of UK Haemophilia Centre Doctors' Organization. Haemophilia 2006; 12: 301–6.
- David JL, Gaspard UJ, Gillain D, Raskinet R, Lepot MR. Hemostasis profile in women taking low-dose oral contraceptives. Am J Obstet Gynaecol 1990; 163: 420–3.
- Lombardi R, Mannucci PM, Seghatchian MJ, Garcia VV, Coppola R. Alterations of factor VIII, von Willebrand factor in clinical conditions associated with an increase in its plasma concentration. Br J Haematol 1981; 49: 61–8.
- Luscher JM. Screening and diagnosis of coagulation disorders.
 Am J Obstet Gynecol 1996; 175: 778–83.

- Fressinaud E, Veyradier A, Truchaud F. Screening for von Willebrand disease with a new analyser using high shear stress; a study of 60 cases. Blood 1998; 91: 1325–31.
- Jayasinghe Y, Moore P, Donath S, Campbell J. Bleeding disorders in teenagers presenting with menorrhagia. Aust NZ J Obstet Gynaecol 2005; 45: 439–43.
- Pasi KJ, Collins PW, Keeling DM, Brown SA. Management of von Willebrand disease: a guideline from the UK Haemophilia Centre Doctors' Organization. Haemophilia 2004; 10: 218–31.
- Bonnar J, Sheppard BL. Treatment of menorrhagia during menstruation: randomised controlled trial of ethamsylate, mefenamic acid, and tranexamic acid. BMJ 1996; 313: 579–82.
- Foster PA. The reproductive health of women with von Willebrand disease unresponsive to DDAVP: results of an international survey. On behalf of the Subcommittee on von Willebrand Factor of the Scienctific and Standardization Committee of the ISTH. Thromb Haemost 1995; 74: 784–90.
- Stewart A, Cummins C, Gold L, Jordan R, Phillips W. The effectiveness of the levonorgestrel-releasing intrauterine system in menorrhagia; a systematic review. BJOG 2001; 108: 74–86.
- Kingman CEC, Kadir RA, Lee CA, Economides DL. The use of levonorgestrel-releasing intrauterine systems for treatment of menorrhagia in women with inherited bleeding disorders. BJOG 2004; 111: 1425–8.
- Kobrinsky N, Goldsmith J. Efficacy of Stimate (desmopressin acetate) nasal spray, 1.5 mg/ml, for the treatment of menorrhagia in women with inherited bleeding disorders. Blood 1997; 90(s1): 106.
- Rose EH, Adelort LM. Nasal spray desmopressin (DDAVP) for mild haemophilia A and Von Willebrand disease. Ann Intern Med 1991; 114: 563–8.
- Rizza CR, Rhymes IL, Austen DE, Kernoff PB, Aroni SA. Detection of carriers of haemophilia: a 'blind' study. Br J Haematol 1975; 30: 447–56.
- 37. Lethagen S. Desmopressin in the treatment of women's bleeding disorders. Haemophilia 1999; 5: 233–7.
- 38. Mauser Bunschotten EP, van Houwelingen JC, Visser EJ, van Dijken PJ. Bleeding symptoms in carriers of hemophilia A and B. Thromb Haemost 1988; 59: 349–52.
- Asakai R, Chang DW, Davie W. Factor XI deficiency in Ashkenazi Jews in Israel. N Engl J Med 1991; 325: 153–8.
- Bolton-Maggs PHB, Young-Wan-Yin B, McCraw AH, Slack J. Inheritance and bleeding in factor XI deficiency. Br J Haematol 1988; 69: 521–8.
- 41. Saxena R, Gupta M, Gupta PK, Kashyap R. Inherited bleeding disorders in Indian women with menorrhagia. Haemophilia 2003; 9: 193–6.
- Alkers JR, Hull SK, Wesley RM. Abnormal uterine bleeding. Am Fam Phys 2004; 69(8): 1915–18.
- Larsen PK, Kronenberg HM, Melmed S, Polonsky KS. Williams Textbook of Endocrinology, 10th edn. Amsterdam: Elsevier, 2003: 615–27.
- 44. Warrell DA, Cox TM, Firth JD, Benz EJ (eds). The reproductive system. Oxford Textbook of Medicine, 4th edn. Oxford: Oxford University Press, 2001.
- Dunaif A. Insulin resistance and the polycystic ovary syndrome; mechanism and implications for pathogenesis. Endocr Rev 1997; 18: 774–800.
- Aldersberg MA, Burrow GN. Focus on primary care. Thyroid function and dysfunction in women. Obstet Gynecol Surv 2002; 57(3 Suppl): S1–7.
- Trokoudes KM, Skordis N, Picolos MK. Infertility and thyroid disorders. Curr Opin Obstet Gynaecol 2006; 18(4): 446–51.

- 48. Krassas GE, Poptikides N, Kaltsas T. Disturbances of menstruation in hypothyroidism. Clin Endocrinol (Oxf) 1999; 50: 655–9.
- Scott JC, Mussey E. Menstrual disturbances in thyrotoxicosis. Clin Endocrinol 1994; 40: 641–4.
- Royal College of Obstetricians and Gynaecologists. The initial management of menorrhagia. Evidence Based Clinical Guidelines. London: RCOG, 1998.
- Davidson AM, Cameron JS, Grunfeld JP, et al. Sexual disorders.
 In: Oxford Textbook of Clinical Nephrology, 3rd edn. Oxford: Oxford University Press, 2005: 1737–53.
- 52. Palmer BF. Sexual dysfunction in uraemia. J Am Soc Nephrol 1999; 10: 1381–8.
- 53. Minetti L, Remuzzi G, Schieppati A. Effect of renal failure on haemostasis. In: Brenner BM, ed. Brenner & Rector's The Kidney, 7th edn. 2004: 2174–8.
- 54. Remuzzi G. Bleeding in renal failure. Lancet 1988; 1: 1205.
- 55. Norris M, Remuzzi G. Uraemic bleeding: closing the circle after 30 years of controversies. Blood 1999; 94(8): 2569–74.
- Vigano GL, Mannucci PM, Lattuada A, Harris A, Remuzzi G. Subcutaneous desmopressin (DDAVP) shortens the bleeding time in uremia. Am J Hematol 1989; 31(1): 32–5.

- 57. Feldmen M, Scharsschmidt BF, Sleisenger MH, Fordtran JS. In: Feldmen, M, Friedman LS, Sleisenger MH, eds Sleisenger and Fordtran's Gastrointestinal and Liver Disease, 7th edn. Philadelphia: WB Saunders, 2002: 1558–62.
- Bell H, Raknerud N, Falch JA, Haug E. Inappropriately low levels of gonadotrophins in amenorrhoeic women with alcoholic and non-alcoholic cirrhosis. Eur J Endocrinol 1995; 132: 444–9.
- Gavaler JS, Van Thiel DH. Hormonal status of postmenopausal women with alcohol-induced cirrhosis; further findings and a review of the literature. Hepatology 1992; 16: 312–19.
- Bradley KA, Badrinath SB, Bush K. Medical risks for women who drink alcohol. J Gen Intern Med 1998; 13(9): 627–39.
- Kadir RA, Sabin CA, Pollard D, Lee CA. Quality of life during menstruation in patients with inherited bleeding disorders. Haemophilia 1998; 4: 836–41.
- 62. Kouides PA, Phatak PD, Burkart P. Gynaecological and obstetrical morbidity in women with type 1 von Willebrand disease: results of a patient survey. Haemophilia 2000; 6: 643–8.

The role of ultrasound in investigating abnormal uterine bleeding

9

Maha Alkatib and Thomas H Bourne

INTRODUCTION

Investigation of abnormal uterine bleeding (AUB) is accountable for a significant proportion of the gynecologist's outpatient workload.1 As the management of AUB diversifies with new, sophisticated medical and surgical approaches, accurate and rapid diagnosis becomes desirable. Ideally, a diagnosis should be reached at the index visit with a specialist, thus requiring various diagnostic tools to aid this. Up to 60% of women will have no identifiable pathology to explain their AUB: to subject such women to a general anesthetic, hysteroscopy, and curettage carries a measure of financial and physical burden, as well as prolonging anxieties and delaying initiation of treatment. Many approaches have been suggested in an attempt to distinguish between women who warrant further operative intervention and women who could be initially managed with medical or conservative treatments.

Outpatient blind endometrial sampling can no longer be considered sufficient in diagnosis, owing to the risk of missing focal pathology such as polyps, fibroids, and focal endometrial hyperplasia. Although such sampling is cheap, quick, and requires little expertise, most clinicians would still not use it as a method of choice to exclude endometrial cancer, but instead consider its use in conjunction with transvaginal sonography (TVS).² The gold standard that has been well established is that of hysteroscopy for diagnosis of endometrial pathology. The development of miniature hysteroscopes allows the use of this tool in the outpatient setting. In addition, the advent of bipolar tools refined enough to be introduced into such scopes has brought the possibility of treatment in a 'one-stop' clinic setting.

However, with regard to diagnosis, various studies have assessed the value of TVS as one such approach. TVS alone is very sensitive at demonstrating intracavity pathology but lacks in specificity. It possesses the great advantage of being relatively painless, less invasive than a

biopsy, and is most acceptable to women. In addition, it provides an opportunity to image the whole pelvis and detect coexisting pathology such as ovarian masses and cervical pathology. Where this is most useful in the investigation of AUB is in women taking tamoxifen and in cases of suspected adenomyosis where the pathologies are subendometrial. The introduction of a negative contrast medium into the endometrial cavity such as normal saline dramatically increases the sensitivity and specificity of TVS. The process of sonohysterography or saline infusion sonography (SIS) brings the diagnostic accuracy of focal pathology up to rates equal to or (in some cases) greater than outpatient hysteroscopy.³⁻⁶

Color Doppler is available on most new-generation ultrasound machines. It has the ability to help characterize focal pathology visualized on TVS, especially in postmenopausal women where the vasculature develops a high-impedance, low-velocity character. Angiogenesis can be seen as areas of color on the B-mode image; this in turn can raise the suspicion of endometrial carcinoma in cases of postmenopausal women found to have a thickened endometrium. Bourne et al demonstrated a low impedance in the uterine arteries in cases of endometrial carcinoma, thereby reducing the false-positive rates of B-mode scanning.⁷

Three-dimensional (3D) ultrasound has made a more recent entry into the diagnostic tools available to the office gynecologist. Studies have mainly compared its ability to detect intracavity pathology vs SIS. However, SIS with 3D or uterine cavities already fluid filled secondary to underlying pathology have been included.⁸ Results have demonstrated comparable figures to two-dimensional (2D) SIS, but the costs incurred financially and in time do not justify its use as a first-line diagnostic tool. Four-dimensional (4D) machines may well reduce the time component, but currently are cost inhibiting. Three-dimensional ultrasound does possess a valuable role in assessing congenital uterine anomalies and leiomyoma volumes pre- and postembolization.

The emphasis in this chapter is on the use of TVS and SIS in investigating AUB, with occasional reference to useful color Doppler findings.

EQUIPMENT AND TECHNIQUE

A conventional B-mode ultrasound machine with a transvaginal (5.0–7.5 MHz) and an abdominal (3.5 MHz) probe is the most basic requirement. Color Doppler is a useful additional function when determining the nature of a focal lesion in the endometrial cavity. SIS requires the additional use of 3–20 ml of normal saline in a syringe, a fine balloon catheter or pediatric gastric feeding tube, a bivalve (Cuscoe's) speculum, and a volsellum in the event that countertraction is indicated. Assistance from a qualified nurse/healthcare assistant is valuable to ensure a smooth and swift procedure.

Conventional TVS involves gentle insertion of the probe up to the cervix and views taken in the coronal and sagittal plane. This ensures complete assessment of the uterus and ovaries. SIS is performed once the conventional scan is complete. A bivalve (Cuscoe's) speculum is inserted and the catheter is primed with saline and inserted

into the external os. This is fed in until it meets resistance at the fundus. The speculum is then carefully removed without dislodging the catheter and the syringe is attached to the distal end of the catheter. The probe is reinserted and a sagittal view of the endometrial cavity is achieved – the saline is then instilled at this point and further coronal and sagittal views are taken to assess any focal endometrial pathology visualized. Antibiotic cover should be prescribed for women of reproductive age.

Contraindications to SIS include a history of unprotected sexual intercourse and current pelvic infection.

NORMAL ENDOMETRIUM

Figure 9.1 demonstrates the endometrium during the various phases of the menstrual cycle. As seen, the echogenicity and thickness of the endometrium increases towards the secretory phase of the cycle. The postmenopausal endometrium in contrast is a thin hyperechoic line less than 5 mm. This can increase in cases of hormone replacement therapy users and should be noted when scanning such women. Measurement of the endometrial thickness is taken from the edge of one endometrial—myometrial

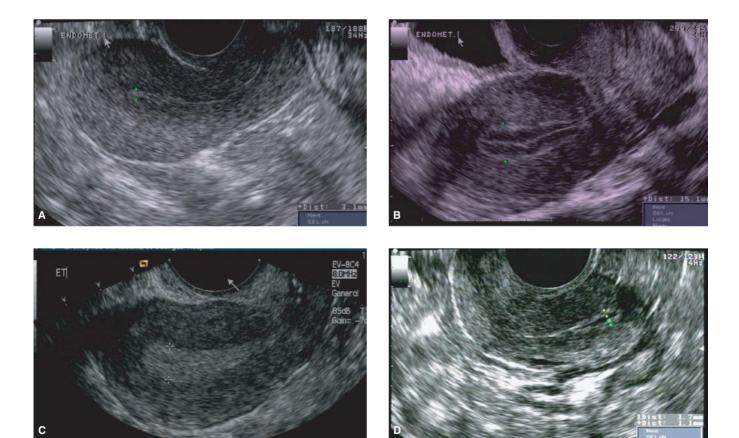


Figure 9.1 Normal endometrium: (A) proliferative, (B) periovulatory, and (C) secretory phase. (D) A postmenopausal endometrium with some fluid in the cavity to demonstrate measurement in such a case.

interface to the perpendicular opposite endometrial—myometrial interface: i.e. a double layer measurement, at its widest point in the cavity. This usually lies just distal to the fundus. Should SIS be used, the measurement would be the sum of the two separated endometrial thicknesses. This can be particularly useful when it is difficult to visualize a calcified postmenopausal endometrium or if the uterus is lying axially to the probe, thus prohibiting a complete longitudinal view.

ENDOMETRIAL POLYPS

Endometrial polyps are characteristically either hyperechoic or cystic areas in the endometrial cavity, disrupting the midline. The optimum time to visualize these polyps is in the proliferative phase of the cycle when the remaining endometrium is at its thinnest. If the endometrium is thickened, visualization may be enhanced with the use of SIS (see Figure 9.2) Color Doppler may demonstrate the presence of a single feeding vessel. The advantage of SIS in this instance is to help differentiate between hyperplasia and a polyp.





Figure 9.2 (A) The initial scan could easily be interpreted as a secretory phase endometrium. (B) Hydrosonography demonstrates a large polyp filling the cavity.

LEIOMYOMAS

Leiomyomas can appear as inhomogeneous, cystic or calcified masses. They tend to be well defined by their capsule, and color Doppler demonstrates a circular blood flow pattern. Care should be taken to ensure no leiomyomas are missed on TVS. Because of the probe frequency, deep penetration to abdominal leiomyomas may fail; thus, the use of a transabdominal probe with abdominal palpation ensures the location of these. TVS can also help to distinguish subserous from pedunculated fibroids if the feeding vessel through the stalk can be located with color Doppler. The main benefit of TVS is in the assessment of submucous leiomyomas. The extent of endometrial disruption can be determined from their outline. The additional use of SIS brought sensitivities of 100% and specificities of 94% in one study,5 providing valuable information when determining those cases that are suitable for transcervical resection. Distinction between fibroid polyps and endometrial polyps, however, may not always be easy to make sonographically, depending on the phase in the cycle the scan was performed (more difficult in the secretory phase). In cases where down-regulation with a gonadotropin-releasing hormone (GnRH) agonist preoperatively is considered, this may prove difficult.

Figure 9.3 shows a submucous fibroid pre- and post-SIS.

ADENOMYOSIS

Historically, adenomyosis was a histopathologic diagnosis. Fedele et al. identified ultrasonographic features characteristic of adenomyosis from the presence of endometrial tissue in the myometrium: in particular, the observation of a bulkier uterus, asymmetrical myometrial thickness, and the presence of hypoechoic spots in the myometrium that occasionally may appear as cystic areas. From the heterogeneous appearance, hypoechoic 'rays' may be demonstrated through the myometrium. Hysteroscopy would be unable to make such a diagnosis. Figure 9.4 illustrates these findings.

ENDOMETRIAL HYPERPLASIA

Endometrial hyperplasia is seen as a globally thickened hyperechoic endometrium with or without cystic changes. The endometrial—myometrial interface is intact throughout; hence, a hypoechoic 'halo' can be seen, which helps in distinguishing it from invasive endometrial carcinoma but not from earlier stages of endometrial cancer (Figure 9.5). TVS, as with hysteroscopy, cannot distinguish between





Figure 9.3 Submucous leiomyoma pre- (A) and post-SIS (B). Accurate assessment of size and protrusion into the cavity can be made.

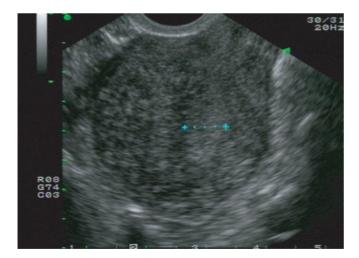


Figure 9.4 Adenomyosis. Asymmetrical myometrium and heterogeneous texture with hypoechoic signals. This could be interpreted as diffuse fibroid change.

benign and atypical hyperplasia. The cutoff for abnormal thickness varies according to the stage in the menstrual cycle, concurrent hormone usage, and menopausal status. Typically, in premenopausal women, an endometrial thickness (ET) of >14–16 mm in the secretory phase is abnormal.





Figure 9.5 Endometrial hyperplasia pre- (A) and post-SIS (B). The endometrial–myometrial interface remains intact. A small polyp is also visualized post-SIS.

Fortunately, in the investigation of postmenopausal bleeding (PMB), far more work has taken place in this area because of the highly negative predictive value TVS possesses in ET measurements. As a result of the hypoestrogenic state, there is little variation in the ET, and cutoff levels of <4 mm in some studies demonstrated a 0% incidence of endometrial cancer.¹⁰ Focal pathology was only noticed in ET >4 mm. This being the case, the authors went on to propose that women with such an ET did not require endometrial sampling and further investigation - a physical and financial cost-saving exercise.11 However, any uncertainty or irregularities in the visualization of the endometrial echo warrants a biopsy. In our unit, an analysis of 86 women attending a 'rapid access' gynecology clinic presenting with PMB, showed 56 (65.1%) had ET < 4 mm and were therefore not biopsied. No malignancies were missed and none of these women re-presented in a 2-year follow-up (unpublished work).

Tamoxifen therapy has remained an ongoing concern of gynecologists due its risk of causing endometrial cancer via its estrogen agonist effect on the endometrium. ^{12,13} Therefore, screening in the form of TVS or hysteroscopy has been suggested during a course of therapy. Studies have demonstrated the advantage of TVS over outpatient hysteroscopy in this matter, hysteroscopy being less sensitive at visualizing subepithelial pseudopolypoid glandulocystic change due to a surface view only. ¹⁴ On TVS, the endometrium can appear thickened with or without the presence of cysts, as seen in Figure 9.6. SIS would be warranted to distinguish between pseudopolypoid glandulocystic endometrium and glandulocystic polyps.

ENDOMETRIAL CANCER

The main purpose of investigation of AUB in postmenopausal women is the exclusion of endometrial cancer. This accounts for less than 10% of women presenting with PMB. As stated previously, diagnosis is not possible on TVS alone due to the sonographic features being indistinguishable from hyperplasia but with the added imaging of color Doppler, a lower suspicion of malignancy is possible. In more advanced cases of endometrial cancer, myometrial invasion can be demonstrated and color Doppler may show the presence of low-resistance, irregular feeding vessels in the subendometrial myometrium in keeping with neovascularization. Figure 9.7 shows such a case.

ARTERIOVENOUS MALFORMATIONS

Although congenital malformations remain rare, iatrogenic arteriovenous malformations (AVMs) have been



Figure 9.6 Thickened endometrium secondary to tamoxifen use. Histology demonstrated normal endometrium with pseudodecidualization.

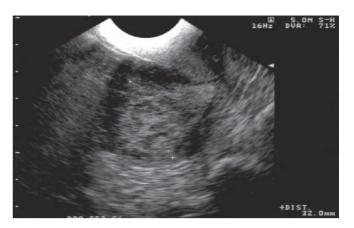


Figure 9.7 Markedly thickened endometrium and loss of endometrial–myometrial interface make this strongly suspicious of malignancy. This was confirmed as FIGO grade III endometrioid endometrial cancer with myometrial penetration up to 3 mm from the serosal surface.





Figure 9.8 An AVM with (A) and without (B) color Doppler.

encountered more frequently in recent years due to their association with uterine evacuations. Such a condition is potentially life-threatening, but, if correctly diagnosed, can be monitored or treated safely in most cases. ^{15,16} TVS and color Doppler are a cheaper and non-invasive

method of detecting AVMs before considering an invasive arteriogram, and have also been used as a means of monitoring resolution of AVMs with time in iatrogenic cases. Figure 9.8 highlights the difficulty in distinguishing an AVM from retained products of conception, as the clinical picture would also convince the clinician that this was the likeliest diagnosis. The superimposed color Doppler, however, presents an entirely different picture.

CONCURRENT PATHOLOGY

As mentioned earlier, TVS provides an opportunity to assess the uterus, cervix, and adnexae at the same visit. One study demonstrated that 14% of women attending a clinic for investigation of AUB had coexisting adnexal pathology.¹⁷

CONCLUSION

Transvaginal sonography, color Doppler, and SIS are recognized methods in the investigation of AUB, with sensitivities and specificities comparable to hysteroscopy for identifying focal pathology. Normal ultrasound appearances of the endometrium act as prevention from further invasive investigations and allow for the pursuit of various medical treatment options instead, thus acting as a form of triage. The procedure is tolerated well by patients and incurs minimal costs once set up and running. Gynecologists should encourage training in TVS in order to combine the expertise in AUB with sonographic findings as well as minimizing the number of attendances to a clinic for investigation of AUB.

The development of 3D scanning may help to improve the mapping of focal abnormalities prior to surgical removal as well as assess coexisting congenital anomalies.

References

- Hallberg L, Hogdall AM, Nilsson L et al. Menstrual blood loss: a population study. Acta Obstet Gynecol Scand 1966; 45: 320–51.
- Goldstein SR, Zelster I, Horan CK et al. Ultrasonography-based triage for perimenopausal patients with abnormal uterine bleeding. Am J Obstet Gynecol 1997; 177: 102–8.
- Nass Duce M, Oz U, Ozer C et al. Diagnostic value of sonohysterography in the evaluation of submucosal fibroids and endometrial polyps. Aust N Z J Obstet Gynaecol 2003; 43(6): 448–52.
- 4. Schwarzler P, Concin H, Bosch H et al. An evaluation of sonohysterography and diagnostic hysteroscopy for the assessment of intrauterine pathology. Ultrasound Obstet Gynecol 1998; 11: 337–42.
- 5. Fedele L, Bianchi S, Dorta M et al. Transvaginal ultrasonography versus hysteroscopy in the diagnosis of uterine submucosal myomas. Obstet Gynecol 1991; 77: 745–8.
- 6. Kelekci S, Kaya E, Alan M et al. Comparison of transvaginal sonography, saline infusion sonography, and office hysteroscopy in reproductive-aged women with or without abnormal uterine bleeding. Fertil Steril 2005; 84(3): 682–6.
- Bourne TH, Campbell S, Steer CV et al. Detection of endometrial cancer by transvaginal ultrasonography with colour flow imaging and blood flow analysis: a preliminary report. Gynecol Oncol 1991; 40: 253–9.
- 8. de Kroon CD, Louwé LA, Trimbos JB et al. The clinical value of 3-dimensional saline infusion sonography in addition to 2-dimensional saline infusion sonography in women with abnormal uterine bleeding: work in progress. J Ultrasound Med 2004; 23: 1433–40.

- Fedele L, Bianchi S, Dorta M et al. Transvaginal ultrasonography in the diagnosis of diffuse adenomyosis. Fert Steril 1992; 58: 94–7.
- Karlsson B, Granberg S, Wikland M et al. Transvaginal ultrasonography of the endometrium in women with postmenopausal bleeding – a Nordic multicenter study. Am J Obstet Gynecol 1995; 172: 1488–94.
- Epstein E, Valentin L. Managing women with post-menopausal bleeding. Best Pract Res Clin Obstet Gynaecol 2004; 18(1): 125–43.
- 12. Hardell L. Tamoxifen as a risk factor for carcinoma of the corpus uteri. Lancet 1989; 60: 126–31.
- 13. Kedar RP, Bourne TH, Powles TJ et al. Effects of tamoxifen on the uterus and ovaries of postmenopausal women in a randomised breast cancer prevention trial. Lancet 1994; 343: 1318–21.
- Timmerman D, Deprest J, Bourne TH et al. A randomized trial on the use of ultrasonography or office hysteroscopy for endometrial assessment in postmenopausal patients with breast cancer who were treated with tamoxifen. Am J Obstet Gynecol 1998; 179: 62–70.
- 15 Maleux G, Timmerman D, Heye S, Wilms G. Acquired uterine vascular malformations: radiological and clinical outcome after transcatheter embolotherapy. Eur Radiol 2006; 16(2): 299–306.
- Yang JJ, Xiang Y, Wan XR, Yang XY. Diagnosis and management of uterine arteriovenous fistulas with massive vaginal bleeding. Int J Gynecol Obstet 2005; 89: 114–19.
- 17. Jones K, Bourne TH. The feasibility of a 'one-stop' ultrasound-based clinic for the diagnosis and management of abnormal uterine bleeding. Ultrasound Obstet Gynecol 2001; 17: 517–21.

10

The role of hysteroscopy in investigating abnormal uterine bleeding

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Normal menstrual cycles in premenopausal women occur every 21–35 days. Menses on average lasts 3–7 days, with a blood loss of <80 ml/cycle. Any variant of the normal cycle is defined as abnormal uterine bleeding (AUB), which is subdivided based on cycle characteristics. Menorrhagia occurs when a women has a menstrual blood loss of >80 ml/cycle. Menometrorrhagia is similar to menorrhagia but menstrual blood loss occurs as irregular cycles. Metrorrhagia is normal flow of menses but occurs at irregular cycles. Oligomenorrhea is defined as a menstrual cycle occurring >35 days. The opposite is polymenorrhea, in which the cycle occurs <21 days. The absence of menses for 6 months is termed amenorrhea. Postmenopausal bleeding occurs in women who have undergone menopause for at least 6 months. Dysfunctional uterine bleeding (DUB) is a diagnosis of exclusion when no organic or structural cause can be determined for a woman's abnormal uterine bleeding. Anovulation is a common cause of DUB that results from a lack of opposing progesterone production to estrogen, leading to thickened endometrium and irregular, heavy bleeding. DUB is the most common cause of AUB in premenopausal women. In perimenopausal and postmenopausal women, endometrial hyperplasia and cancer should be ruled out as causes of AUB. Other causes of AUB are submucosal myomas, endometrial polyps, adenomyosis, endometritis, endocrinopathies, and coagulopathies. After a detailed patient history, physical examination, and appropriate laboratory work-up, imaging or outpatient diagnostic techniques are used to help establish a diagnosis.

Recamier first introduced the evaluation of abnormal uterine bleeding in 1850 by utilizing a mechanical curette; in an inpatient setting, to sample the endometrium. With this method, approximately 60% of the uterine cavity is curetted, often missing focal lesions and leading to an inconclusive diagnosis in approximately 10% of patients. Since the introduction of dilatation and curettage (D&C), multiple outpatient modalities have been developed to improve the accuracy of diagnosis for AUB.

These modalities include the Pipelle endometrial biopsy, magnetic resonance imaging, hysterosalpingogram, two-dimensional (2D) and three-dimensional (3D) transvaginal ultrasound, saline-infused sonohysterogram, and hysteroscopy.

The Pipelle endometrial biopsy (EMB) is a quick, office-based technique that has a high sensitivity for endometrial cancer and hyperplasia but a low sensitivity for focal lesions.³ Even though the Pipelle only samples 10–25% of the uterine cavity, it has been shown by Bradley et al. in a published meta-analysis of 39 studies that the detection rate for endometrial cancer was 99.6% in postmenopausal women and 91% in premenopausal women. The detection rate for atypical hyperplasia was 88% in this study.³ This detection rate is similar in patients who underwent a D&C with endometrial cancer and atypical hyperplasia. If the EMB is inconclusive or negative, other methods of investigation for AUB are necessary.

A less commonly utilized method for diagnosing the cause of abnormal uterine bleeding is the hysterosalpingogram (HSG). This technique evaluates the contour of the uterine cavity and tubal patency, utilizing transcervical injection of contrast media and fluoroscopy. HSG has a sensitivity of 80–98% and a specificity of 35–85% for the detection of intrauterine pathology in premenopausal women when compared with hysteroscopy. ^{4–6} An HSG can be performed in approximately 10 minutes with little discomfort and few complications. This method is typically utilized in patients undergoing an infertility evaluation.

Magnetic resonance imaging (MRI) is another useful tool for evaluating patients with abnormal uterine bleeding. It is highly accurate for the size, location, and number of uterine fibroids. ^{1,7,8} It is perhaps most useful in patients with symptoms suggestive of uterine fibroids (menorrhagia and dysmenorrhea) but where no fibroids are detected by any ultrasound or hysteroscopy and adenomyosis is suspected. MRI has a sensitivity of 88–93% and a specificity of 67–91% in the diagnosis of adenomyosis. ⁸ Owing to the cost, MRI should be limited to a

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select group of patients with AUB, and not utilized as a screening tool.

A simpler and less-expensive radiographic tool that is effective for screening is the transvaginal ultrasound (TVUS). With little discomfort and no complications for the patient, this method permits a rapid assessment of the uterus and adnexa. TVUS is useful for measuring endometrial thickness in postmenopausal women as well as for detecting uterine myomata and polyps in all women. An endometrial thickness cutoff of ≤5 mm can reliably exclude endometrial cancer in postmenopausal women with a sensitivity as high as 98%.^{3,9} The literature shows a wide range of sensitivities and specificities, 21–100% and 12–100%, respectively, in TVUS detection of intrauterine pathology. TVUS has reasonable sensitivity for diffuse and focal lesions, so that it may serve as a practical first step in non-invasive diagnosis for AUB.²

Saline-infused sonohysterogram (SIS) is a minimally invasive technique that enhances the sensitivity and specificity of TVUS.^{2,6} It is recommended in patients with either a thick endometrium and a non-diagnostic EMB, an indeterminate TVUS, or a negative TVUS and EMB with persistent bleeding.² SIS can be completed within 5–10 minutes with minimal patient discomfort. Even though this technique does not allow for direct visualization, it has a sensitivity and specificity in detecting uterine cavity lesions comparable to direct visualization as obtained with hysteroscopy.^{10–12}

Only hysteroscopy (HSC) allows for direct visualization, accurate diagnosis, and targeted biopsies, leading to reduced sampling errors. 1-3,13,14 AUB is the most common indication for outpatient HSC (95.8%) or office HSC (89%).14 The sensitivity of HSC for diagnosing intrauterine pathology ranges from 53 to 100%, with most literature quoting 80–100%. The specificity of HSC for diagnosing intrauterine pathology ranges from 50 to 100%, with most literature quoting 93-100%. For endometrial cancer or hyperplasia detection, the sensitivity and specificity range from 86 to 100% and from 97 to 100%, respectively. The likelihood of endometrial cancer is 0.4–0.5% after a negative hysteroscopy.³ Table 10.1 shows a comparison of sensitivities and specificities of the imaging modalities based on the reported values of various studies. Even though the sensitivities and specificities of HSC are similar to the SIS technique, the advantage of HSC is that, while directly visualizing the lesion within the uterine cavity, a direct biopsy or even removal of the lesion can be performed (Figures 10.1 and 10.2). This may eliminate other studies or procedures necessary to diagnose the cause of AUB. Other advantages include the assessment of endometrial vascularity and the categorization of submucous myomata using different intrauterine pressures (Figures 10.3–10.5). Such presurgical planning can only be accomplished with the direct view obtained with the hysteroscope.

In a review of 19 studies, Hataska averaged the procedure time of HSC to be about 11 minutes, well-tolerated by patients, with 1/770 cases complicated by a tubal infection.² Hysteroscopy can be done in the hospital, as an outpatient surgery, or in the office. In the hospital, the procedure time does not increase but the added time of preoperative registration, anesthesia, procedure, and post-operative recovery lengthen the total time to about 4 hours. By evaluating the patient in the office with HSC, the patient may avoid the operating room time and costs and minimize the disruption in daily activities.

The introduction of small-caliber hysteroscopes in the 1980s has made the office hysteroscope practical. These flexible hysteroscopes have a 2–3.5 mm outer diameter (OD) and permit distal steerability. Using a thumb manipulator, the distal 3–5 cm can typically be deflected 110° in two directions. Because these scopes have small, single-working channels, they are non-continuous flow and are typically used solely for diagnostic purposes. The small diameter (similar to the Pipelle endometrial biopsy) and the steerability create minimal discomfort for the patient. As a result, the uses of a paracervical block and/ or tenaculum are rarely needed in these cases.

Office hysteroscopy can also be performed with standard small-diameter rigid hysteroscopes with an OD of 4–6 mm. The advantage of these systems over the flexible scope is that they are multichanneled and allow for continuous flow of fluid and the passage of instruments such as the semirigid biopsy forceps, scissors, and graspers. These instruments can be placed through the operative port and allow for visually directed biopsies and small procedures, such as a polypectomy. Most often, intravenous (IV) anesthesia is not required for procedures utilizing these small-diameter rigid hysteroscopes. Local anesthesia is useful if the cervix is stenotic or requires dilatation prior to insertion of the hysteroscope. However, in patients with a multiparous cervix, cervical dilatation is infrequently required and anesthesia is a rare necessity.^{15,16} The office hysteroscopy procedure is well tolerated without anesthesia even in nulliparous and postmenopausal patients. 15-17 A vaginoscopic approach to office hysteroscopy requires neither a speculum nor tenaculum and may cause less discomfort to the patient. 15-18

Hysteroscopy should be performed in the early follicular phase of the menstrual cycle just after menses subsides. This is when the endometrium is most thin and visibility optimal. The patient is placed in the dorsal lithotomy position and the vagina prepared with sterile technique. Preferred uterine distention media are either normal saline or lactated ringer's solutions because they are low-viscosity fluids containing physiologic levels of

Table 10.1 Comparison of imaging sensitivities (Sens) and specificities (Spec) for abnormal uterine bleeding

Study	Sens D&C	Spec D&C	Sens HSG	Spec HSG	Sens TVUS	Spec TVUS	Sens SIS	Spec SIS	Sens HSC	Spec HSC
Valle										
 Diagnosis of intrauterine pathology 	%59								%86	
Bettocchi et al ²¹ – 397 patients, mean age 43 years old										
• Diagnosis of intrauterine pathology	46%	100%								
Towbin et al 6 – 149 patients, pre/postmenopausal										
 Diagnosis of intrauterine pathology 			%08	85%	54%	%06			%62	93%
Widrich et al 10 – 113 patients, pre/postmenopausal										
 Diagnosis of intrauterine pathology 							100%	%08	%26	93%
Ceci et al 22 – 443 patients, pre/postmenopausal										
 Diagnosis of intrauterine pathology 									%86	%56
Farquhar et al ¹¹ – 2917 patients, 19 studies, pre/postmenopausal										
• Diagnosis of:										
intrauterine pathology					46–100%	12-100%	85–100%	81-100%	%/6-06	62–93%
submucosal myomas					21–100%	53-100%	57-100%	96–100%	53-100%	97–100%
endometrial cancer or hyperplasia					33-100%	%66-62	29–80%	82-100%	90-100%	97–100%

 Diagnosis of intrauterine pathology in women ≥35 years old 	56.3%	72.0%	81.3%	100%	87.5%	100%
Clark et al ¹⁹ – 26346 patients, 65 studies, pre/postmenopausal • Diagnosis of endometrial cancer					86.4%	%66
• Diagnosis of endometrial disease					%82	95.8%
Bettocchi S et al ¹³ – 925 patients						
Diagnosis of intrauterine pathology in postmenopausal women with:						
endometrium <4 mm					%66	100%
endometrium ≥4 mm					100%	%66
Litta et al 9 – 220 patients						
 Diagnosis of intrauterine pathology in postmenopausal women with 						
endometrial thickness ≥4 mm	55.6%	49.7%			100%	49.6%

Kelekci et al 12 – 50 patients

D&C, dilatation and curettage, HSG, hysterosalpingogram; TVUS, transvaginal ultrasound; SIS, saline-infused sonohysterogram; HSC, hysteroscopy.

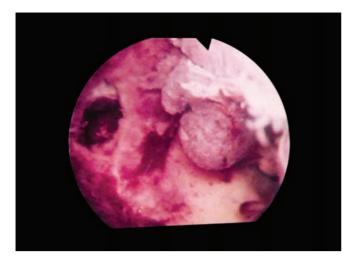


Figure 10.1 Endometrial cancer

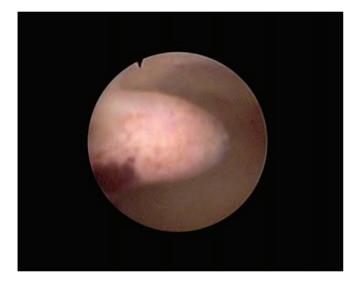


Figure 10.2 Intrauterine polyp

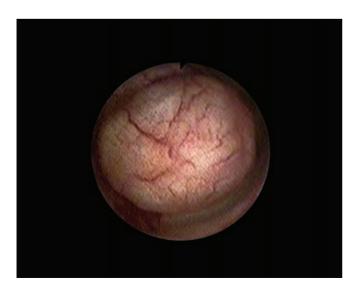


Figure 10.3 Type 0 submucosal myoma



Figure 10.4 Type 1 submucosal myoma

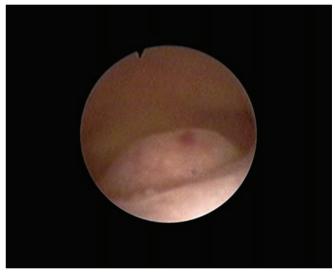


Figure 10.5 Type 2 submucosal myoma

electrolytes. At fluid deficit levels of above 1.5 L, fluid overload and pulmonary edema can occur. However, diagnostic hysteroscopy rarely uses more than a total of 500–1000 ml of fluid media even when performing a minor procedure in the office, such as targeted biopsy and polypectomy. If no more than 1.5 L of fluid is used, strict monitoring of fluids is not warranted. If the fluid loss seems to exceed 1.5 L, a diuretic should be administered, urine output closely monitored, and electrolytes drawn.

Diagnostic hysteroscopy in the office or operating room requires minimal setup. For visualization of the cavity on a monitor, the hysteroscope is attached to a light source (150–300 W halogen or xenon bulb), light cord, and a single-chip video camera. Video printers are available for printing images captured during the hysteroscopy. In the office, a video tower helps organize this setup.

Contraindications to hysteroscopy include pelvic infections, excessive uterine bleeding, cervical cancer, pregnancy, and recent uterine perforation. A relative contraindication is known adenocarcinoma of the endometrium. Complications of hysteroscopy are minimal, but include bleeding from a tenaculum site or uterine cavity if a small procedure is performed, infection, vasovagal reaction, uterine perforation, and creation of a false tract that can lead to perforation or bleeding. These complications typically resolve spontaneously or rarely need treatment: i.e. silver nitrate or a stitch at a tenaculum site or antibiotics for infection. The failure rates for hospital HSC are about 3-3.5%. 14,19 Failure rates for office HSC are minimal as well, and have been reported from as low as 1% to as high as 13%.11,14,19,20 The failure rates of 13% for nulliparous women and 11% for postmenopausal women were found in one study of 473 procedures, performed in the period 1991–1995, using a rigid, 5 mm OD hysteroscope. 14 The more recent studies have shown a less than 5% failure rate with rigid or flexible office hysteroscopy. 11,19,20 The most common conditions responsible for failure to complete the office hysteroscopy include cervical stenosis, poor visualization, and pain.

Although office hysteroscopy has been shown to be a well-tolerated tool with excellent sensitivity and specificity for diagnosing the source of AUB, most gynecologists in the USA continue to perform hysteroscopy in the operating room. The more common office-based evaluation tools include the EMB, MRI, HSG, TVUS, and/or SIS. Towbin et al. compared the cost of different imaging

modalities among 149 procedures performed between July 1993 and December 1994. From this study, the average cost of TVUS was US\$300-400, HSG US\$700, outpatient hospital HSC US\$2000, and office HSC US\$800.6 Hidlebaugh did a cost analysis of 473 procedures from September 1991 to June 1995 between outpatient hospital HSC and office HSC. The average cost for a hospital HSC was US\$1799 (US\$1304-2616) and for office HSC was \$62 per procedure.14 Included in the cost analysis were the anesthesia charges for the hospital HSC and the disposable equipment, staff salary, instrument repair costs, and capital equipment costs (surgical instruments, hysteroscope, light source, and insufflator) for the office HSC. Fortunately, the Centers for Medicare & Medicaid Services (CMS) has realized the cost savings to the healthcare system by performing office-based procedures. As a result, new CPT (Current Procedural Terminology) codes are expected to become available for these office-based procedures in 2007 that will substantially increase the physician reimbursement by covering a facility fee as well as the standard professional fee.

Abnormal uterine bleeding accounts for approximately 33% of women referred to gynecologic clinics, rising to 69% in peri- or postmenopausal women. The role of hysteroscopy in evaluating this common problem continues to be studied and the best diagnostic technique or even combination of techniques is still a debate. The work-up often varies from patient to patient and physician to physician, but each individual patient should be evaluated in a timely and cost-efficient manner.

References

- Valle RF. Office hysteroscopy. Clin Obstet Gynecol 1999; 42(2): 276–89.
- Hataska H. The evaluation of abnormal uterine bleeding. Clin Obstet Gynecol 2005; 48(2): 258–73.
- 3. Bradley LD. Abnormal uterine bleeding. Nurse Pract 2005; 30(10): 38–49.
- Dalfo AR, Ubeda B, Ubeda A, et al. Diagnostic value of hysterosalpingography in the detection of intrauterine abnormalities: a comparison with hysteroscopy. AJR Am J Roentgenol 2004; 183: 1405–9.
- 5. Preutthipan S, Linasmita V. A prospective comparative study between hysterosalpingography and hysteroscopy in the detection of intrauterine pathology in patients with infertility. J Obstet Gynaecol Res 2003; 29(1): 33–7.
- 6. Towbin NA, Gviazda IM, March CM. Office hysteroscopy versus transvaginal ultrasonography in the evaluation of patients with excessive uterine bleeding. Am J Obstet Gynecol 1996; 174(6): 1678–82.
- 7. Imaoka I, Wada A, Matsuo M, et al. MRI imaging of disorders associated with female infertility: use in diagnosis, treatment, and management. Radiographics 2003; 23: 1401–21.

- Spielman AL, Keogh C, Forster BB et al. Comparison of MRI and sonography in the preliminary evaluation for fibroid embolization. AJR Am J Roentgenol 2006; 187: 1499–504.
- 9. Litta P, Merlin F, Saccardi C, et al. Role of hysteroscopy with endometrial biopsy to rule out endometrial cancer in postmenopausal women with abnormal bleeding. Maturitas 2005; 50(2): 117–23.
- Widrich T, Bradley LD, Mitchinson AR, Collins RL. Comparison of saline infusion sonography with office hysteroscopy for the evaluation of the endometrium. Am J Obstet Gynecol 1996; 174(4): 1327–34.
- Farquhar C, Ekeroma A, Furness S, et al. A systematic review of transvaginal ultrasonography, sonohysterography and hysteroscopy for the investigation of abnormal uterine bleeding in premenopausal women. Acta Obstet Gynecol Scand 2003; 82(6): 493–504.
- 12. Kelekci S, Kaya E, Alan Y, et al. Comparison of transvaginal sonography, saline infusion sonography, and office hysteroscopy in reproductive-aged women with or without abnormal uterine bleeding. Fertil Steril 2005; 84(3): 682–6.

- Bettocchi S, Nappi L, Ceci O et al. The role of office hysteroscopy in menopause. J Am Assoc Gynecol Laparosc 2004; 11(1): 103–6.
- Hidlebaugh D. A comparison of clinical outcomes and cost of office versus hospital hysteroscopy. J Am Assoc Gynecol Laparosc 1996; 4(1): 39–45.
- Sagiv R, Sadan O, Boaz M et al. A new approach to office hysteroscopy compared with traditional hysteroscopy. Obstet Gynecol 2006; 108(2): 387–92.
- Bettocchi S, Ceci O, Nappi L et al. Operative office hysteroscopy without anesthesia: analysis of 4863 cases performed with mechanical instruments. J Am Assoc Gynecol Laparosc 2004; 11(1): 59–61.
- 17. Bettocchi S, Ceci O, Di Venere R et al. Advanced operative office hysteroscopy without anaesthesia: analysis of 501 cases treated with a 5 Fr. bipolar electrode. Hum Reprod 2002; 17(9): 2435–8.

- Bettocchi S, Selvaggi L. A vaginoscopic approach to reduce the pain of office hysteroscopy. J Am Assoc Gynecol Laparosc 1997; 4(2): 255–8.
- Clark TJ, Voit D, Gupta J et al. Accuracy of hysteroscopy in the diagnosis of endometrial cancer and hyperplasia. JAMA 2002; 288(13): 1610–21.
- 20. Paschopoulos M, Lolis ED, Alamanos Y et al. Vaginoscopic hysteroscopy and transvaginal sonography in the evaluation of patients with abnormal uterine bleeding. J Am Assoc Gynecol Laparosc 2001; 8(4): 506–10.
- 21. Bettocchi S, Ceci O, Vincino M et al. Diagnostic inadequacy of dilatation and curettage. Fertil Steril 2001; 75(4): 803–5.
- 22. Ceci O, Bettocchi S, Pellegrino A et al. Comparison of hysteroscopic and hysterectomy findings for assessing the diagnostic accuracy of office hysteroscopy. Fertil Steril 2002; 78(3): 628–31.

Medical management of abnormal uterine bleeding

11

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INTRODUCTION

A wide variety of drugs are used to treat abnormal uterine bleeding. Medical therapy is indicated when there is no obvious pelvic abnormality and the woman wishes to retain her fertility. Whereas the number of hysterectomies for menorrhagia has been estimated to have fallen by 36% between 1989 and 2002/3, and the number of endometrial ablations is increasing, some women do not wish to have surgery. Medical treatment avoids surgery, but may have side effects and must be taken long term. Thus, the drug regimen chosen must be effective, have few or mild side effects, and must be acceptable to the patient.

The aims of therapy are to reduce blood loss, reduce the risk of anemia, and improve the quality of life. Menorrhagia is the commonest cause of iron deficiency anemia in Western women, and thus iron therapy is often indicated as well as the options discussed below. It could be argued that menstrual blood loss (MBL) should be reduced to be within the normal range (i.e. less than 80 ml per period). However, women who are keen to avoid surgery may accept a higher loss if they can cope with the flow and any anemia is controlled with iron supplements.

It is important to assess drug therapies in terms of reduction of measured MBL, since, as already discussed in Chapter 5, there is poor correlation between objective and subjective assessment. Well-designed randomized controlled trials provide the best evidence of the efficacy of any intervention, as any differences between groups can be more confidently attributed to differences in treatment.

Medical treatments for abnormal uterine bleeding can be divided into two main classes: non-hormonal and hormonal.

NON-HORMONAL TREATMENTS

Non-hormonal treatments are detailed in Table 11.1.

Non-steroidal anti-inflammatory drugs

Non-steroidal anti-inflammatory drugs (NSAIDs) can be chemically classified into five main groups: salicylates (aspirin), indoleacetic acid analogues (indomethacin), arylproponic acid derivatives (naproxen, ibuprofen), fenamates (mefenamic acid, flufenamic acid, meclofenamic acid), and coxibs (celecoxib, rofecoxib). The first four groups inhibit cyclooxygenase-1 (COX-1) and the last cyclooxygenase-2 (COX-2). Interest in the use of NSAIDs started in the early 1980s when the role of uterine prostaglandins in the genesis of abnormal uterine bleeding was first examined. Excessive levels of prostaglandins were found in menstrual blood and endometrium and prostaglandin E (a vasodilator) receptor concentrations were significantly higher in women with menorrhagia. 4-6

NSAIDs have been evaluated in numerous studies, which to date have been limited to COX-1 inhibitors. It is unlikely that COX-2 inhibitors will be studied in view of concerns of cardiovascular risk.⁷ Patients subjective perception of improvement and decrease of blood loss has been shown in many placebo-controlled trials. A meta-analysis including 16 randomized studies has provided no evidence that one NSAID is superior to another.⁸

Effectiveness in reducing blood loss

Of the NSAIDs, the fenamates (such as mefenamic acid) have been the most extensively studied. The fenamates have the unique property that they inhibit prostaglandin synthesis and also bind to prostaglandin receptors, which are significantly increased in women with menorrhagia. In addition, fenamates are thought to improve endometrial hemostasis. Reductions in menstrual blood flow range from 20% to 50%. 10,11 Furthermore, treatment continues to be effective long term. A follow-up of 12–15 months after commencing treatment showed that mefenamic acid continued to be effective. 12

Other NSAIDs such as naproxen, ibuprofen, sodium diclofenac, and flurbiprofen also reduce blood loss.

 Table 11.1
 Non-hormonal treatments for abnormal uterine

 bleeding

Non-steroidal anti-inflammatory drugs

Mefenamic acid

Meclofenamic acid

Naproxen

Ibuprofen

Flurbiprofen

Diclofenac

Antifibrinolytics

Tranexamic acid

Other

Ethamsylate

The percentage reduction in blood loss varies from 25% to 47%, depending on the agent and dosage used.⁸, ^{13,14} With regard to dosing regimens, most studies have used treatments starting with the first day of menstruation and continuing for 5 days or until the cessation of bleeding. Since NSAIDs are prescribed during menstruation, they are suitable for women trying to conceive. Mefenamic acid and naproxen are typically prescribed in a dose of 250–500 mg two to four times daily; ibuprofen has been studied in doses ranging from 600 mg/day to 1200 mg/day.⁸

Side effects

Gastrointestinal symptoms are a common side effect of NSAIDs and these drugs are therefore contraindicated in women with peptic ulceration. Gastrointestinal effects are less likely with mefenamic acid than naproxen.⁸ Overall, since NSAID use for menorrhagia is intermittent rather than chronic, as for treatments of conditions such as osteoarthritis, the risk of adverse effects in otherwise healthy women is low.

Use in women with inert or copper-bearing intrauterine contraceptive devices

Inert intrauterine contraceptive devices (IUDs) have been shown to at least double the MBL, whereas copper devices increase MBL by an average of 40–50% over 6–12 months compared with preinsertion values. NSAIDs are effective in reducing blood loss in women with a copper or non-hormonal IUD. Mefenamic acid, 500 mg three times a day from the start of bleeding, reduced MBL by 34% in IUD users with a pretreatment MBL >80 ml and by 23% in women with a pretreatment MBL <80 ml. 16

Ibuprofen, 400 mg four times a day, from day 1 gave an average reduction of 32% in MBL, although a greater reduction was seen in the inert as opposed to copper coil users. ¹⁷ Naproxen also reduces blood loss by a third. ¹⁸ Diclofenac reduced MBL by 20% compared with placebo. ¹⁹

NSAIDs combined with other agents

There is no published evidence to support simultaneous use of NSAIDs and other agents such as tranexamic acid or progestogens. They are, however, commonly prescribed together in clinical practice. This pragmatic approach may be of benefit, since NSAIDs also reduce menstrual pain.²⁰

Comparison of NSAIDs and other agents

Randomized studies comparing NSAIDs with other agents for abnormal uterine bleeding suggest both danazol and tranexamic acid to be superior with respect of decreasing blood loss²¹ (Table 11.2). However, danazol and tranexamic acid are more likely to cause adverse events when compared with NSAIDs.

 Table 11.2
 Comparison of medical treatments for abnormal uterine bleeding

Treatment	Reduction of menstrual blood loss
Non-steroidal anti-inflammatory drugs	20–50%
Tranexamic acid	47–54%
Etamsylate	Possibly 13% – not clinically significant
Oral progestogens for 21 days	30-90%
Oral progestogens, luteal adminstration	Ineffective
Long-acting progestogen	50–66% of women with menorrhagia experience amenorrhea between 1 and 2 years of use
Levonorgestrel intrauterine system	74–97%
Combined oral contraceptive pill	43%
Danazol	50-80%
Gonadotropin-releasing hormone agonists	> 90%

Adapted from Reference 20.

In summary, NSAIDs can be an effective first-line treatment in abnormal uterine bleeding. The degree of reduction of menstrual blood loss is modest compared to other agents, but NSAIDs have a low profile of adverse effects in otherwise healthy women. An additional beneficial effect is that these drugs also alleviate menstrual pain.

Antifibrinolytics

The endometrium possesses an active fibrinolytic system. An increase in the levels of plasminogen activators, a group of enzymes that cause fibrinolysis, has been found in the endometrium of women with heavy menstrual bleeding compared to those with normal menstrual loss. ²² Plasminogen activator inhibitors (antifibrinolytic agents) have therefore been promoted as a treatment for menorrhagia.

Effectiveness in reducing blood loss

Tranexamic acid, a synthetic derivate of the amino acid lysine, exerts its antifibrinolytic effect through the reversible blockade of plasminogen. ^{23,24} Tranexamic acid reduces blood loss by 40–50%. ^{25–27} Since it is taken only during menstruation, tranexamic acid is therefore suitable for women trying to conceive.

Side effects

Side effects of antifibrinolytic drugs, mainly gastrointestinal and dose-dependent effects, are reported by about one-third of patients.²⁸ Adverse effects can be reduced by limiting the number of days on which the drug is taken. As about 90% of menstrual blood is lost during the first 3 days, medication could be limited to that time.

The main reported adverse effect of tranexamic acid is thromboembolism. Concerns were fuelled by single case reports about cerebral sinus thrombosis and central venous stasis retinopathy. ^{29,30} However, long-term studies in Scandinavia have shown that the incidence of thrombosis in women treated with tranexamic acid is comparable to the spontaneous frequency of the condition in the female population. ³¹

Use in women with inert or copper-bearing intrauterine contraceptive devices

Tranexamic acid is also effective in women with a copper or an inert intrauterine contraceptive device. The effect is dose dependent, with a 54% reduction in MBL when 3 g daily was used compared to 71% when initially 6 g was given for the first 5 days of bleeding followed, if necessary, by 3 g.

Comparison of antifibrinolytics and other agents

Comparative studies have shown tranexamic acid to be superior to NSAIDs, oral progestogens, and ethamsylate in reducing menstrual blood loss. 11,27 However antifibrinolytics do not alleviate menstrual pain.

Thus, antifibrinolytics should be considered as a first-line treatment for menorrhagia. However, it is probably prudent not to use an antifibrinolytic with the combined oral contraceptive pill (see below).

Ethamsylate

Ethamsylate (ε-aminocaproic acid) is believed to act by reducing capillary fragility, although the precise mechanisms are unknown. However, studies have produced conflicting results, with some showing an increase in blood loss. 11,33 Its use is not recommended in the UK. 20 It has been studied in women with IUDs, but the reduction of blood loss was small (<20%). 34,35

HORMONAL TREATMENTS

Hormonal treatments are detailed in Table 11.3.

Table 11.3 Hormonal treatments for abnormal uterine bleeding

Oral progestogens

Norethisterone

Medroxyprogesterone acetate

Dydrogesterone

Intrauterine progestogens

Levonorgestrel IUD

Progestasert IUD

Combined estrogen/progestogens

Oral contraceptives

Hormone replacement therapy

Other

Danazol

Gestrinone

GnRH analogues

Mifepristone

Progestogens

The use of progestogens is based on the erroneous concept that women with menorrhagia principally have anovulatory cycles.³⁶ However, many studies have shown that most women with regular excessive menstrual bleeding have normal ovulatory cycles.^{37,38}

A variety of routes of administration and dose schedules have been used, ranging from intermittent luteal phase oral administration, through intramuscular injection, to continuous local administration by an IUD, each of which has a different efficacy in distinct clinical situations; the last mentioned also provides contraception. Owing to the lack of objective randomized controlled trials the use of synthetic progestogens has been previously largely empirical.

Oral progestogens

Traditionally, administration was in the luteal phase and studies have mainly examined norethisterone. Studies with measured menstrual loss with luteal administration for 7 days of norethisterone, 5 mg twice daily, show either a slight decrease or even an increase in flow.³⁹ This regimen is not recommended in the UK.²⁰ However, norethisterone, 5 mg three times daily from day 5–26, is effective.⁴⁰ Of note, there have been no studies comparing progestogens to placebo.³⁹ Side effects include weight gain, headache, and bloatedness. There are also concerns that progestogens used in doses greater than those needed in progestogen-only contraception increase the risk of venous thromboembolism.⁴¹ Limited data suggest that medroxyprogesterone acetate reduces MBL, but there are no publications to date regarding dydrogesterone.^{42,43}

Oral progestogens at very large doses, such as 30 mg/day, can be successfully applied to control torrential bleeding. This is usually effective within 24–48 hours, when the dose can be reduced and then finally stopped over the next few days, when another, usually lighter bleed, will occur.

Depot or implant progestogens

Continued use of long-acting progestogens renders most women amenorrheic and therefore could be considered for use in menorrhagia. However, there are no published data with MBL measurements.

Medroxyprogesterone acetate is available as a depot injection (DMPA) for contraception at a dose of 150 mg administered every 3 months. It may cause unpredictable, irregular spotting and bleeding in the first few months of use and can cause heavy bleeding in 1–2% of women. 44-46 However, with repeated administration, amenorrhea

becomes common and hemoglobin levels increase. 46 After 1 year of use, 45-50% of women are likely to be amenorrheic. 44,46 There are concerns about the use of DMPA increasing the risk of osteoporosis.⁴⁷ The bestavailable evidence suggests that the amenorrhea induced by DMPA contraception is associated with a 5-10% loss of bone, which, however, is not progressive. 48,49 Much depends on the patient's risk factors for osteoporosis, such as family history and smoking. In any case, DMPA probably should be discontinued at age 40 years old to allow resumption of ovarian cycling for the remaining 10 years or so up to the natural menopause. The long-term skeletal effects of DMPA in teenagers who have yet to achieve peak bone mass is uncertain. Any fall in bone mineral density (BMD) on starting treatment, however, seems to reverse rapidly on stopping DMPA.

Subdermal implants (such as Implanon) that release etonogestrel over several years are another way of administering long-acting progestogens for contraceptive purposes. Like DPMA, bleeding disturbances such as irregular bleeding and periods of prolonged bleeding are common.⁵⁰

Intrauterine progestogens

Progesterone or progestogen-releasing intrauterine systems (PPRIUS) were initially introduced in an effort to reduce IUD expulsion, by the addition of 'uterine-relaxing hormones'. ⁵¹ Subsequently, prolonged use of both the Progestasert (the first hormonally impregnated device releasing 65 µg of progesterone per day) and Mirena (a device releasing 20 µg of levonorgestrel per day) intrauterine systems was associated with a profound reduction in MBL in women using the IUD for contraception. Twenty percent of the women using the levonorgestrel-releasing intrauterine system were amenorrheic after 1 year's use while still continuing to ovulate. ⁵¹ The levonorgestrel-releasing intrauterine system (Mirena) is discussed in detail in Chapter 13.

Progestasert requires reinsertion approximately annually. The levonorgestrel-releasing intrauterine system has to be replaced every 5 years.

Estrogen/progestogen combinations

Combined oral contraceptive pills consisting of an estrogen/progestogen combination are often used to reduce MBL. When taken in a cyclical fashion, they induce regular shedding of a thinner endometrium and inhibit ovulation. The exact endometrial mode of action of contraceptive pills is unclear, and probably involves induction of endometrial atrophy.

From clinical experience, the beneficial effect of combined oral contraceptive preparations on menorrhagia is

very well known. However, placebo-controlled randomized controlled trials with adequate patient numbers, duration of at least three to six cycles and adequate follow-up have not been conducted.⁵²

One small study of women taking an oral contraceptive containing 30 µg ethinyl estradiol showed a 43% reduction in MBL compared to baseline. No significant difference was found between groups treated with an estrogen/progestogen combination, mefenamic acid, low-dose danazol, or naproxen. Other studies found users of oral contraceptives less likely to experience heavy menstrual bleeding or anemia. 53

However, some trials employed a higher dose than the 30–35 µg ethinyl estradiol of preparations currently in use. It is, therefore, less clear whether low-dose preparations are as effective in reducing MBL as the higher-dose combinations, and whether particular progestogens make any difference. Although there is some indication that the frequency of menstrual disturbances, such as spotting and breakthrough bleeding, is less when the oral contraceptive contains a relatively high dose of progestogen, no evidence is available to suggest that changing the progestogen influences total MBL.

The combined oral contraceptive is probably best used when contraception is also required and it will also reduce menstrual pain. ⁵⁴ This is partly caused by a fear of thromboembolic events, particularly in the older age groups. ⁵⁵ Although withdrawal bleeds induced by sequential estrogen/progestogen hormone replacement therapy regimens are not excessive, there have been no trials in menorrhagia. ⁵⁶

Androgens

Danazol

Danazol is an isoxazol derivative of 17α -ethinyl testosterone, which acts on the hypothalamic–pituitary–ovarian axis, suppressing ovulation, and directly on the endometrium, leading to atrophy.⁵⁷

Danazol was evaluated for the treatment of menor-rhagia in various randomized trials and compared with several other medical treatments. Danazol reduces MBL by up to 80% in a dose-dependent manner. ^{58–60} It usually leads to amenorrhea at doses >400 mg/day. ⁶¹ Danazol reduces MBL more effectively than NSAIDs or oral progestogens. ^{60,62}

Although effective, the clinical use of danazol is limited by its androgenic side effects, which are experienced by up to three-quarters of the patients. Side effects include weight gain, oily skin, acne, and deepening of the voice.⁵⁷ In addition, women must be advised to use barrier methods of contraception because of potential virilization of a fetus if pregnancy occurs while on danazol treatment.

Given these side effects, danazol is probably best restricted to women awaiting surgery. It can also be used as a shortterm endometrial thinning agent prior to endometrial ablation.

Gestrinone

Gestrinone is a 19-nortestosterone derivative which has antiprogestogenic, antiestrogenic, and androgenic activity.

Gestrinone was shown in a placebo-controlled study to successfully diminish MBL and to cause amenorrhea in patients suffering from menorrhagia. However, most women treated with gestrinone experience androgenic side effects such as acne, hirsutism, and weight gain. These side effects preclude long-term therapy. Again, effective contraception needs to be used to prevent potential fetal virilization.

Gonadotropin-releasing hormone agonists

Gonadotropin-releasing hormone (GnRH) agonists administered continuously create a reversible hypogonadotropic state by down-regulation of GnRH receptors, which blocks ovarian function and causes a hypoestrogenic state.⁵⁷ GnRH agonists reduce uterine volume by 40–60%, and many investigators have evaluated their effectiveness in treating bleeding associated with leiomyomas. GnRH agonists frequently induce amenorrhea.⁵⁷

However, there are significant disadvantages to the use of GnRH analogues. The duration of treatment of these agents is limited to 6 months, owing to rapid bone demineralization associated with estrogen withdrawal. Furthermore, the occurrence of side effects associated with the hypoestrogenic state, particularly hot flushes and vaginal dryness, reduce the woman's quality of life.⁵⁷

Concerns about bone loss and poor tolerability of GnRH agonists have led to a number of studies on estrogen and progestogen 'addback therapy' during GnRH agonist treatment. However, there are still concerns about bone loss.⁶⁴

The side effects of GnRH analogues usually preclude their long-term use. However, they are highly effective in short-term therapies such as for preoperative endometrial thinning or fibroid shrinkage.

Antiprogestogens

Mifepristone (RU-486) is a synthetic 19-norsteroid with antiprogestogen activity that has been shown to inhibit ovulation and to disrupt endometrial integrity.⁶⁵ Mifepristone was recently shown to act as a contraceptive agent and to induce amenorrhea at a dose of 5 mg/day in the majority of women studied.⁶⁶ However, there are

concerns that it induces endometrial hyperplasia, and further research is required.⁶⁷

DECISION AIDS AND EDUCATION PACKAGES

Increasing patient participation in treatment decision making is important in view of the wide choices available. Decision aids come in a variety of formats, including leaflets, audiotapes, decision boards, computer programs, videos, websites, and structured interviews. These were examined in a randomized controlled trial of 894 women with 2 years of follow-up.⁶⁸ Women were randomized to the control group, information-alone group (booklet and video), or information + interview group (interview). Hysterectomy rates were lower for women in the interview group (38%) (adjusted odds ratio [OR], 0.60; 95% confidence interval [CI], 0.38-0.96), than in the control group (48%) and women who received the information alone (48%) (adjusted OR, 0.52; 95% CI, 0.33-0.82). The interview group had lower mean costs (US\$1566) than the control group (US\$2751) (mean difference US\$1184; 95% confidence interval [CI], US\$684-2110) and the information group US\$2026 (mean difference US\$461; 95% CI US\$236–696. Thus, providing women with information alone did not affect treatment choices; however, the addition of an interview to clarify values and elicit preferences had a significant effect on women's management and resulted in reduced costs.

Education packages in primary care have also been evaluated. For example in East Anglia in the UK a

randomized trial of 100 general practices was undertaken. The interventions were an educational package based on principles of 'academic detailing' with independent academics and were given in small practice-based interactive groups with a visual presentation, a printed evidence-based summary, a graphic management flow chart, and a follow-up meeting at 6 months. There were significantly fewer referrals (20% vs 29%; OR = 0.64; 95% CI 0.41–0.99) and a significantly higher use of tranexamic acid (OR = 2.38; 95% CI 1.61–3.49).

CONCLUSION

In January 2007 the National Institute for Health and Clinical Excellence published guidelines on heavy menstrual bleeding.⁷⁰ The guideline makes recommendations on a range of medical and surgical treatment treatment options. They recommended that treatments should be considered in the following order:

- (1) levonorgestrel-releasing intrauterine system provided long-term (at least 12 months) use is anticipated;
- tranexamic acid or non-steriodal anti-inflammatory drugs or combined oral contraceptives;
- (3) norethisterone (15 mg) daily from days 5 to 26 of the menstrual cycle, or injected long-acting progestogens.

What would suit an individual patient would of course depend on her contraceptive needs and fertility goals.

References

- Reid PC, Mukri F. Trends in number of hysterectomies performed in England for menorrhagia: examination of health episode statistics, 1989 to 2002-3. BMJ 2005; 330: 938–9.
- Reid PC. Endometrial ablation in England-coming of age? An examination of hospital episode statistics 1989/1990 to 2004/2005.
 Eur J Obstet Gynecol Reprod Biol 2006 Oct 11; [Epub ahead of print].
- Oehler MK, Rees MC. Menorrhagia: an update. Acta Obstet Gynecol Scand 2003; 82: 405–22.
- Rees MCP, Anderson ABM, Demers LM, Turnbull AC. Prostaglandins in menstrual fluid in menorrhagia and dysmenorrhoea. Br J Obstet Gynaecol 1984; 91: 673–80.
- Rees MCP, Anderson ABM, Demers LM, Turnbull AC. Endometrial and myometrial prostaglandin release during menstrual cycle in relation to menstrual blood loss. J Clin Endocrinol Metab 1984; 58: 813–18.
- Adelantado JM, Rees MCP, Lopez-Bernal A, Turnbull AC. Increased uterine prostaglandin E receptors in menorrhagic women. Br J Obstet Gynaecol 1988; 95: 162–5.

- 7. McGettigan P, Henry D. Cardiovascular risk and inhibition of cyclooxygenase: a systematic review of the observational studies of selective and nonselective inhibitors of cyclooxygenase 2. JAMA 2006; 296: 1633–44.
- Lethaby A, Augood C, Duckitt K. Nonsteroidal anti-inflammatory drugs for heavy menstrual bleeding. Cochrane Database Syst Rev 2000; 2: CD000400.
- 9. van Eijkeren MA, Christiaens GC, Geuze HJ, Haspels AA, Sixma JJ. Effects of mefenamic acid on menstrual hemostasis in essential menorrhagia. Am J Obstet Gynecol 1992; 166: 1419–28.
- Cameron IT, Haining R, Lumsden MA, Thomas VR, Smith SK. The effects of mefenamic acid and norethisterone on measured menstrual blood loss. Obstet Gynecol 1990; 76: 85–8.
- 11. Bonnar J, Sheppard BL. Treatment of menorrhagia during menstruation: randomised controlled trial of ethamsylate, mefenamic acid, and tranexamic acid. BMJ 1996; 313: 579–82.
- Fraser IS, McCarron G, Markham R, Robinson M, Smyth E. Long-term treatment of menorrhagia with mefenamic acid. Obstet Gynecol 1983; 61: 109–12.

- Milsom I, Andersson K, Andersch B, Rybo G. A comparison of flurbiprofen, tranexamic acid, and a levonorgestrel-releasing intrauterine contraceptive device in the treatment of idiopathic menorrhagia. Am J Obstet Gynecol 1991; 164: 879–83.
- Fraser IS, McCarron G. Randomized trial of 2 hormonal and 2 prostaglandin-inhibiting agents in women with a complaint of menorrhagia. Aust NZ J Obstet Gynaecol 1991; 31: 66–70.
- Andrade AT, Pizarro Orchard E. Quantitative studies on menstrual blood loss in IUD users. Contraception 1987; 36: 129–44.
- Guillebaud J, Anderson AB, Turnbull AC. Reduction by mefenamic acid of increased menstrual blood loss associated with intrauterine contraception. Br J Obstet Gynaecol 1978; 85: 53–62.
- 17. Roy S, Shaw ST Jr. Role of prostaglandins in IUD-associated uterine bleeding effect of a prostaglandin synthetase inhibitor (ibuprofen). Obstet Gynecol 1981; 58: 101–6.
- 18. Nygren KG, Rybo G. Prostaglandins and menorrhagia. Acta Obstet Gynecol Scand Suppl. 1983; 113: 101–3.
- Ylikorkala O, Viinikka L. Comparison between antifibrinolytic and antiprostaglandin treatment in the reduction of increased menstrual blood loss in women with intrauterine contraceptive devices. Br J Obstet Gynaecol 1983; 90: 78–83.
- Menorrhagia, Prodigy Guidance 2006. http://www.cks.library. nhs.uk/menorrhagia. accessed 06.11.2007.
- Cameron IT, Leask R, Kelly RW, Baird DT. The effects of danazol, mefenamic acid, norethisterone and a progesteroneimpregnated coil on endometrial prostaglandin concentrations in women with menorrhagia. Prostaglandins 1987; 34: 99–110.
- 22. Gleeson N, Devitt M, Sheppard BL, Bonnar J. Endometrial fibrinolytic enzymes in women with normal menstruation and dysfunctional uterine bleeding. Br J Obstet Gynaecol 1993; 100: 768–71.
- 23. Callender ST, Warner GT, Cope E. Treatment of menorrhagia with tranexamic acid. A double-blind trial. Br Med J 1970; 4: 214–16.
- Gleeson NC, Buggy F, Sheppard BL, Bonnar J. The effect of tranexamic acid on measured menstrual loss and endometrial fibrinolytic enzymes in dysfunctional uterine bleeding. Acta Obstet Gynecol Scand 1994; 73: 274–7.
- Edlund M, Andersson K, Rybo G et al. Reduction of menstrual blood loss in women suffering from idiopathic menorrhagia with a novel antifibrinolytic drug (Kabi 2161). Br J Obstet Gynaecol 1995; 102: 913–17.
- Lee JY, Hahn PM, Van Dijk JP, Reid RL. Treatment of menorrhagia with tranexamic acid. J Soc Obstet Gynaecol Can 2000; 22: 794–8.
- Lethaby A, Farquhar C, Cooke I. Antifibrinolytics for heavy menstrual bleeding. Cochrane Database Syst Rev 2000; 4: CD000249.
- Irvine GA, Cameron IT. Medical management of dysfunctional uterine bleeding. Baillières Best Pract Res Clin Obstet Gynaecol 1999; 13: 189–202.
- 29. Rydin E, Lundberg PO. Letter: tranexamic acid and intracranial thrombosis. Lancet 1976; 2: 49.
- Agnelli G, Gresele P, De Cunto M, Gallai V, Nenci GG. Tranexamic acid, intrauterine contraceptive devices and fatal cerebral arterial thrombosis. Case report. Br J Obstet Gynaecol 1982; 89: 681–2.
- Rybo G. Tranexamic acid therapy is effective treatment in heavy menstrual bleeding: clinical update on safety. Ther Adv 1991; 4: 1–8.

- 32. Westrom L, Bengtsson LP. Effect of tranexamic acid (AMCA) in menorrhagia with intrauterine contraceptive devices. J Reprod Med 1970; 5: 154–61.
- Chamberlain G, Freeman R, Price F et al. A comparative study of ethamsylate and mefenamic acid in dysfunctional uterine bleeding. Br J Obstet Gynaecol 1991; 98: 707–11.
- 34. Kasonde JM, Bonnar J. Effect of ethamsylate and aminocaproic acid on menstrual blood loss in women using intrauterine devices. Br Med J 1975; 4: 21–2.
- 35. Harrison RF, Cambell S. A double-blind trial of ethamsylate in the treatment of primary and intrauterine-device menorrhagia. Lancet 1976; 2: 283–5.
- Bishop PM, de Almeida JC. Treatment of functional menstrual disorders with norethisterone. Br Med J 1960; 1: 1103–5.
- 37. Haynes PJ, Anderson AB, Turnbull AC. Patterns of menstrual blood loss in menorrhagia. Res Clin Forums 1979; 1: 73–8.
- 38. Eldred JM, Thomas EJ. Pituitary and ovarian hormone levels in unexplained menorrhagia. Obstet Gynecol 1994; 84: 775–8.
- Lethaby A, Irvine G, Cameron I. Cyclical progestogens for heavy menstrual bleeding. Cochrane Database Syst Rev 2000; 2: CD001016.
- Irvine GA, Campbell-Brown MB, Lumsden MA et al. Randomised comparative trial of the levonorgestrel intrauterine system and norethisterone for treatment of idiopathic menorrhagia. Br J Obstet Gynaecol 1998; 105: 592–8.
- 41. Vasilakis C, Jick H, del Mar Melero-Montes M. Risk of idiopathic venous thromboembolism in users of progestagens alone. Lancet 1999; 354: 1610–1.
- 42. Fraser IS. Treatment of ovulatory and anovulatory dysfunctional uterine bleeding with oral progestogens. Aust NZ J Obstet Gynaecol 1990; 30: 353–6.
- 43. Kriplani A, Kulshrestha V, Agarwal N, Diwakar S. Role of tranexamic acid in management of dysfunctional uterine bleeding in comparison with medroxyprogesterone acetate. J Obstet Gynaecol 2006; 26: 673–8.
- 44. Belsey EM. Vaginal bleeding patterns among women using one natural and eight hormonal methods of contraception. Contraception 1988; 38: 181–206.
- Fraser IS. A survey of different approaches to management of menstrual disturbances in women using injectable contraceptives. Contraception. 1983; 28: 385–97.
- 46. Roy SN, Bhattacharya S. Benefits and risks of pharmacological agents used for the treatment of menorrhagia. Drug Saf 2004; 27: 75–90.
- Rees M, Purdie DW. Management of the Menopause: the Handbook, 4th edn. London: Royal Society of Medicine Press, 2006
- 48. Orr-Walker BJ, Evans MC, Ames RW et al. The effect of past use of the injectable contraceptive depot medroxyprogesterone acetate on bone mineral density in normal post-menopausal women. Clin Endocrinol (Oxf) 1998; 49: 615–18.
- Scholes D, LaCroix AZ, Ichikawa LE et al. Change in bone mineral density among adolescent women using and discontinuing depot medroxyprogesterone acetate contraception. Arch Pediatr Adolesc Med 2005; 159: 139–44.
- 50. Funk S, Miller MM, Mishell DR Jr et al; The Implanon US Study Group. Safety and efficacy of Implanon, a single-rod implantable contraceptive containing etonogestrel. Contraception 2005; 71: 319–26.
- Lethaby AE, Cooke I, Rees M. Progesterone or progestogenreleasing intrauterine systems for heavy menstrual bleeding. Cochrane Database Syst Rev 2005; 4: CD002126.

- Iyer V, Farquhar C, Jepson R. Oral contraceptive pills for heavy menstrual bleeding. The Cochrane Library 2000; 2: CD000154.
- 53. Ramcharan S, Pellegrin FA, Ray RM, Hsu JP. The Walnut Creek Contraceptive Drug Study. A prospective study of the side effects of oral contraceptives. Volume III, an interim report: a comparison of disease occurrence leading to hospitalization or death in users and nonusers of oral contraceptives. J Reprod Med 1980; 25: 345–72.
- Faculty of Family Planning and Reproductive Health Care, Clinical Effectiveness Unit. FFPRHC Guidance (October 2003): first prescription of combined oral contraception. J Fam Plann Reprod Health Care 2003; 29: 209–23.
- Middeldorp S. Oral contraceptives and the risk of venous thromboembolism. Gend Med 2005; 2(Suppl A): S3–9.
- Rees MC, Barlow DH. Quantitation of hormone replacement induced withdrawal bleeds. Br J Obstet Gynaecol 1991; 98: 106–7.
- Singh RH, Blumenthal P. Hormonal management of abnormal uterine bleeding. Clin Obstet Gynecol 2005; 48: 337–52.
- Need JA, Forbes KL, Milazzo L, McKenzie E. Danazol in the treatment of menorrhagia: the effect of a 1 month induction dose (200 mg) and 2 month's maintenance therapy (200 mg, 100 mg, 50 mg or placebo). Aust NZ J Obstet Gynaecol 1992; 32: 346–52.
- Bonduelle M, Walker JJ, Calder AA. A comparative study of danazol and norethisterone in dysfunctional uterine bleeding presenting as menorrhagia. Postgrad Med J 1991; 67: 833–6.
- Dockeray CJ, Sheppard BL, Bonnar J. Comparison between mefenamic acid and danazol in the treatment of established menorrhagia. Br J Obstet Gynaecol 1989; 96: 840–4.
- Chimbira TH, Anderson AB, Cope E, Turnbull AC. Preliminary results on clinical and endocrine studies in the treatment of menorrhagia with danazol. Postgrad Med J 1979; 55: 90–4.

- 62. Higham JM, Shaw RW. A comparative study of danazol, a regimen of decreasing doses of danazol, and norethindrone in the treatment of objectively proven unexplained menorrhagia. Am J Obstet Gynecol 1993; 169: 1134–9.
- 63. Turnbull AC, Rees MC. Gestrinone in the treatment of menorrhagia. Br J Obstet Gynaecol 1990; 97: 713–15.
- Sagsveen M, Farmer JE, Prentice A, Breeze A. Gonadotrophinreleasing hormone analogues for endometriosis: bone mineral density. Cochrane Database Syst Rev 2003; 4: CD001297.
- Chabbert-Buffet N, Meduri G, Bouchard P, Spitz IM. Selective progesterone receptor modulators and progesterone antagonists: mechanisms of action and clinical applications. Hum Reprod Update 2005; 11: 293–307.
- 66. Brown A, Cheng L, Lin S, Baird DT. Daily low-dose mifepristone has contraceptive potential by suppressing ovulation and menstruation: a double-blind randomized control trial of 2 and 5 mg per day for 120 days. J Clin Endocrinol Metab 2002; 87: 63–70.
- 67. Eisinger SH, Bonfiglio T, Fiscella K, Meldrum S, Guzick DS. Twelve-month safety and efficacy of low-dose mifepristone for uterine myomas. J Minim Invasive Gynecol 2005; 12: 227–33.
- 68. Kennedy AD, Sculpher MJ, Coulter A et al. Effects of decision aids for menorrhagia on treatment choices, health outcomes, and costs: a randomized controlled trial. JAMA 2002; 288: 2701–8.
- Fender GR, Prentice A, Gorst T et al. Randomised controlled trial of educational package on management of menorrhagia in primary care: the Anglia menorrhagia education study. BMJ 1999; 318: 1246–50.
- National Institute for Health and Clinical Excellence. Heavy menstrual bleeding investigation and treatment. Clinical guideline 44. London: NICE, January 2007. Also available at http:// www/nice.org.uk/guidance/cg44.

The levonorgestrel intrauterine system

Diana Mansour

INTRODUCTION

Since its launch, more than 9 million women worldwide have used the levonorgestrel IUS for contraception, as a treatment for heavy menstrual bleeding, and as the progestogen component of hormone replacement therapy (HRT). For women in their reproductive years, the IUS has become one of the most acceptable medical treatments for menorrhagia, reducing referrals to specialists and decreasing the need for operative gynecologic surgery.

This chapter outlines the development of the IUS, highlighting the most important recent areas of research covering its use to control menstrual blood loss and pain.

It has taken several millennia of experimentation with different intrauterine devices (IUDs) before the final development of the intrauterine system (IUS), the ideal contraceptive with additional non-contraceptive benefits. Hippocrates made the first reference to the use of IUDs and, over the centuries, numerous materials have been tried, including wood, glass, pewter, ivory, ebony, gold, and wool. In 1909, Richter developed a ring-shaped device made of silkworm and Grafenberg modified the device by covering the silkworm ring with silver wire.

By the early 1960s, inert plastic IUDs, such as the Lippes loop and Saf-T-Coil, were introduced. These large plastic devices were more suitable for multiparous women but caused users to complain of increased dysmenorrhea and menorrhagia. With their replacement by the smaller medicated IUDs containing copper, side effects were decreased but complaints related to menstrual bleeding and pain remain, with about 8% of women citing these as the major reason for discontinuation at 3 years of this contraceptive method.¹

Professor Tapani Luukkainen invented the levonorgestrel IUS in the 1970s. The Population Council backed its development and Bayer Schering Pharma now markets it as Mirena. It was known that continuous administration of progestogens, both orally or by injection, reduced menstrual blood loss and provided effective contraception; however, reports of hormonal side effects along with menstrual irregularity were common. Delivering a progestogen locally within the uterine cavity could potentially increase contraceptive efficacy and decrease bleeding days compared to copper IUDs, with little systemic absorption of hormone.

DESCRIPTION OF THE INTRAUTERINE SYSTEM

Pharmacokinetics of the intrauterine system

The IUS has a similar shape to the Nova-T 380 copper IUD with the vertical stem containing a mixture of 52 mg of levonorgestrel and polydimethylsiloxane (PDMS) surrounded by a rate-controlling PDMS capsule. The total length of the system is 32 mm, with the T-shaped plastic frame impregnated with barium sulfate, making the device radiopaque. Two threads are attached to the loop at the base of the IUS, which aids removal (Figure 12.1).²

This system allows a steady, local release of 20 µg of levonorgestrel per day, initially giving few systemic side effects (approximately the equivalent of taking two progestogen-only pills a week). There is rapid absorption of locally released levonorgestrel from the uterine cavity, via the capillary network in the basal layer of the endometrium into the systemic circulation. Levonorgestrel can be detected in the circulation within 15 minutes of insertion, reaching maximum plasma levels within a few hours. Plasma hormone concentrations plateau within a month (0.4–0.6 nmol/L) and are far lower than those seen with contraceptive implants or progestogen-only contraceptive pills. The initial release rate of levonorgestrel falls to 11 µg/day at the end of 5 years.²

Initially, it was discovered that local release of levonorg-estrel from a prototype IUS (delivering 30 μ g/day) resulted in high concentrations of hormone in the endometrial tissue (470–1500 ng/g), but this fell to 1.8–2.4 ng/g in the myometrium or fallopian tube, and 0.1–0.2 ng/ml in the plasma.³ For comparison, intrauterine concentrations of levonorgestrel with the IUS are 1000 times higher than

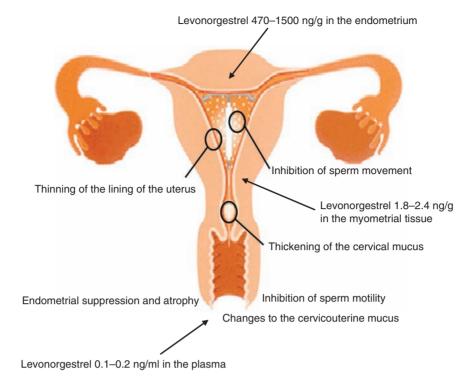


Figure 12.1 The levonorgestrel intrauterine system.

with a levonorgestrel subdermal implant.³ This high concentration of levonorgestrel in the endometrium induces dramatic effects, leading to the unique mode of contraceptive and therapeutic action of the IUS.

Mode of action

Levonorgestrel is derived from 19-nortestosterone; it is a very suitable choice for a small intrauterine system, as it is highly progestational and therefore pharmacologically active at low doses. Locally released levonorgestrel from the IUS alters the cervical mucus and uterotubal fluid, which inhibits sperm migration. It adversely affects sperm motility and function inside the genital tract, preventing fertilization.² There is strong suppression and atrophy of the endometrium, with the stroma becoming swollen and decidual, the mucosa thinning, and the epithelium becoming inactive. Vascular changes also occur with a decrease in mean vascular density but an increase in mean vessel area.⁴

The IUS can suppress ovulation in some women in the first year by possibly reducing the preovulatory luteinizing hormone surge. Most cycles from the second year onwards are ovulatory. This suppressive effect depends on plasma levonorgestrel levels, with marked differences noted between users. However, there is no reduction in plasma estradiol levels during use of the IUS, and the presence or absence of menstrual bleeding does not reflect ovarian activity.²

PRACTICAL ASPECTS OF THE INSERTION AND REMOVAL PROCESS

Insertion

All health professionals providing an intrauterine contraceptive service should receive formal tuition in IUD/IUS insertion and removal and in management of common problems. Careful patient selection will ensure high acceptability and long-term continuance.

The IUS is broader than some copper IUDs such as the Nova-T 380. It measures 4.5 mm in its insertion tube and therefore local anesthesia and dilatation of the cervical canal may be necessary in some nulliparous or perimenopausal woman. The IUS inserter has been modified to enable single-handed insertion and fundal placement. Successful positioning of the IUS is important to ensure uniform exposure of the endometrium to levonorgestrel, improving its efficacy, and to reduce expulsion.

It is recommended that the IUS be inserted within the first 7 days of the menstrual cycle although not during the days of heaviest loss when expulsion is more likely. No additional contraceptive precautions are necessary. It can also be replaced any time during the cycle. If a copper IUD is already in place and the IUS is to be inserted outside of the first 7 days, abstinence/use of a barrier method of contraception for the previous 7 days is advised and continued for the next 7 days after the IUS has been fitted. Insertion of the IUS can take place at any time during the

cycle in women using a hormonal method of contraception or if there is no risk of pregnancy. It is important to remember that, unlike copper IUDs, there are no data to support the use of the IUS as an emergency form of contraception.⁵

The IUS can be inserted immediately after a miscarriage or surgical termination of pregnancy without an increase in side effects.⁵ Postnatally, the insertion of the IUS should be delayed to 6 weeks to reduce the incidence of problematic prolonged bleeding and any potential adverse effects for the baby if the woman is breast-feeding.⁶

Post insertion effects

Following insertion of an IUS, women frequently complain of menstrual disturbance. Approximately 17% of women will complain of prolonged bleeding (>8 days) in the first month of use, with this falling to 3% at month 3.² Recent evidence also suggests that this takes longer to settle in women with heavy menstrual loss (6 months on average).⁷ Some women need to be reassured about the lack of menstruation when using an IUS. Approximately 17% will be amenorrheic at 1 year, with this increasing to 60% in some long-term users.⁸

Although the IUS releases levonorgestrel locally within the uterine cavity, systemic absorption via the capillary network in the basal layer of the endometrium leads to steady plasma levels of 0.4–0.6 nmol/L after the first few weeks.² There is a gradual decline in plasma levonorgestrel levels over time but plasma levels are maintained even up to 72 months following insertion.² For most women this causes few problems, with studies showing that at 1 year between 1 and 2 women out of every 100 will discontinue using the IUS because of hormonal side effects.^{9,10} These progestogenic symptoms are often transient and include mood change, nausea, headache, bloating, breast tenderness, fluid retention, and skin problems.^{8,9}

Removal

The IUS is easily removed by grasping the threads with forceps and gently pulling. It is advisable to remove an IUS at the time of a period in women of reproductive age. Not only will it be easier at this time but it will also reduce the chance of an iatrogenic unplanned pregnancy. If the IUS is removed at any other time and pregnancy is not desired, advice to avoid sexual intercourse for 7 days before removal should be given. Occasionally, the IUS threads are not visible at the external os. Long-handled Spencer Wells forceps may locate the threads if they are within the cervical canal. If this fails, an ultrasound scan will locate the device and IUD retrieval forceps are used to remove the IUS from the uterine cavity.

IN-VITRO AND IN-VIVO STUDIES

At the beginning of the 1970s work began to investigate a progestogen-releasing IUD to provide effective contraception but decrease uterine contractility associated with IUDs and therefore reduce expulsion. Investigators initially developed Progestasert, an IUS delivering progesterone (65 µg/day). This device, however, required replacement every 12 months and was associated with an increased risk of ectopic pregnancies. Other progestogens, such as norethisterone were tried but success was only achieved when Tapani Luukkainen started to consider intrauterine placement of levonorgestrel, within a silastic polymer, as an alternative to subdermal contraceptive implants. A biodegradable polylactate polymer was tested first but its release mechanism was variable. Levonorgestrel was then mixed with silastic and placed in a sleeve around the horizontal arms of a T-shaped plastic device. It proved to be an effective contraceptive, releasing hormone rapidly and causing ovulation suppression. It was also found to be effective when subjects began to ovulate again; however, it was not commercially viable, as it required frequent replacement. Following dose-finding studies and the transfer of the steroid reservoir to the vertical stem of a plastic Nova-T frame, a silastic sheath was added to cover the hormone reservoir, providing a sustained, steady release of levonorgestrel. The modern-day commercial IUS was born.11

CLINICAL STUDIES

Contraception

The IUS is licensed to provide highly effective contraception for a 5-year period with efficacy rates similar to tubal occlusion. One paper quotes a cumulative 7-year pregnancy rate of 1.1%;¹² however, the device studied contained 60 mg of levonorgestrel as against the 52 mg of hormone in the commercially marketed device, Mirena. Recent guidance from the National Institute for Health and Clinical Excellence (NICE) on 'Long-acting reversible contraception' gives a failure rate of less than 10 in 1000 women over 5 years.¹ The IUS is equally effective for all age groups of women, with occasional pregnancies occurring owing to unrecognized expulsion of the device.⁹ It is a very acceptable and immediately reversible contraceptive with 3-year continuation rates of 75–82%.⁵

The levonorgestrel IUS is highly effective but if it fails in situ there is a risk of about 1 in 20 of these pregnancies being ectopic. However, it should be remembered that this risk is far lower in IUS users than in women using no contraceptive method (when the incidence is 1.4 per

100 women).¹ Overall, it is estimated that the incidence of ectopic pregnancy in IUS users is about 1 in 1000 over a 5-year period.¹Recent guidance has also supported the use of the IUS in women who have previously suffered an ectopic pregnancy because using such a highly effective contraceptive will reduce their future absolute risk.¹³

Menorrhagia (including adenomyosis and fibroid-related)

From the very first studies, researchers found both the progesterone-releasing IUD and levonorgestrel IUS reduced menstrual blood flow in women. As early as 1982, Heikkila et al. showed that serum ferritin levels increased in IUS users with normal menstrual blood loss¹⁴ and hemaglobin has also been found to rise in these women who complain of menorrhagia.¹⁵

In 1990, 20 women with objectively measured menorrhagia had an IUS inserted. After 3 months, measured blood loss was reduced by 86% and at 12 months by 97%.16 In 1991, Milsom and co-authors investigated the use of the non-steroidal anti-inflammatory drug (NSAID) flurbiprofen, with the antifibrinolytic agent tranexamic acid and the IUS in women with menorrhagia.¹⁷ At 3 months, the reduction in menstrual blood (a percentage of the mean of two control cycles) was 20.7% for flurbiprofen, 44.4% for tranexamic acid, and 81.6% for the IUS (95.8% by 12 months). The IUS was the only therapy to bring women's mean menstrual blood loss back to within normal range (<80 ml per menstruation). More recent evidence shows that in women with heavy menstrual blood loss the IUS can normalize blood flow, with up to 35% of women being amenorrheic at 24 months. 18 When compared with mefenamic acid, another NSAID, in a six-cycle randomized study, the IUS reduced the median menstrual blood loss to just 5 ml in women with idiopathic menorrhagia (100 ml in the mefenamic acid arm).19 The IUS also appears to be the most effective treatment when compared to other medical therapies used for heavy menstrual blood loss. A three-cycle randomized study compared the IUS with norethisterone (5 mg three times a day from day 5 to day 26 of the cycle). The authors reported that menstrual blood flow was reduced in both groups (94% in the IUS group and 87% in the oral norethisterone group) but only 22% of women wished to continue treatment in the norethisterone arm compared to 76% of women using the IUS.²⁰

In the late 1990s, evidence was accumulating to suggest that the IUS was a safe and effective medical alternative to surgery for the treatment of heavy menstrual blood loss. In one paper, 82% of women fitted with an IUS decided against major surgery for menorrhagia²¹ and in a 6-month randomized open study 64.3% of women with

menorrhagia treated with an IUS compared with 14.3% of controls cancelled their hysterectomy.²² In a 5-year randomized control study, investigating clinical outcomes and costs with the IUS vs hysterectomy for treatment of menorrhagia, 42% of women assigned to the IUS group eventually underwent hysterectomy. However, when direct and indirect costs were calculated, use of the IUS was cheaper than hysterectomy.²³ Health-related quality of life and psychosocial well-being were similar in the two groups.²³

Endometrial resection or ablation has become more popular over the last 15 years. Recovery rates following surgery are far quicker and hospital stay shorter than with hysterectomy. How does the IUS compare with this form of minimally invasive surgery? One of the first papers published on this subject was by Crosignani and colleagues who randomized women to either an endometrial resection or IUS to control their heavy menstrual bleeding.24 At 12 months, the pictorial blood loss assessment chart (PBAC) score was reduced by 79% in the IUS users and by 89% in those women who had undergone a resection. Amenorrhea or infrequent bleeding was reported by 65% of women using the IUS intrauterine device compared with 71% who underwent a resection. Satisfaction was high in both groups, with no significant difference in health-related quality-of-life scores.²⁴ Similar results have been achieved when the IUS and endometrial resection are studied over a 3-year treatment period. In one study, PBAC scores decreased from a baseline median of 261.5 to 7 (p <0.001) for the IUS and from 311 to 4 (p <0.001) for transcervical resection of the endometrium. Sixtythree percent of women using the IUS and 76% of those undergoing a resection completed the study.²⁵ The IUS has also been shown to be equally effective as thermal balloon ablation over a 6-month²⁶ and 24-month study period in European women.¹⁸ However, one paper comparing thermal balloon endometrial ablation (TBEA) with the IUS in a Chinese population of women with menorrhagia over 12 months suggested that mean hemoglobin levels and general/mental health evaluation scores were significantly higher in women treated with TBEA.²⁷

Very recently, a Cochrane systematic review appraised the literature and concluded that:

surgery, especially hysterectomy, reduces menstrual bleeding at one year more than medical treatments but IUS appears equally effective in improving quality of life. The evidence for longer-term comparisons is weak and inconsistent. Oral medication suits a minority of women long term.²⁸

There are data indicating that about 13% of women complaining of heavy menstrual blood loss suffer from von Willebrand's disease, a disorder of hemostasis.

A study investigating the effect of the IUS on hemostatic and fibrinolytic/inhibitor systems in women with menorrhagia has demonstrated high expression of fibrinolytic inhibitors (plasminogen activator inhibitor 1 and 2) and up-regulated urokinase-type plasminogen activator receptor expression in the endometrium, although systemic hemostasis was not significantly altered.²⁹ This may explain why the IUS successfully treats heavy menstrual blood loss where there is known pathologic causes, including inherited bleeding disorders.³⁰

There is some evidence to suggest that long-term use of the IUS may reduce the number of women presenting with fibroid-related problems and need for fibroid-related surgery.³¹ There are also reports indicating that the IUS reduces menstrual blood loss, with a resultant rise in serum ferritin and hemaglobin in women with fibroids, but these effects are variable and dependent on initial fibroid size/position and menstrual blood loss. Although uterine size and fibroid volume is reduced in some women, the IUS has no effect in a significant minority of women.

In the study of Grigorieva et al., women with fibroids (but not necessarily menorrhagia) were recruited from a family planning unit. An IUS was fitted and mean PBAC scores declined from 97 to 16 (p < 0.001) over 12 months.³² A second study recruited women with menorrhagia who had at least one type II myoma according to the European Society of Hysteroscopy but a uterine volume of <380 ml. Following IUS insertion, statistically significant decreases in menstrual blood flow and increases in hemoglobin levels were found.33 A third study recruited women with recurrent fibroid-related menorrhagia lasting more than 3 months. The median monthly PBAC score for two menstrual cycles before treatment was 310 (much higher than in other studies investigating the IUS in fibroid-related menorrhagia). The PBAC score fell to 186 at 3 months post-IUS insertion, 155 at 6 months, 108 at 9 months, and 96 at 12 months of treatment. Heavy menstrual blood loss (PBAC score >100) was still seen in 74% of patients.34 Finally, in a fourth study, 10 women with uterine myomas and increased menstrual bleeding had an IUS inserted. Two women expelled the device and one dropped out of the study as a treatment failure. The seven remaining women had amenorrhea or oligomenorrhea at 6 months and their hematocrit/hemoglobin levels normalized. However, there was no observed reduction in uterine volume or flow velocity assessed by the uterine artery pulsatility index and the series resistance index.³⁵ Therefore, the IUS may be used successfully to treat fibroid-related menorrhagia in the majority of women without necessarily reducing uterine volume.

The IUS may significantly reduce menstrual blood loss in women with adenomyosis-related menorrhagia,

although more studies are required this area.³⁶ The IUS may also be a useful adjuvant therapy following endometrial resection to help adenomyosis-related menorrhagia. In a study of 95 women, those randomized to receiving an IUS following endometrial resection had a higher rate of amenorrhea, with no women requiring further surgery. In the control arm, 19% of women underwent a second procedure.³⁷

Endometriosis

The prevalence of dysmenorrhea and endometriosis is unknown. It is thought that approximately 50% of women in the UK will at some stage complain of moderately painful periods. Endometriosis occurs more frequently among women being investigated for infertility (21%) but still occurs in 'well women' undergoing sterilization (6%).³⁸

The IUS has been shown to reduce dysmenorrhoea in the general population, with one study reporting that menstrual pain fell from 60% before IUS insertion to 29% after 36 months of use.³⁹ The IUS may also be a useful medical treatment for women suffering from endometriosis-related problems, with significant improvements in severity and frequency of pain/menstrual symptoms found in users.

An initial study enrolled women with recurrent dysmenorrhea following conservative surgery for endometriosis.40 The women agreed to have an IUS inserted and, over the next 12 months, reported a significant reduction in blood loss and pain, with 75% of women satisfied or very satisfied. 40 Two other small, non-comparative, studies also suggested that the IUS helped to alleviate pain at 6 and 12 months^{41,42} and improved the disease staging⁴¹ as well as reducing the size of lesions in patients with rectovaginal endometriosis. 42 Other data suggest an improvement in the disease, with CA-125 (a marker for endometriosis) falling over a 6-month period in women using an IUS or treated with a gonadotropin-releasing hormone (GnRH) analogue.43 In one of these studies, however, the 3-year IUS continuation rate was 56%, with most women discontinuing in the first 12 months, citing irregular bleeding and/or persistent pain as the reason for stopping therapy. 44

The first randomized study recruited women with moderate to severe dysmenorrhea after conservative surgery for endometriosis. When assessed 12 months later, moderate or severe dysmenorrhea recurred in 10% of women fitted with an IUS postoperatively compared with 45% in the expectant treatment group. Seventy five percent of women in the IUS group and 50% in the expectant management group were satisfied or very satisfied with the treatment received.⁴⁵

More recently a 6-month multicenter randomized controlled trial (RCT) compared the IUS with a depot GnRH analogue for controlling endometriosis-related

pain. Eighty-two women, aged 18-40 year old suffering from endometriosis and complaining of dysmenorrhea and/or chronic pelvic pain were randomized to receiving the IUS or GnRH analogue. Both therapies significantly reduced chronic pelvic pain from the first month onwards and there was no difference between the groups. In both treatment groups, women with severe endometriosis showed a more rapid improvement in the pain scores than women with stage I or II of the disease. However, women using the IUS had a higher bleeding score throughout the 6-month study at all time points of observation, with only 34% of IUS users being bleed-free in the first month compared to 71% of patients in the GnRH analogue group.46 By 6 months, 70% of IUS users and 98% of those receiving a GnRH analogue reported no bleeding, with both therapies improving quality of life to a similar extent. The reporting of sideeffects was similar for both treatment modalities, with IUS users more likely to report breast tenderness at months 2 and 6.46

Why does the IUS improve endometriosis-related pain? This question has been asked by many, but the answer is still elusive. It is known that systemic and local progestogens reduce the expression of estrogen and progestogen receptors within the endometrium. This action may alter the production of local tissue factors and block endometrial DNA synthesis and mitotic activity, leading to endometrial atrophy in eutopic endometrium, but what about ectopic endometrium? Surely there needs to be sufficient circulating progestogen to suppress ovulation before ectopic endometrium is affected, or perhaps there needs to be high levonorgestrel levels within the peritoneal cavity? A small study showed that women who reported an improvement of endometriosis-related symptoms 6 months after having an IUS fitted had higher peritoneal fluid levels of levonorgestrel (approximately two-thirds the serum levels). 47 We also know that up to 85% of women using the IUS are anovulatory at 3 months but most are ovulating after 1 year; therefore, I am unsure that this successfully explains why the IUS continues to be beneficial at 12 months or more of use.

Finally, a Cochrane systematic review in 2006 concluded that there is initial evidence from one RCT meeting their criteria⁴⁵ that:

postoperative use of the IUS reduces the recurrence of painful periods in women who have had surgery for endometriosis. However there is a need for further well designed RCTs of this approach.⁴⁸

If long-term RCTs prove that the IUS equals other conventional medical therapies for endometriosis, the additional advantages of a treatment potentially lasting 5 years with one device, having a proven contraceptive action and no hypo-estrogen adverse effects, would make it a popular choice for disease sufferers.

Endometrial hyperplasia

The authors of a paper published in 1979 stated that local administration of progestational agents for the treatment of adenomatous hyperplasia of the endometrium was unwise as such a device would not reach the total surface of the endometrium or the deeper layers of the endometrium.⁴⁹ However by 1982 a progesterone intrauterine device had successfully treated 23 out of 25 women with cystic endometrial hyperplasia⁵⁰ and further papers followed suggested that framed and frame-less levonorgestrel intrauterine systems might cause regression of endometrial hyperplasia.

The first paper comparing intrauterine and oral progestogen therapy for endometrial hyperplasia was published in 2003. An historic group of women treated with 10 mg of medroxyprogesterone acetate for 10 days per cycle were compared with 26 women receiving an IUS over a 3-month treatment period. All women receiving an IUS had regression of their disease compared with 14 of 31 women taking oral therapy, with those having the highest malignant potential benefiting most from local intrauterine levonorgestrel.⁵¹ Further studies have investigated cell apoptosis and down-regulation of estrogen and progesterone receptors in women with endometrial hyperplasia. 52,53 It was shown that progestogens regulate the apoptotic cascade and completely down-regulate progesterone receptor expression in endometrial glands and stroma, with considerable downregulation of estrogen receptor expression. This effect was markedly more pronounced when levonorgestrel was administered locally via an IUS. 52,53

These initial results suggest that the IUS has the potential to treat early stage 1 endometrial cancers. However, caution is advised as a small case series showed that only one of four women with stage 1 grade 1 progesterone receptor positive endometrial adenocarcinoma had complete histologic regression of disease within 6 months and one had no response, with superficial myometrial invasion found at the time of surgery. There have also been several case reports in the literature of women with an endometrial adenocarcinoma diagnosed after the fitting of an IUS. This emphasizes the importance of appropriately investigating women with heavy menstrual bleeding before an IUS is inserted.

COMPLICATIONS

Expulsion of the IUS, be it partial or complete, can occur at any time after insertion, but the commonest time is at the first postinsertion menses.

Both expulsion and uterine perforation rates are dependent on the skill of the attendant healthcare professional, with national guidance advising staff to undertake a recognized supervised training program and to continue to regularly fit these devices. In such circumstances the risk of uterine perforation and translocation of the IUS is less than 1 in 1000 fittings. Expulsion should also be low, occurring in about 1 in 20 women over a 5-year period. 1

Initial plasma levonorgestrel levels may disrupt ovulation, delaying follicular atresia and resulting in the development of enlarged follicles in about 12% of women with an IUS.² These simple 'ovarian cysts' occasionally cause pelvic pain or dyspareunia but surgical treatment is rarely needed and the majority (94%) resolve spontaneously over 6 months of observation.⁵⁵

The IUS requires changing every 5 years, with some women finding the procedure invasive and the fitting painful. One randomized study investigating the use of the IUS vs oral contraceptives in nulliparous women found that 64.9% of IUS users complained of mild-to-moderate pain at insertion.⁵⁶ At 12 months, pelvic pain was more likely to be reported in IUS users, with approximately 54% of IUS users reporting abdominal/back pain compared with 40% in the oral contraceptive group.⁵⁶

The risk of developing pelvic inflammatory disease (PID) associated with use of the IUS is low (<1 woman per 100 who are at low risk of sexually transmitted infections [STIs]. Opportunistic screening for chlamydia should be considered prior to inserting an IUS, particularly in women with risk factors for STIs, as uterine instrumentation may reactivate or disseminate the infection. Evidence suggests that the risk of PID is greatest within the first 20 days post IUD/IUS insertion. 5

COSTS

Health service commissioners need to allocate resources effectively, making best use of government and taxpayers' money. As healthcare providers, we are often challenged regarding the 'up-front' costs of providing long-acting reversible contraceptive methods compared to permanent contraceptive options or surgical treatments for heavy menstrual bleeding. Are there any published studies investigating the cost-effectiveness of the IUS in these two clinical areas? There are a small number of studies, but caution is advised when interpreting the findings, as these economic models are based on local costs and an individual country's healthcare provision.

It is known that a small increase in the use of more effective contraceptive methods will improve health, by

preventing gynecologic ill-health, and reduce costs.⁵⁷ Recently, a UK cost-effectiveness analysis was performed.¹ There were some limitations to the model highlighted by the authors, including the exclusion of costs for potential contraceptive side effects, non-contraceptive benefits, and quality-of-life changes. However, the overall conclusions suggested that all long-acting reversible contraceptives are more cost-effective than using oral contraception or condoms even at 1 year – with the IUD, IUS, and implant more cost-effective than injectables.

In an RCT enrolling 236 Finnish women, the health outcomes, quality of life issues, and costs of providing the IUS to treat women with heavy menstrual loss was compared to hysterectomy. The trial participants were monitored for 5 years and both groups were satisfied with their treatment and had a similar improvement in quality of life and psychosocial well-being. When all costs were calculated, including the surgical costs of those women who requested hysterectomy in the IUS group, there was a substantial saving. In those women randomized to receiving the medical treatment, the cost was US\$2817 per participant compared with US\$4660 for those in the hysterectomy group.²³

In New Zealand, a cost-effective analysis comparing the IUS with thermal balloon ablation for the treatment of heavy menstrual bleeding, based on a prospective randomized trial, reported that the IUS appeared more costeffective.58 More recently, a detailed cost analysis investigating hysterectomy, endometrial resection/ablation, the IUS, and oral medical therapy for the management of menorrhagia was performed. The authors used clinical inputs estimated from the medical literature, and the cost analysis was conducted from the perspective of healthcare provision in Hong Kong. They concluded that hysterectomy appears to be the most cost-effective treatment for managing menorrhagia in Hong Kong.⁵⁹ However, a similar analysis was undertaken using US data, with the IUS being the most cost-effective therapy for 'dysfunctional uterine bleeding'.60

CONCLUSIONS

There is no doubt that the IUS is an effective medical treatment for heavy menstrual bleeding; it is now being advocated as the medical treatment of first choice. ⁶¹ It has the advantage of offering additional contraception and treatment 'reversibility' unlike endometrial ablation or hysterectomy. However, women with heavy menstrual blood loss should be actively involved when treatment decisions are being made. Careful preinsertion counseling will improve IUS continuation rates and patient satisfaction.

As healthcare professionals, we should also be aware of the enormous potential for the IUS to help prevent gynecologic disease. Increasing the provision of the IUS as a long-acting reversible method of contraception and offering alternative contraceptive choice at the time of female sterilization will reduce gynecologic intervention long term. In Newcastle-upon-Tyne, where primary and secondary care work closely together, the number of hysterectomies has fallen by over 50% and female sterilization procedures by 75% in the last 10 years. This has been achieved by increasing provision of the long-acting hormonal contraceptive methods, particularly the IUS (Figure 12.2).

Main clinical points

- All health professionals fitting the IUS should receive formal tuition in correct insertion, removal, and management of common problems.
- Careful patient selection and explanation of nuisance side effects will ensure high acceptance of the IUS and long-term continuance.
- Women with heavy menstrual blood loss should be appropriately investigated before an IUS is fitted.
- The levonorgestrel IUS is one of the most effective medical treatments for heavy menstrual bleeding and should be first choice for women requiring contraception but who have not completed their family.
- Approximately 12% of IUS users will develop enlarged follicles in the first year of use, but 94% of these will resolve at 6 months.

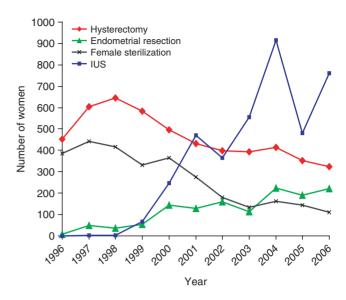


Figure 12.2 Fall in gynecology surgery with associated rise in use of the IUS in Newcastle-upon-Tyne, UK.

Research agenda

- More research is required to investigate the causes and effective treatment of the irregular uterine bleeding that occurs in some IUS users.
- Long-term studies comparing the IUS to surgical treatments for controlling heavy menstrual blood loss are required.
- Long-term comparative studies are required to confirm the efficacy of the IUS in endometriosis sufferers.
- Comparative, prospective studies are required to explore the use of the IUS in women with endometrial hyperplasia.

References

- National Institute for Health and Clinical Excellence. Longacting reversible contraception: NICE clinical guideline 30, developed by the National Collaborating Centre for Women's and Children's Health, London, 2005.
- Product Monograph, Mirena, 5th edn. Finland: Schering AG and Leiras Oy, 2002.
- 3. Nilsson CG, Haukkamaa M, Vierola H, Luukkainen T. Tissue concentrations of levonorgestrel in women using a levonorgestrel-releasing IUD. Clin Endocrinol (Oxf) 1982; 17: 529–36.
- 4. Jondet M, Letellier B, Verdys MT. Endometrial vascularization in levonorgestrel intrauterine device users; computerized microvessel measurement study. Contraception 2005; 7: 60–4.
- Faculty of Family Planning and Reproductive Health Care Clinical Effectiveness Unit. FFPRHC Guidance (April 2004). The

- levonorgestrel-releasing intrauterine system (LNG-IUS) in contraception and reproductive health. J Fam Plann Reprod Health Care 2004; 30: 99–108.
- Shaamash AH, Sayed GH, Hussien MM, Shaaban MM. A comparative study of the levonorgestrel-releasing intrauterine system Mirena versus the Copper T380A intrauterine device during lactation: breast-feeding performance, infant growth and infant development. Contraception 2005; 72: 346–51.
- Ibraheim M, Ikomi A. An evaluation of troublesome inter-menstrual bleeding in menorrhagic users of the LNG-IUS. J Obstet Gynaecol 2005; 25: 384–5.
- 8. Ronnerdag M, Odlind V. Health effects of long-term use of the intrauterine levonorgestrel-releasing system. A follow-up study over 12 years of continuous use. Acta Obstet Gynecol Scand 1999; 78: 716–21.

- Andersson K, Odlind V, Rybo G. Levonorgestrel-releasing and copper-releasing (Nova T) IUDs during five years of use: a randomized comparative trial. Contraception 1994; 49: 56–72.
- Dubuisson JB, Mugnier E. Acceptability of the levonorgestrelreleasing intrauterine system after discontinuation of previous contraception: results of a French clinical study in women aged 35 to 45 years. Contraception 2002; 66: 121–8.
- 11. Luukkainen T. The levonorgestrel-releasing IUD. Br J Fam Plann 1993; 19: 221–4.
- 12. Sivin I, Stern J, Coutinho E et al. Prolonged intrauterine contraception: a seven-year randomized study of the levonorgestrel 20 mcg/day (LNg 20) and the Copper T380 Ag IUDS. Contraception 1991; 44: 473–80.
- The UK Medical Eligibility Criteria for Contraceptive Use (UKMEC 2005/2006). Faculty of Family Planning and Reproductive Health Care, London, July 2006. www.ffprhc.org.uk accessed on 25.9.2006.
- Heikkila M, Nylander P, Luukkainen T. Body iron stores and patterns of bleeding after insertion of a levonorgestrel- or a copper-releasing intrauterine contraceptive device. Contraception 1982; 26: 465–74.
- Xiao B, Wu SC, Chong J et al. Therapeutic effects of the levonorgestrel-releasing intrauterine system in the treatment of idiopathic menorrhagia. Fertil Steril 2003; 79: 963–9.
- Andersson JK, Rybo G. Levonorgestrel-releasing intrauterine device in the treatment of menorrhagia. Br J Obstet Gynaecol 1990; 97: 690–4
- 17. Milsom I, Andersson K, Andersch B, Rybo G. A comparison of flurbiprofen, tranexamic acid, and a levonorgestrel-releasing intrauterine contraceptive device in the treatment of idiopathic menorrhagia. Am J Obstet Gynecol 1991; 164: 879–83.
- Busfield RA, Farquhar CM, Sowter MC et al. A randomised trial comparing the levonorgestrel intrauterine system and thermal balloon ablation for heavy menstrual bleeding. BJOG 2006; 113: 257–63.
- 19. Reid PC, Virtanen-Kari S. Randomised comparative trial of the levonorgestrel intrauterine system and mefenamic acid for the treatment of idiopathic menorrhagia: a multiple analysis using total menstrual fluid loss, menstrual blood loss and pictorial blood loss assessment charts. BJOG 2005; 112: 1121–5.
- Irvine GA, Campbell-Brown MB, Lumsden MA et al. Randomised comparative trial of the levonorgestrel intrauterine system and norethisterone for treatment of idiopathic menorrhagia. Br J Obstet Gynaecol 1998; 105: 592–8.
- 21. Barrington JW, Bowen-Simpkins P. The levonorgestrel intrauterine system in the management of menorrhagia. Br J Obstet Gynaecol 1997; 104: 614–16.
- Lahteenmaki P, Haukkamaa M, Puolakka J et al. Open randomised study of use of levonorgestrel releasing intrauterine system as alternative to hysterectomy. BMJ 1998; 316: 1122–6.
- 23. Hurskainen R, Teperi J, Rissanen P et al. Clinical outcomes and costs with the levonorgestrel-releasing intrauterine system or hysterectomy for treatment of menorrhagia: randomized trial 5-year follow-up. JAMA 2004; 291: 1456–63.
- Crosignani PG, Vercellini P, Mosconi P et al. Levonorgestrelreleasing intrauterine device versus hysteroscopic endometrial resection in the treatment of dysfunctional uterine bleeding. Obstet Gynecol 1997; 90: 257–63.
- 25. Rauramo I, Elo I, Istre O. Long-term treatment of menorrhagia with levonorgestrel intrauterine system versus endometrial resection. Obstet Gynecol 2004; 104: 1314–21.

- Barrington JW, Arunkalaivanan AS, Abdel-Fattah M. Comparison between the levonorgestrel intrauterine system (LNG-IUS) and thermal balloon ablation in the treatment of menorrhagia. Eur J Obstet Gynecol Reprod Biol 2003; 108: 72–4.
- Tam WH, Yuen PM, Shan Ng DP et al. Health status function after treatment with thermal balloon endometrial ablation and levonorgestrel intrauterine system for idiopathic menorrhagia: a randomized study. Gynecol Obstet Invest 2006; 62: 84–8.
- Marjoribanks J, Lethaby A, Farquhar C. Surgery versus medical therapy for heavy menstrual bleeding. Cochrane Database Syst Rev 2006; (2): CD003855.
- 29. Koh SC, Singh K. The effect of levonorgestrel-releasing intrauterine system use on menstrual blood loss and the hemostatic, fibrinolytic/inhibitor systems in women with menorrhagia. J Thromb Haemost 2007; 5: 133–8.
- 30. Kingman CE, Kadir RA, Lee CA, Economides DL. The use of levonorgestrel-releasing intrauterine system for treatment of menorrhagia in women with inherited bleeding disorders. BJOG 2004; 111: 1425–8.
- Sivin I, Stern J. Health during prolonged use of levonorgestrel 20 micrograms/d and the copper TCu 380Ag intrauterine contraceptive devices: a multicenter study. International Committee for Contraception Research (ICCR). Fertil Steril 1994; 61: 70–7.
- 32. Grigorieva V, Chen-Mok M, Tarasova M, Mikhailov A. Use of a levonorgestrel-releasing intrauterine system to treat bleeding related to uterine leiomyomas. Fertil Steril 2003; 79: 1194–8.
- Soysal S, Soysal ME. The efficacy of levonorgestrel-releasing intrauterine device in selected cases of myoma-related menorrhagia: a prospective controlled trial. Gynecol Obstet Invest 2005; 5: 29–35.
- 34. Mercorio F, De Simone R, Di Spiezio Sardo A et al. The effect of a levonorgestrel-releasing intrauterine device in the treatment of myoma-related menorrhagia. Contraception 2003; 67: 277–80.
- 35. Rosa e Silva JC, de Sa Rosa e Silva AC, dos Reis FJ et al. Use of a levonorgestrel-releasing intrauterine device for the symptomatic treatment of uterine myomas. J Reprod Med 2005; 50: 613–17.
- Fedele L, Bianchi S, Raffaelli R, Portuese A, Dorta M. Treatment of adenomyosis-associated menorrhagia with a levonorg-estrel-releasing intrauterine device. Fertil Steril 1997; 68: 426–9.
- 37. Maia H Jr, Maltez A, Coelho G, Athayde C, Coutinho EM. Insertion of Mirena after endometrial resection in patients with adenomyosis. J Am Assoc Gynecol Laparosc 2003; 10: 512–16.
- 38. Mahmood TA, Templeton A. Prevalence and genesis of endometriosis. Hum Reprod 1991; 6: 544–9.
- 39. Baldaszti E, Wimmer-Puchinger B, Loschke K. Acceptability of the long-term contraceptive levonorgestrel-releasing intrauterine system (Mirena): a 3-year follow-up study. Contraception 2003; 67: 87–91.
- 40. Vercellini P, Aimi G, Panazza S et al. A levonorgestrel-releasing intrauterine system for the treatment of dysmenorrhea associated with endometriosis: a pilot study. Fertil Steril 1999; 72: 505–8.
- 41. Lockhat FB, Emembolu JO, Konje JC. The evaluation of the effectiveness of an intrauterine-administered progestogen (levonorgestrel) in the symptomatic treatment of endometriosis and in the staging of the disease. Hum Reprod 2004; 19(1): 179–84.
- 42. Fedele L, Bianchi S, Zanconato G, Portuese A, Raffaelli R. Use of a levonorgestrel-releasing intrauterine device in the treatment of rectovaginal endometriosis. Fertil Steril 2001; 75: 485–8.

- de Sa Rosa e Silva AC, Rosa e Silva JC, Nogueira AA et al. The levonorgestrel-releasing intrauterine device reduces CA-125 serum levels in patients with endometriosis. Fertil Steril 2006; 86: 742–4.
- Lockhat FB, Emembolu JO, Konje JC. The efficacy side-effects and continuation rates in women with symptomatic endometriosis undergoing treatment with an intra-uterine administered progestogen (levonorgestrel): a 3 year follow-up. Hum Reprod 2005; 20: 789–93.
- Vercellini P, Frontino G, De Giorgi O et al. Comparison of a levonorgestrel-releasing intrauterine device versus expectant management after conservative surgery for symptomatic endometriosis: a pilot study. Fertil Steril 2003; 80: 305–9.
- Petta CA, Ferriani RA, Abrao MS et al. Randomized clinical trial of a levonorgestrel-releasing intrauterine system and a depot GnRH analogue for the treatment of chronic pelvic pain in women with endometriosis. Hum Reprod 2005; 20: 1993–8.
- Lockhat FB, Emembolu JE, Konje JC. Serum and peritoneal fluid levels of levonorgestrel in women with endometriosis who were treated with an intrauterine contraceptive device containing levonorgestrel. Fertil Steril 2005; 83: 398–404.
- Abou-Setta AM, Al-Inany HG, Farquhar CM. Levonorgestrelreleasing intrauterine device (LNG-IUD) for symptomatic endometriosis following surgery. Cochrane Database Syst Rev 2006; (4): CD005072.
- 49. Sievers S, Dallenbach-Hellweg G, Schaude H. [The treatment of pre-malignant hyperplasias of the endometrium with progesterone-carrying intra-uterine devices (author's transl)]. Geburtshilfe Frauenheilkd 1979; 39: 389–92 [in German].
- Volpe A, Botticelli A, Abrate M et al. An intrauterine progesterone contraceptive system (52 mg) used in pre- and peri-menopausal patients with endometrial hyperplasia. Maturitas 1982; 4: 73–9.
- Vereide AB, Arnes M, Straume B, Maltau JM, Orbo A. Nuclear morphometric changes and therapy monitoring in patients with endometrial hyperplasia: a study comparing effects of intrauterine levonorgestrel and systemic medroxyprogesterone. Gynecol Oncol 2003; 9: 526–33.

- 52. Vereide AB, Kaino T, Sager G, Orbo A Scottish Gynaecological Clinical Trials Group. Bcl-2, BAX and apoptosis in endometrial hyperplasia after high dose gestagen therapy: a comparison of responses in patients treated with intrauterine levonorgestrel and systemic medroxyprogesterone. Gynecol Oncol 2005; 97: 740–50.
- 53. Vereide AB, Kaino T, Sager G, Arnes M, Orbo A. Effect of levonorgestrel IUD and oral medroxyprogesterone acetate on glandular and stromal progesterone receptors (PRA and PRB), and estrogen receptors (ER-alpha and ER-beta) in human endometrial hyperplasia. Gynecol Oncol 2006; 101: 214–23.
- Dhar KK, NeedhiRajan T, Koslowski M, Woolas RP. Is levonorgestrel intrauterine system effective for treatment of early endometrial cancer? Report of four cases and review of the literature. Gynecol Oncol 2005; 97: 924–7.
- 55. Inki P, Hurskainen R, Palo P et al. Comparison of ovarian cyst formation in women using the levonorgestrel-releasing intrauterine system vs. hysterectomy. Ultrasound Obstet Gynecol 2002; 20: 381–15.
- Suhonen S, Haukkamaa M, Jakobsson T, Rauramo I. Clinical performance of a levonorgestrel-releasing intrauterine system and oral contraceptives in young nulliparous women: a comparative study. Contraception 2004; 69: 407–12.
- Sonnenberg FA, Burkman RT, Hagerty CG, Speroff L, Speroff T. Costs and net health effects of contraceptive methods. Contraception 2004; 69: 447–59.
- Brown PM, Farquhar CM, Lethaby A, Sadler LC, Johnson NP. Cost-effectiveness analysis of levonorgestrel intrauterine system and thermal balloon ablation for heavy menstrual bleeding. BJOG 2006; 113: 797–803.
- You JH, Sahota DS, MoYuen P. A cost-utility analysis of hysterectomy, endometrial resection and ablation and medical therapy for menorrhagia. Hum Reprod 2006; 21: 1878–83.
- 60. Blumenthal PD, Trussell J, Singh RH et al. Cost-effectiveness of treatments for dysfunctional uterine bleeding in women who need contraception. Contraception 2006; 74: 249–58.
- 61. National Institute for Health and Clinical Excellence. Diagnosis and management of heavy menstrual bleeding, developed by the National Collaborating Centre for Women's and Children's Health, London, 2007.

Current surgical treatment options: an evidence-based approach

13

Erik Qvigstad and Olav Istre

INTRODUCTION

Heavy menstrual bleeding (HMB) is the dominant complaint in women with abnormal uterine bleeding (AUB), even though long duration of bleeding and intermenstrual bleeding or spotting may be of concern in some women. These bleeding disturbances are classified as dysfunctional when no pathogenic mechanism can be demonstrated. First-line therapy is usually with drugs described by general practitioners. The efficacy of medical treatment is variable, and surgical treatment often follows failed or ineffective medical therapy. However, there has been concern that unnecessary surgery is being performed and that treatment of this condition is not an evidence-based approach.¹

Hysterectomy has been regarded as the definitive surgical treatment for HMB/AUB and has been a very commonly performed operation.² The uterus may be removed by open abdominal procedure, or laparoscopic or vaginal hysterectomy. There is evidence that the vaginal³ or laparoscopic routes⁴ are associated with shorter recovery time and fewer complications than the abdominal route. Since hysterectomy is a major surgical procedure with certain complications and adverse effects, and HMB is a benign condition, many women request less invasive alternatives. The less invasive surgical techniques, with the purpose of removing the entire thickness of the endometrium, were first introduced in 1981.⁵ Since then, numerous equipments, techniques, and procedures have been developed.

The surgical procedures used in the management of abnormal uterine bleeding are:

- endometrial ablation (using different systems)
- transcervical endometrial resection
- operative hysteroscopy
- hysterectomy
- myomectomy
- uterine artery embolization or occlusion.

Since myomectomy and uterine artery embolization/ occlusion are only indicated in women with fibroids, and are described in detail in other chapters, we will concentrate on the other surgical treatment options with an evidence-based approach.

EVIDENCE-BASED MEDICINE

Evidence-based medicine (EBM) emerged as a clinical discipline in the 1990s. EMB is dependent on the use of randomized controlled trials, systematic reviews, and meta-analyses. Whereas traditional medicine to a large extent has been based on authority, the idea with EBM is research-based practice. EMB is closely linked to the Cochrane Collaboration, which is a worldwide network of centers aimed at promoting EMB.

In evaluating medical practice and treatment options, where a standardized hierarchy of evidence has been established, systematic reviews and meta-analyses of randomized controlled trials have the best strength of evidence in EBM. The randomized controlled trials, which were introduced in clinical research more than 50 years ago, have recently been given increasing importance in EMB.

With the Cochrane Collaboration as the basis for the evidence-based approach, we will evaluate medical therapy vs surgery, hysterectomy vs endometrial resection and ablation, and compare different endometrial destruction techniques for heavy menstrual bleeding.

Medical therapy or surgery

A main factor influencing treatment choice for AUB is whether the woman has used first-line medical treatment with little or no improvement of symptoms. When this happens, women may be reluctant to retry medical treatments.⁶ In such situations, both the woman and the gynecologist will be more likely to choose surgical treatment, and Coulter and co-workers showed that women being referred to hospital clinics had a 60% risk of having a hysterectomy.⁷

The available medical treatments include the levonorgestrel intrauterine system (LNG-IUS), non-steroidal anti-inflammatory drugs (NSAIDs), antifibrinolytic drugs, progestogens, oral contraceptives, and danazol. All these medical therapies are at least partially effective in reducing menstrual blood loss. It has been shown that LNG-IUS ranks much higher than all other medical treatments when effectiveness, side effects, length of treatment, and acceptability are taken into account.⁸ The choice of medical treatment can, however, depend on individual factors such as requirement for contraceptive, dysmenorrhea, or health status.

Even though hysterectomy is a major surgical procedure, it is nevertheless virtually 100% successful in treating bleeding disorders, and for most women postoperative problems are of relatively short duration. Satisfaction rates after hysterectomy are very high, at over 95% up to 3 years after surgery. Following surgery, well-known complications such as hemorrhage, infection, and wound healing problems may occur. There is also a relation between hysterectomy and early ovarian failure. For example, the surgery of the surgery of

Throughout the last 20 years, several less invasive operative techniques have been introduced, chiefly endometrial resection or ablation. Some of these techniques utilize a hysteroscope (first-generation techniques), whereas the 'second-generation' non-hysteroscopic techniques utilize controlled application of heat, cold, microwave, suction, or other forms of energy to destroy the endometrium. Endometrial destruction techniques require shorter operation times, and result in quicker recovery and fewer complications than hysterectomy.¹¹

In the Cochrane Review of surgery vs medical therapy, eight trials have been included.11 The outcome measures were bleeding control, quality of life, satisfaction rate, adverse effects, and requirements for additional surgical or medical treatment. The trials of oral medication vs surgery indicate that surgery is more effective for most women in reducing menstrual bleeding and improving quality of life. 6,12 In the latter trial, 53% of women randomized to medical treatment had received surgery by 2 years. Women on the surgical arms of these trials had a variety of operations, including simple balloon ablation technique, transcervical endometrial resection, and major surgery with hysterectomy. There was, however, no significant variation in the results reported by the trials comparing different types of surgery with LNG-IUS. In a comparison of LNG-IUS vs surgery, conservative surgery was significantly more effective than LNG-IUS in controlling bleeding at 1 year, but there was no statistically significant difference in satisfaction rate or quality of life. 11,13 In a study from 1998, we showed that there was no statistically significant difference between conservative surgery

and LNG-IUS with regard to the number of women who reported amenorrhea at 2 and 3 years. 14

In the study from 2001, Hurskainen et al. compared hysterectomy with LNG-IUS in 228 women.¹³ At 1 year after treatment, no women in the hysterectomy group had, as expected, any further bleeding, whereas 69% of women in the LNG-IUS group had control of bleeding, and 35% of women had nil or negligible bleeding. At 5 years follow-up, 48% still had the LNG-IUS in situ, most of them with no bleeding or minimal spotting. Among the 60 women with the LNG-IUS no longer in situ, 50 had experienced a hysterectomy.

These results suggest that the LNG-IUS system provides a better alternative to surgery than oral medication. Even though transcervical endometrial resection or balloon ablation is more effective than LNG-IUS in reducing bleeding at 1 year, levels of satisfaction and quality of life are quite similar after the different treatment options. A significant proportion of women initially treated by conservative surgery or LNG-IUS will require further interventions, usually hysterectomy. The risk of additional surgery because of failure of the initial treatment was significantly more likely for endometrial destruction when compared with hysterectomy. Even though women treated by conservative surgery may need retreatment, a significant proportion of women will choose these treatment options from a quality of life and satisfaction viewpoint, even knowing that hysterectomy is the definitive treatment for heavy menstrual bleeding.

Hysterectomy or endometrial resection/ablation

In women with ineffective or failed medical therapy for HMB, surgical treatment often follows, and the definitive treatment is hysterectomy. Hysterectomy is associated with an almost 100% primary success rate and high levels of satisfaction. However, at least a third of the patients had a normal uterus removed (no uterine pathology). ¹⁵ In spite of the success rate, hysterectomy is a major surgical procedure with peri- and postoperative complications, in addition to emotional, cultural, social, and economic costs.

The less invasive surgical techniques with the purpose of removing the entire thickness of the endometrium may be performed under direct hysteroscopic view or by ablating the endometrium with some form of thermal energy to produce necrosis of the full thickness of the endometrium. The newer surgical techniques are easier to perform, are associated with fewer complications, and are cost saving for society, although the cost for the device adds extra compared to the first-generation techniques. Compared to hysterectomy, however, since additional surgical treatment is required in a proportion of cases, the

need for retreatment at later stage may reduce the cost saving.

In the Cochrane Collaboration report, five randomized controlled trials of endometrial destruction vs hysterectomy were evaluated: 16 two trials compared transcervical endometrial resection with abdominal hysterectomy, 17,18 one trial compared endometrial resection with vaginal hysterectomy, 19 and two trials compared endometrial resection with abdominal and vaginal hysterectomy. 20,21 Follow-up after surgery for all included studies ranged from 4 months to 4 years.

There was a significant advantage in favor of hysterectomy in improvement of HMB. In women undergoing endometrial destruction, 13% had no effect on menstrual blood loss after 1 year, but there was improvement with longer follow-up. Women who had a hysterectomy were significantly more satisfied both at 1 and 2 years after surgery, when compared with those who had endometrial destruction. However, duration of surgery, hospital stay, and time to return to work were all significantly shorter with endometrial destruction techniques when compared with hysterectomy. Thereby, considerable short-term benefits of endometrial destruction techniques were demonstrated.

The less-invasive surgical techniques have early benefits and high rates of satisfaction, but an increasing proportion of these women require retreatment. In a report from the Aberdeen Endometrial Ablation Trials Group, 38% of women who had endometrial ablation received, at a later stage, surgical treatment of some kind within 4 years compared with 1% of women who had a hysterectomy.²² Thus, even though endometrial resection costs are reduced, the health service provides less compared to hysterectomy for the management of HMB and, over time, the cost gap narrowed because of the retreatment rate for women having an endometrial resection. However, both clinical experience and several reports indicate that the results after transcervical endometrial resection are quite skill-dependent, at least in the early learning phase.

There is good evidence that vaginal hysterectomy is associated with shorter recovery time and fewer complications than hysterectomy by the abdominal route,^{3,23} as there is evidence that the patient will benefit from laparoscopic hysterectomy with respect to hospital stay, recovery, and sick leave.^{4,24} With modern anesthesia, fast-track surgery and hysterectomy being done as day surgery, future studies may reveal further advantages in favor of hysterectomy.

Comparison of different endometrial destruction techniques

As mentioned previously, hysterectomy has traditionally been regarded as the definitive surgical treatment for HMB, but many women prefer less invasive surgical treatment even when they are made aware that the success of the treatment is not always assured.²⁵ Since the first effective ablation technique was reported in 1981,⁵ a large number of techniques have been developed to remove the lining of the endometrium. The gold standard techniques include laser, transcervical resection of the endometrium, and roller ball: they are often referred to as first-generation methods. Several non-hysteroscopic techniques, i.e. second-generation techniques, have recently been introduced to make the procedure easier, quicker, and safer. These techniques include cryoablation, hot saline solution irrigation, microwave ablation, and heated balloon systems. The methods have been introduced to the market with very few randomized controlled trials to assess efficacy, safety, and acceptability.

In the Cochrane Collaboration to compare the different methods, data were extracted from a total of 19 complete studies.²⁶ The first-generation techniques were compared, as were second-generation first-generation techniques.

Apart from differences between techniques, the duration of surgery is likely to be affected by the skill and expertise of the surgeon and hospital policy. The secondgeneration techniques were in all included trials faster to perform than first-generation techniques, regardless of the procedures being compared. First-generation ablation techniques required up to an extra 15 minutes treatment time when compared with second-generation techniques. Women undergoing ablation with some second-generation techniques were more likely to have local anesthesia, compared to more frequent use of general anesthesia with first-generation techniques. However, most of the secondgeneration techniques require pretreatment endometrial thinning agents. Overall, the woman's satisfaction was high with most procedures, and the differences found were unlikely to be clinically significant. There was significant heterogeneity between the trials, and large study numbers would be needed in order to demonstrate a significant difference in satisfaction between different methods of endometrial destruction.

There has been little systematic attempt to compare new methods against the gold standard of established techniques. In the MISTLETOE study, the first-generation methods of endometrial ablation vs resection were compared, and the conclusion was that both methods produced similar outcomes in terms of bleeding and participant satisfaction, but the resection methods have significantly more complications.²⁷ When compared with endometrial resection, NovaSure and microwave ablation methods were quicker and suitable for local rather than general anesthesia.

Women with a normal uterus who wish to reduce HMB and want to retain their uterus should be recommended

endometrial destruction by first- or second-generation techniques. The advantage of the second-generation methods, in particular, of being performed under local anesthesia should be taken into consideration, especially in women who want a simple and quick procedure and in high-risk patients. There is sufficient evidence to confirm that second-generation techniques are technically simpler and quicker than first-generation techniques, whereas satisfaction rates and reduction in HMB are similar. The problem with many of the second-generation techniques is, however, still related to equipment reliability. In addition, many women suffering from AUB have intrauterine pathology, which only can be detected and treated with first-generation endometrial destruction techniques.

CONCLUSIONS

A significant number of women with heavy menstrual bleeding will not benefit from medical treatment. The first-line therapy with drugs has a variable efficacy and, at best, oral medication reduces menstrual blood loss by only 50%. The levonorgestrel-releasing intrauterine system is more effective, and has been shown to be as

effective as endometrial ablation. It could be argued that endometrial surgery is only appropriate for those women who are not suitable (i.e. polyps, fibroids) or for women who do not wish to have treatment with the intrauterine system. A significant number of women with heavy menstrual bleeding are interested in keeping their uterus, and the minor surgical procedures with endometrial destruction are an alternative. The existing evidence suggests that success rates and complication profiles of newer techniques of ablation compare favorably with transcervical resection of the endometrium. The ultimate treatment of heavy menstrual bleeding is hysterectomy, as primary treatment in selected patients or as first choice in the retreatment procedure. Comparison of the more recent types of hysterectomy with endometrial ablation techniques is still to be done.

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References

- Prentice A. Medical management of menorrhagia. BMJ 1999; 319: 1343–5.
- 2. Farquhar C, Steinera C. Hysterectomy rates in the United States 1990 1997. Obstet Gynecol 2002; 99: 229–34.
- Johnson N, Barlow D, Lethaby A et al. Surgical approach to hysterectomy for benign gynaecological disease. Cochrane Database Syst Rev 2005; (1): CD003677.
- Istre O, Langebrekke A, Qvigstad E. Changing hysterectomy technique from open abdominal to laparoscopic. New trend in Oslo, Norway. J Minim Invasive Gynecol 2007; 14: 74–7.
- 5. Goldrath MH, Fuller TA, Segal S. Laser photovaporization of endometrium for the treatment of menorrhagia. Am J Obstet Gynecol 1981; 140: 14–19.
- Cooper KG, Parkin DE, Garrett AM, Grant AM. A randomised comparison of medical and hysteroscopic management in women consulting a gynaecologist for treatment of heavy menstrual loss. Br J Obstet Gyneacol 1997; 104: 1360–6.
- Coulter A, Bradlow J, Agass M, Matin-Bates C, Tulloch A. Outcomes of referrals to gynaecology outpatient clinics for menstrual problems: an audit of general practice. Br J Obstet Gyneacol 1991; 98: 789–96.
- National Health Committee Working Party. Guidelines for the management of heavy menstrual bleeding. Wellington, NZ: National Health Committee, 1998.
- Lethaby A, Shepperd S. Cooke I Endometrial resection and ablation versus hysterectomy for heavy menstrual bleeding. Cochrane Database Syst Rev.

- Farquhar CM, Sadler L, Harvey SA et al. The association of hysterectomy and menopause: a prospective cohort study. Br J Obstet Gynaecol 2005; 112(7): 956–62.
- Marjoribanks J, Lethaby A, Farquhar C. Surgery versus medical therapy for heavy menstrual bleeding. Cochrane Collaboration 2006; Issue 4.
- 12. Kupperman M, Varner RE, Summitt RL et al. Effect of hyster-ectomy vs medical treatment on health-related quality of life and sexual functioning. JAMA 2004; 291(12): 1447–55.
- 13. Hurskainen R, Teperi J, Rissanen P et al. Quality of life and cost-effectiveness of levonorgestrel-releasing intrauterine system versus hysterectomy for treatment of menorrhagia: a randomised trial. Lancet 2001; 357: 273–7.
- Kittelson N, Istre O. A randomized study comparing levonorgestrel intrauterine system (LNG IUS) and transcervical resection of the endometrium (TCRE) in the treatment of menorrhagia: preliminary results. Gynecol Endosc 1998; 7: 61–5.
- Clarke A, Black N, Rowe P et al. Indications for and outcomes of total abdominal hysterectomy for benign disease: a prospective cohort study. Br J Obstet Gynaecol 1995; 102: 611–20.
- Lethaby A, Shepperd S, Cooke I et al. Endometrial resection and ablation versus hysterectomy for heavy menstrual bleeding. Cochrane Collaboration. 2006; Issue 4.
- Dwyer N, Hutton J, Stirrar GM. Randomised controlled trial comparing endometrial resection with abdominal hysterectomy for the surgical treatment of menorrhagia. Br J Obstet Gynaecol 1993; 100: 237–43.

- 18. Gannon MJ, Holt EM, Fairbank J et al. A randomised trial comparing endometrial resection and abdominal hysterectomy for the treatment of menorrhagia. BMJ 1991; 303: 1362–4.
- Crosignani PG, Vercellini P, Apolone G et al. Endometrial resection versus vaginal hysterectomy for menorrhagia: longterm clinical and quality-of-life outcomes. Am J Obstet Gynecol 1997; 177: 95–101.
- Pinion SB, Parkin DE, Abramovich DR et al. Randomised trial of hysterectomy, endometrial laser ablation, and transcervical endometrial resection for dysfunctional uterine bleeding. BMJ 1994; 309: 979–83.
- O'Connor H, Broadbent JA, Magos AL, McPherson K. Medical Research Council randomised trial of endometrial resection versus hysterectomy in management of menorrhagia. Lancet 1997; 349: 897–901
- 22. Aberdeen Endometrial Ablation Trials Group. A randomised trial of endometrial ablation versus hysterectomy for the treatment of dysfunctional uterine bleeding: outcome at four years. Br J Obstet Gynaecol 1999; 106: 360–6.

- 23. Langebrekke A, Eraker R, Nesheim BI et al. Abdominal hyster-ectomy should not be considered as a primary method for uterine removal. A prospective randomised trial of 100 patients refered to hysterectomy. Acta Obstet Gynecol Scand 1996; 75: 404–7.
- Lieng M, Istre O, Langebrekke A, Jangersen M, Bufund B. Outpatient laparoscopic supracervical hysterectomy with assistance of the lap loop. J Minim Invasive Gynecol 2005; 12: 290–4.
- Nagele F, Rubinger T, Magos A. Why do women choose endometrial ablation rather than hysterectomy? Fertil Steril 1998; 69(6): 1063–6.
- Lethaby A, Hickey M, Garry R. Endometrial destruction techniques for heavy menstrual bleeding. Cochrane Collaboration 2006; Issue 4.
- 27. Overton C, Hargreaves J, Maresh M. A national survey of the complications of endometrial destruction for menstrual disorders: the MISTLETOE study. Br J Obstet Gynaecol 1997; 104(12): 1351–9.

14

The use of contemporary energy modalities during operative laparoscopy

Andrew I Brill

INTRODUCTION

Since the inception of operative laparoscopic surgery, the use of energy has remained an essential component of the surgical armamentarium. The demand and evolution of new energy devices continue to grow as surgeons seek technical innovation that is robust, safe, reliable, and effective. Mirroring the fundamental needs of laparotomic and vaginal surgery, contemporary energy modalities are customarily used to control bleeding and to mobilize, secure, incise, and devitalize or ablate living tissues.

Guided by the Hippocratic charge to primum non nocere (first do no harm), the ultimate aim of energy-assisted surgery is the attainment of anatomic dissection and hemostasis with the least amount of collateral damage and subsequent scar tissue formation. Ideally, the surgeon's final view of the operative field should accurately approximate the topography discoverable after postoperative healing. Despite the continued innovation of products borne to reduce thermal damage and then marketed as being comparatively safer, it is the hands and mind of the surgeon that serve to preserve tissue integrity by reducing the burden of delayed thermal necrosis and taking steps to prevent excessive devitalization of tissue. Regardless of the chosen modality, the inseparable and exponentially linked elements of time and the quantity of delivered energy must be integrated while purposefully moderating to attain the desired tissue effect. Ultimately, the reduction of unwanted thermal injury is inherently linked to good surgical judgment and technique, a sound comprehension of the applied energy modality, and the surgeon's ability to recognize anatomic structures within the field of surgical dissection as well as those within the zone of significant thermal change.

During the use of any energy-based device for hemostasis, out of sight must never mean out of mind. If the bowel, bladder, or ureter is in close proximity to a bleeder, they should be sufficiently mobilized before applying energy.

Thermal energy should always be withheld until an orderly sequence of anatomic triage is carried out. Whenever a vital structure cannot be adequately mobilized, hemorrhage is preferentially controlled by using mechanical tamponade or suture ligature.

BIOPHYSICAL PRINCIPLES OF ELECTROSURGERY

Science becomes art and art becomes function when fundamental principles are utilized to dictate surgical practice. Most importantly, the risk for inadvertent thermal injury during electrosurgery can be minimized by a sound comprehension of the predictable behaviors of electricity in living tissue.

Typical household current is low-frequency alternating current (AC) of (60 Hz cycles per second), which on accidental contact causes well-known neuromuscular contraction, the so-called Faradic effects, by sustained nerve depolarization. Since there is insufficient time for current to create sustained depolarization at much higher frequencies of AC (>100 kHz), the contemporary solid-state electrosurgical unit (ESU) generator converts household current (60 Hz) to very high radiofrequency (RF) current (300–600 kHz range) to obviate this phenomenon.

Electrosurgery is achieved by the delivery of a high-frequency AC from an ESU generator into living tissue by an active electrode which is then conducted via low-resistance pathways to a return electrode. The flow of electrons (or electrical current) is set in motion and sustained by an electromotive force (or voltage) to complete the circuit across the significant difference in electrical potential between the two electrodes. Since voltage is the electromotive force that drives the transit of charged particles across a potential difference, a greater voltage has the propensity to produce greater thermal necrosis. Whereas the electrons are simply electromagnetic couriers of charge, their conduction through

the resistance (impedance) of living tissue cause secondary thermodynamic phenomena, all culminating with an increase in tissue temperature.

Quite clearly then, electrocautery is not electrosurgery. Contrary to the ability to create and moderate a variety of thermal tissue effects with electrosurgery, electrocautery uncontrollably heats tissue on contact with a hot electrode that has been primed with a direct current (DC) Figure 14.1.

The capacity of electricity to achieve work in the form of heat in living tissue is termed resistive heating. As living tissue is slowly heated to and maintained at temperatures >50°C, irreversible cellular damage occurs. This is caused by deconfiguration of regulatory proteins and denaturation of cellular proteins. If the tissue is heated to 100°C, cellular water completely evaporates (desiccation), localized hemostasis occurs due to contraction of blood vessels and the surrounding tissues (coagulation), and collagens convert to glucose, which creates an adhesive effect between the tissue and electrode. Temperatures >200°C cause carbonization and charring.

Depending upon the rate of tissue temperature change and magnitude of energy delivery, various surgical endpoints are accomplished, including cutting (vaporization or electrosection), fulguration, and desiccation (coagulation). In fact, the entire spectrum of electrosurgical tissue endpoints is fundamentally realized by the manipulation of current density to change the rate of tissue heating (Figure 14.2). Electricity always seeks ground (the earth) and follows the path of least resistance (e.g. vascular rather than desiccated tissue).

The behavior of electricity in living tissue is generally governed by Ohm's Law: $V = I \times R$. Derivatively, current (*I*) is directly proportional to voltage (*V*) and inversely proportional to resistance (*R*). To complete a circuit,

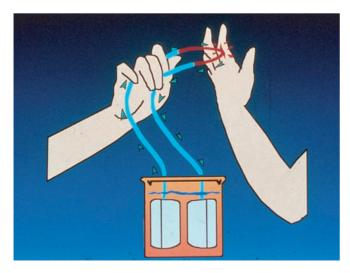


Figure 14.1 Electrocautery.

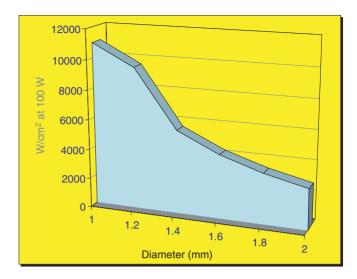


Figure 14.2 Current density = electrode surface area.

greater resistance requires greater electromotive force or voltage. Power settings keyed into the ESU as watts (W) by the surgeon correspond to the rate of work being done. The important relationship between voltage and resistance is reiterated by the derivation of power: $W = I \times V$ and with use of Ohm's Law, $W = I^2 \times R$ and $W = V^2/R$. Hence, as long as the power setting remains constant, circumstances of higher resistance such as fat, fascia, and desiccated or carbonized tissues at the active electrode will require correspondingly higher output voltages to maintain the desired tissue endpoints.

MONOPOLAR ELECTROSURGERY

During monopolar electrosurgery, an electrical current is delivered to tissue via an active electrode (e.g. needle, spatula, and hook) from a solid-state ESU generator and subsequently conducted via a variety of conductive tissues back to the ESU through the return (dispersive) electrode. Although equivalent amounts of current are conducted through each electrode, the dramatic difference in thermal effects between the active and return electrodes is simply explained by the marked discrepancy in surface areas. Just as a magnifier can quickly incinerate a dried leaf by focusing otherwise thermally innocuous sunlight, the rate of heat production in living tissue by electrosurgery is primarily determined by the current density (i.e. surface area): see Figure 14.2.

ELECTROSURGICAL WAVEFORMS

Viewed on an oscilloscope, the bidirectional AC output from an ESU generator is generally sinusoidal in nature. Contrary to commonly held beliefs, each of the typical output settings on the face of a conventional ESU generator, labeled 'cut', 'blend', and 'coag', are not necessarily related to any specific tissue endpoints; rather, these settings simply modulate the output by varying current and voltage in relation to time, resulting in a variety of available waveforms (Figure 14.3). The purely sinusoidal cut waveform output is uninterrupted and has the lowest peak voltage, whereas switching to blend and then coag creates greater intervals of periodic interruption, with correspondingly higher peak voltages. In order to maintain the same power output (W), the relatively lower average currents of higher (i.e. 3 and 4) blend and coag outputs automatically generate higher output voltage (i.e. $W = I \times V$). Since force and voltage are synonymous during electrosurgery, the zone of thermal damage is predictably greater from higher peak voltages associated with blend and then coag waveforms (Figure 14.4). New breeds of modern ESU generators incorporate automatic control circuits to ensure that the output voltage is kept constant (constant or automatic voltage generator). This makes the depth of coagulation relatively independent of the waveform setting.

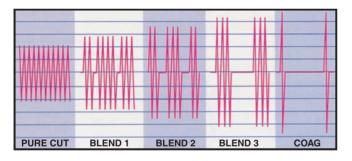


Figure 14.3 Electrosurgical waveforms.

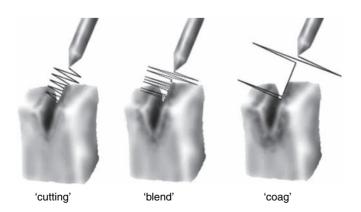


Figure 14.4 Lateral thermal damage during electrosurgical tissue cutting is directly related to the waveform and consequent voltage output that is keyed into the electrosurgical generation.

NON-CONTACT ELECTROSURGICAL PHENOMENA: CUTTING AND FULGURATION

Electrosurgical cutting (vaporization/ablation) is possible whenever voltage is sufficient to create an electrical spark between an electrode and underlying tissue; tissue cutting is more likely to occur if the arcing remains uninterrupted. When it does, cellular water is superheated to temperatures >600°C, causing explosive vaporization secondary to the production of highly disruptive pressure (since steam occupies six times the volume of liquid water). Electrical sparking, the ionization of air into an unstable plasma cloud between the active electrode and underlying tissue, requires only 200 V. Since cut, blend, and coag all deliver this amount of voltage, tissue cutting can be accomplished with any of these waveforms. Using conventional ESU generators, the zone of thermal damage at the margins of a spark-borne cut is determined by the amount of peak voltage associated with a given waveform. Predictably then, the thermal effects at the margin of an incision are greatest using the highly interrupted output of the coag waveform (see Figure 14.4). These effects are amplified by using broad-surface electrodes, which reduce current density. The ability to better insure hemostasis at the cut margins using blend or coag current can be helpful during myomectomy, when operating down the broad ligament and along the vaginal fornices during hysterectomy, across vascular adhesions, and to clarify the space of Retzius in preparation for colposuspension and paravaginal repair. Higher-voltage waveforms also facilitate electrosurgical incision of tissue types with greater resistance, such as the omentum, subcutaneous fat, and desiccated adhesions. On the other hand, it is more prudent to utilize the lower-voltage cut waveform via the edge of an electrode for electrosurgical incision whenever lateral thermal spread may pose extra liability to adjacent tissues, such as the ovarian cortex during cystectomy and the ureter or rectum during excision of endometriosis from the lateral pelvic sidewall or cul-de-sac.

Fulguration is the application of high-voltage sparking using the coag waveform to coagulate a broad surface with open vessels on end (up to 2 mm) where mechanical coaption is not feasible or desirable. Despite the high-voltage output, fulguration is quickly rendered useless in a wet surgical field due to ready conduction and diffusion of net current density. As opposed to the continuous ionization pathway and high current density propagated by the uninterrupted cut waveform, the output of the coag waveform sparks intermittently, resulting in a very dispersed target zone. The higher peak voltage of the coag waveform also creates much higher tissue, temperatures

sufficient to carbonize tissue resulting in an easily dislodged coagulum with superficial crusting. This rapid change in surface temperature self-limits the depth of significant thermal change during fulguration. These characteristics are especially useful for attaining hemostasis of small open bleeders as well as along the undersurface of the ovarian cortex during cystectomy, atop the myometrial bed during myomectomy, and alongside Cooper's ligament during colposuspension. If bleeding in the vicinity of the bowel, bladder, or ureter cannot be controlled with pressure alone, carefully directed short bursts of non-contact coag current with a broad-surface electrode can attain effective hemostasis with the least-possible amount of electrosurgical penetration.

CONTACT ELECTROSURGICAL PHENOMENA: DESICCATION AND COAGULATION

Regardless of the selected waveform, current density is dramatically reduced whenever an active electrode comes into significant contact with a tissue surface. Just as heat is noticeably reduced on withdrawal of a magnifying glass from a curling leaf, tissue is heated more slowly on contact, resulting in gradual cellular dehydration or desiccation. As the rate of tissue heating is substantially slower than during vaporization or fulguration, the depth of thermal damage is predictably deeper and more widespread during contact desiccation. Whereas desiccation is inherently related to manipulation of electrode surface area, the applied waveform can also affect the volume of thermal damage Unsurprisingly, the rapid surface heating from higher peak voltages associated with the blend and coag waveforms precludes deeper current penetration and results in more superficial zones of thermal change. On the other hand, the lowest peak voltage cut waveform heats tissue more gradually, leading to deeper and more effective penetration. These biophysical principles can be used to moderate and direct electrosurgical treatment for endometriosis. Since superficial peritoneal implants commonly penetrate more deeply into the retroperitoneal tissues, these lesions may be best ablated using a large surface electrode in contact using a cut waveform. In contrast, superficial implants on the ovarian cortex may be more prudently ablated using coag waveform to minimize widespread thermal injury to normal follicular cortex. And finally, surgeons should give their highest attention to white rather than blackened areas of electrosurgical injury (e.g. bowel), as these typically represent deeply penetrating injury from inadvertent contact desiccation.

PROBLEMS UNIQUE TO LAPAROSCOPIC MONOPOLAR ELECTROSURGERY

The potential for aberrant and unrecognized injury to tissue such as the viscera during monopolar laparoscopic electrosurgery is magnified by the fact that nearly all of the potential conductors during laparoscopic monopolar electrosurgery are out of the surgeon's field of view. These conductors include the abdominal wall, all metallic trocar sheaths and instruments, an operating laparoscope, adjacent tissue (including bowel), and the active electrode. Not surprisingly, most inadvertent electrosurgical insults are not recognized at the time of the laparoscopic procedure.

Insulation failure

The integrity of insulation along the entire shaft of an active electrode is essential to preclude an alternative pathway for the flow of current. If the defective portion of insulation contacts tissue during electrode activation, an electric arc will bridge directly from the electrode through the defect to this tissue. Thermal damage will occur if the current density is high enough to significantly heat the tissue. Since these defects are usually out of the field of view, this type of injury usually proceeds undetected at the time of insult.

Direct coupling

Direct coupling of current occurs whenever an activated electrode makes unintended contact with another metal object in the area of the surgical field such as a suction-irrigator probe or tissue probe. Provided these instruments are passed within all metal cannulas, coupled currents are conducted back to the dispersive electrode via the abdominal wall. On the other hand, isolation from the abdominal wall by a non-conductive plastic cannula will isolate this current, which may then take an alternative pathway through a point of contact with adjacent tissue such as bowel. Depending upon the current density at the point of contact, a clinically significant burn may evolve.

Capacitive coupling

Capacitive coupling is the induction of current to a surrounding conductor such as a metal trocar through the intact insulation of an active electrode. As in direct coupling, this current can be returned to the dispersive electrode by conduction via the metal cannula and then the abdominal wall. If the metal trocar sheath is attached to the abdominal wall by a non-conductive device, the

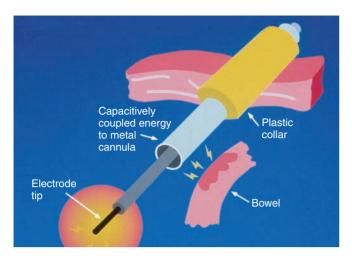


Figure 14.5 Capacitively coupled fault condition hybrid system.

induced current becomes electrically isolated from the abdominal wall (Figure 14.5). Contact between the isolated cannula and the bowel provides an alternative pathway for this stray current to discharge. Provided the current density is sufficiently concentrated by a small area of contact, significant thermal damage can occur. Overall, an all-metal system will serve to safely conduct any induced current back to the dispersive electrode. Capacitive coupling does not occur during bipolar electrosurgery, due to the bidirectionality of the current flow along the active electrode.

BIPOLAR ELECTROSURGERY

Bipolar electrosurgery consolidates an active electrode and return electrode into an instrument which are separated by a small distance. The consequently lower power requirements are customarily matched with the uninterrupted cut waveform. Dissimilar from monopolar electrosurgery, the intervening tissue is part of the electrical circuit rather than the patient. This obviates the need for a dispersive electrode, as current returns to the ESU generator back up the active electrode.

The ability to coaptively heat tissue between two electrodes provides a number of benefits including the ability to limit the volume of affected tissue, a reliable method to occlude and seal blood vessels, and the capacity to effectively heat tissue that is immersed in fluid.

Despite the isolation of tissue between the bipolar electrodes, thermal damage may occur well beyond their confines. Desiccation of tissue percolates heated intracellular water into adjacent tissues. The unabated application of current after attaining this endpoint can propagate a secondary thermal bloom that disruptively bubbles

steam throughout the surrounding parenchyma. Further application of current using older ESU generators may heat enough to carbonize and cause a sticky tissue amalgam. These adverse phenomena are best prevented by terminating current on tissue whitening and when water vapor can no longer be seen to percolate from the heated tissue. Despite its propriety for determining the endpoint for bipolar tubal sterilization, use of an in-line ammeter, which meters the flow of current between the tissue and the jaws of the bipolar grasper, does not prevent this problem. Rather, it tends to promote overdesiccation of tissue. Since larger coapted tissue pedicles generate greater heat, unwanted thermal damage can also be minimized by selectively utilizing the sides or tips of a slightly open bipolar device to directly tamponade and then desiccate with the episodic application of current. Rather than subjecting a desiccated pedicle to mechanical trauma, an electosurgically frozen pedicle can usually be dislodged by activating the active electrodes while immersed in a conductive irrigant.

The latest advances in bipolar electrosurgery arise from the evolution and development of instant feedback technology that delivers either pulsed or continuous electrical output with constant voltage by only moderating the output current. This new breed of ESU generators are paired with a variety of novel ligating-cutting devices which are manufactured to provide continuous feedback about tissue impedance (resistance) at the treatment site. By nearinstantaneous response to incremental changes in tissue resistance, total energy delivery using these newer devices is dramatically less than conventional bipolar systems. Once tonal feedback from the generator signals complete desiccation of the tissue bundle, the pedicle is typically cut by advancing a centrally set mechanical blade. These devices should logically reduce tissue carbonization, sticking, plume, and lateral thermal damage. As a general rule, low-voltage bipolar desiccation of coapted vessels is more effective under reduced tissue tension.

To date, there are three innovative bipolar platforms that utilize low constant voltage and impedance feedback along with paired ligating–cutting devices. Having established that vessel wall fusion can be achieved using electrical energy to denature collagen and elastin in vessel walls to reform into a permanent seal, The LigaSure Vessel Sealing Device (Valleylab, Boulder, CO) applies a high coaptive pressure to the tissue bundle during the generation of tissue temperatures <100°C; hydrogen cross-links are first ruptured and then renature, resulting in a vascular seal that has high tensile strength. The second platform, the PlasmaKinetics Cutting Forceps (Gyrus Medical Minneapolis, MN), delivers pulsed energy with continuous feedback control. A third device, the EnSeal Laparoscopic

Vessel Fusion System (SurgRx, Inc., Palo Alto, CA) utilizes a set of plastic jaws embedded with nanometer-sized spheres of nickel that conduct a locally regulated current. Desiccation is facilitated by simultaneously advancing a mechanical blade that both cuts and squeezes the tissue bundle to eliminate tissue water.

The clinical evaluation of new bipolar ligating—cutting devices should reach well beyond their capacity to simply desiccate and cut tissue. Other pivotal considerations include the relative responsiveness to variable tissue content, tissue tension, and efficacy in fat as well as the propensity for smoke production and tissue sticking. Each instrument should also be evaluated as an operative instrument, including the relative ability to grasp, elevate, dissect, and coapt tissues of variable densities and girth.

ULTRASONIC ENERGY

Using the dynamic tissue effects of applied mechanical energy, ultrasonic blades and shears can be used to effectively coagulate and cut tissue using a number of technical maneuvers that correspondingly alter tissue density. Tissue effects from ultrasonic energy are actuated by a titanium blade of variable excursion that vibrates nearly 60 000 times per second from an in-line piezoelectric crystal housed in the hand-piece of the device. The high-frequency vibration in tissue causes a low-temperature protein denaturation by rupturing the hydrogen bonds of tissue proteins, thereby limiting the extent of lateral thermal

damage. Subsequent tissue separation from cavitational fragmentation naturally evolves from the mechanical vibration and percussive effects of steam that emanates through the adjacent tissue parenchyma. Contrary to the volumetric thermal tissue effects during electrosurgery, lateral thermal damage with ultrasonic energy is limited by the linear nature of energy propagation through the tip of the blade. Available configurations include a 5 mm curved or hook blade and a 5 mm ligating—cutting shears which coaptively desiccates and cuts tissue after being secured between a grooved plastic pad and the vibrating blade. This technology is robust enough to reliably secure the uterine and ovarian vessels using a single cycle of desiccation to seal and then cut.

By using various combinations of blade shapes, blade excursions, and tissue tensions, surgeons can accomplish a variety of specific effects. Cutting velocity is directly proportional to blade excursion, tissue traction, and blade surface area (energy density), and is inversely related to tissue density and elasticity. Thus, the fastest cutting with the least amount of coagulation occurs when tissue is placed on tension and firmly squeezed, lifted, or rotated with the sharpest side of a blade set at maximum excursion. Coagulation is the obverse of cutting: it is inversely related to tissue tension, blade sharpness, blade excursion, and cutting speed. Therefore, coagulation is best achieved by relaxing tension, minimizing blade excursion, and using a blunt edge or flattened blade surface. Premature incision of a vascular core is best avoided by carefully heeding the dynamics of ultrasound transmission in living tissue.

References

- Amaral JF, Chrostek C. Depth of thermal injury: ultrasonically activated scalpel vs electrosurgery. Surg Endosc 1995; 9: 226.
- Brill AI. Energy systems for operative laparoscopy. J Am Assoc Gynecol Laparosc 1998; 5(4): 333–349.
- Friedman J. The technical aspects of electrosurgery. Oral Surg Oral Med Oral Pathol 1973; 36: 177–87.
- 4. Honig WM. The mechanism of cutting in electrosurgery. IEEE Trans Biomed Eng 1975; 22: 58–62.
- Luciano A, Soderstrom R, Martin D. Essential principles of electrosurgery in operative laparoscopy. J Am Assoc Gynecol Laparosc 1994; 1: 189–195.
- 6. McCarus SD. Physiologic mechanism of the ultrasonically activated scalpel. J Am Assoc Gynecol Laparosc 1996; 3: 601–608.
- 7. Odell RC. Pearls, pitfalls, and advancement in the delivery of electrosurgical energy during laparoscopy. Probl Gen Surg 2002; 19(2): 5–17.

- 8. Phipps JH. Thermometry studies with bipolar diathermy during hysterectomy. Gynaecol Endosc 1994; 3: 5–7.
- Sigel B, Dunn MR. The mechanism of bleed vessel closure by high frequency electrocoagulation. Surg Gynecol Obstet 1965; 121: 823–31.
- Soderstrom RM. Electrosurgical injuries during laparoscopy: prevention and management. Curr Opin Obstet Gynecol. 1994; 6: 248–250.
- Tulandi T, Chan KL, Arseneau J. Histopathological and adhesion formation after incision using ultrasonic vibrating scalpel and regular scalpel in the rat. Fertil Steril 1994; 61: 548–560.
- Vancaillie TG. Electrosurgery at laparoscopy: guidelines to avoid complications. Gynaecol Endos 1994, 3:1143–150.
- Wu MP, Ou CS, Chen SL, Yen YET, Rowbotham R. Complications and recommended practices for electrosurgery in laparoscopy. Am J Surg. 2000; 179(1): 67–73.

Hysteroscopic rollerball endometrial ablation

15

George A Vilos, Jackie Hollett-Caines, and Fawaz Edris

HISTORICAL

Abnormal uterine bleeding (AUB) affects approximately 20–25% of premenopausal women. The prevalence increases with age and peaks just prior to menopause.¹ Traditionally, treatment of AUB included a variety of medical therapies, dilatation and curettage (D&C), and hysterectomy. Hysterectomy is a definitive treatment of AUB and is associated with high rates of patient satisfaction. However, public attention to inflated hysterectomy rates and evaluations of its risk and cost benefits has shifted the philosophy and practice of healthcare providers to exploring alternative therapies to hysterectomy, including endometrial ablation.²

Hysteroscopic endometrial ablation using the Nd:YAG (neodymium–yttrium aluminum garnet) laser was described by Goldrath in 1981. Resection with a loop electrode was described by Hallez in 1985 and electrocoagulation, first with a loop electrode and subsequently with a rollerball electrode, were described by DeCherney and Polan in 1983 in the USA and by Lin et al. in 1988 in Japan, respectively.²

In 1985, Hallez et al. described the continuous flow gynecologic resectoscope. The initial instrument consisted of a 2.7 mm diameter telescope, a working element with passive action that allowed articulation of the active electrode, an inner sheath allowing inflow of irrigation/distention liquid, and an outer sheath for outflow of the irrigant liquid (diameter 6.3 mm).³ This system, in contradistinction to the urologic resectoscope, allowed continuous irrigation of the uterine cavity. The irrigant solution used was glycine (1.5%). In December 1989, the Food and Drug Administration (FDA) approved the use of the resectoscope in the USA for gynecologic indications.

In the USA, electrocoagulation of the endometrium with the rollerball electrode was first reported by Vancaillie in 1989.⁴ He used a 2 mm rollerball at power outputs of 40–70 W coagulation waveform and a combination of dextran 70 and 10% dextrose irrigation solution. After 6–11 months of follow-up, 14 of 15 treated women reported amenorrhea (66.7%) or hypomenorrhea

(26.7%).⁴ In 1990, McLucas reported on 12 women with menorrhagia treated with endometrial ablation, under concomitant laparoscopic observation, using a 2.2 mm rollerball at 100 W of cutting waveform and sorbitol 3% to irrigate the uterus. Nine patients were pretreated with danazol (800 mg/day) for 1 month prior to ablation. The short-term results were amenorrhea in 8 (67%) women and hypomenorrhea in 4 (33%) women.⁵

In 1990, Townsend and colleagues performed rollerball coagulation of the endometrium in 50 women with menorrhagia.⁶ The endometrium was thinned preoperatively with danazol (800 mg/day), oral contraceptives, or Provera (medroxyprogesterone acetate; 400 mg, intramuscularly [IM]). The authors used a 2.5 mm rollerball with varied coagulation power, between 50 and 100 W, and various uterine irrigation liquids (primarily sorbitol 3%). They noted that with 50 W of power there was a 'fair' degree of endometrial coagulation, whereas with 70 W and 100 W there was 'moderate' and 'thorough' coagulation, respectively. Therefore, they adapted 90-100 W as the most effective coagulation power for endometrial ablation. At 12 months of follow-up, 10 of 25 (40%) women had amenorrhea, 10 of 25 (40%) had spotting, and 5 of 25 (20%) had light menses. The other 25 women also received medroxyprogesterone acetate (400 mg IM) in the recovery room following rollerball ablation, and all were amenorrheic at 12 months.⁶

In 1992, Daniell and associates reported on hysteroscopic endometrial rollerball ablation in 64 women with menorrhagia. The ablations were performed using a 2.5 mm or 4 mm rollerball, 1.5% glycine irrigant solution, and 100 W of cutting waveform supplemented, at times, with 50 W of coagulation waveform. At 18 months follow-up, women reported amenorrhea (30%), spotting (26%), hypomenorrhea (34%), no change (6.6%), or increased menstrual flow (3.3%). Seven women (11%) received repeat ablation and 4 (6%) required subsequent hysterectomy.⁷

By the mid 1990s, the technique of hysteroscopic endometrial ablation was adopted worldwide by many gynecologists as an alternative therapy in women with AUB who had failed medical therapies or D&C, who were at risk for hysterectomy, or who wished to retain their uterus. The technique, referred to as rollerball ablation, uses various size and shapes of electrodes (rollerballs-bars-barrels, some with grooves or spikes) has enjoyed the most popularity amongst gynecologists.

PRE-ENDOMETRIAL ABLATION ASSESSMENT

The aim of rollerball ablation is to destroy, rather than to remove, endometrial tissue. Thus, the endometrial cavity should be adequately assessed and evaluated prior to ablation in accordance with established clinical practice guidelines.¹ In addition to the standard history, physical and pelvic examination, Papanicolaou smear, complete blood count, and coagulation profile, it is good clinical practice to perform endometrial sampling within the past 6 months (e.g. office biopsy, D&C), pelvic imaging (e.g. sonography on days 5–7 of the cycle, magnetic resonance imaging [MRI], computed tomography [CT] scan), and/or hysteroscopy prior to rollerball ablation.^{1,2}

PATIENT COUNSELING, EDUCATION, AND INFORMED CONSENT

Prior to endometrial ablation, women should be made aware that the procedure is irreversible and relatively safe (complication rates lower than hysterectomy) and that the goal is to reduce bleeding, not to produce amenorrhea. Conversely, patients should be advised that amenorrhea is a possible outcome of the treatment. Women should also be informed that there may be a need for further treatment, including medical therapies, repeat ablation, and/or hysterectomy, if initial ablation fails to control their bleeding.

It should also be emphasized that rollerball ablation should not be performed in women who wish to preserve their fertility, nor should it be used as a means for contraception. Additional methods of family planning should be addressed and documented, since intrauterine and ectopic pregnancies have been reported after endometrial ablation. Although shrinkage and fibrosis of the uterine cavity occur after endometrial ablation/resection, a significant number of women have patent fallopian tubes (13%) despite coagulation of the tubal ostia. Therefore, concomitant laparoscopic or hysteroscopic tubal occlusion should be offered in patients who require contraception. The nature of rollerball ablation, possible complications, clinical outcomes, and alternative treatments should be outlined. Specific complications associated with rollerball

ablation, such as cervical tears, partial (false passages) or complete uterine perforations, hemorrhage, excessive fluid absorption, and thermal injuries to viscera and/or lower genital tract, should be disclosed. Major complications may require the need for possible exploratory laparoscopy, laparotomy, and additional corrective surgery, such as the need for hysterectomy. All of these potential but serious risks should be disclosed.

CONTRAINDICATIONS TO ROLLERBALL ABLATION

Rollerball ablation should not be performed in the presence of undiagnosed intrauterine pathology such as endometrial hyperplasia, polyps, myomas, known genital tract malignancy, acute pelvic inflammatory disease (PID), intrauterine pregnancy, women wishing to preserve their fertility, and those who expect amenorrhea as a clinical outcome. Inadequate training, unfamiliarity with the ablation technique, and lack of appropriate equipment are also a contraindication to rollerball ablation.

PREABLATION ENDOMETRIAL THINNING

Intuitively, a smaller endometrial cavity with thin endometrium should be faster and easier to coagulate. In addition, it has been theorized that a thin endometrium may be associated with less irrigant fluid absorption, fewer intraoperative complications, and possibly result in better clinical outcomes. The initial impression of the pioneers of hysteroscopic endometrial ablation was that the use of progestins resulted in the poorest preparation of the endometrium and that gonadotropin-releasing hormone agonists (GnRH-a) provided the best preparation.^{6,10}

In one study, the authors pretreated 25 women with AUB with one of medroxyprogesterone acetate (200 mg IM), norethindrone acetate (5 mg/day), danazol (600-800 mg/day), or leuprolide acetate (7.5 mg IM) at least 6 weeks prior to hysteroscopic endometrial resection using 110 W of cutting waveform. Histologically, progestin therapy was the least successful in suppressing any of the elements studied (vessels, glands, stroma, thickness). After progestin therapy, the endometrium appeared decidualized and the stroma showed diffuse vascular proliferation and edema. The suppressive effect of danazol was inconsistent, and the effects were correlated to differences in dose and duration of therapy. The histologic findings in the GnRH-a group were the most consistent and effective in thinning the endometrium. However, measurements of the thermal damage revealed that the specimens pretreated with progestins had the greatest

extent of thermal effect, with a mean depth of thermal damage of $217\,\mu m$ as contrasted with the mean damage in danazol-treated tissue and leuprolide-treated tissue of 175 and $141\,\mu m$, respectively. The significance of the thermal injury to tissue remains unresolved.

A Cochrane review concluded that, in general, a GnRH-a produces slightly more consistent endometrial thinning than danazol, whereas both GnRH-a and danazol were more effective in inducing endometrial thinning than progestogens, placebo, or no pretreatment. There was no difference between progestogens and no pretreatment in inducing atrophy of endometrial glands, adequate endometrial thinning, and reducing endometrial thickness. 11 The reviewers concluded that endometrial thinning prior to hysteroscopic endometrial ablation improves both the operating conditions for the surgeon and short-term postoperative outcome. The beneficial effects of pretreatment with GnRH-a or danazol on longer-term postoperative outcomes, such as amenorrhea and the need for further surgical intervention, reduces with time.¹¹ The Cochrane review reported that, in general, when compared with no pretreatment, the GnRH-a drugs are associated with a shorter duration of surgery, greater ease of surgery, and a higher rate of postoperative amenorrhea at 12 months. Postoperative dysmenorrhea also appears to be reduced. The use of GnRH-a has no effect on intraoperative complication rates and patient satisfaction is high regardless of the use of any preoperative thinning agent.¹¹

Data on endometrial thinning prior to rollerball ablation are very limited. One randomized study reported outcomes following pretreatment with GnRH-a (n=30) vs danazol (n=30)¹² and another study following GnRH-a (n=10), danazol (n=10), progestogen (n=10), and no treatment (n=10). The studies concluded that GnRH-a and danazol provided adequate endometrial preparation before rollerball endometrial ablation.

TECHNIQUE OF ROLLERBALL ABLATION

Cervical priming/ripening

Prior to introducing a 24–27 Fr (8–9 mm) resectoscope, the cervical os must be dilated up to 10 mm in diameter. To prevent vaginal and/or cervical tears caused by the tenaculum, or lateral cervical tears and/or cervical and uterine perforation caused by the dilator, cervical priming or ripening is recommended. The use of 400 µg of misoprostol, given 12 hours prior to operative hysteroscopy (orally or as vaginal suppository), has been shown to be beneficial over placebo in the ease of cervical dilatation. This benefit was seen in both premenopausal and postmenopausal women, and in those pretreated with GnRH-a. In a randomized

study, both misoprostol and laminaria were shown to be equally effective in inducing proper cervical priming prior to operative hysteroscopy.¹⁵ Cervical priming should be considered in women who are nulliparous, did not have a vaginal delivery, were pretreated with GnRH-a, or had cervical surgery for dysplasia, and in all postmenopausal women.

Anesthesia and patient positioning

Cervical dilatation and rollerball ablation can be performed under general anesthesia, regional analgesia (epidural or spinal), or conscious sedation with or without para-(intra)-cervical block. Once the patient has been adequately anesthetized, the surgical table must remain in horizontal position to avoid air or gas embolism through the uterus. This rare but potentially lethal complication may occur when air or gas bubbles intravasate when the patient is in Trendelenburg position (placing the uterus above heart level).¹⁶

Cervical dilatation

Prior to attempting cervical dilation, the size, shape, mobility, and especially the uterine position must be determined by bimanual examination. A double-toothed tenaculum is then applied to the anterior lip of the cervix. The double-toothed tenaculum may be less prone to cause cervical tears because of its four-point attachment rather than the two-point attachment of the single-toothed tenaculum. If excessive traction on the cervix is required, and the tenaculum attachment is tearing, a single-toothed tenaculum may be applied to the posterior lip of the cervix. This simultaneous traction on both tenaculi frequently avoids cervical tears during difficult dilatation of the cervix.

Cervical stiffness encountered during dilatation can be minimized by intracervical injection of 10–15 ml of vasopressin or Xylocaine (lidocaine) with 1:200 000 epinephrine solution. ¹⁴ The initial smaller dilator or uterine sound should pass freely with no resistance through the cervical canal. If resistance to the initial dilator/uterine sound is encountered, the cervical canal should be visualized with a smaller diagnostic hysteroscope, and dilatation can be achieved once the opening is visualized. Once the desired dilatation is achieved, the last dilator should be left in place to avoid air embolism through possible cervical tears or perforations.

Irrigation/distention liquids

The use of 'monopolar' radiofrequency (RF) resectoscopes requires non-conductive (salt-free) solutions.

Non-electrolytic or non-ionic solutions include amino acids (glycine 1.5%, 3%) or several sugars alone or in combination (sorbitol 3.3%, mannitol 5%, and dextrose in water 5%). The preference of the solution varies in accordance with physician training and experience, local preference, and personal bias. All solutions are nonphysiologic and hypotonic, except mannitol, and all result in hyponatremia when excessive intravasation occurs. 16 From a theoretical point of view, mannitol may be a safer solution to use because it is isotonic and induces diuresis. However, acute hyponatremia in rabbits resulted in equal mortality (approximately 30%) following either isotonic or hypotonic hyponatremia, although there was less brain edema caused by mannitol.¹⁷ In our center, we have used glycine (1.5%) in over 5000 operative hysteroscopic procedures with no major complications and no deaths attributable to the irrigant solution.

Electrosurgical generators/units

For rollerball endometrial ablation, any modern electrosurgical unit (ESU) can be used. The two main safety features that an ESU should have are isolated circuitry and contact quality monitoring system (CQMS). Two frequently used CQMS are the return electrode monitoring (REM) system and the neutral electrode safety system (NESSY). The CQMS use a small alternating current (AC) and voltage across the two halves of the split pad to evaluate the electrode-to-patient contact impedance. All modern ESUs are isolated, meaning they are not referenced to ground. The electrosurgical AC flows between the ESU, the active electrode (rollerball, bar, barrel, etc.), through the uterus and patient, and back to the ESU, through the dispersive split pad electrode attached to the patient's thigh or buttocks.

Electrosurgical power (wattage)

The power output of the ESU is given in watts:

Power (W) = voltage (V) \times current (A)

Energy = $1 \text{ W} \times 1 \text{ second} = 1 \text{ Joule.}$

All ESUs are designed to deliver two waveforms of voltage: a continuous waveform, having low peak-to-peak voltage (<3500 V p-p uploaded), used to cut and referred to as cut or low-voltage waveform; and an intermittent, modulated (damped) waveform, peak-to-peak voltage, up to 10 000 V to fulgurate capillary bleeding beds (coagulate). This latter waveform is referred to as coag or high voltage and is designed to coagulate or fulgurate tissue. These intermittent bursts of the coag waveform are delivered at 30 000 to 40 000 per second. By varying the time duration interval and peak-to-peak voltage of each burst

of power, electrical engineers have created a variety of combinations of waveforms, frequently referred to as blended waveforms. For example, most ESUs deliver five modes: pure cut (low-voltage) continuous waveform, blend 1, blend 2, blend 3, and coag (higher-voltage) waveforms; the corresponding duration delivery for the currents are on 100%, 80% on 20% off, 60% on 40% off, 50% on 50% off, 6% on 94% off duty cycle in time. The ESU modes deliver the wattage displayed regardless of mode, and the number of joules is the same provided that the control settings are equal. Therefore, the pure cut mode will cut or vaporize tissue at a lower setting than blend or coag modes due to continuous (100%) delivery of current.¹⁸

Electrosurgical power density

Power density (PD) is power delivered in watts, divided by the surface area of the active electrode:

 $PD = W/cm^2$

This means that a 2.5 mm diameter rollerball electrode delivers four times higher power density to the tissue than a 5 mm diameter rollerball. This explains the paradox that a smaller electrode may perform the ablation faster and more efficiently than a larger one. Furthermore, electrons tend to marginate on the edges of some specially shaped electrodes called grooved or spiked electrodes. This phenomenon of electron margination increases the power density in the edges, referred to as edge density, and causes vaporization of tissue with these electrodes rather than desiccation or fulguration. However, the power required to vaporize tissue is in excess of 200 W of cut (low-voltage) waveform. Such electrodes are frequently referred to as vaporizing electrodes.^{18,19}

Electrosurgical power and waveforms

Controversy exists as to what power (wattage) and waveform (cut, blend, or coag) surgeons should use during rollerball endometrial ablation to optimize ease and speed of ablation, patient safety, and clinical outcomes. An invivo study of uterine electrosurgery demonstrated that rollerball coagulation at 75 or 100 W applied for 1–5 seconds results in endomyometrial necrosis of 3.30–3.77 mm depth (mean = 3.59 mm).²⁰ Therefore, it has been recognized that approximately $100 \text{ W} \pm 20 \text{ W}$ of power is required to cause sufficient desiccation of endomyometrial tissue for the desired clinical effect.

The use of wattage in the cut mode to ablate the endometrium with rollerball is more difficult and frustrating for the surgeon. With the use of wattage in the cut mode, the rollerball (bar) electrode very rapidly becomes covered by coagulated tissue and debris, which increases the electrode–endometrium interface impedance and decreases

further desiccation of endomyometrium. Many surgeons know that the easiest way to clean such a 'gummed up' electrode is to briefly step on the coag mode of the ESU. The high voltage (plasma) of the coag mode burns away all the desiccated tissue and debris, producing a very shiny clean rollerball (bar) and eliminates the need to withdraw the resectoscope and clean the electrode manually. Furthermore, this 'gumming up' of the electrode may cause arcing and burning of the insulation next to the rollerball. This, in turn, may cause arcing/coupling to the telescope or outer sheaths/cannulae, which may result in vaginal burns.^{21,22} During rollerball endometrial ablation, it is important to have a consistent low impedance between the electrode and the tissue to be desiccated, to ensure uniform delivery of the ESU's output power. Coagulated tissue built up on the electrode will clearly affect uniform desiccation of the endometrium with each pass of the rollerball.

There is controversy on whether the use of low-voltage (cut) waveform is safer than high-voltage (coag) waveform on minimizing genital tract burns due to stray currents associated with all monopolar RF resectoscopes. 22-25 Recent evidence indicates that in the presence of normal electrodes, the magnitude of surge currents into the working elements of resectoscopes is the same (up to 500–600 mA) whether one uses high- or low-voltage waveforms. 26 Furthermore, genital tract burns have been experienced from the use of both high-voltage (coag) waveform during rollerball ablation and low-voltage (cut) waveform during endometrial resection with loop electrodes. 22

The final controversy is whether the low-voltage (cut) or high-voltage (coag) waveforms desiccate endomyometrial tissue deeper and produce better clinical outcomes. There have been limited in-vivo studies addressing the degree of thermal injury to the uterine wall. One study addressed the effects of power (wattage) and waveforms (cut and coag modes) during endometrial ablation.²⁷ This in-vitro study, using a small number of extirpated hysterectomy specimens, concluded that the amount of thermal injury correlated linearly but weakly with the amount of wattage used for either current (waveform). The correlation coefficients of thermal myometrial injury vs wattage were 0.36 (15-80 W) and 0.38 (40-160 W) for the coag and cut waveforms, respectively.²⁷ The cut (low-voltage) waveform required >90 W for a 3 mm depth of myometrial injury compared to a required 55 W of coag (high-voltage) waveform for the same result. Higher levels did not result in a significant difference in depth of damage, with a maximum depth of damage of 4.2 mm or 18% of the myometrium. Power and waveform alone do not appear to be clinically significant determinants of the amount of thermal injury occurring during endometrial ablation.27

There have been no reported clinical trials on the outcomes of using cut vs coag waveforms during rollerball endometrial ablation. However, in a randomized pilot study in our hospital we found that, in addition to our frustration with 'gumming up' of the electrode with the use of the cut mode, the preliminary clinical results in terms of menstrual reduction were inferior with the use of cutting waveform.

Rollerball (bar) endometrial ablation

Once the resectoscope is introduced into the uterine cavity, the surgeon must identify certain landmarks prior to commencing ablation. The landmarks include the tubal ostia, the internal cervical os, and the cervical canal. Thickened, polypoid, or inadequately prepared endometrium may be curreted with a sharp curette, or suctioned to facilitate rollerball ablation or resected with a loop electrode. Unexpected findings such as polyps, myomas, or other suspicious neoplastic lesions should be removed for histologic examination prior to rollerball ablation. Alternatively, the surgeon may switch to a loop electrode to resect both the lesions and endometrium at the same time. Some myomas may be treated by vaporizing electrodes, whereas larger myomas can be coagulated over their protruding surface in conjunction with the endometrium. A rollerbarrel (bar) provides more uniform contact with the endometrium than the rollerball, but it may not adequately ablate the cornua and fundus of the uterus. A 2-3 mm rollerball is more effective than a 4-5 mm ball because it provides higher current density for a given electrosurgical power.

The technique of roller ablation involves the ball or barrel being extended by thumb motion and allowed to passively return towards the sheath at speeds of approximately 1–1.5 mm/s. However, the final effect on the tissue is judged visually by the surgeon as a dark brown honeycomb appearance of the ablated/desiccated myometrial surface. Repeated passes may be necessary to produce the desired effect. The depth of myometrial thermal necrosis is limited by the increased impedance of the desiccated tissue. There is no evidence that repeated passes of the rollerball over the same areas increase the risk of visceral injury without uterine perforation.

To perform a rollerball ablation, you need a 3 or 5 mm rollerball attached to a $12{\text -}30^\circ$ telescope with a swivel camera and $100~\text{W}~(\pm~20~\text{W})$ of power in the coag (high-voltage) mode. After the cervical canal, tubal ostia, and internal cervical os are identified, the lower margins of ablation, at the level of the internal os, are circumferentially marked with active rollerball. Rollerball ablation then proceeds in a systematic fashion, starting at either the left or right tubal ostia. The resectoscope is first rotated

and held horizontally - palm pointing downwards - with the 12-30° scope visualizing the left tubal ostium. The rollerball is positioned at the mid fundus of the uterus and is progressively moved towards the left tubal ostium. Once the left fundal area and tubal ostium are thoroughly ablated, the resectoscope is pulled outwards, ablating the left uterine wall all the way to the previously marked internal os. Then the entire posterior wall is thoroughly ablated using long passes in a clockwise rotation of the resectoscope from the fundus to the internal os. At the completion of ablating the left and posterior uterine walls, the resectoscope is rotated 180° and is regrasped with the palm pointing again downwards but the lens looking to the right tubal ostium. Ablation is then completed from the right tubal ostium, right and anterior uterine wall, in a systematic clockwise fashion. By using this technique, reapplication of the surgeon's hand to the resectoscope occurs only once. Some surgeons prefer to ablate the endometrium in short strokes, using thumb action to control the rollerball, while others prefer long passes by withdrawing the entire resectoscope like a curette. Other surgeons use a combination of short and long passes. The most important thing to remember is that the rollerball is activated only when moved outwards and never when it is moved inwards. This is to minimize perforation and thermal injury to viscera.

Bubbles in solution

During rollerball tissue desiccation, smoke is generated and is seen as bubbles in the solution. These bubbles can accumulate at the tip of the telescope, trapped under the ceramic insulating tip of the internal sheath, or float upwards to the anterior uterine wall or fundus, impairing visibility. Bubbles trapped at the tip of the telescope are easily dislodged by rotating the resectoscope 180°, allowing the bubbles to float upwards. Bubbles on the anterior uterine wall or fundus can impair visibility but are frequently suctioned out by advancing the resectoscope forwards through the bubbles. One must remember that the outflow holes of the external sheath of the resectoscope are approximately 1–2 cm behind the field of vision of the telescope. Vigorous shaking of the telescope does not dislodge or suction these troublesome bubbles.

Bleeding during ablation

Excessive bleeding during rollerball ablation is rare since small and larger vessels are coagulated rather than resected. However, if bleeding is thought to be excessive at the completion of the procedure, individual vessels can be identified and recoagulated. Other helpful maneuvers may be a bimanual compression and massage of the uterus for a few seconds or an injection of vasopressor agents intracervically. However, the most reliable method to control bleeding in the operating room or recovery room is the insertion of a Foley catheter into the uterine cavity, which is then inflated with 20–40 ml of sterile fluid until the bleeding stops. After 1 hour, the Foley can be deflated and, if there is no further bleeding, it can be removed. If bleeding persists, the Foley can be reinflated to tamponade the uterus for a longer period of time.

CLINICAL OUTCOMES

One study reported on 200 women with menorrhagia who were candidates for hysterectomy and were treated with rollerball ablation from 1988 to 1993.28 All women were pretreated with various thinning agents, and ablation was performed using 120 W of coag waveform and sorbitol (3%). Complications were minimal. At mean follow-up of 2.5 years, improvement in menstrual bleeding was achieved in 90% of patients. Eight (4%) patients required a repeat ablation and one of these eight patients subsequently went on to have a hysterectomy. A total of 10 (5%) women had hysterectomy following rollerball ablation.²⁸ Another study reported medium-term results on 142 women who presented with menorrhagia and were treated by rollerball ablation, from 1990 to 1993.²⁹ All women were pretreated with either danazol or GnRH-a. Follow-up was obtained on 128 patients (90%) from 12 up to 52 months. The amenorrhea rate was 25%, while the satisfaction rate decreased gradually from 95% within the first 2 years to 75% after 3 years. The rate of repeat ablation and hysterectomy within the first 3 years was 8.5% for both. The hysterectomy rate (8.5%) increased gradually with time over the first 3 years, but not thereafter. There were no significant differences in menstrual outcomes among different age groups, types of endometrial preparation, endometrial thickness, presence or absence of 'adenomyosis' or myomas, or performance of myoma resection.²⁹

In another study, significant menstrual blood reduction was reported in 39 women presenting with menorrhagia, treated by rollerball ablation.³⁰ All women were pretreated with either danazol or GnRH-a. The mean (\pm standard deviation) menstrual blood loss (per menstrual period) was reduced from 90 \pm 14.4 ml before ablation to 3.8 \pm 2.1 ml at 3 months, 1.8 \pm 1.0 ml at 6 months, and 3.3 \pm 1.3 ml at 5–6 years after ablation. In menstruating women, the mean hemoglobin rose significantly from 126 to 135 g/dL (p=0.022). The amenorrhea rate was 65%, 62%, and 46% at 3, 6, and 60–72 months, respectively.³⁰

One study reported on a retrospective review of 240 women, presenting with menorrhagia, treated by rollerball

ablation with a mean follow-up of 31.2 months.³¹ Overall, the probability of no hysterectomy in the first 5 years was 71%. Ablation was repeated in 10 (4.2%) patients, six of whom eventually underwent hysterectomy (60%). Multivariate analysis identified previous tubal ligation as a statistically significant positive predictor of the risk of hysterectomy (hazard ratio = 2.20, 95% confidence interval [CI] 1.18–4.09). Women \geq 45 years old had a lower risk of subsequent hysterectomy than those >35 years old (HR = 0.28, 95% CI 0.10–0.75). The authors concluded that previous tubal ligation, repeat ablation, and a younger age at the time of ablation increase the risk of requiring subsequent hysterectomy.³¹

One randomized clinical trial reported on 2- and 5-year follow-up of endometrial rollerball ablation (n =61) vs endometrial resection (n = 59) in women presenting with menorrrhagia.²⁹ The mean operating time for the rollerball and resection groups was 13 and 30 minutes, respectively (p < 0.05). Rollerball ablation was performed with a 4 mm rollerball and 100 W of coag power. At 5 years, 113 women answered a questionnaire. At 2-year follow-up, 14.8% vs 16.9% of women had repeat ablation and 9.8% vs 6.8% had a hysterectomy in the rollerball ablation vs resection groups, respectively. At 5-year follow-up, the corresponding rates for repeat ablation and hysterectomy were 16.4% and 13.6%, respectively, in both rollerball ablation and resection groups. One patient absorbed excessive irrigant fluid, developed sepsis, and died.³²

Another study reported on a randomized comparison of vaporizing electrode (n = 47) and cutting loop (n = 44) for endometrial ablation in menorrhagic women.³³ At 1-year follow-up, the menstrual pattern was amenorrhea (36%), hypomenorrhea (43%), eumenorrhea (21%), and menorrhagia (0%) in the vaporization group. The corresponding rates with the loop electrode were 48%, 32%, 16%, and 5%, respectively.³³

A small cohort study (n = 64) reported that 3 years following rollerbar endometrial ablation, women experienced significant improvement of their perimenstrual symptoms in conjunction with menstrual reduction.³⁴

The effect of rollerball ablation on dysmenorrhea has also been reported. At 12 months after rollerball ablation, dysmenorrhea decreased in 75% of women, while it remained the same or worsened in 25% of women. After 5 years, mild, moderate, and severe dysmenorrhea was reported by 26%, 13%, and 8% of patients, respectively.³⁵

Several randomized clinical trials compared second-generation endometrial ablation technologies (SEATs), also called global endometrial ablation (GEA), vs roller-ball ablation.² The overall amenorrhea rate following rollerball ablation varied from 27% to 56% and the hysterectomy rate was up to 16% at 5 years follow-up.²

A Cochrane review also reported on endometrial destruction techniques.³⁶ When balloon endometrial ablation was compared to rollerball, the amenorrhea rate was less likely after balloon than after rollerball ablation at both 12 and 36 months, but there was no significant difference between the groups 24 months and 5 years after treatment. At 5 years, the odds of satisfaction with treatment were significantly less in the balloon group when compared with the rollerball group and the hysterectomy rate was 16% in both groups.^{35,36}

COMPLICATIONS

Immediate complications

Immediate complications can be classified under traumatic complications, distending media complications, or thermal injuries.

Traumatic complications

Cervical tears, false passages, and/or partial or complete uterine perforations with dilators, uterine sound, or resectoscope have been reported to occur at frequencies of 0.8–2%.² Midline or fundal perforations do not usually result in significant sequelae. In the presence of excessive bleeding or larger rents, the perforation may require suturing. Lateral perforations involve the risk of hemorrhage and should be inspected laparoscopically.^{37,38} Such injuries, if unrecognized, may lead to excessive bleeding, air embolism, excessive fluid absorption, and injuries to adjacent organs such as ureters and bladder. Tips to avoid and/or recognize such complications have been discussed previously.¹⁶

Distending media complications

Air or gas embolism Mechanical trauma to the cervix or uterus may allow the intravasation of room air or gas bubbles generated during rollerball ablation, especially when the patient is positioned in the Trendelenburg position.

To prevent air embolism, the patient should remain in the horizontal position throughout surgery. The last dilator should be left in the cervix and air should be purged from the inflow tubing prior to insertion of the resectoscope. Furthermore, surgeons should minimize the number of insertions and withdrawals of the resectoscope and avoid the use of non-collapsible distention media containers such as glass or solid plastic bottles. The use of outflow suction (80–100 mmHg) to evacuate generated bubbles during surgery may also reduce the risk of gas embolism.¹⁶

Excessive fluid absorption Complications related to distention media occur in 0.14–4% of the procedures. Several factors have been found to minimize fluid absorption during resectoscopic surgery. These include pretreatment with a GnRH-a or intraoperative injection of vasopressors into the cervix (Pitressin [vasopressin] solution 0.05–0.4 U/ml, epinephrine 1:200 000). Other important factors to minimize fluid absorption are intrauterine pressure below the mean arterial pressure (MAP <75 mmHg) of the patient and outflow suction (80–100 mmHg). 14,16

The surgeon may use a variety of non-conductive fluids during rollerball ablation. It is good clinical practice that the surgeon is aware of the physiology and biochemistry of whichever fluid is chosen, so that the clinical sequelae can be appropriately treated should the need arise. The fluid deficit should be diligently monitored every 1000 ml of fluid used rather than by an arbitrary time of every 5–10 minutes. Fluid irrigates the uterus at rates of up to 300 ml/min and intravasation can occur very rapidly if the endomyometrial integrity is breached by the electrode.

Electronic fluid monitoring systems, which allow regulation of the rate of flow, infusion pressure, and outflow suction as well as fluid deficit, may be advantageous over gravity infusion systems and manual estimation of fluid deficit. With the use of salt-free (non-conductive) solutions, the serum sodium decreases by approximately 1 mEq/100 ml of fluid absorbed. To avoid moderate hyponatremia ($Na^+=120-130 \text{ mEq/L}$), the procedure should be expeditiously completed at a fluid deficit of approximately 1000 ml and serum electrolytes should be evaluated. When the fluid deficit exceeds 1500 ml, the procedure should be terminated, electrolytes should be assessed, and the patient should be given intravenous furosemide. Severe hyponatremia (Na+<120 mEq/L) requires intensive therapy and monitoring to avoid cognitive brain damage and even death.¹⁶

Thermal injuries

Visceral injuries Thermal injuries to viscera occur when the uterus is perforated with an active rollerball. The response to uterine perforation with a dilator, sound, or inactive rollerball/resectoscope is expectant treatment. However, when the surgeon is not sure whether the electrode was activated or not during perforation, responses should include intensive monitoring of the patient for several days or immediate exploration of the bowel through laparoscopy or laparotomy.

Genital tract burns Lower genital tract burns to cervix, vagina, and vulva have been reported.²¹ These burns are caused by a variety of stray currents, some of which are unique to the RF resectoscopes. Stray currents can occur by capacitive leakage, electrode insulation defects, and ionic

currents generated by blood mixing with the non-conductive solutions during rollerball ablation. 18,21–26

Baseline stray currents are present all the time. Several signs may warn the surgeon of the presence of excessive stray currents, including electrical interference (diagonal lines or sparks on the TV monitor caused by a short circuit), the patient twitching or jumping (caused by harmonic demodulation of the frequency to <100 kHz), or the inadequate effect of the rollerball on the tissue (caused by loss of electrons elsewhere) when the electrode is activated. When any of these signs are present, the procedure should be stopped and the entire electrical circuit/system should be evaluated. A simple way to minimize the risk of genital tract burns is to keep the weighted speculum in the vagina throughout the procedure. The larger surface area of the weighted speculum dissipates these currents without harm to the patient.

Dispersive electrode skin burns As a rule, during rollerball ablation, dispersive pad electrode burns to the skin do not occur when using a CQMS split-pad electrode. However, when a high-power output is required (>200 W in cut mode) with vaporizing electrodes or in the presence of inadvertently used saline solution to irrigate the uterus, return electrode burns have been encountered.¹⁹

Delayed Complications

Intrauterine contracture, scarring/synechiae

In one study, 9 of 13 hysterectomy specimens assessed more than 3 months after rollerball ablation had significant scarring of the cavity and two had complete obliteration of the cavity. Taskin et al. reported on long-term histopathologic and morphologic changes after rollerball endometrial ablation in 26 women. Mean follow-up time to second-look hysteroscopy after rollerball ablation was 33.4 ± 2.1 months. Complete atrophy, partial adhesions, or obliteration of the cavity and fibrosis were observed at second-look hysteroscopy. Whereas all random biopsies were normal before ablation, biopsies after ablation revealed diminished endometrial glands with necrosis and scarring. The number of endometrial glands was not correlated with amount of bleeding or menstrual pattern. 40

Postablation tubal sterilization syndrome

Townsend and associates reported on six patients who had prior tubal ligation and presented with cyclic severe unilateral lower abdominal pain 6–10 months after rollerball endometrial ablation. Hysteroscopic evaluation revealed a contracted, scarred cavity while laparoscopy identified hematosalpinx of the proximal tubal stump. A recent review reported that this syndrome occurs after hysteroscopic and non-hysteroscopic endometrial ablation.

The true incidence of PATSS is unknown but it has been estimated to occur in up to 10% of cases.⁴³ The treatment of PATSS is either laparoscopic proximal salpingectomy or hysterectomy.

Hematometra

Hematometra can occur when there is complete occlusion of the lower uterine segment or cervix postablation with persistent or regenerating endometrium from deep adenomyosis within the uterine cavity. Women presenting with cyclic central pain with or without vaginal bleeding and imaging indicates single or multiple fluid collection pockets within the uterus. The treatment is either repeat endomyometrial resection by experienced surgeons or hysterectomy. Adenomyosis is confirmed histologically in up to 52% of hysterectomy specimens.⁴⁴ The risk of hematometra may be minimized by avoiding rollerball ablation to the lower uterine segment and cervix.⁴⁵

Repeat ablations

The rate of repeat ablations has been reported by numerous investigators to be 3–16.3%. ^{28–32,35,46} In general, there are fewer repeat ablations than hysterectomy following treatment failures. ⁴⁷

Hysterectomy

Following rollerball endometrial ablation, hysterectomy rates of up to 16% have been reported. 28–32,35 One

cohort study reported that 14 of 41 women (34%) underwent hysterectomy within 5 years after rollerball ablation. However, 11 of the 14 cases of hysterectomy were associated with gross abnormalities such as myomas, adenomyosis, endometriosis, and chronic hematosalpinx.⁴⁸ It has been noted that women who require hysterectomy after rollerball ablation will present within the first 3 years after the ablation procedure.^{29,32,35} Previous tubal ligation is a risk factor for hysterectomy after rollerball ablation.^{31,49}

SUMMARY

In general, rollerball ablation is the easiest and most frequently used technique of all the hysteroscopic methods.⁵⁰ It has the lowest risk of hemorrhage, perforation, gas embolism, excessive fluid absorption visceral damage, and emergency surgery.^{37,38} A general anesthetic is used in 99% of cases.³⁷ Compared with hysterectomy, rollerball ablation is quicker to perform and results in shorter hospitalization.⁴⁷ Satisfaction with hysterectomy is initially higher than rollerball ablation, but there is no significant difference after 2 years.⁴⁷

Compared with thermal balloon endometrial ablation, amenorrhea was more likely in the rollerball group at 12 and 36 months but not at 24 months.⁴⁷ Likewise, additional surgery was significantly more likely in the rollerball group at 24 months; this was not seen at 12 or 36 months.⁴⁷

References

- Vilos GA, Lefebvre G, Graves G. Guidelines for the management of abnormal uterine bleeding. SOGC Clinical Practice Guidelines No. 106, August 2001. J Obstet Gynecol Can 2001; 23: 704–9.
- Vilos GA. Hysteroscopic and nonhysteroscopic endometrial ablation. Obstet Gynecol Clin North Am 2004; 31: 687–704.
- Hallez JP, Netter A, Cartier R. Resection endo-uterine. Rapport preliminaire. Gynecologie 1985; 36: 127.
- 4. Vancaillie TG. Electrocoagulation of the endometrium with the ball end resectoscope. Obstet Gynecol 1989; 74: 425–7.
- McLucas B. Endometrial ablation with the rollerball electrode. J Reprod Med 1990; 35(11): 1055–8.
- Townsend DE, Richart RM, Paskowitz RA, Woolfork RE. "Rollerball" coagulation of the endometrium. Obstet Gynecol 1990; 76: 310–13.
- Daniell JF, Kurtz BR, Ke RW. Hysteroscopic endometrial ablation using the rollerball electrode. Obstet Gynecol 1992; 80: 329–32.
- 8. Vilos GA. Intrauterine pregnancy following rollerball endometrial ablation. J Soc Obstet Gynecol Can 1995; 17: 479–80.

- Istre O, Daleng W, Forman A. The incidence of fallopian tube patency after transcervical resection of the endometrium including rollerball diathermy to the tubal ostia. Fertil Steril 1996; 65: 198–200.
- Brooks PG, Serden S, Davos I. Hormonal inhibition of the endometrium for resectoscopic endometrial ablation. Am J Obstet Gynecol 1991; 164: 1601–6.
- Sowter MC, Lethaby A, Singla AA. Pre-operative endometrial thinning agents before endometrial destruction for heavy menstrual bleeding. The Cochrane Library. 2006; Volume 3.
- 12. Fraser IS, Healey DL, Torode H et al. Depot goserelin and danazol, pre-treatment before rollerball endometrial ablation for menorrhagia. Obstet Gynecol 1996; 87: 544–50.
- Fomer T, Muller B, Bojahr B, Schwesinger G, Lober R. [Hormonal pretreatment for endometrial ablation results of a prospective comparative study]. Zentralblatt für Gynakologie 1996; 118: 291–4. [in German]
- Vilos GA, Abu-Rafea B. New developments in ambulatory hysteroscopic surgery. Best Pract Res Clin Obstet Gynecol 2005; 19(5): 727–42.

- 15. Darwish AM, Ahmad AM, Mohammad AM. Cervical priming prior to operative hysteroscopy: a randomized comparison of laminaria versus misoprostol. Hum Reprod 2004; 19: 2391–4.
- Vilos GA. Hysteroscopic surgery: indications, contraindications and complications. In: Pasic RP, Levine RL, eds. A Practical Manual of Hysteroscopy and Endometrial Ablation Techniques. A Clinical Cookbook, 1st edn. London: Taylor & Francis, 2004; 237–58.
- Pollock AS, Arieff AL. Abnormalities of cell volume regulation and their functional consequences. Am J Physiol 1980; 239: 195–205.
- Vilos GA, McCulloch S, Borg S, Zheng W, Denstedt JD. Intended and stray radiofrequency electrical currents during resectoscopic surgery. J Am Assoc Gynecol Laparosc 2000; 7: 55–63
- Vilos GA, Raders J. Dispersive pad injuries associated with hysteroscopic surgery. J Am Assoc Gynecol Laparosc 1999; 6(3): 363–6.
- 20. Duffy S, Reid PC, Sharp E. In-vivo studies of uterine electrosurgery. Br J Obstet Gynaecol 1992; 99: 579–82.
- Vilos GA, D'Souza I, Huband D. Genital tract burns during rollerball endometrial coagulation. J Am Assoc Gynecol Laparosc 1997; 4: 273–6.
- Vilos GA, Brown S, Graham G et al. Genital tract electrical burns during hysteroscopic endometrial ablation: report of 13 cases in the United States and Canada. J Am Assoc Gynecol Laparosc 2000; 7: 141–7.
- Munro MG. Factors affecting capacitive current diversion with a uterine resectoscope. An in vitro study. J Am Assoc Gynecol Laparosc 2003; 10: 450–60.
- Munro MG. Capacitive coupling: a comparison of measurements in four uterine resectoscopes. J Am Assoc Gynecol Laparosc 2004; 11(3): 379–87.
- Munro MG. Mechanisms of thermal injury to the lower genital tract with radiofrequency resectoscopic surgery. J Minim Invasive Gynecol 2006; 13: 36–42.
- Vilos GA, Newton DW, Odell RC, Abu-Rafea B, Vilos AG. Characterization and mitigation of stray radiofrequency currents during monopolar resectoscopic electrosurgery. J Minim Invasive Gynecol 2006; 13: 134–40.
- Onbargi LC, Hayden R, Valle RF, Del Priore G. Effects of power and electrical current density variations in an vitro endometrial ablation model. Obstet Gynecol 1993; 82: 912–18.
- 28. Paskowitz RA. "Rollerball" ablation of the endometrium. J Reprod Med 1995; 40: 333–6.
- Chullapran T, Song JY, Fraser IS. Medium-term follow-up of women with menorrhagia treated by rollerball endometrial ablation. Obstet Gynecol 1996; 88: 71–6.
- Teirney R, Arachchi GJ, Fraser IS. Menstrual blood loss measured 5–6 years after endometrial ablation. Obstet Gynecol 2000; 95: 251–4.
- 31. Dutton C, Ackerson L, Phelps-Sandall B. Outcomes after rollerball endometrial ablation for menorrhagia. Obstet Gynecol 2001; 98: 35–9.
- 32. Boujida VH, Philipson T, Pelle J, Joergensen JC. Five-year follow-up of endometrial ablation: endometrial coagulation versus endometrial resection. Obstet Gynecol 2002; 99: 988–92.
- 33. Vercellini P, Oldani S, Yaylayan L, Zaima B, De Giorgi O. Randomized comparison of vaporizing electrode and cutting

- loop for endometrial ablation. Obstet Gynecol 1999; 94: 521–7.
- 34. Lefler HT, Lefler CF. Ablation of the endometrium. Three-year follow-up for perimenstrual symptoms. J Reprod Med 1992; 37(2): 147–50.
- 35. Loffer FD, Grainger D. Five-year follow-up of patients participating in a randomized trial of uterine balloon therapy versus rollerball ablation for treatment of menorrhagia. J Am Assoc Gynecol Laparosc 2002; 9: 429–35.
- Lethaby A, Hickey M, Garry R. Endometrial destruction techniques for heavy menstrual bleeding. The Cochrane Library. 2006; Volume 3.
- Overton C, Hargreaves J, Maresh M. A national survey of the complications of endometrial destruction for menstrual disorders: The MISTLETOE study. Br J Obstet Gynaecol 1997; 104: 1351–9.
- 38. Jansen FW, Vredevoogd CB, van Ulzen K et al. Complications of hysteroscopy: a prospective multicenter study. Obstet Gynecol 2000; 96: 266–70.
- Colgan TJ, Shah R, Leyland N. Post-hysteroscopic ablation reaction: a histopathologic study of the effects of electrosurgical ablation. Int J Gynecol Pathol 1999; 18: 325–31.
- Taskin O, Onoglu A, Inal M et al. Long-term histopathologic and morphologic changes after thermal endometrial ablation. J Am Assoc Gynecol Laparosc 2002; 9(2): 186–90.
- Townsend DE, McCausland VM, McCausland AM. Post-ablation-tubal-sterilization syndrome. Obstet Gynecol 1993; 82: 422–24.
- 42. Gurtcheff SE, Sharp HT. Complications associated with the global endometrial ablation: the utility of the MAUDE database. Obstet Gynecol 2003; 102: 1278–82.
- 43. McCausland AM, McCausland VM. Frequency of symptomatic cornual hematometra and post ablation tubal sterilization syndrome after total rollerball endometrial ablation a 10 year follow-up. Am J Obstet Gynecol 2002; 186: 1274–83.
- 44. Vilos GA, Abu-Rafea B, Ettler H, Ahmad R. Indications for hysterectomy and uterine histopathology following hysteroscopic endometrial ablation. J Minim Invasive Gynecol 2005; 12: S9.
- 45. McCausland AM, McCausland VM. Partial rollerball endometrial ablation: a modification of total ablation to treat menorrhagia without causing complications from intrauterine adhesions. Am J Obstet Gynecol 1999; 180: 1512–21.
- Vilos GA, Vilos EC, King JH. Experience with 800 hysteroscopic endometrial ablations. J Am Assoc Gynecol Laparosc 1996; 4(1): 33–8.
- 47. Garside R, Stein K, Round A, Price A. The effectiveness and cost-effectiveness of microwave and thermal balloon endometrial ablation for heavy menstrual bleeding: a systematic review and economic modeling. Health Technol Assess 2004; 8(8): 1–155.
- 48. Unger JB, Meeks RG. Hysterectomy after endometrial ablation. Am J Obstet Gynecol 1996; 17: 1432–7.
- Moll A, Shirk G, Bradley J, Voorhis BV. Previous tubal ligation is a risk factor for hysterectomy after rollerball endometrial ablation. Obstet Gynecol 2002; 100: 659–64.
- 50. Garry R for the Endometrial Ablation Group. Evidence and techniques in endometrial ablation. Consensus. Gynecol Endosc 2002; 11: 5–17.

Hysteroscopic electrosurgical resection

Nikolaos P Papadopoulos and Adam Magos

INTRODUCTION

The development of the intrauterine resection of submucous fibroids by Neuwirth in 1978 was the first use of the urologic resectoscope in the uterine cavity and led to its adaptation to treat the whole endometrial cavity with what is commonly referred to as transcervical resection of the endometrium (TCRE).1 Although Neuwirth extended the procedure to electrocoagulation of the endometrium,2 it was DeCherney who, in 1983, 2 years after Goldrath's seminal paper on laser endometrial ablation, first formally described burning the entire endometrial cavity hysteroscopically using the loop electrode in women with intractable menorrhagia who were unfit for hysterectomy.3 The subsequent history of the technique is a little unclear, but at some stage the endometrium began to be resected rather than electrocoagulated, and rather than using a single-flow resectoscope with Hyskon (dextran 70) for uterine distention, continuous-flow resectoscopes with low-viscosity fluids for uterine distention (e.g. 1.5% glycine) became more popular. Indeed, the first gynecologic resectoscope sold by Karl Storz was just such an instrument designed by the urologist Jean-Pierre Hallez, who used it to perform hysteroscopic myomectomy.4 What is known is that the technique of TCRE was introduced into Europe by the famous Parisian gynecologist, Jacques Hamou, who advocated what has become known as 'partial TCRE', while Adam Magos et al. in Oxford described 'total TCRE' in 1989.5

Whatever the exact history, hysteroscopic methods of endometrial ablation soon became established as an effective alternative to more invasive surgery such as hysterectomy, and studies have since shown that around three-quarters of women with abnormal uterine bleeding can avoid hysterectomy with these techniques. The Royal College of Obstetricians and Gynaecologists (RCOG) in London recognized the role of these procedures in an evidence-based guideline published in 1999, stating that, 'endometrial ablative procedures are effective in treating menorrhagia'.

As a result of the success of these hysteroscopic interventions (endometrial resection, rollerball ablation, and

laser ablation), now referred to as first-generation ablation techniques, they are still considered as the gold standard by which the newer, less skill-dependent second-generation endometrial ablation methods (e.g. thermal balloon, radiofrequency, cryotherapy, etc.), must be judged.^{8,9}

INDICATIONS AND CONTRAINDICATIONS

Not all women with menorrhagia are suitable for TCRE and, as with all the ablation procedures, certain criteria have to be met; these are outlined in Table 16.1. TCRE has been shown to be effective in cases of dysfunctional uterine bleeding, and even if the uterus is slightly enlarged with small fibroids. Conversely, concurrent pathologies such as uterovaginal prolapse or endometriosis, to take but two examples, are better treated by more radical surgery. Similarly, malignant or premalignant changes in the endometrium are considered by most surgeons to be absolute contraindications to TCRE, although the opposite view is held by some. 10 Pregnancies have been reported after endometrial ablation as it does not guarantee sterility, but it is universally agreed that the procedure should not be contemplated in those women who may want to become pregnant in the future because of a much higher incidence of pregnancy complications (see later).

It is important for any woman contemplating endometrial ablation, by whatever technique, to understand that amenorrhea cannot be guaranteed; the principal aim of surgery is to make periods lighter and improve the quality of life and, even today, only hysterectomy can promise cessation of menstruation.

PREOPERATIVE PREPARATION

There is no universal agreement regarding the need for preoperative endometrial preparation to thin the endometrium. Some, such as Hamou, do not pretreat their

Table 16.1 Indications and contraindications for electrosurgical endometrial resection

Indications	Contraindications
Menorrhagia severe enough to warrant treatment	Concurrent pathology (e.g. uterovaginal prolapse, ovarian pathology, pelvic inflammatory disease, cervical atypia)
Failure of or contraindication to medical treatment	Submucous fibroids >5 cm
No desire for future pregnancies	Uterine size >12 weeks
Benign endometrial histology	Anovulation, endometrial hyperplasia
	Endometrial atypia and cancer

patients, whereas others time the intervention to just after menses when the endometrium is at its thinnest. If this proves not possible, surgical preparation by sharp or suction curettage at the time of the TCRE can reduce the endometrial thickness and thereby facilitate the resection. However, all these approaches leave a 'fluffy' endometrium that is prone to blocking the narrow suction holes on the resectoscope outflow sheath. For these reasons, as well as the simple fact that it is difficult to time surgery to a particular phase of the menstrual cycle in a busy clinical setting, a case can be made for routinely preparing the endometrium with drugs such as gonadotropin-releasing hormone (GnRH) analogues (e.g. goserelin, nafarelin), danazol, progestogens, and even the combined contraceptive pill, starting 6 weeks or so prior to surgery. 11 Such pretreatment has a number of advantages that facilitate surgery: it reduces endometrial thickness to less than 4 mm, corrects anemia, provides a better surgical view by reducing endometrial debris, and decreases the vascularity of the endometrium and uterus, leading to a shorter operating time, less bleeding, and less fluid absorption. 12 Apart from facilitating the surgery and reducing complications, pretreatment may lead to a better short-term and possibly long-term outcome. 13,14 Evidence also exists showing a higher amenorrhea rate when postoperative endometrial suppression is used.^{15,16} However, as with so much in medicine, contradictory evidence exists to suggest that there is no real difference in surgical or menstrual outcomes with preoperative endometrial thinning, and there are the obvious disadvantages of cost, side effects, and delay of surgery. 17,18

Cervical priming

Another, less-discussed aspect of preoperative preparation is cervical priming. The standard resectoscope has an outer diameter of 8–9 mm, which means that the cervix almost always has to be dilated to allow the instrument to be inserted into the uterine cavity. In nulliparous women, or those who have undergone cervical surgery (e.g. cone biopsy), this may be difficult because of cervical stenosis and scarring, with the risk of cervical tearing. In such cases, various techniques can be used for priming the cervix to facilitate dilatation of the canal such as the intracervical placement of laminaria, prostaglandins, and oral or vaginal misoprostol. ^{19–21}

Obtaining informed consent

The RCOG has published guidelines on the subject of informed consent for diagnostic hysteroscopy under general anesthesia.²² The consent for TCRE can be based on this document with some modifications, in particular with regard to the likely menstrual outcome, failure of the procedure, and fertility. Complications must also be discussed, in particular uterine perforation, fluid overload, and hemorrhage, which are unlikely with diagnostic hysteroscopy but are recognized complications of operative procedures. If the uterus is perforated, the patient must accept that a laparoscopy or laparotomy may have to be carried out, and even hysterectomy may be necessary (although this is extremely uncommon).

In addition, as we like to record all surgery that we perform on a personal computer (PC) in the operating theater, we routinely ask our patients for consent in order to record the procedure.²³

Anesthesia

Hysteroscopic procedures can be done under general anesthesia, spinal anesthesia, or local anesthesia using intra- and/or paracervical block in association with intravenous sedation. There is, for instance, no reason why even TCRE should not be performed under local anesthesia combined with sedation,²⁴ and we have summarized our protocol in Table 16.2. There are two aspects of this scheme worthy of comment. First, the dose of the anxiolytic midazolam should be titrated so that the minimum dose is used to ensure that the patient is relaxed (but not asleep!). Secondly, arguably the most important component of the local anesthetic injections is the intrauterine infiltration. This is done under direct vision using an injection needle that is available for certain resectoscopes; in the case of TCRE, the entire uterine cavity, particularly the fundal and cornual areas, are infiltrated about 10 mm under the endometrial surface (Figure 16.1).

Table 16.2 Protocol for intrauterine surgery under sedoanalgesia

Time	Drugs
1 hour before surgery	Diclofenac 100 mg pr
	Temazepam 20 mg po
In operating theater	Midazolam 2–10 mg IV
	Alfentanil 50 μg IV
Local infiltration	1% Lidocaine
	intracervical 10 ml
	paracervical 10 ml
	intrauterine 20 ml



Figure 16.1 Injecting intrauterine local anesthetic before hysteroscopic surgery.

In our experience, this protocol works very well provided the patient is motivated, and we have never had to convert a procedure to general anesthesia.

Antibiotic prophylaxis

Many surgeons routinely administer prophylactic antibiotics for TCRE to reduce the possibility of ascending infection from the lower to the upper genital tract during surgery (e.g. amoxicillin + clavulanic acid).²⁵ In reality, as with diagnostic hysteroscopy, the risk of infection is extremely small, and as far as the authors are aware, this practice is not an evidence-based approach, and may be unnecessary.

Equipment and instruments

The following equipment is required for TCRE.

Continuous flow resectoscope

A continuous flow resectoscope consists of five components: the handle mechanism, inflow sheath and outflow sheath, electrodes, and optic. The handle mechanism can be of the passive or active type (Figure 16.2). With the passive handle, the electrode is pulled into the sheath at rest, while with the active resectoscope, the handle pushes the electrode to the outside. Although urologists tend to use an active resectoscope, it makes more sense to use a passive handle inside the narrow confines of the uterus; as the electrode is naturally sited inside the instrument, it does not obstruct the view and is inherently safer from the point of view of accidental activation and perforation.

The sheathing system comes in different sizes, but most gynecologists use a 26 or 27 Fr gauge instrument (3 Fr [French] gauge = 1 mm). It is important to connect the irrigation and suction tubes correctly, remembering that the 'inner' sheath is for 'inflow' and the 'outer' sheath is for 'outflow'.

The typical loop for a 26 Fr resectoscope has a diameter of 24 Fr. Other options include the small or large rollerball, and rollerbar electrodes which are used for ablation (cf. resection) or vaporization.²⁶ Most currently used resectoscopes are monopolar, but bipolar instruments are now also available and, as they are safer, they should become the standard instrument (Figure 16.3).

A 4 mm optic is the usual diameter for a 26/27 Fr resectoscope. It can have a straight view or be fore-oblique at 12°, 15°, or 30° angles; angled optics give a better view of the ostial areas and are preferred by most gynecologists.

Uterine distention

Only electrolyte-free solutions (e.g. 1.5 glycine, 3% sorbitol, 5% mannitol) can be used with monopolar electrosurgery,

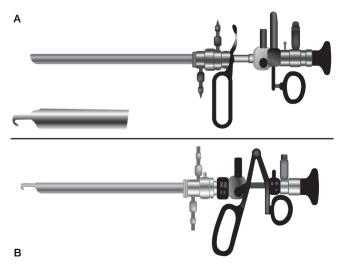


Figure 16.2 Passive handle resectoscope (A) and active handle resectoscope (B).



Figure 16.3 Bipolar resectoscopes and loop electrodes for use with bipolar current (inset pictures).

whereas normal saline is safe with the newer bipolar resectoscope.²⁷ Distention of the uterine cavity is facilitated by a dedicated automatic pump able to control intrauterine pressure and thereby the flow rate of the distention fluid. A basic rule of thumb is to use the lowest pressure that produces an adequate view, which in most cases means an inflow pressure of 80–120 mmHg. Sometimes, particularly if the uterus is relatively non-compliant because of fibroids, a higher pressure is required, but this is associated with greater fluid absorption and therefore risks fluid overload. Conversely, the suction pressure on the outflow tubing should be low to avoid deflating the uterine cavity, and there are some who only use gravity (the outflow should still be measured in an outflow bag).

Whatever set-up is used, it is essential to monitor fluid balance continuously during surgery to avoid fluid overload, and this is best done by a dedicated member of staff (see below). Apart from documenting in-flow and out-flow, the same person also has to ensure that air bubbles do not get into the in-flow system, as this risks air embolism.

Electrosurgical generator

Unlike the 'spark generators' of old, the modern electrosurgical generator is a safe device provided certain safety rules are adhered to. As with intrauterine distention pressure, the lowest power setting should be used which adequately cuts the endometrium without dragging (it should be like cutting through butter). For instance, we use 100–120 W of pure cut or blend 1 current with our Storz monopolar resectoscope and Valleylab Force 4 generator, but the optimum power setting can vary with different brands of resectoscopes and generators.

The use of bipolar resectoscopes is not only safer because more physiologic solutions can be used for uterine distention but also because bipolar electrosurgery is inherently safer than monopolar electrosurgery. The proximity of the active and return electrodes means that a lower voltage can be applied, and this makes accidental electrical or thermal injury less likely.

Camera unit and documentation systems

A three-chip CCD video camera (possibly to be superseded by the newest high-definition endoscopic cameras in the near future), a fiberoptic light lead, a tungsten, metal halide, or more usually xenon cold light source, and a medical monitor are all essential equipment for diagnostic and operative hysteroscopy. It can also be useful to record procedures and images to document the procedure. This can be done with rather expensive dedicated 'off the shelf' systems (e.g. Storz OR1), but is also possible for a fraction of the cost using a standard PC.²³

Theater organization and patient position

One scheme for theater organization in terms of positioning of the equipment trolley, patient, and staff is shown in Figure 16.4. Note that there is a clear provision for an experienced person who is going to be responsible for the fluid management. The patient must be placed in a dorsal lithotomy position with the hips at 90° angulation, with the trunk and buttocks over the edge of the operating table. This positioning allows good exposure of the female external genitalia and, most importantly, facilitates the free movement and manipulation of the resectoscope. Urinary bladder catheterization is rarely necessary unless the bladder is full or if there is concern about fluid overload (see below).

THE TRANSCERVICAL RESECTION OF THE ENDOMETRIUM TECHNIQUE

Initially, the perineum and vagina is cleaned with antiseptic solution and the cervix is dilated to accept a Hegar 10 dilator. The uterine cavity is inspected for its anatomic landmarks or any anomalies; any small submucous fibroids or polyps are generally resected at this stage. The presence of larger fibroids is not an absolute contraindication for surgery but may result in suboptimal treatment and compromise outcome.²⁸

Resection of the endometrium is commenced at the fundus with a forward angled loop, or alternatively, the area is rollerballed. The rollerball is arguably less likely to perforate the uterus at the cornual region where the myometrium is at its thinnest. The rest of the uterus is systematically resected with the conventional loop, following a clockwise or counterclockwise course, down towards the internal cervical os (Figure 16.5). Amenorrhea can only be achieved with resection of the whole uterine cavity,

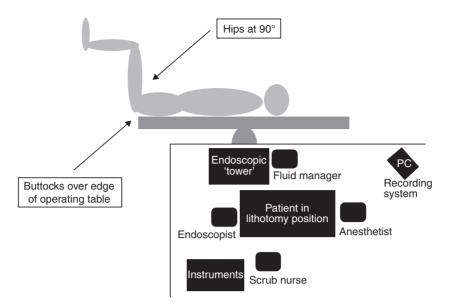


Figure 16.4 Correct patient positioning and theatre oganization (inset picture) for operative hysteroscopy.

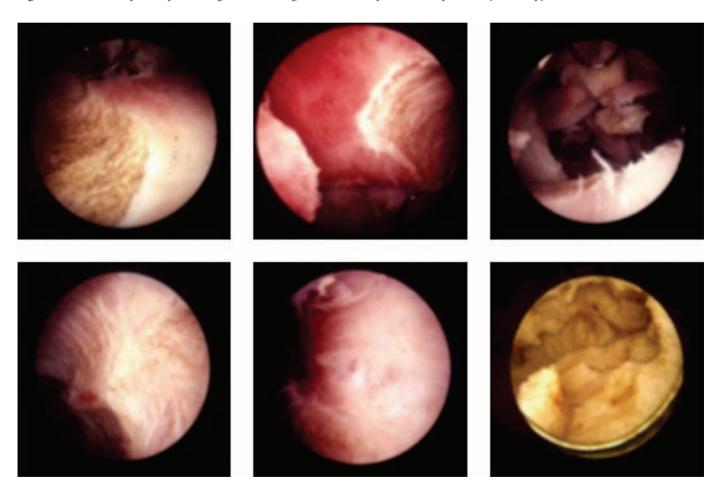


Figure 16.5 Different stages of TCRE using the loop electrode.

and to ensure that endometrium has not been left near the isthmus, we routinely continue the resection into the upper part of the endocervical canal; surgery in the cervix should be more superficial to avoid hemorrhage from the rich cervical vasculature. The cardinal principle of safe resectoscopy is to only activate the electrode as it is being pulled into the sheath, i.e. towards the cervix. Cutting away from the instrument, towards the uterine fundus or into the side walls of the uterus, risks perforation. As previously noted, the risk

of perforation resulting from unintentional activation of the loop electrode is reduced by using a passive handle mechanism.

The depth of resection is judged by the appearance of the circular myometrial fibers, and it is important not to cut too deep as this could lead to hemorrhage and ultimately also to uterine perforation. Isolated bleeding points can be coagulated with the loop electrode using the same cutting mode in 'contact mode', and it is rarely necessary to change to coag, which is more risky as it is at a higher voltage. As high-tech instruments are used during resection, many practical problems may arise. These are outlined in Table 16.3, together with proposed solutions.

The resected tissue chips are pushed up towards the fundus of the uterine cavity to enable visualization of the unresected part of the endometrial cavity and are ideally removed at the end of the procedure using polyp forceps, or even better, an old-fashioned flushing curette. This technique is preferable to removing the resectoscope with every cut as this increases the operation time, bleeding, and the chance of cervical trauma. The above is our preferred technique, but if the endometrium is very thickened, it is often easier to cut full-length endometrial chips

and remove them with each pass of the resectoscope; we use a similar technique in cases of repeat TCRE.

At the end of surgery the uterine cavity must be inspected carefully for any pulsating arteriolar bleeding or untreated islets of endometrium. In rare cases, postoperative hemorrhage requires tamponade and we use a large urinary catheter balloon inflated with 30 ml of N/saline, which is left inside the uterine cavity for 6–24 hours.

POSTOPERATIVE PATIENT MANAGEMENT

In the vast majority of cases TCRE is day-case procedure. Arising problems or minor complications such as pain, nausea and vomiting and bleeding after surgery (usually heavy only for the first 24 hours), can be managed easily with mild analgesics (e.g. mefenamic acid). Vaginal bleeding usually continues for a few weeks, but is rarely heavy. It is said that there is less discharge after resection than ablation techniques which are associated with a necrotic coagulum inside the uterine cavity. Normal activities and work can be resumed very soon after surgery. We no longer review our patients after surgery, and it is certainly not worthwhile arranging a follow-up for at least 3 months.

Table 16.3 Troubleshooting chart

Problem	Reason	Action
Poor uterine distention	Low distention pressure	Increase pressure
	Cervical incompetence	Suture or clamp cervix
	Uterine perforation	Stop surgery and check
Slow clearance of debris	Low suction pressure	Increase suction pressure
	Blocked suction holes in outflow sheath	Remove resectoscope and clear
Inefficient cutting	Cutting power too low	Increase power or reduce blend
	Electrode broken	Replace electrode
	Cutting loop bent forward	Bend back towards beak
Bleeding during surgery	Low distention pressure	Increase distention pressure
	Insufficient coagulation	Increase cutting blend
	Resection too deep	Cut more superficially
	Myomectomy	Coagulate vessels around base of fibroid
Rapid fluid absorption	High distention pressure	Reduce distention pressure
	Uterine perforation	Stop surgery and check for perforation
Hemorrhage after surgery	Resection too deep	Uterine tamponade with balloon
	Infection	Give antibiotics
	Tissue chips in cavity	Evacuate

Complications

As with all surgical procedures, complications can be reduced by proper patient selection and preparation, as previously outlined. Similarly, adequate training and experience with using a resectoscope is also mandatory, and there is little doubt that TCRE is more skill dependent with a longer learning curve than is the case with second-generation ablation techniques.²⁹ Nonetheless, even proper patient selection and preparation and careful surgery cannot totally protect against complications, some even fatal.^{30–32}

Intraoperative complications

The most serious intraoperative complications of TCRE are uterine perforation, hemorrhage, fluid overload, electrosurgical burns, and air embolism (Table 16.4).

Uterine perforation can occur during cervical dilation and during tissue chip retrieval and usually does not require any intervention except for hospitalization and close observation for signs of bleeding for the next 24 hours. In contrast, perforation occurring as the loop electrode is being activated is potentially very serious, as there is the possibility of extrauterine injury to surrounding structures such as bowel, bladder, and major blood vessels; this type of perforation requires immediate investigation by laparoscopy, and arguably by laparotomy.

Warning signs that uterine perforation has occurred include a sudden loss of uterine distention pressure and immediate loss of view accompanied by sudden fluid absorption. In that case, surgery should stop immediately and only be continued if perforation has been excluded.

Excessive bleeding from transected myometrial vessels tends to occur when the resection is too deep, and is more

 Table 16.4
 Endometrial resection complications (intraoperative, early, and late)

Intraoperative	Early	Late
Uterine perforation	Infection	Intrauterine adhesions
Fluid overload	Bleeding	Pelvic pain
Hemorrhage		Hematometra
Gas embolism		Postablation sterilization syndrome
Cervical trauma		
Electrosurgical burn		Pregnancy
		(Cancer)

likely during repeat surgery. Electrocoagulation is usually effective in stopping the bleeding, either with the loop electrode or a rollerball. Excessive bleeding at the end of the procedure can be managed with a urinary catheter balloon, as already discussed.³³

Fluid overload results from excessive intravasation of the distention fluid through the opened myometrial blood vessels into the general circulation, and to a lesser extent through transtubal loss. The phenomenon of intravasation is explained by the fact that intrauterine distention pressures during TCRE tend to be higher than the mean arterial pressure, so fluid is pushed from the cavity into the vascular system. The volume of intravasation correlates with the depth of endometrial resection, intrauterine pressure, and duration of the procedure, whereas there is an inverse correlation with prior treatment with GnRH analogues and the menopause. 14,27,34 It is possible to identify women at low risk of fluid overload based on parameters such as parity, endometrial preparation, uterine cavity length, and the presence of submucous fibroids. 35

The results of fluid overload are two-fold, a volume effect and a biochemical effect, the latter depending on the constituents of the uterine irrigant. The volume effect would be cardiac failure with pulmonary edema.

The precise definition of what constitutes fluid overload is arguable, and depends on several factors, including the general condition of the patient and the nature of the fluid. Everyone would agree that all otherwise healthy women could tolerate 1 L absorption without any adverse effects. Greater care has to be taken when operating on women with cardiac or renal disease, who would only tolerate a smaller volume. Similarly, the risk associated with absorbing large volumes of an electrolyte-free solution such as 1.5% glycine is more than if normal saline was the distention medium. Our protocol for glycine solution during resectoscopic surgery is summarized in Table 16.5.

As is evident from the above, the clinical implication of fluid overload is not just related to volume but also to the nature of the medium. Dilutional hyponatremia and hypokalemia are conditions more likely to occur with electrolyte-free solutions such as glycine and sorbitol, as used with standard (monopolar) resectoscopy. For instance, the absorption of 1 L of glycine solution is associated with a drop in serum sodium concentration of approximately 10 mmol/L.³⁶

Hyponatremia and other biochemical dilutional changes are the basic pathophysiologic conditions leading to cerebral edema, which might be fatal if unrecognized or left untreated.³⁷ In addition, ammonia, a breakdown product of glycine, can also produce an encephalopathy manifest by confusion, coma, and ultimately death. Solutions such as normal saline do not suffer from these risks, but it is still important to avoid overloading the patient

Table 16.5 Management of fluid overload with 1.5% glycine

Absorption of <1000 ml of distention fluid	Hyponatremia and fluid overload unlikely
	Continue surgery unlikely
Absorption of 1000–2000 ml of distention fluid	Mild hyponatremia and fluid overload likely
	Complete as soon as possible
	Check urea electrolytes (e.g. Na ⁺)
	Catheterize bladder and monitor urine output
	Give IV diuretics if >1500 ml absorbed
Absorption of >2000 ml of distention fluid	Severe hyponatremia and fluid overload likely
	Stop surgery immediately
	Manage as above
	Close observation of vital signs

with volume and therefore careful monitoring of fluid balance is still important.

There are several methods for monitoring fluid balance, from the simple to the complicated. The simplest, and the one we favor, is merely to monitor inflow and outflow continuously and record the balance every time a new bag or bottle of distention medium is started; there are now hysteroscopic pumps available that measure balance automatically. Other more complex and invasive techniques include weighing the patient, using tracer substances in the irrigant (e.g. ethanol), using central venous pressure (CVP) measurements, or measuring serum sodium.^{27,38} Any biochemical method of monitoring will not detect delayed transperitoneal absorption, and therefore can mislead.³⁹

Air embolism during TCRE is a rare but very serious complication which can be fatal.⁴⁰ Air is relatively insoluble, and if air bubbles gain entry in the irrigation circuit (e.g. when starting a new bag of irrigant), they can intravasate across resected opened blood vessels and travel to the heart. Intravasation is promoted by head-down tilt of the patient.^{34,41} It is therefore important to purge the inflow circuit of air at the start of surgery and to ensure that bubbles do not gain entry during surgery. In contrast to air, gas derivatives with the use of monopolar and bipolar cutting electrodes are highly soluble in blood and

are unlikely to result in gas embolism.^{34,42} In all cases, theater staff should check the inflow tubes for air bubbles, especially during fluid bag changes, and alert the surgeon to remove them from the system.

Early postoperative complications

Infection in the form of endometritis or pelvic inflammatory disease (tubo-ovarian abscess, hematosalpinx, pyometra) may sometimes occur. 43 Most gynecologists prescribe prophylactic antibiotics to prevent this complication, although this practice is, as yet, not an evidence-based approach. Secondary uterine bleeding often accompanies sepsis, and its management is to treat the infection and preserve the patient's hemodynamic and iron status.

Late postoperative complications

Pelvic pain and recurrent menorrhagia are certainly the major reasons for treatment failure and the need for repeat endometrial resection or hysterectomy. Hematometra is the painful collection of blood in the endometrial cavity and tends to result from residual endometrium in the cornu or cervical stenosis. 44 The treatment options include repeat resection and cervical dilatation in the knowledge that the repeat resection carries a higher risk of uterine perforation.45 Pelvic pain in the absence of hematometra could be due to fibroid degeneration, adenomyosis, and endometriosis or more rarely due to pelvic vein congestion syndrome.⁴³ Pregnancy after endometrial resection has been reported; a recent study from China reported 39 pregnancies in 1621 women who underwent TCRE, most pregnancies occurring during the first postoperative year.46 Pregnancy complications chiefly related to abnormal placentation are relatively common, so women should be discouraged from becoming pregnant.³⁸ Unfortunately, while sterilization is a very effective contraceptive, it is associated with post-ablation sterilization syndrome secondary to the development of a hematosalpinx.⁴⁷

Ectopic pregnancy and rare instances of endometrial cancer have also been reported. 43,48,49

Costs

It is generally known that the initial costs of hysteroscopic ablation techniques are less than the costs of hysterectomy, although, considering the reoperation rate of these methods and comparing it with the definitive solution of hysterectomy, the financial gap between them becomes smaller with time. ⁵⁰ One of the advantages of TCRE in this field is that surgery is done with a reusable instrument rather than a single-use device.

Outcome of intervention

The majority of women experience an improvement in menstrual flow after TCRE, with about one-third becoming amenorrheic. The menstrual improvement tends to be better in older women, as does the long-term outcome; this is perhaps not unexpected, as older patients will become menopausal sooner. Results from our unit, for instance, with a follow-up of up to 10 years, have shown that, overall, 20% of patients ultimately undergo hysterectomy after their initial TCRE, but this figure increases to around 40% for women who are <35 years old at the time of their initial surgery. Repeat TCRE is more usually effective than not, with only one-third of patients eventually requiring hysterectomy. Endometrial preparation and the presence or absence of smaller fibroids do not have any significant effect on outcome, but results are worse once uterine size ≥10 weeks' gestation equivalent.⁵¹ Surgical experience appears to influence the success of TCRE, with one study reporting failure rates of 17% and 25% when surgery is performed by experienced and less experienced surgeons, respectively, and 90% short-term effectiveness.⁴¹

These results have largely been replicated by other authors. Amenorrhea is usually achieved in about 30–40% of women if allowance is taken of the duration of follow-up. An Italian study published in 2005 showed a 77.4% rate of success after 5 years follow-up (94% success in women >49 years old, while this success rate decreased to 70% in younger women),⁵² and another recent study with follow-up between 4 and 10 years, and including patients with fibroids, revealed a success rate of 83.4%, with a hysterectomy rate of 16.4% within the same period, with half the hysterectomies being done during the first 2 years after the initial procedure. 53 These results confirm our impression that the failure rate of endometrial resection largely plateaus after 4 years. Nevertheless, even in the case of treatment failure, a repeat procedure constitutes a reliable option to avoiding hysterectomy, with good results.⁴⁵

Women's satisfaction rate after the procedure was reported in various studies as 70–90%, 79–87%, and 91–94%. 43,54–56

Intra- and postoperative complications are not common. For instance, a large prospective national audit of hysteroscopic endometrial ablation in the UK, the MIS-TLETOE study, involving 3776 TCREs and 4291 TCREs with rollerball ablation, out of a total of 10 686 hysteroscopic ablations, reported overall immediate complication rates of 6.4% and 4.2%.⁵⁷ Other studies have reported higher complication rates of up to 12%.^{43,58}

The most common and feared complications of TCRE are uterine perforation and fluid overload, with published rates of between 2 and 8% for perforation and 1.3 and

4% for fluid overload. ^{31,43,53,57,59–61} Repeat surgery appears to be associated with an increased rate of uterine perforation (up to 9%), but a lesser risk of fluid overload (up to 4%). ⁴³

There have been numerous comparative trials of TCRE with other treatments for menorrhagia, both medical and surgical. Cooper et al. compared endometrial resection with medical treatment and found that TCRE had higher patient satisfaction rates, while surgical intervention rates at 5 years were 77% in women with medical treatment and 27% in the TCRE group. 62 A Cochrane Systematic Review in 2006 also showed that endometrial resection was more effective and less likely to cause side effects than medical treatment. 63

The early comparative trials of TCRE were principally against hysterectomy. All the studies essentially came to the same conclusions: namely, that TCRE was associated with less postoperative morbidity, faster recovery, and was more cost-effective in the short term, whereas hysterectomy had greater satisfaction rates and a lesser need for further surgical intervention. ^{59,61} However, it must not be assumed that hysterectomy is a 'final' solution, as such cases frequently require readmission to hospital. ⁶⁴ It should also be noted that in a study investigating patients' preferences for endometrial ablation, the levonorgestrel-releasing intrauterine system (LNG-IUS; Mirena), or hysterectomy, the majority of the women chose TCRE (66.7%) compared with only 17.3% who preferred hysterectomy, and 16% who favored the Mirena. ⁶⁵

TCRE has also been compared with the LNG-IUS by several authors, the first study being published by Crosginani et al. in 1997. The conclusion of that study was that both treatments are effective, having high satisfaction rates, with the LNG-IUS being somewhat less satisfactory than TCRE (satisfaction rates of 85% and 94%, respectively).⁶⁶ At the same time, the IUS requires less operator skills and entails no operative hazards while providing effective contraception.^{67,68} Both methods are comparable and highly effective and have their own relative merits.

Various studies have shown that there are also no significant differences between TCRE, rollerball, and Nd:YAG (neodymium–yttrium aluminum garnet) laser ablation regarding rates of amenorrhea, patient satisfaction, improvement of dysmenorrhea, and the need for further surgery. Laser ablation tends to take longer, whereas rollerballing the endometrium is generally considered a quicker procedure than resection, but this does depend on operator experience.^{8,27} Certainly, laser ablation is the procedure associated with the greater fluid absorption and higher rates of equipment failure,⁸ whereas the risk of perforation is reported to be greater with TCRE.⁶⁹

As TCRE constitutes the gold standard for endometrial ablation, it has become the standard by which the

more recent second-generation methods of endometrial ablation such as thermal balloon, microwaves, radiofrequency, and cryotherapy are judged. Data from the Cochrane Database of Systematic Reviews 2005 showed that, overall, second-generation devices were associated with a shorter procedure time by 15 minutes, greater use of local anesthesia, but also higher rates of equipment failure. Complications such as fluid overload, cervical lacerations, and hematometra were less likely. Uterine perforation, which is the commonest major complication of uterine ablation, is rarer with the second-generation techniques, but still cannot be excluded.8 It must certainly not be thought that the new, non-hysteroscopic ablation techniques are totally safe. The US Food and Drug Administration's (FDA's) MAUDE database, a useful source of information on complications, makes it clear that complications such as thermal bowel injury, sepsis, and, most worryingly, uterine perforation (which would tend to be undiagnosed as most of the new techniques are performed blindly), and laparotomy are all potential risks.⁷⁰

To give some examples of these studies, comparisons between TCRE and thermal balloon systems such as ThermaChoice (Gynaecare, Inc., Menlo Park, CA, USA) and Cavaterm (Wallsten Medical SA, Morges, Switzerland) showed the hysteroscopic and non-hysteroscopic techniques to be equally effective. Microwave endometrial ablation (MEA) has also proved to be a reliable alternative to resection. A recently published study with a follow-up of up to 5 years reported significantly higher satisfaction rates with MEA compared with TCRE (86%)

vs 74%, respectively); although a higher percentage of patients ultimately underwent hysterectomy after TCRE (25%) than MEA (16%), this difference was not statistically significant.⁷³

Finally, another study reported that endometrial laser intrauterine thermotherapy (ELITT) is as effective as TCRE in terms of patient satisfaction but is associated with significantly higher rates of amenorrhea after 12 and 36 months postoperatively.⁷⁴

CONCLUSIONS

TCRE is considered as a level III hysteroscopic procedure according to the revised classification of hysteroscopic surgery by the RCOG in London (1999). This means that a high level of competence is required from the endoscopist. It is certainly a proven alternative to hysterectomy and continues to keep its place in the treatment of heavy menstrual bleeding.^{57,59} However, newer, less skill-dependent treatments have become available which have reduced the role of hysteroscopic ablation techniques such as TCRE. Nonetheless, it is important for gynecologists to remain skilled in the use of the resectoscope, as it is such a versatile instrument for the management of other gynecologic problems apart from dysfunctional uterine bleeding (e.g. hysteroscopic myomectomy). Consequently, for those familiar with the art, there seems little reason to abandon this valuable instrument, even for endometrial ablation.

References

- 1. Neuwirth RS. A new technique for and additional experience with hysteroscopic resection of submucous fibroids. Am J Obstet Gynecol 1978; 131: 91–4.
- Derman SG, Rehnstrom J, Neuwirth RS. The long-term effectiveness of hysteroscopic treatment of menorrhagia and leiomyomas. Obstet Gynecol 1991; 77: 591–4.
- 3. DeCherney A, Polan HL. Hysteroscopic management of intrauterine lesions and intractable uterine bleeding. Obstet Gynecol 1983; 61: 392–7.
- 4. Hallez JP. Single-stage total hysteroscopic myomectomies: indications, techniques, and results. Fertil Steril 1995; 63: 703–8.
- Magos AL, Baumann R, Turnbull AC. Transcervical resection of endometrium in women with menorrhagia. BMJ 1989; 298: 1209–12.
- 6. Aberdeen Endometrial Ablation Trials Group. A randomised trial of endometrial ablation versus hysterectomy for the treatment of dysfunctional uterine bleeding: outcome at four years. Br J Obstet Gynaecol 1999; 106: 360–6.
- Royal College of Obstetricians and Gynaecologists. The management of menorrhagia in secondary care. National evidence-based clinical guidelines, 1999.

- Lethaby A, Hickey M, Garry R. Endometrial destruction techniques for heavy menstrual bleeding. Cochrane Database Syst Rev 2005; 4: CD001501.
- Bradley LD. New endometrial ablation techniques for treatment of menorrhagia. Surg Technol Int 2004; 12: 161–70.
- Sui L, Xie F, Cao B. Management of abnormal uterine hemorrhage with atypical endometrial hyperplasia by transcervical resection of endometrium. Int J Gynecol Cancer 2006; 16: 1482–6.
- Grow DR, Iromloo K. Oral contraceptives maintain a very thin endometrium before operative hysteroscopy. Fertil Steril 2006; 85: 204–7.
- Kriplani A, Manchanda R, Nath J et al. A randomized trial of danazol pre-treatment prior to endometrial resection. Eur J Obstet Gynecol Reprod Biol 2002; 103: 68–71.
- 13. Donnez J, Vilos G, Gannon MJ et al. Goserelin acetate (Zoladex) plus endometrial ablation for dysfunctional uterine bleeding: a 3-year follow-up evaluation Fertil Steril 2001; 75: 620–2.
- Sowter MC, Lethaby A, Singla AA. Pre-operative endometrial thinning agents before endometrial destruction for heavy

- menstrual bleeding. Cochrane Database Syst Rev 2002; (3): CD001124.
- Townsend DE, Richart RM, Paskowitz RA et al. "Rollerball" coagulation of the endometrium. Obstet Gynecol 1990; 76: 310–3.
- Erian MM, Thomas IL, Buck RJ et al. The effects of danazol after endometrial resection – results of a randomized, placebocontrolled, double-blind study. Aust NZ J Obstet Gynaecol 1998; 38: 210–14.
- Molnar B, Kormanyos Z, Kovacs L et al. Long-term efficacy of transcervical endometrial resection with no preoperative hormonal preparation. Eur J Obstet Gynecol Reprod Biol 2006; 127: 115–22.
- Zapico A, Grassa A, Martinez Eet al. Endometrial resection and preoperative LH-RH agonists: a prospective 5 year trial. Eur J Obstet Gynecol Reprod Biol 2005; 119: 114–18.
- Crane JM, Healey S. Use of misoprostol before hysteroscopy: a systematic review. J Obstet Gynaecol Can 2006; 28: 373–9.
- Barcaite E, Bartusevicius A, Railaite DR et al.. Vaginal misoprostol for cervical priming before hysteroscopy in perimenopausal and postmenopausal women. Int J Gynaecol Obstet 2005; 91: 141–5.
- Preutthipan S, Herabutya Y. A randomized comparison of vaginal misoprostol and dinoprostone for cervical priming in nulliparous women before operative hysteroscopy. Fertil Steril 2006; 86: 990–4.
- Royal College of Obstetricians and Gynaecologists. Diagnostic hysteroscopy under general anaesthesia. RCOG Consent Advice 1 October 2004.
- 23. Magos A, Kosmas I, Sharma M et al. Digital recording of surgical procedures using a personal computer. Eur J Obstet Gynecol Reprod Biol 2005; 120: 206–9.
- Lockwood GM, Baumann R, Turnbull AC et al. Extensive hysteroscopic surgery under local anaesthesia. Gynaecol Endosc 1992; 1: 15–21.
- Thinkamrop J, Laopaiboon M, Lumbiganon P. Prophylactic antibiotics for transcervical intrauterine procedures (Protocol). Cochrane Database Syst Rev 2006; (1): CD005637.
- Vercellini P, Oldani S, Yaylayan L et al. Randomized comparison of vaporizing electrode and cutting loop for endometrial ablation. Obstet Gynecol 1999; 94: 521–7.
- Munro GM. Endometrial ablation for heavy menstrual bleeding. Curr Opin Obstet Gynecol 2005; 17: 381–94.
- Loffer FD. Endometrial ablation in patients with myomas. Curr Opin Obstet Gynecol 2006; 18: 391–3.
- van Dongen H, Kolkman W, Jansen FW. Hysteroscopic surgery: perspectives on skills training. J Minim Invasive Gynecol 2006; 13: 121–5.
- Isaacson KB. Complications of hysteroscopy. Obstet Gynecol Clin North Am 1999; 26: 39–51.
- Propst AM, Liberman RF, Harlow BL et al. Complications of hysteroscopic surgery: predicting patients at risk. Obstet Gynecol 2000: 96: 517–20.
- Indman PD, Brooks PG, Cooper JM et al. Complications of fluid overload from resectoscopic surgery. J Am Assoc Gynecol Laparosc 1998; 5: 63–7.
- Pasini A, Belloni C. Intraoperative complications of 697 consecutive operative hysteroscopies. Minerva Ginecol 2001; 53: 13–20.
- Murakami T, Tamura M, Ozawa Y et al. Safe techniques in surgery for hysteroscopic myomectomy. J Obstet Gynaecol Res 2005; 31: 216–23.

- Molnar BG, Broadbent JAM, Magos AL. Fluid overload risk score for endometrial resection. Gynaecol Endosc 1992; 1: 133–8.
- Magos AL, Baumann R, Lockwood GM et al. Experience with 250 endometrial resections for menorrhagia. Lancet 1991; 337: 1074–9.
- 37. Istre O. Fluid balance during hysteroscopic surgery. Curr Opin Obstet Gynecol 1997; 9: 219–25.
- Bradley LD. Complications in hysteroscopy: prevention, treatment and legal risk. Curr Opin Obstet Gynecol 2002; 14: 409–15.
- Molnar BG, Magos AL, Kay J. Monitoring fluid absorption using 1% ethanol-tagged glycine during operative hysteroscopy. J Am Assoc Gynecol Laparosc 1997; 4: 357–62.
- Brooks PG. Venous air embolism during operative hysteroscopy. J Am Assoc Gynecol Laparosc 1997; 4: 399–402.
- 41. Sutton C. Hysteroscopic surgery. Best Pract Res Clin Obstet Gynaecol 2006; 20: 105–37.
- 42. Munro MG, Brill AI, Ryan T et al. Electrosurgery-induced generation of gases: comparison of in vitro rates of production using bipolar and monopolar electrodes. J Am Assoc Gynecol Laparosc 2003; 10: 252–9.
- O'Connor H, Magos AL. Endometrial resection for menorrhagia. N Engl J Med 1996; 335: 151–6.
- 44. Cooper JM, Brady RM. Late complications of operative hysteroscopy. Obstet Gynecol Clin North Am 2000; 27: 367–74.
- Wortman M, Daggett A. Reoperative hysteroscopic surgery in the management of patients who fail endometrial ablation and resection. J Am Assoc Gynecol Laparosc 2001; 8: 272–7.
- 46. Xia E, Li TC, Yu D et al.. The occurrence and outcome of 39 pregnancies after 1621 cases of transcervical resection of endometrium. Hum Reprod 2006; 21: 3282–6.
- Townsend DE, McCausland V, McCausland A et al. Postablation-tubal sterilization syndrome. Obstet Gynecol 1993; 82: 422–43.
- Sagiv R, Ben-Shem E, Condrea Aet al.. Endometrial carcinoma after endometrial resection for dysfunctional uterine bleeding. Obstet Gynecol 2005; 106: 1174–6.
- 49. Neuwirth RS, Loffer FD, Trenhaile T et al. The incidence of endometrial cancer after endometrial ablation in a low-risk population. J Am Assoc Gynecol Laparosc 2004; 11: 492–4.
- 50. Lethaby A, Shepperd S, Cooke I et al. Endometrial resection and ablation versus hysterectomy for heavy menstrual bleeding. Cochrane Database Syst Rev 1999; 2: CD000329.
- Taylor A, Magos A. Control of menorrhagia by endometrial resection. In: Bieber E, Loffer F, eds. Hysteroscopy, Resectoscopy and Endometrial Ablation. London: Parthenon Publishing, 2003: 149–70.
- 52. Litta P, Merlin F, Pozzan C et al. Transcervical endometrial resection in women with menorrhagia: long-term follow-up. Eur J Obstet Gynecol Reprod Biol 2006; 125: 99–102.
- 53. Boe Engelsen I, Woie K, Hordnes K. Transcervical endometrial resection: long-term results of 390 procedures. Acta Obstet Gynecol Scand 2006; 85: 82–7.
- Pinion SB, Parkin DE, Abramovich DR et al. Randomised trial of hysterectomy, endometrial laser ablation, and transcervical endometrial resection for dysfunctional uterine bleeding. BMJ 1994; 309: 979–83.
- 55. Istre O. Transcervical resection of endometrium and fibroids: the outcome of 412 operations performed over 5 years. Acta Obstet Gynecol Scand 1996; 75: 567–74.
- Ravi B, Schiavello H, Chandra P et al. Safety and efficacy of hysteroscopic endomyometrial resection-ablation for menorrhagia. J Reprod Med 2001; 46: 717–23.

- 57. Overton C, Hargreaves J, Maresh M. A national survey of the complications of endometrial destruction for menstrual disorders: the MISTLETOE study. Minimally Invasive Surgical Techniques—Laser, EndoThermal or Endorescetion. Br J Obstet Gynaecol 1997; 104: 1351–9.
- A Scottish audit of hysteroscopic surgery for menorrhagia: complications and follow up. Scottish Hysteroscopy Audit Group. Br J Obstet Gynaecol 1995; 102: 249–54.
- O'Connor H, Broadbent JA, Magos AL et al. Medical Research Council randomised trial of endometrial resection versus hysterectomy in management of menorrhagia. Lancet 1997; 349: 897–901.
- Pooley AS, Ewen SP, Sutton CJ. Does transcervical resection of the endometrium for menorrhagia really avoid hysterectomy? Life table analysis of a large series. J Am Assoc Gynecol Laparosc 1998; 5: 229–35.
- 61. Zupi E, Zullo F, Marconi D et al. Hysteroscopic endometrial resection versus laparoscopic supracervical hysterectomy for menorrhagia: a prospective randomized trial. Am J Obstet Gynecol 2003; 188: 7–12.
- Cooper KG, Parkin DE, Garratt AM et al. Five-year follow up of women randomised to medical management or transcervical resection of the endometrium for heavy menstrual loss: clinical and quality of life outcomes. Br J Obstet Gynaecol 2001; 108: 1222–8.
- Marjoribanks J, Lethaby A, Farquhar C. Surgery versus medical therapy for heavy menstrual bleeding. Cochrane Database Syst Rev 2006; (2): CD003855.
- 64. Clarke A, Judge A, Herbert A et al. Readmission to hospital 5 years after hysterectomy or endometrial resection in a national cohort study. Qual Saf Health Care 2005; 14: 41–7.
- Bourdrez P, Bongers MY, Mol BW. Treatment of dysfunctional uterine bleeding: patient preferences for endometrial ablation,

- a levonorgestrel-releasing intrauterine device or hysterectomy. Fertil Steril 2004; 82: 160–6.
- 66. Crosignani PG, Vercellini P, Mosconi P et al. Levonorgestrelreleasing intrauterine device versus hysteroscopic endometrial resection in the treatment of dysfunctional uterine bleeding. Obstet Gynecol 1997; 90: 257–63.
- 67. Rauramo I, Elo I, Istre O. Long-term treatment of menorrhagia with levonorgestrel intrauterine system versus endometrial resection. Obstet Gynecol 2004; 104: 1314–21.
- 68. Istre O, Trolle B. Treatment of menorrhagia with the levonorgestrel intrauterine system versus endometrial resection. Fertil Steril 2001; 76: 304–9.
- Abbott JA, Garry R. The surgical management of menorrhagia. Hum Reprod 2002; 8: 68–78.
- Gurtcheff SE, Sharp HT. Complications associated with global endometrial ablation: the utility of the MAUDE database. Obstet Gynecol 2003; 102: 1278–82.
- 71. Gervaise A, Fernandez H, Capella-Allouc S et al. Thermal balloon ablation versus endometrial resection for the treatment of abnormal uterine bleeding. Hum Reprod 1999; 14: 2743–7.
- 72. Brun JL, Raynal J, Burlet G et al. Cavaterm thermal balloon endometrial ablation versus hysteroscopic endometrial resection to treat menorrhagia: the French, multicenter, randomized study. J Minim Invasive Gynecol 2006; 13: 424–30.
- 73. Cooper KG, Bain C, Lawrie L et al. A randomised comparison of microwave endometrial ablation with transcervical resection of the endometrium; follow up at a minimum of five years. BJOG 2005; 112: 470–5.
- Perino A, Castelli A, Cucinella G et al. A randomized comparison of endometrial laser intrauterine thermotherapy and hysteroscopic endometrial resection. Fertil Steril 2004; 82: 731–4.

Hysteroscopic laser ablation technique

David C Hunter

INTRODUCTION

Lasers were used therapeutically in medicine for some time before Goldrath et al. first described their use for destruction of the endometrium in 1981. The potential of endometrial laser ablation (ELA) was recognized as an alternative to hysterectomy by the early 1990s and endometrial ablation for dysfunctional uterine bleeding, in one form or another, now represents a significant proportion of the gynecologist's workload. The increasing number of ablation procedures using varying second-generation techniques has meant that fewer first-generation ablation procedures (laser ablation, transcervical resection, and rollerball) are now performed and that fewer doctors are being trained in their use. This will ultimately have an impact on the ability of gynecologists to treat fibroids, septa, and uterine synechiae.

The principle of all ablation procedures is much the same: to deliver energy to the endometrium in order to induce its destruction. Most frequently, the energy employed is thermal, but cryocoagulation and light energy are also used. This chapter deals with endometrial destruction using light energy in the form of lasers.

Laser is an acronym for light amplification by the stimulated emission of radiation. Electrons are encouraged to leave their orbit around the nuclei of atoms by the application of an electrical voltage differential. When the electrons return to their orbit, each atom releases a photon packet of energy. These photon packets are collimated (all of the light waves are in phase and synchronous) and laser light is thus produced as a parallel and non-divergent beam. This may be in the visible or non-visible spectrum, depending on the wavelength of the light produced, which is dependent on the substance from which the light is produced. Argon and potassium titanyl phosphate (argon titanyl phosphate (ATP) and KTP at 500 and 532 nm respectively) lasers produce light of wavelengths that are in the visible (approximately 400–700nm) blue-green region of the electromagnetic spectrum. Neodymium:yttrium-aluminum-garnet (Nd:YAG) and carbon dioxide lasers produce light that is not visible to the human eye (1060 and 10600 nm, respectively).

Differing wavelengths determine the characteristics of the laser, how the energy can be transmitted, and the tissue effects. The primary factors to be considered when determining the suitability of any laser for a medical therapeutic purpose are the degree of tissue scatter and the ability to transmit the energy from the source to the point of delivery. It is the absorbed energy that produces the tissue effect following its conversion to heat energy and mechanical energy. This effect produces a zone of tissue vaporization surrounded by a zone of thermal necrosis and a further, more peripheral, zone of edema and inflammation that does not receive sufficient energy to cause thermal necrosis and therefore recovers. Beyond this is tissue unaffected by the laser energy (Figure 17.1).

When using the light produced by the Nd:YAG laser for endometrial ablation, 25–30% of the inherent energy scatter is forward, 30–40% is reflected, and 30–45% of the energy is absorbed by the tissue being treated (Figure 17.2). The relatively high proportion of forward scatter and absorption of the Nd:YAG laser allows for the controlled destruction by vaporization and thermal necrosis of tissue up to a depth of 4–5mm. Such controlled destruction of the endometrium and underlying myometrial tissue causes minimal temperature rises on the serosal surface of the endometrium.^{1,4,5} Carbon dioxide and KTP/ATP lasers have much lower proportions of forward scatter of energy and therefore are ineffective for the destruction of the basal endometrial glandular structures.

Endometrial glands penetrate the myometrium to a depth of 4–5 mm in a normal uterus (the depth of penetration is greater in patients with adenomyosis). To prevent regeneration of the endometrium from these basal glands or basal lamina, tissue destruction must be to at least this depth.^{1,6,7} This makes the Nd:YAG laser ideal for the destruction of the endometrium.

In addition, the wavelength of the laser light produced also determines how the light may be transmitted from source to its point of delivery. The carbon dioxide laser beam is transmitted using mirrors and swinging arms. ATP, KTP, and Nd:YAG may be transmitted using flexible fibers, making them much less cumbersome to use.

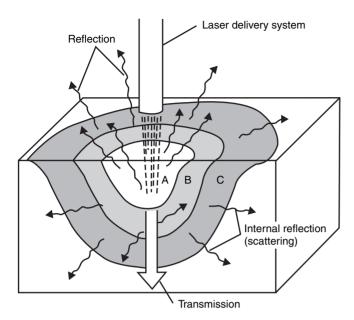


Figure 17.1 Reflection, scattering, and forward transmission of laser energy with zones of thermal effect: A, zone of vaporization; B, zone of thermal necrosis; and C, zone of inflammation and recovery.

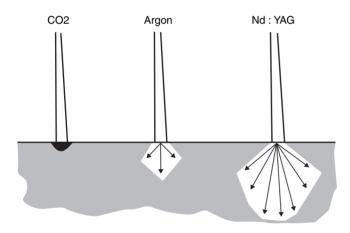


Figure 17.2 Characteristics of beam scattering for different lasers.

LASER SAFETY

Lasers are potentially dangerous, so it is important that all members of the theater team involved with their use are appropriately trained, familiar with the potential hazards of their use, and that appropriate protocols are developed to avoid laser hazards.

The suppliers of the laser and the medical physics department of each hospital should ensure that the equipment is correctly installed and that all staff members are familiar with the operational procedures for the equipment. A laser safety committee must be established

and only surgeons who have attended didactic sessions on laser safety should be permitted to use the laser. The theater should have a nominated laser safety officer or officers who must be accredited in the use of medical lasers. The key for the laser should be kept in a locked cupboard when the laser is not in use or by the nominated laser safety officer(s) when the laser is to be activated.

The Nd:YAG laser is a class IV laser and the main hazard to staff is eye damage: injury to the cornea or macula is permanent. It is imperative that all staff members understand the risks posed and wear the appropriate eye protection at all times when the laser is in the theater, whether the laser is active or not. Laser goggles are specific for the wavelengths of individual lasers and should not, therefore, be exchanged between theaters using different types of lasers. To prevent accidental injury to staff members not directly involved in the patient's care, all doors to the theater should be locked from the inside. Alert signs should be hung (Figure 17.3) on the outside of the doors of theater alerting those who may wish to enter the theater that a laser is in use. If the doors have windows, these should be blacked out or covered.

INSTRUMENTATION

The equipment described above forms an integral part of the treatment of each patient, and absence of or damage to any of the safety equipment should be treated seriously.

The laser generator is a bulky piece of equipment and is removed from theatre when not in use. A commonly used laser generator is the SLT CL100 Nd:YAG laser (Surgical Laser Technologies, Inc., Malvern, PA). The maximum power output of this machine is 80 W (see below). The electrical supply to the laser generator requires



Figure 17.3 Alert sign for theater entrances and exits.

a specific electrical socket and lead capable of delivering a current of 40 A and voltage of 415 V. The socket for the laser generator should be sited near where the generator is placed during surgery.

The energy is delivered through a 600 µm bare quartz fiber, with fiber transmission rates of >95% being essential for economic and effective use of the generator. The tip of the fiber heats during operation and may occasionally fragment; the risk of this occurrence can be reduced by continuous flow of cool fluid over the tip of the fiber during the procedure. The tip of the fiber is cut to ensure a 'clean' working surface for each patient.

Pressure-controlled continuous flow of irrigating fluid allows for distention of the uterine cavity with minimal risk of inducing fluid overload, clears endometrial debris from the operative field, and cools the tip of the fiber. Such flow is achieved using a WOM hysteroflator (HYS SUR-GIMAT) and Aquasens Fluid Monitoring System (Aquintel Inc., Mountain View, CA) which allows for accurate and instantaneous monitoring of fluid deficit throughout the procedure and reduces the risk of sudden and unexpected fluid overload.8 A steady intrauterine pressure is maintained throughout the procedure, facilitating clear visualization of the uterine cavity. Fluid loss due to spillage is minimized by the use of a plastic drape placed beneath the patient's buttocks from which leaked fluid is returned to the monitoring system. The fluid used is normal saline, which reduces the risk of electrolyte disturbance if excessive fluid absorption does occur.

The hysteroscope used should be a three-channel operating scope such as that described by Baggish. Separate inflow and outflow channels permit the maintenance of a continuous flow of fluid, with the evacuation of blood, tissue, and gas produced by the vaporization of tissue. A third channel is necessary for the delivery of the laser fiber and its sheath. Passage of the fiber through a channel used for insufflation or evacuation of fluid will result in reduced or increased pressures, respectively, and reduced flow rates. Good-quality three-channel scopes are now available with diameters of approximately 5.5 mm. Images obtained with a 0° straightforward scope under video vision permit the laser fiber to be dragged from the cornua or fundus to the isthmus in one movement, but some operators prefer to use a 30° scope.

A good-quality camera and video system are recommended, a lighter camera being preferred to prevent tiring or strain of the surgeon's arm and shoulder. The stack or pendulum holding the light source, camera system, and monitor are all placed on the patient's right side (for a right-handed operator) and the fluid irrigation system and laser generator to the patient's left for ease of access.

The operating table should have surgical 'boots' fitted in order that the patient's legs may be flexed and abducted at the hips by the surgeon to permit access to the uterine cornua.

PATIENT SELECTION AND PREOPERATIVE PREPARATION

Patients are assessed with bimanual examination and transvaginal ultrasound scanning prior to surgery to exclude intracavitary or large fibroids and adnexal pathology. Some gynecologists prefer a formal assessment of the cavity by hysteroscopy before arranging for laser ablation. A biopsy sample of the endometrium is taken in the outpatient department; if the result of this is not conclusive, or insufficient, or the sampler cannot be passed through the cervix, the endometrium is biopsied by curettage at the time of surgery. An up-to-date cervical smear result must be normal. Patients should have completed their family and have employed a reliable method of contraception. This avoids subsequent complications in pregnancy following endometrial destruction. Inclusion and exclusion criteria for endometrial laser ablation are listed below in Table 17.1.

Fibroids, septa, and polypi may be treated with the laser. However, larger fibroids are associated with increased operating times and increased volumes of fluid absorption. Patients should be alerted to the possibility that the procedure may require two or more stages and that there is an increased risk of uterine perforation.

Having described the mechanism of action of the laser above, it will be clear to the reader that to administer effective treatment the depth of thermal injury should extend to approximately 4-5 mm into the myometrium. The endometrium should therefore be pretreated to ensure that it is as thin as possible prior to surgery, facilitating destruction of the basal lamina with a single pass of the laser. This can be achieved chemically by the use of danazol at a dose of 400-800 mg/day for 4-5 weeks preoperatively or by the use of a single injection of a gonadotropin-releasing hormone (GnRH) analogue such as goserelin 3.6 mg 4 weeks preoperatively. 10,11 The injectable preparation can be administered, or a prescription for danazol issued at the patient's preoperative pre-assessment visit (usually 4 weeks prior to surgery). If the patient is reluctant to take preop preparation, the procedure should be timed for the immediate postmenstrual phase of the cycle.

In Garry et al's trial comparing danazol and goserelin there was no difference in clinical outcomes but it was noted that better operating conditions were achieved with the use of two doses of goserelin. The use of two doses of goserelin resulted in significant side effects and there are cost implications, but these were felt to be offset by

Table 17.1.

Criteria for treatment	Exclusion criteria (relative)
Dysfunctional uterine bleeding	• Uterine size >12 weeks
• Intracavitary fibroids <5 cm	Intracavitary fibroids>5 cm
Family completed	• Concomitant gynecologic pathology
 Bleeding primary complaint (not pain or premenstrual syndrome) 	 Endometrial hyperplasia or malignancy (all stages of endometrial atypia)
	 Active pelvic infection
	 Patient request for amenrrhoea

the better operating conditions achieved and improved long-term outcomes following ablation.¹³

OPERATIVE PROCEDURE

The operation is performed under general anesthesia. The patient is placed in the lithotomy position with the hips flexed and moderately abducted, permitting access to the uterine cornua. The basic principles of the procedure follow that described by Garry.¹⁴

As the patient is being anesthetized and positioned, the surgeon assembles the scope, connecting the fluid inflow and outflow tubing and light lead. The laser fiber is fed through first its sheath and then the operating channel of the hysteroscope. The fluid inflow should be connected peripherally to a warmed 3L bag of saline using a wide bore giving set fed through the fluid insufflator. The maximum flow rate is set at 250 ml/min (this should not be increased) and the initial maximum pressure at 75 mmHg (this may be increased or decreased during the procedure). Increasing the operating pressure increases the rate at which fluid is forced into the intravascular compartment, and thus increases the risk of fluid overload. The scope is connected to the camera system, and the camera and lead covered with a sterile drape to prevent contamination of the camera and keep the camera lens dry during the procedure.

A non-flammable solution is used to cleanse the perineum and vagina and the patient is draped in the usual fashion but with a plastic pocket drape under the buttocks. The cervix is dilated to a size which will just permit the passage of the operating hysteroscope.

The hysteroscope is inserted under direct vision with the fluid running. The laser fiber is then introduced into the uterine cavity through the operating channel and its flexible metal sheath. Care should be taken to ensure that the operating channel valve is open before attempts at insertion of the fiber to prevent damage to the tip. Only then should the laser generator be switched from standby to active mode and the power set at 80 W. The foot pedal should be placed at the surgeon's dominant foot.

Two techniques for application of the laser energy may be employed: dragging, when the tip of the fiber is in contact with the endometrium; and blanching, when the tip of the fiber does not come into contact with the endometrium. Some authors have suggested the use of the laser and rollerball. Only one study has compared the two methods of ELA, and the conclusion from this study was that the blanching technique was easier to perform and more effective. Despite this, the dragging technique remains more commonly used.

Using the dragging technique, the tip of the laser fiber is placed on the endometrium and the laser discharged as the tip of the fiber is dragged over the surface of the endometrium. The camera system is held in the non-dominant (left) hand, leaving the right (dominant) hand free to withdraw and apply pressure to the fiber tip with each pass of the fiber. Each pass of the fiber tip over the endometrium creates a vaporized furrow, and repeated passes produce a series of parallel furrows over the entire surface of the endometrium with a golden brown base of char (Figure 17.4). The order in which the cavity is treated is as follows: the cornua are treated first with radial furrows, beginning at the tubal ostia and extending outwards; The fundus is treated with horizontal (lateral) movements; and the anterior, lateral and posterior walls are treated with vertical passes of the fiber tip to the level of the internal cervical os (Figure 17.5).



Figure 17.4 Completely treated uterine cavity. The tip of the laser fiber can be seen in the middle of the picture.

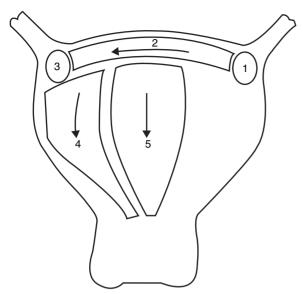


Figure 17.5 Representation of the order in which the cavity is treated.

With the blanching technique, the tip of the laser fiber does not come into contact with the endometrium. 15 The laser is discharged as the tip of the fiber is moved or 'airbrushed' slowly over the surface of the endometrium without coming into contact with it. To achieve an optimal depth of thermal injury, the fiber should be held perpendicular to the surface of the endometrium: while this is achievable at the fundus and cornua, application of laser energy to the anterior, posterior, and lateral walls is more difficult to achieve using this technique. As the endometrium is systematically treated, the surface turns white in color but there is little difference in its appearance. It can therefore be difficult to determine which areas have been treated, particularly as the endometrium will often appear white following pretreatment with GnRH analogues or danazol.

A number of safety rules are applied, regardless of the technique used or the anatomy of the cavity:

- the laser should only be fired when the tip of the fiber is being dragged or moved towards the scope and NEVER when the tip is being pushed away from the scope
- the laser should not be fired when the tip of the fiber is not in vision
- the tip of the fiber should be kept in constant slow motion when the laser is being fired.

Extreme caution should be exercised if an area is retreated and when treating the anterior wall of the cavity, which is often obscured by the presence of gas bubbles.

The power settings of the laser can be altered, with outputs of between 30 W and 80 W having been

suggested. 18,19,20 The author prefers to use the dragging technique throughout, with a power setting of 80 W and slow passage of the laser tip with gentle pressure applied to the surface of the endometrium.

Average operating times using this technique are 19–32 minutes. 18,21,22

RESULTS

The effect of the laser on the endometrium and underlying myometrium has been poorly documented. The studies of Goldrath et al., ¹ Davis, ¹⁹ and Indman ¹⁸ on the tissue effects of laser energy suggest that the depth of thermal necrosis is 4–5 mm with a power output of 80 W using the dragging technique, and reduced depths of thermal necrosis with lower-power outputs.

Long-term follow-up results have been published by a number of authors, with studies reporting on outcomes after periods of between 6 months and 12 years. Some of these studies are summarized below.

In Garry et al's series of 859 patients, follow-up ranged from 6 months to 3 years.²³ The amenorrhea rate was 60% and a further 32% of patients had ongoing but acceptable menstrual bleeding. Only 39 patients had ongoing menorrhagia following treatment, and 26 of these responded to a second ablation. Thirteen (3%) of 479 patients followed up for at least 6 months required hysterectomy by 3 years. The mean treatment time was 24 minutes and the complication rates were low (minor fluid overload 0.4%, infection 0.4%, perforation 0.3%). In two follow-up publications, the same authors concluded that the principal reason for treatment failure was persistent menstrual pain, and that increasing patient age increased the likelihood of a successful outcome.^{24,25} Uterine size or operating time were not important factors in predicting outcome.

Pinion et al. randomized patients planned for hysterectomy for menorrhagia to hysterectomy, transcervical resection of the endometrium (TCRE), and ELA, with the randomization ratio being 1:1 for hysterectomy and hysteroscopic surgery and 1:1 within the hysteroscopic surgery arm of the trial.²⁶ There were no reported statistically significant differences between the ELA and TCRE groups, but there was less intraoperative and early postoperative morbidity in the hysteroscopic surgery arm of the trial and a more rapid recovery than in the hysterectomy group (2–4 weeks vs 2–3 months, p < 0.001). Seventeen patients in the hysteroscopic surgery arm subsequently underwent hysterectomy and 11 repeat hysteroscopic procedures. Seventy-five of 96 (78%) and 89% (79/89) patients in the hysteroscopic surgery and hysterectomy groups were satisfied with their treatment

(p < 0.001) at 12 months and 95% and 90%, respectively, felt that there had been an acceptable improvement in their symptoms.

In 1995, Goldrath reported results of 427 ablations performed on 407 women.²⁷ Excellent results were obtained in 379 women (89%) and only 35 (8.2%) patients had poor outcomes. This study also showed a significant reduction in the number of treatment failures if a single dose of medroxyprogesterone acetate was administered at the time of surgery (p < 0.04).

The rate of hysterectomy following ELA in Jourdain et al's study of 137 patients was 13.3%, and 85% of patients were satisfied with their treatment with a mean follow-up of 32 months. However, 35 (29.2%) of patients in whom treatment was deemed to be a success had serologic evidence of menopause. Treatment failures in this study were attributed to adenomyosis and fibroids, in contrast to other studies where the treatment of fibroids was associated with increased amenorrhea rates following treatment.

Bhattacharya et al. compared TCRE with ELA in a randomized controlled trial with 184 women randomized to treatment with TCRE and 188 to ELA.²⁸ There were no reported differences in further surgical intervention (20% vs 16%) but only 9 (5%) women in the ELA group required hysterectomy, as opposed to 25 (14%) in the TCRE group. Satisfaction rates at 12 months were similar (90% ELA vs 91% TCRE).

Phillips et al. reported on a series of 1003 consecutive ablations performed on 873 patients, a single procedure being performed on 746 women, two ablations on 124 (14.2%), and three procedures in three women (0.4%).²¹ Using survival curve analysis to compensate for varying follow-up times, it was estimated that the hysterectomy rate (for all indications) at 6.5 years was 21%. Having adjusted for confounding factors such as age and dysmenorrhea, factors affecting the risk of subsequently undergoing hysterectomy were repeat ablation (relative risk [RR] = 2.93; 95% confidence interval [CI] 1.59–5.40; p = 0.0015), which increased the risk, and the presence of intracavitary fibroids (RR = 0.26; 95% CI 0.08-0.86; p = 0.0082), which reduced the risk. Shankar et al. demonstrated a similar hysterectomy rate at 4 years, with 79.3% of patients satisfied with the results of treatment and 76.2% remaining 'free of failure' at 4 years.²⁹ This study also demonstrated a higher rate of success in older patients.

Baggish and Sze reported a 58% amenorrhea rate, with a further 34% patients noting reductions in menstrual flow.³⁰ The complication rate was very low (0% uterine perforation, <1% fluid overload) and the average follow-up in this study was 4.5 years. The number of subsequent hysterectomies is not noted.

ELA has, more recently, also been compared to thermal balloon ablation: amenorrhea rates for ELA were 39% vs 29% for balloon therapy.³¹ First-generation ablation techniques remain the benchmark against which second-generation technologies are tested.

Historically, amenorrhea rates and rate of subsequent hysterectomy have been used as the primary outcome measures. Other factors are also important, including economic analysis and effect of treatment on the patient's quality of life, perception of body image, and sexual activity. It has recently been suggested that quality of life assessment, rather than amenorrhea or subsequent hysterectomy rate, should be used to determine treatment efficacy.³²

COMPLICATIONS AND ADVERSE INCIDENTS

When the safety principles outlined above are followed, the rates of adverse incidents and complications are low. The risk of blunt uterine perforation at cervical dilatation is reported at 1% but at ELA the reported rate is somewhat lower (0-0.3%). 23,30,33 Uterine perforation with the hysteroscope or laser fiber is rare in the absence of fibroids. The Royal College of Obstetricians and Gynaecologists' Clinical Audit Unit examined data from more than 10000 ablations in the MISTLETOE study; of these, 1793 were endometrial laser ablation procedures.34 The overall rate of immediate complications (hemorrhage, perforation, cardiorespiratory problems, and visceral burn) with laser and rollerball ablation were significantly lower than with resection. In addition, the rate of emergency surgical intervention was significantly lower during laser ablation than all the other techniques assessed. 0.34% vs 1.11% (rollerball); 1.36% (loop and ball); 2.39% (loop alone); and 2.86% (radiofrequency ablation).

Fluid absorption complicates all procedures when liquid is used to distend the uterine cavity. Hasham et al. studied in detail the rates of fluid absorption at varying flow rates and pressures employed for ablative techniques: rate of flow of fluid through the uterus, the uterine pressure, and the depth of thermal injury were all found to be linked to the rate at which fluid is absorbed.³⁵ The risk of sudden and unexpected fluid loss can be reduced by the use of fluid insufflation and monitoring systems.8 When fluid monitoring systems are not used, large volumes of fluid can be rapidly absorbed, as demonstrated in the study by Osborne et al. when up to 5.1 L were lost during uncomplicated procedures.³⁶ The use of electrolyte solutions such as Hartmann's or saline is possible with ELA, and this markedly reduces the risk of TURP (transurethral resection of the prostate) syndrome and dilutional hyponatremia in the presence of excessive fluid absorption. What

is defined as excessive is dependent on the operator and unit policy: the author uses 1500 ml of deficit as a first alarm level. At this point, a single dose of furosemide (20 mg) is administered intravenously and a urinary catheter inserted. The volume of urine subsequently excreted is subtracted from the calculated deficit and the resulting figure taken as the true fluid deficit (the bladder having been emptied at the beginning of the procedure). Volumes of >2500 ml are not tolerated and surgery is discontinued, even if incomplete when this figure is reached.

Extrauterine visceral injury occurs very infrequently but is a serious complication.^{34,37} Enterotomy or thermal bowel injury will require laparotomy in the majority of patients. This permits inspection of the entire bowel and facilitates repair of any small or large bowel injury that has occurred. Failure to recognize uterine perforation may result in a delayed presentation of fecal peritonitis, with a patient in a moribund state.

The uterine vessels can be injured, particularly if lateral wall fibroids are being treated, and such injuries are more common than pelvic wall vessel injury. Most cases of intraoperative hemorrhage can be controlled with the use of electrocautery or the placement of a urinary catheter within the uterine cavity and inflation of its balloon. Hysterectomy, however, is sometimes necessary to control bleeding, and should be considered early if a patient becomes hemodynamically unstable.

Reported cases of postoperative endometritis are uncommon (<1%) and antibiotics reduce the incidence of such infections further.^{22,23,30} When infection does occur, it should be treated aggressively to prevent the development of profound sepsis.³⁴ A bloody watery discharge may persist for up to 6 weeks following surgery but this rarely infected or problematic.

Intravasation of gas produced by the rapid vaporization of tissue may rarely result in gas embolism, a potentially

fatal complication: this has been reported with the use of a carbon dioxide cooled coaxial fiber with an exposed tip but is most unlikely to occur when the tip of the fiber is cooled in liquid.³⁸

Late complications include:

- failure, with recurrence of dysfunctional bleeding
- pelvic pain as a result of tubal syndrome³⁹
- dysmenorrhea (often related to the presence of adenomyosis)
- the formation of uterine granulomata. 40

Following laser ablation, hysteroscopic assessment of the cavity for abnormal bleeding should be carried out because pockets of endometrium may be obscured by the scaring that results from the primary surgery.

CONCLUSIONS

Endometrial laser ablation is a safe and effective alternative to hysterectomy for the treatment of heavy menstrual loss, uterine fibroids, and polypi. The procedure has a longer learning curve than for the currently available second-generation endometrial ablation techniques and a high initial set-up cost. The technique does, however, have a long track record, and more than 75% of women have endometrial laser ablation for treatment of menstrual dysfunction and will avoid the need for hysterectomy.

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References

- Goldrath MH, Fuller TA, Segal S. Laser photovaporization of the endometrium for the treatment of menorrhagia. Am J Obstet Gynecol 1981; 140: 14–19.
- Bent AE, Ostergard DR. Endometrial ablation with the neodymium:YAG laser. Obstet Gynecol 1990; 75: 923–25.
- Bernhard LA Laser endometrial ablation: an alternative to hysterectomy. Health Care Women Int 1994; 15: 123–33.
- Davis J. The principles of use of the Nd:YAG laser in gynaecological surgery. Baillière's Clin Obstet Gynaecol 1987; 1: 331–52.
- Indman PD, Lovoi PA, Brown WW et al. Uterine surface temperature changes caused by endometrial treatment with the Nd:YAG laser. J Reprod Med 1991; 36: 505–12.

- Davis JR, Maynard KK, Brainard CP et al. Effects of thermal endometrial ablation: clinicopathologic correlations. Am J Clin Pathol 1998; 109: 96–100.
- Indman PD. High-power Nd:YAG laser ablation of the endometrium. J Reprod Med 1991; 36: 501–7.
- Hawe JA, Chien PF, Martin D et al. The validity of continuous automated fluid monitoring during endometrial surgery: luxury or necessity? Br J Obstet Gynaecol 1998; 105: 797–801.
- 9. Baggish MS. New laser hysteroscope for neodymium:YAG endometrial ablation. Laser Surg Med 1988; 8: 99–103.
- Erian J. Endometrial ablation in the treatment of menorrhagia.
 Br J Obstet Gynaecol 1994; 101 (Suppl 11): 19–22.

- Valle RF. Endometrial ablation for dysfunctional uterine bleeding: role of GnRH agonists. Int J Gynaecol Obstet 1993; 41: 3–15.
- Garry R, Khair A, Mooney P et al. A comparison of goserelin and danazol as endometrial thinning agents prior to endometrial laser ablation. Br J Obstet Gynaecol 1996; 103: 339–44.
- Sculpher M, Thompson E, Brown J et al. A cost effectiveness analysis of goserelin compared with danazol as endometrial thinning agents. BJOG 2000; 107: 340–46.
- Garry R. Endometrial laser ablation. Baillière's Clin Obstet Gynaecol 1995; 9: 317–28.
- Loffer FD. Hysteroscopic endometrial ablation with the Nd:YAG laser using a nontouch technique. Obstet Gynecol 1987; 69: 679–82.
- Taylor RH. Endometrial ablation with the combined Nd:YAG laser-rollerball. J Am Assoc Gynecol Laparosc 1996; 4: 589– 92.
- Lomano JM. Dragging technique versus blanching technique for endometrial ablation with the Nd:YAG laser in the treatment of chronic menorrhagia. Am J Obstet Gynecol 1998; 159: 152-5
- Indman PD. High power Nd:YAG laser ablation of the endometrium. J Reprod Med 1991; 36: 501–4.
- Davis JA. Hysteroscopic endometrial ablation with the neodymium:YAG laser. Br J Obstet Gynaecol 1989; 96: 928–32.
- Taylor RH. Endometrial ablation: combination procedure (Nd:YAG laser and rollerball together). J Am Assoc Gynecol Laparosc 1994; 4: S35.
- Phillips G, Chien PF, Garry R. Risk of hysterectomy after 1000 consecutive endometrial laser ablations. Obstet Gynecol 1998; 105: 897–903.
- Jourdain O, Joyeux P, Lajus C et al. Endometrial Nd:YAG laser ablation by hysterofibroscopy: long term results of 137 cases. Eur J Obstet Gynecol Reprod Biol 1996; 68: 103–7.
- 23. Garry R, Erian J, Grochmal SA. A multi-centre collaborative study into the treatment of menorrhagia by Nd:YAG laser ablation of the endometrium. Br J Obstet Gynaecol 1991; 98: 357–62
- Shelley-Jones D, Mooney P, Garry R et al. Factors affecting the outcome of endometrial laser ablation. J Gynecol Surg 1994; 10: 211–15.
- 25. Garry , Shelley-Jones D, Mooney P. Factors influencing the outcome after endometrial laser ablation: a review of 600 cases. J Am Assoc Gynecol Laparosc 1994; 4: S11.

- Pinion SB, Parkin DE, Abramovich DR et al. Randomised trial of hysterectomy, endometrial laser ablation and transcervical endometrial resection for dysfunctional uterine bleeding. Br Med J 1994; 309: 979–83.
- 27. Goldrath MH. Hysteroscopic endometrial ablation. Obstet Gynecol Clin North Am 1995; 22: 559–72.
- 28. Bhattacharya S, Cameron IM, Parkin DE et al. A pragmatic randomised comparison of transcervical resection of the endometrium with endometrial laser ablation for the treatment of menorrhagia. Br J Obstet Gynaecol 1997; 104: 601–7.
- Shankar M, Naftalin NJ, Taub N et al. The long term effectiveness of endometrial laser ablation: a survival analysis. Eur J
 Obstet Gynecol Reprod Biol 2003; 108: 75–9.
- Baggish MS, Sze EH. Endometrial ablation: a series of 568 patients treated over an 11-year period. Am J obstet Gynecol 1996; 174: 908–13.
- 31. Hawe J, Abbott J, Hunter D et al. A randomised controlled trial comparing the Cavaterm endometrial ablation system with the Nd:YAG laser for the treatment of dysfunctional uterine bleeding. BJOG 2003; 110: 350–7.
- 32. Abbott JA, Hawe J, Garry R. Quality of life should be considered the primary outcome for measuring success of endometrial ablation. J Am Assoc Gynecol Laparosc 2003; 4: 491–95.
- Garry R, Shelley Jones D, Mooney P et al. Six hundred endometrial laser ablations. Obstet Gynecol 1995; 85: 24–9.
- Overtone C, Hargreaves J, Maresh M. A national survey of the complications of endometrial destruction for menstrual disorders: the MISTLETOE study. Br J Obstet Gynaecol 1997; 104: 1352–9.
- 35. Hasham F, Garry R, Kokri MS et al. Fluid absorption during laser ablation of the endometrium in the treatment of menorrhagia. Br J Anaesth 1992; 68: 151–4.
- 36. Osborne GA, Rudkin GE, Moran P Fluid uptake in laser endometrial ablation. Anaesth Intensive Care 1991; 19: 217–19.
- Petrucco OM, Gillespie A. The neodymium: YAG laser and the resectoscope for the treatment of menorrhagia. Med J Aust 1991; 154: 518–20.
- 38. Kelly M, Matthews HM, Weir P. Carbon dioxide embolism during endometrial laser ablation. Anaesthesia 1997; 52: 65–7.
- McCausland AM, McCausland VM. Long-term complications of endometrial ablation: cause, diagnosis, treatment and prevention. J Minim Invasive Gynecol 2007; 14: 399–406.
- 40. Silvernagel SW, Harshbarger KE, Shevlin DW. Postoperative granulomas of the endometrium: histological features after endometrial ablation. Ann Diagnostic Pathol 1997; 1: 82–90.

ThermaChoice balloon endometrial ablation

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INTRODUCTION

Abnormal uterine bleeding (AUB) from benign causes is experienced by approximately one in four premenopausal women. The prevalence increases with age and peaks just prior to menopause. When menstrual blood loss (MBL) exceeds 80 ml, approximately two-thirds of women develop iron deficiency anemia. In addition, AUB adversely affects women's quality of life and can lead to significant utilization of healthcare resources. In the past, menorrhagia was treated by dilatation and curettage (D&C) and/or hysterectomy. It has been shown that D&C has no therapeutic effect on menorrhagia. Hysterectomy is a definitive therapy for menorrhagia, with high rates of patient satisfaction; however, it is associated with inflated rates of morbidity and costs. I

Hysteroscopic endometrial ablation (HEA) was introduced in the 1980s as an alternative to hysterectomy in women with AUB of benign causes. Initially, there was rapid and wide interest in this procedure. This enthusiasm came to a halt, and even a decline in some countries (e.g. Australia), due to a realization that HEA required additional training and surgical expertise to avoid emergent procedure-related complications such as excessive fluid absorption, uterine perforations^{4,5} and thermal injuries.⁶ A prospective study (MISTLETOE) captured about 80% of HEA performed in the UK up to the mid 1990s. The efficacy of HEA and risk of complications were strongly related to skill and training of the surgeon. Severe complications, especially with use of the loop electrode, were more common in the first 100 cases of the surgeon.7 To overcome these difficulties and concerns, a thermal balloon (ThermaChoice, Gynecare, Division of Ethicon, Somerville, NJ) invented by Neuwirth and Bolduc and described in 1994, was utilized that required skills similar to inserting an intrauterine contraceptive device (IUCD).8

HISTORY OF THE THERMACHOICE BALLOON

Development of balloon endometrial ablation

The invention consisted of a plastic catheter, 16 cm long × 3 mm in diameter, which was connected to a latex balloon on one side and to a control unit on the other. The latex balloon was designed to conform to the uterine cavity at an intraluminal pressure of approximately 70 mmHg. The distal end of the catheter formed the center axis of the balloon, inside of which there was a heating element and a thermistor surrounded by a perforated heat shield. The control unit monitored intra-balloon pressure, temperature, and duration of treatment. Initially, it was thought that the most appropriate intra-balloon pressure should be 70-80 mmHg. The initial six cases were conducted in the high altitude of Mexico City; thus, the temperatures within the balloon were kept below 100°C to avoid boiling of the liquid (5% dextrose in water) and any potential sequelae of steam formation. Subsequently, the control unit was programmed to provide a temperature range of 87 ± 5°C via a feedback thermistor/heating element software system.

Initial studies

The duration of treatment in six prehysterectomy specimens in Mexico City varied from 6 to 12 minutes at temperatures of 87.7–97.2°C. An additional four prehysterectomy cases were performed in London, UK, and the duration of treatment was limited to 6 minutes with intra-balloon temperatures of 87.7–89.4°C. During treatment in all 10 cases, the uterine serosal temperature was measured by thermocouples, and varied from 31.7°C to 37°C. Once the hysterectomy was completed, sections of the uterine wall were taken for histochemical assessment of tissue destruction by diaphorase stains. Visual measurements

of thermal destruction correlated with histochemical findings, indicating a zone of destruction ranging from 3.3 mm up to 10 mm (average 5.5 mm).8

Following prehysterectomy studies, a feasibility study was conducted in 18 women with menorrhagia in five centers (Mexico, Canada, USA, and UK).9 All except two procedures were performed in the operating room under general anesthesia; one patient had regional anesthesia while another had local anesthesia. Four women were treated under laparoscopic observation. The intra-balloon pressure was stabilized at 80 mmHg, the temperature was kept at 170-190°F (76.6-87.8°C) for at least 4 minutes, and the duration of treatment varied from 6 to 9 minutes. At follow-up of 6-34 months, there were no reported complications and seven of 18 women (39%) reported light menses, eight (44%) reported spotting or amenorrhea, and three women (17%) reported no change in menstrual pattern. Two women (11%) subsequently had hysterectomy.9

The first feasibility/efficacy pilot study was conducted by Vilos at St. Joseph's Health Care, London, Canada, in June and July of 1994. After Institutional Review Board (IRB) approval, 30 women with menorrhagia who met inclusion and exclusion criteria were treated with the ThermaChoice balloon. Nine women were pretreated with danazol 100-200 mg/day for 1-2 months prior to surgery. The controller had been programmed to provide a temperature range of 87 ± 5°C for 8 minutes. The first nine women were treated under general anesthesia while the subsequent 21 women were treated under conscious intravenous (IV) sedation and paracervical block. The first seven patients experienced severe uterine cramps in the immediate postoperative period. A single, preoperative dose of indomethacin (100 mg) rectal suppository markedly reduced intra- and postoperative cramps and was given routinely to all subsequent women.

The balloon was pressurized between 80 and 140 mmHg in the first 15 patients. Routine post-balloon ablation hysteroscopy indicated variable thermal tissue effects on the endometrium. Flattening of the endometrium with more uniform coverage of the balloon and thermal necrosis was noted at higher pressures. By plotting pressure–volume curves, it was determined that the natural capacity of the uterus was reached at approximately 160–170 mmHg. Therefore, in the last 15 women and all subsequent studies, the balloon was inflated until the pressure was stable at 160–180 mmHg. ¹⁰

The feasibility pilot study was expanded to include a total of 121 women treated by the ThermaChoice balloon in 3 centers in Canada. No intraoperative complications occurred and minor postoperative morbidity was reported in 4% of patients. Success of the procedure was constant over the year (range 86–90%). Treatment led to

significant decreases in menstrual flow, duration, and pain (p <0.001). No significant effects of parity, uterine position or cavity length, timing, or various endometrial-thinning regimens were found. Increasing age was significantly associated with increased odds of success (p <0.05). 11

The safety and efficacy of thermal balloon ablation was further evaluated by an international prospective observational study, including five European countries, Canada, and Australia. The 121 patients from the Canadian trial were included. Follow-up data at 3 and/or 6 and/or 12 months were required for inclusion in the analysis. 12 Between June 1994 and August 1996, 321 women were treated and 296 were eligible for analysis. No intraoperative complications occurred and postoperative morbidity was minimal. Success of the procedure was constant over the year (range 88-91%) and treatment led to a significant decrease in the duration of menstrual flow and severity of pain (p < 0.0001). Increasing age, higher balloon pressure, smaller uterine cavity, and a lesser degree of preprocedure menorrhagia were associated with significantly improved results. Pretreatment with a gonadotropinreleasing hormone agonist (GnRH-a) increased amenorrhea and spotting rates (p = 0.03), but was only used in 5% of patients.12

A multicenter randomized controlled trial (RCT) randomization 1:1 - comparing ThermaChoice and rollerball ablation, for treatment of menorrhagia in premenopausal women (n = 255), was conducted in 12 centers in the USA and two in Canada. 13 At 12 months of follow-up, 239 women were evaluable. Results indicated that both techniques significantly reduced menstrual blood flow, with no clinically significant differences between the two groups as reflected by return to normal or less bleeding (balloon 80.2% and rollerball ablation 84.3%). Intraoperative complications occurred in 3.2% of rollerball-treated patients, whereas no intraoperative complications occurred in the ThermaChoice group. The study concluded that uterine balloon therapy is as efficacious as hysteroscopic rollerball ablation, and may actually be safer, in the treatment of dysfunctional uterine bleeding (DUB).¹³

Based on the above evidence, the FDA (Food and Drug Administration) approved the use of ThermaChoice balloon endometrial ablation in the USA in December 1997. It had been approved in other parts of the world in 1995.

TEMPERATURE SAFETY ASPECTS

Initially, thermal injury by the hot liquid balloon was evaluated in a variety of non-perfused tissues. Approximately 5 mm of coagulation necrosis was noted when the liquid inside the balloon was heated to 92°C for 5 minutes.

Similar coagulation effects were seen in extirpated uterine specimens.⁸

Safety aspects of the ThermaChoice balloon were further studied by Andersen and colleagues in Denmark, and Shah and colleagues in the USA. Andersen et al. measured uterine serosal temperatures in eight women undergoing balloon ablation just prior to abdominal hysterectomy for benign AUB and/or dysmenorrhea. Balloon therapy was completed at 87±5°C, a pressure of 100-160 mmHg, and treatment duration of 8, 14, 15, and 16 minutes. The highest uterine serosal temperature recorded was 39.1°C at the left cornua after 13 minutes in one patient. The rate of increase and the gradients of serosal temperature varied between patients; however, the temperature peaked at 10-12 minutes and stabilized at 9–11 minutes. The average coagulation zone in the uterine corpus was 3.5 mm, and one patient showed 11.5 mm of coagulation at the fundus. In this patient, the serosal temperature was 38.8°C at 16 minutes of treatment.14

Shah and colleagues reported on 20 women undergoing abdominal hysterectomy. Eleven extirpated uterine specimens were treated with the ThermaChoice balloon for 8 minutes at pressures of 150–179 mmHg. The heating cycle was not activated in two specimens, which were used as controls. Data collected from seven cases indicated that the serosal temperatures remained below 45°C, with the greatest depth of myometrial necrosis being 5–8 mm. In-vivo measurements in nine prehysterectomy uteri revealed a mean (±SD) peak serosal temperature of 36.1±1.6°C. Histochemical studies indicated that the greatest depth of myometrial injury occurred in the mid fundus at 3.4 mm.¹⁵

EFFECTS OF BALLOON PRESSURIZATION

Initially, the balloon was pressurized at 70–80 mmHg.⁸ The control unit was programmed, so that when pressure was outside the 45–165 mmHg range, the heating unit would default and shut down.⁸

In the initial studies by Vilos et al., 18 women were treated for 8 minutes at 80–150 mmHg pressure and 15 women at 151–180 mmHg. At 12–24 months follow-up, persistent menorrhagia was reported in 56% of women in the low-pressure-treated group compared with 20% in the high-pressure-treated group (p = 0.01). To determine the natural capacity of the uterus, pressure–volume curves were performed by incremental infusion of small volumes of 5% dextrose and water in nine women. The natural uterine capacity was reached at 170–180 mmHg. Attempts to infuse even a small portion of liquid after this pressure induced uterine contractions and rapid increases in intrauterine pressure (IUP). 16

It was speculated that the improved clinical outcome at higher pressures may be due to flattening of the endometrium, better contact of the balloon with the uterine cavity, and restriction of local blood circulation, allowing deeper and more uniform distribution of heat. ¹⁶ The effects of blood flow, balloon pressure, and blood vessel damage were studied in a geometric uterine model. The model predicted that higher intra-balloon pressures (>166 mmHg) strangulate endomyometrial capillary vessels by local stress, allowing deeper penetration of thermal coagulation and necrosis. ¹⁷

The intra-treatment characteristics and the effects of ThermaChoice intra-balloon pressure on the clinical outcomes were also reported from a prospective observational study of 72 women with menorrhagia. The mean (\pm SD) starting pressure was 174.8 ± 8.3 mmHg, which decreased to a mean end pressure of 143.1 ± 18.1 mmHg. A spontaneous decrease in IUP was observed in 67 patients (93%), with the mean reduction being 34.1 ± 14.9 mmHg or $19.5\pm9.1\%$. An increase in IUP at the end of the cycle was seen in two (3%) and no change in IUP in three patients (4%). The end pressure decreased to <140 mmHg in 29 patients (35%) and to \leq 120 mmHg in 8 patients (11%). The end pressure remained >160 mmHg in only 12 patients (17%). The

With up to 36 months of follow-up, life-table analysis of the data indicated that the mean end pressure was significantly lower in patients with treatment failure than in those with successful treatment (131.1 \pm 14.1 mmHg vs $145.1 \pm 18.0 \text{ mmHg}, p = 0.02$). The failure rate was 37.5% when the end pressure decreased to ≤120 mmHg, whereas it was 4.7% if the pressure remained at ≥140 mmHg. No patient experienced treatment failure if the end pressure was >160 mmHg.¹⁸ Amenorrhea rates of 33% vs 5% (p < 0.01) were experienced if the end pressures were >160 and <160 mmHg, respectively. Univariate analysis of the data demonstrated that the rates of success of treatment with ThermaChoice were significantly lower when the end pressure was <140 mmHg, the intrauterine volume was >10 ml, and the uterus was retroverted.18

The importance of adequate balloon pressurization and maintenance of high pressure throughout the 8-minute treatment cycle was recognized quite early. 10,16 It was suggested that the balloon be pressurized slowly up to 200 mmHg and the pressure titrated downwards to 180 mmHg prior to starting treatment. If the pressure decreases to <160 mmHg during the treatment cycle, some surgeons reinstate and maintain the pressure between 160 and 180 mmHg by small incremental infusion or withdrawal of liquid throughout the 8-minute cycle. 16,19 However, addition of liquid during a therapy cycle is not recommended by the manufacturer of ThermaChoice.

EFFECTS OF DURATION OF TREATMENT

The initial studies on various tissues, extirpated uterine specimens, prehysterectomy-treated uteri, and in vivo pilot studies indicated that an effective duration of treatment should be approximately 8 minutes. The 8-minute duration has been programmed into the control unit and has been used in all subsequent treatments. Vilos and colleagues compared 15 women treated for 8 minutes with 33 women treated for 12–16 minutes at 151–180 mmHg pressure. Success was not affected or influenced by increasing the duration of treatment from 8 to 12 minutes or more. ¹⁶

Bongers et al compared 63 women treated for 8 minutes with 67 treated for 16 minutes. Hysteroscopy, performed immediately after treatment, showed a thermal effect on both the anterior wall and fundal region in both groups. The posterior wall appeared non-treated in 25% of women after 8 minutes, whereas it was only 8% in the 16-minute group (not statistically significant). At 3, 6, 12, and 24 months of follow-up, failure rates, defined by hysterectomy (six in each group) or patient dissatisfaction (n = 11) with the treatment result, were similar in the two groups.²⁰

A warning by the manufacturer of ThermaChoice states not to treat patients for more than one therapy cycle in a given treatment session because of the potential for transmural injury to the uterus or injury to adjacent viscera.

PRETREATMENT ASPECTS

Patient assessment

Prior to endometrial ablation, by any technology, women with AUB should be assessed and inclusion and exclusion criteria should be applied in accordance with established clinical practice guidelines^{1,21} and manufacturer's specifications. In addition to the standard history, physical and pelvic examination, Papanicolaou smear, vaginal/cervical swabs and endometrial biopsy, when indicated, the uterine cavity should be thoroughly assessed prior to Therma-Choice treatment. Imaging by sonography (saline infusion sonography, 'SIS', transvaginal ultrasound 'TVS') and/or office hysteroscopy is mandatory to assess the shape, size, and condition of the uterine cavity.

Indications and contraindications

The indications and contraindications for ThermaChoice endometrial ablation are listed in Tables 18.1 and 18.2, respectively.

Table 18.1 Indications for ThermaChoice ablation

- Dysfunctional uterine bleeding (DUB)
- Failed traditional therapies (e.g. medical, D&C)
- Contraindications to traditional therapies
- · Poor surgical risk for anesthesia, HEA, hysterectomy
- To preserve the uterus

Table 18.2 Contraindications for ThermaChoice

- Genital tract malignancy (cervical, uterine, tubal, ovarian)
- Unresolved endometrial hyperplasia
- Women with anatomic or pathologic uterine anomalies
- Women with history of previous classical cesarean section or transmural myomectomy
- Intrauterine pregnancy
- Acute genital and/or urinary tract infection
- Women wishing to preserve their fertility
- Women expecting amenorrhea as an outcome
- Women with IUCD in place
- Failed previous endometrial ablation

Patient counseling, education, and informed consent

Prior to ThermaChoice ablation, women should be informed that the procedure is irreversible and that the clinical outcome is reduction of menstrual bleeding, rather than amenorrhea, although amenorrhea is a possible outcome. The need for further treatments such as medications, repeat hysteroscopic endometrial ablation, and/or hysterectomy in approximately 20–25% of women should be discussed.

It should be emphasized that ThermaChoice ablation should not be performed in women who wish to preserve their fertility, nor should it be used as a means for contraception. Additional methods of family planning should be discussed and documented, since pregnancies after ThermaChoice balloon ablation have been reported to occur at a frequency of approximately 5%.²² Pregnancies after ablation can be dangerous for both mother and fetus. Concomitant laparoscopic or hysteroscopic tubal occlusion should be offered in patients who require contraception.²³ The nature of ThermaChoice ablation, possible complications, clinical outcomes, and alternative therapies should be outlined. Specific complications, such as infections, hemorrhage, hematometra, postablation tubal

sterilization syndrome (PATSS), cervical and/or uterine perforations, and thermal injuries to viscera and/or lower genital tract, should be disclosed prior to the procedure.

Patient selection

One of the advantages of ThermaChoice balloon ablation is that it is a minimally invasive procedure requiring skills similar to those of inserting an IUCD. However, knowledge and training on its application, use, limitations, and safety are mandatory. The small-diameter catheter/balloon (4–5 mm) requires minimal cervical dilatation and obviates the need for major analgesia/anesthesia and the use of resource-intensive operating rooms. The ideal patients for ThermaChoice endometrial ablation should be women with menorrhagia, over 40 years old, normal size and shape of uterine cavity, who have had at least one normal vaginal delivery, and family planning is not an issue.

The pain tolerance of women, their eligibility for outpatient balloon ablation, and their requirements for analgesia/anesthesia may be assessed during office visits by pelvic and vaginal speculum examination, particularly by the ease or difficulty of performing endometrial biopsy and/or office hysteroscopy.

Cervical stenosis, due to lack of vaginal deliveries, may be overcome by preoperative misoprostol administration (orally or vaginally) or insertion of laminaria, ^{24,25} whereas cervical scarring from previous surgery would be better dealt with under conscious sedation or general anesthesia.

Preoperative endometrial preparation

Intuitively, a thin endometrium should allow deeper thermal endomyometrial necrosis and result in better clinical outcomes. In the initial Canadian trial, no significant effects of various endometrial thinning regimens were noted. The international study (n = 296 women) suggested that pretreatment with GnRH-a (n = 15 women) increased amenorrhea and spotting rates (p = 0.03). The international study (n = 296 women) increased amenorrhea and spotting rates (n = 296).

Lok et al. reported on 72 women treated by Therma-Choice after endometrial preparation with danazol 600 mg daily for 6 weeks or a single injection of GnRH-a 6 weeks prior to ThermaChoice balloon ablation. Transvaginal ultrasound, performed on the day of treatment, showed a mean (\pm SD) endometrial thickness of 3.7 ± 1.1 mm, whereas the mean (\pm SD) uterine volume was 10.0 ± 4.6 ml. At a median follow-up of 18 months (range 6–26 months), the amenorrhea rate was 33% if the pressure was >160 mmHg and 5% if it was <160 mmHg. Compared with other RCTs and cohort studies reporting amenorrhea rates of 5–20%, the high amenorrhea rate of 33% in the present study may be due to the thin pretreated endometrium.

Lissak and associates treated 30 women with menorrhagia using the ThermaChoice balloon. Women were randomized into receiving a GnRH-a (n = 17, Lupron 'leuprolide acetate' 3.75 mg, 30 days prior) vs immediate treatment without a GnRH-a (n = 13). After 6 months of follow-up, the amenorrhea, hypomenorrhea, and eumenorrhea rates were 23%, 61.5%, and 15.3% vs 23.5%, 70.5%, and 5.8% in the GnRH-a and control groups, respectively (NS). The corresponding satisfaction rates were 92% and 88%.²⁶

In the FDA pivotal trial of ThermaChoice vs rollerball ablation, patients randomized to ThermaChoice balloon ablation were required to undergo suction curettage for 3 minutes. No standard pretreatment was given to patients undergoing rollerball ablation. At 12 months of follow-up, amenorrhea rates were 15.2% and 27.2% in the Therma-Choice and rollerball groups, respectively.¹³

Therefore, the use of preoperative endometrial preparation prior to ThermaChoice is optional. However, if endometrial thickness of 3–4 mm is thought to be beneficial, as suggested by the study conducted by Lok et al., a uniformly thin endometrium of 4 mm can be achieved by oral contraceptives.²⁷

ANALGESIA/ANESTHESIA

During a surgical procedure, the goal of the use of analgesia/anesthesia is to reduce the patient's anxiety, create amnesia, and control pain. Pain threshold and pain tolerance may be expressed by interaction of biologic, psychological, and social factors. Pain can be alleviated by a variety of pharmacologic agents and techniques, including analgesics, local anesthetics, conscious sedation, general anesthesia, and possibly acupuncture. Analgesia is defined as the reduction of pain in the conscious patient and can be achieved by a variety of medications, including anxiolytics, opioids, and non-steroidal anti-inflammatory drugs (NSAIDs). Local anesthesia during endometrial ablation eliminates sensation from the cervix and uterus, and can be achieved by a variety of injectable or spray solutions and gels.²⁵

A suggested cocktail for local anesthesia prior to thermal balloon endometrial ablation is shown in Table 18.3.

Conscious sedation is defined as minimal reduction in the level of consciousness while the patient retains her own airway and responds to physical and verbal stimuli. Suggested medications for conscious sedation are shown in Table 18.4.

Caution should be exercised when a combination of medications is used. Various drugs, given by different routes, peak at different times, and anxiolytics and narcotics may potentiate each other's contribution to respiratory

Table 18.3 Solution for paracervical block

•	10 ml	lidocaine 1% with 1:200 000 epinephrine
•	10 ml	bupivacaine 0.2%
•	50 ml	(1 ampule) sodium bicarbonate
•	1 ml	(1 ampule) atropine (0.5 mg)

71 ml total solution; inject 10-20 ml around the cervix

Table 18.4 Medications for conscious sedation

- Fentanyl citrate 1 (μg/kg IV)
- Atropine 0.5–0.6 mg IV
- Midazolam 4 m IV
- Antiemetic:

Dimenhydrinate 50 mg IV Prochlorperazine 10 mg IV or IM

and cardiac dysfunction. Cardiopulmonary monitoring (blood pressure, heart rate) and pulse oximetry are recommended during treatment when patients are given combined medications by any route.

From the beginning of ThermaChoice utilization, it became apparent that the majority of women could be treated without the need for a general anesthetic and operating room. ^{10,11} In the FDA's pivotal RCT, local anesthesia, plus or minus IV sedation, was used in 38.8% of patients undergoing ThermaChoice balloon ablation. ¹³ Various protocols used a combination of agents and techniques, including NSAIDs, opioids, and paracervical blocks with or without conscious sedation in an outpatient setting (outside operating theaters).

Fernandez et al. treated 18 women with menorrhagia using the ThermaChoice balloon under preoperative indomethacin (100 mg) rectal suppository and ketoprofen or paracetamol followed by 40 ml of 1% lidocaine paracervical/intracervical block. The mean visual analogue score (VAS) during the procedure was 3.8.²⁸ Duggan and Dodd treated 16 women with the ThermaChoice balloon under local analgesia with light IV sedation. The procedure was well tolerated in 80% of women. The median VAS for intraoperative discomfort was 0.5 (range 0–5.1) and 5.6 (range 1.4–10) for discomfort assessed 2 hours following the procedure.⁴

Soysal et al. treated 45 women with myoma-induced menorrhagia using the ThermaChoice balloon under intracervical/paracervical block (1% lidocaine with 1:200 000 epinephrine) and fentanyl citrate intravenously. The procedure was well tolerated by all patients.²⁹

Lok and associates treated 30 women with menorrhagia using the ThermaChoice balloon under indomethacin (100 mg) rectal suppository, midazolam 7.5 mg given 2 hours preoperatively, and PCA (patient-controlled analgesia) pump (propofol 10 mg/ml, alfentanil 500 μ g/ml). Over 85% of women did not think that general anesthesia was necessary.³⁰

Laberge and colleagues compared intra and postoperative pain in women with menorrhagia treated by Therma-Choice (n = 30) or the NovaSure device (n = 37, Novacept, Palo Alto, CA). All patients received indomethacin (100 mg rectal suppository, 1 hour pretreatment), paracervical block, and IV sedation. Patients treated with Therma-Choice reported higher intra- and postoperative pain than those treated with the NovaSure system. Serum prostaglandin $F_{2\alpha}$ (PGF $_{2\alpha}$) values did not differ between the two groups. ³¹

In 2004, Clark and Gupta reported on 68 women with menorrhagia, given the option of having treatment with the ThermaChoice balloon under general or local anesthesia. Fifty-three women chose local anesthesia, consisting of indomethacin (100 mg) rectal suppository and intracervical/paracervical block. No IV sedation or narcotic analgesia was given. The treatment was successfully completed in 50 women (94%). One (2%) woman could not tolerate treatment because of severe discomfort. One woman was not treated due to equipment failure, and, in one case, the balloon/catheter system could not be inserted through the cervix. ¹⁹

A retrospective study reported on 226 women with menorrhagia treated with either ThermaChoice (n = 161) or HEA (n = 65). Most patients (88%) were treated under IV sedation, paracervical block, and Toradol (ketorolac tromethamine). Patients who underwent HEA were less likely to require postoperative analgesics (14% vs 33%, p = 0.003), whereas more patients were admitted for pain control after ThermaChoice treatment (13.7% vs 3.1%, p = 0.02). Preoperative Toradol use did not influence the rate of admission to hospital.³²

Finally, Marsh and colleagues reported on Therma-Choice endometrial ablation (n = 27 women) in the outpatient setting, without local anesthesia or IV sedation.³³ The first cohort of 14 women underwent ThermaChoice without elective analgesia (i.e. awake, with no premedication, IV sedation, or local anesthetic). Uterine cramping, both during and after ThermaChoice, was most commonly responsible for women requiring 'rescue' analgesia (n = 4 women) or requesting to terminate treatment (n = 1). Successful 8-minute treatment was achieved in 12 women (86%). A second cohort of 13 women underwent ThermaChoice ablation after taking elective ibuprofen only. Patients were asked to take ibuprofen (600 mg) the evening before treatment, 600 mg 1 hour prior to treatment,

and 600 mg 4 hours after treatment. In one woman, the cervix could not be dilated. Eight-minute treatment in the second group was successful in 12 women (92%).³³

Throughout treatment, there was little difference between the two groups with regards to VAS pain scores, with an overall pain score of 3.6. The most uncomfortable part of the procedure in both groups was the insertion of the ThermaChoice, with an average pain score for all women of 4.2. The VAS pain scores for the first cohort gradually increased during the procedure from the initiation of therapy to the end of 8 minutes. Nausea was experienced by 42% and 8% (p = 0.059) and vomiting by 25% and 8% (NS) in the first and second group, respectively. Overall, ThermaChoice treatment was successful in 24 of 27 (89%) women. Of the 92% of women who replied to a questionnaire, 100% would recommend it to a friend and 77% would have it again.³³

The study by Marsh and associates indicates that, in properly selected women, ThermaChoice endometrial ablation can be safely performed in an outpatient setting without local anesthesia or IV sedation. One could speculate whether the addition of misoprostol (400 µg vaginal suppository) or laminaria given the evening before treatment would have facilitated cervical dilatation and successfully treated the two women in whom the procedure was abandoned due to inability to access the uterine cavity. No other non-hysteroscopic endometrial ablation device has been reported to be feasible under no analgesia at all, or oral or local anesthetic alone. We have successfully treated several women with menorrhagia using Therma-Choice without any form of analgesia or anesthesia.

TECHNIQUE

The ThermaChoice balloon and required components come in a sterilized package. After appropriate anesthesia and pelvic examination, the cervix is grasped with a single-toothed tenaculum and the uterine cavity is sounded. The cervix should easily allow passage of a 5 mm dilator. Postdilatation hysteroscopy, just prior to insertion of the balloon, is performed by some surgeons to determine the integrity of the cervical canal and uterine cavity.

The balloon–catheter is first tested for leaks. The system is primed by inflation with 30 ml of 5% dextrose and water, and it is then deflated to 180 mmHg negative pressure to remove any air. If an ionic/electrolytic solution is used inadvertently (e.g. saline, Ringer's lactate), the controller faults due to electrical shorting within the balloon. The balloon is then inserted through the cervix until the tip touches the fundus. The centimeter marking in the catheter should match the predetermined uterine sounding. The balloon is then inflated manually with a syringe

until the pressure remains stable at 180 mmHg. The treatment cycle is activated and the catheter–balloon system is maintained in position for the 8-minute cycle. Some surgeons add liquid to the balloon against the manufacturer's recommendation to maintain the pressure >160 mmHg throughout the treatment cycle. Presently, the software-controlled device alarms at balloon pressures of 200 and 100 mmHg and faults if balloon pressure exceeds 210 mmHg or falls below 70 mmHg for 2 seconds during treatment. In addition, the procedure self-terminates if the intra-balloon temperature >95°C for 2 seconds, or <75°C for 15 seconds, or if a temperature of 87°C cannot be achieved after 4 minutes of preheating.

At the completion of treatment, the balloon is deflated, withdrawn from the cavity, and discarded. Some surgeons perform post-treatment hysteroscopy to determine whether the balloon treated the uterine cavity rather than a false passage. 10,11

CLINICAL OUTCOMES

Post-ThermaChoice hysteroscopic appearance

During the first 3 months following HEA, the endometrium undergoes necrosis, with variable degrees of acute and chronic inflammation, followed by repair and regeneration with foreign body and granulomatous reaction.^{34,35} These changes lead to various configurations of the uterine cavity, from intrauterine synechia, shortening, and narrowing, to partial or complete obliteration with or without entrapment of viable endometrial tissue remnants.^{36–38}

The hysteroscopic appearance of the endometrial cavity 6 months after ThermaChoice ablations was reported on 22 women.³⁹ In two women (9%) the cavity could not be accessed due to cervical stenosis. In 10 women (45.5%) the appearance of the uterine cavity was reported as normal, whereas in four women (18%) the cavity was reported as fibrotic and atrophic. Six women (27.3%) had intrauterine adhesions. The menstrual outcome correlated with postablation appearance.³⁹

Randomized controlled trials

ThermaChoice vs rollerball ablation

A multicenter RCT reported on 255 women with menorrhagia treated by ThermaChoice or rollerball ablation. ¹³ At 12 months of follow-up (n = 239 evaluable women), results indicated that there was no clinically significant difference between the two groups as reflected by return to normal bleeding or less (balloon 80.2% vs rollerball 84.3%). Quality of life results were also similar. Satisfaction rates were 85.6% and 86.7% in the balloon and rollerball groups, respectively. The corresponding amenorrhea rates were 15.2% and 27.2%, respectively. Dysmenorrhea and postmenstrual syndrome (PMS) symptoms decreased significantly in both groups. The study concluded that ThermaChoice therapy is as efficacious as rollerball ablation and it may be safer. At 2 years of follow-up (n = 255 evaluable women), patient satisfaction with both treatments was consistently high. Only 15 hysterectomies had been performed (six for menorrhagia), 11 in the rollerball group, and four in the balloon group. Additional benefits were reduction in dysmenorrhea and PMS. At 3 years of follow-up (n = 214 women) the results were consistent and remained similar in both groups. There were 14 hysterectomies in the rollerball group and eight in the ThermaChoice group.

At 5 years of follow-up there were 147 women who were interviewed. Of these, 25 reported hysterectomy, repeat ablation or D&C between years 3 and 5, leaving 122 eligible for analysis (61 balloon, 61 rollerball): of these, 58 (95%) having balloon ablation and 59 (95%) having rollerball ablation reported normal or less bleeding. Similarly, 93% and 100%, respectively, were satisfied with the procedure. Among the total population of 255 women, originally randomized, 42 hysterectomies (21 balloon, 21 rollerball), five repeat ablations (three balloon, two rollerball) and one D&C (rollerball) were reported by year 5. Thirty-five hysterectomies (83%) were performed because of bleeding and/or pelvic pain, one-third of them associated with myomas. Overall success rates at 5 years were 68% (58/85) for ThermaChoice and 69% (59/85) for rollerball.⁴²

van Zon-Rabelink et al. randomized 139 women with menorrhagia and treated 77 with ThermaChoice and 60 with rollerball ablation. All patients were pretreated with Zoladex (goserelin), GnRH-a, 6 and 2 weeks prior to surgery. The type of anesthesia was not stated. At 24 months, significant reduction in menstrual blood loss (pictorial blood loss assessment chart [PBAC] <185) was experienced by 79% and 76% of the ThermaChoice- and rollerball-treated patients, respectively. Additional surgical treatment was required by 17% and 15% of women, respectively. Postoperative complication rates in both groups were low, but postoperative analgesics were prescribed significantly more in the ThermaChoice groups. 43,44

ThermaChoice vs TCRE

Gervaise et al. reported on an RCT of 73 women with menorrhagia treated by ThermaChoice ablation and 74 women treated by transcervical resection of the endometrium (TCRE).⁴⁵ There were no intraoperative complications in either group. At 2 years of follow-up, an amenorrhea rate of 36.4% was reported by 44 evaluable

women treated by ThermaChoice and amenorrhea rate of 38.8% by 47 women treated by TCRE. The corresponding hysterectomy rates were 15.9% (7/44) and 10.6% (5/47), respectively. The overall success rates were 83.0 ± 5% for ThermaChoice balloon ablation and 76.3 ± 6% for TCRE. 45 Another study compared 77 women with menorrhagia treated by ThermaChoice with 75 women treated by TCRE (non-randomized). At 2 years of follow-up, amenorrhea rates of 13% vs 17% and menometrorrhagia of 12% vs 21% were reported for ThermaChoice and TCRE, respectively. 46

ThermaChoice vs NovaSure ablation

Bongers and colleagues randomized 126 women with menorrhagia into treatment by ThermaChoice (n = 43) or the NovaSure system (n = 83). All patients were treated in a daycare program under spinal or general anesthesia. Suction curettage was performed in the ThermaChoice group. There were no complications in either group. 47,48

At 12 months of follow-up, amenorrhea rates were 8% and 43% in the ThermaChoice and NovaSure groups, respectively (p<0.001). The corresponding satisfaction rates were 79% and 90% (p=0.003), respectively. Severe dysmenorrhea, present in >30% of the women at baseline, was reduced in both groups (p=0.001).⁴⁷ Both methods of treatment significantly improved health-related quality of life (HRQoL). However, despite better amenorrhea and satisfaction rates after the NovaSure ablation, there was no difference in HRQoL between the two groups.⁴⁸

ThermaChoice vs LNG-IUS (Mirena)

Soysal et al. randomized 72 women with menorrhagia into treatment with ThermaChoice ablation (n = 36) or the insertion of the levonorgestrel intrauterine system (n = 36, LNG-IUS, Schering AG, Berlin, Germany). Both therapies were found to be significantly effective in reducing MBL, increasing hemoglobin levels, and improving HRQoL. However, at 12 months the ThermaChoice ablation was significantly more effective in the reduction of MBL and improvement of HRQoL.⁴⁹

Barrington et al. randomized 50 women with menorrhagia into treatment by ThermaChoice endometrial ablation (n = 25) or the insertion of LNG-IUS (n = 25). By 6 months of follow-up, two patients in the Mirena group requested removal of Mirena and received hysterectomy. Two women in each group were lost to follow-up. At 6 months, 3 of 21 (14.3%) women with Mirena in place were amenorrheic, 16 were improved, and two were unchanged. Two (8.7%) of the women who had Therma-Choice treatment were amenorrheic, 16 were improved,

and five experienced exacerbation of their bleeding. All five women requested hysterectomy (21.7%). The authors concluded that ThermaChoice endometrial ablation and Mirena LNG-IUS are equally effective in the management of menorrhagia. ⁵⁰

Busfield et al. randomized 79 women with menorrhagia into treatment with ThermaChoice (n = 39) or LNG-IUS (n = 40). Both treatments resulted in a significant reduction in MBL. At 12 and 24 months, the PBAC scores were significantly lower in women treated with the LNG-IUS compared with women treated by Therma-Choice ablation (11.5 vs 60.0 at 12 months, p = 0.002; 12.0 vs 56.5, p = 0.002 at 24 months). At 24 months, nine of 26 (35%) women still using the LNG-IUS had amenorrhea compared with one (5%) woman successfully treated by the ThermaChoice balloon (p = 0.025). There were no significant differences in patient satisfaction between the two groups. Treatment failed in 11 (28%) women using LNG-IUS and in 10 (26%) women treated by ThermaChoice. Overall, women in both groups experienced an increased quality of life.51

ThermaChoice in myoma-induced menorrhagia

Soysal and colleagues randomized women with myomatous uteri and menorrhagia into endometrial ablation by ThermaChoice (n = 45) or rollerball (n = 48). The uterine size was smaller than at 12 weeks' pregnancy and ≤380 ml total uterine volume with myomas <5 cm diameter by ultrasound assessment. All patients received GnRH-a (goserelin 3.6 mg, two monthly injections) before treatment. ThermaChoice ablation was performed under local anesthesia and IV sedation, whereas HEA was performed under general anesthesia. At 12 months of follow-up, the authors concluded that ThermaChoice ablation for myoma-induced menorrhagia provided both significant and statistically similar reductions in MBL and increases in hemoglobin values with no intraoperative complications compared with rollerball endometrial ablation. There were five (10%) intraoperative complications during rollerball ablation: two cases of fluid overload, two cases of bleeding requiring an intrauterine Foley catheter, and one cervical laceration requiring suturing. There were four hysterectomies in each group. Amenorrhea rates were 11.1% and 16.7% for ThermaChoice and rollerball ablation, respectively.²⁹

Long-term results

Amso et al. reported on a multicenter, long-term (4–6 years), case series of women with menorrhagia treated with ThermaChoice balloon ablation. Of the 260 eligible women, 188 (72%) were evaluable. By life-table analysis, the

probability of avoiding hysterectomy was 86% for all women. The probability of avoiding reablation was 88% for all women who did not have a hysterectomy. The probability of avoiding any surgery was 75%. The probability varied with uterine position, being the lowest (61%) in women with retroverted uteri and highest (80%) in women with an anteverted uterus.⁵²

Prognostic factors

Differences in treatment outcomes reported by various cohort and randomized studies may be due to a variety of factors, including patient age, parity, and uterine factors such as congenital anomalies, uterine position, cavity size, and endometrial thickness at the time of treatment.

Bongers et al. reported on prognostic factors for successful ThermaChoice treatment in 130 women with menorrhagia. Young age, retroverted uterus, endometrial thickness of at least 4 mm, and prolonged duration of menstruation were associated with an increased risk of treatment failure. Uterine depth and associated dysmenorrhea had limited impact on the effectiveness of ThermaChoice balloon ablation.⁵³

In a multicenter randomized comparison (n = 245 women) of ThermaChoice (n = 117) vs rollerball ablation (n = 128), stepwise logistic regression was performed to explore the effects of certain baseline characteristics on predicting clinical outcomes. Neither gravidity, parity, Higham score, uterine position, years of menorrhagia, sound measurement, procedure duration, age, and body mass index (BMI) strongly predicted treatment outcome.⁴²

A cohort study on 72 women with menorrhagia treated with the ThermaChoice balloon reported that the chance of success of treatment was significantly lower when the end pressure was <140 mmHg (odds ratio [OR] = 0.42; 95% confidence interval 'CI' 0.27–0.68; p = 0.01), the intrauterine volume was >10 ml (OR = 0.43; 95% CI 0.22–0.83; p = 0.058), and the uterus was retroverted (OR = 0.36; 95% CI 0.20–0.65; p = 0.008). ¹⁸

An additional cohort study of 45 women treated with ThermaChoice also reported that the chance for a successful treatment increased significantly with increased age (p = 0.044), shorter uterine depth (p = 0.049), and adequate balloon pressure. Parity, uterine volume, and endometrial thickness were not predictive factors.⁵⁴

COMPLICATIONS

Gurtcheff and Sharp reviewed complications associated with global endometrial ablation reported on MEDLINE up to May 2003 and on the FDA MAUDE database. The combined MEDLINE and MAUDE data identified

85 complications. According to the MAUDE database, there were 64 complications in 50 patients attributed to ThermaChoice balloon ablation. Complications comprised thermal bowel injury (5), other thermal injury (7), hemorrhage (2), hematometra (9), endometritis (4), sepsis (1), intensive care unit [ICU] admissions (1), uterine perforation (25), adnexal uterine necrosis (1), required laparotomy (8), and 1 death. The estimated denominator was 150 000 ThermaChoice procedures performed during the same period. The estimated incidence of complications was 88 per 150 000, or 0.59 per 1000 procedures.⁵⁵ However in a letter to the editor, Weisberg pointed out that the manufacturer of the ThermaChoice (Gynecare) submits all worldwide complications to the MAUDE database. Therefore, based on 271638 ThermaChoice catheters sold worldwide through May 2003, the incidence of complications is 0.03%.56

Infection

According to a review by Garside et al., the median rate of endometritis following thermal balloon ablation was 2% (range 1–4%), compared with a median 3% (range 2–4%) after rollerball.^{57,58}

Hematometra

According to RCTs, following thermal balloon ablation, hematometra has been reported at rates of 1% and 4% in comparison to 0% and 2% after rollerball ablation. 57,58

Repeat hysteroscopic ablation

As a rule, following endometrial ablation of any kind, the endometrial cavity is distorted. Therefore, repeat ablation should only be performed by a skilled hysteroscopic surgeon with a loop electrode under hysteroscopic observation. At 5 years of follow-up, the FDA RCT reported 3% repeat ablations in both ThermaChoice and rollerball ablation groups.

Hysterectomy

Following ThermaChoice balloon ablation, hysterectomy rates up to 25% have been reported at 5 years of follow-up. These rates are similar to those reported following TCRE and/or rollerball ablation.^{57,58}

COST-EFFECTIVENESS OF THERMACHOICE

Fernandez et al. compared the overall effectiveness and direct economic costs of vaginal hysterectomy (VH, n = 50),

hysteroscopic endometrial ablation (HEA, n = 50), and ThermaChoice ablation (TC, n = 47) in the treatment of 147 women with menorrhagia in France. The two ablation procedures had the same cure rate of approximately 80%. The total cost (without reintervention for persistent menorrhagia) was €5315 for VH, €1098 for HEA, and €921 for TC. The total cost with reintervention, calculated on a failure rate of 20%, was €1263 for HEA and €1320 for TC.⁵⁹

A cost-utility analysis by Garside et al. also suggested that second-generation ablation technologies (SEATs) are likely to be more cost-effective than first-generation ablation technologies (FEATs) in most cases.⁶⁰

THERMACHOICE II

During the initial studies of ThermaChoice, it was noted by hysteroscopy performed immediately after treatment that the uterine cavity was not treated in a uniform fashion. It became immediately apparent that gravity-dependent areas of the endometrial cavity were less blanched and even appeared quite normal with no visible thermal effects on the endometrium. 10,11 Bongers et al. reported that hysteroscopy, performed immediately after treatment with ThermaChoice, showed thermal effect on both the anterior wall and fundal regions but the posterior wall appeared non-treated in 25% of women.²⁰ Furthermore, several studies reported that a retroverted uterus was associated with an increased risk of treatment failure. 30,52,53 It was suspected early on, and confirmed by thermographic pictures taken by infrared cameras, that the static nature of the liquid within the balloon was responsible for the above observations in accordance with the laws of physics that hot fluids tend to rise while cold fluids gravitate downwards.

In the ThermaChoice II system, introduced in 1998, the balloon was changed from latex to silicone and the liquid was agitated with a small impeller inside the balloon. The impeller was driven mechanically by a wire inside the catheter and a motor within the control unit. In addition, the handle of the catheter was more ergonomic and a pressure relief valve was added to the pressure line.

ThermaChoice II was initially validated by thermographic pictures confirming uniform distribution of the heat energy within the balloon. Furthermore, it was shown in extirpated uteri that the endomyometrial necrosis was uniform throughout the uterine cavity with the ThermaChoice II compared to the ThermaChoice. Vilos et al. reported on a randomized comparison of goserelin (3.6 mg) vs suction curettage prior to ThermaChoice II balloon ablation in 105 women. At 1 year of follow-up, the median reduction in menstrual scores was 97% and 95%,

respectively. The combined amenorrhea–hypomenorrhea rates (Higham scores 0–35), eumenorrhea (Higham 36–75), and menorrhagia (Higham >75) for goserelin were 85%, 9%, and 6%, and for curettage were 76%, 16%, and 9%, respectively. Patient satisfaction was 89% for the goserelin vs 95% for the curettage group. The overall success rates were 88% for goserelin and 89% for curettage.⁶¹

Olah et al. reported on 87 women with menorrhagia treated by ThermaChoice II. All patients were treated by indomethacin (100 mg rectal suppository) given 1 hour prior to procedure and paracervical block using prilocaine 4% (40 mg/ml, 4 ml injected around the cervix). At 2 years of follow-up, reduction in MBL was reported by 94% of women. Amenorrhea rates of 10%, 13%, and 24% were reported at 6, 12, and 24 months, respectively. Both dysmenorrhea and PMS improved significantly (p < 0.001) and the satisfaction rate remained at 94%. 62

THERMACHOICE III

Following clinical evaluation of ThermaChoice II, it was noted that the amenorrhea rate still remained quite low when compared to other second-generation ablation devices. It was hypothesized that the tear-shaped silicone balloon did not expand to cover the endometrial areas around the tubal ostia at the specified pressure treatment of 160-180 mmHg. Initial histochemical studies on extirpated uteri, treated by ThermaChoice II, demonstrated that the mean overall depth of tissue necrosis was 5.2 mm in the body of the uterus and 1.9 mm in the cornual area. Hysteroscopy immediately following treatment with ThermaChoice II also confirmed inadequate thermal effect in the cornual areas. Lack of thermal effect was particularly evident in arcuate-shaped uteri. During concomitant ultrasonic observations, it was also demonstrated that the ThermaChoice II silicone balloon did not expand to herniate into the cornual areas. Therefore, the silicone balloon was modified to allow better expansion and coverage of the uterine cavity and to improve amenorrhea rates under the same parameters of pressure, temperature, and duration of treatment. ThermaChoice III was introduced in 2004.

The efficacy of ThermaChoice III was evaluated in a study of 25 extirpated uteri (Gynecare files). The ThermaChoice III balloon demonstrated greater coverage of the uterine cavity than the previous generations. The average distance from the tubal ostium to first observed location >1 mm depth of necrosis from ThermaChoice III was 3.5 mm vs 4.8 mm and 6.3 mm for ThermaChoice II circulating and ThermaChoice I non-circulating catheters, respectively. Greater average depth of

necrosis was observed for ThermaChoice III, with average mid-body depth of necrosis 0.3 mm and 1.5 mm greater than ThermaChoice II and ThermaChoice I, respectively. Circulation of the liquid was significant in promoting even treatment at the extremes of the uterine cavity. ⁶³

Marsh and associates randomized 73 women eligible for ThermaChoice III endometrial ablation into an outpatient setting (n = 39) receiving only ibuprofen 800 mg the evening before, and 1 hour before treatment, and in a daycase (n = 34) under general anesthesia. They concluded that outpatient ThermaChoice III could be performed in 87% of women, and was associated with similar overall pain scores as daycase ThermaChoice III (VAS mean = 5.9; range 0–10 vs 5.3; range 0–10). Outpatient ThermaChoice III was associated with significantly less nausea, vomiting, need for antiemetics, and time spent in hospital than was the daycase procedure.⁶⁴

Clinical studies of ThermaChoice III are limited. Valle et al. reported on feasibility, safety, and concomitant Essure tubal sterilization and ThermaChoice III endometrial ablation in 49 women undergoing hysterectomy. No disturbance of the intratubal insert devices was noted by the balloon ablation. Endometrial ablation was complete visually and histologically, although small areas near the tubal ostia exhibited less endometrial destruction. Mean tubal serosal temperatures, measured by thermocouples, ranged from 37.1°C to 37.5°C.²³

Clinical evaluation of ThermaChoice III was conducted in a multicenter study (12 in the USA, one in Mexico). Women with menorrhagia (n = 250) were randomized into post-ThermaChoice III ablation curettage vs no curettage. ThermaChoice III had an observed rate of 12.4% of equipment-related events compared with 18.6% observed with ThermaChoice I and 31.7% with ThermaChoice II. Clinical outcomes from this study have not been reported.⁶⁵

SUMMARY

The advantages of the ThermaChoice balloon device include portability, ease of use, and short learning curve. The small-diameter catheter requires minimal cervical dilatation (5 mm) and allows treatment under minimal analgesia/anesthesia requirements, including no local anesthesia or IV sedation. The minimal requirements for anesthesia/analgesia allow treatment in an outpatient setting without the use of resource-intensive operating rooms.

The ThermaChoice balloon ablation device is the most extensively used ablative technology worldwide, with over 400 000 procedures performed to date. The rate of reported complications is 0.31 per 1000 cases, the lowest

of all FDA-approved endometrial ablation technologies. Long-term (4–6 years) analysis indicates that the probability of avoiding hysterectomy is 86% for all women, with a probability of avoiding any kind of surgery of 75%. The cost-effectiveness of ThermaChoice balloon ablation has been estimated to be similar to HEA.

References

- Vilos GA, Lefebvre G, Graves GR. Guidlines for the management of abnormal uterine bleeding. Society of Obstetrics and Gynaecology of Canada (SOGC) Clinical Practice Guidlines. J Obstet Gynaecol Can 2001; 23: 704–9.
- Hallberg L, Hogdahl AM, Nilsson L, Rybo G. Menstrual blood loss – a population study. Variation at different ages and attempts to define normality. Acta Obstet Gynecol Scand 1966; 45: 320–51.
- Coulter A, Kelland A, Long A. The management of menorrhagia. Effective Health Care Bull 1995; 9.1: 1–14.
- Duggan PM, Dodd J. Endometrial balloon ablation under local analgesia and intravenous sedation. Aust NZ J Obstet Gynaecol 1999; 39: 123–26.
- Jansen FW, Vredevoogd CB, van Ulzen K et al. Complications of hysteroscopy: a prospective multicenter study. Obstet Gynecol 2000; 96: 266–70.
- Vilos GA, Brown S, Graham G, McCulloch S, Borg P. Genital tract electrical burns during hysteroscopic endometrial ablation: report of 13 cases in the United States and Canada. J Am Assoc Gynecol Laparosc 2000; 7: 141–7.
- Overton C, Hargreaves J, Maresh M. A national survey of the complications of endometrial destruction for menstrual disorders: the MISTLETOE study. Minimally Invasive Surgical Techniques – Laser, EndoThermal or Endorescetion. Br J Obstet Gynaecol 1997; 104: 1351–9.
- 8. Neuwirth RS, Duran AA, Singer A, MacDonald R, Bolduc L. The endometrial ablator: a new instrument. Obstet Gynecol 1994; 83: 792–6.
- 9. Singer A, Almanza R, Gutierrez A et al. Preliminary clinical experience with a thermal balloon endometrial ablation method to treat menorrhagia. Obstet Gynecol 1994; 83: 732–4.
- Vilos GA, Vilos EC, Pendley L. Endometrial ablation with a thermal balloon for the treatment of menorrhagia. J Am Assoc Gynecol Laparosc 1996; 3: 383–7.
- Vilos GA, Fortin CA, Sanders B, Pendley L, Stabinsky SA. Clinical trial of the uterine thermal balloon for treatment of menorrhagia. J Am Assoc Gynecol Laparosc 1997; 4: 559–65.
- Amso NN, Stabinsky SA, McFaul P et al. Uterine thermal balloon therapy for the treatment of menorrhagia: the first 300 patients from a multi-centre study. International Collaborative Uterine Thermal Balloon Working Group. Br J Obstet Gynaecol 1998; 105: 517–23.
- Meyer WR, Walsh BW, Grainger DA. Thermal balloon and rollerball ablation to treat menorrhagia: a multicenter comparison. Obstet Gynecol 1998; 92: 98–103.
- 14. Andersen LF, Meinert L, Rygaard C et al. Thermal balloon endometrial ablation: safety aspects evaluated by serosal temperature, light microscopy and electron microscopy. Eur J Obstet Gynecol Reprod Biol 1998; 79: 63–8.
- Shah AA, Stabinsky SA, Klusak T et al. Measurement of serosal temperatures and depth of thermal injury generated by thermal

- balloon endometrial ablation in ex vivo and in vivo models. Fertil Steril 1998; 70: 692–7.
- Vilos GA, Aletebi FA, Eskandar MA. Endometrial thermal balloon ablation with the ThermaChoice system: effect of intrauterine pressure and duration of treatment. J Am Assoc Gynecol Laparosc 2000; 7: 325–9.
- 17. Persson BR, Friberg B, Olsrud J, Rioseco J, Ahlgren M. Numerical calculation of temperature distribution resulting from intracavitory heating of the uterus. Gynaecol Endosc 1998; 7: 203–9.
- Lok IH, Leung PL, Ng PS, Yuen PM. Life-table analysis of the success of thermal balloon endometrial ablation in the treatment of menorrhagia. Fertil Steril 2003; 80: 1255–9.
- Clark TJ, Gupta JK. Outpatient thermal balloon ablation of the endometrium. Fertil Steril 2004; 82: 1395–401.
- 20. Bongers MY, Mol BW, Brolmann HA. Comparison of 8 versus 16 minutes heating in the treatment of menorrhagia with hot fluid balloon ablation. J Gynecol Surg 1999; 15: 143–7.
- Vilos GA. Hysteroscopic and nonhysteroscopic endometrial ablation. Obstet Gynecol Clin North Am 2004; 31: 687–704, xi.
- 22. Gervaise A, de Tayrac R, Fernandez H. Contraceptive information after endometrial ablation. Fertil Steril 2005; 84: 1746–7.
- Valle RF, Valdez J, Wright TC, Kenney M. Concomitant Essure tubal sterilization and ThermaChoice endometrial ablation: feasibility and safety. Fertil Steril 2006; 86: 152–8.
- Darwish AM, Ahmad AM, Mohammad AM. Cervical priming prior to operative hysteroscopy: a randomized comparison of laminaria versus misoprostol. Hum Reprod 2004; 19: 2391–4.
- Vilos GA, Abu-Rafea B. New developments in ambulatory hysteroscopic surgery. Best Pract Res Clin Obstet Gynaecol 2005; 19: 727–42.
- Lissak A, Fruchter O, Mashiach S et al. Immediate versus delayed treatment of perimenopausal bleeding due to benign causes by balloon thermal ablation. J Am Assoc Gynecol Laparosc 1999; 6: 145–50.
- Grow DR, Iromloo K. Oral contraceptives maintain a very thin endometrium before operative hysteroscopy. Fertil Steril 2006; 85: 204–7.
- 28. Fernandez H, Capella S, Audibert F. Uterine thermal balloon therapy under local anaesthesia for the treatment of menorrhagia: a pilot study. Hum Reprod 1997; 12: 2511–14.
- Soysal ME, Soysal SK, Vicdan K. Thermal balloon ablation in myoma-induced menorrhagia under local anesthesia. Gynecol Obstet Invest 2001; 51: 128–33.
- Lok IH, Chan M, Tam WH, Leung PL, Yuen PM. Patientcontrolled sedation for outpatient thermal balloon endometrial ablation. J Am Assoc Gynecol Laparosc 2002; 9: 436–41.
- 31. Laberge PY, Sabbah R, Fortin C, Gallinat A. Assessment and comparison of intraoperative and postoperative pain associated with NovaSure and ThermaChoice endometrial ablation systems. J Am Assoc Gynecol Laparosc 2003; 10: 223–32.

- Solnik JM, Guido RS, Sanfilippo JS, Krohn MA. The impact of endometrial ablation technique at a large university women's hospital. Am J Obstet Gynecol 2005; 193: 98–102.
- Marsh F, Thewlis J, Duffy S. ThermaChoice endometrial ablation in the outpatient setting, without local anesthesia or intravenous sedation: a prospective cohort study. Fertil Steril 2005; 83: 715–20.
- Davis JR, Maynard KK, Brainard CP et al. Effects of thermal endometrial ablation. Clinicopathologic correlations. Am J Clin Pathol 1998; 109: 96–100.
- Colgan TJ, Shah R, Leyland N. Post-hysteroscopic ablation reaction: a histopathologic study of the effects of electrosurgical ablation. Int J Gynecol Pathol 1999; 18: 325–31.
- Magos AL, Baumann R, Lockwood GM, Turnbull AC. Experience with the first 250 endometrial resections for menorrhagia. Lancet 1991; 337: 1074–78.
- Istre O, Skajaa K, Holm-Nielsen P, Forman A. The second look appearance of the uterine cavity after resection of the endometrium. Gynaecol Endosc 1993; 2: 189–91.
- Taskin O, Onoglu A, Inal M et al. Long-term histopathologic and morphologic changes after thermal endometrial ablation. J Am Assoc Gynecol Laparosc 2002; 9: 186–90.
- Leung PL, Tam WH, Yuen PM. Hysteroscopic appearance of the endometrial cavity following thermal balloon endometrial ablation. Fertil Steril 2003; 79: 1226–8.
- 40. Grainger DA, Tjaden BL, Rowland C, Meyer WR. Thermal balloon and rollerball ablation to treat menorrhagia: two-year results of a multicenter, prospective, randomized, clinical trial. J Am Assoc Gynecol Laparosc 2000; 7: 175–9.
- Loffer FD. Three-year comparison of thermal balloon and rollerball ablation in treatment of menorrhagia. J Am Assoc Gynecol Laparosc 2001; 8: 48–54.
- Loffer FD, Grainger D. Five-year follow-up of patients participating in a randomized trial of uterine balloon therapy versus rollerball ablation for treatment of menorrhagia. J Am Assoc Gynecol Laparosc 2002; 9: 429–35.
- Zon-Rabelink IA, Vleugels MP, Merkus HM, de Graaf R. Endometrial ablation by rollerball electrocoagulation compared to uterine balloon thermal ablation. Technical and safety aspects. Eur J Obstet Gynecol Reprod Biol 2003; 110: 220–3.
- Zon-Rabelink IA, Vleugels MP, Merkus HM, de Graaf R. Efficacy and satisfaction rate comparing endometrial ablation by rollerball electrocoagulation to uterine balloon thermal ablation in a randomized controlled trial. Eur J Obstet Gynecol Reprod Biol 2004; 114: 97–103.
- Gervaise A, Fernandez H, Capella-Allouc S et al. Thermal balloon ablation versus endometrial resection for the treatment of abnormal uterine bleeding. Hum Reprod 1999; 14: 2743–7.
- Bongers MY, Mol BW, Dijkhuizen FP, Brolmann HA. Is balloon ablation as effective as endometrial electroresection in the treatment of menorrhagia? J Laparoendosc Adv Surg Tech A 2000; 10: 85–92.
- Bongers MY, Bourdrez P, Mol BW, Heintz AP, Brolmann HA. Randomised controlled trial of bipolar radio-frequency endometrial ablation and balloon endometrial ablation. BJOG 2004; 111: 1095–102.
- Bongers MY, Bourdrez P, Heintz AP, Brolmann HA, Mol BW. Bipolar radio frequency endometrial ablation compared with balloon endometrial ablation in dysfunctional uterine bleeding: impact on patients' health-related quality of life. Fertil Steril 2005; 83: 724–34.

- Soysal M, Soysal S, Ozer S. A randomized controlled trial of levonorgestrel releasing IUD and thermal balloon ablation in the treatment of menorrhagia. Zentralbl Gynakol 2002; 124: 213–19
- Barrington JW, Arunkalaivanan AS, Abdel-Fattah M. Comparison between the levonorgestrel intrauterine system (LNG-IUS) and thermal balloon ablation in the treatment of menorrhagia.
 Eur J Obstet Gynecol Reprod Biol 2003; 108: 72–4.
- 51. Busfield RA, Farquhar CM, Sowter MC et al. A randomised trial comparing the levonorgestrel intrauterine system and thermal balloon ablation for heavy menstrual bleeding. BJOG 2006; 113: 257–63.
- Amso NN, Fernandez H, Vilos G et al. Uterine endometrial thermal balloon therapy for the treatment of menorrhagia: longterm multicentre follow-up study. Hum Reprod 2003; 18: 1082–7.
- 53. Bongers MY, Mol BW, Brolmann HA. Prognostic factors for the success of thermal balloon ablation in the treatment of menorrhagia. Obstet Gynecol 2002; 99: 1060–6.
- Shaamash AH, Sayed EH. Prediction of successful menorrhagia treatment after thermal balloon endometrial ablation. J Obstet Gynaecol Res 2004; 30: 210–16.
- Gurtcheff SE, Sharp HT. Complications associated with global endometrial ablation: the utility of the MAUDE database. Obstet Gynecol 2003; 102: 1278–82.
- Weisberg M. Complications associated with global endometrial ablations: the utility of the MAUDE database. Obstet Gynecol 2004; 103: 995.
- Garside R, Stein K, Wyatt K, Round A, Price A. The effectiveness and cost-effectiveness of microwave and thermal balloon endometrial ablation for heavy menstrual bleeding: a systematic review and economic modelling. Health Technol Assess 2004; 8: iii, 1–155.
- 58. Garside R, Stein K, Wyatt K, Round A. Microwave and thermal balloon ablation for heavy menstrual bleeding: a systematic review. BJOG 2005; 112: 12–23.
- Fernandez H, Kobelt G, Gervaise A. Economic evaluation of three surgical interventions for menorrhagia. Hum Reprod 2003; 18: 583–7.
- Garside R, Stein K, Wyatt K, Round A, Pitt M. A cost-utility analysis of microwave and thermal balloon endometrial ablation techniques for the treatment of heavy menstrual bleeding. BJOG 2004; 111: 1103–14.
- 61. Vilos GA, Vilos EC. Comparison of goserelin acetate and suction curettage pretreatment for endometrial ablation. J Am Assoc Gynecol Laparosc 2001; 8: S73.
- 62. Olah KS, Alliston J, Jones J, Stewart G, Mavrommatis R. Thermal ablation performed in a primary care setting: the South Warwickshire Experience. BJOG 2005; 112: 1117–20.
- Nohilly MJ, Grainger D, Simmons G, Martinez D. Extirpated uteri study of next generation confirming ThermaChoice 3 uterine balloon therapy catheter. J Am Assoc Gynecol Laparosc 2003; 10: S35.
- Marsh F, Thewlis J, Duffy S. Randomized controlled trial comparing ThermaChoice III in the outpatient versus daycase setting. Fertil Steril 2007; 87: 642–50.
- Garza Leal JG, Pena A, Donovan A, Cash C Jr. Clinical evaluation of Gynecare ThermaChoice III uterine balloon therapy system for menorrhagia. J Minim Invasive Gynecol 2006; 13: S55–46.

Britt Friberg

INTRODUCTION

The Cavaterm thermal balloon ablation system (produced by Pnn Medical SA, former Wallsten Medical, Switzerland) was manufactured for the treatment of dysfunctional uterine bleeding. The Cavaterm system was invented by the Swedish inventor Hans Wallstén. The first study on extirpated uteri was performed in 1992. The first clinical treatment was done in 1993. The original Cavaterm catheter has been replaced by a second-generation catheter, the Cavaterm plus catheter. Since 1995, the treatment time using the original Cavaterm system has been 15 minutes. The treatment time with the Cavaterm plus system is 10 minutes. Other improved features in the Cavaterm plus system are the diameter of the catheter, which is less, and the balloon is preshaped in an attempt to fit better to the uterine cavity. Until September 2007 approximately 31000 treatments using the Cavaterm system have been performed.

DESCRIPTION OF TECHNOLOGY

The Cavaterm plus system consists of two major components – a balloon catheter (Figure 19.1) and a central unit (Figure 19.2). The length of the preformed highly flexible, antiallergenic, silicone balloon is adjustable to fit the cavity. Thus, it complies with the uterine cavity, ensuring good balloon/cavity surface contact and protecting the cervical canal and vagina from heat effects. Also, the catheter is insulated below the balloon to protect the cervical canal and vagina. The diameter of the catheter is 6 mm and the balloon length can be adjusted between 4 and 8 cm. A device in the central unit generates pulses through the liquid in the catheter that promotes vigorous circulation in the balloon. This ensures an even temperature on the balloon surface and uniform heat treatment. Therefore, a uniform degree of thermal damage will be reached. If there is no circulation, temperature differences of up to 18°C within the balloon have been noted.1 The heat is generated from self-regulating Soft Heat elements. These

are thin lamellae of a semiconductive ceramic/metal material. Above the working temperature, the electric conductivity decreases rapidly, limiting the heating power, and thus automatically maintaining the desired temperature during the treatment phase. The large surface area, of the Soft Heat elements, combined with the circulation of the liquid, enables them to act as high-performance heat exchangers. The elements heat the circulating fluid to working temperature quickly, while the elements themselves only reach a temperature of a few degrees higher than the target temperature of 78°C. The fluid used is 5% glucose. The catheter is equipped with a pressure-regulating syringe, which allows continuous and precise pressure adjustment to maintain the optimal balloon pressure, 230-240 mmHg, which ensures optimal heat penetration through the tissues. An overpressure safety valve is automatically and quickly activated if an overpressure is sensed, thus maintaining a safe working pressure at all times during the treatment.

The Cavaterm *plus* system is mains or battery operated. The integrated low-voltage battery delivers sufficient power for one procedure and is automatically charged when the mains cable is connected. Software included in the central unit makes treatment data printout possible.

PRACTICAL ASPECTS OF PROCEDURE

Preoperative

Cavaterm patients are treated on arbitrary menstrual cycle days. Patients receive no pretreatment medication. Before treatment, either hysteroscopy or vaginal sonography is recommended, preferably with saline infusion sonography added. This is performed to exclude intracavitary changes, i.e. polyps or pedunculated leiomyomas. Preoperative sonography is also recommended to evaluate uterine wall thickness and diagnose submucosal leiomyomas or other leiomyomas. A curettage has to be done either preoperatively or at surgery prior to insertion of the



Figure 19.1 The Cavaterm *plus* balloon catheter. (Reproduced with permission of Engineers & Doctors Wallsten Medical Group.)



Figure 19.2 The Cavaterm *plus* central unit and balloon catheter. (Reproduced with permission of Engineers & Doctors Wallsten Medical Group.)

balloon catheter. The Cavaterm treatment is an outpatient procedure.

Operative

The first generation Cavaterm treatment was often performed under general anesthesia. The second generation,

Cavaterm *plus*, can be used with only paracervical block and intravenous sedation. The former is more often used for treatment with the first-generation Cavaterm catheter and the latter is usually used with the second-generation catheter, Cavaterm *plus*.

Surgery starts with measurement of cavity length and cervical dilatation to 6 mm. Curettage is performed if not done preoperatively. The length of the catheter is adjusted and the balloon purged. The balloon catheter is inserted to the fundus uteri. The balloon is filled with liquid, 5% glucose, until a pressure of 230–240 mmHg. Circulation is commenced and heating started to the target temperature, 78°C. Treatment time is 10 minutes at working temperature. When treatment is finished, the balloon is deflated and the balloon catheter removed from the uterine cavity.

Postoperative

Patients usually need medication against pain in the first hours after surgery. They can return home as soon as the sedation during surgery has disappeared. Usually, there are no postoperative symptoms besides vaginal discharge.

IN VITRO AND IN VIVO STUDIES

The first experimental study was performed in 1992–93.² The Cavaterm treatment effect in vitro was studied in five extirpated uteri and in vivo in three patients treated preoperatively just before hysterectomy. After 30 minutes heating of the endometrium to 58-65°C and a balloon pressure of 180 mmHg, histologic examination showed destruction of cells in the corpus uteri to a maximum depth of 8 mm. The 36 patients first treated were treated for 30 minutes, and thereafter treatment time was 15 minutes, as no major difference was seen in the outcome after 30 or 15 minutes' treatment. In 2003, Hawe et al.3 studied treatment result immediately post- and prehysterectomy. The serosal temperatures did not demonstrate any temperature rise above 44.1°C and macroscopic examination showed no thermal injury to the serosa. Results suggested that treatment time could be reduced to 10 minutes.

Thermal conductivity and the water content of uterine tissue in vitro have been studied.⁴ It was found that endometrial and myometrial tissues have similar thermal conductivities and water contents. It was also indicated that coagulation causes dehydration, resulting in a lower thermal conductivity. In another study⁵ numerical calculations provided a basis for estimation of the optimal intracavitary temperature and treatment time when performing thermal endometrial destruction by means of a balloon catheter.

CLINICAL STUDIES

Published in 2000 were the first clinical results in 116 women followed up 10–46 months after treatment between 1993 and 1996.⁶ The success rate was defined as amenorrhea, minimal or normal bleeding, at patients' maximal bleeding assessment at final follow-up after treatment. The success rate was 94%, excluding women with preoperative intracavitary changes and pretreatment ultrasonographically identified submucosal leiomyomas. Lifetable analysis showed that the probability of assessing the treatment as 'excellent' or 'good' and avoiding hysterectomy over a 49-month period was 81%, and the probability of avoiding hysterectomy over the same period was 85% when no exclusions were made.

The satisfaction rate and the effectiveness of transcervical hysteroscopic endometrial resection have been compared with thermal destruction of the endometrium by means of the Cavaterm balloon catheter.⁷ The satisfaction rate was significantly higher, the operative time significantly shorter, and the intraoperative blood loss was significantly lower in the thermal destruction group.

Mettler evaluated 48-month follow-up in the treatment of menorrhagia and hypermenorrhea for patients treated with the Cavaterm technique.⁸ In 60 women treated with this method, 58% reported amenorrhea, 33% hypomenorrhea, and 9% remained eumenorrheic. The study included another 10 women with adenomyosis and uterine fibroids; i.e. women who before treatment were informed that the treatment might not be successful concerning diminished bleeding volume. Fifty percent of women treated in this group had to undergo hysterectomy. Another 50% were hypomenorrheic.

Cavaterm has been compared to another method for thermoablation (Menotreat) in a 6-month follow-up period. About 70% of the patients described the result of the treatment as 'very good'. In this study, the two methods showed similar and good efficacy and patient acceptance.⁹

Another study compares Cavaterm treatment to Nd:YAG (neodymium–yttrium aluminum garnet) laser. ¹⁰ The results with the Cavaterm balloon endometrial ablation system are as good as those obtained with the Nd:YAG laser in a study of 72 women in 12 months follow-up. The Cavaterm treatment resulted in a significant reduction in menstrual blood loss, high patient satisfaction, and improvement in the patient's quality of life.

Abbott et al. in 2003 published a study comparing the Cavaterm and the NovaSure systems. ¹¹ Both treatments are effective in reducing menstrual blood loss and achieving high rates of patient satisfaction. Thirty-seven women were treated with the NovaSure system and 18 with the Cavaterm system.

A French study randomized women with menorrhagia to Cavaterm treatment or to hysteroscopic endometrial resection. Both treatments significantly reduced uterine bleeding. The 12-month decrease in the Cavaterm group was higher than in the resection group. Also, patients' satisfaction was higher in the Cavaterm group. 12

Alaily, in a prospective study, showed a 24-month 90% satisfaction rate and 46% amenorrhea, 39% light periods, 4% normal, and 10% heavy periods.¹³

A study of Cavaterm *plus*, the second-generation Cavaterm catheter, was performed by El-Toukhy et al. ¹⁴ The study included 220 patients. The mean follow-up time was 19 months (range 6–24 months). The amenorrheahypomenorrhea rates at the various follow-up periods ranged between 74% and 93%. At the end of follow-up, 83% of patients were satisfied with the procedure.

In a review, microwave endometrial ablation and thermal balloon endometrial ablation vs transcervical resection and rollerball ablation were compared as regards their effectiveness for treating heavy menstrual bleeding. No significant differences were found in terms of amenorrhea, bleeding patterns, premenstrual symptoms, patient satisfaction, or quality of life. Microwave endometrial ablation and thermal balloon endometrial ablation had significantly shorter operating and theater times than transcervical resection and rollerball ablation.

COMPLICATIONS

The Cavaterm system has been designed to be simple to use. The learning curve is very short. There is no risk of fluid absorption. When introducing the balloon catheter, there is a risk of making a false passage. If in doubt, an ultrasound or a hysteroscopy should be performed before starting the treatment. There is also a risk of uterine wall perforation. If this occurs, it should be impossible to reach the treatment pressure even when the balloon has been filled to the maximal volume of 30 ml.

In case of an uncontrolled rise in balloon pressure, the overpressure valve opens.

Thermal injuries should be avoided in the cervical area because of the insulation of the balloon shaft. No thermal effects on the outer uterine surface or on adjacent organs were found in experimental studies.² When treating a patient who has used gonadotropin-releasing hormone (GnRH) analogues or other hormonal pre-treatment, it is recommended to perform a preoperative ultrasound to measure the uterine wall thickness which has to be a minimum of 15 mm.

From a technological point of view, the method is safe, as the self-regulating heating elements make overheating

impossible and they are furthermore placed in the catheter handle outside the body.

During the first 2–4 hours postoperatively, pain may be intense, and patients should be informed of this prior to treatment. Pain is successfully treated by prostaglandin synthetase inhibitors, which also can be given prior to treatment to reduce pain postoperatively. Occasionally, postoperative endometritis has been reported, and has been successfully treated with antibiotics. 6,16

Another uncommon complication reported after Cavaterm treatment is cervical stenosis, resulting in hematometra, 17 which has also been described after transcervical endometrial resection. 18,19

Since 1997, when Cavaterm was first marketed, six cases of uterine rupture and one case of bowel burn in connection with rupture have been reported to the manufacturer (personal information from manufacturer February 18th, 2007). Potential complications such as fluid overload and hemorrhage should be avoided and treatment time is short. This means that the Cavaterm treatment is well suited for patients with intercurrent disease such as cardiac problems, bleeding disorders, and anticoagulation therapy.

COST

The standard end-user price for the disposable Cavaterm *plus* catheter is €585 exclusive of VAT. There are no studies published comparing the cost of the Cavaterm treatment with other treatments. In the late 1990s when the Cavaterm system was used in the Department of

Obstetrics and Gynecology at Lund University in Sweden, an estimation of costs of Cavaterm treatment and hysterectomy was carried out. Ahlgren and Friberg (pers comm) showed that costs for Cavaterm treatment were half those for hysterectomy. In those days, the treatment was performed in the operating theater. If carried out in the consultation room, costs ought to be even lower for the Cavaterm treatment. Studies comparing endometrial laser ablation, rollerball and endometrial resection to hysterectomy have shown lower costs for the hysteroscopic techniques.^{20,21}

CONCLUSIONS

The Cavaterm plus thermal balloon ablation system is simple and easy to use. It is a reliable and safe system. The balloon length is adjustable, depending on the size of the uterine cavity. The fluid circulation system and the heating element are unique. The technique is well suited for patients with intercurrent disease, who are at high risk at surgery. Success and the patient satisfaction rate are high. The balloon endometrial techniques offer effective options in the surgical treatment of women with heavy menstrual bleeding. The endometrial ablation techniques offer an alternative to women with menorrhagia who prefer minimal operative and recovery time. The National Institute of Clinical Excellence (NICE) in the United Kingdom is recommending Cavaterm (and other second generation endometrial ablation devices) as the preferred surgical treatment for dysfunctional uterine bleeding (www.nice. org.uk/TA078).

References

- Friberg B, Wallstén H, Henriksson P et al. A new, simple, safe, and efficient device for the treatment of menorrhagia. J Gynecol Tech 1996; 2: 103–8.
- Friberg B, Persson BRR, Willén R, Ahlgren M. Endometrial destruction by hyperthermia – a possible treatment of menorrhagia. An experimental study. Acta Obstet Gynecol Scand 1996; 75: 330–5.
- 3. Hawe J, Abbott J, Phillips G et al. In-vitro and in-vivo histochemical and thermal studies using a thermal balloon endometrial ablation system for varying treatment times. Hum Reprod 2003; 18: 2603–7.
- Olsrud J, Friberg B, Ahlgren M, Persson BRR. Thermal conductivity of uterine tissue *in vitro*. Phys Med Biol 1998; 43: 2397–406.
- Persson BRR, Friberg B, Olsrud J, Rioseco J, Ahlgren M. Numerical calculations of temperature distribution resulting from intracavitary heating of the uterus. Gynecol Endosc 1998; 7: 203–9.

- Friberg B, Ahlgren M. Thermal balloon endometrial destruction: the outcome of treatment of 117 women followed up for a maximum period of 4 years. Gynecol Endosc 2000; 9: 389–95.
- Pellicano M, Guida M, Acunzo G et al. Hysteroscopic transcervical endometrial resection versus thermal destruction for menorrhagia: a prospective randomized trial on satisfaction rate. Am J Obstet Gynecol 2002; 187: 545–50.
- 8. Mettler L. Long-term results in the treatment of menorrhagia and hypermenorrhea with a thermal balloon endometrial ablation technique. JSLS 2002; 6: 305–9.
- Vihko KK, Raitala R, Taina E. Endometrial thermoablation for treatment of menorrhagia: comparison of two methods in outpatient setting. Acta Obstet Gynecol Scand 2003; 82: 269–74.
- Hawe J, Abbott J, Hunter D, Phillips G, Garry R. A randomised controlled trial comparing the Cavaterm endometrial ablation system with the Nd:YAG laser for the treatment of dysfunctional uterine bleeding. Br J Obstet Gynaecol 2003; 110: 350–7.

- Abbott J, Hawe J, Hunter D, Garry R. A double-blind randomized trial comparing the CavatermTM and the NovaSureTM endometrial ablation systems for the treatment of dysfunctional uterine bleeding. Fertil Steril 2003; 80: 203–8.
- 12. Brun JL, Raynal J, Burlet G et al. Cavaterm thermal balloon endometrial ablation versus hysteroscopic endometrial resection to treat menorrhagia: the French multicenter, randomized study. J Minim Invasive Gynecol 2006; 13: 424–30.
- Alaily AB, Auld BJ, Diab Y. Endometrial ablation with the CavatermTM thermal balloon. J Obstet Gynecol 2003; 23: 51–4.
- 14. El-Toukhy T, Chandakas S, Grigoriadis T, Hill N, Erian J. Outcome of the first 220 cases of endometrial balloon ablation using CavatermTM plus. J Obstet Gynaecol 2004; 24: 680–3.
- Garside R, Stein K, Wyatt K, Round A. Microwave and thermal balloon ablation for heavy menstrual bleeding: a systematic review. Br J Obstet Gynaecol 2005; 112: 12–23.
- Hawe JA, Phillips AG, Erian J, Garry R. Cavaterm[™] thermal balloon ablation for the treatment of menorrhagia. Br J Obstet Gynaecol 1999; 105: 1143–8.

- 17. Friberg B, Joergensen C, Ahlgren M. Endometrial thermal coagulation degree of uterine fibrosis predicts treatment outcome. Gynecol Obstet Invest 1998; 45: 54–7.
- Rådestad A, Svenberg T. [Hematometra. Complication after transervical resection of the endomentrium]. Läkartidningen 1995; 92: 513. [in Swedish]
- Jacobs SA, Blumenthal NJ. Endometrial resection follow-up. Late onset of pain and the effect of depot medroxyprogesterone acetate. Br J Obstet Gynaecol 1994; 101: 605–9.
- Sculpher M. The cost-effectiveness of preference-based treatment allocation: the case of hysterectomy versus endometrial resection in the treatment of menorrhagia. Health Econ 1998; 7: 129–42.
- Cameron IM, Mollison J, Pinion SB et al. A cost comparison of hysterectomy and hysteroscopic surgery for the treatment of menorrhagia. Eur J Obstet Gynecol Reprod Biol 1996; 70: 87–92.

Thermablate EAS balloon endometrial ablation

George A Vilos, Jackie Hollett-Caines, and Fawaz Edris

INTRODUCTION

Abnormal uterine bleeding (AUB) from benign causes effects 20–25% of premenopausal women.¹ It is one of the most common presenting symptoms for gynecology patients, accounting for 15% of gynecology clinic patients, and is the major indication for 25% of gynecologic operations.² Menstrual disorders is listed as the second most common indication for hysterectomy (15–20%) and, together with uterine fibroids, accounts for up to 70% of all hysterectomies.^{3–6}

First-line treatment for dysfunctional uterine bleeding (DUB) consists of medical management with non-steroidal anti-inflammatory drugs (NSAIDs),^{2,7-9} antifibrinolytics,⁹⁻¹¹ progestins, 12-14 combined estrogens and progestins, 15,16 androgens,¹⁷ or antiprogestational agents.¹⁸ If a patient fails or has a contraindication to medical therapy, surgical therapy is utilized. Up until the 1980s, dilatation and curettage (D&C) had been widely used as a treatment for DUB. However, D&C has since been shown to have diagnostic value and no therapeutic effect on DUB. Hysterectomy was the definitive surgical standard for the treatment of menorrhagia and was associated with a high rate of satisfaction. Hysterectomy can be associated with many potential adverse events, such as death, significant blood loss requiring transfusion, deep venous thrombosis, pulmonary embolism or infarction, myocardial infarction, abscess formation, sepsis, injury to bowel, bladder, or major blood vessels, longer postoperative recovery times, potentially long-term implications, 19-24 and high direct and indirect costs.^{25–27} Over the last few decades, the trend in gynecology has been towards minimally invasive therapies for the treatment of common gynecologic conditions such as menorrhagia. Endometrial ablation has been developed as an alternative to hysterectomy for the management of menorrhagia. The gold standard for ablation of the endometrium is hysteroscopically directed rollerball ablation or resection. It is safe, effective, and durable but requires significant technical skill. In addition, endometrial ablation is more cost-effective than hysterectomy as therapy for menorrhagia. 25-27 Global endometrial ablation

or second-generation endometrial ablation technologies (SEATs) were introduced as equally safe and effective as hysteroscopically directed ablation, but are less skill-intensive. ^{28–30}

Endometrial ablation with hot liquid balloons was investigated in the early 1990s and was introduced into clinical practice in the mid 1990s. Three hot liquid balloons were available: ThermaChoice (Gynecare, Division of Ethicon, Somerville, NJ), Cavaterm (Wallsten, Medical SA, Morges, Switzerland), and MenoTreat (Atos, Medical AB, Horby, Sweden). After 10 years of clinical practice, a review concluded that balloon endometrial ablation may be the preferred first-time surgical treatment in appropriate candidates who have failed or have refused pharmacologic therapy for chronic AUB.³¹

Garside et al. conducted a systematic review and economic cost-effectiveness of microwave endometrial ablation (MEA) and thermal balloon endometrial ablation (TBEA) for heavy menstrual bleeding.³² They reported that satisfaction and effectiveness were high for both MEA and TBEA. The economic model suggested that MEA and TBEA are more cost-effective than hysteroscopic endometrial ablation (HEA) techniques for heavy menstrual bleeding (HMB).³²

Although the hot liquid balloon devices were shown to be safe, efficacious, and cost-effective, several shortcomings were identified with each existing product. Examples included problems with heating of the liquid used by the ThermaChoice balloon, resulting in non-uniform treatment of the endometrium, and poor control of both intraballoon inflation pressure and the length of treatment time (8–15 minutes). Another concern expressed by clinicians and healthcare providers was the relatively high costs for both reusable and disposable components of the existing balloon devices.

The objectives of the Thermablate EAS balloon were to shorten procedure times, provide more uniform and consistent treatment, improve clinical outcomes, allow the procedure to be performed under no or minimal analgesia/ anesthesia (outside the operating room), and reduce costs as compared to existing SEATs.

HISTORY OF THE THERMABLATE BALLOON

The Thermablate hot liquid balloon system was designed by MDMI Technologies in 1998 (MDMI Technologies Inc, Richmond, BC, Canada). Requirements included portability (light weight, handheld system), user friendliness (minimal clinician involvement), and fulfillment of the shortcomings of the existing balloons such as temperature gradients, manual balloon control, and duration of the treatment cycle.

MDMI engineers had substantiated uneven temperature distribution using the ThermaChoice balloon. This was done by using both a thermocouple test frame (uterine model with 62 thermocouples) and tissue uterine models. The non-circulating liquid of the ThermaChoice device developed significant temperature gradients which affected treatment, particularly if the catheter was resting towards the anterior surface of the uterus or if the uterus was retroverted.

It was also noted that the ThermaChoice and Cavaterm balloon technologies required manual inflation and pressure control of the balloon both before and during treatment. As a rule, when the uterus is heated it tends to relax and expand. This results in a significant decrease of intra-balloon pressure during treatment, which can affect clinical outcomes.^{33,34} However, the fluid pressure in the Thermablate balloon is monitored continuously and adjusted automatically.

The treatment cycle of the existing balloons varied from 8 to 15 minutes. Although this duration of treatment is shorter than for the first-generation endometrial ablation technologies (FEATs), clinicians objected because there was not much to do other than hold the device. An important requirement of the Thermablate system was to shorten the duration of treatment.

A heat transfer model of TBEA, taking into account conduction through the uterine wall, cooling due to uterine blood perfusion, and metabolic heat generation, predicted a 4 mm burn depth with increased temperature (130°C) and shorter treatment time (1.4 minutes).35 Reinders et al. also reported on another mathematical model of the Thermablate system. The model predicted that high temperature and pulsed treatment resulted in consistent immediate tissue death (coagulation) of 3.4 + 0.1 mm for uterine cavity volumes of up to 26 ml. Furthermore, eventual necrosis (tissue death that would occur 1–5 days postablation) could occur to depths of 6.5 ± 0.2 mm. Similarly, the high-temperature pulsed treatment was less sensitive to blood perfusion rate than the lowtemperature treatment. Predicted eventual necrosis depth was 1.5 mm less for the high-temperature pulsed treatment than that predicted for a low-temperature treatment (constant 87°C for 7 min) for the same immediate tissue death depth (3–5 mm), indicating that the new high-temperature treatment may result in less damage to non-targeted tissues.³⁶

Throughout 1999, progress continued in developing and testing prototypes in various tissue models and, by the beginning of 2000, a final prototype was ready for prehysterectomy safety trials (Phase 1). Phase 1 safety studies were carried out in seven women undergoing hysterectomy at Delta Hospital in Vancouver, Canada, and seven women at the University Hospital in Monterrey, Mexico. Histopathologic examination of the extirpated uteri confirmed that the most satisfactory tissue necrosis was obtained with the preheated liquid at 173°C for a treatment duration of 128 seconds (2 minutes 8 seconds). 37,38

In 2001, a Phase II pilot feasibility/efficacy study was carried out in Bombay, India, in 16 women with menorrhagia. Following Thermablate treatment, only one woman reported persistent menorrhagia and mild dysmenorrhea. There were no adverse events and the overall satisfaction rate was 94%.³⁹

From March to July 2003, two pilot feasibility/safety studies were conducted in China. Women (n = 120) with menorrhagia were treated by Thermablate ablation in two centers. Ten patients from each site had hysterectomy immediately after treatment for histochemical evaluation of the thermal effects. Fifty women from each site were followed to determine clinical outcomes. There were no complications or device malfunctions. At 2–3 months of follow-up, menstrual reduction was experienced by 98% of women at both sites. Based on these studies, the Thermablate was approved for use by the State Drug Administration (SDA) of China in the fall of 2003.

The Thermablate system was approved for use in Canada in May 2003, in the European Union in October 2004, and has since been approved for the treatment of menorrhagia in several other countries. The Food and Drug Administration (FDA) has approved Investigational Device Exemption (IDE) and associated clinical trial/PMA is pending.

DESCRIPTION OF THE THERMABLATE

The Thermablate EAS is a hot liquid balloon system that allows for ablation of the endometrial lining, using thermal energy, without the need for direct visualization of the uterine cavity. The device consists of a handheld treatment control unit (TCU, weight 700 g); a catheter balloon disposable cartridge (weight 110 g), power supply, and TCU stand (Figure 20.1). The TCU is electrically powered, with voltage at an intrinsically safe level to protect the user and the patient from electrical injuries.



Figure 20.1 Thermablate EAS device.

The TCU is reusable and controls treatment settings such as time, pressure, and temperature for the heating and pumping/draining subsystems. The treatment is automatically controlled by a microprocessor with no physician input or adjustment required. It also has liquid crystal display (LCD) that provides information and instructions to the user, including warm-up cycle, readiness for treatment, leak checks, treatment cycle and completion, and withdrawal of balloon. The TCU preheats 28 ml of glycerine solution to 173°C within 8 minutes. The unit remains in the treatment-ready mode for 35 minutes and automatically turns itself off if treatment has not been initiated. The unit can be restarted. The treatment component of the device is the catheter/balloons/cartridge, which consists of a 6 mm diameter and 12 cm insertional length catheter with a preshaped, single-use, silicone balloon used for treatment on one end and a second reservoir balloon located inside the heating canister at the other end. The catheter is heat shielded to avoid genital tract burns, and has a soft tip to minimize risk of uterine perforation. Once the treatment liquid is heated to 173°C, the balloon is inserted into the uterus to the sounded depth. Treatment is initiated by a finger trigger action on the TCU which is held for 5 seconds. Following this, a 15-second balloon leak check is automatically performed to confirm balloon integrity. The TCU then pneumatically forces the heated liquid from the reservoir balloon through the catheter into the uterine balloon until a controlled set point of liquid pressure of 180-200 mmHg is reached. The rationale for using these pressures was provided by studies involving the ThermaChoice and Cavaterm balloons.

A geometric uterine model predicted that higher intraballoon pressures (>166 mmHg) strangulate endometrial capillary vessels by local stress, which in turn decreases uterine blood circulation allowing deeper penetration of thermal coagulation and necrosis. 40 Clinical data from ThermaChoice balloon ablation also demonstrated that the rate of treatment success was directly related to intrauterine pressure (>160 mmHg) during treatment. 33,34 Throughout the Thermablate treatment cycle, fluid pressure in the balloon is continuously monitored by two pressure transducers and is automatically controlled via the system pneumatics to remain within a small window of the desired value. In the event that the uterus relaxes, causing the uterine volume to increase and fluid pressure to drop, the system reacts immediately to inject more fluid into the balloon to maintain the fluid pressure at 180 mmHg. In the event of a sudden contraction of the uterus, the system immediately withdraws fluid from the balloon.

As the liquid travels through the catheter, the temperature of the liquid entering the balloon decreases to approximately 150°C and intrauterine treatment temperatures have been measured at 100°C. The TCU maintains a homogenized temperature within the balloon during the treatment cycle through a series of pressurization and depressurization 10-second cycles. The amount of heat energy stored within the uterus at any given time is not much greater than that with water-based fluid systems because of glycerine's lower specific heat capacity (2.4 J/g/°C compared to 4.2 J/g/°C for water). A typical Thermablate treatment has 247 J/g available to heat tissue, which is not significantly greater than the 210 J/g for water-based fluid.

The Thermablate EAS achieves a depth of tissue necrosis into the myometrium of 4–5 mm in the uterine cavity and 2–3 mm at the level of the internal os and cornual region within 128 seconds (2 minutes and 8 seconds). Once the treatment has concluded, the glycerine is automatically withdrawn from the balloon into the canister, and the balloon is removed from the uterine cavity.³⁷

PRETREATMENT ASPECTS

Patient assessment

Prior to endometrial ablation, by any technology, women with AUB should be assessed and inclusion and exclusion criteria should be applied in accordance with established clinical practice guidelines, ^{1,41} and manufacturer's specifications. In addition to the standard history, physical and pelvic examination, Papanicolaou smear, vaginal/cervical swabs and endometrial biopsy, when indicated, the uterine cavity should be thoroughly assessed prior to Thermablate treatment. Imaging by sonography (saline infusion sonography [SIS], transvaginal ultrasound [TVS]) and/or office hysteroscopy is mandatory to assess the shape, size, and condition of the uterine cavity.

Indications and contraindications

The indications and contraindications for Thermablate endometrial ablation are listed in Tables 20.1 and 20.2, respectively.

Patient counseling, education, and informed consent

Prior to Thermablate ablation, women should be informed that the procedure is irreversible and that the clinical outcome is reduction of menstrual bleeding, not amenorrhea. However, women should be informed that amenorrhea is a possible outcome. The need for further treatments such as medications, repeat hysteroscopic endometrial ablation, and/or hysterectomy in approximately 20–25% of women should also be discussed.⁴¹

It must be emphasized that Thermablate ablation should not be performed in women who wish to preserve their fertility, nor should it be used as a means for contraception. Additional methods of family planning should be

Table 20.1 Indications for Thermablate Ablation

Dysfunctional uterine bleeding (DUB)
Failed traditional therapies (e.g. medical, D&C)
Contraindications to traditional therapies
Poor surgical risk for anesthesia, HEA, hysterectomy
To preserve the uterus

Table 20.2 Contraindications for Thermablate

- Uterine fundal sounding <7 cm or >12 cm or uterine, cavity <5 cm
- Genital tract malignancy (cervical, uterine, tubal, ovarian)
- Unresolved endometrial hyperplasia
- Women with anatomic or pathologic uterine anomalies
- Myomas >3 cm distorting the uterine cavity
- Women with history of previous classical cesarean section or transmural myomectomy
- Intrauterine pregnancy
- Acute genital and/or urinary tract infection
- Women wishing to preserve their fertility
- Women expecting amenorrhea as an outcome
- Women with IUCD in place
- Failed previous endometrial ablation

discussed and documented since pregnancies after Thermal balloon ablation have been reported to occur at a frequency of approximately 5%. Pregnancies after ablation can be dangerous for both mother and fetus due to early pregnancy loss, abnormal placentation, and fetal intrauterine growth restriction. Concomitant laparoscopic or hysteroscopic tubal occlusion should be offered in patients who require contraception. The nature of Thermablate ablation, possible complications, clinical outcomes, and alternative therapies should be outlined. Specific complications, such as infections, hemorrhage, hematometra, postablation tubal sterilization syndrome (PATSS), cervical and/or uterine perforations, thermal injuries to viscera and/or lower genital tract, should also be disclosed. In

Patient selection

One of the advantages of Thermablate balloon ablation is that it is a minimally invasive procedure requiring skills similar to those of inserting an intrauterine contraceptive device (IUCD). However, knowledge and training on its application, use, limitations, and safety are mandatory. The small-diameter catheter/balloon (6 mm) requires minimal cervical dilation and obviates the need for major analgesia/anesthesia and the use of resource-intensive operating rooms. The ideal patients for Thermablate endometrial ablation should be women with menorrhagia, over 40 years old, normal size and shape of uterine cavity, who have had at least one normal vaginal delivery, and family planning is not an issue.

The pain tolerance of women, their eligibility for outpatient balloon ablation, and their requirements for analgesia/anesthesia may be assessed during office visits by pelvic and vaginal speculum examination, particularly by the ease or difficulty of performing endometrial biopsy and/or office hysteroscopy.

Cervical stenosis, due to lack of vaginal deliveries, may be overcome by preoperative misoprostol administration (orally or vaginally) or laminaria inserted in the cervix at least 4 hours prior to treatment. Conscious sedation or general anesthesia would be recommended for women with cervical scarring from previous surgery.⁴⁴

Preoperative endometrial preparation

Intuitively, a thin endometrium should allow deeper thermal endomyometrial necrosis and result in better clinical outcomes. However, endometrial thinning prior to Thermablate balloon treatment has not been assessed. Randomized comparison using the ThermaChoice balloon has indicated that pretreatment thinning of the endometrium with gonadotropin-releasing hormone

agonist GnRH-a vs no treatment⁴⁵ and GnRH-a vs suction curettage did not significantly alter the clinical outcomes.⁴⁶

ANALGESIA/ANESTHESIA

During a surgical procedure, the goal of the use of analgesia/anesthesia is to reduce the patient's anxiety, create amnesia, and control pain. Pain threshold and pain tolerance may be expressed by interaction of biologic, psychological, and social factors. Pain can be alleviated by a variety of pharmachologic agents and techniques, including analgesics, local anesthetics, conscious sedation, general anesthesia, and possibly acupuncture. Analgesia is defined as the reduction of pain in the conscious patient and can be achieved by a variety of medications, including anxiolytics, opioids, and NSAIDs. Local anesthesia (elimination of sensation) from the cervix and uterus can be achieved by a variety of injectable or spray solutions and gels.⁴⁴

A suggested cocktail for local anesthesia prior to TBEA is shown in Table 20.3.

Conscious sedation is defined as minimal reduction in the level of consciousness while the patient retains her own airway and responds to physical and verbal stimuli. Suggested medications for conscious sedation are shown in Table 20.4.

Caution should be exercised when a combination of medications is used. Various drugs, given by different routes, peak at different times, and anxiolytics and narcotics may potentiate each other's contribution to respiratory and cardiac dysfunction. Cardiopulmonary monitoring (blood

 Table 20.3
 Solution for paracervical block

• 10 ml	lidocaine 1% with 1:200 000 epinephrine
• 10 ml	bupivacaine 0.2%
• 50 ml	(1 ampule) sodium bicarbonate
• 1 ml	(1 ampule) atropine (0.5 mg)
• 71 ml	total solution; inject 10-20 ml around the cervix

Table 20.4 Medications for conscious sedation

- Fentanyl citrate 1 μg/kg IV
- Atropine 0.5–0.6 mg IV
- Midazolam 4 m IV
- Antiemetic:
- Dimenhydrinate 50 mg IV
- Prochlorperazine 10 mg IV or IM

pressure, heart rate) and pulse oximetry are recommended during treatment when patients are given combined medications by any route.

Leyland evaluated the feasibility, safety, and pain tolerance of Thermablate endometrial ablation in an office setting under local anesthesia. Forty-two women with menorrhagia, who met eligibility criteria, received a preop oral dose of oxycodone/acetaminophen combination and paracervical block immediately before ablation consisting of a 50/50 mixture of Marcaine (bupivacaine) 0.25% and lidocaine 1%. Patient pain tolerance, measured using visual analogue scale (VAS), showed lower pain levels both intra- and postoperatively for Thermablate EAS when compared with 122 women who had been treated with the NovaSure (Cytyc Surgical Products, Palo Alto, CA) system using the same protocol.⁴⁷

A study by Laberge and colleagues compared pain associated with the NovaSure bipoplar radiofrequency system and the ThermaChoice balloon system. Using VAS, the authors reported that the NovaSure system had significantly lower intra- and postoperative pain than the ThermaChoice balloon. However, Leyland's study inferred that pain levels associated with the Thermablate balloon offer a significant improvement over both the NovaSure and the ThermaChoice treatments.

PROTOCOL FOR THERMABLATE BALLOON ABLATION

Vilos and associates conducted a pilot study to determine the feasibility, safety, and efficacy in 60 women with menorrhagia treated under local anesthesia in a clinical setting. Patient assessment and selection included the presence of menorrhagia for more than three cycles with no intramenstrual bleeding. Since hot liquid balloons tend to decrease rather than eliminate menstrual bleeding, women with menometrorrhagia may express dissatisfaction with treatment if they experience spotting between reduced menstruations. The uterine cavity was assessed by SIS. In the absence of contraindications, women were given oral contraceptives to be taken until the day of treatment. It has been shown that oral contraceptives prior to hysteroscopy maintain a very thin endometrium (mean 4.1 ± 1.6 mm) compared with endometrium observed in the late follicular phase (11 \pm 2.0 mm) or luteal phase (12 \pm 2.3 mm).⁴⁹ All women were prescribed misoprostol 400 µg vaginal suppositories and were instructed to insert into the vagina with a moist tampon the evening before treatment. In addition, they were instructed to take ibuprofen orally (400-600 mg) the evening before and 1 hour prior to treatment. One tablet of Ativan (lorazepam) orally or sublingually was also given just before treatment.

The treatment protocol included a pelvic examination to reconfirm the position of the uterus prior to sounding and cervical dilatation. The cervix was infiltrated with 15-20 ml of the solution listed in Table 20.3. After a minimum waiting period of 3-5 minutes, a single-toothed tenaculum was applied, the uterine cavity was sounded, and the cervix was dilated to 7 mm. Hysteroscopy just prior to balloon ablation is desirable but it was not performed in this group of women. The balloon/catheter was inserted to the fundus, ensuring that the centimeter markings on the catheter matched the predetermined uterine depth. Currently, we are investigating the introduction of transabdominal sonography for confirmation of correct placement of the balloon prior to initiating treatment. The use of ultrasound monitoring for other hysteroscopic procedures has been reported.⁵⁰

Post-treatment analgesia included the use of mild opioids with ibuprofen (400–600 mg) orally every 4 hours. Adverse events reported within the first 24 hours following ThermaChoice balloon ablation included nausea and vomiting (25% of women) and cramping abdominal and pelvic pain (92% of women).⁵¹ Therefore, ibuprofen has been chosen as the NSAID of choice for the Thermablate balloon, since it has been shown to be the most effective prostaglandin inhibitor, with a low incidence of side effects, for treating dysmenorrhea.⁵²

Fifty-nine women were successfully treated in the clinic using the above protocol. In one patient, the cervix could not be accessed due to cervical scarring. There were no adverse events intraoperatively or in the immediate postoperative period. All women were discharged within 2 hours after treatment. Our treatment protocol was similar to those used by other investigators with the ThermaChoice balloon.⁵³

In 2004, Clark and Gupta reported on 68 women with menorrhagia having treatment with the ThermaChoice balloon under general or local anesthesia. Fifty-three women chose local anesthesia, consisting of indomethacin (100 mg) rectal suppository and intracervical/paracervical block. No intravenous (IV) sedation or narcotic analgesia was given. The treatment was successfully completed under local anesthesia in 50 women (94%); one (2%) woman could not tolerate treatment because of severe discomfort, another was not treated due to equipment failure, and in the third woman the balloon/catheter system could not be inserted through the cervix.⁵³

Marsh et al. reported on ThermaChoice endometrial ablation (n = 27 women) in the outpatient setting, without local anesthesia or IV sedation.⁵⁴ The first cohort of 14 women underwent ThermaChoice without elective analgesia (i.e. awake, with no premedication, IV sedation, or local anesthetic). Uterine cramping, both during and after ThermaChoice, was most commonly responsible for

women requiring 'rescue' analgesia (n=4 women) or requesting to terminate treatment (n=1). Successful 8-minute treatment was achieved in 12 women (86%). A second cohort of 13 women underwent ThermaChoice ablation after taking elective ibuprofen only. Patients were asked to take ibuprofen (600 mg) the evening before treatment, 600 mg 1 hour prior to treatment, and 600 mg 4 hours after treatment. In one woman, the cervix could not be dilated. Eight-minute treatment in the second group was successful in 12 women (92%).

Throughout treatment there was little difference between the two groups with regard to VAS pain scores, with an overall pain score of 3.6. The most uncomfortable part of the procedure in both groups was the insertion of the ThermaChoice, with an average pain score for all women of 4.2. The VAS pain scores for the first cohort gradually increased during the procedure from the initiation of therapy to the end of 8 minutes. Nausea was experienced by 42% and 8% (p=0.059) and vomiting by 25% and 8% (NS) in the first and second group, respectively. Overall, ThermaChoice treatment was successful in 24 of 27 (89%) women. Of the 92% of women who replied to a questionnaire, 100% would recommend it to a friend and 77% would have it again.⁵⁴

The studies by Marsh and associates,⁵⁴ Leyland,⁴⁷ and Vilos (unpublished study) indicate that, in properly selected women, balloon endometrial ablation can be safely performed in an outpatient setting without local anesthesia or IV sedation. One could speculate whether the addition of misoprostol (400 µg vaginal suppository) given the evening before treatment would have fascilitated cervical dilatation and successfully treated the two women in whom the procedure was abandoned due to inability to access the uterine cavity.⁵⁴ No other non-hysteroscopic endometrial ablation device has been reported to be feasible under absence of analgesia or oral/local anesthetic alone.

CLINICAL OUTCOMES

There have been no randomized controlled trials (RCTs) reported to compare clinical outcomes of Thermablate EAS to any other of the first- or second-generation endometrial ablation technologies. There have been five cohort studies performed to assess the safety and efficacy of the Thermablate EAS device for the treatment of menorrhagia. 38,39,47,55,56

A study in China compared outcomes in 90 women with menorrhagia treated by Thermablate endometrial ablation with 92 women treated by transcervical resection of the endometrium (TCRE) between October 2003 and June 2005. At 6–27 months of follow-up, improvement

of menstrual bleeding and dysmenorrhea was significantly higher in the Thermablate-treated women than in the TCRE group.⁵⁷

The first cohort study consisted of 16 patients with menorrhagia and a uterine sound of ≥7 cm and ≤12 cm.³⁹ Six-month follow-up after the ablation procedure showed a 50% amenorrhea rate (8/16), a 38% hypomenorrhea rate (6/16), and one patient with eumenorrhea. One patient failed treatment with the Thermablate procedure and had persistent menorrhagia. This patient had cystic endometrial hyperplasia documented by endometrial biopsy 2 weeks prior to Thermablate treatment and confirmed by hysteroscopy at the time of ablation. Patient satisfaction rate was 94% and there were no reported complications of the procedure. These results remained unchanged at 1 and 2 years of follow-up (pers comm).

Prior to approval for general use of the Thermablate by Health Canada in May 2003, a series of women were treated under the Special Access Program of the Device Evaluation division of the Therapeutic Products Directorate for Health Canada.³⁸ From September 26, 2002, through to April 28, 2003, 54 patients were approved for treatment with Thermablate. Treatment was carried out by 10 gynecologists in six university and community hospitals. Various medical conditions included morbid obesity (body mass index [BMI] >40 kg/m2), sleep apnea, previous history of thromboembolism, cardiopulmonary dysfunction, and unsuitability or refusal for general anesthesia or other treatment for AUB. Anesthesia provided comprised general (39%), intravenous sedation (IVS, 26%), paracervical block (PCB, 31%), and IVS with PCB (4%). Sixteen patients (30%) were treated in an office or outpatient setting with no anesthesiologist present. There were no intra- or postoperative complications. Patients were discharged within 4-6 hours after ablation and required minimal postoperative analgesia. At 6 months of follow-up (n = 49 patients), the rates of amenorrhea, hypomenorrhea, eumenorrhea, and menorrhagia were 20%, 57%, 16%, and 6%, respectively. Three patients had hysterectomy. 38,55

Leyland compared clinical outcomes of 42 women with menorrhagia treated in the office with the Thermablate balloon with 122 women treated with the NovaSure system. At 12 months of follow-up, amenorrhea, hypomenorrhea, eumenorrhea, and failure rates in women treated with Thermablate were 35%, 50%, 12%, and 3%, respectively. The corresponding rates with the NovaSure system were 37%, 54%, 7%, and 2%. 47

The safety and efficacy of the Thermablate EAS was also evaluated by Vilos and associates. From March through December 2003, 60 women with menorrhagia were treated with Thermablate EAS. The average patient age was 41.2 years old (range 16–53 years old) and the average gravidity

was 2.2 (range 0–5). The average BMI in 30 of the women was 34.5 kg/m2 (range 27–47 kg/m2). Other comorbid conditions included cardiopulmonary disease (7), ileostomy (3), multiple sclerosis (3), thromboembolism (2), and renal transplant (1). Patients were treated under conscious sedation (80%), with or without paracervical block, or general anesthetic (20%). At 6 months of follow-up (n = 60), the rates of amenorrhea, hypomenorrhea, eumenorrhea, and menorrhagia were 15.5%, 33.3%, 37.7%, and 15.5%, respectively. Repeat hysteroscopic ablation was performed in 15% of women and 3.3% received hysterectomy. At 12 months of follow-up (n = 17 women), rates of amenorrhea, dysmenorrhea, eumenorrhea and menorrhagia were 22.2%, 33.3%, 39%, and 5.5%, respectively. Repeat HEA was performed in 16.6% of women.

The study concluded that Thermablate EAS was feasible and safe in all women, including 30 at high risk for other therapies. The 6 mm diameter catheter and the 2-minute duration of treatment allowed treatment under minimal analgesia/anesthesia in 80% of women. At least 80% of women with menorrhagia avoided hysterectomy or other surgical interventions at 6 and 12 months of follow-up. 56

It should be pointed out that endometrial ablation was introduced as an alternative to hysterectomy and the objective of endometrial ablation, by any method, is reduction of menstrual bleeding rather than amenorrhea. The National Women's Health Resource Center in the USA reported on women's preferences for AUB treatment and their definition of a successful outcome compared to gynecologist's recommendations. Of 401 women who had not been treated for AUB, 33% would prefer amenorrhea, 36% would prefer reduction of bleeding, and 32% would be 'OK' with either result or were 'not sure'. Of 400 women who had been treated for AUB, 80% told their physicians that they wanted reduction of bleeding and only 18% preferred amenorrhea. Similarly, 77% of physicians told those patients that success was less bleeding and 21% told those women that amenorrhea defined success.⁵⁸ Furthermore, a study comparing four different methods of endometrial ablation concluded that quality of life should be considered the primary outcome for measuring success of endometrial ablation.⁵⁹

COMPLICATIONS

Intraoperative adverse events with the Thermablate EAS have not been reported. In the immediate postoperative period, minor complications such as those reported with the other hot liquid balloons have been experienced. These include cramps, nausea, vomiting, endomyometritis, dysmenorrhea, hematometra, and PATSS. There have been no incidents of balloon rupture and no genital tract

burns. According to company records, six bowel injuries have been experienced in over 7000 procedures performed worldwide. In all six cases, the injuries were associated with uterine perforations. In four of the six cases, there was protocol violation. In two cases the Thermablate was used in two previously failed endometrial ablation cases; one had prior ThermaChoice and the other Thermablate ablation.

To minimize the risk of visceral injury, structural and procedural changes have been introduced by MDMI. For example, the cervical stopper along the catheter has been fixed at 8.0 cm to avoid fundal perforation. In addition, it is recommended that hysteroscopy be performed prior to inserting the catheter to determine the integrity of the cervical canal and uterine cavity. Alternatively, intrauterine placement of the Thermablate balloon may be

confirmed by ultrasound just prior to activating the treatment cycle.

SUMMARY

The Thermablate EAS is an easy-to-use, handheld, light-weight device which is fully automated and has a self-contained control unit. It is an effective treatment for women with menorrhagia, with clinical results similar to other technologies. The small-diameter catheter (6 mm) and the short duration of treatment (2 minutes) allow treatment in a clinic setting with minimal requirements for analgesia/anesthesia. The use of Thermablate is cost-effective because of its simple design and its ability to be used in a clinic setting.

References

- Vilos GA, Lefebvre G, Graves GR. Guidlines for the management of abnormal uterine bleeding. Society of Obstetrics and Gynaecology of Canada (SOGC) Clinical Practice Guidelines. J Obstet Gynaecol Can 2001; 23: 704–9.
- Haynes PJ, Hodgson H, Anderson AB, Turnbull AC. Measurement of menstrual blood loss in patients complaining of menorrhagia. Br J Obstet Gynaecol 1977; 84: 763–8.
- Lee NC, Dicker RC, Rubin GL, Ory HW. Confirmation of the preoperative diagnoses for hysterectomy. Am J Obstet Gynecol 1984; 150: 283–7.
- Carlson KJ, Nichols DH, Schiff I. Indications for hysterectomy. N Engl J Med 1993; 328: 856–60.
- Vayda E, Gentleman JF, Walsh MN, Parson GF. Hysterectomy rates by diagnosis: variations among Canadian census divisions. J Obstet Gynaecol Can 1996; 18: 315–25.
- Kovac SR. Hysterectomy outcomes in patients with similar indications. Obstet Gynecol 2000; 95: 787–93.
- Hallberg L, Hogdahl AM, Nilsson L, Rybo G. Menstrual blood loss – a population study. Variation at different ages and attempts to define normality. Acta Obstet Gynecol Scand 1966; 45: 320–51.
- 8. Munro MG. Abnormal uterine bleeding in the reproductive years. Part I pathogenesis and clinical investigation. J Am Assoc Gynecol Laparosc 1999; 6: 393–416.
- 9. An evidence-based guideline for the management of heavy menstrual bleeding. Working Party for Guidelines for the Management of Heavy Menstrual Bleeding. NZ Med J 1999; 112: 174–7.
- Callender ST, Warner GT, Cope E. Treatment of menorrhagia with tranexamic acid. A double-blind trial. Br Med J 1970; 4: 214–16.
- 11. Edlund M, Andersson K, Rybo G et al.. Reduction of menstrual blood loss in women suffering from idiopathic menorrhagia with a novel antifibrinolytic drug (Kabi 2161). Br J Obstet Gynaecol 1995; 102: 913–17.

- Fraser IS. Treatment of ovulatory and anovulatory dysfunctional uterine bleeding with oral progestogens. Aust NZ J Obstet Gynaecol 1990; 30: 353–6.
- Preston JT, Cameron IT, Adams EJ, Smith SK. Comparative study of tranexamic acid and norethisterone in the treatment of ovulatory menorrhagia. Br J Obstet Gynaecol 1995; 102: 401–6.
- Kaunitz AM. Injectable depot medroxyprogesterone acetate contraception: an update for U.S. clinicians. Int J Fertil Womens Med 1998; 43: 73–83.
- 15. Ramcharan S, Pellegrin FA, Ray RM, Hsu JP. The Walnut Creek Contraceptive Drug Study. A prospective study of the side effects of oral contraceptives. Volume III, an interim report: a comparison of disease occurrence leading to hospitalization or death in users and nonusers of oral contraceptives. J Reprod Med 1980; 25: 345–72.
- Fraser IS, McCarron G. Randomized trial of 2 hormonal and 2 prostaglandin-inhibiting agents in women with a complaint of menorrhagia. Aust NZ J Obstet Gynaecol 1991; 31: 66–70.
- Lamb MP. Danazol in menorrhagia: a double blind placebo controlled trial. J Obstet Gynecol 1987; 7: 212–16.
- 18. Murphy AA, Kettel LM, Morales AJ, Roberts VJ, Yen SS. Regression of uterine leiomyomata in response to the antiprogesterone RU 486. J Clin Endocrinol Metab 1993; 76: 513–17.
- Dicker RC, Greenspan JR, Strauss LT et al.. Complications of abdominal and vaginal hysterectomy among women of reproductive age in the United States. The Collaborative Review of Sterilization. Am J Obstet Gynecol 1982; 144: 841–8.
- Harris WJ. Early complications of abdominal and vaginal hysterectomy. Obstet Gynecol Surv 1995; 50: 795–805.
- 21. Harkki-Siren P, Sjoberg J, Makinen J et al.. Finnish national register of laparoscopic hysterectomies: a review and complications of 1165 operations. Am J Obstet Gynecol 1997; 176: 118–22.

- Meikle SF, Nugent EW, Orleans M. Complications and recovery from laparoscopy-assisted vaginal hysterectomy compared with abdominal and vaginal hysterectomy. Obstet Gynecol 1997; 89: 304–11.
- Makinen J, Johansson J, Tomas C et al. Morbidity of 10110 hysterectomies by type of approach. Hum Reprod 2001; 16: 1473–8.
- Shen CC, Wu MP, Kung FT et al. Major complications associated with laparoscopic-assisted vaginal hysterectomy: ten-year experience. J Am Assoc Gynecol Laparosc 2003; 10: 147–53.
- Vilos GA, Pispidikis JT, Botz CK. Economic evaluation of hysteroscopic endometrial ablation versus vaginal hysterectomy for menorrhagia. Obstet Gynecol 1996; 88: 241–5.
- 26. Sculpher MJ, Dwyer N, Byford S, Stirrat GM. Randomised trial comparing hysterectomy and transcervical endometrial resection: effect on health related quality of life and costs two years after surgery. Br J Obstet Gynaecol 1996; 103: 142–9.
- Hidlebaugh DA, Orr RK. Long-term economic evaluation of resectoscopic endometrial ablation versus hysterectomy for the treatment of menorrhagia. J Am Assoc Gynecol Laparosc 1998; 5: 351–6.
- Lethaby A, Hickey M. Endometrial destruction techniques for heavy menstrual bleeding: a Cochrane review. Hum Reprod 2002; 17: 2795–806.
- Garry R for the Endometrial Ablation Group. Evidence and techniques in endometrial ablation: Consensus. Gynaecol Endosc 2002; 11: 9–17.
- Lethaby A, Hickey M, Garry R. Endometrial destruction techniques for heavy menstrual bleeding. Cochrane Database Syst Rev 2005; (4): CD001501.
- 31. Munro MG. Endometrial ablation with a thermal balloon: the first 10 years. J Am Assoc Gynecol Laparosc 2004; 11: 8–22.
- 32. Garside R, Stein K, Wyatt K, Round A, Price A. The effectiveness and cost-effectiveness of microwave and thermal balloon endometrial ablation for heavy menstrual bleeding: a systematic review and economic modelling. Health Technol Assess 2004; 8: iii, 1–155.
- Vilos GA, Aletebi FA, Eskandar MA. Endometrial thermal balloon ablation with the ThermaChoice system: effect of intrauterine pressure and duration of treatment. J Am Assoc Gynecol Laparosc 2000; 7: 325–9.
- 34. Lok IH, Leung PL, Ng PS, Yuen PM. Life-table analysis of the success of thermal balloon endometrial ablation in the treatment of menorrhagia. Fertil Steril 2003; 80: 1255–9.
- Baldwin SA, Pelman A, Bert JL. A heat transfer model of thermal balloon endometrial ablation. Ann Biomed Eng 2001; 29: 1009–18.
- Reinders DM, Baldwin SA, Bert JL. Endometrial thermal balloon ablation using a high temperature, pulsed system: a mathematical model. J Biomech Eng 2003; 125: 841–51.
- Yackel DB, Elliott JR. Thermablate, a new thermal balloon endometrial ablation method and instrument. J Am Assoc Gynecol Laparosc 2001; 8: S77–8.
- Yackel DB, Vilos GA. Thermablate EAS: a new endometrial ablation system. Gynecol Surg 2004; 1: 129–32.
- Mangeshikar PS, Kapur A, Yackel DB. Endometrial ablation with a new thermal balloon system. J Am Assoc Gynecol Laparosc 2003; 10: 27–32.
- 40. Persson BR, Friberg B, Olsrud J, Rioseco J, Ahlgren M. Numerical calculations of temperature distribution resulting from

- intracavitary heating of the uterus. Gynaecol Endosc 1998; 7: 203–9.
- Vilos GA. Hysteroscopic and nonhysteroscopic endometrial ablation. Obstet Gynecol Clin North Am 2004; 31: 687–704, xi.
- Gervaise A, de Tayrac R, Fernandez H. Contraceptive information after endometrial ablation. Fertil Steril 2005; 84: 1746–7.
- Valle RF, Valdez J, Wright TC, Kenney M. Concomitant Essure tubal sterilization and Thermachoice endometrial ablation: feasibility and safety. Fertil Steril 2006; 86: 152–8.
- Vilos GA, Abu-Rafea B. New developments in ambulatory hysteroscopic surgery. Best Pract Res Clin Obstet Gynaecol 2005; 19: 727–42.
- Lissak A, Fruchter O, Mashiach S et al. Immediate versus delayed treatment of perimenopausal bleeding due to benign causes by balloon thermal ablation. J Am Assoc Gynecol Laparosc 1999; 6: 145–50.
- Vilos GA, Vilos EC. Comparison of goserelin acetate and suction curettage pretreatment for endometrial ablation. J Am Assoc Gynecol Laparosc 2001; 8: S73.
- Leyland N. Office based global endometrial ablation: feasibility and outcomes for 3 modalities. J Obstet Gynaecol Can 2004; 26: S22.
- 48. Laberge PY, Sabbah R, Fortin C, Gallinat A. Assessment and comparison of intraoperative and postoperative pain associated with NovaSure and ThermaChoice endometrial ablation systems. J Am Assoc Gynecol Laparosc 2003; 10: 223–32.
- Grow DR, Iromloo K. Oral contraceptives maintain a very thin endometrium before operative hysteroscopy. Fertil Steril 2006; 85: 204–7.
- Xia E, Duan H, Zhang D. Study of Beta-ultrasound monitoring for hysteroscopic surgeries. J Am Assoc Gynecol Laparosc 2001; 8: S77.
- Cooper J, Gimpelson RJ. Summary of safety and effectiveness data from FDA: a valuable source of information on the performance of global endometrial ablation devices. J Reprod Med 2004; 49: 267–73.
- Zhang WY, Li Wan PA. Efficacy of minor analgesics in primary dysmenorrhoea: a systematic review. Br J Obstet Gynaecol 1998; 105: 780–9.
- Clark TJ, Gupta JK. Outpatient thermal balloon ablation of the endometrium. Fertil Steril 2004; 82: 1395–401.
- Marsh F, Thewlis J, Duffy S. Thermachoice endometrial ablation in the outpatient setting, without local anesthesia or intravenous sedation: a prospective cohort study. Fertil Steril 2005; 83: 715–20.
- 55. Vilos GA. Endometrial ablation with a new balloon (Thermablate EAS) to treat menorrhagia in high-risk surgical candidates. J Am Assoc Gynecol Laparosc 2003; 10: S36.
- Vilos GA, Abu-Rafea B, Hauqe A. Endometrial thermal ablation: a two minute balloon treatment. J Am Assoc Gynecol Laparosc 2004; 11: S89–90.
- 57. Feng LM, Gao WL, Yang BJ et al. Clinical analysis of abnormal uterine bleeding treatment with Thermablate EAS. Beijing Da Xue Xue Bao 2006; 38(4): 432–5 [in Chinese].
- Niles A. Women's preferences for AUB treatment and their definitions of a successful outcome compared to Ob/Gyn recommendations. J Minim Invasive Gynecol 2005; 12: S24.
- Abbott J, Hawe J, Garry R. Quality of life should be considered the primary outcome for measuring success of endometrial ablation. J Am Assoc Gynecol Laparosc 2003; 10(4): 491–5.

Microwave endometrial ablation

Nicholas C Sharp

INTRODUCTION

Microwave endometrial ablation (MEA) owes its origin to an initial report in the *Lancet* by Phipps et al¹ describing the use of radio waves for the treatment of menorrhagia. Radiofrequency endometrial ablation (RaFEA) used electromagnetic energy at a frequency of 27.12 MHz to heat the endometrium and to destroy the regenerative basalis layer. This report prompted the formation of the research team in Bath, UK, to explore the possibility of using microwaves to achieve the same objective, with the expectation that it should potentially have advantages over the use of radiofrequency. Microwave energy lies in the millimeter waveband, with a frequency in the GHz range.

At the same time, RaFEA was trialled in the Bath Royal United Hospital as the first endometrial ablation technique in the department, and considerable experience was obtained with it while the microwave research was being completed. Despite the two technologies being in adjacent parts of the electromagnetic spectrum, the difference in frequency considerably altered how the energy behaved in use, and this was reflected in the safety margins: microwaves are inherently safe; radio waves, we found, are inherently dangerous.

The microwave research turned out to be fruitful, not only living up to the research team's expectations but also exceeding them and making it one of the foremost types of endometrial ablation today.

It is interesting to compare the features of MEA against RaFEA (Table 21.1), to show the differences in the technologies.

Owing to an unacceptably high incidence of complications with RaFEA, it was withdrawn from the market in 1995. MEA, however, was taken through all research stages and initial trials without adverse events, and the first report of a successful clinical study was published in 1995.²

MICROWAVE THEORY

Microwaves, like most other forms of electromagnetic energy, penetrate tissues, and the depth of penetration is

a function of their wavelength. Microwaves are non-ionizing, but the absorption in tissues causes heating, largely due to energizing of water molecules. A domestic microwave oven uses a frequency of 2.3 GHz to penetrate deeply into the food to be cooked. If the frequency is raised and the wavelength therefore decreased, penetration is reduced, and by choosing the correct frequency, penetration can be restricted to a specific depth. Using a frequency of 9.2 GHz, with a wavelength of approximately 3 cm, tissue penetration is restricted to 5–6 mm.³ This penetration is determined purely by microwave physics, and is essentially independent of the power setting.

Microwaves can be emitted by an antenna arrangement - a variation on a bare wire, or transferred by a waveguide. An antenna arrangement was judged to be an ineffective approach for endometrial ablation, and waveguide technology was the favored approach. An air-filled waveguide would need to be about 30 mm in diameter to transfer microwaves at 9.2 GHz.³ The preferred diameter for the microwave device was 8 mm - a compromise between feasible cervical dilation, but adequate 'bluntness' to avoid uterine perforation. To 'pipe' microwaves down an 8 mm waveguide, it was necessary to find an appropriate dielectric filler for the waveguide. Initially, a ceramic rod was used as the dielectric. This was effective, but liable to fracture with rough handling, and further refinements produced a more robust, easily manufactured applicator.

More recently, a disposable waveguide (FemWave) has been introduced (Figures 21.1 and 21.2), and reusable applicators will be phased out.

MICROWAVE RESEARCH

The microwave research was divided into a series of steps (with full Research Ethical Committee approval):

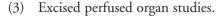
- (1) Measurements of 'permittivity' of endometrium.
- (2) Excised unperfused organ studies.

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Characteristic	Microwave endometrial ablation	Radiofrequency endometrial ablation
Frequency	9.2 GHz	27.12 MHz
Power	22 W (emitted)	200–350 W
Warm-up time	None	6–8 minutes
Treatment time	3.5 minutes (average)	12 minutes
Energy used	4.6 kJ (average)	240–420 kJ
Applicator diameter	8.2 mm	10 mm
Earthing	No	Yes, and capable of 'earthing' through electrically insulated items
Earth return belt required	No	Yes
Endometrial temperature	100°C	63–68°C
Uterine perfusion	Irrelevant	Essential to prevent thermal spread to serosa, with adjacent organ damage
Vaginal contact with applicator	Safe	Had to be avoided to prevent serious burns due to 'earthing'
Energy field	Confined to 5 mm of endometrium	Filled entire operating theater, affecting anesthetic alarm systems and other electrical equipment
Waveguide	Yes	No
Antenna	No	Yes. Patient would emit energy as part of the system. Simple touch would cause significant warming due to energy transfer



Figure 21.1 Disposable waveguide (FemWave) of the MEA.



- (4) Treatment of patients immediately prior to hyster-ectomy.
- (5) Clinical trial.



Figure 21.2 The MEA Control Unit.

Step 1

Samples of endometrium were obtained by simple curettage, and laboratory measurements of tissue permittivity made. It was found that most soft tissues registered similar values and, subsequently, raw animal liver made a very useful trial material, with easily visible and measurable thermal effects.

Step 2

After obtaining informed consent, normal uteri from hysterectomy (usually for menorrhagia) were instrumented, and the microwaves applied to the cavity before despatch to histology. Serosal temperature measurements confirmed the absence of serosal heating despite high cavity temperatures. Histology confirmed major thermal effects and tissue destruction of endometrium.

Step 3

Identical to Step 2, but perfusion of the uterus with warm saline at 37°C was undertaken to establish that the 'coolant' effect of uterine blood flow would not reduce the microwave effects.

To prepare a uterus for this experiment, it was necessary to try and leave a bit of uterine artery leading to the specimen – this would then be flushed with heparinized solution as soon as the uterus was removed, to retain the vascular bed. This study confirmed that uterine blood flow had no impact on the microwave effects.

Step 4

After opening the abdomen, prior to hysterectomy, the bowel would be packed clear of the uterus. Thermocouples were then secured to the uterine serosa and placed into the myometrium. Microwave energy was then applied using the prototype applicator introduced through the dilated cervix. The uterus was observed directly during this process, in addition to the continuous multiple placement thermometry.

It quickly became apparent during this stage that 80 W power was too much: not only because of any serosal heating but also because of loud noises coming from the uterus owing to rapid expansion of pockets of superheated steam and because of very rapid, and difficult-to-control heating of the cavity. A setting of 30 W (lower than anticipated) was found to be very workable. In fact, at this setting, the actual emitted power at the applicator tip is about 22 W, as a result of power losses in the system.

These studies confirmed that the system behaved entirely as predicted by the microwave theory, and penetration was no greater than 6 mm with complete tissue destruction in this narrow zone.

Histologic staining with Nitrazolium tetra-blue gave a good visual representation of the effects of microwave heating. Whereas viable tissue stains blue, as a result of

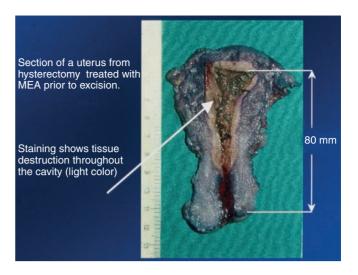


Figure 21.3 Tissue distruction from in-vivo trial: white uterus.

the activity of the intracellular enzyme succinic dehydrogenase, non-vital tissue does not stain due to thermal degradation of cellular enzymes (Figure 21.3).

MICROWAVE EFFECTS

The rapid heating induced by microwaves has a coagulative effect on tissue – there is therefore no bleeding (Figure 21.4). Following treatment, patients have a light watery discharge, which lasts from 1 to 6 weeks. With an effective treatment, there is a hyaline, cicatricil fibrosis of the cavity, with total cavity occlusion (Figure 21.5). The cavity may not occlude entirely but is usually very scarred, much reduced, and lined mainly by fibrous tissue.

MICROWAVE ENDOMETRIAL ABLATION TECHNIQUE

The technique of MEA has been well described elsewhere. 2,4-7

A brief description is appropriate, however; MEA is different to all other second-generation ablation systems in that it is iterative, rather than global. All first-generation ablation techniques – transcervical resection of the endometrium (TCRE), rollerball, and laser – treated the endometrium bit by bit, i.e. iteratively. All second-generation systems aim to treat the entire endometrial cavity at once, i.e. global treatment, apart from MEA.

After safely instrumenting the uterine cavity, with hysteroscopy if necessary, the microwave applicator is inserted until the tip reaches the fundus. It is then activated with a foot switch. The cavity is treated from the fundus downwards, with lateral side-to-side motions to evenly cover

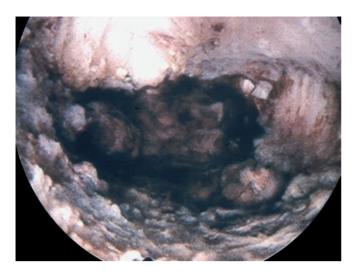


Figure 21.4 Coagulative effect or tissue



Figure 21.5 Uterus 6 months after MEA–hysterectomy following ovarian cystadenoma.

the endometrial surface with the microwave energy field. This process is guided by the continuous thermometry display on the system's plasma screen. The therapeutic zone is displayed as a band from 70 to 80°C. However, the applicator thermocouple is heat-sunk onto the applicator shaft, and covered with a fluoropolymer sheath, and the actual tissue temperature at the applicator–tissue interface is 100°C; this produces micropockets of superheated steam – the effect of which is cratering in the coagulum seen after MEA (see Figure 21.4).

The system prints a documentary record of the treatment profile for inclusion in the patient's medical record.

The mean treatment time is approximately 3.5 minutes, but is dependent on cavity length: bigger cavities take longer (Figure 21.6) Significant fibroids tend to lengthen treatment time, as the increased blood flow may have a slight coolant effect. Pretreatment with gonadotrophin-releasing hormone (GnRH) agonists tends to shorten treatment time by thinning the endometrium and reducing vascularity.

Patient selection

Like all ablation techniques, MEA is a treatment for menorrhagia. Patients presenting with abnormal uterine bleeding (AUB) must have pathology excluded before simple menorrhagia can be diagnosed. Vaginal ultrasound examination in the outpatient clinic with endometrial biopsy is the preferred assessment protocol. Some practitioners may prefer hysteroscopy, but skilled ultrasound examination is less invasive and is more informative in most cases.

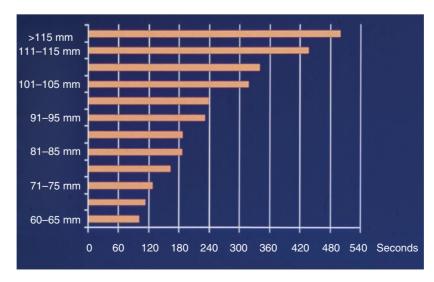


Figure 21.6 MEA: Cavity length vs treatment time

Fibroids

Fibroids are not a contraindication to MEA, provided there is no excessive cavity distortion. If the applicator tip can be placed in contact with the all the endometrium, MEA is feasible. This applies with submucous fibroids, as long as cavity protrusion is less than one-third. Hysteroscopy may be required to evaluate the cavity in such cases. Very large cavities may be difficult to treat fully within the 8 minutes maximum treatment time, and cavities beyond 11 cm in length are unlikely to get the best response, although treatment of cavities up to 14 cm is feasible with MEA.

Cesarean section

Previous cesarean section is not a contraindication to treatment, but the scar integrity must be assessed by ultrasound to ensure safety. The scar is easily visualized on sagittal ultrasound section and is found adjacent to the empty bladder fold (Figure 21.7). Since microwave penetration is limited to 6 mm, a minimum scar thickness of 8 mm has been a safe working minimum. Microsulis protocol now stipulates 10 mm (giving a good margin of safety).

Most patients with a single previous cesarean section will have an adequate scar thickness; the incidence of defective scars increases with the number of cesarean sections, and many women with three cesarean sections will be ineligible, but not all.

Uterine abnormality

Congenital uterine anomalies such as unicornuate, bicornuate, subseptate, or didelphys can be safely treated with

MEA. Hysteroscopic control is required to ensure safe instrumentation and proper access. The treatment technique is modified to a simple slow steady withdrawal, and care must be taken not to allow the temperature to rise outside the therapeutic band. MEA is one of the few second-generation techniques applicable to such cases.

Contraindications

- Abnormal endometrial histology.
- Hysterectomy indicated for other reasons.
- Previous uterine surgery.
- Fertility required.

Special precautions

- Uterine retroversion increased risk of uterine perforation: extra care required.
- Chronic steroid use increased risk of uterine perforation.
- Connective tissue disorder, e.g. Ehlers—Danlos syndrome, osteogenesis imperfecta etc. increased risk of uterine perforation.

RESULTS OF TREATMENT

Initial follow-up of patients after the introduction of MEA into clinical practice was fairly intense, with several visits in the first year, and then annually. It became clear





Figure 21.7 Cesarean scar measurements on vaginal ultrasound assessment.

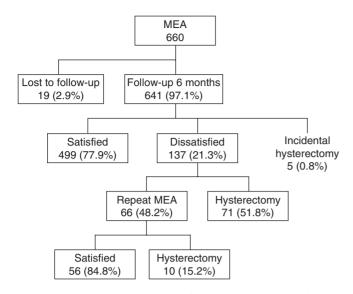


Figure 21.8 Outcomes at 6 years following introduction of MEA.

that there were no major concerns in the follow-up, and patients now receive a simple questionnaire by post 3 months after MEA, the results of which are entered on the database. Those patients unsatisfied with their outcome are offered a review consultation, or may be referred back.

The flow chart (Figure 21.8) shows outcomes at 6 years following introduction of MEA:

- Satisfaction total = 555 (86.6%)
- Hysterectomy total = 86 (13.4%)

Although an initial amenorrhea rate of 57% was reported for an early cohort, the amenorrhea rate has settled to a consistent 41–42% over the longer term.

Apart from incidental causes, the main indication for hysterectomy in this group is regrowth of cornual endometrium which has become trapped behind scar tissue in the lower uterine cavity. Such patients typically present about 18 months post-MEA with steadily worsening cyclical pain, despite good menstrual outcome. The pain is unresponsive to analgesics; vaginal ultrasound reveals the cornual pockets with retained menstrual fluid. It is therefore important to warn patients undergoing MEA that avoidance of hysterectomy cannot be guaranteed, although a good outcome may be anticipated.

RANDOMIZED CONTROLLED TRIALS

Comparison with endometrial resection

The initial report of Cooper et al⁸ compared 123 patients receiving MEA with 132 receiving TCRE. Amenorrhea

results were identical: 40% at 12 months, with satisfaction rates of 78% for MEA and 76% for TCRE. Operating times were significantly less for MEA.

Two-year follow-up of this study group⁹ showed continuing satisfaction, with 47% amenorrhea for MEA, and 41% for TCRE, with satisfaction rates of 79% and 67%, respectively. Actual acceptability of treatment was greater for MEA (96% vs 88%).

Comparison with rollerball endometrial ablation

A comparison with rollerball undertaken for Food and Drug Administration(FDA) approval at eight sites in the UK and USA¹⁰ showed high satisfaction rates with both techniques (MEA 98%, rollerball 99%); amenorrhea rates were 55% for MEA and 46% for rollerball. Treatment times were again significantly shorter for MEA: 3½ minutes compared with 20½ minutes.

Comparison with Mirena Intrauterine system

A recent small randomized controlled trial¹¹ comparing MEA (43 patients) with the levonorgestrel-releasing intrauterine device (44 patients) showed a higher satisfaction rate using quality of life questionnaires. Of 38 patients fitted with Mirena for whom 12 months' follow-up was concluded, six had hysterectomies and seven opted for MEA, compared with three hysterectomies in the microwave group.

OUTPATIENT/OFFICE MEA UNDER LOCAL ANESTHETIC

The brevity of the MEA treatment quickly led to the application of a local anesthetic approach. The local anesthetic technique used is a refinement of that described by Ferry and Rankin.¹²

Cervical block

The block required for MEA is an intracervical block – this blocks not only the cervix but also, when correctly established, provides a good uterine blockade. However, the cervix is fairly vascular in a proportion of patients, and intravascular absorption affects the choice of local anesthetic agents that can be used.

Local anesthetic agents to avoid are:

Those containing epinephrine – patients will frequently experience the side effects of intravenous epinephrine: palpations, tachycardia, and a very unpleasant feeling of panic, or impending doom.

Bupivacaine 0.5% – absorption of which causes muscular excitability with twitching and clouding or loss of consciousness, both of which can lead to a 'grand mal' seizure.

The anaesthetic agents used are:

- A quick-acting, short-acting agent: for a long time prilocaine 3% with felypressin (Citanest with Octapressin; Astra) was used. Now mepivacaine 3% (Scandonest; Septodont) has been substituted.
- A slow-acting, long-acting agent: either bupivacaine (Marcain; Astra) 0.25%, or levobupivacaine (Chirocaine; Abbott) 0.25%, administered slowly with 'draw-back'. Administration is halted if the patient experiences any intravasation symptoms (buzzing in ears, blurring of vision, tingling in lips/face, feeling of floating, etc.).

After positioning the patient, the vagina is cleansed with warmed antiseptic solution and the cervix exposed. Using a dental syringe, a small amount of Citanest or Scandonest is administered into the anterior cervical lip centrally. After a few moments, this area may be grasped with volsellum forceps and the cervix brought into full view. The cervical block is then initiated with one cartridge of local anesthetic (2.2 ml) administered as deeply as possible into each cervical quadrant - the aim being to establish a 'ringblock' at the internal cervical os. This administration can be quick. Next, the slower-acting bupivacaine or levobupivacaine 0.25% is administered with a 20 ml syringe and 22 gauge needle, 5 ml per quadrant, starting with the posterior quadrants (the uterosacral ligaments being the most important to block). If the patient develops any symptoms with this phase, further administration is then withheld until completion of the MEA procedure; the main purpose of this second local anesthetic is to enhance postoperative pain relief. This second block is also given to all patients having general anesthetic, to minimize postoperative discomfort.

Drugs

All patients for local anesthesia have diclofenac (Voltarol; Geigy) 1 hour preoperatively (100 mg suppository, self-administered).

Occasionally, during the MEA treatment, the patient may still experience discomfort despite the local anesthetic; in such cases Entonox (nitrous oxide/oxygen mixture) by inhalation may be sufficient to overcome this, especially if it is only the central fundus that has escaped the blockade, and should therefore be readily available.

For some patients, these measures will be insufficient, and sedation with midazolam (Hypnovel; Roche) and alfentanil (Rapifen; Janssen) intravenously will enable the treatment to be completed. For this reason all patients have an intravenous (IV) cannula sited routinely preprocedure, so that sedation can be readily administered if required.

All patients receiving these agents must have pulse oximetry and supplemental oxygen at 4 L/min. Anexate (Flumazenil; Roche) and naloxone (Narcan; DuPont) must be available as the reversants for midazolam and alfentanil. Atropine should also be available, in case of vagal bradycardia (very uncommon).

In our reported study of outpatient local anesthesia,¹³ cavities up to 12 cm were treated. The mean treatment time was about 4 minutes (254 seconds).

Of the 116 patients reported in the study, 94 had local anesthesia alone (81%). Entonox alone was sufficient for a further seven (6.1%), and 15 had IV sedation (12.9%). All procedures were completed in the Outpatient Department, and there was no anesthetist in attendance; any sedation was given by the operator, who then regloved to complete the MEA.

Follow-up was completed in 114 patients (two lost to follow-up). Of those, 101 were satisfied, 12 disappointed, and there was one incidental hysterectomy. Of the 12 dissatisfied patients, five had repeat MEA and seven opted for hysterectomy. Following repeat MEA, one patient was satisfied and four were not and had hysterectomy. Overall satisfaction was 89.5%, with a hysterectomy rate of 10.5% at 4 years.

Before treatment, 74% reported moderate or severe dysmenorrhea. After treatment, this was reduced to 21%, with 61.5% reporting no dysmenorrhea.

Patient selection for outpatient/office treatment

Experience has shown that careful patient selection is critical to smooth running of an outpatient treatment session. Initial selection was unrefined, and difficulties were encountered. The exclusion criteria developed for use in our outpatient clinic are given in Table 21.2.

Practical aspects of outpatient treatment

- Four people are required for an outpatient session:
 - surgeon
 - assistant to operate the equipment, connect the cables, generally assist the surgeon
 - treatment nurse to distract the patient with conversation, administer inhalational agent, or top up IV sedation under surgeon's instruction

 Table 21.2
 Exclusion criteria for outpatient/office MEA

Access issues

Overweight

Virgo intacta

Nulliparous

No vaginal birth

Previous vaginal surgery

Restricted hip/knee mobility

Tolerance issues

Previous unpleasant experience in delivery or termination of pregnancy

Previous unwelcome sexual contact

History of mental illness

Vaginal infection

Analgesia issues

Intolerance of NSAIDs

Difficulty dilating cervix

Long-standing GnRH agonist therapy (>5 weeks)

Other

Coexisting medical problem (warfarin therapy is not an exclusion)

NSAIDs, non-steroidal anti-inflammatory drugs, GnRH, gonadotropin-releasing hormone.

- · recovery nurse.
- Background music is helpful to provide a soothing atmosphere.
- Experience with MEA should be gained with patients fully anesthetised first.
- Experience with local anesthesia should be gained in the operating theater initially, with an anesthetist present.
- Experience with sedation (midazolam and alfentanil) should be under the supervision of an anesthetist initially.

INCIDENCE OF UPPER GENITAL TRACT OCCLUSION AFTER MEA

A study using hysterosalpingogram (HSG) ≥3 months after MEA has shown a high incidence of upper genital tract occlusion following treatment, due to the subsequent scarring. ¹⁴ The results are shown in Table 21.3.

Table 21.3 Incidence of upper genital tract occlusion after MEA, and its relationship to menstrual outcome

Outcome	Number	Occluded	Percent
Amenorrhea	16	16	100
Scanty menses	9	9	100
Satisfied with light menses	10	5	50
Total	35	30	85.7

The finding of upper genital tract occlusion so often after MEA means that, for many women, further contraception post-treatment may be unnecessary, and concomitant sterilization may be inappropriate. However, all women should have an HSG before contraception is discontinued, as pregnancy can occur in amenorrheic women. Because of the small recognized false-negative rate of HSG, all women ceasing contraception should be advised to report symptoms of pregnancy early.

SUMMARY

Inherently safe
Microwave physics
Steady applicator withdrawal
Continuous thermometry
Low power (22 W)
Lower energy dose
Uterine blood cooling unimportant
Penetration depth limited to 6 mm
No heated fluids (no scalding risk)
No earthing risks

Clean

No bleeding

No hysteroscopic fluids

Quick

3–4 minutes for an average cavity

Simple

Good outcomes are not operator dependent

Interactive

The surgeon is guided by the thermometry display on screen

No 'warm-up' phase

Treatment commences with 'power on'

Few exclusions

Can treat large cavities

Can treat fibroid uteri

Can treat bicornuate uteri Can treat subseptate uteri Can treat unicornuate uteri Can treat didelphys uteri

Amenorrhea Around 40%

Satisfaction Around 85%

Dysmenorrhea Often improved

Randomized controlled trials

Compares favorably in all randomized controlled trials to date.

CONCLUSION

Microwave endometrial ablation was introduced in 1994 and 55 000 women have now been treated worldwide,

with 30 000 treated in the UK. Whereas most of these procedures have been undertaken under general anesthesia, the ability to perform MEA so quickly under local anesthesia is likely to make it a treatment of choice in an increasingly cost-conscious healthcare market.

ACKNOWLEDGMENTS

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Research nurse: Sr Fran Jones.

Research assistant: Mrs Rosemary Reader.

I also acknowledge an enormous debt of gratitude to the patients, especially in the early days, who willingly allowed us to experiment on the hysterectomy specimens, or to treat them with our new 'microwave device'. They were fearless – unlike their surgeon, who was at times a bit anxious. But for them, MEA would not have been possible.

References

- 1. Phipps JH, Lewis BV, Roberts T et al. Treatment of functional menorrhagia by radiofrequency-induced thermal endometrial ablation. Lancet 1990; 335: 374–6.
- Sharp NC, Cronin N, Feldberg I et al. Microwaves for menorrhagia: a new fast technique for endometrial ablation. Lancet 1995; 346: 1003–4.
- Feldberg IB, Cronin NJ. A 9.2 GHz microwave applicator for the treatment of menorrhagia. IEEE MTT-S Digest 1998; WEZE-I; 755–758.
- Sharp NC, Feldberg IB, Hodgson DA et al. Microwave endometrial ablation. In: Sutton C, Diamond MP, eds. Endoscopic Surgery for Gynaecologists, 2nd edn. Philadelpia: WB Saunders, 1998: 630–7.
- Sharp N, Hodgson DA, Ellard ME et al. Microwave endometrial ablation: prospective study covering 4 years' experience of over 300 patients. Alternatives to Hysterectomy, Proceedings from the World Congress on Alternatives to Hysterectomy, Miami, Florida, 2000: 183–6.
- Sharp N. Microwave endometrial ablation in the out-patient setting, In: O'Donovan PJ, Downes E, eds. Advances in Gynaecological Surgery. London: Greenwich Medical Media, 2002: 189–96.
- Sharp N. MEA: microwave endometrial ablation. In: O'Donovan P, McGurgan P, Prendiville W, eds. Conservative Surgery for Menorrhagia, London: Greenwich Medical Media, 2003: 143–50.

- 8. Cooper KG, Bain C, Parkin DE. Comparison of microwave endometrial ablation and transcervical resection of the endometrium for treatment of heavy menstrual loss: a randomised trial. Lancet 1999; 354: 1859–63.
- Bain C, Cooper KG, Parkin DE. Microwave endometrial ablation versus endometrial resection: a randomised controlled trial. Obstet Gynaecol 2002; 99(6): 983–7.
- Microsulis Americas. Microwave Endometrial Ablation. FDA Trial. Coral Springs, Fl: Microsulis Americas, 2002.
- Behnia-Willison F, Cook J, Seman C et al. A randomised controlled trial comparing microwave endometrial ablation (MEATM) and Mirena® (levonorgestrel-releasing intra-uterine device) in the treatment of menorrhagia. RANZCOG 2006 Annual Scientific Meeting, Perth, Western Australia (oral presentation).
- 12. Ferry J, Rankin L. Transcervical resection of the endometrium using intracervical block only. A review of 278 procedures. Aust NZ J Obstet Gynaecol 1994; 34: 457–61.
- Tawfeek S, Hayes T, Sharp N. Three-year experience in outpatient microwave endometrial ablation. Gynaecol Surg 2004; 1: 243–7.
- 14. Tawfeek S, Sholapurkar S, Sharp N. Incidence of upper genital tract occlusion following microwave endometrial ablation (MEA). BJOG 2006; 113: 958–960.

NovaSure endometrial ablation

Adolf Gallinat

INTRODUCTION

Over decades, various methods have been described for the treatment of dysfunctional uterine bleeding (DUB), and authors have reported good results using technical equipment. The introduction of new technologies, the improvement in different techniques, and the application and skill of surgeons have facilitated the progress in the development of endometrial ablation. Modern endometrial ablation began in 1981 with the introduction of the neodymium-yttrium-aluminum-garnet (Nd:YAG) laser in hysteroscopic surgery for photocoagulation of the endometrium by Goldrath et al.² In the 1980s, hysteroscopic electrotechniques,3-5 later called first-generation techniques (FEATs), were described. Collected studies 6 showed that photocoagulation was still superior. These methods were not performed by the majority of gynecologists because of perceived technique-related difficulties.

Over the past decade, less complicated methods have been developed. Sources of energy used to permanently destroy the endometrial lining of the uterus are those of the FEATs^{7,8} using high temperatures created by heat convection or using freezing.¹² The advantage of these global ablation techniques is that there is no need for skill in operative hysteroscopy. Furthermore, after secure application of the device in the uterine cavity, there are no moving parts of any instrument to cause additional perforation.¹³ During the development of second-generation endometrial ablation techniques (SEATs), microwave energy (by blind application), as described for electroball coagulation, 1,14 was introduced. The technology employed, approach, treatment time, outcome, and risks associated with these procedures vary from one method to another. Large-scale studies are continuously conducted to assess the safety and efficiency of these systems.¹⁵

Although the SEATs are significantly easier to perform and do not require extensive hysteroscopy skills, each system has a number of limiting factors. To receive good results, all of the SEATs require endometrial ablation of some kind. But most important is the lack of a

reliable safety mechanism before the process of endometrial ablation starts. In the case of a false passage or an undetected uterine perforation, no energy is should be delivered, to avoid severe complications such as bowel burns.

TECHNOLOGY

The NovaSure system consists of a single-use, threedimensional bipolar ablation device and a radiofrequency (RF) multifunctional controller that enables a controlled endometrial ablation in an average time of 90 seconds.

Disposable device

The NovaSure ablation device consists of a conformable bipolar gold-plated porous mesh mounted on an expandable frame fitting to the shape of the uterine cavity (Figure 22.1). The special design and configuration of electrodes of porous mesh provides a deeper ablation in the mid body of the uterus, where endometrium is thickest, and a shallower depth of myometrial desiccation in the cornual areas and lower uterine segment. The adjustable sheath accommodates and protects the cervical channel, eliminating the possibility of an endocervical burn. After intrauterine placement of the device, the width of the fundus (cornu-to-cornu distance) is determined.

Via connecting cables and prior high-frequency (HF) application, CO₂ is insufflated for the 'cavity integrity assessment system'. From the start of bipolar coagulation, using continuous vacuum aspiration, blood, mucus, and cell contents of vaporized endometrium are removed during the entire operation.

Radiofrequency generator

The NovaSure controller contains a constant power output generator that functions independent of tissue resistancy (Figure 22.2). The maximum power delivery is fixed by the geometry of the uterine cavity at 180 W. Power



Figure 22.1 NovaSure handset, showing the bipolar gold-plated porous mesh at the tip. On the left, the intrauterine measuring device determines the cornu-to-cornu distance. Connections for RF energy, CO₂ insufflation (cavity integrity assessment system), and the suction system are shown.



Figure 22.2 NovaSure controller. The function is demonstrated by LEDs. An automatic power calculation is made according to the geometry (length and width) of the treated cavity.

delivery is calculated automatically on the basis of the uterine cavity length (measured during sounding and dilation) and the uterine width (measured by the device).

These two values are keyed into the controller and the exact power level required is automatically calculated for an optimal ablation of the uterine cavity of a given size.

The power delivery, and automatic procedure termination concept, is based on monitoring of specific well-analyzed physical characteristics of the tissue (impedance/resistance), allowing for a controlled predictable depth of tissue destruction.

The coagulation of the endometrial layer is a low-impedance process, owing a high level of liquid, electrolytes, and hormones present in the endometrial tissue. The endometrium (and cell contents) are vaporized during the high-power ablation and evacuated from the uterine cavity by continuous suction. As the ablation front advances and reaches the myometrial layer, the tissue can no longer be vaporized (because of its higher density), and therefore is desiccated. When overall tissue impedance (resistance) reaches 50 Ω (which is equivalent to the impedance of the ablated superficial myometrium), the NovaSure system automatically terminates the ablation process. The vacuum is continuously generated, maintained, and monitored within the uterine cavity throughout the endometrial ablation procedure. By this vacuum (suction), an intimate apposition between the endometrium and later myometrium is assured. The presence of a constant vacuum facilitates removal of the contents of the uterine cavity (blood, electrolytes, hormones) as well as vaporization of by-products (steam) generated during the bipolar electrosurgical ablation process.

The cavity integrity assessment system is an integral part of the NovaSure system. This automatic safety feature was developed and implemented to assist the physician in the timely detection of uterine wall perforation, thus preventing energy delivery. It uses a hysteroflatertype technology.16 Carbon dioxide is insufflated into the uterine cavity (via the porous device) at a safe flow rate and pressure. Once the proper intrauterine pressure (50 mmHg) is reached and maintained for 4 seconds, confirming the integrity of the uterine wall, the RF controller proceeds with the ablation process, which lasts 90 seconds on average. Exclusion of perforation takes about 6-8 seconds and does not prolong the entire procedure. A validated pictorial blood loss assessment chart (PBAC) scoring system described by Higham¹⁷ was used for a precise and objective quantification of menstrual blood loss before and after ablation.

Only premenopausal women with menorrhagia secondary to DUB that is unresponsive to medical therapy were treated; all patients had completed childbearing at the time of procedure. All patients had their follicle-stimulating hormone (FSH) levels determined before the procedure, to assure their premenopausal status (FSH >40 U/L).

Patients received no hormonal or surgical (i.e. curettage) endometrial pretreatment. The procedure performance was not timed to a particular menstrual cycle day.

In November 1998, we started a prospective study, ¹⁸ while Bongers started in November 1999. ¹⁹ A randomized, multicenter clinical trial compared with wire loop resection followed by rollerball endometrial ablation was undertaken at nine investigational sites, four in the USA, four in Canada, and one in Mexico. ²⁰

Inclusion and exclusion criteria were the same for all studies. Only premenopausal women (the premenopausal condition was confirmed by FSH determination) after completed family planning were included. The remaining diagnosis evaluation of the patients was similar to that which is standard for women deemed to be candidates for endometrial ablation: i.e. exclusion of endometrial malignancies as well as premalignant histologies. Patients were excluded if they had bacteremia, sepsis, or some other active systemic infection, or active or recurrent chronic pelvic inflammatory disease. Furthermore, coagulopathies or a history of uterine surgery that would have interrupted the integrity of the uterine wall (classic cesarian section, myomectomy) meant exclusion. Women who had previously undergone endometrial ablation were also excluded. Also, patients were excluded if they had an abnormal Papanicolaou smear, were taking anticoagulants, or were taking drugs that could thin myometrial muscle, such as long-term steroids. Patients with abnormal or obstructed uterine cavity (submucous myomas, polypys >2 cm) or if uterine sound measurement (external os to fundus) was <6.0 cm or >10.0 cm were excluded. Menorrhagia was verified by validated PBAC. Patients eligible for enrollment were required to have a history of failed medical therapy and a PBAC score ≥150.

Between November 1998 and July 2000, 107 patients were treated in a prospective study. A randomization against the Vesta electrocoagulation-balloon was started. As the Autosuture Company stopped the Vesta project the same month, directly after the start of the study, we continued as a single-arm study: 107 premenopausal women (median age 42.2 years) with menorrhagia secondary to DUB were enrolled. The mean PBAC score was 563 (range 194–2590). With respect to the position of the uterus, the distribution within this patient population was as follows: anteverted 52%, retroverted 22%, and mid position 26%.

OPERATIVE PROCEDURE

The uterine cavity was evaluated by means of hysteroscopy to exclude patients with submucous fibroids, polyps, and synechiae that would heavily distort the uterine cavity. The average cornu-to-cornu distance was 3.98 cm (range 2.5–5.3 cm). The anesthesia regimen was uniform for all patients, consisting of total intravenous anesthesia

(TIVA) with induction with Versed (midazolam 2.0 mg) + propofol 1% (1.5–2.5 mg/kg) + remifentanil (1 μg/kg/min). The intraoperative anesthesia was maintained with propofol 1% (5–7 mg/kg/hr) + remifentanil (0.2 μg/kg/min). A 50/50 oxygen/air mix was delivered by using a larynx mask.

A vaginal speculum was inserted and the cervix was grasped with a tenaculum. The cavity was sounded and the measurement recorded. The length of the cervix was assessed during cerival dilatation to 7.5 mm by measuring the distance between the internal and external cervical ora. Cavity length (sound measurement - length of cervix) was entered into the RF controller. The NovaSure device was inserted, deployed, and properly seated in the uterine cavity. The cornu-to-cornu measurement was determined by the intrauterine measurement device and entered into the RF controller to allow a precise automatic calculation of power setting required for optimal treatment of a cavity of that size. The controller was activated by pressing the foot switch, and the perforationdetection cycle was followed by the ablation cycle (Figure 22.3).

At the end of the ablation cycle, the controller automatically terminated energy delivery and the device was closed and withdrawn from the cavity. The tenaculum and vaginal speculum were removed to conclude the procedure. No prophylactic antibiotics were administered.

Treatment was measured from the start to the end of RF energy application. The average treatment time was 94 seconds (range 40–119 seconds). All adverse events and/or complications during and after the procedure were

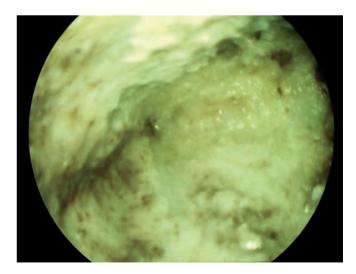


Figure 22.3 Hysteroscopic close-up view of the right cornual area. The entire cavity appears whitish. By the special design of the device, coagulation is performed until the tubal ostium. The endometrium is vaporized, and the underlying myometrium coagulated.

recorded. After surgery, patients were required to maintain a menstrual diary for 12 months, even those who reported amenorrhea. In addition to a 4-week contact, follow-up visits were scheduled at 6 and 12 months. The PBAC was used to assess the amount of bleeding to correlate to the classification approved by the World Health Organization (amenorrhea, spotting, hypomenorrhea, eumenorrhea, menorrhagia). All patients were required to have FSH measured at the 12-month visit to eliminate the possibilty of false interpretation of amenorrhea.

RESULTS AT 12 AND 36 MONTHS

No intraoperative or postoperative complications or complications associated with anesthesia occurred. All patients were discharged in 1–4 hours. They experienced a sero-sanguineous discharge for approximately 2–4 weeks after the procedure.

No patients withdrew from the study and 106 completed the 6-month follow-up. At that time, 49 women (46.2%) were amenorrheic, 45 (42.5%) were hypomenorrheic (PBAC-1–30), and three (2.9%) were eumenorrheic (PBAC-31–75). Nine (8.4%) were still menorrhagic (PBAC >75). Of 45 hypomenorrheic women, 36 had spotting only (PBAC-1–10).

One patient was lost to follow-up at 12 months. Of the 105 women, 62 (58.6%) were amenorrheic, 35 (33.3%) were hypomenorrheic, and four (3.9%) were eumenorrheic. Most hypomenorrheic patients (31/35) experienced only spotting. Only four women (3.9%) were still menorrhagic (Figure 22.4).

Data comparison indicated that between 6- and 12-month follow-up the clinical results changed. Therefore, it is safe to conclude that a steady state (clinical durability plateau) is reached ≥12 months after the

procedure, ¹⁸ with clinical outcome becoming significantly better with time.

We also stratified patients by age (<40 years old, ≥ 40 years old) and analyzed data based on this factor (Figure 22.5). In women <40 years old, amenorrhea was achieved in 43% and hypomenorrhea in 47% (45% spotting, 2% hypomenorrhea); in women ≥ 40 years old, the hypomenorrhea rate dropped to 24% (19% spotting, 5% hypomenorrhea) and amenorrhea increased to 70%. The distribution and bleeding patterns between age groups was statistically significant using the likelihood ratio χ^2 (L=8.94, p=0.0114). This difference was due primarily to distributional differences in amenorrhea rates (L=7.60, p=0.005).

One patient experienced hematometra 5 months after treatment, which resulted in hysterectomy. After the fact, it was clear that hysterectomy was not the procedure of choice in her management. No other hysterectomies were performed for any reason. Thus, hysterectomy or retreatment was avoided in 103 patients (97%) at 12-month follow-up.

In 2003, the 3-year follow-up data of this group were collected. As mean age at primary treatment was 42 years old, it can be assumed that nearly all patients are still premenopausal.²²

Only two patients reported climacteric symptoms whereas one women was on hormone replacement therapy (HRT). A successful bleeding reduction with the use of NovaSure bipolar ablation was achieved in 98% of patients at 1-year follow-up, compared with a success rate of 97.2% at 3-year follow-up (Figure 22.6). Increase in the amenorrhea rate between 6 and 36 months after ablation was found to be statistically significant ($\chi^2 p > 0.004$). Because no significant difference in success rates has been observed when comparing the data for 6, 12, and 36 months, it is safe to conclude that, although becoming better with



Figure 22.4 Results at 6 and 12 months follow-up.

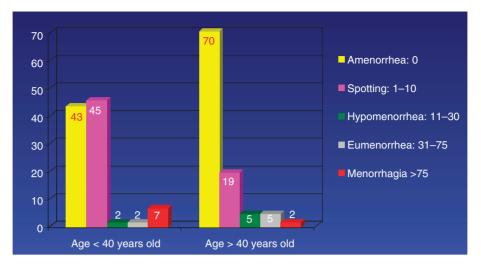


Figure 22.5 Results at 12 months according to age.

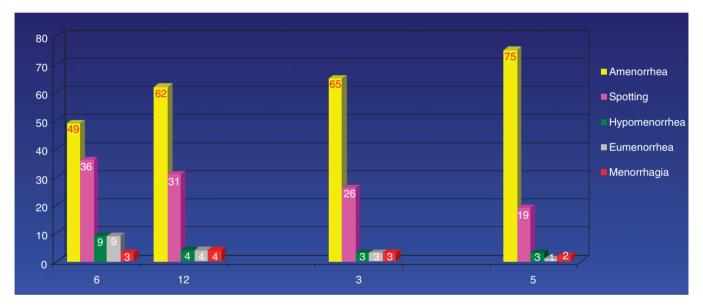


Figure 22.6 Late results: steady state between 6 and 12 months; plateau phase is between 1 and 3 years; increase of amenorrhea after 5 years.

time with respect of amenorrhea, a successful steady state is reached 6 months after the NovaSure procedure.

FAILURES

Four patients were considered failures, with PBAC scores >75 at 12-month follow-up. One woman had a PBAC score of 800. A substantial reduction in bleeding was seen in all other patients. One woman (PBAC-250) required a second ablation, and two others were satisfied with their final bleeding status (PBAC-219 and 125) (Figure 22.7). During the 3-year follow-up, three hysterectomies and one reablation were performed. One patient presented with hematometra at 5 months after ablation. The second

hysterectomy was performed in the patient who failed the ablation procedure (PBAC = 800). A third hysterectomy was performed on an amenorrheic patient, who presented with symptoms of a fast-growing myoma (preasure on the bladder) requiring surgical intervention. Therefore, at 3 years after NovaSure ablation, hysterectomy and the need for any additional surgical intervention was avoided in 97.2% and 96.3% of patients, respectively (see Figure 22.7).

LATE RESULTS

In 2005, 5-year follow-up data were collected to demonstrate the long-term follow-up results. Mean follow-up

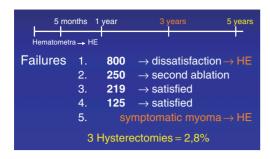


Figure 22.7 Failures (*n* = 107) at 36 months after NovaSure endometrial ablation. Failures: at 12 months; four patients PBAC >75, one hematometra; at 36 months; one symptomatic myoma; and at 60 months; no change. (Source: Center of Gynaecological Endoscopy, Hamburg, Germany.)

time at the time that this chapter was submitted was 5.8 (± 2.5 months).²³ Eight Patients reported climacteric symptoms. At this 5-year follow-up, data were available for 103 of the 107 patients enrolled in the study. Four patients were lost to follow-up between 3 and 5 years of follow-up. Of the patients lost to follow-up, two were amenorrheic, one patient was eumenorrheic, and one patient reported menorrhagia at 3-year follow-up.

At 5 years after the NovaSure procedure, 75% of patients available for follow-up reported amenorrhea (PBAC = 0). Spotting (PBAC = 1–10) was reported by 19% of patients, with an additional 3% reporting hypomenorrhea (PBAC = 11–30). Reduction to normal bleeding (PBAC = 31–75) was reported by 1% of patients, whereas 2% continued to be menorrhagic (see Figure 22.6).

Direct comparison of the previously reported 1- and 3-year follow-up data suggests strong results stability when compared with the 5-year follow-up results (see Figure 22.6).

Statistical analyses were conducted using the McNemar test for the significance of change. This test was selected as an optimal and most applicable test due to its design pecifics and best applicability in comparing the patterns of responses of two nominal variables obtained from dependent samples (repeated measures in the same group). Controlling for an experiment-wise error (α = 0.05) for the three comparisons of interest (6 months vs 12 months, 12 months vs 36 months, and 36 months vs 60 months), the α per comparison was set at $\alpha = 0.015$. The results obtained suggest that improvement in amenorrhea rate observed between 6- and 12-month follow-up (46.2% and 58.6%, respectively) was statistically significant (p = 0.0003). A statistically significant improvement in amenorrhea was again observed between 12 and 36 months (58% and 65%, respectively) (p = 0.0253), as well as between 36 and 60 months (65% and 75%, respectively) (p = 0.0047). Because no significant difference in success

rates has been observed when comparing 6, 12, 36, and 60 months data (91.6%, 96.1%, 97%, and 98%, respectively) it is safe to conclude that, while becoming significantly better with time with respect of amenorrhea, a steady success state (clinical durability plateau) is reached at about 6 months after NovaSure procedure.

The hysterectomy rate of 2.9%, as well as the overall retreatment rate of 3.8%, was very low at 5-year follow-up. Considering that no additional surgical interventions were required between 3- and 5-year follow-up, it is safe to assume that the probability of need for additional surgical intervention after 3 years post-NovaSure ablation is negligible.

The efficacy of an endometrial ablation device is primarily measured by clinical outcomes. For this ongoing follow-up evaluation, we report on 5-year amenorrhea rates, spotting rates, hypomenorrhea, and reduction to normal bleeding, as determined by PBAC. We observed a 75% amenorrhea rate in this cohort at 5 years post procedure and an overall successful reduction of DUB was achieved in 98% of patients. Hysterectomy was avoided in 97.1% of patients (Figure 22.8) and the need for any additional surgical intervention was less than 4%. This is quite a striking improvement when compared with similar outcomes when this condition is treated with other solutions.

LATEST DEVELOPMENTS

While the classical indication for endometrial ablation is 'dysfunctional uterine bleeding disorders', the latest reports show the efficacy of NovaSure bipolar coagulation in the presence of polyps and myomata. Off-label use in the treatment of menometrorrhagia caused by type I and type II myomas ≤3 cm in diameter demonstrated a 95% satisfaction rate at 12-month follow-up.²⁴ But indications for treatment in the presence of intracavitary diseases and late results are still missing. As the uterine cavity is more or less distorted, endometrial ablation in the presence of myomata should only be performed by very experienced surgeons to avoid complications.

As we performed all operations under general anesthesia (TIVA), there are first reports of bipolar endometrial ablation in an office setting under local anesthesia. Patients are prepared with a painkiller in the form of a suppository followed by a paracervical block. To avoid systemic side effects and even for a better local effect after the paracervical block, an intrauterine gel is applied for pain treatment of the upper uterine part. As the operation (bipolar coagulation) only takes about 90 seconds, the results are satisfying. Development of pain after NovaSure ablation is less than after other global ablation techniques. By the continous suction system, cell debris of vaporized endometrium is

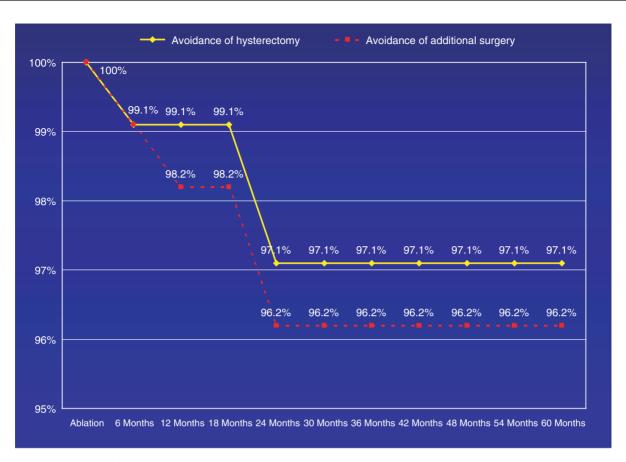


Figure 22.8 Avoidance of additional surgery and avoidance of hysterectomy.

removed out of the uterine cavity. In this way, prostaglandins synthesized in the endometrium are not set free, which would lead to contraction of uterine muscle.²⁵

CONCLUSION

For more than 20 years, literature data have demonstrated that endometrial ablation is an effective alternative in the treatment of excessive menstrual bleeding. Hysteroscopic ablation techniques were followed by the development of global ablation modalities. Introduction of the validated PBAC scoring system allowed for an objective comparison of the clinical outcomes achieved with different methods of endometrial ablation. Current literature data indicate that the SEATs are equal or superior to hysteroscopic ablation and deliver good clinical results, lower complication rates, and shorten operating room time, allowing for a quick recovery period.

Pretreatment with gonadotropin-releasing hormone (GnRH) agonists has proven to be advantageous in hysteroscopic ablation and was also found to be essential in the effectiveness of all other SEATs. NovaSure is the only endometrial ablation modality that does not require endometrial pretreatment. Published data suggest that

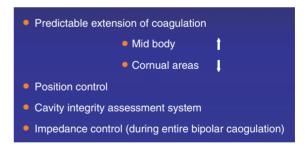


Figure 22.9 Safety features of the NovaSure system. (Source: Center of Gynaecological Endoscopy, Hamburg, Germany.)

the NovaSure system can be successfully used and provide excellent results ^{19,20,23} without the need for preoperative GnRH shrinkage of the endometrium. ²⁶ The significant risk of inadvertent energy application to the organs of the abdominal cavity as a result of an undetected uterine perforation is always present during blind intrauterine manipulation.

NovaSure technology incorporates several imporant safety features, such as device position feedback feature and the cavity integrity assessment system (Figure 22.9). Implementation of the cavity integrity assessment system is a revolutionary step in bringing the safety of endometrial ablation to a new, higher level. This safety feature

virtually eliminates the possibility of RF energy delivery in the case of an uterine wall perforation.

The geometry and size of each uterine cavity determine the precise amount of power required to achieve optimal ablation depths and profile. The power level is automatically calculated based on each woman's uterine cavity size. Regardless of power and energy requirements, the depth of endomyometrial ablation is consistent from patient to patient, as it depends on achieving adequate dessication and coagulation of endomyometrial tissues equating to an impedance of $50\,\Omega$. In all cases, the procedure (energy delivery) self-terminates in ≤ 2 minutes. Specific to NovaSure is the ability to achieve a reproducible depth of ablation, independent of endometrial thickness.

Different studies have demonstrated excellent success and patient satisfaction rates achieved with NovaSure treatment. This method continues to be proven as a safe and very effective method of treatment for patients suffering from menorrhagia and secondary DUB. Efficacy is demonstrated by high amenorrhea and a very low retreatment rate. High amenorrhea, which appears to most accurately represent the efficacy of a system, and low-score hypomenorrhea rates are prerequisites for consistant and good long-term results.

The advantage of the very short treatment time, which in turn allows for short procedure and operating room times, low complication rates, the special safety features, and the favorable results are convincing evidence that the NovaSure system can be an attractive treatment option for patients and their physicians.

References

- Badenheuer FH Elektrokoagulation der Uterusschleimhaut zur Behandlung klimakterischer Blutungen. Zentralblatt für Gynäkologie 1937; 4: 209–11.
- Goldrath MH, Fuller TA, Segal S. Laser photovaporization of endometrium for the treatment of menorrhagia. Am J Obstet Gynecol. 1981; 140: 14–19.
- DeCherney AH, Diamond MP, Lavy G, Polan ML. Endometrial ablation for intractable uterine bleeing: hysteroscopic resection. Obstet Gynecol 1987; 70: 668–70.
- 4. Lin BL, Miyamoto N, Tomomatsu M et al. The development of a new hysteroscopic resectoscope and its clinical application on transcervical resection (TCR) and endometrial ablation (EA). Jpn, J Gynecol Obstet Endosc 1988; 4: 56.
- 5. Vancaillie TG. Electrocoagulation of the endometrium with the ball-end resectoscope. Obstet Gynecol 1980; 74: 425–7.
- 6. Loffer FD. A comparison of hysteroscopic techniques. In: Lewis BV, Magos AL, eds. Churchill Livingstone. Edinburgh: Endometrial Ablation 1993: 143–50.
- Donnez J, Polet R, Rabinovitz R et al. Endometrial laser intrauterine thermotherapy: the first series of 100 patients observed for one year. Fertil Steril 2000; 74: 791–6.
- Gallinat A, Cosgriff N. Endometrial ablation by electroballoon coagulation: long term results. Gynecol Endosc 2001; 10: 37–43.
- Loffer FD. Three-year comparison of thermal balloon and rollerball ablation in treatment of menorrhagia. J Am Assoc Gynecol Laparosc 2001; 8(1): 48–54.
- Hawe JA. Cavaterm thermal balloon ablation for the treatment of menorrhagia. Br J Obstet Gynaecol. 1999; 106(11): 143– 148.
- Corson SL. A multicenter evaluation of endometrial ablation by Hydro ThermAblator and rollerball for treatment of menorrhagia. J Am Assoc Gynecol Laparosc 2001; 8(3): 359–367.
- 12. Heppard M. Data on 222 patients from a multicenter study using cryogen first option uterine cryoblation therapy in women with abnormal uterine bleeding. Obstet Gynecol 2001; 97(4): 21.

- 13. O'Connor H, Magos A. Endometrial resection for the treatment of menorrhagia. N Engl J Med 1996; 355: 151–6.
- Sharp NC, Cronin N, Feldberg I et al. Microwaves for menorrhagia: a new fast technique for endometrial ablation. Lancet 1995; 246: 1003–4.
- Garry R. Evidence and techniques in endometrial ablation: consensus. Gynecol Endosc 2002; 11: 5–17.
- 16. Gallinat A. Carbon dioxide hysteroscopy: principles and physiology. In: Siegler AM, Lindemann HJ, eds. Hysteroscopy Principles and Practice. Philadelphia: JB Lippincott, 1984: 45–7.
- 17. Higham JM, O'Brien PMS, Shaw RW. Assessment of menstrual blood loss using a pictorial chart. Br J Obstet Gynacol 1990; 97: 734–9
- Gallinat A, Nugent W. NovaSure impedance-controlled system for endometrial ablation. J Am Assoc Gynecol Laparosc 2002; 9(3): 283–9.
- Bongers MY, Bourdrez P, Mol BWJ et al. Randomised controlled trial of bipolar radio frequency endometrial ablation and balloon endometrial ablation. In: Bongers MY, eds. Thermal Endometrial Ablation. Veldhoven: Verhagen 2003: 99–115.
- 20. Cooper J, Gimpelson R, Laberge P et al. A randomized, multicenter trial of safety and efficacy of the NovaSure system in the treatment of menorrhagia. J Am Assoc Gynecol Laparosc 2002; 9(4): 418–28.
- 21. Wortmann M, Daggett A. Reoperative hysteroscopic surgery in the management of patients who fail endometrial ablation and resection. J Am Assoc Gynecol Laparosc. 2001; 8(2): 272–7.
- 22. Gallinat A. NovaSure impedance controlled system for endometrial ablation: three-year follow-up on 107 patients. Am J Obstet Gynecol. 2004; 191: 1585–9.
- Gallinat A. NovaSure impedance controlled system for endometrial ablation. five-year follow-up on 107 patients. J Reprod Med 2007; in press.
- 24. Sabbah R, Desaulniers G. Use of the NovaSure Impedance Controlled Endometrial Ablation System in patients with

- intracavitary disease: 12-month follow-up result of a prospective, single-arm clinical study. J Minim Invative Gynecol 2006; 13: 467–71.
- 25. Laberge PY, Sabbah R, Fortin C et al. Assessment and comparison of intraoperative, and postoperative pain associated with
- NovaSure and ThermaChoice endometrial ablation systems. J Am Assoc Gynecol Laparosc 2003; 10: 223–32.
- 26. Cooper J, Brill A, Fulop T. Is endometrial pretreatment necessary in NovaSure 3-D endometrial ablation? Gynecol Endosc 2001; 10: 179–83.

Hydrothermablation

Mark H Glasser

INTRODUCTION

Menorrhagia has an enormous impact on women's lives. Not only does it have an overall impact on health by causing anemia but also it creates anger, embarrassment, fear, lost work days, lost family time, decreased sexuality, and an overall loss of sense of well-being. In an analysis of the 1999 National Health Interview Survey (NHIS) done by the National Center for Health Statistics, it was estimated that women with heavy bleeding would work an average of 3.6 weeks less per year. The expected value of lost wages annually associated with heavy bleeding was estimated to be US\$1692 per woman. Approximately 2.5 million visits to gynecologists in the USA annually are for the treatment of menorrhagia and another 1 million women visit their family practitioner with the primary complaint of abnormal uterine bleeding.

Menorrhagia with no recognizable uterine pathology accounts for 20–25% of all hysterectomies performed each year in the USA. Another 40% of hysterectomies are done for leiomyomata; this number increases to almost 70% in the African-American population.² In the 45–54 years old age group, regardless of race, 53% of all hysterectomies are done for leiomyomata.³ The reported incidence of uterine leiomyomata in the USA is between 20% and 70%, and one of the most common symptoms these women have is abnormal uterine bleeding.⁴

The Hydro ThermAblator (HTA) system (Boston Scientific, Marlborough, MA) developed by BEI Medical Systems (Teterboro, NJ) is a hysteroscopic thermal ablation device intended to ablate the endometrial lining of the uterus in premenopausal women, for whom childbearing is complete, with menorrhagia (excessive uterine bleeding) due to benign causes. It is the only procedure for 'global' endometrial ablation that is performed under direct hysteroscopic control (Figure 23.1). The system introduces free-flowing normal saline into the endometrial cavity via a disposable 8 mm polycarbonate sheath which accommodates a standard rigid 3 mm hysteroscope (Figure 23.2). Adaptors are available that allow use of hysteroscopes made by the major manufacturers. After a 2-minute diagnostic phase (which can be

lengthened or shortened depending on the surgeon's preference), the fluid is heated to 90°C and circulated for 10 minutes, thereby treating the entire endometrium by a thermal effect. The fluid is maintained at low pressure to prevent egress either through the fallopian tubes or through the cervical canal. Circulation of fluid (0.9% saline solution) is controlled by gravity, based on the height of the fluid container above the patient's uterus, with actual intrauterine pressure reduced from hydrostatic pressure by the effect of the evacuation pump that recirculates fluid to the elevated reservoir. The fluid reservoir, mounted on the unit's dedicated intravenous (IV) pole, is adjusted to a height of 115 cm (45 inches) above the patient's uterus to provide a net intrauterine pressure in the range of 50-55 mmHg, well below the minimum pressure of 70 mmHg required to open the fallopian tubes. With the operating table at a typical height for hysteroscopic procedures, and with an average-size patient, the uterus is approximately 85 cm (34 inches) above the floor. The fluid reservoir may be elevated to a maximum height of 221 cm (87 inches) above the floor when the connecting tubing set is fully extended. Consequently, maximum net intrauterine pressure obtainable during HTA treatment is <70 mm Hg. The typical tubal opening pressure is 70 mmHg, whereas the HTA system operates in the range of about 50 mmHg. The fluid is gravity-fed and the height of the reservoir above the level of the patient's uterus determines the intrauterine pressure. Concurrent laparoscopy performed during the phase II clinical trials showed no transtubal leakage.5 The fact that this system operates at low pressure and involves a 'no-touch' technique makes it ideally suited for use in the office treatment room. This is discussed at length later in the chapter.

PATIENT SELECTION AND PREOPERATIVE WORK-UP

The HTA system is contraindicated for use in a patient:

 who is pregnant or wants to be pregnant in the future, as pregnancy after ablation can be dangerous to both the mother and fetus



Figure 23.1 The HTA control unit with a 3L bag of normal saline hanging from the integrated IV pole.



Figure 23.2 The HTA sheath with tubing connected and hysteroscope in the sheath. Note the ratcheted tenaculum stabilizer at the top of the sheath.

- who is known or suspected of having endometrial carcinoma or premalignant change of the endometrium, such as atypical adenomatous hyperplasia
- who has active pelvic inflammatory disease or pyosalpinx

- who has hydrosalpinx
- who has an intrauterine device in place
- who has active genital or urinary tract infection at the time of treatment.

All patients with menorrhagia should be offered a trial of hormones before being scheduled for endometrial ablation. The fear that this would not occur, given the ease of use of the second-generation ablation devices, is largely unfounded. In a study from Glasgow, Scotland, UK, where published guidelines for the management of menorrhagia exist, the majority (86%) of women undergoing a second-generation endometrial ablation technique received at least one effective medical therapy before surgical intervention, indicating a high level of compliance with published guidelines.⁶ We favor oral contraceptives, given either continuously or cyclically. An alternative is oral or intramuscular progestins. Norethindrone acetate (Aygestin; Duramed Pharmaceuticals, Pomona, NY) is a very effective treatment for abnormal uterine bleeding when given in a dose of 10 mg/day for 21 days initially and then 5 mg/day on days 15-25 of each cycle. Depot medroxyprogesterone acetate (DPMA, Depo-Provera; Pharmacia & Upjohn, Kalamazoo, MI) can also be used. If the patient continues to bleed after 1–2 weeks on the initial course of norethindrone acetate or after the second month of oral contraceptives or DMPA, she is scheduled for an office diagnostic hysteroscopy and endometrial biopsy. These patients will often have polyps or small submucous myomas. All patients with known myomas should undergo diagnostic hysteroscopy to assess whether or not they are candidates for HTA. If the tubal ostea can be seen and the physician determines that fluid can circulate around the myoma, HTA can be done. Patients with submucous myomas were not included in the phase III FDA (Food and Drug Administration) trials, so the use of the device for this indication must be considered 'off label'. The use of HTA in patients with submucous myomas is discussed later in the chapter.

Pretreatment:

In our early experience, most patients were pretreated with a gonadotropin-releasing hormone (GnRh) agonist using a single injection of Lupron Depot (leuprolide acetate) 3.75 mg (TAP Pharmaceuticals, Deerfield, IL) given in the late luteal phase, and the procedure performed 4–6 weeks following the injection. This was according to the protocol submitted to the FDA for the phase III clinical trials of the HTA system. Alternative medical pretreatments are danazol 600 mg/day for 3–4 weeks, starting day 1 of the cycle, continuous oral contraceptives (OCs), or norethindrone acetate 10 mg/day for 4 weeks.

In a search of the Cochrane database by the Menstrual Disorders and Subfertility Group in Auckland, New Zealand in 2002, the authors concluded that:

Endometrial thinning prior to hysteroscopic surgery in the early proliferative phase of the menstrual cycle for menorrhagia improves both the operating conditions for the surgeon and short term post-operative outcome. Gonadotrophin-releasing hormone analogues produce slightly more consistent endometrial thinning than danazol, though both agents produce satisfactory results. The effect of these agents on longer term post-operative outcomes such as amenorrhoea and the need for further surgical intervention reduces with time.⁷

In the last 2 years we have attempted to schedule the patients in the early proliferative phase of the cycle, with no difference in outcome. In a series of 89 patients presented at the World Congress of Gynecologic Endoscopy in 2004, William Crowder found no significant difference in patient satisfaction (87%, 90.3%, 92.9%) 15 months following HTA in the groups treated with leuprolide depot, continuous OCs, or cycle timing.⁸ If excessive endometrium or clots are noted during the diagnostic phase of the HTA procedure, they can be removed with a light suction curettage using the Milex Handy-Vac (Cooper Surgical, Trumbull, CT) with a 7 mm rigid vacurette.

HTA PROCEDURE

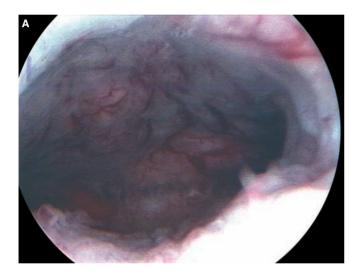
The set up of the HTA unit is very simple, as each step is prompted by instructions displayed on the LED monitor. All of the necessary components are shipped in a sterile 'peel pack' container and the tubing connections are color-coded. When the power is turned on, the unit goes through a brief self-diagnostic phase. The medical assistant is then prompted to connect the disposable heater canister, reservoir, and drain bag in their proper receptacles. A 3L bag of normal saline is then hung from the system's integrated IV pole and the in-line cassette containing the recirculating pump is connected to the unit and locked into place. The disposable sheath (see Figure 23.2) is packed separately and connected to the inflow and outflow tubing by the physician just prior to beginning the procedure. Not only are the connections colorcoded but also they are male and female, so they cannot be connected incorrectly. Room temperature saline then purges air from the system. This step also checks all components for leakage and fills the heater canister and fluid measurement reservoir. The fluid is then heated to body temperature to check the fluid heating rod and thermocouples that monitor fluid temperature.

After the cervix is dilated to 8 mm to accept the insulated 7.8 mm outer diameter hysteroscopic sheath, containing a standard 3 mm or smaller hysteroscope, flow of room temperature saline is started to allow visualization of the cervical canal and the uterine cavity. It is most important not to overdilate the cervix, which should not be dilated beyond 8 mm (24 Fr). The junction of the HTA sheath with the external cervical os should be carefully observed during the flushing stage to confirm a good seal and no fluid leakage. Visualization of both tubal ostea confirms correct intracavitary placement of the device. The microprocessor-controlled system monitors the fluid volume by a series of sensors and automatically stops the flow of saline when a 10 ml deficit is detected. It is not recommended that one does sharp curettage prior to the procedure, since this may open sinuses and lead to intravasation of saline. Although this is not dangerous, the machine will automatically stop and a fluid loss alarm will sound. Also, tissue debris created during sharp curettage may clog the outflow of the sheath, causing a fluid excess alarm. Fluid monitoring begins during the heating phase, which starts at room temperature. If a fluid loss alarm sounds, the deficit is displayed on the LED screen at the front of the control unit as well as the rate of fluid loss. This safety feature allows the surgeon to immediately suspect a perforation if the rate of fluid loss is high (>20 ml/min). The HTA system will not function in the event of uterine perforation and it cannot be overridden, since it will again shut off when another 10 ml deficit is detected. Since the procedure is performed under direct hysteroscopic guidance, uterine perforation, false passage, and intrauterine pathology can be detected immediately by the surgeon. It is always possible to create a false passage or a perforation while passing dilators through the cervix. Direct visual introduction should eliminate the possibility of creating a false passage or a perforation while introducing the HTA sheath, unlike blindly introduced probes. The flushing cycle is preset for 2 minutes. Additional 1 minute flushing cycles can be obtained if needed by pressing 'Start' once the message, 'Reached Recommended Flushing Time, Press Start for Additional Time' appears. After flushing has been completed, a minimum of 1.5 L of saline must remain available.

As saline is heated in the heater canister, the temperature is displayed on the panel. Saline moves through the closed looped system at 300 ml/min, maintaining therapeutic temperature in the tubing system and uterine cavity. Earlier testing established less than a 2°C difference in temperature between saline in the heater canister and the input port on the sheath, so a thermocouple is not needed in the uterine cavity. It takes approximately 3 minutes to heat the fluid to ablating temperature. Once the temperature reaches 80°C, the timer on the microprocessor begins,

even though the temperature of the saline continues to climb for approximately 1 minute until it reaches 90°C. The ablation cycle lasts for 10 minutes. The optimum time and temperature were determined from earlier studies. During the ablation cycle, blanching of the endometrium is noted on the video monitor. This is fascinating to the patient observing the screen during an office procedure under local anesthesia and provides 'video analgesia' as well as reassuring the physician and patient that the ablation is occurring normally (Figure 23.3). The junction of the HTA sheath with the external cervical os should be carefully observed during the heating period to confirm a good seal and no fluid leakage.

It is most important for the physician to maintain a steady, central position within the uterus during the ablation cycle and not radically deviate the sheath. Lateral movement of the sheath can result in stretching of the internal os, which makes leakage possible. Also, when



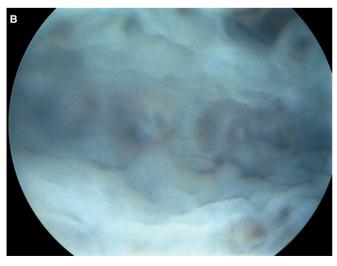


Figure 23.3 Pre- (A) and post-HTA(B) uterine cavity in a 41-year-old woman with severe menorrhagia. Note the large vessels at the fundus completely obliterated post treatment.

the sheath is deviated horizontally or vertically, it is likely to come into contact with the uterine wall, resulting in contractions. Not only is this uncomfortable for the patient, but also it may cause difficulty distending the uterus, which may result in some areas not being completely ablated. At any time, the procedure may be interrupted by pressing 'Stop', and terminated by pressing 'Stop' a second time. To continue after interrupting the procedure, press 'Start'. The timer will resume and continue until completion of the ablation cycle. Following the 10-minute ablation cycle, a 1-minute cool-down cycle begins. During this cycle the sheath can be moved about in the cavity to assure complete ablation effect. The fluid in the uterus and tubing is hot, so the sheath must not be removed until the cooling cycle is complete and the machine prompts the physician to remove the sheath. If areas of unablated native endometrium are noted (as would occur if there was poor distention or a fibroid opposing the sidewall shrinks to reveal it), the machine can be shut off and restarted for additional ablation time (off-label indication). If visualization is compromised or if the patient is uncomfortable during the HTA procedure, the cycle can be interrupted by pressing the 'stop' button twice, the sheath removed after cooldown, and the machine restarted to complete the cycle after the scope is cleaned or the patient given additional analgesia. To complete the ablation, use the following 'hot restart technique'.

Hot restart technique

- Press 'Stop' twice to abort procedure and allow cooling to take place note ablation time.
- Remove sheath from patient, clean lens and back flush with syringe – administer additional anesthetic if necessary.
- Turn off the power to the unit and turn back on after 5 seconds.
- Repeatedly press 'Start' as machine goes through initial start-up instructions.
- During filling phase, press 'Start' when fluid reaches 80 ml mark.
- When 'Insert sheath' message appears, press 'Start' and make sure there is good flow before reinserting sheath.
- Make sure there is enough saline in supply bag and enough capacity in outflow bag. If the collection bag is full, drain the bag and reconnect tubing.
- Ablate for remaining time or for reablation, until the unablated endometrium blanches completely.

Cervical control

A tight cervical seal is necessary to prevent leakage of fluid from the cervix into the vagina. The use of laminaria tents and misoprostol should be avoided, since both of these agents can soften the cervix, making it difficult to maintain a tight seal. I prefer to dilate the cervix using Hegar dilators, which are non-tapered. The use of Pratt or Hanks dilators will result in the mid cervix and external os being dilated to 9 mm and 10 mm, respectively, if the internal os is dilated to the requisite 8 mm. The use of a Gimpleson four-pronged tenaculum will often help maintain the cervical seal in a multiparous patient with a wide patulous cervix.¹⁰ Another simple technique to employ for the patulous cervix is to grasp the cervix laterally with one tenaculum held vertically and compressing the anterior to the posterior lip; inserting the sheath to its proper position and then applying a second tenaculum to compress the anterior and posterior lips of the cervix on the opposite side of the sheath creates a tight cervical seal. If either of these methods is unsuccessful, the use of an endoscopic loop cinched tightly around the cervix after the sheath is inserted into the cavity is often effective. As a last resort, a McDonald circlage suture can be placed in the cervix and tied following insertion of the sheath to its proper intracavitary position beyond the internal os.

The integrated tenaculum stabilizer at the top of the sheath (see Figure 23.2) prevents inadvertent removal of the device from the cervix during the procedure while heated saline is being circulated. The physician must actively release this ratcheted holder before the device can be removed. The next-generation HTA sheath, which is awaiting FDA approval, will have a cervical sealing device built into the sheath, which will eliminate any possibility of transcervical leakage. In the author's personal experience of 286 HTAs, there has not been any instance of saline leakage resulting in cervical or vaginal burn.

OFFICE ABLATION UNDER LOCAL ANESTHESIA USING THE HTA SYSTEM

While minimally invasive gynecologic surgery has dramatically decreased hospitalization and shortened disability for countless numbers of women over the last two decades, many gynecologists have been reluctant to move some of these procedures out of the formal operating rooms of hospitals and ambulatory surgical centers to their offices. In an informal survey at four recent 'hands on' postgraduate hysteroscopy courses sponsored by the American College of Obstetricians and Gynecologists (ACOG), only 5–10% of participants did any office hysteroscopy, while approximately 70% were experienced

hysteroscopists. 11 This is true despite studies in the literature which show patients having hysteroscopy in an outpatient setting compared to those done in a day case setting (surgicenter) have a more rapid return to normal activities and require no greater amount of postoperative analgesia.¹² There are also economic benefits to patients, their employers, and to the healthcare system by performing hysteroscopy in the outpatient setting rather than in a day case setting.¹³ The outpatient group in this study from the UK required significantly less time off work compared with the day case group, resulting in the average loss of income being twice as much in the day case group. Travel costs incurred by the women were 74% more in the day case group compared with the outpatient group. Day case hysteroscopy costs to the British National Health Service were significantly more per patient than performing an outpatient hysteroscopy.

There are several other benefits to the patient of having a surgical procedure performed in the office rather than in the operating room (OR). In addition to eliminating the risk of general anesthesia, having the procedure performed in the familiar surroundings of the gynecologist's office is far less intimidating than the OR, thus reducing anxiety. Also, the ability to have a support person in the room and to converse with the physician further reduces anxiety and the discomfort which, conversely, is magnified by anxiety.

There are many physician benefits of office-based surgery as well, such as avoiding the hassle of scheduling, dictation, and 'down time' in the OR caused by cases running overtime or being 'bumped' from the schedule. Time commuting to the hospital is better spent increasing office productivity and accessibility.

There are many barriers to performing procedures in the physician's office, including equipment costs and maintenance, rapid obsolescence of technologies, lack of procedure room space, staffing and staff training, and anesthesia requirements. Traditionally, office procedures were reimbursed at rates equal to or lower than those rates for procedures performed in a hospital or surgicenter, which made it economically disadvantageous for the physician to perform procedures with high disposable kit costs in the office. Fortunately, this is changing in the USA, with the publication of the 2006 National Physician Fee Schedule Relative Value Guide. Hysteroscopic endometrial ablation (resection, electrosurgical ablation, thermoablation - CPT 58563) performed in the office is now reimbursed at 63.09 RVU (relative value units) compared to 9.65 RVU for the same procedure performed in a facility. Similarly, thermal endometrial ablation without hysteroscopic guidance (CPT 58353) is now reimbursed at 39.63 RVU for the procedure performed in the office compared to 6.02 RVU for the same procedure performed

in a facility. The office RVU for hysteroscopic sterilization (CPT 58565) is 57.77 compared to the facility RVU of 12.11. Insurance companies are slowly adopting these rates, making it economically advantageous to perform procedures in the office setting, especially diagnostic hysteroscopy, hysteroscopic endometrial ablation, and hysteroscopic sterilization. Phillip Brooks MD, one of the pioneers of hysteroscopy said:

If possible, the ideal role for the new 'simple' or 'global' ablation should be for office or treatment room use thereby avoiding the use and risks of general or regional anesthesia.¹⁵

The control of pain seems to be the greatest concern of physicians attempting to perform hysteroscopic procedures in the office setting. The early experience in setting up an ambulatory hysteroscopy service at a large endoscopy unit in Australia provoked a review of the literature, due to an unacceptably high failure rate. The review was undertaken to establish the accepted success rates and reasons for failure, and to assess evidence for various analgesic protocols through randomized controlled trials. Twenty-nine separate studies were reviewed, which included 10232 patients. The success rate varied between 69% and 100%, with most studies citing a 90-100% success rate. Failures were due predominantly to pain (29.4%), stenosis (28.2%), and poor view (20.8%). The authors concluded that most failures were probably due to inadequate analgesia.¹⁶

The sensory innervation of the uterus derives both from the sympathetic and parasympathetic nervous systems. Pain in the first stage of labor stems largely from the uterus. Sensory fibers to the cervix accompany the parasympathetic fibers arising from the S2-S4 region of the spinal cord to the pelvic plexus and travel through Frankenhauser's ganglion to innervate the cervix and myometrium. Pain in the cervix is referred to the sacral region. The uterus is also innervated by sympathetic fibers arising from the lower thoracic and upper lumbar regions of the spinal cord (T12-L2), which follow the same pathway. The paracervical block (PCB), sometimes called a uterosacral block, places the local anesthetic at the base of the broad ligament and lateral walls of the lower uterine segment, blocking the afferent pathways which lead to Frankenhauser's ganglion. For many years this was a very popular anesthetic for the first and second stages of labor. With the advent of fetal monitoring, deep decelerations in fetal heart rate were noted after administration of the block, and thus PCB fell into disfavor for obstetrical analgesia. However, its use for gynecologic procedures is based on sound physiologic principles.

The cervix and uterus are sensitive to stretch but insensitive to heat.

The HTA system, because it operates at low pressure (50 mmHg) and works by circulating free-flowing saline in the uterine cavity at 90°C without any instruments touching the uterine wall, is ideally suited for office use under local anesthesia. In a study of 40 patients to assess and establish the feasibility of outpatient global endometrial ablation using the HTA device with local cervical block and oral non-steroidal anti-inflammatory drugs (NSAIDs), Farrugia and Hussain concluded that, since the HTA system operates at a low intrauterine pressure, and no manipulation of the device is required during the ablation cycle, it is ideal for performing endometrial ablation in an outpatient clinic. This initial study shows the feasibility and patient acceptability of this procedure under local anesthesia.¹⁷

There are numerous protocols for administering paracervical/intracervical blocks described in the literature for office procedures. Several are outlined in a review article by Leclair. ¹⁸ At the Kaiser Permanente Medical Center in San Rafael, California, we have performed over 12 000 gynecologic office procedures under local anesthesia with minimal oral sedation over a 25-year period. These procedures included pregnancy termination, both elective and for missed and incomplete abortions, diagnostic hysteroscopies, hysteroscopic sterilizations, and, to date, 286 HTAs.

Protocol for office anesthesia

All procedures were done in the medical office treatment room under local anesthesia after oral premedication at home and intramuscular (IM) premedication in the office. Our oral premedication regimen consists of 800 mg of ibuprofen (Motrin; Pharmacia & Upjohn, Kalamazoo, MI), 10 mg of diazepam (Valium; Roche, Nutley, NJ) and two hydrocodone/acetominophen (Vicodin; Abbott, North Chicago, IL) tablets taken at home 1-2 hours prior to the procedure. The patients are instructed to arrive 30 minutes prior to their scheduled appointment and are given an IM injection of ketorolac (Toradol; Roche, Nutley, NJ) 30 mg and atropine 0.4 mg at that time. Toradol has peripheral effect as well as being a prostaglandin synthetase inhibitor and is very effective for office endometrial ablation. Atropine is used to prevent vasovagal reactions. A paracervical/intracervical block with 1% mepivacaine (Polocaine; AstraZeneca, Wilmington, DE) using a 10 ml control-top syringe and a 22 gauge spinal needle is then administered. We chose mepivacaine since it is relatively safe (75% protein bound) and is longer acting than lidocaine. First, 2 ml is given in the anterior lip of the cervix before it is grasped with a single-toothed tenaculum. The needle is placed against the cervix and the patient is instructed to cough, which results in 'self-injection'.

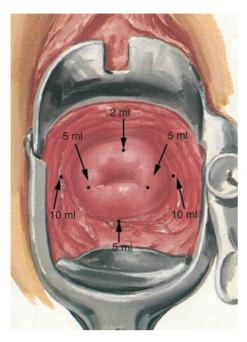


Figure 23.4 A graphic representation of the cervix and vagina, indicating the injection sites and the amounts of 1% mepivacaine to be injected.

Then, 10 ml of mepivacaine is given in the cervicovaginal junction on each side at 3:00 and 9:00. These injections are given superficially, just under the mucosa to raise a weal. An additional 5 ml is given intracervically about 1-2 cm deep at 8:00 and 4:00, and 5 ml is given submucosally at 6:00 between the uterosacrals (Figure 23.4). The total amount of mepivacaine given is 37 ml or 370 mg. We use a large-volume PCB so that the mepivacaine can disperse freely around the cervix and lower parametrium. The total of 370 mg used is under the manufacturer's recommended maximum dose of 400 mg. However, the package insert, as listed in the Physician's Desk Reference, states that up to 550 mg has been given without adverse effect.¹⁹ We have not had any adverse anesthetic reactions in our patients in 286 HTAs done over 5.5 years, or in the 12 000 other patients given similar PCBs for office gynecologic procedures over 25 years. It is most important that dilatation of the cervix is not begun until 10–15 minutes has elapsed, to permit the block to set properly.²⁰ We recommend that the physician actually leave the room for that period of time while the patient is monitored by the nurse and encouraged to relax.

Precautions for paracervical/intracervical block

Strict guidelines should be followed when administering a PCB to avoid intravascular injection, which can result in convulsions with cardiovascular collapse and death:

 It is most important to administer the block using a control top syringe, which allows frequent aspiration and confirmation that the injection is not intravascular.

- The lowest concentration of drug should be given in small increments.
- Avoid the use of Marcaine (bupivacaine), since it is the most cardiotoxic of the local anesthetics and a small amount injected intravascularly can lead to convulsions and rapid cardiac collapse.²¹
- Inject superficially. A deep PCB into the lower segment advocated by some authors^{22,23} runs the risk of direct injection into the uterine vessels or large myometrial sinuses. This technique should be avoided!
- Premedicate with diazepam. Not only is this an anxiolytic but also it is a potent anticonvulsant and raises
 the threshold for convulsions in case of inadvertent
 intravascular injection.
- Have basic resuscitative equipment in the treatment room, including an oxygen supply and a positive pressure manual resuscitator (Ambu bag).

Not all patients are candidates for office HTA, and the physician must assess which patients will tolerate an office operative procedure. Those patients who are excessively apprehensive and have low pain tolerance, as evidenced by their experience during endometrial biopsy, should be a good indication that they will not tolerate office ablation well. This can certainly be mitigated by good patient education and counseling and the use of video and printed material. In our 5.5 years of performing HTA in the office, we have only had three patients refuse to have it done without general anesthesia. Also we've only had to discontinue one procedure after 8 minutes of ablation because of patient discomfort: parenthetically, the patient had a good clinical outcome.

Most patients feel well enough to leave for home almost immediately after the conclusion of the procedure. Of 286 patients, 280 were discharged within 30 minutes of the end of the procedure, four were discharged within 2 hours, and two were admitted overnight for nausea, vomiting, and cramping. All patients were discharged with only oral analgesics and most required them only for 6-8 hours following the procedure. Post-procedure nausea, which occurred in about 15% of patients, was controlled with oral diphenhydramine or hydroxyzine (Atarax; Pfizer, New York,). Patients are instructed to take an additional ibuprofen 800 mg as soon as they get home and to take Vicodin, as required, needed for cramping. They are instructed to call if they experience any temperature >100.4° F (37.6°C), severe abdominal pain, or heavy bleeding. They are also instructed to expect a period approximately 4 weeks after the procedure and sloughing of necrotic endometrium. Occasionally, the patient will have a pink discharge for 4-6 weeks following the procedure. Patients are also instructed to call if they experience no discharge at all accompanied by cramping within the first 3 days following the procedure, since this may be a sign of an obstruction at the internal os, which can lead to endometritis.

CLINICAL OUTCOMES

When considering clinical outcomes of the various global ablation technologies, the prime consideration should be improvement in the patient's quality of life rather than absolute amenorrhea rate. In fact, in some cultures, amenorrhea is not the desired outcome and is detrimental to the patient's psyche. In a study comparing four different endometrial ablation techniques in 139 women in Sydney, Australia, the authors found quality of life, measured preoperatively by the EQ-5D index and EQ-5D vas, SF-12 physical and mental component scores, and sexual activity questionnaires; pleasure, habit, and discomfort scores, were substantially improved 12 months after treatment. No significant differences were seen in quality of life scores between women after endometrial ablation and the general population. Their conclusion was: 'Quality of life for women with menorrhagia is improved to a normal level by treatment with either first- or second-generation endometrial ablation'.24

In a review of 500 cases of the use of the HTA system for the treatment of menorrhagia presented at the Global Congress of Minimally Invasive Gynecology in November 2006, the author reported amenorrhea or light spotting in 70% of patients and an overall success rate of 88%. Two other studies – 200 patients with a median follow-up of 27 months and 139 patients carried out over a 5-year period – showed satisfaction and success rates of 92% and 88%, respectively. In a 3-year follow-up of the patients enrolled in the original FDA trial, the HTA system was found to have a similar success rate and amenorrhea rate when compared with rollerball endometrial ablation (Table 23.1). Since the HTA system works by circulating free-flowing heated (90°C) saline, it is capable of treating

Table 23.1 Success and satisfaction rates at 36 months for patients in the phase III FDA trial undergoing HTA and rollerball endometrial ablation²⁸

	HTA (n = 135)	Rollerball (n = 68)
Patient Satisfaction	97.8%	97.1%
Success rate	94.1%	91.2%
Amenorrhea	53.3%	45.9%

patients with irregular uterine cavities and those with benign intrauterine pathology.²⁹ This increases the versatility of the device, since it can be used in a broader patient population, thus avoiding hysterectomies in those patients whose physicians are not skilled in resection of submucous myomas or intrauterine septae. The success rate and patient satisfaction rate in patients with irregular cavities and benign intrauterine pathology is similar to patients with normal cavities.³⁰ In our own clinical experience at the Kaiser Permanente Medical Center in San Rafael, California, we have performed 286 HTAs over the last 5.5 years. In that group, nine patients have had repeat HTAs and 13 patients have undergone hysterectomies for a success rate of 93.3%; 120 of those patients had submucous myomas (42%).

THE USE OF HTA IN PATIENTS WITH SUBMUCOUS MYOMAS

Global ablation technologies were developed in order to ameliorate the complications of operative hysteroscopy. They offer the promise of success rates similar to rollerball ablation for menorrhagia without requiring the surgical skill necessary for performing operative hysteroscopy. These technologies have been embraced by many gynecologists uncomfortable with operative hysteroscopy, especially resection of submucous myomas, in order to offer their patients a simple, safe alternative to hysterectomy. However, the significant shortcoming of these devices, with the exception of the HTA system, is the inability to treat irregular uterine cavities or those with large type 0 or type 1 submucous myomas. Fixed architecture devices or those that depend on movement of a probe across the endometrial cavity are, by virtue of their design, not suitable for treating intracavitary lesions which would prevent deployment or movement of the probe. Also, the HTA system is the only global ablation technique done under direct visualization with the hysteroscope rather than ablating the cavity blindly or with only ultrasound guidance. Some physicians may be reluctant to apply thermal, electrosurgical, microwave, or cryothermic energy to the endometrial cavity without visual confirmation that the energy is being delivered where intended. Whereas other global ablation technologies have been used to treat submucous myomas, all of those myomas have had >50% of their volume within the myometrium (type 2).31,32 It must be stated that this is not described in the manufacturer's manual or is it recommended by the manufacturer, but rather an off-label use by the author (MG). The technique employed in patients with submucous myomata is exactly the same as that described above and used in patients

with normal cavities, so, logically, there should be no increase in complications. Parenthetically, this technique has been used successfully at several facilities throughout the Kaiser system with good results and no adverse consequences. Several of the studies cited above included large numbers of patients with submucous myomata with no significant difference in the success rate, satisfaction rate, or complication rate compared with those patients with normal cavities. 17,25,26,30 The author has reported on a 12-20 month follow-up of the first 22 patients with submucous myomas ≤4 cm in diameter and menorrhagia treated with HTA system and found a 92% success rate and an amenorrhea rate of 58% overall and 46% in the premenopausal group.³³ A 60-month follow-up of the original group plus an additional 11 patients found a hysterectomy rate of 12% (four patients), three for persistent menorrhagia and one for bulk symptoms. The overall success rate was 88%, comparable to the author's series of electrosurgical vaporization procedures which had been our standard technique for the hysteroscopic management of submucous myomas at Kaiser permanente Medical Center, San Rafael, in the period 1995-2001.34 A large multicenter prospective trial of the use of the HTA system in patients with submucous myomas has been funded and is now being organized.

Why HTA works in patients with submucous myomas

In a recent report of a large cohort of women in Washington, DC, women with leiomyomata were more likely to report gushing-type bleeding and high pad/tampon use compared with women without leiomyomata. The risk of heavy bleeding increased with size of the myomas but was the same for submucosal as non-submucosal leiomyomata. However, size and location of the myomas was determined using abdominal and transvaginal ultrasound, not hysteroscopy.³⁵ In that paper, Wegienka et al. also discuss several theories of how leiomyomata cause bleeding, including increased uterine and endometrial vascularization, increased endometrial surface area, or interference with the normal sequence of uterine contractions. We have directly observed large vessels bleeding on the surface of submucous myomas and this may very well be one of the reasons why patients with submucous myomas have abnormal bleeding. The bleeding stops during the HTA procedure, as blood clots in the surface vessels of the submucous myomata, and eventually the vessels are completely obliterated (Figure 23.5). In addition, the myomas are observed to markedly shrink in volume and some actually crumble (Figure 23.6). The reason for this clinically observed phenomenon may be explained by a recent in-vivo study of the effect of



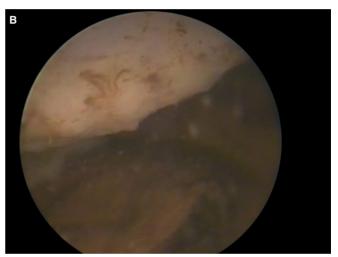


Figure 23.5 Preoperative (A) and postoperative (B) appearance of a 4 cm submucous myoma in a 42-year-old woman with menorrhagia and anemia (hct. 24%). The patient has been amenorrheic for 5.5 years.

cryothermic and hyperthermic treatments on human leiomyomata and adjacent myometrium. Leiomyomata cell death increased from 17% to 88% when exposed to progressive temperature increases from 45°C to 80°C for 10 minutes. Leiomyoma cell death increased from 12% to 27% over the cryothermic temperature range of -20°C to -80°C for 10 minutes.36 The HTA system circulates heated saline at 90°C for 10 minutes. The compression of the myoma volume observed during the procedure may also compress internal vasculature and lead to further hypoxia and myoma death. To date, no prehysterectomy studies have been done on patients with submucous myomas following HTA. It would be interesting to carry out leiomyoma cell viability studies in myomas removed hysteroscopically immediately after HTA.





Figure 23.6 Preoperative (A) and postoperative (B) appearance of a 3 cm type 0 fundal myoma in a 49-year-old patient. The patient has been amenorrheic for 3 years.

COMPLICATIONS OF GLOBAL ABLATION DEVICES

The global ablation technologies were developed in order to extend the ability to perform endometrial ablation to gynecologists with limited operative hysteroscopy skills as well as making endometrial ablation safer for the patient. The use of these technologies completely eliminates the risk of distention media complications. However, their widespread use has resulted in another set of complications which have been reported only to a limited extent. Most of the published articles on global endometrial ablation are from the original FDA trials. These clinical trials were performed by experts in the field under strict protocol monitored by local Institutional Review Boards (IRBs) as well as the manufacturer's clinical research associates. The widespread commercial use of these technologies since FDA approval, especially by those with limited

hysteoscopy skills, has resulted in a dramatic increase in complications. These occur most often when devices are misused or safety systems are overridden. Also, the fear of litigation makes physicians unwilling to report complications. There is a significant time lag from occurrence of complications to their publication in the literature.³⁷ The complications reported in the FDA MAUDE database (http://fda.gov/cdrh/maude.html) include bowel burns occurring after unrecognized perforation as well as bowel burns occurring with electosurgical, microwave energy, or heat transferred through intact myometrium. Vaginal burns, uterine necrosis with myometritis requiring hysterectomy, and death from an unrecognized bowel burn have also been reported in this database.³⁸ When assessing devices for the potential for serious injury, one must certainly take into account the type and number of injuries reported for each device and be cognizant of the fact that the reports only represent a small portion of the injuries which actually occur in clinical practice. Most of these procedures are performed blindly and some physicians fail to do a diagnostic hysteroscopy in these patients to assess the cavity preoperatively and override built-in safety systems. HTA is the only global ablation technique performed under direct observation with the hysteroscope and is therefore my procedure of choice. In 286 procedures done to date in our office under local anesthesia, our only complications were two false passages and four cases of post-procedure endometritis. Both false passages were promptly diagnosed during the diagnostic hysteroscopy phase of the procedure, allowing us to stop and reschedule 2-3 months later. One patient with endometritis had a pyometrium secondary to a stenotic cervix and was hospitalized for a course of IV antibiotics.

CONCLUSIONS

HTA using free-flowing, heated (90°C) saline is a safe and effective treatment for women with menorrhagia as well as submucous myomas ≤4 cm in diameter. The 91% success rate and 58% amenorrhea rate in the latter group of patients is similar to that achieved using this technology in patients with normal uterine cavities as well as that achieved with rollerball endometrial ablation. 28,33 It offers advantages over hysterectomy and electrosurgical resection since it is an office-based procedure with a very low complication rate. Also, there are very significant advantages to HTA over other global ablation technologies, which, by their design, are unable to treat significantly distorted uterine cavities. Also, unlike the other devices, it is inserted into the uterine cavity and the procedure performed under direct hysteroscopic visualization. It can easily be done by physicians with only basic hysteroscopy

skills. Patients tolerate treatment in the medical office procedure room under local anesthesia with oral analgesia/ sedation and intramuscular ketorolac (Toradol). There is a high degree of patient satisfaction with the procedure whether done in the office or the operating room. Increased

reimbursements have now made it economically advantageous to physicians to perform hysteroscopic ablation in the medical office. Moving procedures out of the operating room into the physician's office also results in significant cost savings to the healthcare system.

References

- Cote I, Jocobi P, Cumming D Work loss associated with increased menstrual loss in the United States. Obstet Gynecol 2002; 100: 683–67.
- Wilcox LS, LM, Pokros Ret al. Hysterectomy in the United States, 1988–1990. Obstet Gynecol 1994; 83:(4) 549–55.
- 3. Pokras R Hysterectomy: past, present and future. Stat Bull Metrop Insur Co 1989; 70(4): 12.
- Buttram VC, Reiter RC. Uterine leiomyomata: etiology, symptomatology and management. Fertil Steril 1981; 36: 433–445.
- Weisberg M, Goldrath MH, Berman Jet al. Hysteroscopic endometrial ablation using free heated saline for treatment of menorrhagia. J Am Assoc Gynecol Laparosc 2000: 7: 311–316.
- Hardwick JC, Owen P. Adherence to published guidelines for the management of menorrhagia in women undergoing second generation endometrial ablation. J Obstet Gynaecol 2004; 24(3): 279–80.
- Sowter MC, Lethaby A, Sinla AA. Pre-operative endometrial thinning agents before endometrial destruction for heavy menstrual bleeding. Cochrane Database Syst Rev 2002; (3) CD001124.
- 8. Crowder WJ, Meyer JRet al. Evaluation of pretreatment methods for endometrial ablation using the HTA system. World Congress of Gynecologic Endoscopy, San Francisco, CA, November 2004.
- Richart RM, Botacini das Doras G, Nicolau SM et al. Histologic studies of the effects of circulating hot saline on the uterus before hysterectomy. J Am Assoc Gynecol Laparosc 1999; 6: 269–273
- Gimpelson RJ. Preventing cervical reflux of the distention medium during panoramic hysteroscopy. J Reprod Med 1986; 31(7): 592–4.
- Breitkopf D. 'No Frills' Hands-on operative hysteroscopy. ACOG; Philadelphia, 2004, San Francisco, 2005, Chicago, IL 2005, Las Vegas, 2006.
- Kremer C, Duffy S, Moroney M. Patient satisfaction with outpatient hysteroscopy versus day case hysteroscopy: randomised controlled trial. BMJ 2000; 320(7230): 279–82.
- 13. Marsh F, Kremer C, Duffy S. Delivering an effective outpatient service in gynaecology. A randomised controlled trial analysing the cost of outpatient versus daycase hysteroscopy. BJOG 2004 111(3): 243–8.
- 14. US Department of Health and Human Services Centers for Medicare and Medicaid Services. Physicians Fee Schedule Relative Value Units 2006.
- Brooks PM. Cosgrove Lecture. American College of Obstetricians and Gynecologists, Annual Clinical Meeting. Philadelphia, 2004.
- Readman E, Maher PJ. Pain relief and outpatient hysteroscopy: a literature review. J Am Assoc Gynecol Laparosc 2004; 11(3): 315–319.

- 17. Farrugia M, Hussain SY. Hysteroscopic endometrial ablation using the Hydro ThermAblator in an outpatient hysteroscopy clinic: feasibility and acceptability. J Minim Invasive Gynecol 2006; 13(3): 178–82.
- 18. Leclair C. Anesthesia for office endometrial procedures: a review of the literature. Curr Women's Health 2002; 2: 429–433.
- Physician's Desk Reference. Mountvale, NJ: Thompson PDR, 2004 58: 630–631.
- Eastman NJ, Hellman LM. Williams Obstetrics, 13th edn. New York: Appleton-Century-Crofts, 1966. From Moore Anesthetic Technique for Obstetrical Anesthesia and Analgesia, Ch 18, 452.
- 21. Albright GA. Cardiac arrest following regional anesthesia with etidocaine or bupivacaine. Anesthesiology 1979; 51: 285–7.
- 22. Stubblefield PG. Control of pain for women undergoing abortion. Int Gynecol Obstet suppl 1989; 3: 131–140.
- 23. Glick E. Paracervical and lower uterine field block anesthesia for therapeutic abortions and office D&C. In: Eleventh Annual Convention of the National Abortion Federation. Salt Lake City, Utah: National Abortion Federation, 1987.
- 24. Abbott JA, Hawe J, Garry R. Quality of life should be considered the primary outcome for measuring success of endometrial ablation. J Am Assoc Gynecol Laparosc 2003; 10(4): 491–5.
- Donovan JJ. Review of 500 cases of endometrial ablation with the use of the HTA system for the treatment of menorrhagia. J Minim Invasive Gynecol 2006; 13(5): S55.
- 26. Kahn BS, Flinn A. Efficacy of hydrothermal ablation in patients with abnormal uterine bleeding. J Minim Invasive Gynecol 2006; 13(5): S102.
- 27. Talvacchia J, Iddenden J. Five year clinical experience with the HTA endometrial ablation system. J Minim Invasive Gynecol 2006; 13(5): S102–3.
- 28. Goldrath MH, M, Husain M. Endometrial ablation by hysteroscopic instillation of hot saline solution. J Am Assoc Gynecol Laparosc 1997; 4: 235–240.
- Corson SL. A multicenter evaluation of of endometrial ablation by Hydro ThermAblator and rollerball for treatment of menorrhagia. J Am Assoc Gynecol Laparosc 2001; 8(3): 359–67.
- Rosenbaum SP, Fried M, Munro MG. Endometrial hydrothermablation: a comparison of short-term clinical effectiveness in patients with normal endometrial cavities and those with intracavitary pathology. J Minim Invasive Gynecol 2005; 12(2): 144–9.
- Soysal EA, Soysal SE, Vicdan K. Thermal balloon ablation in myoma-induced menorrhegia under local anesthesia. Gynecol Obstet Invest 2001; 51: 126–33.
- 32. Sabbah R, Desaulniers G. Use of the NovaSure Impedance Controlled Endometrial Ablation System in patients with intracavitary disease: 12-month follow-up results of a prospective, single-arm clinical study. J Minim Invasive Gynecol 2006; 13(5): 467–71.

- Glasser MH, Zimmerman JD. The HydroThermAblator system for management of menorrhagia in women with submucous myomas: 12- to 20-month follow-up. J Am Assoc Gynecol Laparosc 2003; 10(4): 521–7.
- Glasser MH. Endometrial ablation and hysteroscopic myomectomy by electrosurgical vaporization. J Am Assoc Gynecol Laparosc 1997; 4(3): 369–374.
- Wegienka G, Baird DD, Hertz-Picciotto I et al. Self-reported heavy bleeding associated with uterine leiomyomata. Obstet Gynecol 2003; 101: 431–437.
- Rupp CC, Nagel TC, Swanland DJ, Bischof JC, Coad JE. Cryothermic and hyperthermic treatments of human leiomyomata and adjacent myometrium and their implications for laparoscopic surgery. J Am Assoc Gynecol Laparosc 2003; 10(1): 90–8.
- 37. Gurtcheff SE, Sharp MT. Complications associated with global endometrial ablation: the utility of the MAUDE database. Obstet Gynecol 2003; 102(6): 1278–82.
- 38. http://fda.gov/cdrh/maude.html Search by individual device name.

Endometrial cryoablation

Andrea S Lukes

INTRODUCTION

The challenge for all endometrial ablation technologies is the unique and impressive ability of the endometrium to regenerate. The endometrium is predominantly an endocrine organ that responds to a sequence of orchestrated hormonal signals which then result in normal menstruation. In addition, there is growing evidence regarding the important role of both hematologic and immunologic factors within normal menstruation. The goal of endometrial ablation is to destroy the endometrium. The now well-established technology of cryoablation is one of many technologies designed to destroy the endometrium. Cryoablation provides an effective treatment for heavy menstrual bleeding and other menstrual disorders. Cryoablation is unique in that it uses freezing as a method to destroy the endometrium, compared to other technologies which either remove or destroy the endometrium using heating or microwave energy. Furthermore, it provides an opportunity for physicians to transition this procedure to an office setting.

This chapter:

- (1) Reviews the history of endometrial cryoablation.
- (2) Discusses the clinical experience with Her Option Cryoablation Therapy (American Medical Systems).
- (3) Discusses the Her Option device and disposable.
- (4) Provides a review of ultrasound use during endometrial cryoablation.
- (5) Summarizes the unique reasons why endometrial cryoablation is ideally suited for in-office procedures.

HISTORY OF ENDOMETRIAL CRYOABLATION

Cryosurgery is used to treat many disorders: e.g. breast, prostate, liver, and kidney malignancies. Its use within gynecology began as a treatment for chronic cervicitis and

cervical dysplasia. The first reported use of cryosurgery within the uterine cavity to destroy the endometrium was presented by Cahan and Brockunier in 1967.¹

Cahan and Brockunier at Memorial-Sloan-Kettering Cancer Center reviewed 5 years of their experience using cryosurgery to treat the endometrium. The equipment used by Cahan for endometrial cryoablation included a probe that was curved, yet rigid, and made of stainless steel (Figure 24.1). Liquid nitrogen was used for cooling. The heating phase or thawing was done with the same probe, and it is one of the first devices that not to rely on spontaneous rewarming. Cahan described two cryoablations performed in hysterectomy specimens in addition to six clinical cases.

During the clinical cases, the cervix was minimally dilated to a No. 6 Hegar. Several freeze and heat cycles were recommended for development of tissue necrosis; specifically, five separate positions were used (separate freezes in both cornua, two closer to midline, and one in the endocervix). Furthermore, perioperative antibiotics were given. It was recommended in this first article on endometrial cryoablation that females undergoing treatment should no longer desire children, given that treatment may compromise future pregnancies. This recommendation is true decades later.

- Other important findings from Cahan's work are:
- endometrial cryoablation is *safe*
- endometrial cryoablation improves symptoms by reducing menstrual flow
- thicker endometrium probably reduces the clinical affect of the ablation.

These basic principles set forth by Cahan in 1967 continue to be proved today. The greatest limitation of the technology, as used by Cahan, is that liquid nitrogen was not easy to control and it was not easy to monitor the temperatures or the process of freezing.

Additional studies on endometrial cryoablation were carried out by Droegemueller and colleagues,²⁻⁵ including attempts at destruction of endometrium to treat heavy

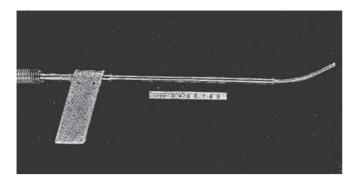


Figure 24.1 Uterine cryosurgical probe. (Reproduced with permission from Cohan and Brockunier.¹)

menses and investigation of permanent sterilization. Freon was the first substance used for freezing, but was found to be inadequate. Nitrous oxide was investigated next, which brought the probe temperature to -50° C.² Although some scarring was noted, follow-up studies showed areas of endometrium that were not destroyed. Findings included necrosis limited to the endometrium with minimal impact on the myometrium,² which is critical to the success of endometrial cryoablation. A key limitation with this method was the inability for the probe to reach low enough temperatures to assure more thorough endometrial destruction. Owing to limited scarring, it was also determined that this technology was not suited for permanent contraception.

Interestingly, Droegemueller used two different cryoprobes in his later work using nitrous oxide as the cooling agent:³ one probe was curved and smaller, at 0.5 cm in diameter, and was designed to be used in the corneal regions; the second probe was straight and 1.0 cm at its widest diameter, and was designed to be used for the anterior and posterior walls in the midline of the uterus (Figure 24.2). This allowed Droegemueller to address the need for reaching all areas of the endometrium. Probably, however, incomplete destruction of the endometrium resulted from not having cold enough temperatures.

An in-depth review of cryosurgery theory is beyond the scope of this chapter, although, as mentioned, the early work of both Cahan and Droegemueller used temperatures that were not cold enough for effective depth of tissue destruction. An effective ablation technology must destroy a tissue that has an impressive ability to regenerate. In general, for cryosurgery, the minimum temperature needed to destroy endometrial tissue is below –20 to –30°C. An excellent description of the *physiology* of cryosurgery and how it results in cell death is provided by Droegemueller et al:⁵

Cryosurgery causes coagulation necrosis of the tissue due to the severe biochemical and biophysical

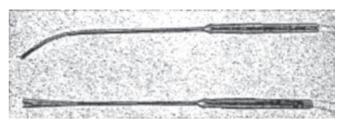


Figure 24.2 Endometrial cryoprobes.

changes produced by the subfreezing temperatures. Primarily, a physical rupture of the cell wall is produced by the formation of intracellular and extracellular ice crystals. Subsequently, abrupt changes in pH and electrolyte concentrations occur with alterations of the cell membrane and cytoplamic structures. Secondarily, there is avascular necrosis of the endometrium produced by circulatory changes due to capillary obstruction and stasis.⁵

The three dominant theories related to the mechanism of cell death during cryosurgery are intracellular ice formation, dehydration, and ischemia. Probably, all three of these contribute to the process of cell death. Beyond the actual temperature applied to the tissue, there are factors which impact outcome, including the type of tissue, whether cells are normal, inflammatory, or malignant, but also the *rate* of freezing and thawing.

The next development with endometrial cryoablation occurred in the early 1990s. Pittrof and Majid⁶ evaluated 15 instances where cryosurgery was performed in cases where a hysterectomy was indicated. In these cases, a uterine distention medium, saline, was used to improve the results of endometrial ablation using cryosurgery technology. It was clear that contact between the probe and the endometrium was important to the success, and liquid allowed for better 'contact' compared to air or space. The method of freezing used by Pittrof involved nitrous oxide, and was based on the principle of the expansion of this gas. Temperatures were as low as -70°C and approximately -40°C at the interface between ice and the endometrium. This 'feasibility' study provided additional confirmation that cryoablation technology is safe. Saline is still used with Her Option In-Office Cryoablation Therapy in limited fashion and may provide some advantage for visualization and cryozone propagation.

Finally, an important breakthrough for endometrial cryoablation occurred with the success of a new closed-loop device made by CryoGen Inc. (San Diego, CA). Dobak and colleagues presented a series of manuscripts describing this technique.^{7–9} This device offered important advantages over older systems that had warmer temperatures and/or very high pressures. Additionally, prior systems were based on either liquid nitrogen or expansion

of high-pressure gases such as nitrous oxide or argon with the coolant exhausted to the atmosphere. The new closedloop cryosurgical device solved these issues.

HER OPTION CRYOABLATION SYSTEM THERAPY

The system relies on the Joule–Thomson effect, which involves expansion of gases under pressure through an opening, resulting in marked reduction in temperature. The gas used is a proprietary compressed gas mixture that generates temperatures between –90 and –120°C at the tip of the probe. These cold temperatures help achieve more complete destruction of the endometrium, which is an improvement from earlier systems. The compressor console is small and portable and supports use of the system for in-office procedures. Furthermore, the narrow probe also further supports in-office use, given that cervical dilation is not necessary. This system gained approval from the US Food and Drug Administration (FDA) in April 2001. It is now called the Her Option In-Office Cryoablation Therapy (American Medical Systems).

A large prospective, randomized trial in approximately 300 females with heavy menstrual bleeding using this new technology was published in 2003. The trial randomized eligible females with heavy menses to treatment with either endometrial cryoablation or electroablation. Subjects were randomized at a ratio of 2:1 (193 subjects within the cryoablation group, and 86 within the electroablation group). Heavy menses was defined by a semiobjective pictorial blood assessment chart (PBAC) score >150. Pretreatment was used in this study, with a single 1-month dose of a gonadotropin-releasing hormone (GnRH) agonist. This was administered 3–4 weeks before treatment, given without consideration of menstrual cycle stage.

Success for this trial was defined as a PBAC score of ≤75, similar to comparable technologies in other pivotal clinical trials. Although an intent-to-treat analysis is not provided, those subjects evaluated at 12-month follow-up (156 subjects within the cryoablation, 72 within electroablation) showed significantly lower PBAC scores of ≤75 in the majority of evaluated subjects (85% of cryoablation group and 89% of electroablation group). Measures used for quality of life also showed improvement in both treatments.

Minimal anesthesia was required in this trial with cryoablation compared to the electroablation system (Figure 24.3). This finding is unique to cryoablation compared to other pivotal trials using heat technologies for endometrial ablation. Cryoanesthetic properties associated with the technology may be a factor in the need for

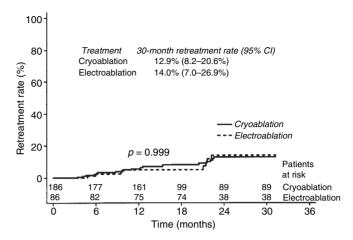


Figure 24.3 Retreatment rates and 95% CI for all patients receiving stydy treatment. Overall retreatment experience and 30-month point estimate of retreatment rate were determined by Kaplan-Meier analysis using all available retreatment status data, including those from patients monitored for longer than 24 months. Indicated p value is for comparison of overall retreatment experience by log-rank test. (Reproduced with permission from Duseba et al.¹⁰)

minimal anesthesia and patient comfort. Furthermore, the percentage of females who underwent cervical dilatation was significantly different, with 11% of females who received cryoablation vs all or 100% of females who received electroablation (p = 0.001). Both minimal anesthesia and little to no cervical dilatation are ideally suited for in-office procedures.

Follow-up analysis on the durability of findings from this large clinical trial was published by Townsend et al. in 2003. 12 As would be expected, follow-up is incomplete because of patient drop out, but the results for both groups, cryoablation and rollerball electroablation, are good at 2 years follow-up. Specifically, in 94 evaluable subjects who received cryoablation and in 43 evaluable subjects who received electroblation, the percentage that did not have abnormal bleeding was 94% and 93%, respectively. The authors do not define abnormal bleeding within the publication (pers comm, this was determined by patient assessment of menstrual levels). Although some bias may exist in that those subjects with favorable outcomes may be more likely to cooperate with follow-up, it is important to recognize that a very significant proportion of both groups were doing well at 2 years post-treatment.

This study by Townsend also provides interesting follow-up information on the proportion of subjects who were *re*treated. Of the subjects who received cryoablation, 7% underwent hysterectomy and 2.7% had a repeat ablation. In the subjects who received electroablation, 8.1% underwent hysterectomy and 1.2% underwent

repeat ablation. The median risk for retreatment was 20.7 months, (range 0.5–31.3 months). At 30 months, retreatment rates were similar: 12.9% for cryoablation and 14.0% for electroablation.

The Her Option Office Cryoablation Therapy System is the only endometrial cryoablation available

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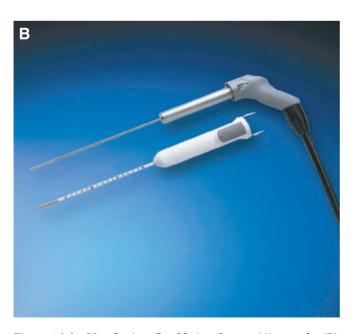


Figure 24.4 Her Option Cryoblation System (A) console; (B) cryoprobe.

within the USA. Furthermore, it is FDA approved for *in-office* use.

HER OPTION CRYOABLATION SYSTEM EQUIPMENT

As seen in Figure 24.4, the console for this system is small and portable; furthermore, the cryoprobe is narrow, measuring 5.5 mm. This allows for minimal discomfort and usually no cervical dilation during treatment. The cryoprobe is disposable and sterile. In addition, the probe has a tip surface monitoring system that allows for direct temperature measurements during freezing and heating cycles. This feature provides the user with continuous temperature readings throughout the freezing and rewarming phases of treatment. Also, the probe tip is hyperechoic, allowing visualization of probe placement via ultrasonography. The probe has a saline flush port, allowing injection of small amounts of sterile saline that may (1) help with visibility during ultrasound monitoring and also (2) increases contact between the endometrium and the probe, which may improve outcome.

The system is easy to use – with an option for voice automation that can guide the physician through the procedure. The cryoprobe has only two buttons, a minus (–) for freezing and a plus (+) for warming. Only basic ultrasound skills are needed and comfort with performing office-based procedures.

FREEZE PATTERNS

During the first large trial with the Her Option Cryoablation System, the investigators used a 4-minute freeze in one cornua followed by a 6-minute freeze in the contralateral cornua (4×4 freeze pattern). As clinical experience has grown, more extensive or slightly longer freeze times have been shown to improve the reduction of symptoms of heavy menstrual bleeding. Often, users perform longer freezes, up to 7 or 8 minutes, and may also perform a central fundal freeze and/or a pull-back freeze (the cryoprobe is pulled back 2 or 3 cm) in larger cavities.

In order to develop a protocol to help clinicians to use this device most effectively, a second large clinical trial was begun by American Medical Systems in late 2004. Follow-up is ongoing at the time of writing. Briefly, this study involves seven different sites within the USA. The primary goal for this study is to evaluate extended freeze regimens during endometrial cryoablation. The author of this chapter was a principal investigator – and both amenorrhea and overall bleeding patterns are improved compared with the first large clinical trial.

ULTRASOUND MONITORING WITH ENDOMETRIAL CRYOABLATION

Ultrasound monitoring is recommended during cryoablation. This safety feature allows for increased confidence with cryoprobe placement, as well as real-time measurements of 'effect' in that the dimensions of the iceball can be visualized. Distance of the leading edge of the iceball from the serosal surface of the uterus is also recorded. The iceball produced during Her Option In-Office Cryoablation Therapy has a predictable size, which aids the clinician in development of a tailored freeze regimen for individual patients based on uterine dimensions. Certainly this enhances the safety of the endometrial cryoablation procedure, but also allows the clinician to show and describe to the subject what she is experiencing during the procedure.

Research based on cryablation in extirpated uteri has provided information relating the size of the iceball created during this procedure.⁸ This study confirmed that the iceball created is symmetric, even in the face of significant myomatous disease. Furthermore, specimens were sectioned and stained with tetrazolium red to determine regions of non-viable tissue. The average maximal diameter of non-viable tissue was 24 mm (range 21.4–28.4 mm), with depth of tissue destruction ranging from 6 to 12 mm. The average size of the cryozones is shown in Figure 24.5.

As part of the previously mentioned extended freeze pattern study begun in 2004 conducted at seven sites within the USA, Lukes et al¹³ evaluated the use of three dimensional (3D) imaging during the procedure (presentation, 2005 AAGL meeting). We found that 3D imaging provided superior results compared with two dimensional (2D) imaging – and practices using a 3D 'sweep' that could be manipulated *after* the procedure to measure closeness to the serosa and measures of iceball dimension. An example of this is provided in Figure 24.6. We relied on the 2D images for real-time feedback during the procedure regarding safety. Once the procedure was stopped

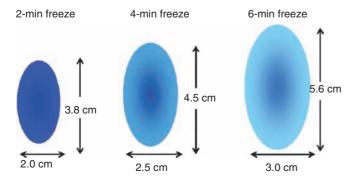


Figure 24.5 Ice balls.

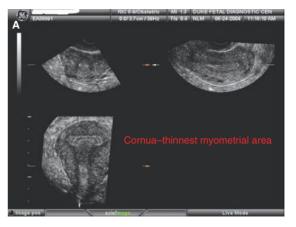








Figure 24.6 Ultrasound monitoring with endometrial cryoblation.

early due to inadequate visualization, not because the iceball was close to the serosa.

The 3D images illustrate that the most narrow part of the myometrial wall is at the corneal regions. Also, at Duke University we never found that the leading edge of the iceball reached within 2 mm of the serosa (including up to 10 minutes in one area). At the leading edge, however, this is not destructive to tissue – it is at least 2 mm back from this edge that destroys tissue. Although we did perform 3D images, these had limited impact during the procedure, other than being a topic of great interest for both clinician and patient.

PERFORMING ENDOMETRIAL CRYOABLATION IN-OFFICE

The Her Option In-Office Cryoablation Therapy system is ideal for in-office procedures. The unique analgesic properties of cryotherapy, small-diameter probe size, and the ease of use make it appropriate for use in an office setting. Oral or intramuscular (IM) analgesia and/or sedation with and without paracervical block has been demonstrated to be highly effective, and patients are typically discharged home within an hour of completion of treatment.

Reimbursement to the physician for this procedure is now favorable throughout the USA. The procedure is generally approved by payers for in-office use under current procedural terminology (CPT) code 58356. Also, the manufacturer provides assistance to clinicians seeking reimbursement.

The author has experience with approximately 100 procedures using this system, and favors only oral pain medication (non-steroidal for postoperative cramping and low-strength benzodiazepine for a calming/anxiolytic effect). There has never been a requirement for cervical dilation. Furthermore, the author recommends a onedose treatment with an oral antibiotic perioperatively to minimize risk of infection, in line with current ACOG (American College of Obstetricions and Gynecologists) recommendations. As with all global ablation procedures, endometrial sampling should be done prior to the procedure with documented normal results. Childbearing must be complete. Survey data (unpublished) was collected on approximately 70% of these cases performed by Lukes at Duke University – this showed that less than 8% (6/71) of females failed treatment (needed for retreatment or patient dissatisfaction). Follow-up ranged from 4 months to 5 years.

In summary, the technology of endometrial cryoablation has advanced over the last 40 years. The Her Option Cryoablation Therapy System provides clinicians with an effective treatment for abnormal uterine bleeding in females who have completed childbearing. Compared to the global ablation devices using heating or microwave technologies, this system is the best suited for in-office treatment.

References

- Cahan WG, Brockunier A Jr. Cryosurgery of the uterine cavity. Am J Obstet Gynecol 1967; 99: 138–53.
- Droegemueller W, Greer BE, Makowski EL. Preliminary observations of cryocoagulation of the endometrium. Am J Obst Gynecol 1970; 107: 958–61.
- Droegemueller W, Greer B, Makowski E. Cryosurgery in patients with dysfunctional uterine bleeding. Obstet Gynecol 1971; 38: 256–8.
- Droegemueller W, Makowski E, Macsalka R. Destruction of the endometrium by cryosurgery. Am J Obstet Gynecol 1971; 110: 467–9.
- Droegemueller W, Greer BE, Davis JR et al. Cryocoagulation of the endometrium at the uterine cornua. Am J Obstet Gynecol 1978; 131: 1–9.
- Pittrof R, Majid S. Endometrial cryoablation using 0.9% saline as a uterine distension medium: a feasibility study. Minim Invasive Ther 1992; 1: 283–286.
- Dobak JD, Ryba E, Kovalcheck S. A new closed-loop cryosurgical device for endometrial ablation. J Amer Assoc Gynecol Laparosc 2000; 7: 245–9.
- 8. Dobak JD, Willems J. Extirpated uterine endometrial cryoablation with ultrasound visualization. J Amer Assoc Gynecol Laparosc 2000; 7: 95–101.

- 9. Dobak JD, Willems J, Howard R, Shea C, Townsend DE. Endometrial cryoablation with ultrasound visualization in women undergoing hysterectomy. J Am Assoc Gynecol Laparosc 2000; 7: 89–93.
- Duleba AJ, Heppard MC, Soderstrom RM, Townsend DE. A randomized study comparing endometrial cryoablation and rollerball electroablation for treatment of dysfunctional uterine bleeding. J Am Assoc Gynecol Laparosc 2003; 10: 17–26.
- Higham JM, O'Brien PM, Shaw RW. Assessment of menstrual blood loss using a pictorial chart. Br J Obstet Gynaecol 1990; 97: 734–9.
- Townsend DE, Duleba AJ, Wilkes MM. Durability of treatment effects after endometrial cryoablation versus rollerball electroablation for abnormal uterine bleeding: two-year results of a multicenter randomized trial. Am J Obstet Gynecol 2003; 188: 699–701.
- Lukes A. 3-D Ultrasound imaging during extended freezes for cryoblation. AAGL meeting, November, 2005.

25

Vesta: distensible multielectrode balloon endometrial ablation

Kevin Jones

INTRODUCTION

The Vesta system (Vallylab, Boulder, CO) is no longer available commercially. However, before it was removed from clinical practice, it was assessed in a randomized controlled trail (RCT) where it was compared with electrosurgical endometrial ablation in the treatment of dysfunctional uterine bleeding (DUB). It has also been evaluated in a long-term follow-up report. In both these studies the safety features, cost-effectiveness, and efficacy were comparable to the gold standard minimum access technique for DUB.

INSTRUMENTATION AND ANCILLARY DEVICES

The Vesta system consists of an electrosurgical generator and a handpiece that fits into the uterine cavity (Figure 25.1A–C). Its components are:

- (1) A Valleylab force II electrosurgical generator set to supply 'pure cut' mode (undampened) current at 45–50 W (Figure 25.1A).
- (2) A disposable handset for the introduction of an electrode carrier.
- (3) A cable connecting the handset to the generator (Figure 25.1B)
- (4) A patient return electrode pad.
- (5) A controller to monitor and distribute the electrical energy (Figure 25.1C).

The silicone inflatable electrode pad carry has an inverted triangle shape that unfurls when its insertion sheath is withdrawn.

The through tube traverses the center for access to the uterine cavity, while the carrier is in place to check for potential perforation or residual space. There are six ventral and six dorsal flexible electrode plates covering the surface of the carrier, each with its own thermistor. The

controller functions in two phases: warm-up and treatment. The monitor generates output as well as the temperature and impedances of the 12 electrodes throughout both phases.

If an impedance for any one electrode is too high, indicating poor tissue contact, the control will not permit treatment to begin. The electrode is monitored three times per second and the generator will energize the electrode, that is farthest below its set point temperature each cycle. Warm-up is programmed to occur within 3 minutes. The controller automatically shifts to 4-minute treatment phase as soon as all electrodes have reached their set points and ends the procedure when treatment is completed.

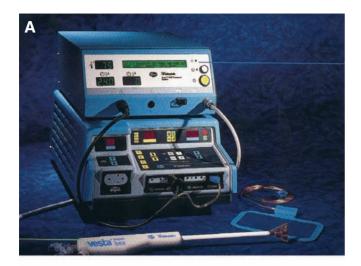
SAFETY FEATURES

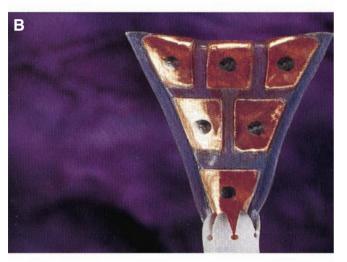
- (1) The electrode balloon expands to fit the uterine cavity, ensuring a uniform depth of desiccation.
- (2) The silicone balloon is properly positioned and the uterine wall is intact. The through tube should not accept air.
- (3) A stationary electrode system reduces the risk of uterine perforation while the electrode is activated.
- (4) The electrosurgical energy moves through the endometrium, allowing the minimum amount of power required to be used.
- (5) The system provides continuous and automatic monitoring of temperature (measured three times per second), electrical power, and electrode and electrode tissue impedance.

PRACTICAL ASPECTS OF TREATMENT

Technique

The cervical canal is dilated to 9–10 mm. The handset (the sheath containing the electrode balloon) is introduced





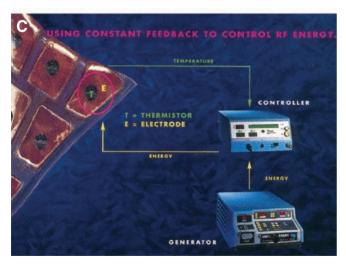


Figure 25.1 The Vesta system: (A) electrosurgical generator; (B) cubic; and (C) controller.

into the uterine cavity and advanced until its tip reaches the fundus. The sheath is withdrawn, and this deploys the silicone balloon, which is then inflated with 8–12 ml of air. This brings the 12 electrodes into contact with the

uterine wall. An attempt is then made to introduce air into the through tube. If the carrier is properly positioned and the uterine wall is intact, the through tubes should not accept air; the controller is turned on and indicates a ready condition when it has checked the generator output and all connections. Warm-up is initiated by pressing a start button. The operator has to maintain pressure on the syringe plunger attached to the carrier inflation port throughout the warm-up and treatment phases. The electrosurgical generator is set at 40-45 W in an unimpeded waveform. The warm-up time lasts approximately 1 minute and this is followed by a 4-minute therapeutic phase radiofrequency (RF) energy applied to the electrodes by the generator. The electrodes apply the RF to the tissue, which is then returned to the generator by the patient return electrode pad. The RF current heats the uterine tissue, causing the endometrial ablation.

Because the myometrium near the tubal ostia is relatively thin, the corneal electrodes have set temperatures of 72°C whereas the remaining eight electrodes have set temperatures of 74°C. Automated maintenance of these temperatures for 4 minutes with constant distention of the carrier lumen to keep the electrodes in intimate surface contact produces uniform thermal destruction to a depth of 4–5 mm in the myometrium. When the controller ends treatment, the silicone balloon is deflated and the handset is withdrawn without resheathing the carrier.

Endometrial preparation

In clinical evaluation studies conducted in Europe and in the USA, investigators were free to use timing alone, oral contraceptive cycling, depot progesterones, or gonadatropin-releasing hormone (GnRH) agonists.³ In the studies carried out in Mexico and the USA, oral contraceptives were taken for at least 2 weeks and discontinued for at least 1 week before the procedure to allow for endometrial sloughing.^{1,4}.

Analgesic requirements

In the clinical studies to evaluate the Vesta system^{1,3} general anesthesia was used five times as commonly as paracervical block under sedation. Where a paracervical block was used, it was commonly supplemented with topical mepivacaine injected into the electrode carrier through tube before inflation. During the RCT, general or epidural anesthesia was used in only 16.7% of Vesta procedures; 20% of rollerball resection group (R-R) procedures were done with a paracervical block and intravenous sedation. No difference in result was noted in either case as a function of anesthesia employed.

EX-VIVO AND IN-VITRO STUDIES

Laboratory and initial clinical testing was carried out to establish safety parameters prior to in-vivo studies and laboratory test conducted on animal tissue and extirpated uteri.⁴ Once the safety parameters had been established, in-vivo studies were performed. These studies took place in Mexico, the UK, and the Netherlands in 30 women scheduled for hysterectomy. Uterine serosal temperatures were monitored in 17 women during the procedure. Treatment variables ranged from 30 to 45 W, 90 to 240 seconds' duration, and 65 to 75°C. After hysterectomy, the uterus was dissected into sections to determine the depth of narcosis with six alternate sections analysed histochemically. The extent and depth of tissue narcosis were measured to establish the optimum preselected temperature time and power.

Initial findings

No significant serosal temperature increases were reported and no complications occurred as a result of the procedures. The extent of narcosis varies, depending on the treatment variables and the degree to which the electrode balloon conformed to the uterine cavity. Residual narcotic endometrium measured approximately 0.2 mm. The depth of myometrial narcosis varied from 1 to 6 mm, with 88% of dissections averaging from 2 to 4 mm. An intermediate layer of cells between the viable and nonviable tissue was evident. This intermediate layer of cells has been excluded from measurements of depth of narcosis and would be expected to slough.

In-vivo studies

With regard to inclusion and exclusion criteria used in the clinical evaluation studies, all the patients in the initial in-vivo studies were screened by preoperative hysteroscopy or ultrasound and endometrial biopsy to rule out abnormal uterine cavities and unexplained malignancy or atypical hyperplasia.⁴

Subsequently, a multicentered single-armed evaluation study was carried out.³ Patients were admitted to the study if they failed to respond to medical therapy and they had no systemic or local cause for their excessive bleeding. All the patients were booked to undergo a hysterectomy; patients were generally excluded if they had distorted uterine cavity or a sounding length >10 cm but 12 women with <3 cm submucosal myomas were elected to have laser myomectomies immediately preceding ablations.

A multicenter prospective RCT was then carried out.¹ Women between the ages of 30 and 49 years old were

recruited. All the patients had completed their families and were using non-hormonal contraception or one of the partners had been sterilized. Women with Follicle stimulating hormone (FSH) levels > 40 mu/ml were excluded from the study group. A previously validated pictorial blood loss assessment chart (PBAC) was used to quantitly monthly menstrual blood loss. Women used the same brand of sanitary pad or tampons (New Freedom Superior or Tampax Superior). After 3 months of completing a menstrual diary, if the score was >150 the patients were then evaluated with hysteroscopy or ultrasonography. Patients with distorted uterine cavities, myomas, or polyps or a cavity in excess of 9.75 cm were excluded from the study. Other exclusion criteria included:

- (1) Significant systemic medical disease.
- (2) Pregnancies.
- (3) Pelvic inflammatory disease.
- (4) Carcinoma.
- (5) Clotting studies.
- (6) Previously unsuccessful endometrial ablation.
- (7) Myomectomy.
- (8) Uterine reconstruction/hormonal therapy within 3 months of enrollment.

All patients had endometrial sampling performed, and the findings of any hyperplasia were causes for exclusion.

THERPAPEUTIC STUDIES

Follow-up data for 3–24 months is available on 246 patients recruited into the multicenter single-armed evaluation study conducted in Europe and Mexico.³ Stability data from the study have been analyzed on the same 117 patients at 6, 12, 18, and 24 months. At each time interval, the classification and blood loss has been checked by menstrual diaries' sampling. During the 24-month follow-up period, the proportion of patients who reported amenorrhea, hypomenorrhea, and eumenorrhea remained constant. In particular, the amenorrhea rate remained at between 40 and 45%.

During the randomization process for the trial carried out in the USA,¹ 126 patients were allocated endometrial resection and coagulation, with 150 randomized to Vesta ablation. In the Vesta group, 144 patients reached the point of anesthesia and 132 patients were treated according to the study protocol. Of these, 122 had 12-month follow-up. In the R-R group, 123 patients were treated according to the study protocol; of these 122, had a 12-month follow-up.

Table 25.1 shows the results of the US RCT of Vesta vs rollerball resection at 12 months. In the Vesta-treated group 87% of patients had menstrual scores <75 and did not require any additional treatment during the initial 12 months following treatment, whereas 83% of patients in the R-R group had scores <75 at the 12-month follow-up visit. The amenorrhea (defined as a menstrual score of 0) was 31% in the Vesta group and 35% in the R-R group.

Follow up data

Long-term follow-up data on the patients treated at the Royal Surrey County Hospital, Guildford, UK² were compared with a life-table analysis of patients, during the initial 24 months, who took part in the European trial.³

A cohort of 25 patients were followed up prospectively for an average of 4.2 (3.5–5) years. The patients were asked to complete a short questionnaire detailing their medical history since the initial Vesta system procedure, together with a validated PBAC. Menstrual status was defined according to the PBAC score. Amenorrhea was defined as a PBAC score of 0, spotting 1–10, hypomenorrhea 11–30, eumenorrhea 31–75, and menorrhagia as >75. A life-table analysis of the patients enrolled into the European evaluation study has also been carried out (Table 25.2).

The mean age of the patients was 46.3 years old, compared with 42 years old at the time of the original operation. Of the 25 patients, a transcervical endometrial resection of the endometrium had to be carried out as a second operation in two patients because of continuing menorrhagia, and one patient had a PBAC of >150 but did not want further treatment at 5 years. Therefore, treatment with the Vesta system failed to relieve the original symptoms or avoid second surgery in 3/25 (12%) of the patients in the long term. Two (8%) patients were eumenorrheic, 6 (24%) had hypomenorrhae, and 14 (56%) patients were amenorrheic (five of these women

Table 25.1 Randomized controlled trial of Vesta vs rollerball resection – US clinical study results at 12 months

	Vesta	R/R	P value
Age (years)	41 (±4.19)	40.1 (±4.7)	0.11
Pretreatment PBAC	520 ± 600	447 (±316)	0.23
Post-treatment PBAC	18 ± 37	28 (±60)	0.13
Patients with PBAC <75	86.9%	83%	0.46
Amenorrhea at 12 months	31.1%	34.8%	0.58

R/R, rollerball resection group; PBAC, pictorial blood loss assessment chart.

Table 25.2 In the whole of Europe 305 patients have been treated as part of the trial, and 192 have been followed up for 24 months, and subjected to life-table analysis	of Europe 305 patient	s have been treated	as part of the trial, a	nd 192 have been follo	owed up for 24 months.	, and subjected to life-ta	ıble analysis
Interval (months) from Vesta treatment	No. of patients	Lost/ withdrawn	Patients with menorrhagia	Probability of developing menorrhagia	Probability of not developing menorrhagia	Cumulative probability of no menorrhagia	Cumulative probability of menorraghia
0–3	305	09	8	0.029	0.971	0.971	0.029
4-6	237	5	9	0.026	0.974	0.946	0.054
7–12	226	~	7	0.032	896.0	0.916	0.084
13–18	211	18	1	0.005	0.995	0.911	0.089
19–24	192	32	1	9000	0.994	906.0	0.094

were >54 years old and were assumed to be menopausal). This represents an 88% success rate.

In the whole of Europe, 305 patients have been treated as part of the trial, and 192 have been followed up for 24 months, and subjected to life-table analysis (Table 25.2).

Instead of presenting a crude success rate, life-table analysis can be carried out. The advantage of this type of analysis is that it takes into account patients who have already undergone reoperation and who have been lost to follow-up at a given time. Table 25.2 shows a life-table analysis of the patients enrolled into the European evaluation study. The cumulative probability of having no menorrhagia is 0.906 during the initial 24 months after the Vesta procedure, whereas the cumulative probability of having menorrhagia is 0.094. From a statistical point of view, the endpoint for life-table analysis should be irreversible, e.g. hysterectomy, rather than a subjective endpoint such as menorrhagia. However, the definition of menorrhagia in this study was quantifiable (PBAC score >150), and therefore acceptable. In this long-term follow-up report, we did not loose data on any patients. Three (12%) of our patients had treatment failures when followed up for >3.5 years, which is similar to the rate at 2 years.

Our long-term results suggest that the efficacy of the Vesta system at 2 years is likley to persist at 3.5–5 years following treatment. The results for the Vesta procedure are better than the results in a life-table analysis of transcervical electrosurgical endometrial ablation patients carried out within this unit.⁵ In that study, the failure rate increased to around 20% at an average of 4 years. The results could reflect the fact that the second-generation devices are less operator- and therefore more skill-dependent. However, the numbers of patients involved in the two studies are very different, and the small numbers in this report limit the clinical application of the information.

COMPLICATIONS

During the single-armed evaluation study,³ no perforations of the uterus occurred. Most patients experienced a serious discharge for 3–5 weeks following treatment, but no cases of endometritis occurred. There were eight device failures during the first 60 attempts at treatment. In these cases, the warm-up phase could not be completed within 3 minutes or the controller detected too much variability in electrode temperatures and the controller would not permit conversion to the treatment phase. These situations were resolved by precalibration of the generators and by allowing a 5 W increment in generator output setting if warm-up cannot be achieved within 3 minutes at 45 W.

One patient experienced painful muscular twitching during treatment in the single-armed evaluation study³ and in 18 cases during the trial carried out in the USA¹. In only one of these cases was it necessary to halt the procedure because of pain. The other patients were simply aware of it. RF current oscillates too rapidly for muscle to respond and, following these adverse events, sources of low-frequency transients were identified in some controllers and then eliminated by more restrictive testing. However, as with all electrosurgical procedure performed in the absence of pharmacologic neuromuscular blockage, minor fasciculations can still occur: typically, in the thigh muscles, on the side where the dispersive pad is applied.

In addition to the two patients who had hysterectomies for hemetometra listed as failures, two other patients developed cervical stenosis and minimal menstrual blood retention that responded to a single cervical dilatation; they both continue to be hypomenorrheic.

During the trial carried out in the USA, there was a total of 16 device failures in 12 of the 144 treatments. The inflatable tip of the Vesta device failed to fully deploy and the electrodes failed to come to satisfactory operating temperatures. One Vesta procedure was halted because the balloon entered what appeared to be a weak cesarean section scar.

There were six adverse events during the electrosurgical procedures in the same trial: two cases of cervical lacerations; one case of hematometra; a fluid deficit of 1300 ml without electrolyte disturbance; one myometritis; and one small fundal perforation.

CONCLUSION

The Vesta system is designed to provide highly predictable repeatable endometrial ablation. It compares favorably with other devices and, prior to its removal from clinical practice for commercial reasons, it was a valid method for the conservative management of menorrhagia. It uses 12 temperature-controlled electrodes to treat all the areas of endometrial lining simultaneously. Each of the electrodes is independently controlled to adapt to differences in perfusion within the individual uteri and conventional electrosurgery is used to treat the endometrium for a preset duration.

The data that was collected while the device was in clinical practice demonstrated that thermoregulated RF endometrial ablation produces comparable results to those reported for hysteroscopic electrosurgical ablation. The results were sustained over a medium-term follow-up period. The amenorrhea rate was 39% and, if the hypomenorrhea rate was included, the success rate was 85.2%. The failure rate at 24 months was 11%.

References

- Corson SL, Brill AI, Brooks PG et al. Interim results of the American Vesta trial of endometrial ablation. J Am Assoc Gynecol Laparosc 1999; 6(1): 45–9.
- 2. Jones KD, Spangler L, Sutton CJG. Endometrial ablation using a distensible multielectrode balloon: a long term follow up report. Gynaecol Endosco 2002; 11(1): 43–7.
- Desquesne J, Gallinat A, Garza-Leal et al. Thermo regulated radiofrequency endometrial ablation. Int J Fertil 1997; 42: 311–8.
- Sonderstrom RM, Brooks PG, Corson SL et al. Endometrial ablation using a distensible multielectrode balloon. J Am Assoc Gynecol Laparosc 1996; 3: 403–7.
- 5. Pooley A, Ewen S, Sutton CJG. Does trans-cervical resection of the endometrium really avoid a hysterectomy?: Life table analysis of a large series. J Am Assoc Gynecol Laparosc 1999; 5(3): 229–35.
- Jones KD, Spangler L, Sutton CJG. Vesta: distensible multielectrode balloon endometrial ablation. In: O'Donovan P, McGurgan P, Prendiville W (eds). London: Greenwich Medical Media; 2003: 121–9.

26

Randomized controlled trials in second-generation endometrial ablation

Paul McGurgan and Peter Joseph O'Donovan

Not wrung from speculations and subtleties, but from common sense, and observation.

T. Browne (1663–1704)

INTRODUCTION

The role of evidence-based practice

In clinical practice, the paradigm of evidence-based medicine currently holds sway. Evidence-based medicine implies not only the application of effective treatments but also their rational use within a comprehensive management framework. One of the paradoxes in the modern surgical management of excessive menstrual blood loss is that it was not until the surgical alternatives to hysterectomy were being evaluated, that a proper critical reappraisal for our existing methods of treatment (both medical and surgical) occurred. Evidence is now classified (Tables 26.1 and 26.2), based on the scientific robustness of the source. A well-conducted randomized controlled trial (RCT) – or preferably a few, thereby increasing the generalizability – is the pinnacle of the evidence pyramid.

Why destroy the endometrium?

The idea of destroying the endometrium and creating an iatrogenic 'Asherman's syndrome' as a treatment for dysfunctional bleeding is not new. Many attempts have been made in the past using a variety of chemical and physical agents – ethanol, formalin, copper sulfate, talc, quinacrine, fibroblast-impregnated sponges, and even radiotherapy. These methods were best characterized by their variable efficacy, and high complication rates, and it is only since the 1980s that endometrial destruction procedures have possessed adequate efficacy and sufficient safety to successfully compete with hysterectomy, as a surgical treatment.

The so-called 'first-generation' techniques (resection,² laser,³ and rollerball⁴) have been extensively evaluated in national audits,^{5,6} RCTs^{7–10} and meta-analysis.¹¹ Indeed, endometrial ablation has been described as 'one of the most carefully evaluated surgical procedures'.¹² However, despite their efficacy, the first-generation methods have a number of drawbacks. They require a skilled hysteroscopic surgeon, and despite having a significantly lower morbidity than conventional hysterectomy, the national audits demonstrated incidences of uterine perforation ranging from 0.6 to 2.5%, and fluid deficits >2 L ranging from 1 to 5%.^{5,6}. Based on these findings, there was a need to develop alternative methods that could compare to the efficacy of the first-generation techniques, but be safer and technically simpler to perform.

Menorrhagia is precisely defined as a menstrual loss of >80 ml per month; population studies have shown that this amount of loss is present in 10% of the population, ¹³ yet, nearly a third of menstruating women consider their periods to be excessive. ¹⁴ This symptom thus creates a significant workload for health services.

For a successful technique, the potential market is huge; menorrhagia is a significant healthcare problem in the developed world. In the United Kingdom alone, 5% of women of reproductive age will seek help for this symptom annually, 15 and by the end of reproductive life the risk of hysterectomy (primarily for menstrual disorders) is 20%. 16 The VALUE study 17 examined outcomes of more than 37 000 hysterectomies performed for benign disease, and reported a mortality of 0.38 per 1000 operations and a serious morbidity of 3% (return to theater, visceral injury, and other life-threatening complications). This study showed that while hysterectomy is a very effective treatment for menorrhagia, it is not without significant

Table 26.1 Classification of Evidence Levels

- Ia Evidence obtained from meta-analysis of randomized controlled trials
- Ib Evidence obtained from at least one randomized controlled trial
- IIa Evidence obtained from at least one well-designed controlled study without randomization
- IIb Evidence obtained from at least one other type of well-designed quasi-experimental study
- III Evidence obtained from well-designed nonexperimental descriptive studies, such as comparative studies, correlation studies, and case studies
- IV Evidence obtained from expert committee reports or opinions and/or clinical experience of respected authorities

Table 26.2 Grades of recommendations

- A Requires at least one randomized controlled trial as part of a body of literature of overall good quality and consistency addressing the specific recommendation (Evidence Levels Ia, Ib)
- B Requires the availability of well-controlled clinical studies but no randomized clinical trials on the topic of recommendations (Evidence Levels IIa, IIb, III)
- C Requires evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities
 Indicates an absence of directly applicable clinical studies of good quality (Evidence Level IV)

complications; indeed, the authors of the VALUE study concluded by stating that the 'various methods of endometrial ablations or resections, would need to meet the current low levels of clinical complications in order to replace hysterectomy.'

THE PRINCIPLES OF SECOND-GENERATION ENDOMETRIAL ABLATION

All of the ablative techniques rely on destroying the endometrium's regenerative capacity (usually this needs a depth of destruction of 4 mm). The devices are all licensed for the treatment of heavy periods due to benign causes in premenopausal women when fertility is no longer wanted. Some manufacturers recommend pretreatment with medications which decrease the endometrial thickness in an effort to improve efficacy. Individual devices vary importantly in the size of uteri they can safely treat and also

whether intracavity pathology (e.g. fibroids) are exclusion criteria.

To provide an estimate for the incidence of women with these features, we can use results from Wilcox et al.'s research which analyzed the indications for women requiring hysterectomy for benign disease. This study found that 29% and 61% of Caucasian and black women, respectively, had coexistent fibroids¹⁸ that would preclude the use of some second-generation ablation treatments.

The role of guidelines

Increasingly in clinical practice, decision making occurs in the context of a framework devised by regulatory bodies such as the National Institute for Clinical Excellence (NICE) in the UK. These clinical guidelines are systematically developed statements which assist clinicians and patients in making decisions about appropriate treatment for specific conditions. The principal aim is to improve the effectiveness and efficiency of clinical care through the identification of good clinical practice and desired clinical outcomes.¹⁹

One of the strengths of these bodies' recommendations is that they have had sufficient quality published data in the form of RCTs to provide mainly grade A recommendations for practice in general. This includes their recommendations on the use of endometrial ablation techniques. Based on the extensive cohort and randomized data for the first-generation techniques, the RCOG (Royal college of Obstetricians and Gynaecologists) Guideline Development Group has stated as a grade A recommendation that 'endometrial ablative procedures are effective in treating menorrhagia'. Of course, this raises the issue of the generalizability of this statement concerning the newer second-generation methods.

THE TECHNIQUES OF SECOND-GENERATION ENDOMETRIAL ABLATION

The current methods of second-generation endometrial ablation are:

- (1) Cryotherapy Her Option, Soprano.
- (2) Fluid balloon Cavaterm, ThermaChoice, MenoTreat.
- (3) Microwave MEA.
- (4) Electrode: mesh NovaSure.
- (5) Interstitial laser ELITT.
- (6) Hydrothermal ablation Hydro ThermAblator.
- (7) Photodynamic therapy in development.

The evidence base supporting the safety and efficacy of these devices is variable (Table 26.3). The clinical trials, (with particular emphasis on any RCTs performed, are discussed below.

Cryotherapy

Cryotherapy is a non-hysteroscopic technique that uses cold temperatures to destroy the endometrium. It can be performed under local, regional, or general anesthesia. The endometrium can be prepared for treatment by giving a gonadotropin-releasing hormone analogue (GnRH-a) or by pretreatment curettage. The cryoprobe is inserted into the fundus of the uterus and cooled to −90°C by perfusing it with liquid nitrogen or a compressed gas mixture to create an iceball. The tip of the probe is placed initially in one cornu, and then in the other, to generate an ice-ball that destroys the endometrial tissue (necrosis temperature is ≤−20°C); this is typically monitored using ultrasound. Each freeze cycle is followed by a thaw cycle, which allows the probe to be removed.

The effectiveness of the treatment was evaluated in an RCT between cryotherapy (Her Option) and rollerball electrosurgery. At 12 months, the success rate (assessed using a pictorial blood loss assessment chart [PBAC]) was 67% (130/193 patients) and 73% (63/86 patients) in the cryotherapy- and electrosurgery-treated patients, respectively. Patient satisfaction with the cryotherapy treatment was 91% at 24 months. Retreatment was reported in 10% (18/186) of patients at 24 months. During the

 Table 26.3
 Published studies on second generation endometrial ablation

Instrument	Type of study
Hydro ThermAblator	RCT
ThermaChoice	RCT
Cavaterm	RCT
MEA	RCT
Novasure	RCT
Vesta	RCT
ELITT	RCT
Her Option	RCT
Menotreat	Cohort
Photodynamic therapy	Case reports

RCT, randomized controlled trial.

RCT, 54% of patients treated with Her Option avoided a general anesthetic.

Fluid balloon –ThermaChoice, Cavaterm, MenoTreat

These devices all share a common mechanism – a balloon is inserted into the endometrial cavity and filled with heated fluid under pressure for a variable time. The fluid, heat, pressure, and time vary according to the device; the net result is endometrial destruction by the conducted heat (Table 26.4). Due to the predefined shape of the balloon, these devices require a regular uterine cavity with size limitations. Vilos et al²³ have published in-vivo work assessing the clinical effectiveness of modifying the various ThermaChoice balloon parameters (pressure and time used). They found that balloon pressure >150 mmHg increased the effectiveness of treatment; however, therapeutic success was not affected or influenced by increasing the duration of treatment from 8 to 12 minutes or more.

ThermaChoice III

The ThermaChoice device involves a handpiece with a catheter, and controller. The catheter is 16 cm long and 4.5 mm in diameter. On the end of the catheter is a latex balloon. The catheter is inserted blindly through the cervical canal to the level of the uterine fundus. The balloon is then inflated to a pressure of 180 mmHg (90–190 mmHg) with 5% dextrose in water. The control unit is then activated, heating the fluid to $87 \pm 5^{\circ}$ C for 8 minutes. The activated cycle will terminate if the pressure drops to 45 mmHg. This protects against inadvertent balloon rupture, or perforation of the uterus.

Marketed by Johnson and Johnson, this device has a large share of the world market. It is easy to use and appears to be safe. ThermaChoice requires an anatomically normal uterine cavity between 4 and 10 cm in

Table 26.4 Fluid balloon devices and specifications

Device	Specifications for treatment
Thermachoice III	Limited to a regular cavity, 180 mmHg, 87°C for 8 minutes
Cavaterm plus	Limited to a regular cavity, 220–240 mmHg, 75°C for 10 minutes
Menotreat	Limited to a regular cavity, 200 mmHg, 85°C for 11 minutes

length. The endometrial preparation used is curettage. The choice of anesthesia is left to the individual surgeon; studies examining the device's suitability for outpatient-based treatment have shown that up to 90% of patients can be treated in this way.²⁴

ThermaChoice was the first of the new second-generation devices to undergo RCT comparison with a first-generation technique.²⁵ When evaluated against the first-generation techniques (specifically rollerball ablation), ThermaChoice was shown to compare favorably,²⁵ beeing significantly quicker to perform (p < 0.05). In spite of a low amenorrhea rate, at 1 year the reported post-treatment menstrual blood loss is significantly decreased in 91% and 85% for the rollerball- and ThermaChoice-treated women, respectively, and more than 85% of women are satisfied with the treatment (Table 26.5).

Cavaterm plus

The apparatus consists of a control unit containing the electronics and the battery source, and a handpiece with the balloon attachment. The balloon-carrying end is 6 mm in diameter, and has a silicone balloon of adjustable length at the distal end. The handpiece unit contains a self-regulating semiconductive ceramic/metal material that automatically maintains the temperature at the desired level (65–78°C). An impeller fan contained in the handle ensures uniform distribution of heat. Once the balloon is placed within the cavity, it is inflated with 5% dextrose and the pressure is maintained at 220–240 mmHg. Heating is maintained for 10 minutes, after which the catheter is withdrawn.

Similar to ThermaChoice, Cavaterm has been compared with a first-generation technique (resection) in an

RCT.²⁶ Women were excluded if they had any intrauterine abnormalities (submucous myomas, uterine septae, suspicion of uterine wall weakness, or uterine cavity length <4 cm or >10 cm) or histologic pathology,

Results showed an amenorrhea rate of 36% and 29% in the Cavaterm and the endometrial resection groups at 12 months, respectively. Both treatments significantly reduced uterine bleeding. The median decrease in Higham PBAC scores at 12 months were significantly higher in women treated by Cavaterm than in women treated by resection (p = 0.006). The rate of women reporting good or excellent satisfaction was 89% in the Cavaterm group and 79% in the resection group at 12 months. Discharge time was significantly lower in women treated by Cavaterm, although postoperative pain at 1 hour was higher. There were no major complications in either group. The authors concluded that Cavaterm thermal balloon ablation was as effective as hysteroscopic endometrial resection in treating menorrhagia, both resulting in a significant reduction in menstrual blood loss and high patient satisfaction.

Menotreat

This device was designed by Ulmsten. There is no need for pretreatment; the silicon balloon heats up to 85°C at a pressure of 200 mmHg for 11 minutes. There is relatively little research published on it. A cohort-based study published by Ulmsten et al. quoted amenorrhea in 10%²⁷ and treatment success in 84% of patients

Microwave - MEA

Microwave endometrial ablation (MEA) was pioneered in the UK by Sharp, who published his first cohort results in 1995.²⁸ The method utilizes the local heating effect

Table 26.5 Results of randomized controlled trials in endometrial ablation – ThermaChoice

	ThermaChoice $(n = 128)$	$Rollerball\ (n=117)$
Procedure time	<30 minutes in 71%	<30 minutes in 29%
General anesthesia used	53%	84%
Perioperative complications	0	4
Postoperative hysterectomy	2	3
Results at 1 year $(n = 239)$		
Mean menstrual diary scores decreased	85.5%	91.7%
Menstrual diary score <100	80.2%	84.3%
Amenorrhea	15.2%	27.2%
Dysmenorrhea decreased	70.4%	75.4%
Satisfaction	85.6%	86.7%

(temperature 75–80°C) of microwaves released from an 8 mm applicator. This gives a consistent, reproducible maximum depth of coagulation of 6 mm at 9.2 GHz frequency,²⁹ hence, it is important that the myometrial thickness is ≥10 mm. Cooper et al. published their results from an RCT comparing MEA to rollerball/resection in 1999³⁰ (Table 26.6).

Cooper's study was performed on a pragmatic basis to enable results to be as generalizable as possible. Therefore, trial exclusion criteria were minimal: patients were deemed eligible for trial entry if they were premenopausal, with no wish for fertility, and had intolerable dysfunctional uterine bleeding (defined in this study as the complaint of menorrhagia in women with normal endometrial histopathology, and a uterine size ≤10 weeks' pregnancy).

All of the women received 3.6 mg goserelin 5 weeks preoperatively in order to promote endometrial thinning (this is now not used routinely as a pretreatment).

Blunt perforation with an inactive hysteroscope or MEA probe occurred to one patient in each group; the MEA patient with perforation declined an attempt at a repeat procedure, and later requested a hysterectomy. The perforation in the rollerball/resection patient caused bleeding into the broad ligament, which was managed intraoperatively by converting to a hysterectomy. A hysterectomy was also required in another of the rollerball/resection-treated patients, who presented 2 weeks after the original procedure with abdominal/pelvic pain.

Rates of satisfaction with and acceptability of treatment were high for both techniques at 12-month follow-up

Table 26.6 Results of randomized controlled trials in endometrial ablation – MEA

	MEA (n = 129)	Rollerball/ resection (n = 134)
Procedure time	11.4 ± 10.5	15 ± 7.2
General anesthesia used	100%	100%
Perioperative complications	17	14
Postoperative hysterectomy	9	12
Results at 1 year	n = 116	n = 124
Mean menstrual diary scores	92%	91%
Menstrual diary score <100	Not noted	Not noted
Amenorrhea	40%	40%
Dysmenorrhea	80%	82%
Satisfaction	77%	75%

(more than 75%), and the results were similar to previous trials of endometrial ablation. Although amenorrhea was not used as an outcome to define success, this was achieved in 40% of treated patients for both techniques. Dysmenorrhea and perimenstrual symptoms also improved in most treated women, with only 4% and 8% of MEA- and rollerball/resection-treated women, respectively, complaining of 'new' pelvic pain after treatment.

At 5-year follow-up,³¹ women allocated to MEA were significantly more likely to be totally or generally satisfied with treatment (86% vs 74%), to find it acceptable (97% vs 91%), and would recommend it (97% vs 89%). Bleeding and pain scores were highly significantly reduced following both MEA and transcervical resection of the endometrium (TCRE), achieving amenorrhea rates of 65% and 69%, respectively. The hysterectomy rate after a minimum of 5 years was 16% in the MEA and 25% in the TCRE arm. On the basis of this RCT, MEA is a more effective and efficient treatment for heavy menstrual loss than TCRE.

MEA has also been evaluated in the outpatient setting with no endometrial pretreatment in a randomized comparison to an inpatient procedure with hormonal pretreatment. Jack et al.³² found that more than 90% of women treated as out patients were satisfied with equivalent therapeutic efficacy.

Unlike many of the endometrial ablation manufacturers, MEA has an independent users group which monitors significant complications. Downes and O'Donovan³³ reviewed 1364 MEA procedures in 13 units by 25 different surgeons and found a low incidence of complications (one bowel injury).

NovaSure system

The NovaSure system consists of a disposable handpiece and a computerized generator. The handpiece incorporates a catheter that carries an expandable skeleton over which is draped a metallic membrane, electrically isolated into 4 quadrants. The generator delivers power at up to 180W, establishing a swirl of energy around the expanded membrane. The generator automatically calculates the required power from uterine length and width measurement.

This system is novel, in that the generator applies suction to draw the endometrium into contact with the electrode. This process also removes steam and moisture from the tissue, allowing efficient desiccation. The procedure is terminated when a preset impedance of 50 Ω is reached, indicating an adequate depth of endometrial destruction. Treatment times range from 40 to 120 seconds, making this the fastest global ablation system available.

Results from cohort studies quote an average treatment time of 94 seconds, with an amenorrhea rate of

65% and a subsequent hysterectomy rate of <3% at 3 years follow-up.³⁴

When NovaSure was compared with rollerball/resection in an RCT,³⁵ NovaSure had an equivalent beneficial effect on menstrual blood loss (assessed by PBAC seconds), with 41% becoming amenorrheic. The mean procedure time was 4.2 minutes (average 84 seconds) in the NovaSure group and 24.2 minutes in the rollerball/resection group. Local and/or intravenous sedation was administered in 73% of NovaSure patients and 18% of rollerball patients. Intraoperative complications occurred less frequently with NovaSure (0.6%) than with rollerball (6.7%). Thus, NovaSure was shown to be a safe, effective, and quick treatment for women with menorrhagia.

NovaSure has also been compared to ThermaChoice and Cavaterm in RCTs. The results of these studies are discussed later in the Randomised comparisons of second-generation devices section.

Hydrothermablation

The Hydro ThermAblator (HTA) differs from the other ablation devices in that heated saline circulates freely within the uterine cavity, and the process is monitored hysteroscopically. Thinning of the endometrium prior to hydrothermablation is essential, as there is no endometrial compressive effect during treatment. Pretreatment curettage is insufficient, as the induced bleeding interferes with the effectiveness of the procedure. Medical treatment with either danazol or a GnRH-a can be given to achieve this endometrial effect. During the treatment, an insulated hysteroscope sheath (7.8 mm in diameter) is inserted into the uterine cavity, and a Gimpelson (four-pronged) clamp is applied to the cervix to create a water-tight seal around the apparatus.

The fluid flows into the uterine cavity through the insulated sheath surrounding a 3 mm hysteroscope. A computerized controller monitors the treatment cycle; the saline is instilled under an adjustable pole height pressure and actively pumped from the uterus to create a circulation. The adjustable height allows for intrauterine operating pressures of 40–50 mmHg to be obtained, which are below the tubal opening pressure of 70–75 mmHg. Therefore, heated fluid is not lost through the fallopian tubes or from the sealed cervix.

The fluid volumes are constantly monitored, such that the system will shut down if it detects a 10 ml fluid loss, either through the fallopian tube, the cervix, or a uterine perforation. A typical treatment cycle takes 10 minutes at a temperature of 80–90°C.

Hydrothermablation is the only second-generation technique which hysteroscopically visualizes the endometrial cavity during treatment. Corson,³⁶ in the RCT for

the device comparing it to rollerball ablation, found that although the hydrothermablation procedure time was 6 minutes shorter on average, the amenorrhea rates and satisfaction scores were very similar between the two techniques. At 12 months, the amenorrhoea rate was 40%, with an overall satisfaction rate of 77% (compared with 51% and 82%, respectively, for rollerball).

Unlike the majority of global ablation devices, hydrothermablation is not confined to anatomically normal uterine cavities. Rosenbaum et al. compared the short-term clinical effectiveness of hydrothermablation in patients with normal endometrial cavities and those with intracavitary pathology.³⁷ In both groups, baseline and follow-up scores were similar, with satisfaction scores of 80% in the subjects with normal endometrial cavities and 73% in those with abnormal cavities.

Farrugia and Hussain conducted a study to assess the acceptability of hydrothermablation as an outpatient treatment.³⁸ Eighty-eight percent of patients found the procedure acceptable, there were no serious complications, and all patients were discharged home within 2 hours of the procedure.

ELITT

Endometrial laser intrauterine thermotherapy (ELITT) was introduced by GyneLase, Needham MA, USA, and uses fiberoptic technology to deliver 830 nm diode laser energy to the endometrium with a power of 20 W.

This is a blind procedure (the endometrium is not visualized during the technique), which takes approximately 7 minutes. Temperatures within the uterine cavity reach 102°C, but the temperatures within 6–7 mm of the device do not exceed 60°C. The foldaway arm design allows the laser energy to be transmitted via three optical light diffusers, which also means that it can be performed in an outpatient setting if required (the cervix needs to be dilated up to 7 mm); however, the device is limited to women with regular uterine cavities. In initial cohort studies, amenorrhea rates of 71% at 12 months have been reported.³⁹

ELITT has been compared with TCRE in a randomized fashion after pretreatment with a GnRH-a. ⁴⁰ Although the trial was underpowered (58 patients in each group), the authors found that at 1-year follow-up, the amenor-rhea rate was an impressive 56% in the ELITT group and 23% in the TCRE group; there were no significant complications were recorded for either procedure.

Photodynamic therapy

Gannon and Brown⁴¹ reported that photodynamic therapy with topical 5-aminolevulinic acid could be used to

achieve endometrial ablation. This photosensitizing agent is preferentially taken up by the endometrium, reaching a level sufficient for ablation. The ablative effect achieved can reach the basalis layer; however, incomplete uptake of the photosensitizing agent throughout the endometrium may limit the clinical usefulness of this therapy. There are no large studies addressing safety or long-term effectiveness of this technique.

RANDOMIZED COMPARISONS OF SECOND-GENERATION DEVICES

All of the devices discussed above that have been evaluated in RCTs have been shown to have equivalent results to the first-generation techniques (resection, rollerball, or laser). However, effectiveness is difficult to assess in a clinical sense, and studies vary as to whether they measure menstrual blood loss (usually with surrogate measures such as (PBAC), satisfaction with the treatment, or effect on quality of life (often assessed using the validated SF-36.⁴²)

The lack of a consistent measure of effectiveness between the studies of the second-generation devices means that it is difficult to compare techniques. The standard solution for this problem is to perform an RCT between the second-generation devices; however, there is a surprising lack of trials in this area. This may be partly due to the intrinsic differences between the devices regarding their ability to treat women with fibroids or other intrauterine abnormalities, e.g. MEA or hydrothermablation has a greater versatility than the balloon devices. However, it would seem likely that there is some commercial resistance to comparing devices, given the likely effect on the market share for the inferior treatment.

NovaSure is the device with the best comparative data, as it has been evaluated in two RCTs (ThermaChoice and Cavaterm). In the ThermaChoice RCT,⁴³ the main outcome measure was amenorrhea at 12-month follow-up; 83 women were treated with NovaSure, with 43 in the balloon group. No significant complications occurred with either treatment. At 1-year follow-up, the amenorrhea rates were 41% (34/83) in the NovaSure group and 7% (3/43) in the balloon group. Also, 90% of the patients in the bipolar group were satisfied with the result of the treatment against 79% in the ThermaChoice group at this time. The authors (Bongers et al.) concluded that the NovaSure system was more effective than ThermaChoice balloon ablation in the treatment of menorrhagia.

In comparison, Abbott et al.'s study compared Cavaterm with NovaSure.⁴⁴ Of the 55 women followed up at 1-year post treatment, 11 vs 43% were amenorrheic, and 83% vs 92% of women were either satisfied or very satisfied in the Cavaterm or NovaSure groups, respectively.

The authors concluded that both the Cavaterm and NovaSure endometrial ablation systems were effective in reducing menstrual loss in women and achieved high rates of patient satisfaction. Similar to the findings in the ThermaChoice RCT, the NovaSure system achieved a statistically significantly higher rate of amenorrhea.

There is one RCT that has evaluated the thermal balloon devices (Cavaterm and Menotreat).⁴⁵ Although the study was very underpowered to detect any significant differences (with only 31 patients), both thermal balloon treatments were well accepted by patients and had good efficacy (about 70% satisfaction in both treatment groups).

Second-generation techniques compared to other treatments

Until the mid 1980s menorrhagia treatments consisted of either hormonal treatment or hysterectomy. Parallel to the developments in endometrial ablation, there have been developments in medical alternatives, the main one being the levonorgestrel-releasing intrauterine system (LNG-IUS, Mirena).

Cooper et al. evaluated the quality of life outcomes in women randomized to endometrial ablation (TCRE) or medical management of menorrhagia in the 1990s. 46 At 2-year follow-up, women allocated medical treatment were less likely to be satisfied (57% vs 79%), to find their management acceptable (77% vs 93%), or to recommend their allocated treatment (24% vs 78%) compared to women treated by TCRE. Of note, in the medical cohort after 2 years, 59% of women had subsequently undergone TCRE, hysterectomy, or both, whereas 83% in the TCRE cohort avoided further surgery. The Short Form-36 (SF-36) health survey scores were significantly improved from baseline for five of the eight health scores in the medical arm, and seven in the TCRE arm. Cooper et al. concluded that the results at 2 years showed that a policy of early TCRE is effective and safe and does not result in an increase in hysterectomies. It should not be routinely withheld in an effort to try alternative medical therapies.

The introduction of Mirena has had a marked effect on surgical treatments for heavy periods (a reported 43% reduction in the UK rates of surgical treatments for menorrhagia⁴⁷). However, Mirena is not a panacea. Has another UK-based study, following up women using the Mirena primarily for menorrhagia, 21% had the IUS removed prematurely. Hurskainen et al⁴⁹ reviewed the literature in this area and estimated that the use of Mirena avoids hysterectomy in 60% of women using it as a treatment for menorrhagia.

How do the endometrial ablation treatments compare with the Mirena IUS? Their effectiveness, patient satisfaction and cost-effectiveness when compared with Mirena have been assessed in four trials.^{50–52}

The first study examining this area was by Crosignani et al; they compared the effect of a levonorgestrel-releasing intrauterine device (IUD) with that of endometrial resection (a first-generation technique) on menstrual bleeding, patient satisfaction, and quality of life (using the SF-36 General Health Survey) in an RCT on 70 menorrhagic women with 12 months of follow-up.⁵⁰

Amenorrhea or hypomenorrhea at 1 year was reported by 65% of the women with an IUD compared with 71% who underwent endometrial resection. The degree of satisfaction with treatment was high in both groups, with 29 of 34 (85%) women being satisfied or very satisfied in the IUD group vs 33 of 35 (94%) in the resection group. The SF-36 health-related quality of life perception was not significantly different in the two treatment groups. The authors concluded that somewhat less satisfactory results were obtained with an LNG-IUS compared with endometrial resection for dysfunctional uterine bleeding at 1 year of follow-up.

The only second-generation device to be compared to Mirena is ThermaChoice: two RCTs were performed. The first (smaller) study, published in 2003 by Barrington et al, ⁵¹ followed up 50 women randomized to either ThermaChoice or an LNG-IUS (Mirena) at 6 months post-treatment. Treatment efficacy was assessed by the change in PBAC scores. Barrington et al. found that both ThermaChoice and Mirena were equally effective in the management of menorrhagia, and concluded that the choice of treatment should be tailored to the woman's needs and preferences.

Busfield et al. from New Zealand performed a larger RCT on 79 women, comparing ThermaChoice and Mirena.⁵² Treatment efficacy was assessed once more by the change in PBAC scores, but in this study there was up to 2-year follow-up. Busfield et al. found that at 24 months, nine (35%) women still using the LNG-IUS had amenorrhea compared with one (5%) woman successfully treated by ThermaChoice (p = 0.025). There were no significant differences in patient satisfaction between two treatments during follow-up. Treatment failed in 11 (28%) women using the LNG-IUS and in 10 (26%) women treated with thermal balloon ablation. Overall, women in both groups showed an increased quality of life as a result of the treatment, with SF-36 scores increasing from 63.7 at randomization to 76.1 at 24 months. The authors summarized their results by stating that at 1- and 2-year follow-up, women with heavy menstrual bleeding treated with Mirena had significantly lower PBAC scores than women treated with ThermaChoice. However, both treatments resulted in a significant improvement in overall quality of life, with no significant differences between either treatment in this respect.

As a follow-up to Busfield et al's RCT,⁵² Brown et al. evaluated the cost-effectiveness of the two modalities of

treatment (ThermaChoice and Mirena). 42 The trial examined the direct and indirect costs of medical treatment, including treatment costs, subsequent medical procedures, lost income, and medical treatment for failed procedures. The change in quality of life (as assessed by the SF-36) measured between time of treatment and 24 months was the primary outcome measure. Economic modeling was used to examine the expected cost and therapeutic outcome for a woman entering each treatment. Brown et al. found that the expected cost of treatment was NZ\$1241 (US\$869) for the Mirena and NZ\$2418 (US\$1693) for ThermaChoice treatment. The LNG-IUS was associated with an increase of 15 points on the SF-36 scale, compared with 12 points for the thermal balloon ablation. A sensitivity analysis was also performed, which indicated that the results were robust to a 25% decrease in the price of the primary cost factors and to variations in the rates of failed treatment between the conditions. The trial concluded that Mirena was cost-effective when compared with the ThermaChoice in the treatment of heavy menstrual bleeding.

Costs

The issue of cost of a surgical treatment is notoriously difficult to evaluate, owing to the inherent differences in the set-up and administration costs between different health systems. The largest study in the UK, which examined the economics of a number of the second-generation techniques (all of which have potentially costly disposable outlay costs), when compared with the established firstgeneration techniques (all of which have minimal disposable outlay costs, but take longer and usually involve a general anesthetic), was published in 2004.53 The Peninsula Technology Assessment Group found that both MEA and thermal balloons cost less and accrue more QALYs (quality-adjusted life years) than the first-generation techniques. However, the group noted that small changes in values may have a marked effect on cost. In comparison, the group noted that hysterectomy (when a woman finds this option acceptable) remained a very cost-effective procedure compared with all the ablation methods.53

Ablation compared to hysterectomy

In marked contrast to the first-generation techniques, there are no RCTs evaluating the second-generation techniques to hysterectomy. This is because a wealth of comparative data from the first-generation techniques has shown that ablation is superior in terms of operating time, postoperative complications/recovery and, short-term costs.^{7–11} However, it should be noted that hysterectomy

is superior in terms of long-term satisfaction and is cost-effective in the long term. 11,53,54

DOES A RCT PROVIDE ALL THE ANSWERS?

Unlike the first-generation techniques, which underwent large audits to determine the likelihood of rare complications (e.g. perforation, visceral trauma), relatively soon after their introduction,5,6 there is little published data about the second-generation devices in this regard.³³ This may be for a number of reasons: the studies evaluating these newer devices (mainly RCTs) have not shown any cause for concern; also, the device manufacturers operate in a very competitive market (e.g. Menostat, an early global ablation device, was withdrawn because of safety concerns due to alternate site burns⁵⁵). However, rare complications in these treatments can have devastating consequences: e.g. we have accurate data on the incidence of uterine perforation with the first-generation techniques from the national audits (ranging from 0.6 to 2.5%^{5,6}). The relative infrequency of this complication means that in the numbers used in most RCTs (about 300 patients in total), this complication may not be seen in either group. Nonetheless, if a perforation occurs, in most second-generation methods, the cavity is not routinely visualized during the procedure. Hence, an unrecognized incorrect placement may go undetected. The perforated instrument when activated may then damage the bowel. This will typically cause problems within 12–48 hours, often when the patient has been discharged. Whereas abdominal signs may then be present, their significance might not be recognized; the resultant diagnostic and therapeutic delay can easily convert a 'sick' patient into a moribund patient.

In the USA the Food and Drug Administration (FDA) operates the MAUDE (Manufacturer and User Facility Device Experience) database,⁵⁶ which mandates all devices manufacturers as a federal directive to report any complications that they are informed about by their users. Although this is useful, it does not provide any denominator data by which the relative frequency of these complications can be compared between the devices.

SUMMARY AND CONCLUSIONS

The ideal technique for endometrial ablation would be:

- safe
- scientifically validated

- simple
- economical
- outpatient based
- provide contraception.

At present no device fulfills these criteria completely. This review seeks to emphasize four key messages regarding the second-generation endometrial ablation techniques:

- (1) Most second-generation ablation systems have been compared with classical endometrial ablation/resection in an RCT setting. The clinical results in the medium term have shown no statistically significant difference. However, the different second-generation devices vary in their ability to treat non-standard uteri (e.g. fibroids, scarred uteri).
- (2) There is very little RCT data analyzing the clinical efficacy and patient satisfaction between the various second-generation treatments available. The available evidence shows no statistically significant differences in their short-term outcomes, with a trend for ThermaChoice to show a lower amenorrhea rate than the other systems.
- (3) All of the ablation techniques have shown a very low morbidity rate in RCTs, but the data for long-term safety and the denominator data needed to define the incidences for rare complications such as perforation and visceral injury are lacking with most devices (the exception being MEA).
- (4) Cost must be considered in these comparisons. This is a difficult analysis, as most of the companies producing global ablation systems are willing to amortize the cost of computers and controllers, against a guaranteed rate of disposable utilization. The cost of pretreatment and disposables must then be compared with outcomes of endometrial ablation by first-generation methods. The available data show that the second-generation devices do appear to be cost-effective.

Thus, there is a need for ongoing comparative studies among the second-generation devices to determine which modality is the safest and most cost-effective. In addition, there is an obvious need to develop systems whereby denominator data for these devices can be obtained so that the relative frequency of rare complications can be assessed among the techniques.

References

- 1. Punnonen R, Gronroos M. Cathetron and radium in the treatment of functional uterine bleeding. Ann Chir Gynaecol Fenn 1972; 61: 215–19.
- Neuwirth RS, Amin HK. Excision of submucus fibroids with hysteroscopic control. Am J Obstet Gynecol 1976; 126(1): 95–19.
- Goldrath MH, Fuller TA, Segal S. Laser photovaporization of endometrium for the treatment of menorrhagia. Am J Obstet Gynecol 1981; 140(1): 14–19.
- 4. Vancaillie TG Electrocoagulation of the endometrium with the ball-end resectoscope. Obstet Gynecol 1989; 74(3 Pt 1): 425–7.
- Scottish Hysteroscopy Audit GroupA Scottish audit of hysteroscopic surgery for menorrhagia: complications and follow-up. Br J Obstet Gynaecol 1995; 102: 249–54.
- Overton C, Hargreaves J, Maresh M. A national survey of complications of endometrial destruction for menstrual disorders: the MISTLETOE study. Br J Obstet Gynaecol 1997; 104: 1351–9;.
- Gannon MJ, Holt EM, Fairbank J. A randomised trial comparing endometrial resection and abdominal hysterectomy for the management of menorrhagia. BMJ 1991; 303: 1362–4.
- Dwyer N, Hutton J, Stirrat GM. Randomised controlled trial comparing endometrial resection with abdominal hysterectomy for the surgical treatment of menorrhagia. Br J Obstet Gynaecol 1993; 100: 237–43.
- Pinion SB, Parkin DE, Abramovich DR et al. Randomised trial of hysterectomy, endometrial laser ablation, and transcervical resection for dysfunctional uterine bleeding. BMJ 1994; 309: 979–83.
- O'Connor H, Broadbent JAM, Magos AL, McPherson K. Medical Research Council randomised trial of endometrial resection versus hysterectomy in the management of menorrhagia. Lancet 1997; 349: 897–901.
- 11. Lethaby A, Shepherd S, Cooke I, Farquhar C. Endometrial resection and ablation versus hysterectomy for heavy menstrual bleeding. Cochrane Menstrual Disorders & Subfertility Group, Update Software, 1999.
- Garry R. Endometrial ablation and resection: validation of a new surgical concept. Br J Obstet Gynaecol 1997; 104: 1329–21.
- Hallberg L, Hogdahl A, Nilsson L, Rybo G. Menstrual blood loss – a population study: variation at different ages and attempts to define normality. Acta Obstet Gynecol Scand 1966; 45: 320–51.
- MORI. Women's health in 1990. Market Opinion and Research International, 1990. (Research study conducted on behalf of Parke-Davis Research Laboratories.)
- Vessey MP, Villard-Mackintosh L, McPherson K, Coulter A, Yeates D The epidemiology of hysterectomy: findings in a large cohort study. Br J Obstet Gynaecol 1992; 99: 402–7.
- Coulter A, McPherson K, Vessey M. Do British women undergo too many or too few hysterectomies? Soc Sci Med 1988; 27: 987–94
- McPherson K, Metcalfe MA, Herbert A et al. Severe complications of hysterectomy: the VALUE study. BJOG 2004; 111(7): 688–94.
- 18. Wilcox LS, Koonin LM, Pokras R et al. Hysterectomy in the United States, 1988–1990. Obstet Gynecol 1994; 83(4): 549–55.

- RCOG Press. Guidance for the development of RCOG Clinical Guidelines. August 1999. http://www.rcog.org.uk/guidelines/ gt_guidelines.html.
- 20. RCOG Press. The Initial Management of Menorrhagia. Evidence-Based Clinical Guideline No. 1. 1998. http://www.rcog.org.uk/guidelines/menorrhagia.html.
- RCOG Press. The management of menorrhagia in secondary care. Evidence-Based Clinical Guideline No. 5. 1999. http:// www.rcog.org.uk/guidelines/menorrhagiasc.html.
- Townsend DE, Duleba AJ, Wilkes MM. Durability of treatment effects after endometrial cryoablation versus rollerball electroablation for abnormal uterine bleeding: two-year results of a multicenter randomized trial. Am J Obstet Gynecol 2003; 188(3): 699–701.
- 23. Vilos GA, Aletebi FA, Eskandar MA. Endometrial thermal balloon ablation with the ThermaChoice system: effect of intrauterine pressure and duration of treatment. J Am Assoc Gynecol Laparosc 2000; 7(3): 325–9.
- 24. Marsh F, Thewlis J, Duffy S. Randomized controlled trial comparing Thermachoice III in the outpatient versus daycase setting. Fertil Steril 2007; 87(3): 642–50.
- Meyer WR, Walsh BM, Grainger DA et al. Thermal balloon and rollerball ablation to treat menorrhagia: a multicentre comparison. Obstet Gynecol 1998; 92(1): 98–103.
- Brun JL, Raynal J, Burlet G et al. Cavaterm thermal balloon endometrial ablation versus hysteroscopic endometrial resection to treat menorrhagia: the French, multicenter, randomized study. J Minim Invasive Gynecol 2006; 13(5): 424–30.
- 27. Ulmsten U, Carstensen H, Falconer C et al. The safety and efficacy of MenoTreat, a new balloon device for thermal endometrial ablation. Acta Obstet Gynecolo Scand 2001; 80(1): 52–7.
- Sharp NC, Cronin N, Feldberg I et al. Microwaves for menorrhagia: a new fast technique for endometrial ablation. Lancet 1995; (346)14: 1003–4.
- 29. Hodgson D, Feldberg IB, Sharp N et al. Microwave endometrial ablation: development, clinical trials and outcomes at three years. Br J Obstet Gynaecol 1999; 106: 684–94.
- Cooper KG, Bain C, Parkin DE. Comparison of microwave endometrial ablation and transcervical resection of the endometrium for treatment of heavy menstrual loss: a randomised trial. Lancet 1999; 354: 1859–63.
- 31. Cooper KG, Bain C, Lawrie L, Parkin DE. A randomised comparison of microwave endometrial ablation with transcervical resection of the endometrium; follow up at a minimum of five years. BJOG 2005; 112(4): 470–5.
- 32. Jack SA, Cooper KG, Seymour J et al. A randomised controlled trial of microwave endometrial ablation without endometrial preparation in the outpatient setting: patient acceptability, treatment outcome and costs. BJOG. 2005; 112(8): 1109–16.
- Downes E, O'Donovan P. Microwave endometrial ablation in the management of menorrhagia: current status. Curr Opin Obstet Gynecol 2000; 12: 293–6.
- Gallinat A. NovaSure impedance controlled system for endometrial ablation: 3 year follow-up on 107 patients. Am J Obstet Gynecol 2004; 191(5): 1585–9.
- Cooper J, Gimpelson R, Laberge P et al. A randomized, multicenter trial of safety and efficacy of the NovaSure system in the

- treatment of menorrhagia. J Am Assoc Gynecol Laparosc 2002; 9(4): 418–28.
- Corson SL. A multicenter evaluation of endometrial ablation by Hydro ThermAblator and rollerball for treatment of menorrhagia. J Am Assoc Gynecol Laparosc 2001; 8(3): 359–67.
- Rosenbaum SP, Fried M, Munro MG. Endometrial hydrothermablation: a comparison of short-term clinical effectiveness in patients with normal endometrial cavities and those with intracavitary pathology. J Minim Invasive Gynecol 2005; 12(2): 144–9.
- 38. Farrugia M, Hussain SY. Hysteroscopic endometrial ablation using the Hydro ThermAblator in an outpatient hysteroscopy clinic: feasibility and acceptability. J Minim Invasive Gynecol 2006; 13(3): 178–82.
- 39. Donnez, J, Polet R, Rabinovitz R et al. Endometrial laser intrauterine thermotherapy: the first series of 100 patients observed for 1 year. Fertil Steril 2000; 74(4): 791–6.
- Perino A, Castelli A, Cucinella G et al. A randomized comparison of endometrial laser intrauterine thermotherapy and hysteroscopic endometrial resection. Fertil Steril 2004; 82(3): 731–4.
- Gannon MJ, Brown SB. Photodynamic therapy and its applications in gynaecology. Br J Obstet Gynaecol 1999; 106(12): 1246–54.
- Brown PM, Farquhar CM, Lethaby A, Sadler LC, Johnson NP. Cost-effectiveness analysis of levonorgestrel intrauterine system and thermal balloon ablation for heavy menstrual bleeding. BJOG 2006; 113(7): 797–803.
- 43. Bongers MY, Bourdrez P, Mol BW, Heintz AP, Brolmann HA. Randomised controlled trial of bipolar radio-frequency endometrial ablation and balloon endometrial ablation. BJOG 2004; 111(10): 1095–102.
- Abbott J, Hawe J, Hunter D, Garry R. A double-blind randomized trial comparing the Cavaterm and the NovaSure endometrial ablation systems for the treatment of dysfunctional uterine bleeding. Fertil Steril 2003; 80(1): 203–8.
- 45. Vihko K, Raitala R, Taina E Endometrial thermoablation for treatment of menorrhagia: comparison of two methods in outpatient setting. Acta Obstet Gynecol Scand 2003; 82(3): 269–74.

- Cooper KG, Parkin DE, Garratt AM, Grant AM Two-year follow up of women randomised to medical management or transcervical resection of the endometrium for heavy menstrual loss: clinical and quality of life outcomes. Br J Obstet Gynaecol 1999; 106(3): 258–65.
- Reid PC, Mukri F. Trends in number of hysterectomies performed in England for menorrhagia: examination of health episode statistics, 1989 to 2002-3. BMJ 2005; 330: 938–9
- 48. Mukherjee K, Jones K. The treatment of dysfunctional uterine bleeding with the Mirena IUS: a survival analysis. Gynecol Surg 2005; 2(4): 251–4.
- Hurskainen R, Paavonen J. Levonorgestrel-releasing intrauterine system in the treatment of heavy menstrual bleeding. Curr Opin Obstet Gynecol. 2004; 16(6): 487–90.
- Crosignani PG, Vercellini P, Mosconi P et al. Levonorgestrelreleasing intrauterine device versus hysteroscopic endometrial resection in the treatment of dysfunctional uterine bleeding. Obstet Gynecol 1997; 90(2): 257–63.
- 51. Barrington JW, Arunkalaivanan AS, Abdel-Fattah M. Comparison between the levonorgestrel intrauterine system (LNG-IUS) and thermal balloon ablation in the treatment of menorrhagia. Eur J Obstet Gynecol Reprod Biol 2003: 108(1): 72–4.
- 52. Busfield RA, Farquhar CM, Sowter MC et al. A randomised trial comparing the levonorgestrel intrauterine system and thermal balloon ablation for heavy menstrual bleeding. BJOG 2006; 113(3): 257–63.
- Garside R, Stein K, Wyatt K, Round A, Pitt M. A cost-utility analysis of microwave and thermal balloon endometrial ablation techniques for the treatment of heavy menstrual bleeding. BJOG 2004; 111(10): 1103–14.
- Lethaby A, Hickey M, Garry R. Endometrial destruction techniques for heavy menstrual bleeding. Cochrane Database Syst Rev 2005; 4: CD001501.
- 55. Thijssen RF. Radiofrequency induced endometrial ablation: an update. Br J Obstet Gynaecol 1997; 104(5): 608–13.
- 56. Gurtcheff SE, Sharp HT. Complications associated with global endometrial ablation: the utility of the MAUDE database. Obstet Gynecol 2003; 102(6): 1278–2.

Photodynamic therapy

Michael J Gannon

INTRODUCTION

Administration of a sensitizer in addition to light has long been known to have a beneficial effect. The ancient Egyptians ingested plants containing light-activated psoralens and sat in strong sunlight to treat vitiligo. Four thousand years later, psoralen activated by ultraviolet A radiation (PUVA) was used in the treatment of psoriasis. Photodynamic therapy (PDT), first described just over 100 years ago, is distinguished by being an oxygen-dependent phenomenon. Low-power light produces necrosis of tissue that has been rendered photosensitive by administration of a drug. Photosensitizers accumulate preferentially in rapidly dividing cells, thus labeling them for destruction. The toxic effect is brought about by release of singlet oxygen.

Research into PDT was commenced by two American groups in 1972. Diamond and colleagues reported that the administration of hematoporphyrin followed by visible light therapy proved lethal to glioma cells in culture and produced massive destruction of porphyrin-containing gliomas which had been transplanted subcutaneously in rats. This paper brought the term 'photodynamic therapy' into general use.² Dougherty et al. demonstrated eradication of a transplanted mouse mammary tumor using hematoporphyrin derivative (HpD) activated by red light from a filtered xenon arc lamp and treated various malignant tumors with intravenous HpD and laser light.³ The longer-wavelength red light (650 nm) was chosen for treatment as it had better tissue penetration properties than the shorter-wavelength blue or green light.

Photosensitizers, in general, tend to accumulate in neoplastic tissues. The ratio of photosensitizer concentration between tumor and surrounding normal tissue varies with the photosensitizer and the tissue and forms the basis for successful PDT. Selective photosensitizer uptake in vascular, proliferative tissues is used to target certain non-neoplastic tissues, as well as tumors, for destruction. As a rule, it can be stated that practically all photosensitizers that have been studied have a pronounced affinity for non-neoplastic tissues, which are high in reticuloendothelial components.⁴

PHOTOSENSITISERS FOR ENDOMETRIAL ABLATION

The first attempt at photodynamic endometrial ablation was carried out on ovariectomized rats. Dihematoporphyrin ether (DHE) was taken up by the endometrial layer of the estrogen-primed rat uterus. Photoradiation of the uterine surface 72 hours after DHE administration caused selective coagulation necrosis in the entire endometrium and the inner part of the muscularis.⁵ PDT endometrial ablation was also studied in rabbits, which, like rats, have a double uterus, providing a convenient treatment and control uterine horn in each animal. Bhatta et al⁶ showed that Photofrin (porfimer sodium) was retained preferentially by the endometrium, with the greatest concentration observed in the stroma. Laser light was delivered using an optical fiber with a diffusing tip inserted in the rabbit uterus. When the uterus was examined after treatment, endometrial necrosis was confirmed and related to the dose of Photofrin. Despite the rabbit's relatively thin myometrium, there was no full-thickness uterine destruction.

Many early studies were carried out using HpD, which is a complex mixture of porphyrins that includes esters and ethers. A more efficient photosensitizer was obtained by removal of the monomers, to yield the proprietary preparation Photofrin. Regulatory approval for PDT using Photofrin for patients with early- and advanced-stage cancer of the lung, digestive tract, and genitourinary tract has been obtained in Canada, the Netherlands, France, Germany, Japan, and the USA. UK approval was obtained in January 1999.

Photofrin has specificity for malignant tissue, although it also accumulates in liver, spleen, kidneys, and skin. The latter may lead to photosensitization lasting up to 6 weeks, thus restricting the wider use of this photosensitizer. Tumor selectivity over surrounding normal tissues is not always optimal. Moreover, Photofrin absorbs only weakly above 600 nm, where light exhibits the deepest penetration of tissues.

The ideal tumor photosensitizer should be a pure, single substance, selective for tumor tissue over surrounding normal tissue, that achieves efficient photosensitization, is non-toxic in the dark, and is rapidly excreted from the body. It is desirable that the sensitizer has a high triplet quantum yield and efficient transfer of excitation energy to produce singlet oxygen.² It should absorb well in the red part of the visible spectrum for optimum effect. Red light has less absorption and scattering and penetrates tissue more deeply than shorter-wavelength blue or green light.⁹

Several strategies have been employed to increase porphyrin absorption in the red. The search for new photosensitizers is concentrated on preparations with relatively intense bands in the longer-wavelength 650-800 nm region.¹⁰ Chlorins and bacteriochlorins are formed by progressive reduction of porphyrins. The chlorin absorption spectrum shows a strong band in the red (650 nm), giving the substance a green color. As its natural parent compound chlorophyll is sensitive to autoxidation, studies have been performed on the PDT activity of less-fragile derivatives such as the synthetic chlorin meso-tetra(mhydroxyphenyl)chlorin (m-THPC) or temoporfin. It is a powerful photosensitizer that causes better tumor necrosis than Photofrin during in-vivo tests and is available commercially as Foscan (Scotia Pharmaceuticals Ltd, Guildford, UK). The structure is highly efficient, with a short treatment time and body clearance in days. However, the powerful effect may also make patients susceptible to a strong photosensitivity reaction, even in ambient light.

Benzoporphyrin derivative (BPD), a chlorin in spite of its name, is also being developed commercially as BPd monoacid ring A (BPD-MA; QLT PhotoTherapeutics Inc., Vancouver, Canada). The drug light interval is short, and generalized photosensitization is low. In a dose-ranging study in rats, intravenous BPD-MA (verteporfin) was followed after 5 minutes by effective endometrial destruction using 630 nm light treatment.¹¹

Chlorin substitution gives a puce-colored series of compounds called purpurins. The most active is the hydrophobic tin complex of etiopurpurin (SnEt2; Miravant Inc., formerly PDT Inc., Santa Barbara, CA, USA). Further reduction produces the bacteriochlorins with an intensified absorption band, which is shifted further to the red at around 735 nm. More extensive changes to the porphyrin structure produce the azaporphyrin derivatives phthalocyanine (Pc) and the closely related naphthalocyanine (Nc). Sulfonation of the metal complex renders these extremely hydrophobic compounds water soluble. Various complexes of Pc with non-transition elements such as zinc (Zn phthalocyanine; Ciba Geigy, Basel, Switzerland), aluminium, and silicon show photobiologic activity against tumors. Absorption maxima are red shifted to around 670 nm for Pc and 750 nm for Nc. Although

there is also a greater magnitude of light absorption than shown by Photofrin, the evidence for its translation into photodynamic effect in vivo is limited.¹²

An alternative approach uses 5-aminolevulinic acid (ALA) to produce protoporphyrin IX (PpIX), a precursor of heme in most body cells.¹³ Administration of excess ALA leads to accumulation of PpIX, which acts as an endogenous photosensitizer. Like the other porphyrins, PpIX accumulates preferentially in tumor tissue. As ALA is a natural body compound that is completely metabolized within 24 hours, the problem of prolonged skin sensitivity is avoided by its use. ALA is commercially available as Levulan (DUSA Pharmaceuticals Inc., Valhala, New York, USA). Kennedy and Pottier¹³ studied the distribution of ALA-induced PpIX in normal tissues and found that fluorescence occurred primarily in surface and glandular epithelium of the skin and the lining of hollow organs. Systemic ALA administration has been shown to induce a five-fold greater PpIX fluorescence in rabbit endometrium than in myometrium or stroma.¹⁴

Topical administration has been investigated as a means of minimizing photosensitizer-induced skin sensitivity. ¹⁵ Rats were randomized to receive intravenous, intraperitoneal, or intrauterine Photofrin, and the uterine porphyrin levels were determined. Intrauterine administration provided the best uptake and distribution within the uterus, at lower drug doses. The powerful photosensitizer BPD, when instilled into the uterine cavity of rabbits, was shown to accumulate in higher concentration in the endometrium than in the myometrium. ¹⁶ After PDT, substantial, persistent endometrial destruction was generally observed, although there were regional variations in re-epithelialization.

Intrauterine administration of ALA in rats enabled selective PDT endometrial ablation.¹⁷ There was preservation of some glandular elements after treatment, yet no regeneration of endometrium was evident at 10 days. The functional effect was confirmed by comparing pregnancy implantation in treated and untreated uterine horns. Those treated by means of ALA PDT showed a profoundly decreased rate of implantation as well as the absence of functioning endometrium.¹⁸ This study suggests that, although complete endometrial destruction was not immediate, photoablation of the endometrium was achieved by direct tissue destruction combined with the effect of local toxicity from photoablated tissue.

A study of ALA PDT in rats and rabbits explored the pharmacokinetics and effective distribution of intrauterine ALA.¹⁹ Peak endometrial fluorescence, and hence PpIX conversion, was observed at 3 hours in both animal models. No significant dose-dependent fluctuations were observed in glandular, stromal, and myometrial fluorescence when the ALA concentration was increased from

100 to 400 mg/ml. However, glandular uptake was significantly higher than that of the other structures regardless of drug concentration. Although the solution of ALA was highly acidic and potentially toxic, buffering to pH 5.5 did not affect the fluorescence levels. Histologic appearances of the uteri were similar at 3 and 7 days, showing destruction of glandular epithelium with moderate stromal scarring.

Endometrial PpIX fluorescence was measured in monkeys after ALA was administered either via a needle into the uterine fundus, transcervically, or by intravenous injection. Hysterectomy specimens after 3 hours showed selective accumulation of PpIX in endometrium and not in myometrium. Peak fluorescence occurred 4–5 hours after injection and decreased gradually to less than 20% at 8 hours. Monkeys were shown to tolerate large doses of ALA without ill effect. The same group went on to study ALA-induced endometrial ablation in non-human primates. In monkeys were shown in non-human primates.

We investigated the use of ALA PDT of the endometrium in model systems and in a series of patients.²² In all of this work, the ALA was administered directly into the uterine cavity to reduce any possibility of systemic photosensitization. In a series of experiments in perfused ex-vivo uteri, ALA was introduced into the cavity and protoporphyrin formation was measured in the endometrium, the underlying myometrium, and the perfusate. ALA transfer into the perfusate was also measured. This work demonstrated that protoporphyrin formation in the endometrium was approximately 10-fold that in the underlying myometrium and that systemic photosensitization would be unlikely to result from transfer of administered ALA from the uterus into the circulation. Similar results were found in studies carried out in vivo, where ALA was administered to patients scheduled for hysterectomy.

LIGHT DELIVERY FOR PHOTODYNAMIC THERAPY

It is convenient to generate a fixed dose of visible light with a laser and deliver this to the target area via a fiber. The wavelength chosen for treatment depends on a number of considerations. Porphyrins generally absorb well in the low-wavelength, blue range of the visible spectrum. The porphyrin photosensitizers are thus most efficiently activated by blue light. Unfortunately, endogenous tissue chromophobes, including hemoglobin, also absorb well in the blue. The ubiquitous nature of hemoglobin means that blue light has a very limited capacity for penetration in living tissue. The hemoglobin absorption spectrum falls off rapidly above a wavelength of 600 nm in the red. Longer wavelengths are therefore chosen for PDT, even though most photosensitizers absorb less well at these

levels. The increased penetration depth of longer-wavelength light is a major incentive for the development of new photosensitizers absorbing at such wavelengths.

About 30% of the incident light at wavelengths of 600–800 nm reflects off the surface layer. This leaves about 70% of photons free to propagate into the tissue. These photons are subject to multiple scattering before they are absorbed. Scattering is caused by variations in refractive index that alter the direction of travel of individual photons. The initial forward direction is altered after about 1–2 mm to a nearly isotropic light distribution in most tissues. The path traveled by a photon is much longer than the linear distance covered. Thus, scattering leads to increased absorption, even though the process itself occurs without loss.

The fluence rate measures the quantity of photons per second passing through a defined area (mW/cm2).²³ Light fluence in tissue decreases exponentially with distance due to absorption and scattering. The effective penetration depth of light is the distance (in millimeters) corresponding to a decrease in the fluence rate by a factor of 1/e equivalent to 0.37 (where e = 2.718). Since it is determined by absorption and scattering and, as both of these parameters differ between tissues, there is a characteristic optical penetration depth for each tissue. The average light penetration depth is about 1–3 mm at 630 nm and 2–6 mm at 700–850 nm of light.

Optical dose is a product of the incident fluence rate and the exposure time.²³ The amount of light delivered to a tissue is also influenced by propagation properties and geometry of the particular tissue. Back-scattered light enhances the fluence rate near the surface, increasing light delivered to a superficial tissue. The suitability of PDT for the treatment of surface lesions has been exploited in recent studies of PDT for superficial lesions that are extensive or prove difficult to eradicate, such as premalignant conditions²⁴ and endometriosis.²⁵ Furthermore, in a hollow organ such as the uterus, the surface fluence rate may be increased by a factor of 5-6 due to the reflection of light from surrounding walls. The accessibility of the endometrium and the buffer provided by the myometrium make the prospect of safe endometrial destruction by PDT appealing.

In our studies, the optical parameters required for clinical treatment were estimated from previous experience of PDT of the esophagus and the bladder, both of which can be treated as hollow organs. We carried out investigations on a posthysterectomy uterus to characterize the distribution of light and to predict an adequate treatment time. ²⁶ A light delivery system was constructed using a balloon catheter, and later developed into a shaped latex balloon. The catheter was introduced through the cervix and the balloon inflated inside the uterine cavity.

Intralipid in solution was injected into the balloon to scatter light. Other workers designed a balloon made of elastomer loaded with highly scattering particles for intrauterine PDT.²⁷ Reflecting and scattering of light inside the balloon achieved an even fluence rate over the balloon surface. The same principle of optical integration by multiple internal diffuse reflections to achieve uniform output illumination was employed to design a silicone balloon for intrauterine use.²⁸

Clinical activation of the photosensitizer was generally achieved by visible light derived from a laser and directed to the site by optical fiber.²⁶ In our studies, a fiber modification was designed to emit light over a cylindrical terminal section 2 cm in length. When the tip was activated in the Intralipid-filled balloon, a homogeneous light delivery was ensured.²⁹ Tromberg et al. derived a mathematical model to describe homogeneous light distribution in the uterus without balloon distention.³⁰ It proved possible to apply sufficient light to the entire endometrium with three separate cylindrical diffusers placed horizontally in the uterine cavity in a manner similar to the introduction of an intrauterine device.³¹ Two lateral fibers with 2 cm diffusing tips fed into the cornua and a 4 cm central diffusing tip extended from the central fiber. The intrauterine light probe's ability to deliver the required light dose for PDT was demonstrated on three surgically removed human uteri.

Until recently, large, complex laser systems were needed to deliver sufficient power (up to about 1 W) for effective treatment. A primary pumping laser such as an argonion or a coppervapor laser was coupled to a separate, tunable, dye laser.³² The high capital and maintenance costs associated with these laser systems was a limiting factor in the widespread application of PDT. Simpler, more compact and less expensive sources such as diode lasers³³ and filtered arc lamps³⁴ are now becoming available for use in PDT.³⁵

CONCLUSION

Current methods for endometrial ablation generally require anesthesia, and despite meticulous technique, about one in five women subsequently need hysterectomy.³⁶ PDT is simple to perform and may give better results because of endometrial targeting.

Successful PDT depends on the critical interaction of several complex, interrelated factors, including tissue thickness, which determines penetration of both drugs and light. Preoperative manipulation of endometrial depth is common to many endometrial ablation techniques. It may be that hormonal suppression of endometrium impairs oxygenation for PDT. Furthermore, estrogen activation has been shown to be of benefit in some experiments. The choice of photosensitizer, vehicle, and route of administration must be made. There has been a trend towards topical photosensitizer administration for accessible lesions. The major drawback to topical administration is the limited and variable penetration achieved.

Each photosensitizer has an optimal wavelength for activation. Light penetration also varies with wavelength, and should be at least 500 nm for in-situ lesions and 600 nm or more for deeper lesions up to 10 mm or more. Light delivery will be facilitated by the various purpose-made devices that are becoming available for the treatment of the uterine cavity. Perhaps the biggest recent advance which will allow more widespread use of PDT is the development of a new generation of compact diode lasers capable of producing light at more than 600 nm on a narrow wavelength. This will allow the more widespread use of this very promising technique and, perhaps, the development of the ideal outpatient method of endometrial ablation.

References

- Gannon MJ, Brown SB. Photodynamic therapy and its applications in gynaecology. Br J Obstet Gynaecol 1999; 106: 1246–54.
- 2. Bonnett R. Photodynamic therapy in historical perspective. *Rev Contemp Pharmacother* 1999; 10: 1–17.
- Dougherty TJ, Kaufman JE, Goldfarb A et al. Photoradiation therapy for the treatment of malignant tumors. *Cancer Res* 1978; 38: 2628–35.
- Henderson BW, Dougherty TJ. How does photodynamic therapy work? *Photochem Photobiol* 1992; 55: 145–57.
- Schneider DF, Schellhas HF, Wesseler TA, Moulton BC. Endometrial ablation by DHE photoradiation therapy in estrogen-treated ovariectomized rats. Colposcopy Gynecol Laser Surg 1988; 4: 73–7.
- Bhatta N, Anderson RR, Flotte T et al. Endometrial ablation by means of photodynamic therapy with photofrin II. Am J Obstet Gynecol 1992; 167: 1856–63.

- Dougherty TJ, Gomer CJ, Henderson BW et al. Photodynamic therapy. J Natl Cancer Inst 1998; 90: 889–905.
- 8. Kennedy JG, Pottier RH. Endogenous protoporphyrin IX, a clinically useful photosensitizer for photodynamic therapy. *J Photochem Photobiol B: Biol* 1992; 14: 275–92.
- Wan S, Parrish JA, Anderson RR, Madden M. Transmittance of non-ionising radiation in human tissues. *Photochem Photobiol* 1981; 34: 679–81.
- Bonnett RPhotosensitizers of the porphyrin and phthalocyanine series for photodynamic therapy. Chem Soc Rev 1995; 24: 19–33.
- Mhawech P, Renaud A, Sene C et al. High efficacy of photodynamic therapy on rat endometrium after systemic administration of benzoporphyrin derivative monoacid ring A. *Hum Reprod* 2003; 18: 1707–11.
- 12. Schmidt S, Wagner U, Oehr P, Krebs D. Clinical application of photodynamic therapy in patients with gynaecologic

- tumors antibody-targeted photodynamic laser therapy as a new oncological treatment modality. *Zentbl Gynakol* 1992; 114: 307–11.
- Kennedy JC, Marcus SL, Pottier RH. Photodynamic therapy (PDT) and photodiagnosis (PD) using endogenous photosensitization induced by 5-aminolevulinic acid (ALA): mechanisms and clinical results. J Clin Laser Med Surg 1996; 14: 289–304.
- Judd MD, Bedwell J, MacRobert AJ. Comparison of the distribution of phthalocyanine and ALA-induced porphyrin sensitisers within the rabbit uterus. *Lasers Med Sci* 1992; 7: 203–11.
- Chapman JA, Tadir Y, Tromberg BJ et al. Effect of administration route and estrogen manipulation on endometrial uptake of Photofrin porfimer sodium. Am J Obstet Gynecol 1993; 168: 685–92.
- Wyss P, Tadir Y, Tromberg BJ et al. Benzoporphyrin derivative (BPD): a potent photosensitizer for photodynamic destruction of the rabbit endometrium. *Obstet Gynecol* 1994; 84: 409–14.
- 17. Yang JZ, Van Vugt DA, Kennedy JC, Reid RL. Intrauterine 5-aminolevulinic acid induces selective fluorescence and photodynamic ablation of the rat endometrium. *Photochem Photobiol* 1993; 57: 803–07.
- Yang JZ, Van Vugt DA, Kennedy JC, Reid RL. Evidence of lasting functional destruction of the rat endometrium after 5-aminolevulinic acid-induced photodynamic ablation: Prevention of implantation. Am J Obstet Gynecol 1993; 168: 995–1001.
- Wyss P, Tromberg BJ, Wyss MT et al. Photodynamic destruction of endometrial tissue with topical 5-aminolevulinic acid in rats and rabbits. Am J Obstet Gynecol 1994; 171: 1176–83.
- 20. Yang JZ, Van Vugt DA, Roy BN et al. Intrauterine 5-aminolae-vulinic acid induces selective endometrial fluorescence in the rhesus and cynomolgus monkey. *J Soc Gynecol Invest* 1996; 3: 152–7.
- Van Vugt DA, Krzemien A, Roy BN et al. Photodynamic endometrial ablation in the nonhuman primate. J Soc Gynecol Investig 2000; 7: 125–30.
- Gannon MJ, Johnson N, Roberts DJH et al. Photosensitization of the endometrium with topical 5-aminolevulinic acid. Am J Obstet Gynecol 1995; 173: 1826–8.
- Wyss P, Svaasand LO, Tadir Y et al. Photomedicine of the endometrium: experimental concepts. *Hum Reprod* 1995; 10: 221–6.

- Martin-Hirsch PL, Whitehurst C, Buckley CH, Moore JV, Kitchener HC. Photodynamic treatment for lower genital tract intraepithelial neoplasia. *Lancet* 1998; 351: 1403.
- 25. Yang JZ, Van Dijk-Smith JP, Van Vugt DA, Kennedy JC, Reid RL. Fluorescence and photosensitization of experimental endometriosis in the rat after systemic 5-aminolevulinic acid administration: a potential new approach to the diagnosis and treatment of endometriosis. *Am J Obstet Gynecol* 1996; 174: 154–60.
- Stringer MR, Hudson EJ, Dunkley CP et al. Light delivery schemes for uterine photodynamic therapy. In: Jori G, Moan J, Star WM, eds. *Photodynamic Therapy of Cancer. Proc SPIE* 1994; 2078: 41–9.
- Bays R, Woodtli A, Mosimann L et al. A light distributor for photodynamic endometrial ablation. In: Wyss P, Tadir Y, Tromberg BJ, Haller U, eds. *Photomedicine in Gynecology and Reproduction*. Basel: Karger, 2000; pp 243–5.
- Dwyer PJ, White WM, Fabian RL, Anderson RR. Optical integrating balloon device for photodynamic therapy. *Lasers Surg Med* 2000; 26: 58–66.
- Gannon MJ, Vernon DI, Holroyd JA et al. PDT of the endometrium using ALA. *Proc SPIE* 1997; 2972: 2–13.
- Tromberg BJ, Svaasand LO, Fehr MK et al. A mathematical model for light dosimetry in photodynamic destruction of human endometrium. *Phys Med Biol* 1996; 41: 223–7.
- 31. Tadir Y, Hornung R, Pham TH, Tromberg BJ. Intrauterine light probe for photodynamic ablation therapy. *Obstet Gynecol* 1999; 93: 299–303.
- 32. Fehr MK, Madsen SJ, Svaasand LO et al. Intrauterine light delivery for photodynamic therapy of the human endometrium. *Hum Reprod* 1995; 10: 3067–72.
- Ripley PM. The physics of diode lasers. *Lasers Med Sci* 1996; 11:
- De Jode ML, McGilligan JA, Dilkes MG et al. A comparison of novel light sources for photodynamic therapy. *Lasers Med Sci* 1997; 12: 260–8.
- Mang TS. Lasers and light sources for PDT: past, present and future. Photodiagn Photodyn Ther 2004; 1: 43–8.
- Gannon MJ, Holt EM, Fairbank J et al. A randomised trial comparing endometrial resection and abdominal hysterectomy for the treatment of menorrhagia. BMJ 1991; 303: 1362–64.

Charles E Miller

INTRODUCTION

Abnormal uterine bleeding is one of the most common gynecologic complaints in contemporary gynecology. It has been reported that 30% of all premenopausal women perceive their menses to be in excess. Recently, the World Health Organization stated that 18 million women aged 30–55 years old perceive their menstrual bleeding to be exorbitant. Interestingly, 10% of these women experience blood loss severe enough to be clinically defined as menorrhagia. Approximately one-third of this population will have intracavitary lesions. The majority of these cases (90%) will have endometrial polyps or submucous myomas <3 cm in diameter. In the remaining 10% of cases, submucous myomas with deep intramural involvement or diameter >3 cm will be noted.

DIAGNOSTICS

When a patient presents with menorrhagia or metrorrhagia, it is incumbent upon the practitioner to rule out endometrial polyps or uterine fibroids. While ultrasound or magnetic resonance imaging (MRI) can be acceptable in establishing the diagnosis, saline infused sonohysterography (Figure 28.1), either in two or three dimensions (2D or 3D), improves visualization. Endometrial biopsy should also be considered. The author does not routinely perform endometrial biopsy on women who present with ovulatory bleeding (menorrhagia). As per the ACOG (American Association of Gynecologic Laparoscopists) Practice Bulletin on Management of Anovulatory Bleeding, the author recommends endometrial sampling for all women over 35 years old with anovulatory type bleeding (metrorrhagia) or women younger who are non-responsive to therapy.

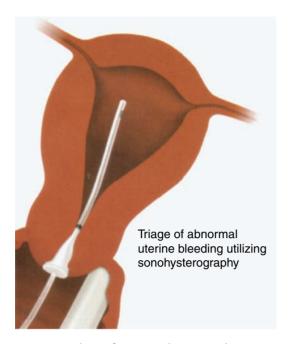
TREATMENT ALTERNATIVES: HYSTEROSCOPIC RESECTOSCOPY

With over 25 years of experience, it is apparent that the resectoscope can be used effectively to treat both intrauterine polyps as well as submucosal uterine fibroids, both pedunculated and sessile. Moreover, in the same setting, endometrial ablation or resection can be performed. If bleeding is noted, the resectoscope can be used to coagulate the vessel. Moreover, when resectoscopy is performed, a specimen is available for histologic evaluation.

Despite these advantages, resectoscopy does offer challenges. It is because of these disadvantages that only 5% of gynecologists perform electrical resectoscopy. There is a long learning curve. Perforation is especially concerning if it occurs when energy is activated. An inadvertent bowel burn can occur. While resectoscopy is underway, specimen fragments can disrupt visualization. Moreover, to extirpate these chips, multiple insertions of the hysteroscope may be required. This activity can lead to cervical trauma and increased risk of air embolism secondary to vessel tear. In addition to tissue fragments disrupting visibility, cervical mucus, gas bubbles and blood clots may also prove to be problematic. Fluid intravasation can be particularly hazardous, especially with monopolar resectoscopy. Since bipolar electrosurgery is performed with the ionic solution saline as the distention medium, fluid overload exists. On the other hand, monopolar electrosurgery requires a non-ionic fluid. Thus, not only is fluid overload a risk but also the hypoosmolar state can lead to hyponatremia, brainstem infarct, and death. Finally, the bubbles created at the time of resectoscopy increase the risk of gas embolism. It is no wonder that only 5% of gynecologists utilize the resectoscope.

Treatment Alternatives: Hysteroscopic Morcellation

The current hysteroscopic morcellation system, developed by Smith & Nephew, consists of a continuous-flow hysteroscope (Figure 28.2) which connects to a high-flow (up to 700 ml/min) fluid management system (Figure 28.3). This system enables the surgeon to accurately choose an intrauterine pressure which enables cavity-distention while minimizing fluid extravasation.



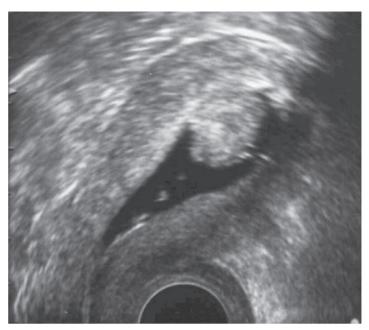


Figure 28.1 Saline infusion sonohysterography.



Figure 28.2 Continuous-flow hysteroscope.

Through the hysteroscope's working channel, a rotating cutting device is placed (either a rotary blade or reciprocating blade) that not only allows mechanical extirpation of tissue but also continues evacuation of the excised specimen chip.

There are multiple advantages of hysteroscopic morcellation over the conventional resectoscope. Unlike the need to use a non-ionic distention medium with monopolar resectoscopy, hysteroscopic morcellation is performed in an ionic environment with normal saline. Instantaneous tissue removal as well as the ability to remove blood clots enhances visualization. Moreover, the gynecologic surgeon remains focused on the task, as chips do not require retrieval and the cavity does not require redistention. Inevitably, the ability to continuously evacuate specimen chips and blood clots provides a time saving as well. Because the hysteroscope need not be reinserted



Figure 28.3 Fluid management system with morcellation control unit.

multiple times during a procedure, secondary to continuous chip and clot removal, the risk of cervical trauma is reduced. As risk of air embolism increases with trauma to the cervical vessels, hysteroscopic morcellation is a safe alternative.

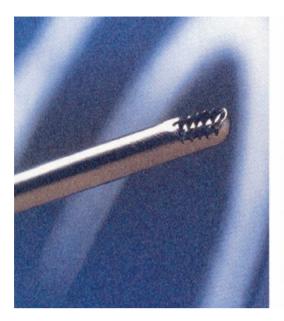




Figure 28.4 Rotary blade.

The working part of the blade opens to the side. The blade is therefore placed against the tissue laterally, in full view, rather than behind: this lowers perforation risk. Because saline is the distention medium and the pressure noted is truly that of the intrauterine cavity, there are fewer fluid-related complications. Finally, the author who has performed and taught resectoscopy for nearly 25 years, notes a shorter learning curve with hysteroscopic morcellation and thus more physicians are willing to avail themselves of this technology.

At present there are two types of blades that can be used for hysteroscopic morcellation. The rotary blade (Figure 28.4) is the initial blade created for the system; however, because its ability to cut through dense tissue is limited, it is most useful in removing endometrial polyps. The newer reciprocating blade (Figure 28.5) is designed for myoma evacuation: not only does the blade rotate at 1100 times per second but also it moves in a forward–backward direction at one-seventh (157 cpm) the rate. This blade configuration enables morcellation of more fibrous tissue.

PATIENT SELECTION CRITERIA

Hysteroscopic morcellation is most efficient for patients presenting with endometrial polyps or a type 0 or type I submucosal leiomyoma, as defined by Wamsteker et al² (Figure 28.6). As it is difficult for either blade to go beneath the surface of the cavity, the type II submucosal myoma must be undermined and positioned above the surface to enable complete morcellation.

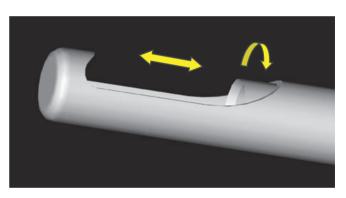


Figure 28.5 Reciprocating blade. Smith & Nephew: completely redesigned morcellator for gynecology (myomas); optimum performance at 1100 rpm (157 cpm).

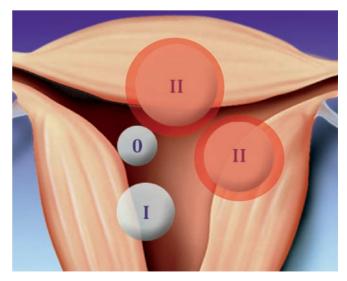


Figure 28.6 Hysteroscopic morcellation – Types of submucosal leiomyomas: O, I, and II.

Volume = $4/3\pi r^3$ First 10 cm³ diameter 0–2.7 cm Second 10 cm³ diameter 2.7–3.4 cm Third 10 cm³ diameter 3.4–3.9 cm Fourth 10 cm³ diameter 3.9–4.2 cm

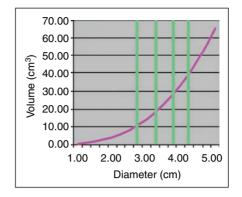


Figure 28.7 Effect of fibroid diameter on fibroid volume.

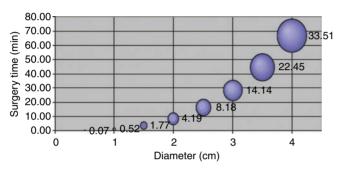


Figure 28.8 Diameter vs surgery time for morcellation rate of O.S. cm³/min.

Fibroid size also must be considered. One can see from (Figure 28.7) that the fibroid volume doubles as the fibroid diameter increases from 2.7 cm to 3.4 cm. Furthermore, the volume doubles yet again from 3.4 cm to 4.2 cm. As according to the manufacturers, morcellation can be expected to proceed at approximately 0.5 cm³/min, a 2 cm fibroid, with a volume of 4.2 cm³, would be completely evacuated in 8.4 min (Figure 28.8). On the other hand, a 3 cm fibroid would be completely morcellated in 28.2 minutes, as its volume is 14.1 cm³. Thus, with a 50% increase in fibroid diameter, morcellation time will be more than tripled. As a 4 cm fibroid would require 1 hour of morcellation time, the recommendation is to use this technique for fibroids ≤3 cm.

PRE-TREATMENT CONSIDERATIONS

The author routinely does not pretreat the endometrium, but rather performs hysteroscopic morcellation in the early follicular phase. If desired, the endometrium can be pretreated effectively either with an oral contraceptive or a gonedotropin-releasing hormone (GnRH) agonist.

Because the diameter of the hysteroscopic morcellation system is 9 mm, the author recommends use of misoprostol 200 mg taken orally or placed vaginally,

the night prior to the procedure and the morning of the surgery. With the softening of the cervix, dilatation can be accomplished more safely, with less risk of tearing the cervix. Use of *Laminaria* is not recommended because of the potential risk of increasing the infection rate.

HYSTEROSCOPIC MORCELLATION RISKS

As with the resectoscope, hysteroscopic morcellation can be associated with perforation, cervical trauma, intravasation leading to fluid overload, infection, and bleeding. It is the author's opinion that such complications are lessened with hysteroscopic morcellation. The hysteroscope is brought in and out of the cervix and endometrial cavity far less when using the morcellation system. This reduces risk of perforation, cervix trauma, infection, and bleeding. Since the system is based on mechanical energy inside the uterus, not electrical energy, gas embolism risk is far less. Moreover, the side opening of the blade decreases perforation risk. Furthermore, if perforation does occur, the risk of electrosurgical burn is a non-factor.

Despite the inability to coagulate a bleeding vessel, as the electrical energy is converted to mechanical energy, no reported bleeding has occurred. Generally, contraction of the uterus stops bleeding. In addition, the continuous high-flow system will clear the image if bleeding is noted. Given that vessel size increases as one proceeds away from the endometrium toward the serosa (Figure 28.9) it is best to utilize the hysteroscopic morcellation to remove type 0 and type I submucosal myomata. In this way, the blade remains superficial and therefore risks of bleeding are reduced.

TECHNIQUE TIPS

When inserting the instrument, since the hysteroscope is 0° (non-beveled) and large (9 mm), to minimize cervical

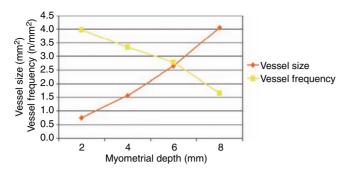


Figure 28.9 Myometrial vascular achitecture.

trauma, insert the hysteroscope sheath with the obturator in place. The curved edge causes less cervical trauma.

Open the inflow valve as the well as outflow valve with insertion of the hysteroscope: not only does the saline flow aid insertion but also it assists in achieving proper visualization in an expeditious fashion. The flow of fluid will flush blood and clots and assist in fluid exchange.

Increasing the intrauterine pressure at the start of the procedure will rapidly aid in achieving adequate visualization. Once this occurs, intrauterine pressure should be reduced to the lowest setting that allows maintenance of adequate distention and provides good visualization. Ultimately, lower pressure enables less intravasation of fluid.

If clot or debris is noted to negatively impact on visualization, the morcellator can be activated in an open cavity. The fluid will clear quickly. This certainly is a distinct advantage of hysteroscopic morcellation.

When morcellating a fibroid or polyp, the surgeon is advised to work from the periphery to the base. In this way, there is no risk of having to retrieve a specimen that is circulating freely in the uterine cavity.

CLINICAL STUDIES

In 2005, Emanuel and Wamsteker reported on a retrospective comparison of hysteroscopic intrauterine

morcellation with conventional resectoscopy³: 55 women were evaluated (27 with endometrial polyps, 28 with submucous myomas). The mean operating time was 8.7 minutes for the removal of endometrial polyps compared with 30.9 minutes for resectoscopy, and 16.4 minutes for submucous myomas compared with 42.2 minutes for resectoscopy. All procedures were uneventful.

The European Pilot Study Group reported on 51 patients undergoing hysteroscopic morcellation from October 2003 until July 2004: 97% of the 109 lesions (83 polyps and 26 myomas) were successfully completed.⁴ The mean operative time was 9.4 minutes and the mean fluid deficit was 329 ml. No intra- or postoperative hemorrhage was noted. No obvious electrolyte abnormalities were noted. All patients underwent uneventful recoveries

In a randomized controlled multicenter study that included the author (C.M), hysteroscopic morcellation was compared to conventional loop resectoscopy for the removal of endometrial polyps and fibroids within the uterine cavity.⁵ A total of 167 lesions were treated in 97 patients: 94 lesions in 48 patients (73 polyps, 21 fibroids) were treated via hysteroscopic morcellation. 73 lesions (51 polyps, 22 myomas) were removed in 49 patients treated by conventional loop resectoscopy.

The operating time for the morcellation technique was 10.2 minutes and the mean fluid deficit for these procedures was 313 ml. The operative duration for the loop resection was 12.7 minutes, with a fluid deficit of 232 ml. Essentially, the operating time as well as the fluid deficit were similar between patients in both the hysteroscopic morcellation and the loop resectoscopy group. Thus, hysteroscopic morcellation is an effective technique for treatment of endometrial polyps and fibroids contained in the uterine cavity. It can be offered as a safe alternative to conventional hysteroscopic resectoscopy.

References

- American Association of Gynecologic Laparoscopists. Management of anovulatory bleeding. ACOG Practice Bulletin, Clinical management guidelines for obstetrician-gynecologists, No. 14, March 2000.
- Wamsteker K, Emanuel MH, de Kruif JH. Transcervical hysteroscopic resection of submucous fibroids for abnormal uterine bleeding: results regarding the degree of intramural extension. Obstet Gynecol 1993; 82(5): 736–40
- Emanuel M, Wamsteker K. The Intra Uterine Morcellator: a new hysteroscopic operating technique to remove intrauterine
- polyps and myomas. J Minim Invasive Gynecol 2005; 12: 62–66
- European Pilot Study Group. Personal communications with Dr Mark Hans Emanuel.
- Bradley LD, Gimpelson RJ, Lukes A et al. J Minim Invasive Gynecol 2006 Suppl. Abstracts of the Global Congress of Minimally Invasive Gynecology 35th Annual Meeting of the AAGL. Advancing Minimally Invasive Gynecology Worldwide, Abstract No. 36, PS18.

Uterine artery embolization – the evidence

Anju Sinha and Janesh Gupta

INTRODUCTION

Uterine artery embolization (UAE) is an emerging minimally invasive technology for reducing symptoms from uterine fibroids. It was first introduced in 1995 as an alternative technique for treating fibroids. Since then, more than 100000 procedures have been carried out worldwide, mainly in the USA and the Western Europe.² In the UK, the National Institute for Clinical Excellence (NICE) issued guidance in October 2004 that UAE could be used in routine practice as there is symptomatic benefit in the majority of patients in the short term.³ A subsequent NICE guideline published in January 2007 recommends UAE, along with surgery, to be considered as first-line treatment.4 However, a Cochrane review on UAE emphasizes the need for longer term and larger randomized controlled trials of UAE vs surgical treatments, as this information is crucial to determine the long-term efficacy and safety of the procedure.5

The aim of this chapter is to review the available literature on uterine artery embolization and provide some guidelines for its use in clinical practice.

BACKGROUND

Uterine fibroids are the most commonly found gynecological benign tumors. At least 25% of all women of childbearing age are clinically affected.⁶ They can cause heavy and prolonged uterine bleeding, pain and pressure symptoms, and subfertility.⁷ Treatment is generally reserved for symptomatic women, as fibroids are usually regarded as a benign condition.

Currently available medical therapies for fibroids have not demonstrated long-term efficacy, while surgical therapies are commonly associated with complications. Hysterectomy is the traditional treatment for women who have completed their families. In the UK, approximately 42 500 hysterectomies are performed annually, with fibroids being the second most frequent indication. For women wishing to maintain their fertility, myomectomy

is the principal option. Hysterectomy has an approximately 3% incidence of major complications, although that for myomectomy is less well defined. Myomectomy is associated with long-term problems such as fibroid recurrence, adhesion formation, and the increased possibility of uterine rupture during pregnancy and vaginal delivery. delivery.

Uterine artery embolization, like myomectomy, spares the uterus. It offers an alternative treatment in women who want to conserve their uterus or have medical contraindications to major surgery.³

CURRENT EVIDENCE

The evidence for UAE is mainly derived from several large uncontrolled series. These have demonstrated the efficacy and safety of uterine artery embolization in the management of fibroids. This is also supported by the systematic review of the efficacy and safety of uterine artery embolization in the treatment of fibroids commissioned by NICE.11 The review states that there is a reduction in mean uterine volume by 26-59% and fibroid volume by 40–75% in the first 6 months following UAE. In studies with longer follow-up, this was shown to continue in most women. UAE also results in the improvement of symptoms, mainly menorrhagia (60%-90%). The overall complication rate reported is 10.5%, with the rate of major complications being 1.5%. The review was based on one randomized controlled trial, two comparative studies, one patient questionnaire survey, and 32 papers from 25 case series.

Whereas some useful information can be deduced from the results of uncontrolled studies, we have concentrated on the evidence available from randomized controlled trials. We have identified four randomized controlled trials^{13–16} for the purposes of this review.

There are two randomized controlled trials (Pinto¹² and the EMMY trial¹³) with 57 and 177 women, respectively, comparing UAE to abdominal hysterectomy with regards to length of hospital stay and associated complications.

The EMMY trial has only reported on the peri- and postprocedural complications up to 6-week follow-up. The Pinto trial duration of follow-up was intended to be 2 years but published results that are currently available are only for 6-month follow-up.

There is one randomized controlled trial (Mara et al. ¹⁴) with 63 women comparing UAE with myomectomy (open abdominal in 18 women and laparoscopic in 15 women). Outcome measures reported were procedure duration, length of hospital stay, technical success, fibroid-related symptom relief, and early and late complications (which included therapy failures, recurrences, and reinterventions). The minimum follow-up was 6 months, with a mean of 17 months (range 6–36 months).

The largest and most recent REST trial¹⁵ included 157 women and compared UAE with surgery (43 hysterectomy and 8 myomectomy). The primary outcome measure was quality of life at 1 year, while secondary outcome measures included the length of hospital stay, time to resume normal activities, symptom relief, and treatment failures.

Efficacy – fibroid volume and symptom improvement

In the Pinto trial the mean dominant fibroid volume decreased by 46% (95% confidence internal [CI] 27–66%) at 6-month follow-up. The EMMY trial fails to discuss the efficacy of the embolization procedure.

In the Mara trial, the mean shrinkage of dominant fibroid at 6 months after embolization was assessed in all 30 UAE women: $29.7\pm14.1\%$ (range 5%-57%). Mean shrinkage at 12 months after UAE was assessed in only 13 women (due to excluding women with secondary myomectomy and with shorter follow-up): $38.9\pm18.1\%$ (range 7%-63%).

Based on data from the Pinto trial only, the clinical success rate for women who underwent UAE, based on the reduction in bleeding, was 86% (31 of 36 women). This equates to normalization of menorrhagia in 56% (20 of 36 women), reduction of menorrhagia in 14% (5 of 35 women), and amenorrhea in 17% (6 of 36 women).

In the Mara trial, which compared UAE with myomectomy, both methods were shown to be highly effective in treating symptoms: 21 out of 24 women (87.5%) with previous symptoms had significant relief 6 months after embolization and 28 out of 30 women (93.3%) after myomectomy. There was a higher proportion of completely asymptomatic women after myomectomy (70%) compared to those after UAE (46%), but the difference was not significant (p < 0.1).

The primary outcome measure (12-month Short Form 36 [SF-36] score) for the REST trial was available for 140 (89%) of the 157 women. There were no significant

differences between the groups in any of the eight components of the SF-36 score at 1 year. However, symptom relief scores were better in the surgical arm at 12 months. This can be explained as the majority of women in the surgical arm underwent hysterectomy.

Safety

The establishment of safety for any new procedure is of vital importance before the procedure can be introduced into routine clinical practice. Safety can be divided into primary (complications that occur as result of the procedure) or secondary (complications where there is a delay before patients can resume their normal activities). The four randomized controlled trials have commented on the safety aspect of the procedure by comparing the complication rates. Also, all the trials have commented on the return to daily activity following UAE, indicating indirectly improved symptoms after this procedure.

In the Pinto trial, there were no significant differences in intraprocedural complications (25% in the UAE and 20% in the hysterectomy group, p = 0.8). Postprocedurally, complications were recorded in 29 (72%) patients who underwent UAE and for nine (45%) patients who underwent hysterectomy (p = 0.05). These were vaginal discharge, postpuncture hematoma, and postembolization syndrome.

In the EMMY trial, the overall rate of minor complications was 64.2% in the UAE group and 56.0% in the hysterectomy group (p = 0.38). UAE had more minor complications within 42 days of discharge, such as vaginal discharge, postpuncture hematoma, and postembolization syndrome (pain, fever, nausea, vomiting), compared with the hysterectomy group. The overall major complication rate was 4.9% and 2.7% for UAE and hysterectomy, respectively.

In the MARA trial, no significant differences were found between the embolization and myomectomy groups with regard to febrile morbidity, need for antibiotics, or frequency of prolonged hospitalization or rehospitalization. The frequency of early postoperative adverse events was relatively high, occurring in 23% of the embolization and 27% of the myomectomy group. The mean follow-up was more than 17 (±9.3) months in both groups and longer than 1 year in 63% and 61% of women in the embolization and myomectomy groups, respectively. There were no significant differences between the groups in the frequency of late complications, with no cases of a life-threatening complication, hysterectomy, or other urgent surgery in the entire study population.

In the first year of the REST trial, minor complications were reported by 34% of women in the embolization group and 20% of women in the surgical group (p = 0.06).

These were usually related to the postembolization syndrome (52%) in the embolization group and to minor infections (25%) in the surgical group. In a similar time frame, there were 12% major adverse events in the embolization group and 20% in the surgical group (p = 0.22), mostly related to the intervention. Overall, the rate of minor complications after uterine artery embolization is around 48% considering the complication rates from the four trials.

The results from the Pinto and EMMY trials, both of which compared UAE vs hysterectomy, indicate that UAE reduces hospital stay by 3.37 days (p <0.001). This significant difference in hospital stay was further maintained in the MARA and REST trials (p <0.001). In the Pinto trial, the mean duration of resumption to routine activities was significantly shorter for the UAE group (9.5 ± 7.2 days) vs the hysterectomy group (36.2 ± 20.5 days) (p <0.001). In the MARA trial, the return to normal activity was markedly longer after myomectomy (13.6 ± 5.1 days vs 30.0 ± 12.9 days, p <0.0001). The REST trial also showed a shorter time to resume normal activities including return to work (p <0.001).

Patient satisfaction

Patient satisfaction after UAE and the comparator surgical intervention was elicited by asking women whether they would undergo the same treatment again. In the Pinto trial, this is similar in both UAE and hysterectomy groups (86% and 88%) at 6-month follow-up and 88% and 93%, respectively, in the REST trial at 12-month follow-up (p = 0.32). This is in keeping with the results of a large prospective multicenter study which reported that 85% of patients(n = 414/487) were willing to undergo another UAE procedure if necessary.¹⁶

Pregnancy

There is limited information about successful pregnancies from the reported randomized controlled trials. However, there are small numbers of case reports and case series of fertility restoration and successful delivery of normally grown infants.^{17,18}

In the MARA trial, 18 gestations from 17 women with eight live born and five uncomplicated pregnancies had resulted in the entire study population. They did not define the number of pregnancies in each group and have commented that the effect of both methods on reproductive outcome cannot yet be sufficiently evaluated. In the REST trial, by September 2005, eight pregnancies had occurred in five women (7/106 in the UAE group and 1/8 in the myomectomy group): four women had miscarried, three had successful live births and one pregnancy was ongoing.

Ovarian failure

Only the MARA trial reported on ovarian failure, with two patients undergoing temporary elevations of follicle-stimulating harmone (FSH) levels, with one patient showing poor response to ovarian stimulation. In their study, there was no difference in postprocedural FSH levels between the embolization and myomectomy groups, nor a significant increase in the mean FSH level 6 months after the procedure in comparison with the results prior to embolization. They also feel that the risk of permanent amenorrhea and of ovarian failure in UAE most probably relates to women >40 years old or to those with significantly decreased ovarian reserve. 19,20

Postembolization pregnancy chances

The RCOG (Royal College of Obstetricians and Gynaecologists) joint working party²¹ suggested that women who elected to undergo fibroid embolization should be fully informed about the uncertain effects of UAE on pregnancy and that there may be long-term implications for the health and development of their offspring. The conclusion was that patients should be advised not to try to conceive after UAE and should only contemplate the procedure if they had completed their family. They also suggested that patients should be warned of the potential complications of the procedure, including the risk of late complications such as ovarian damage due to impairment of ovarian blood flow and infection leading to fallopian tube damage and subsequent infertility. Because of the theoretical risk of adverse effects of UAE on placental blood flow, any pregnancy following the procedure may be complicated by intrauterine growth restriction, premature labor, and postpartum hemorrhage, with possible long-term sequelae for the child.²²

Hence, UAE is currently only recommended for women with fibroids who have completed their families, with a primary complaint of menorrhagia, dysmenorrhea, and pressure effects. However, in patients with large and/ or multiple submucous or interstitial fibroids, where resection would be difficult and likely to recur, and in those with failed previous fibroid surgery, UAE could be considered as an option with warnings about the chances of successful pregnancy.²³

Baseline investigations before UAE

Accurate pretreatment diagnosis is essential, and endometrial biopsy should be taken to ensure that bleeding irregularities are not due to any other pathology other than the fibroids. Magnetic resonance imaging, is superior to ultrasound in determining the size of the fibroids

and their extension into the myometrium and the presence of adenomyosis, which is a relative contraindication to embolization. Gonadotropin-releasing hormone analogues should be avoided in the preceding 2 months. Other relative contraindications are pedunculated subserous fibroids and very large (>8 cm) fibroids, which respond less well to the technique.²⁴ Absolute contraindications to performing the procedure would be pregnancy, any evidence of current or recent infection in the genital tract, refusal to consent to hysterectomy under any circumstances, and allergy to contrast media.

Technique

The aim of successful uterine artery embolization is to totally occlude both uterine arteries. The normal myometrium rapidly establishes a new blood supply through collateral vessels from the ovarian and vaginal circulations. As fibroids appear to be supplied by end arteries, without the collateral flow found in normal myometrium, they are preferentially affected by the reduction in flow.

Uterine artery embolization involves with the use of particulate emboli to cause ischemic necrosis of the uterine fibroids with the aim of avoiding permanent adverse effect on the otherwise normal uterus. This has been performed using either general anesthesia, conscious sedation, epidural, or spinal anesthesia. Some practitioners administer prophylactic antibiotics. An angiography catheter is inserted directly into the woman's femoral artery and the contralateral uterine artery is then selectively catheterized. The catheter is then maneuvered to the opposite uterine artery (ipsilateral to the femoral puncture site) and the process repeated. The most commonly used agent is polyvinyl alcohol (PVA), a non-biodegradable agent available in a variety of sizes (normally 150-1000 µm for this procedure) and suspended in a contrast solution. Occlusion (blockage) of the uterine vessels is confirmed by angiography (X -ray dye test) and the catheter removed. The procedure takes between 45 and 135 minutes to complete and the woman is exposed to approximately 20 rads (20 cGy) of ionizing radiation to the ovaries.²⁵ Women are observed for up to 24 hours postprocedure and treated with narcotics for pain.

Technical failure

In the Pinto trial the technical success rate was 90% with unilateral embolization performed in four cases (10%), due to technical difficulties such as spasm and/or anatomic abnormalities of the uterine artery. The EMMY trial success rate was 89% (72/81) while the technical failure rate was 11% (9/81) due to failure to embolize both arteries in four (5%) patients. The Mara trial reported successful

bilateral occlusion of ascending branches of the uterine arteries in 87% of cases. In four women (13.3%) embolization was only unilateral, mainly due to arterial abnormalities (atypical branching, spasm not reacting to vasodilators), and in one case for a large utero—ovarian anastomosis. There was a low technical failure rate in the REST trial (3/101) due to difficulty identifying or catheterizing one or both uterine arteries. Overall, the technical success rate is around 92% (237/257) and the failure rate is 8% (20/257).

Repeat intervention or treatment failure rates

This is defined as the number of women who need an additional invasive procedure such as hysterectomy, myomectomy, or repeat uterine artery embolization.

In the Pinto trial, three women needed hysterectomy while two were waiting decision regarding further management after having UAE, giving a treatment failure rate of 12.5%. The EMMY trial had a low treatment failure rate of 5% (4/81), but this was only at 6 weeks of follow-up. There was a high reintervention rate in the Mara trial. Eleven women (37%), including four who had unilateral embolization, underwent secondary myomectomy. No case required hysterectomy. This high failure rate could be explained by the characteristic nature of the study sample, which included women wishing to retain fertility and the need for elective secondary myomectomy in seven cases. Adjusting for these cases gave a treatment failure rate of 13% (4/30). In the REST trial, 10 (9%) women needed repeat embolization or hysterectomy for inadequate symptom control by 12 months. This figure increases to 21% after the first year of follow-up, suggesting that long-term follow-up results are essential.

Overall, the treatment failure or the procedural failure rate is around 11.5%. The EMMY trial has been excluded, as it only had 6 weeks of follow-up.

Complications from UAE

The commonest immediate side effect of UAE is moderate to severe pain associated with nausea, vomiting, and a low-grade fever. This is known as postembolization syndrome. Usually, it is mild, lasts for a few days, and is controlled with analgesia, antiemetics, and intravenous fluids. There is a risk of infection from necrosis of the fibroids, leading to endometritis, which may require hospitalization and treatment with intravenous antibiotics. Bruising and hematoma formation at the site of incision may occur. The patient may suffer from persistent vaginal discharge due to infected necrotic tissue inside the uterus. She may complain of fibroid expulsion or may need surgical removal of a partially expelled fibroid or even hysterectomy for chronic discharge or pain.

There is also a concern about causing unintended ovarian damage, resulting from embolic material migrating to the ovaries. This can be linked to future infertility and premature menopause. Rarely, subacute bowel obstruction has occurred. ²⁶ Very rarely, death has been reported due to septicemia. ²⁷

CONCLUSION

Uterine artery embolization is gaining popularity, both among clinicians and women, as an option for managing symptomatic fibroids. There is definitive evidence of its efficacy and safety in the short term. However, the use of UAE as a fertility-sparing option for women with symptomatic fibroids is debatable. Although, there are reports of successful pregnancy after UAE, reliable long-term data are not available. There is only one randomized controlled trial comparing UAE with myomectomy (Mara trial) which suggests that myomectomy may be indicated over UAE when fertility is desired. The effect of UAE on premature ovarian failure has not been established. There is still a need for long-term follow-up studies to ascertain the efficacy, treatment success rate, and safety of UAE.

SUMMARY OF RECOMMENDATIONS²¹

- While the early results of UAE are encouraging, no long-term data exist.
- UAE should be considered only for women with symptomatic fibroids who might otherwise be advised surgical treatment.

- UAE as treatment for fibroids in infertile patients should be within a controlled clinical trial.
- The procedure is contraindicated in women who have evidence of current or recent infection and women who are unwilling to have a hysterectomy in any circumstances.
- Infection is the predominant cause of serious morbidity and mortality. Further research on the place of prophylactic antibiotic therapy and the value of pretreatment screening for infection is needed.
- Patients should be seen by a gynecologist in the first instance and accurate pretreatment diagnosis is essential.
- The procedure should only be undertaken by radiologists with specialized embolization experience or who have undergone appropriate training.
- The particular responsibilities of both gynecologist and radiologist should be established prior to treatment and be set out in a relevant hospital protocol. The patient must be under a named responsible consultant at all times.
- All cases of UAE must be part of a primary research program and be registered with the Safety and Efficacy Register of New Interventional Procedures (SERNIP), class C procedure.
- The collection of data relating to methodology, outcome, complications, and pregnancy following UAE is essential; a national register is recommended.

References

- Ravina JH, Herbreteau D, Ciraru-Vigneron N et al. Arterial embolisation to treat uterine myomata. Lancet 1995; 346: 671–2.
- Committee on Gynecologic Practice, American College of Obstetricians and Gynecologists. ACOG Committee Opinion. Uterine artery embolization. Obstet Gynecol 2004; 103(2): 403–4.
- National Institute for Clinical Excellence. Uterine artery embolisation for the treatment of fibroids. NICE Interventional Procedures Guidance: Issue date October 2004. Available from www.nice.org.uk/ip020overview (accessed January 30, 2006).
- 4. National Institute for Clinical Excellence. Heavy menstrual bleeding. Issue date January 2007. Available from http://guidance.nice.org.uk/CG44.
- Gupta JK, Sinha AS, Lumsden MA et al. Uterine artery embolization for symptomatic uterine fibroids. Cochrane Database Syst Rev 2006; 1: CD005073.

- 6. Stewart EA. Uterine fibroids. Lancet 2001; 357: 293-8.
- Lumsden MA, Wallace EM. Clinical presentation of uterine fibroids. Baillieres Clin Obst Gynaecol 1998; 12(2): 177–95.
- Edozien LC. Hysterectomy for benign conditions. BMJ 2005; 330(7506): 1457–8.
- Garry R, Fountain J, Mason S et al. The eVALuate study: two
 parallel randomised trials, one comparing laparoscopic with
 abdominal hysterectomy, the other comparing laparoscopic with
 vaginal hysterectomy. BMJ 2004; 328(7432): 129.
- Gehlbach DL, Sousa RC, Carpenter SE, Rock JA. Abdominal myomectomy in the treatment of infertility. Int J Gynaecol Obstet 1993; 40(1): 45–50.
- 11. Coleman P. Review Body for Interventional Procedures. Sheffield: National Institute for Clinical Excellence, 2004.
- 12. Pinto I, Chimeno P, Romo L et al. Uterine fibroids: uterine artery embolization versus abdominal hysterectomy for treatment.

- A prospective randomized and controlled trial. Radiology 2003; 226(2): 425–31.
- 13. Hehenkamp WJK, Volkers NA, Donderwinkel PFJ et al. Uterine artery embolization versus hysterectomy in the treatment of symptomatic uterine fibroids (EMMY trial): peri- and postprocedural results from a randomized controlled trial. Am J Obstet Gynecol 2005; 193: 1618–29.
- 14. Mara M, Fucikova Z, Maskova J, Kuzel D, Haakova L. Uterine fibroid embolization versus myomectomy in women wishing to preserve fertility: preliminary results of a randomized controlled trial. Eur J Obstet Gynecol Reprod Biol 2006; 126: 226–33.
- Edwards RD, Moss JG, Lumsden MA et al. Committee of the Randomized Trial of Embolization versus Surgical Treatment for Fibroids. Uterine-artery embolization versus surgery for symptomatic uterine fibroids. N Engl J Med 2007; 356: 360–70.
- Pron G, Bennett J, Common A et al. Ontario Uterine Fibroid Embolization Collaborative Group. The Ontario Uterine Fibroid Embolization Trial. Part 2 Uterine fibroid reduction and symptom relief after uterine artery embolization for fibroids. Fertil Steril 2003; 79(1): 120–7.
- McLucas B, Goodwin S, Adler L et al. Pregnancy following uterine fibroid embolization. Int J Gynecol Obstet 2001; 74: 1–7.
- Ravina JH, Vigneron NC, Aymard A et al. Pregnancy after embolisation of uterine myoma: report of 12 cases. Fertil Steril 2000; 73: 1241–3.
- Spies JB, Roth AR, Gonsalves SM, Murphy-Skrzyniarz KM. Ovarian function after uterine artery embolization for leiomyo-

- mata: assessment with use of serum follicle stimulating hormone assay. J Vasc Interv Radiol 2001; 12: 437–42.
- Tropeano G, Di Stasi C, Litwicka K et al. Uterine artery embolization for fibroids does not have adverse effects on ovarian reserve in regularly cycling women younger than 40 years. Fertil Steril 2004; 81: 1055–61.
- Royal College of Radiologists and Royal College of Obstetricians and Gynaecologists. Clinical recommendations on the use of uterine artery embolisation in the management of fibroids. Report of a joint working party. (Royal College Joint Report) 2000.
- 22. Goldberg J, Pereira L, Berghella V. Pregnancy after uterine artery embolization. Obstet Gynecol 2002; 100(5): 869–72.
- Walker W, McDowell SJPregnancy after uterine artery embolization for leiomyomata: a series of 56 completed pregnancies.
 Am J Obstet Gynecol 2006; 195: 1266–71.
- Al-Fozan H, Tulandi T. Factors affecting early surgical intervention after uterine artery embolization. Obstet Gynecol Surv 2002; 57: 810–15.
- Spies JB, Warren EH, Mathias SD et al. Uterine fibroid embolization: measurement of health-related quality of life before and after therapy. J Vasc Interv Radiol 1999; 10(10): 1293–303.
- Payne JF, Haney AF. Serious complications of uterine artery embolization for conservative treatment of fibroids. Fertil Steril 2003; 79: 128–31.
- Vashisht A, Studd J, Carey A et al. Fatal septicaemia after fibroid embolization. Lancet 1999; 354: 307–8.

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Avoiding and managing laparoscopic complications in gynecologic surgery

Paul Tulikangas and Tommaso Falcone

INTRODUCTION

Complications are inevitable in surgery. The skilled surgeon takes key steps to limit their number, but when a complication does occur it is important that it is recognized intraoperatively and corrected to reduce patient morbidity. In this chapter, we review techniques for avoiding complications and basic concepts in managing most common complications in laparoscopic surgery for menorrhagia.

The complication rate for diagnostic laparoscopy and tubal sterilization is significantly lower than the rate for operative laparoscopy (Table 30.1) When an operative laparoscopy is performed, complications are typically reported as those related to initial entry into the peritoneal cavity and those related to specific organ systems: the urinary, gastrointestinal, and vascular systems. Rates of complications from a review of 70 607 procedures are noted in Table 30.2.

NEUROPATHY

Nerve injuries are uncommon problems after laparoscopic surgery. Most are due to positioning of the patient and can be avoided. Some occur as a result of direct trauma to nerves. Patients with medical disorders that predispose to neurologic disorders should be evaluated preoperatively. The physical forces that cause nerve injury are typically compression, stretching, or direct trauma. Shoulder braces that are meant to prevent patient movement during deep Trendelenburg position can cause brachial nerve palsy if placed medial to the acromioclavicular joint. Compression of the peroneal nerve can occur with inadequate protection of the head of the fibula. Femoral nerve compression under the inguinal ligament is the result of hyperflexion or hyperextension of the leg at the hip.

Hyperextension of the leg can also stretch the sciatic nerve. Excessive abduction of the legs during the vaginal part of a laparoscopic-assisted vaginal hysterectomy can cause stretching of the obturator nerve with subsequent adductor muscle weakness. Direct injury to the nerves of the anterior abdominal wall can cause severe pain postoperatively. The ilioinguinal and iliohypogastric nerves run between the external oblique and internal oblique aponeurosis. Cadaver studies have demonstrated that the nerves pierce the fascia approximately 2 cm medial to the anterior superior iliac spine (ASIS) and run towards the pubis. Trocars should be placed above the ASIS to decrease the incidence of nerve injury either from direct trauma or compression with sutures when closing the fascia of the port site.

The genitofemoral nerve is found on the psoas muscle. Injuries to this retroperitoneal nerve can occur during dissection on the psoas muscle, such as during an appendectomy on the right side or incision of the sigmoid reflection on the left. The latter is sometimes erroneously diagnosed as an adhesion. Injury to the obturator nerve can occur during a lymph node dissection.

TROCAR-RELATED INJURY

The majority of complications in laparoscopy occur with laparoscopic entry into the abdomen and pelvis. In one review of 2324 laparoscopic gynecologic procedures, 21 complications were noted and 18 occurred during laparoscopic trocar insertion.² Patients should be positioned supine on the operating table for the primary access. If the patient has general anesthesia, a gastric drainage tube should be placed to decompress the stomach. The bladder should be drained. If a long surgery is anticipated, the arms are typically tucked by the patient's side. This will avoid potential hyperextension of the arms and possible nerve injury. The patient's legs should be carefully placed in stirrups to avoid hyperflexion at the hips or possible compression of the peroneal nerve in the popliteal fossa. For operative laparoscopy, we routinely use pneumatic compression stockings. If a patient is high risk for deep vein thrombosis (malignancy, history of prior clot, or clotting disorder), we also use prophylactic subcutaneous heparin.

Most gynecologists establish a pneumoperitoneum through the umbilicus. This is typically done with either

Table 30.1 Annual major complication rates¹⁵

Diagnostic laparoscopy	0.6/1000	
Tubal sterilization	0.8/1000	
Operative laparoscopy	10.1/1000	

Table 30.2 Types of major laparoscopic complications¹⁵

Intestinal injuries	0.6/1000
Urinary tract injuries	0.6/1000
Vascular injuries	0.1/1000

a Verres needle into the abdomen or a trocar directly into the abdomen. Some surgeons recommend an 'open' technique, which involves a peritoneal cut-down incision followed by trocar insertion under direct visualization. A systemic review of multiple studies has found no superior method for entering the abdomen.³ There do appear to be fewer vascular complications with the 'open' technique. We recommend that the surgeon routinely perform the technique that they are most comfortable with if there are no apparent contraindications.

When a Verres needle is used as the primary entry procedure, it should be held gently like a pen. The small muscles of the hand are used to advance it into the abdomen. Insertion of the trocar will typically require more force. An adequate abdominal incision is needed to prevent resistance at the level of the skin. The trocar is best held in the palm, with the middle finger or index finger along the sleeve to control entry. The patient should be flat for the initial trocar insertion.

If the patient has had prior abdominal incisions or adhesions are suspected, one should consider either open laparoscopy at the umbilicus or primary trocar insertion in the left upper quadrant. In patients with prior lower abdominal incisions, the incidence of adhesions in the periumbilical area is about 20%.⁴ We prefer the left upper quadrant technique because it gives us a panoramic view of the potential lower abdominal and pelvic adhesions. The most common organ injuries with left upper quadrant trocar insertion are the stomach, the left lobe of the liver, and the lung.⁵

An optical-guided trocar is available which allows the laparoscope to be inserted into the trocar to view the planes of the abdominal wall as you enter the abdomen. No study has shown a significant benefit with this technique and a number of major complications have occurred with this technique.⁶

The most common vascular injuries during primary umbilical trocar insertion are the common iliac vessels,

the aorta, and the vena cava. In thin women, the great vessels are located directly below the umbilicus.

To avoid vessel injury, the trocar or Verres needle should be advanced at a 45° angle in the sagittal plane. In obese women, the angle of the trocar can be adjusted to 90° because the umbilicus is more caudad. Advancing the needle perpendicular to the abdominal wall in obese patients decreases the length of the abdominal wall the trocar must travel and increases the chance of successful pneumonia insufflation. Hurd et al. demonstrated this relationship in a review of computed tomography (CT) scans of women with different body mass indices BMIs.⁷

The accessory trocars are typically placed either in the suprapubic area or laterally under direct vision. Suprapubic ports should be placed 5 cm above the pubic symphysis and lateral ports should be placed 8 cm lateral to the midline and 5 cm above the pubic symphysis. These locations limit the risk of injury to the superficial and inferior epigastric and circumflex blood vessels.⁸

At the end of surgery we typically release the pneumoperitoneum and recheck hemostasis. To avoid drawing intestines into the abdominal wall, we remove our accessory trocars under direct visualization. The umbilical trocar is removed over the laparoscope and the scope is withdrawn last. Facial defects of trocar sites ≥8 mm are closed to avoid incisional hernia.⁹

VASCULAR INJURIES

Vascular injuries at laparoscopy are the result of entry into the peritoneal cavity or trauma to blood vessels during surgery. Injuries due to entry into the peritoneal cavity can be avoided but not entirely eliminated with sound knowledge of anterior abdominal wall anatomy, principally the relationship of the umbilicus to the retroperitoneal vascular anatomy and the relationship of the inferior epigastric vessels to the abdominal musculature and facsia.

The umbilical relationship to the bifurcation of the aorta was discussed above. Injury to a large retroperitoneal vessel requires immediate action. The anesthesiologist should be notified that a potential vascular injury has occurred, the patient placed in the Trendelenburg position, and an immediate laparotomy with a midline incision should be performed. Pressure should be placed on the site of the bleeding and a vascular surgeon called. Blood should be ordered and resuscitation initiated.

The lower abdominal wall has two major vessel systems, one derived from the external iliac artery and one derived from the femoral artery. The femoral artery gives rise to the superficial epigastric and circumflex iliac vessels. These superficial vessels can sometimes be transilluminated with the laparoscopic light, but the deep vessels

can never be transilluminated. Injury to the superficial vessels can lead to a hematoma anterior to the fascial components of the anterior abdominal wall. The hematoma is visible and blood can track down the subcutaneous tissues into the labia.

The inferior (deep) epigastric vessels come off the external iliac artery. There are typically two veins and one artery. They lie posterior to the fascias (external oblique and internal oblique) of the anterior abdominal. They can be visualized laparoscopically medial to the insertion of the round ligament into the deep inguinal ring. In obese patients they may not be visualized but can be assumed to be in their anatomic relationship to the round ligament. They course medially to lay posterior to the rectus muscle in the rectus sheath. If the vessels cannot be visualized laparoscopically, the best placement of the lateral accessor trocars would be approximately 8 cm from the midline at a height of 5 cm from the pubic symphysis.

Injury to the superficial epigastric vessels can be managed with simple compression. Injury to the deep vessels can be diagnosed by blood dripping down the trocar sleeve. Sometimes there is sufficient intraperitoneal pressure to occlude a partial injury. Therefore it is important to inspect the lateral incision sites after removing the trocars and, with decreased pressure, to confirm no injury to the vessels.

If an injury is diagnosed, vessels should be occluded with bipolar cautery if visible or with suture of not visible. A Foley catheter through the incision site can be used to temporarily occlude the vessels, so that more definitive measures can be taken. It is not recommended to leave the catheter in situ to be removed postoperatively. A fascial closure device (such as a Carter—Thompson fascial closure device [Karl Storz GmbH and Co., Tuttlingen, Germany) can be used to occlude the vessels above and below the incision site. If it is not possible to control the bleeding with these methods, the trocar site should be extended and the vessel identified and occluded.

Insertion of the lateral trocars should be directed towards the vesicouterine fold to avoid the external iliac vessels. Decreasing resistance of the trocar entry site, such as with thin abdominal walls or after multiple reinsertions, can lead to injury because of the decreasing force required to place the trocar through the incision. Injuries have been reported with all trocars available on the market.

Bleeding during laparoscopic surgery can usually be controlled by bipolar cautery. The concept is the same as open surgery: i.e. dissecting the area and visualizing the vessel. The ureter should be identified throughout the dissection and before energy is applied. In cases of severe pelvic disease, such as endometriosis, this may be difficult.

Dissection around the presacral area such as with a prescral neurectomy or suture of the mesh for vaginal suspension may lead to a vascular injury. The left com-

mon iliac vein is located below the bifurcation of the aorta. The prescral nerves are located on it. There may be other vessels around this area that will bleed. Bipolar cautery is usually used first. Special thumbtacks are available to control bleeding in this area.

COMPLICATIONS SECONDARY TO PNEUMOPERITONEUM

A pneumoperitoneum is usually established with CO₂. This gas is rapidly absorbed and is ideal for laparoscopy. The insufflation pressure should be maintained at ≤15 mmHg. Laparoscopy in pregnant patients will require less pressure. After establishing a pneumoperitoneum, CO₂ is rapidly absorbed and the arterial pCO₂ will increase. The anesthesiologist compensates by increasing minute ventilation.

Complications associated with a pneumoperitoneum are usually due to the increase in intraperitoneal pressure to >15 mmHg that results in decreased venous return and decreased cardiac output. The anesthesiologist may have difficulties in ventilating an obese patient placed in the Trendelenburg position, even if the pressure is \leq 15 mmHg. The ventilation perfusion mismatch may cause an increase in pCO₂ and potentially hypoxemia. There is no clear way to adjust for this, except to position the patient in less Trendelenburg.

A gas embolism can occur during laparoscopic surgery and is due to air or CO₂ entering the venous system. This is an uncommon cause of increasing pCO₂ and is usually due to the pneumoperitoneal needle directly entering a large vein. The insufflation pressure is higher than the venous pressure but is less than the arterial pressure. A gas embolism is accompanied by a decrease in end-tidal pCO₂. If the anesthesiologist reports this finding, it should not be ignored, and the surgeon should be prepared for management of the potential complications of a gas embolism – typically, arrhythmia and cardiovascular collapse.

URINARY TRACT INJURIES

Several steps should be taken to avoid injury to the bladder and ureters during gynecologic surgery. Prior to surgery, we often perform imaging studies to evaluate the bladder and ureters if abnormalities are anticipated (examples known endometriosis or large pelvic mass). An intravenous urogram is our study of choice. The bladder should be drained prior to surgery. If a long surgery is anticipated, an indwelling catheter should be left to gravity drainage.

Laparoscopic hysterectomy is a particularly high-risk procedure for urinary tract injuries. As noted in Table 30.3

Table 30.3 Urinary tract complications from hysterectomy¹⁶

16.1/1000
1.4/1000
0.3/1000
0.4/1000

LAVH, laparoscopic-assisted vaginal hysterectomy.

the incidence is greater with total laparoscopic hysterectomy than with supracervical hysterectomy. In one series of 126 total laparoscopic hysterectomies (AAGL classification IVe) where routine cystoscopy was performed, there was 4% incidence of lower urinary tract injury. Of the five injuries detected, three were not identified until cystoscopy was performed. Ocystoscopy should be considered after any difficult laparoscopic surgery to evaluate the bladder and ureters.

During hysterectomy, we try to use only sharp dissection to mobilize the bladder off the lower uterine segment and cervix. If there is a question of a possible bladder injury, the bladder is backfilled via the urethral catheter with indigo carmine diluted in 300 ml of sterile saline. Another helpful trick to identify the bladder during dissection is to place a mandarin-style rigid catheter guide into the urethral catheter. This allows the surgeon to probe the outline of the bladder to avoid cystotomy. The catheter drainage bag should also be observed for air, which may be a sign of a cystotomy.

If there is a cystotomy, the location and size will determine the type of repair needed. As a general concept, cystotomies in the dependent portion of the bladder near the trigone are more prone to fistula formation than cystotomies near the dome of the bladder. A cystotomy near a suture line is also more likely to form a fistula. In surgery for menorrhagia, this is most commonly near the vaginal cuff incision. A cystotomy that involves an energy source (laser, electrocautery, or harmonic energy) should be managed cautiously. Collateral spread from an energy source could slow healing times, so we typically leave the bladder to gravity drainage for a longer time in these cases.

A simple needle puncturing the bladder rarely requires any intervention. If leakage of urine is noted intraperitoneally, a urethral catheter to gravity drainage for 1 week followed by a cystogram is a reasonable plan. If there is a tear through the bladder wall into the epithelium, we perform a double-layer closure. The first layer is a running absorbable suture and the second is usually interrupted sutures to imbricate the suture line.

Special care must be taken if there is a bladder injury near the trigone. These injuries are often close to the ureter. We stent both ureters in this situation. We are careful not to obstruct the ureters when closing the cystotomy. This often requires interrupted sutures instead of a running suture. If possible, a layer of peritoneum is interposed on top of the suture line.

A closed suction drain is left outside the bladder adjacent to the repair. After any cystotomy, we leave the bladder on gravity drainage for at least 1 week and perform a cystogram prior to removing the catheter. If the cystogram identifies a leak in the bladder, the catheter is left in place for an additional week and the X-ray is repeated.

Injury to the pelvic ureter is an unfortunate complication in any gynecologic surgery: 12 to avoid this, we identify and dissect the ureter from its surrounding peritoneum whenever this is needed to keep the ureter in clear view. This may also mobilize the ureter away from the area of dissection. We do not routinely use ureteral stents, although some surgeons find them helpful. We find that a ureter with a stent in it is more rigid and difficult to dissect. Advocates for ureteral stenting claim that visualization of a stent will allow prompt recognition of ureteral injury and that, if an injury occurs, having a stent already in place facilitates repairs.

We identify the ureter at the pelvic brim near the bifurcation of the iliac vessels and then follow its course until it passes under the uterine artery. The most common places to injure a ureter are at the pelvic brim and near the uterine artery. If there is a suspicion that a ureteral injury has occurred, we perform cystoscopy. Prior to cystoscopy, the patient receives one ampule of intravenous indigo carmine. Cystoscopy will assure us that no bladder injury has occurred and also allows us to visualize each ureteral orifice for efflux of urine to confirm ureteral patency. The ureter is also observed laparoscopically for any intraperitoneal loss of urine.

Much like for the bladder, the location and size of a ureteric injury will dictate the type of repair needed. For small tears of the ureteral sheath or a simple needlestick injury where no extravasation of urine is seen, a simple ureteral stent for 2 weeks followed by a urogram to document normal anatomy is all that is needed. A common injury to the ureter is a crush injury with a clamp or a temporary kinking of the ureter by a suture. If peristalsis and color return to the ureter, we simply place a ureteral stent for 2 weeks and perform a follow-up urogram.

For more serious ureteral injuries that occur close to the bladder (example: near the uterine artery) we recommend ureteral reimplantation to the bladder. In this procedure, the injured segment of ureter is excised and the distal end of the ureter is reimplanted into the base of the bladder. This can be performed laparoscopically or through an abdominal incision. For ureteral injuries higher in the pelvis, we have had good success with excision of the ureteral segment and direct end-to-end anastomosis of the ends of the ureter.¹³ With this procedure, it is critical that the ureter not be on tension. If there is tension on the ureter, mobilization of the upper ureter and kidney may be needed.

The ureter is repaired by first placing a retrograde ureteral stent. Both ends of the ureter are spatulated, then repaired with 4–6 fine interrupted absorbable sutures. For large ureteral injuries, interposition of a loop of bowel has been successful, as has transureteral ureterostomy. Most surgeons try to avoid transureteroureterostomy because a problem at the ureter anastomotic sight could potentially put the kidney from the previously uninjured side in jeopardy.

Like cystotomy repairs, a drain is left adjacent but not touching the repaired ureter. After ureteral repairs, a stent is placed for at least 2 weeks. A follow-up urogram is performed to identify leaks, strictures, or ureteral reflux, which can occur postoperatively.

BOWEL INJURIES

Most patients undergoing laparoscopic surgery will have some form of bowel preparation so as to decompress the bowel. However, recent data have questioned the value of this 'prep' to diminish the chances of wound infection or proper bowel healing with an inadvertent enterotomy. Primary closure of an enterotomy is now performed routinely with an 'unprepped' bowel. The main preventive measures to avoid bowel injury are to decompress the stomach with an orogastric tube and to use alternative methods for primary peritoneal entry. Patients with peritoneal adhesions or endometriosis are at risk for bowel injury during dissection.

Inadvertent bowel injuries during laparoscopic surgery are typically due to direct trocar trauma or burn injury. Bowel injury can also occur during the operative procedure itself, such as excision of endometriosis, especially with extensive adhesions. The frequency of injury in these cases is similar whether it is performed by laparotomy or laparoscopy. However, recognition of the injury may be diminished by laparoscopy.

Small serosal tears with the muscularis intact need not be repaired unless extensive. A small puncture wound with the Verres needle need not be sutured unless there is an obvious leak of intestinal fluid. Larger injuries require closure, typically with a one-layered technique using a delayed absorbable suture. Large defects should be closed perpendicular to the long axis of the bowel. Some defects may require a segmental resection. Burn injuries require careful assessment with possible bowel resection. At the end of a difficult surgical dissection around the sigmoid or rectum, it is wise to assess for any leak by insufflation of the rectum and flooding the pelvis with fluid. A laparoscopic bowel clamp should be placed across the sigmoid so as to keep the air within the lower bowel. If there is a hole in the bowel, air bubbles would be seen.

Unrecognized bowel injury can lead to significant postoperative morbidity and mortality. Symptoms associated with bowel injury include nausea, vomiting, abdominal pain, and fever. Symptoms can be relatively non-specific and it is the trend that is important. Return to bowel function may be slow even after laparoscopic surgery. The report of some bowel function such as diarrhea does not exclude bowel injury. Patients should be getting better after surgery. Lack of progress requires evaluation.

Injuries due to direct trauma from the trocar or the actual surgical procedure usually present earlier than burn injury. As a general rule, unrecognized injuries due to direct trauma present within the first 12–36 hours. Burn injuries are usually more delayed and can present as late as 1 week. There are three general types of burn injury secondary to electrosurgery: direct burn of an organ with the electrosurgical instrument; capacitance coupling; and defective insulation.

Reports of the length of time free air remains in the abdomen after laparoscopic surgery are conflicting. Most patients will have resolution of free air within 24 hours after surgery. Free air is seen in small amounts up to 1 week after surgery. ¹⁴ Therefore it is again the trend that is important if the clinical signs are equivocal. Large quantities of air on radiologic evaluation or increasing air with serial evaluation should be suspect.

WOUND COMPLICATIONS

Wound infection is uncommon after laparoscopic injury but can occur in patients with predisposing factors such as obesity and diabetes. Wound hematoma can occur after injury to the superficial abdominal vessels, as described above. Metastases to port sites have been reported when laparoscopic surgery was performed in patients with ovarian cancer.

Wound dehiscence of the trocar sites is uncommon and usually occurs with larger port sites or with the site used to insert a large-bore morcellator. Acute dehiscence can lead to bowel herniation and bowel obstruction. Chronic dehiscence is associated with hernia formation. Hernia formation can be reduced with adequate closure of large trocar sites. However, hernias can still occur even with proper closure of the fascia of the port site. Most hernias occur at the extraumbilical port sites. Acute

dehiscence of the vaginal cuff can lead to postoperative shock or bowel prolapse. It is unclear what the predisposing factors are.

SUMMARY

Simple routines such as careful attention to patient positioning and trocar placement can help to minimize

surgical complications. Knowledge of pelvic and anterior wall anatomy will diminish the risk of injury. Additional steps such as cystoscopy or insufflation of the rectum will help the surgeon to identify complications intraoperatively. Prompt recognition and repair are critical for reducing patient morbidity from complications.

References

- Whiteside JL, Barber MD, Walters MD, Falcone T. Anatomy of ilioinguinal and iliohypogastric nerves in relation to trocar placement and low transverse incisions. Am J of Obstet Gynecol 2003; 189: 1574

 –8.
- Bateman BG, Kolp LA, Hoeger K. Complications of laparoscopy

 operative and diagnostic. Fertil Steril 1996; 66(1): 30–35.
- Merlin TL, Hiller JE, Maddern GJ et al. Systemic review of the safety and effectiveness of methods used to establish pneumoperitoneum in laparoscopic surgery. Br J Surg 2003; 90: 668–79.
- 4. Tulikangas PK, Robinson DS, Falcone T. Left upper quadrant cannula insertion. Fertil Steril 2003; 79(2): 411–12.
- Tulikangas PK, Nicklas A, Falcone T, Price LL. Anatomy of the left upper quadrant for cannula insertion. J Am Assoc Gynecol Laparosc 2000; 7: 211–14.
- 6. Sharp HT, Dodson MK, Draper ML et al. Complications associated with optical access laparoscopic trocars. Obstet Gynecol 2002; 99(4): 553–5.
- 7. Hurd WW, Bude RO, DeLancey JOL, Pearl ML. The relationship of the umbilicus to the aortic bifurcation: implications for laparoscopic technique. Obstet Gynecol 1992; 80(1): 48–51.
- Hurd WW, Bude RO, DeLancey JOL, Newman JS. The location of abdominal wall blood vessels in relationship to abdominal

- landmarks apparent at laparoscopy. Am J Obstet Gynecol 1994; 171(3): 642–6.
- Boike GM, Miller CE, Spirtos NM et al. Incisional bowel herniations after operative laparoscopy: a series of 19 cases and review of the literature. Am J Obstet Gynecol 1995; 172(6): 1726–33.
- Jelovsek JE, Chen CCG, Roberts SL, Paraiso MFR, Falcone T. Incidence of lower urinary tract injury and the value of routine intraoperative cystoscopy at the time of total laparoscopic hysterectomy. J Minim Invasive Gynecol 2006; 13(5); S6.
- Tulikangas PK, Beesley S, Boparai N, Falcone T. Assessment of laparoscopic injuries by three methods. Fertil Steril 2001; 76(4): 817–19.
- Ostrzenski A, Radolinski B, Ostrzenski KM. A review of laparoscopic ureteral injury in pelvic surgery. Obstet Gynecol Surv 2003; 58: 794–9.
- 13. Tulikangas PK, Gill IS, Falcone T. Laparoscopic repair of ureteral injuries. J Am Assoc Gynecol Laparosc 2001; 8(2): 259–62.
- Farooqui MO, Bazzoli JM. Significance of radiologic evidence of free air following laparoscopy. J Reprod Med 1976; 16: 119–25.
- Harkki-Siren P, Kurki T. A nationwide analysis of laparoscopic complications. Obstet Gynecol 1997; 89: 108–11.
- Harkki-Siren P, Kurki T. Urinary tract injuries after hysterectomy. Obstet Gynecol 1998; 92: 113–118.

Charles E Miller

INTRODUCTION

It has long been appreciated that uterine leiomyomata can cause both menorrhagia and metrorrhagia.¹⁻⁸

Over 75 years ago, the distinguished gynecologic surgeon Victor Bonney,¹ reported on 210 cases presenting with menorrhagia and uterine leiomyomata. Postmyomectomy via laparotomy, less than 5% of patients had recurrent symptoms. Fifty years later, Robert Neuwirth outlined the use of the hysteroscopic resectoscope for the treatment of submucosal uterine leiomyomata causing abnormal uterine bleeding.⁹

Although the laparoscope has been utilized for myomectomy for 25 years, ¹⁰ little is written specifically on the impact of laparoscopic myomectomy on menometrorrhagia. Despite this, the author has been effectively treating abnormal bleeding secondary to type II submucosal and intramural leiomyomata via laparoscopic myomectomy for 18 years.

PREOPERATIVE EVALUATION

Due to the diminishment in tactile feedback prior to laparoscopic myomectomy, it is especially important to know the number, site, and location of all leiomyomata. Leiomyomata mapping lessens the risk of errant incisions, or overlooking significant deep intramural leiomyomata. Furthermore, the site of the combined mass of the uterus and all leiomyomata must be determined so that instruments can be properly placed; i.e. above and lateral to the conglomerate. Various preoperative studies have been recommended throughout the years to properly evaluate the uterus with leiomyomata.

METHODS OF LEIOMYOMATA EVALUATION

The following techniques can be used to evaluate leiomyomata:

(1) Hysteroscopy.

- (2) Two-dimensional (2D) ultrasound (transabdominal, transvaginal).
- (3) Three dimensional (3D) ultrasound (transabdominal, transvaginal).
- (4) 2D saline infusion sonogram (2D SIS).
- (5) 3D saline infusion sonogram (3D SIS).
- (6) Magnetic resonance imaging (MRI).

Whereas hysteroscopy is the 'gold standard' for the evaluation of intracavitary pathology, it does not enable evaluation of the myometrium. Vercellini et al. noted that transvaginal ultrasonography had 96% sensitivity, 87% specificity, 91% positive predictive value, and 94% negative predictive value in the diagnosis of intrauterine abnormality.¹¹

On the other hand, in a study by Schwartz and colleagues, ultrasound results were inconclusive in 20% of cases and did not yield a definite diagnosis in 59% of cases. ¹² They went on to note that MRI was more definite in all cases. Especially in cases where contradictions arise comparing previous ultrasound scans, or when confidence in ultrasound technique is questioned, as noted by Hutchins, MRI can be utilized. ¹³ Hricak and co-workers, by MRI, were able to properly identify nine of nine subserosal leiomyomata, all intramural leiomyomata, and 10 of 11 submucosal leiomyomata. ¹⁴

The above comments certainly suggest that MRI is the imaging study of choice for the evaluation of uterine leiomyomata, but the author is somewhat skeptical. Although they are comfortable evaluating ultrasound, most gynecologists are dependent on radiologists to interpret MRI. Given this premise, the author's imaging study of choice, currently, is 3D saline infusion sonohysterography with fibroid mapping (3D SIS). Saline infusion sonogram enhances endometrial visualization during transvaginal ultrasound examination, and is particularly helpful in finding focal endometrial abnormalities.^{15–17} In the author's experience, the addition of 3D viewing further enhances fibroid mapping (Figure 31.1).

Given the fact that the type 0, type I, and certain type II myomata are better evacuated via hysteroscopy, it is important that the endometrial cavity be evaluated prior to or at the time of myomectomy surgery. Preoperatively, the physician can choose saline infusion sonohysterography (2D SIS, 3D SIS), hysterosalpingogram, or hysteroscopy. At the time of surgery, hysteroscopy or an intraoperative hysterosalpingogram can be performed. It is important to note that only the saline-infused sonogram (2D SIS, 3D SIS) allows evaluation of the myometrium.

Finally, prior to surgery, it is imperative that the patient's hematologic status be determined. Although in the author's experience the risk of transfusion is less than 0.5%, the patient with a normal hemoglobin should be given the opportunity to store autologous blood 2 weeks prior to the procedure. If a patient's leiomyomata is causing anemia, a gonadotropin-releasing hormone (GnRH) agonist can be utilized with iron supplementation to raise preoperative hemoglobin levels. From the work of Friedman et al., if 'addback' therapy is required, secondary to hypoestrogenic symptoms, it is important to use an estrogen/progesterone combination rather than progesterone alone. ¹⁸

Concepts

Concept 1

Utilize a uterine manipulator to enable mobility of the uterus, anteriorly, posteriorly, as well as laterally. In order to accomplish this goal, the manipulator must be long enough so it can be positioned well inside the uterus.

Concept 2

The viewing port (laparoscope port) must be placed above the myomata in the midline; if necessary, place the port above the umbilicus. Secondary ports are also positioned above and lateral to the total mass. Particularly when the leiomyomata are large, lateral ports must be placed across the abdomen rather than vertically on the same side. Placing ports too low not only makes visualization difficult, as the myomata are extracted, but also can disrupt instrument positioning as well (i.e. one cannot work around the myomata and uterus).

Concept 3

Use 5 mm lateral ports if possible. Morcellation can be performed through the 12 mm umbilical port. Smaller lateral ports are not only more cosmetic but also are associated with less risk of hernia.

Concept 4

When dissecting out the myomata, utilize an energy system that maximizes cutting and minimizes tissue desiccation.

Ultimately, hemostasis is gained via repair; i.e. suturing the defect rather than tissue desiccation. Overzealous use of energy and resultant tissue destruction is felt to place the patient at greater risk of uterine rupture during pregnancy.

Because of the respective profiles in tissue, the author utilizes the Harmonic Scalpel to dissect out myomata; bipolar energy is not used.

Concept 5

Minimize adhesions near the adnexa. Therefore, utilize midline vertical incisions or anterior uterine incision when possible. Whereas a horizontal incision can be closed more easily when ports are placed vertically, when ports are placed laterally across the abdomen, a vertical incision is more simply repaired.



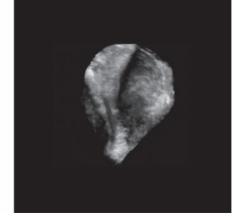


Figure 31.1 3D saline-infused sonogram.

Concept 6

Remove as many myomata as possible through each incision: this not only makes the repair more efficient, but given less serosa trauma decreases the risk of subsequent adhesion formation as well.

Concept 7

Repair the uterine defect in multiple layers. At the same time, do not strangulate tissue.

While other laparoscopists favor repair in one or (at most) two layers, the author is adamant about multilayer closure. It is imperative that the dead space be eliminated to minimize hematoma formation and to maximize tissue repair.

If the endometrial cavity is violated, the author places an initial layer of simple sutures of 3–0 polydioxanone monofilament suture (PDS) in the myometrium directly above the endometrium. These are placed approximately 1–2 mm apart.

The myometrium is then closed in multiple layers using 3–0 polydioxanone monofilament suture (PDS). Depending on the defect shape and site, one can use an interrupted 'purse-string' suture, intraperitoneal 'mattress' suture, or a continuous suture. Avoid 'figure-of-eight' sutures, as tissue will more likely be crushed, strangulated, and necrose. Moreover, place sutures superficially in myometrium, not deep, to avoid needless tissue destruction and necroses.

Finally, repair the serosa in a separate layer, utilizing interrupted 'mattress' or continuous 3–0 or 4–0 polydioxanone monofilament suture (PDS).

Concept 8

Complete repair of the uterine defect prior to myomata morcellation. The one exception occurs when the fibroid is so large that morcellation must occur in situ (midway through the myoma extraction) to enable visualization.

Steps

Having an understanding conceptually of the approach, requirements, and goals for a laparoscopic myomectomy enables a step-by-step discussion of the procedure itself. Remember, laparoscopic myomectomy can only be performed after a meticulous evaluation of the uterus; site number and myoma location must be noted prior to the procedure.

Step 1

Place the Foley catheter into the bladder.

Step 2

Perform hysteroscopy to rule out any submucosal fibroids, polyps, or adhesions not previously recognized. If noted, remove these masses or adhesions prior to laparoscopic myomectomy.

Step 3

Place the intrauterine manipulator deep into the uterine cavity.

Step 4

Place the laparoscope through the 12 mm umbilical port. Consider a 'supra' umbilical port for visualization if the myoma mass is truly large.

Step 5

Place bilateral ports above and lateral to the myoma mass. If required, place ports above the umbilicus. Ideally use 5 mm ports if possible (Figure 31.2).

Step 6

Prior to myomectomy, normalize the pelvis; i.e. perform adhesiolysis, resection of endometriosis, ovarian cystectomy, etc.

Step 7

Infiltrate the myometrium around the fibroid with a dilute vasopressin solution (mix 100 cc of saline with 30 units of vasopressin). Utilize an 18-gauge spiral needle



Figure 31.2 Ports are placed above the umbilicus secondary to the large uterus with fibroids.

placed through a skin 'nick'. Look for the myometrium to expand, then blanch (Figure 31.3).

Remember to aspirate with vasopressin injection. Vascular injection of vasopressin can be fatal.

Step 8

Incise the serosa and myometrium to the level of the fibroid. Ideally use a midline vertical incision to minimize subsequent adnexal adhesions. When the correct plane has been reached, the myoma will begin to protrude out of its pseudocapsule (Figures 31.4 and 31.5).

Step 9

Remove as many leiomyomata as possible through a single incision (Figure 31.6).

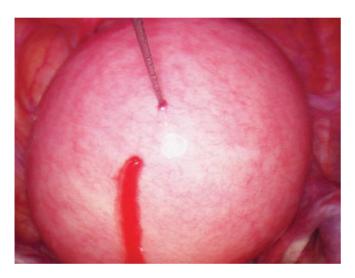


Figure 31.3 Dilute vasopressin is infiltrated between myoma and capsule.

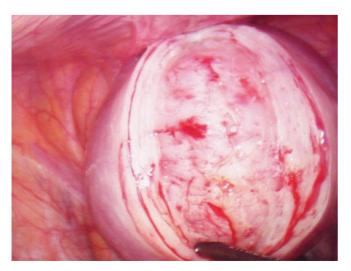


Figure 31.4 Curved blade of Harmonic Scalpel used to make incision to level of myoma.

Step 10

If the endometrial cavity is entered, reapproximate the endometrium by placing simple interrupted sutures of 3–0 polydioxanone monofilament suture (PDS) 1–2 mm apart.

Step 11

Repair the myometrium in multiple layers as needed to close the 'dead space' and properly approximate the tissue. Do not strangulate tissue. Use mattress suture, purse-string suture, continuous purse-string suture, or continuous running suture of 3–0 polydioxanone suture (PDS) as needed (Figures 31.7 and 31.8).

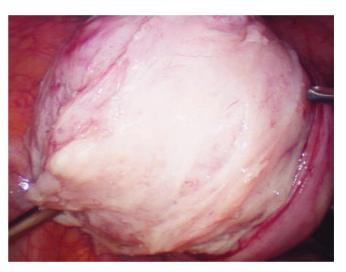


Figure 31.5 Further dissection of myoma from myometrium.

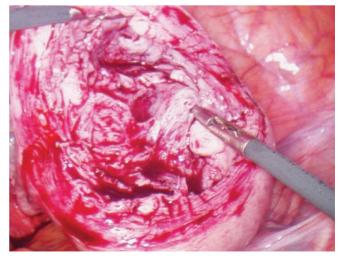


Figure 31.6 Myoma completely removed – myometrium evaluated for entry into endometrium.

Step 12

Repair the serosa via interrupted sutures with buried knots, mattress style closure, 'baseball-style' continuous closure, or a continuous imbricating suture (Figure 31.9).

Note: to only tie a continuous suture once, suture from one end to the other and then return (Figure 31.10).

Step 13

If all secondary ports are 5 mm, morcellate through the 12 mm umbilical port. Otherwise, utilize one of the lateral 12 mm ports (Figure 31.11).

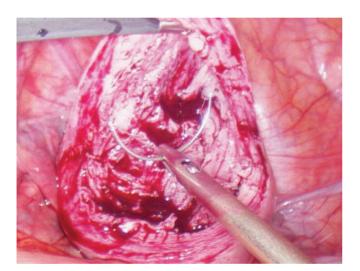


Figure 31.7 First layer of closure using 3–0 polydioxanone suture in a purse-string manner.

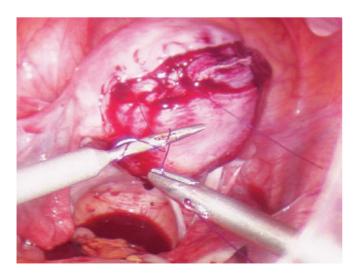


Figure 31.8 Second layer of closure utilizing a baseball style closure of 3–0 polydioxanone suture.

Step 14

Irrigate and gain meticulous hemostasis.

Step 15

Place an antiadhesive barrier or antiadhesive agent (Interceed) or agent (Figure 31.12).

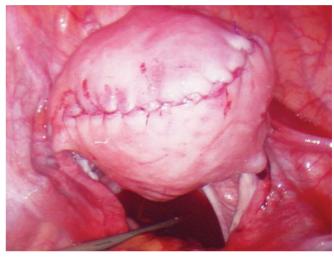


Figure 31.9 Repair of serosa with 3–0 polydiaxanone suture in a baseball-style closure.

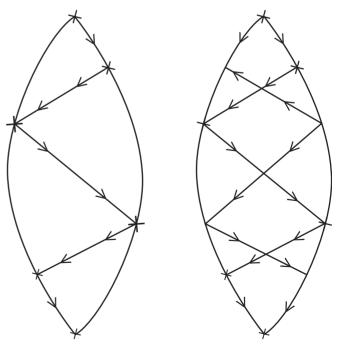


Figure 31.10 To tie a continous suture once, suture from one end to the other and then return.

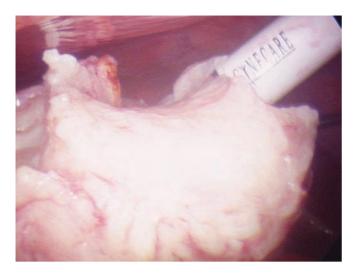


Figure 31.11 Morcellation of fibroid with morcellator (GYNECARE)

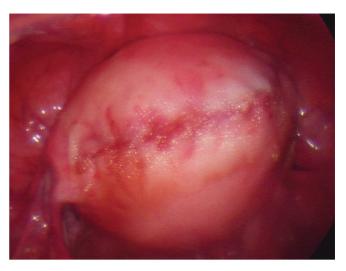


Figure 31.12 Placement of barrier (Interceed) to reduce adhesions.

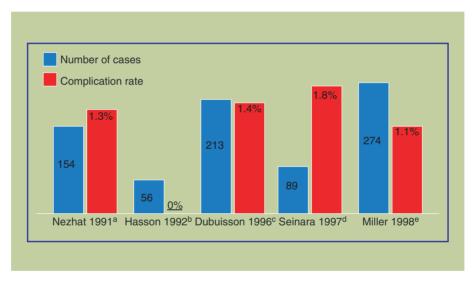


Figure 31.13 Myomectomy complications: laparoscopic myomectomy major complication rate.

- ^a Nezhat C, Nezhat F, Silfen SL, Schaffer N, Evans D. Laparoscopic myomectomy. Int J Fertil 1991; 36(5): 275–80.
- b Hasson HM, Rotman C, Rana N, Sistos F, Dmoswki WP. Laparoscopic myomectomy. Obstet Gynecol 1992; 80(5): 884–8.
- ^c Dubuisson JB, Chapron C. Laparoscopic myomectomy today. A good technique when correctly indicated. Hum Reprod 1996; 11(5): 934-5.
- d Seinara P, et al. Laparoscopic myomectomy: indications surgical technique and complications. Hum Reprod 1997; 12(9): 1927–30.
- ^e Miller CD, Davies. Laparoscopic myomectomy with uterine reconstruction is a safe surgical procedure. J Am Gynecol Laparosc 1998; 55(3): S113.

OUTCOMES

Utilizing variations of the above technique, the author performed 715 laparoscopic myomectomies from August 1999 through September 2006. Data were collected in 698 cases. In 13% of cases, five or more myomata were removed.

Three patients had 43, 34, and 30 fibroids excised, respectively. Myoma weight was recorded in 432 patients:

30% of these patients had myoma weight ≥250 g. Finally, 24% of patients had fibroids ≥8 cm.

Major complications were noted in 13 patients (1.85%). Included in this group are two patients with postoperative bleeds, a 5 mm lateral port hernia, a pulmonary embolism, and a pelvic a abscess.

In a previous study, utilizing a similar technique, the author noted pregnancy rates postlaparoscopic myomectomy of 75% and delivery rates of 70%.

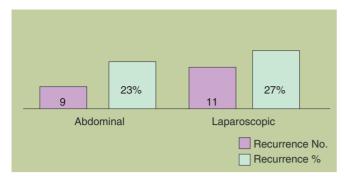


Figure 31.14 Myoma recurrence post myomectomy: Laparoscopic myomectomy vs abdominal myomectomy. Eighty-one patients were randomized between laparoscopy and laparotomy. The follow-up period was 40 months. (Reproduced from Rosetti et al, ²⁴ with permission.)

DISCUSSION

Laparoscopic myomectomy offers distinct advantages over open myomectomy. In multiple studies, complication rates have been noted to be low (Figure 31.13). Like any other minimally invasive surgical procedure, recovery is lessened. Risk of subsequent adhesions formation is diminished. Tulandi et al. noted a postoperative adhesion rate of 93% when a posterior incision is made on the uterus.¹⁹ In a prospective study, Dubuisson reported an

overall adhesion rate of 35.6% in patients undergoing laparoscopic myomectomy: 16.7% per site.²⁰ Other studies by Bulletti et al. Mais et al. and Seracchiolo et al. also indicate decreased adhesions with a laparoscopic approach to myomectomy.^{21–23}

Finally, it would appear that myoma recurrence is not increased when a laparoscopic approach is performed instead of the conventional minilaparotomy. Rosetti et al evaluated 81 patients randomized between laparoscopic myomectomy and abdominal myomectomy. Leiomyomata were at least 3 cm in site, and no more than seven myomas were noted per patient. Figure 31.14 shows the recurrence rate and percent recurrence at 40 months. Essentially, no difference was reported in the two groups.

CONCLUSIONS

With the proper preoperative evaluation, laparoscopic myomectomy can be performed safely and successfully. Of course, the physician must be facile in laparoscopic suturing technique and have an understanding of energy systems. Ultimately, laparoscopic myomectomy is an excellent choice for women interested in future fertility or concerned with potential compromise of ovarian function with hysterectomy.

References

- Bonney V. The technique and results of myomectomy. Lancet 1931; 220: 171–7.
- Bonney V. The fruits of consevatism. J Obstet Gynaecol Brit Emp 1937; 44: 1–12.
- Finn W. Abdominal myomectomy: special reference to subsequent pregnancy and to the reappearance of fibromyomas of the uterus. Am J Obstet Gynecol, 1950; 60(1): 109–16.
- Munnell E. Abdominal myomectomy, advantages and disadvantages. Am J Obstet Gynecol 1951; 62(1): 109–20.
- Hillesmaa V. Abdominal myomectomy in the treatment of uterine fibroids. Ann Chir Gynaecol Fenn 1960; 49: 254–69.
- Brown JM. Abdominal myomectomy. Am J Obstet Gynecol 1967; 99(1): 126–9.
- ACOG Practice Bulletin, Clinical Management Guidelines for Obstetrician-Gynecologists, Surgical Alternatives to Hysterectomy in the Management of Leiomyomas, No. 16, May 2000.
- Rock J. Leiomyomata Uteri and myomectomy. In: Te Linde's Operative Gynecology. Lippincott, Williams and Wilkins, 2003
- Neuwirth RS, Amin HK. Excision of submucous fibroids with hysteroscopic control. Am J Obstet Gynecol 1976; 126(1): 95–9
- Semm K. Course of endoscopic abdominal surgery. In: Operative Manual For Endoscopic Abdominal Surgery. Year Book Medical Publishers Inc., 1987.

- 11. Vercellini P, Cortesi I, Oldani S et al. The role of transvaginal ultrasonography and outpatient diagnostic hysteroscopy in the evaluation of patients with menorrhagia. Hum Reprod 1997; 12(8): 1768–71.
- 12. Schwartz LB, Panageas E, Lange R et al. Female pelvis: impact of MR imaging on treatment decisions and net cost analysis. Radiology 1994; 192: 55.
- Hutchins FL. Uterine fibroids. Diagnosis and indications for treatment. Obstet Gynecol Clin North Am. 1995; 22(4): 659– 65.
- Hricak H, Tscholakoff D, Heinrich L et al. Uterine leiomyomas: correlation of MR, histopathologic findings, and symptoms. Radiology 1986; 158(2): 385–91.
- Parsons AK, Lense JJ. Sonohysterography for endometrial abnormalities: preliminary results. J Clin Ultrasound 1993; 21(2): 87–95.
- 16. Syrop CH, Sahakian V. Transvaginal sonographic detection of endometrial polyps with fluid contrast augmentation. Obstet Gynecol 1992; 79(6): 1041–3.
- Goldstein RB, Bree RL, Benson CB et al. Evaluation of the woman with post menopausal bleeding. J Ultrasound Med 2001; 20: 1025
- Friedman AJ, Daly M, Juneau-Norcross M et al. Long-term medical therapy for leiomyomata uteri: a prospective, randomized

- study of leuprolide acetate depot plus either oestrogen-progestin or progestin 'add-back' for 2 years. Hum Reprod 1994; 9(9): 1618–25.
- Tulandi T, Murray C, Guralnick M. Adhesions formation and reproductive outcome after myomectomy and second-look laparoscopy. Obstet Gynecol 1993; 82(2): 213–15.
- Dubuisson JB, Fauconnier A, Chapron C, Kreiker G, Norgaard C. Second look after laparoscopic myomectomy. Hum Reprod 1998; 13(8): 2102–6.
- Bulletti C, Polli V, Negrini V, Giacomucci E, Flamigni C. Adhesion formation after laparoscopic myomectomy. J Am Assoc Gynecol Laparosc 1996; 3(4): 533–6
- 22. Mais V, Ajossa S, Guerriero S et al. Laparoscopic versus abdominal myomectomy: a prospective, randomized trial to evaluate benefits in early outcome. Am J Obstet Gynecol 1996; 174(2): 654–8.
- 23. Seracchioli R, Rossi S, Govoni F et al. Fertility and obstetric outcome after laparoscopic myomectomy of large myomata: a randomized comparison with abdominal myomectomy. Hum Reprod 2000; 15(12): 2663–8.
- Rosetti A, Sizzi O, Soranna L et al. Long-term results of laparoscopic myomectomy: recurrence rate in comparison with abdominal myomectomy. Hum Reprod 2001; 16(4): 770–4.

Hysteroscopic myomectomy: indications, technique, outcome, and complications

Aethele Khunda and Peter Joseph O'Donovan

INTRODUCTION

The first hysteroscopic examination was done in 1869. But it was not until almost a century later, in 1957, that William Norment performed the first transcervical myomectomy using a cutting loop. Subsequently, in 1976, Neuwirth and Amin reported the first excision of submucous fibroids under hysteroscopic control. Two years later Neuwirth reported the first use of a resectoscope to morcellate a myoma. This heralded a revolution in the management of menstrual problems. Over the last two decades the resectoscope has established itself as the gold standard method for dealing with submucous myomas. Alongside this, was the introduction of laser to vaporize myomas, which has also established its place in hysteroscopic surgery. The high success rate of the above two techniques has meant that recent advances have focused more on making the procedure safer, more user friendly, and more compatible with outpatient use. This chapter briefly discusses hysteroscopic myomectomy: its indications, technique, outcome measures, and complications.

CLASSIFICATION OF MYOMAS WITH A SUBMUCOUS COMPONENT

Hysteroscopic myomectomy is only indicated for myomas with a submucous component. Anatomically, these can be of three types:

- Type 0: pedunculated submucous myoma without intramural extension.
- Type 1: sessile submucous myoma, ≤50% of which is intramural.
- Type 2: sessile submucous myoma, >50% of which is intramural.

The above classification, initially suggested by Wamsteker et al. was later adopted by the European Society of

Hysteroscopy because of its clinical applications.¹ Other classifications have been proposed as being more predictive of resectability and complication rate,² but have not been widely tested.

Histologically, myomas are tumors of myometrial origin. They are usually benign (leiomyoma) and generally referred to as fibroids. The words myoma and fibroid are used interchangeably in this chapter. Other rare tumors of the same origin are malignant leiomyosarcoma and atypical myomas.

INDICATIONS

Abnormal uterine bleeding

Myomas can cause heavy, irregular, intermenstrual, postmenopausal or even, rarely, postcoital bleeding.

Infertility and recurrent pregnancy loss

The effect of myomas and their removal on fertility is still a topic for debate. In a meta-analysis published in 2001, Pritts showed that if all types of fibroids were analyzed together, the only effect fibroids would have on fertility was reduced implantation rate in in-vitro fertilization (IVF) patients. Subgroup analysis demonstrated a lower pregnancy rate in the group of women with submucous myomas compared to infertile controls. This pregnancy rate improved upon myoma resection. This subgroup analysis, however, only included two studies.³ A recent review of 106 articles found only one randomized controlled trial (RCT), which showed an improvement in pregnancy rate from 11% in women with unexplained infertility and fibroids to 42% in infertile women who underwent myomectomy. This compared favorably with a pregnancy rate of 25% in women with unexplained infertility and no fibroids. This study, however, had a small number of patients and a limited follow-up. The overall

pregnancy rate following hysteroscopic myomectomy, from six studies in this review, was 45%. The same review identified seven articles studying the effect of uterine fibroids on IVF success rate. Four studies concluded that myomas do not affect pregnancy rate when they do not distort the endometrial cavity, while three other studies concluded that myomas have a detrimental effect on pregnancy rate even if they do not distort the endometrial cavity.4 More recently, a Cochrane review concluded that there are no good RCTs to support hysteroscopic removal of fibroids compared to other surgical modalities for fertility efficacy.5 Evidence regarding the effect of fibroids on pregnancy loss is scarce; Buttram et al. reviewed 1941 patients who had abdominal myomectomy and found that fetal wastage was reduced from 41% preoperatively to 19% postoperatively.6 Although RCTs are lacking, it seems reasonable to offer removal of a submucous myoma in a woman presenting with recurrent miscarriage when other causes have been excluded.

Pain and Pressure effect

Pain is uncommon. It can result from acute degeneration of the fibroid or from to uterine contraction in an attempt to expel a pedunculated submucous fibroid. Large myomas can exert pressure on surrounding organs, leading to symptoms; however, hysteroscopic myomectomy tends to be contraindicated in these myomas by virtue of their size or location.

Sarcomatous changes in a fibroid are generally considered a myth. Reviewing the available evidence in 2003, Lefebvre et al. found that the risk of malignancy in what is thought to be an asymptomatic leiomyoma is approximate to the surgical mortality of a hysterectomy for benign disease.⁷ It has therefore been accepted that removal of a myoma has to be justified on the basis of symptoms. The relatively low mortality and morbidity of hysteroscopic surgery have led some clinicians to lower the threshold for intervention.

CONTRAINDICATIONS

In addition to contraindications to hysteroscopy in general, the followings are considered contraindications to hysteroscopic myomectomy:

- uterine size more than 12 weeks of gestation (these are usually difficult to distend and associated with large amounts of fluid deficit)
- myomas which have no submucous component, or are embedded in one of the uterine horns (these are associated with high risk of perforation).

PATIENT SELECTION AND PREPARATION

Patient selection and preparation is the key to high success rate and low complication rate. Myomas are usually evaluated sonographically to determine their number, size, type and location. The efficiency of conventional transvaginal sonography in preoperative evaluation of submucous myomas was found to correlate well with hysteroscopic assessment ($\kappa = 0.48$). Its sensitivity, specificity, positive predictive value, and negative predictive value in identifying operable submucous myomas were found to be 80%, 69%, 83%, and 64%, respectively.8 The efficiency of sonography can be enhanced by contrast media (sonohysterography). Leone et al. showed that complete accurate preoperative assessment was possible in 79/80 cases with single submucous myoma using sonohysterography, while in cases with multiple myoma, 2/13 were misclassified.9 Another study, however, showed lack of conformity between the latter and hysteroscopy, especially when myoma diameter was >3 cm, myoma grade was 1-2, and when endometrial thickness was >8 mm.¹⁰ Hysteroscopic evaluation of submucous myomas is considered the gold standard preoperative assessment. In addition to mapping the uterine cavity and assessing the feasibility of hysteroscopic myomectomy, it allows taking a directed endometrial biopsy if indicated.

Other experimental preoperative assessment techniques include three-dimensional (3D) contrast sonohysterography, magnetic resonance imaging (MRI), and virtual hysteroscopy.

Early studies suggested the superiority of 3D sonography over conventional transvaginal sonography, but not that of 3D contrast sonohysterography over two-dimensional (2D) saline contrast sonohysterography. Pretoruis et al. reported that hysteroscopic myomectomy was performed in 21/45 cases with myomas, described as being operable on 3D saline contrast sonohysterography, and in only 2/39 women with unfavorable ultrasound findings.¹¹ MRI is superior to transvaginal ultrasound mainly in cases with multiple myomas (>4) or when uterine volume is large (≥375 ml). It is therefore unlikely to be of benefit for cases being considered for hysteroscopic myomectomy. Virtual hysteroscopy is the most recent development in preoperative evaluation of submucous myomas. It uses a 16-slice computed tomography (CT) scanner to reconstitute a 3D image. Analysis can be done in either the hysteroscopic mode or the volume mode. The latter is preferred as it aids classification of the myoma.¹²

Fibroid polyps are generally amenable to hysteroscopic treatment. In 1995, Neuwirth set the selection criteria for safe hysteroscopic myomectomy as follows: the cross section of the base area of the myoma should be $\leq 4 \times 4$ cm, the myomas should not be on opposite surfaces, and

hysterometry should be ≤10 cm.¹³ With experience and technological advances, these criteria were relaxed. In 2003, Munez et al. reported selection criteria which included a myoma size <6 cm and, in the presence of multiple myomas, <50% of the endometrial surface should be affected.¹⁴ More recently, Ludwin et al. reported extending hysteroscopic myomectomy to type 2 myomas, of which only 1/5 protrude into the uterine cavity provided that the myoma is ≥ 5 mm from the serosal surface. ¹⁰ Interestingly, Yang and Lin showed that the thickness of the myometrium between the myoma and the serosal surface increases significantly during the procedure - from an average of 6.7 mm prior to resection to 16.1 mm just after resection - therefore providing a thicker safety zone. 15 Case reports of bigger and deeper myomas have been described, but great caution should be exercised when trying to push the boundaries of inclusion criteria at the expense of safety. Type 2 myomas should only be operated on by the very experienced hysteroscopist.

Preoperative treatment with progestational agents, danazol, or gonadotropin-releasing hormone analogues (GnRHa) has been extensively debated. A review of 16 controlled trials found that preoperative medical treatment helped decrease operative time and fluid absorption and resulted in a higher incidence of long-term amenorrhea (in cases undergoing endometrial resection). The advantages of preoperative GnRHa treatment can be summarized as follows:

- reduction in myoma size (which reduces operative time, potentially reduces bleeding, and helps to bring large myomas into the range of operability)
- · decrease in the risk of fluid overload
- restoration of normal preoperative hemoglobin concentration.

The drawbacks are:

- menopausal side effects
- small risk of severe hemorrhage due to fibroid necrosis
- shrinking small myomas may make them less submucous and therefore less detectable hysteroscopically
- GnRHa treatment may render the capsule surrounding the myomas more fibrous, making resection more difficult
- difficulty in dilating the cervix.

Interestingly, Propst et al. found that patients who were pretreated with GnRHa had at least four-fold increase in risk of complications.¹⁷ Another study, by Campo et al., suggested that 2 months of GnRHa pretreatment did not improve short- or long-term outcome of hysteroscopic

myomectomy, but increased operative time, probably due to difficulty in cervical dilatation.¹⁸ The general consensus is that GnRHa is indicated to correct anemia and in large myomas. Vaginal misoprostol priming before operative hysteroscopy reduces the need for cervical dilatation, and minimizes cervical complications according to one RCT.¹⁹

TECHNIQUE

A description of the basic set-up of a hysteroscopy theater is beyond the scope of this chapter; however, a summary of the techniques used is presented below. Before the start of any procedure, a thorough examination of the cavity and the lesion should be done in order to plan the procedure well. There are three main modalities of removing myomas hysteroscopically, each of which uses a different energy source.

Electric/thermal energy (Resectoscopic myomectomy)

This is the most popular method of dealing with myomas hysteroscopically. Some surgeons advise sealing the tubal ostia before starting, when fertility is not an issue, to prevent fluid escaping into the peritoneal cavity. The resection is usually done by shaving the myoma in the direction of the lens until it is level with the rest of the surrounding endometrium. The chippings can be removed with a polyp forceps during the procedure, if they interfere with visualization; otherwise, this is best done at the end. An interesting development is the Master-resectoscope, which removes chips from the operative field as they are cut. This is done by suction into a separate removal channel. The overall diameter is still 9 mm. The remaining part of the myoma will then project into the uterine cavity, aided with uterine contractions, especially in type 1 myomas. If this does not happen spontaneously, it may be achieved with bimanual uterine massage, 20 or intraoperative injection of prostaglandin (carboprost). If the above fails to deliver the rest of the myoma into the cavity, the surgeon may proceed in one of four ways:

- Devascularize the rest of the myoma by inserting the electrode 5–10 mm deep into it at multiple points (preferably aided with sonographic guidance). A second-look hysteroscopy may then be performed after an 8-week period of GnRHa therapy and, if not already expelled the remaining part of the myoma will have become intracavitay and easy to remove.
- Proceed with caution, shaving under ultrasound or laparoscopic control. When laparoscopic monitoring

is used, the light of the laparoscope should be dimmed so that it becomes easy to recognize the light of the hysteroscope through the uterine wall when the myometrium becomes thin just before perforation. It is also good practice to use the suction to retrieve any hysteroscopic fluid that had escaped through the fallopian tubes into the peritoneal cavity. Duan et al. reported on the combined use of laparoscopy and hysteroscopy in 235 cases; there were 10 uterine perforations.²¹ Ultrasound monitoring can be performed via a transabdominal, transvaginal, or even transrectal approach. The skilled hysteroscopist is usually able to differentiate the remaining part of the myoma from the adjacent myometrium through color contrast and by gentle touching with the inactive electrode: the myoma is usually harder.

- Cold-loop enucleation: Mazzon described this technique using a special (Mazzon) electrode. This is introduced into the cleavage plane between the myoma and its adjacent myometrium while it is inactive. The myoma is then detached progressively from its bed until it becomes inside the uterine cavity, where it can be dealt with. Ordinary electrodes should not be used for this purpose as they may bend or break. Being devoid of electrothermal energy, it can be argued that this technique is safer (less risk of perforation and less risk of damage to the bowel in case of perforation) and that it causes less damage to the myometrial wall.²² A rather similar technique was described, specifically for type 2 myomas, by Litta et al. and named enucleation in toto; an elliptical incision is made into the endometrial mucosa overlying the myoma at the level of its reflection on the uterine wall until the cleavage plane is reached. The bridges connecting the myoma to the myometrial wall are then divided, allowing the myoma to protrude into the uterine cavity and be dealt with in the usual manner.²³
- In 2006, Van Dongen et al. reported on a wait-andsee policy in these cases and showed that 44.2% of incomplete resection cases were still surgery-free 3 years after the index operation. The size of the fibroid preoperatively had a significant effect on the need for repeat surgery in these cases.²⁴

When the procedure is completed, the intrauterine pressure is lowered gradually by reducing inflow of fluid. This will reveal any bleeding points, which can then be coagulated. As a general principle, small myomas are resected before large ones and lower segment ones before upper segment ones,¹³ but an individualized plan should be made after careful assessment of the cavity in cases with multiple myomas. When dealing with cornual myomas, care must be taken to avoid perforation. Baggish retractile

loop and Mazzon's loop have been described for use in these circumstances.

The more recent bipolar system is now gaining popularity as it allows the use of normal saline as distention fluid. It therefore carries a minimal risk of electrolyte disturbances; fluid overload is usually easily treated with loop diuretics. This technique also allows vaporization of small (≤2 cm) myomas. When activated in normal saline, a high-resistance air pocket is created and the circuit is only completed upon contact with tissue. Its efficacy is similar to that of the monopolar system and its uptake is spreading rapidly. In 2002, Bettocchi et al. reported on 501 women treated in outpatient hysteroscopy, without anesthesia, using a bipolar system; 47.6-79.3% of the patients reported no discomfort.²⁵ Another recent development is the intrauterine morcellator. Emanuel and Wamsteker reported that it reduced mean operating time for submucous myomas from 42.2 minutes (when using the resectoscope) to 16.4 minutes.²⁶

Mechanical energy (hysteroscopic scissors or ring forceps)

This technique uses either hysteroscopic scissors or a ring forceps (twist and avulse, then look in again with the hysteroscope), and is mainly used for small pedunculated myomas. If the myoma is too large to be delivered through the cervix and if dilating the cervix is to be avoided, it can either be removed in pieces or left inside to be expelled at a later date. A modified combination of the mechanical and resectoscopic modalities was reported by Darwish. He concluded that removal of the myoma using a ring forceps, after excising its base, led to reductions in the need for two-stage procedures and in the complication rate, but a higher cervical laceration rate, when compared with the standard resection technique.²⁷

Laser energy

The Nd:YAG (neodymium: yttrium-aluminum-garnet) laser is the commonest one used in hysteroscopic surgery. Its main advantages over other lasers lie in its deep penetration (4 mm) and excellent coagulation effect. It can also cut when a sculpted tip is used. A beam of 1.32 µm wavelength is usually used in operative hysteroscopy. The main advantage of laser over the resectoscope is its safety (laser permits the use of electrolyte-containing fluid), myolysis effect, and the fact that it causes minimal bleeding. Its main drawbacks are cost and time. For polyps and type 0 myomas, the laser fiber is used in a manner similar to the resectoscope. For myomas with a residual intramural component that fails to be delivered into the uterine cavity after resecting the submucous portion, the laser

fiber is inserted 5–10 mm deep into the residual part of the myoma and activated while being withdrawn. This will devitalize the remaining part of the myoma, making its removal easier at a later date. The procedure is called transhysteroscopic myolysis. ²⁸ Laser is used to best effect in cases with small cornual myomas or those with fundal myomas. Protective goggles must be worn by all theater staff.

Outcome measures

The success rate of hysteroscopic myomectomy depends on many factors:

- (1) Factors related to the patient: for the outcome of menstrual disturbances, these include age and menopausal status, while for the outcome of infertility they include age, the type of subfertility (primary or secondary),²⁰ and the presence of other subfertility factors.²⁹
- (2) The indication it is performed for: removing a type 0 myoma will almost invariably cure intermenstrual bleeding, but may not cure heavy periods or infertility.
- (3) Confounding factors related to the myomas, such as their number, size, location, and type.
- (4) The type and length of follow-up: longer follow-up is likely to improve pregnancy rate, but may result in higher rate of anatomic failure (recurrence of myomas) or clinical failure (recurrence of heavy periods whether due to myomas or hormonal disturbances). Reoperation could mean repeat hysteroscopic myomectomy, any subsequent myomectomy, or even any subsequent operation. Also, satisfaction questionnaires do not necessarily correlate to objective assessment of blood loss, or even second-look hysteroscopy.

The heterogeneity caused by variation in the above factors has made pooling of data from different studies inappropriate. Therefore, individualized, operator-specific figures should be used when counseling patients. Table 32.1 lists studies which examined primarily the outcomes of control of abnormal uterine bleeding and reoperation rate (in ≥200 cases). Patient satisfaction and improvement in bleeding pattern ranged between 67 and 100%, while reoperation rate ranged between 0.2 and 16.3 %. Three major preoperative factors influence the success of hysteroscopic myomectomy in alleviating menstrual disorders. The first factor is the number of myomas: multiple myomas reduce success rate and increase reoperation rate. Smets et al. reported a 27%

recurrence of menometrorrhagia in patients with more than two myomas (compared with only 5% for type 1 myomas and 2% for type 2 myomas)²⁸ while Emanuel et al. reported that the presence of three or more myomas on hysteroscopy was an independent risk factor for reoperation.³⁴ This led some authors to suggest alternative therapy in these cases. The second factor is the type of the myoma: type 2 myomas are usually associated with a lower success rate, 30 a higher reoperation rate, and a higher two-stage procedure rate.³³ Vercellini et al. found that 50% of type 2 myomas needed more than one procedure for complete removal compared to 26% of type 1 myomas.³⁵ The third factor is the size of the uterine cavity: a hysterometry >12 cm has been found to be associated with a lower success rate and a higher reoperation rate.³⁴ Patients undergoing repeat myoma resection should be assessed and counseled properly, as 36% of them end up having a hysterectomy.³⁶ The commonest indication for hysterectomy is pain (usually caused by deep adenomyosis). Cravello et al. followed up 181 cases of hysteroscopic myomectomy for 50-104 months and compared those with good results to those with unfavorable results. The two significant predictors of unfavorable results were incomplete resection (judged intraoperatively) and the presence of a residual part of the myoma on control (follow-up) hysteroscopy.³⁷

Table 32.2 lists studies of ≥40 cases which examined fertility rate following hysteroscopic myomectomy. Pregnancy rate ranged between 27 and 66%, delivery rate ranged between 10 and 73%, while term delivery rate ranged between 10 and 56%. Ubaldi et al. pooled data from 10 studies to accumulate 134 cases of hysteroscopic myomectomy. The resultant pregnancy rate was 58.9% the live birth rate was 75%, and the miscarriage rate was 21.5%.³⁹ Giatras et al. found no relationship between the size of the myoma and pregnancy rate,³⁸ while Fernandez et al. reported that pregnancy rate was significantly better when the myoma was the exclusive etiology of infertility and when it was ≥50 mm in size.²⁹ Vercellini et al. reported that the difference in the cumulative conception rate over 3 years according to the type of myoma was not statistically significant. The rates were 49%, 36%, and 33% for type 0, 1, and 2 myomas, respectively.³⁵

COMPLICATIONS

A multicenter prospective study from the Netherlands, involving 13 600 hysteroscopy procedures, reported a complication rate of 0.95% for operative hysteroscopy compared with only 0.28% for diagnostic hysteroscopy. Hysteroscopic myomectomy had a complication rate of 0.75%, which was lower than that of hysteroscopic

Table 32.1 Menstrual outcome following hysteroscopic myomectomy

First author (year)	N(n)	Size (cm)	Procedure	FU in months	Control of abnormal Bleeding (%)	Reoperation rate (%)
Xia ³⁰ (2005)	962	≤7.2	TCRM	>6	Type 0 (100%)	2/962*
					Type 1 (99.1%)	(0.2%)
					Type 2 (94.02%)	
					Multiple and intramural myoma (84%)	
Barbot ³¹ (1994)	825 (823)	1–6	Laser	8-84	(90%)	(5%)
Cravello ³² (1995)	239 (221)	0.5–6	TCRM	6–67	159/181 (87.8%) premenopausal 24/26 (92.3%) postmenopausal	39/239** (16.3%)
Hallez ²⁰ (1996)	284	1–6.5	TCRM	6–≥82	(95.6%) at 6 months	(6.6%***)
					(67.6%) at ≥ 7 years	
Philips ³³ (1995)	208 (185)	1–8.5	TCRM (concomitant ER in 88)	6–78	198/208 (95.2%) at 6 months	0/208* (0%)
					159/185 (85.9%) at a mean of 34 months	6/185* (3.2%)
						9/185** (4.8%)
						14/185**** (7.5%)
Smets ²⁸ (1996)	366	<5	Laser myomectomy and EA	24	355/366 (96.9%)	6/366* (1.6%)
						8/366**** (2.1%)
Emanuel ³⁴ (1999)	283 (266)	?	TCRM	1–104 median 46	With one procedure: 219/266 (82.3%)	41/266**** (15.4%)
					With up to two procedures: 262/266 (98.4%)	

N, Number of cases in study; n, actual number of cases available for follow-up for the outcome of bleeding; FU, Follow-up, TCRM, transcervical resection of myoma; ER, endometrial resection; EA, endometrial ablation.

^{*}Repeat TCRM.

^{**}Repeat hysteroscopic procedures only (14 hysterectomies in this study, but total reoperation rate not clear due to potential overlapping).

^{***}Additional intervention rate.

^{****} Repeat surgery for recurrence.

First author (year)	N	Pregnancy rate (%)	Delivery per patient (Delivery-patient ratio*)	Term delivery per patient (Term delivery- patient ratio*)
Emanuel ^{34**} (1999)	124	57/124 (46.0%)	?	?
		82/124*** (66.1%)	(66 /124 = 53.2% ***)	
Fernandez ²⁹ (2001)	59	16/59 (27.1%)	6/59 = 10.2%	6/59 = 10.2%
Giatras ³⁸ (1999)	41	25/41 (60.9%)	23/41 = 56.0% (30/41 = 73.1%)	20/40 (23/41 = 56%*)
Vercellini ³⁵ (1999)	40	15/40 (37.5%)	13/40 = 32.5%	(9–14/40 = 22.5–35%****)
		16/40 (40%)***	$(14/40 = 35\%^{***})$	

Table 32.2 Fertility outcome following hysteroscopic myomectomy

adhesiolysis and of endometrial resection, but higher than that of polypectomy.⁴⁰ The experience of the surgeon is an important factor in avoiding complications. The complications of hysteroscopic myomectomy can be divided into early and late; below is a brief overview of these complications.

Early complications

Bleeding

A review of 2116 cases of operative hysteroscopy found 13 cases complicated by heavy bleeding (0.6%).⁴¹ Bleeding can occur either preoperatively as a rare complication of GnRHa treatment (1.9%), intraoperatively (the commonest) or postoperatively. Phillips et al., in a doubleblind RCT in 1996, showed that dilute vasopressin administration to the cervical stroma significantly reduced intraoperative blood loss, distention media intravasation, and operative time. 42 Postoperatively, infection could be a causative factor. In cases of intraoperative bleeding, care should be taken to exclude uterine perforation. The bleeding can usually be stopped by applying electrodiathermy to the bleeding point. Insertion of an intrauterine catheter, which can be left in situ for 24-48 hours, has also been reported, but care must be taken as it may extend an overlooked perforation and divert bleeding to the peritoneal cavity. Other options include vaginal uterine artery ligation, laparotomy and repair of the uterus, or even hysterectomy.

Mechanical and/or thermal injury

There are two types of mechanical injury: uterine perforation and cervical laceration. In the Netherlands study, perforation was the most frequent operative complication (33 in 13600). Half of the perforations are usually entry-related. 40,43 It could be argued that ultrasound or laparoscopic control may help reduce the rate of perforation, especially perforations that are not entry-related. A recent review of 797 myoma resection cases done under laparoscopic or ultrasound guidance reported only one perforation (0.13%).43 If a perforation is suspected, then laparoscopy should be performed to rule it out. Laparoscopy can also help exclude bowel and visceral injury. A review of 547 cases from different studies by Ubaldi et al.39 found seven uterine perforations leading to two bowel injuries. A perforation site can usually be left to heal unless it is bleeding or is >5mm and future pregnancy is contemplated. Bleeding from the forceps site on the cervix can usually be controlled with pressure applied with a ring forceps or by the application of sliver nitrate. The application of two rather than one pair of forceps on the cervix, to stabilize it, minimizes the risk of cervical laceration. Tears usually require suturing.

Distention media complications

Although the Netherlands study reported an incidence of only 0.20% distention media overload, a recent literature

N, number of cases in the study.

^{*}Including all deliveries from multiple pregnancies.

^{**}Patients in this study had menstrual disorders and were desirous of a pregnancy, but no details were given regarding their fertility status.

^{***}Including women who conceived more than once.

^{****} Nine term vaginal deliveries and five cesarean section for which gestation was not specified.

review revealed higher figures.⁴⁴ Distention media complications depend on the type of fluid used.

High-molecular-weight dextran The major complication associated with the use of Hyskon is anaphylactic shock (1 in 10000). However, this medium has also been associated with non-cardiogenic pulmonary edema and coagulation disorders. It is therefore rarely used nowadays.

Low-viscosity, non-electrolyte fluid media The media frequently used are glycine, sorbitol, and mannitol. The complications can be divided into electrolyte disturbances (mainly hyponatremia), volume overload (pulmonary edema), and neurologic symptoms (visual disturbances and encephalopathy) caused by the neurotoxic effect of glycine metabolites. It has been suggested that an increase in the size of the myoma expressed as a percent of uterine size increases the risk of fluid retention. The uterine distention pressure should be maintained just above the diastolic blood pressure to minimize intravasation. Fatalities have been reported with large deficits; it is therefore agreed that when the fluid deficit reaches 1000 ml, the procedure should be drawn to conclusion and that if fluid deficit is 1500 ml, the procedure should be stopped immediately. Treatment of hyponatremia depends on the severity of the case. Most cases are asymptomatic, and observation is all that is required. If the patient is symptomatic or the sodium level is <120 mmol/L, treatment in the form of fluid restriction, intravenous diuretics, and hypertonic saline administration is indicated. Very rapid correction can precipitate central pontine myelinolysis. It has been suggested that the Nd:YAG laser is associated with less fluid absorption, as it coagulates deeper vessels than the resectoscope.⁴⁵ It is also superior in this regard, as it uses electrolyte media rather than low-viscosity media.

Electrolyte fluid media The advantage of using normal saline with the new bipolar operative hysteroscopy system is that it is unlikely to cause electrolyte disturbances or neurologic symptoms. Volume overload is easily treated with intravenous diuretics.

Infection

Infection can be introduced to the patient by the procedure or spread from the cervix into the pelvic cavity during the procedure. In a review of 2116 operative hysteroscopy cases, out of which 782 were hysteroscopic myomectomies, in 2002, Agostini et al.⁴⁶ reported a post-operative infection rate of 1.42% (30/1116). There were 18 cases of endometritis (0.85%) and 12 cases of urinary

tract infections. The risk of early-onset endometritis was similar in myomectomy, septa resection, and transcervical resection of the endometrium, but it was higher for synechiae lysis. No major infection complications were detected in this series, but toxic shock syndrome, septicemia, pyometra, and broad ligament abscess have all been reported following operative hysteroscopy.

Air/gas embolism

Fatal embolism has been reported following diagnostic hysteroscopy using $\mathrm{CO_2}^{47}$ and also in association with operative hysteroscopy with normal saline as the distention medium. It has been suggested that deep Trendelenburg position should be avoided, the cervix should be sealed over the hysteroscope, multiple exit and entry with the scope into the cavity should be avoided, and the distention pressure should be kept <100 mmHg, in order to minimize the risk of this rare complication.

Late complications

Uterine adhesions, pain, and adenomyosis

It is estimated that 13.4% of hysteroscopic myomectomies are complicated by intrauterine synechiae. These can be divided at second look hysteroscopy if routinely done. There is evidence that adenomyosis can complicate uterine surgery, but this is thought to be associated mainly with endomyometrial resection. McLucas et al. found newly developed adenomyosis when performing repeat endometrial resections. Some surgeons therefore argue against endometrial resection when performing hysteroscopic myomectomy.

Uterine rupture in subsequent pregnancy

There are a number of case reports of this complication during the antenatal period and in labor. However, in most of these cases, the index hysteroscopy was complicated by uterine perforation.

Spread of uterine malignancy or delaying its presentation

This is a very controversial subject. There is evidence that hysteroscopy with fluid distention carries cancer cells into the peritoneal cavity, but the case for effect of this on cancer staging or even outcome is not proven. The delayed presentation is related to the embedding of endometrial cells within uterine synechiae.

References

- Wamsteker K, Emanuel MH, de Kruif JH. Transcervical hysteroscopic resection of submucous fibroids for abnormal uterine bleeding: results regarding the degree of intramural extension. Obstet Gynecol 1993; 82: 736–40.
- Lasmar RB, Barrozo PR, Dias R, Oliveira MA. Submucous myomas: a new presurgical classification to evaluate the viability of hysteroscopic surgical treatment – preliminary report. J Minim Invasive Gynecol 2005; 12(4): 308–11.
- Pritts EA. Fibroids and infertility: a systemic review of the evidence. Obstet and Gynecol Surv 2001; 8: 483–91.
- Donnez J, Jadoul P. What are the implications of myomas on fertility? A need for a debate? Hum Reprod 2002; 17(6): 1424– 30.
- Griffiths A, D'Angelo A, Amso N. Surgical treatment of fibroids for subfertility. Cochrane Database Syst Rev 2006; 3: CD003857.
- Buttram VJ, Reiter R. Uterine leiomyomata: etiology, symptomatology and management. Fertil Steril 1981; 36: 433

 45.
- Lefebvre G, Vilos G, Allaire C et al. The management of uterine leiomyomas. J Obstet Gynaecol Can 2003; 128: 396–405.
- Vercellini P, Cortesi I, Oldani S et al. The role of transvaginal ultrasonography and outpatient diagnostic hysteroscopy in the evaluation of patients with menorrhagia. Hum Reprod 1997; 12: 1768–71.
- Leone F, Lanzani C, Ferrazzi E. Sonohysterography with endometrial sampling in the pre-operative assessment of submucous myomas. Ultrasound Obstet Gynecol 2004; 24: 305.
- Ludwin A, Basta A, Basta P et al. The accuracy of sonohysterographical versus hysteroscopic evaluation of submucous myomas penetrating myometrium in therapeutic qualification. Ultrasound Obstet Gynecol 2004; 24: 305.
- Pretoruis D, Becker E, Lev-Toaff A. Impact of sonohysterography on the management of women with uterine myomas. Ultrasound Obstet Gynaecol 2001; 18(Suppl): 2.
- Tadeka A, Manabe S, Hosono S et al. Preoperative evaluation of submucosal myoma by virtual hysteroscopy. J Am Assoc Gynecol Laparosc 2004; 11(3): 404–9.
- Neuwirth RS. Hysteroscopic submucous myomectomy. Obstet Gynecol Clin North Am 1995; 22(3): 541–58.
- Munez J, Jimenez J, Hernandez C et al. Hysteroscopic myomectomy; our experience and review. JSLS 2003; 7: 39–48.
- Yang J, Lin B. Changes in myometrial thickness during hysteroscopic resection of deeply invasive submucous myomas. J Am Assoc Gynecol Laparosc 2001; 8(4): 501–5.
- 16. Parazzini F, Vercellini P, De Giorgi O et al. Efficacy of preoperative medical treatment in facilitating hysteroscopic endometrial resection, myomectomy and metroplasty: literature review. Hum Reprod 1998; 13: 2592–7.
- Propst A, Liberman R, Harlow B et al. Complications of hysteroscopic surgery: predicting patients at risk. Obstet Gynecol 2000; 96: 517–20.
- Campo S, Campo V, Gambadauro P. Short-term and long-term results of resectoscopic myomectomy with and without pretreatment with GnRH analogues in premenopausal women. Acta Obstet Gynecol Scand 2005; 84(8): 756–60.
- Preutthipan S, Herabutya Y. Vaginal misoprostol for cervical priming before operative hysteroscopy: a randomized controlled trial. Obstet Gynecol 2000; 96(6): 890

 –4.

- Hallez JP. Myomectomy by endo-uterine resection. Curr Opin Obstet Gynecol 1996; 8: 250–6.
- 21. Duan H, Xia E, Wang L, Duan H. Clinical study on 235 cases performed under hysteroscopy combined with laparoscopy. Zhonghua Fu Chan Ke Za Zhi 2002; 37(6): 342–5. [In Chinese.]
- Mazzon I. Mechanically cutting loops. Gynecology. 4th edn. Karl Storz, 2003.
- 23. Litta P, Vasile C, Merlin F et al. A new technique of hysteroscopic myomectomy with enucleation in toto. J Am Assoc Gynecol Laparosc 2003; 10(2): 263–70.
- Van Dongen H, Emanuel MH, Smeets MJ, Trimbos B, Jansen FW. Follow-up after incomplete hysteroscopic removal of uterine fibroids. Acta Obstet Gynecol Scand 2006; 85(12): 1463–7.
- 25. Bettocchi S, Ceci O, Di Venere R et al. Advanced operative office hysteroscopy without anaesthesia: analysis of 501 cases treated with a 5 Fr. bipolar electrode. Hum Reprod 2002; 17(9): 2435–8.
- Emanuel MH, Wamsteker K. The Intra Uterine Morcellator: a new hysteroscopic operating technique to remove intrauterine polyps and myomas. J Minim Invasive Gynecol 2005; 12(1): 62–6.
- Darwish A. Modified hysteroscopic myomectomy of large submucous fibroids. Gynecol Obstet Invest 2003; 56(4): 192–6.
- Smets M, Nisolle M, Bassil S, Dunnez J. Expansive benign lesions: treatment by laser. Eur Journal Obstet Gynecol Reprod Biol 1996; 65: 101–5.
- 29. Fernandez H, Sefrioui O, Virelizier C et al. Hysteroscopic resection of submucosal myomas in patients with infertility. Hum Reprod 2001; 16(7): 1489–92.
- Xia EL, Duan H, Huang XW, Zhang J, Yu D. [Transcervical resection of myoma in treatment of hysteromyoma, experience in 962 xcases]. Zhonghua Yi Xue Za Zhi 2005; 85(3): 173–6. [In Chinese.]
- Barbot J, Parent B. Failure and/or recurrence following hysteroscopic myomectomy. In: Dubuisson JB, Chapron C, Bouquet de Joliniere, eds. Les Fibromes Uterins. Paris: Arnette, 1994: 67–75. [In French.]
- 32. Cravello L, D'Ercole C, Boubli L et al. Hysteroscopic treatment of uterine fibroids. J Gynecol Surg 1995; 11: 227.
- Phillips D, Nathanson H, Meltzer S et al. Transcervical electrosurgical resection of submucous leiomyomas for chronic menorrhagia. J Am Assoc Gynecol Laparosc 1995; 2(2): 147–53.
- 34. Emanuel M, Wamsteker K, Hart A, Metz G, Lammes FB. Long-term results of hysteroscopic myomectomy for abnormal uterine bleeding. Obstet Gynecol 1999; 93(5 Pt 1): 743–8.
- Vercellini P, Zaina B, Yaylayan L et al. Hysteroscopic myomectomy: long-term effects on menstrual pattern and fertility. Obstet Gynecol 1999; 94(3): 341–7.
- Istre O, Langebrekke A. Repeat hysteroscopic surgery reduces the hysterectomy rate after endometrial and myoma resection. J Am Assoc Gynecol Laparosc 2003; 10(2): 247–51.
- 37. Cravello L, Farnarier J, De Montgolfier R et al. Hysteroscopic resection of fibroids: results with a 6 year follow-up period. J Gynecol Surg 1999; 15(1): 1–5.
- Giatras K, Berkeley A, Noyes N et al. Fertility after hysteroscopic resection of submucous myomas. J Am Assoc Gynecol Laparosc 1999; 6(2): 155–8.

- 39. Ubaldi F, Tournaye H, Camus M et al. Fertility after hysteroscopic myomectomy. Hum Reprod 1995; 1(1): 81–90.
- Jansen FW, Vredevoogd CB, van Ulzen K et al. Complications of hysteroscopy: a prospective, multicenter study. Obstet Gynecol 2000; 96(2): 266–70.
- Agostini A, Cravello L, Desbriere R et al. Hemorrhage risk during operative hysteroscopy. Acta Obstet Gynecol Scand 2002; 81(9): 878–81.
- 42. Phillips DR, Nathanson HG, Milim SJ et al. The effect of dilute vasopressin solution on blood loss during operative hysteroscopy: a randomized controlled trial. Obstet Gynecol 1996; 88(5): 761–6.
- 43. Xia EL, Duan H, Zhang J et al. [Analysis of 16 cases of uterine perforation during hysteroscopic electro-surgeries]. Zhonghua Fu Chan Ke Za Zhi 2003; 38(5): 280–3. [In Chinese.]

- 44. Batra N, Khunda A, O'Donovan PJ. Hysteroscopic myomectomy. Obstet Gynecol Clin North Am 2004; 31(3): 669–85.
- 45. Donnez J, Polet R, Smets M et al. Hysteroscopic myomectomy. Curr Opin Obstet Gynecol 1995; 7(4): 311–6.
- 46. Agostini A, Cravello L, Shojai R et al. Postoperative infection and surgical hysteroscopy. Fertil Steril 2002; 77(4): 766–8.
- 47. Nishiyama T, Hanaoka KGas embolism during hysteroscopy. Can J Anaesth 1999; 46(4): 379–81.
- Hallez JP. Single-stage total hysteroscopic myomectomies: indications, techniques, and results. Fertil Steril 1995; 63(4): 703–8.
- 49. McLucas B. Does endometrial resection cause adenomyosis? J Am Assoc Gynecol Laparosc 1994; 1(4, Part 2): S21.
- Selvaggi L, Cormio G, Ceci O et al. Hysteroscopy does not increase the risk of microscopic extrauterine spread in endometrial carcinoma. Int J Gynecol Cancer 2003; 13(2): 223–7.

Laparoscopic uterine artery occlusion

Moises Lichtinger

INTRODUCTION AND MECHANISM OF ACTION

Uterine leiomyomas are the most common neoplasms of the female reproductive system.¹ with a prevalence from 20% to 77%.² Between 35% and 50% of women with fibroids are symptomatic, experiencing excessive vaginal bleeding, pelvic pain or pressure, constipation, bloating, and/or infertility, and pregnancy loss.³ The traditional treatment has been medical; and when it fails, resective surgery by hysterectomy or myomectomy. Many women with leiomyoma-related symptoms are now seeking alternative, less-invasive treatment.

Laparoscopic uterine artery occlusion is a minimally invasive outpatient procedure to treat leiomyoma-related symptoms. The uterine arteries provide most of the uterine blood supply. When both uterine arteries are occluded, blood flow is blocked, resulting in uterine ischemia. Blood throughout the uterus and myoma clots. After several hours to days of clotted stasis, the uterus is able to lyse clotted blood and is reperfused by fresh blood flow from ovarian and collateral arterial circulation. Myomas cannot lyse clotted blood and reperfuse and eventually suffer infarction and die. Clinically, this translates in a significant decrease in symptoms and imaging-proven fibroid shrinkage.⁴

During reproductive life, the human uterus undergoes multiple periods of hyperperfusion without negative effects. Transient uterine ischemia with myometrial clotting is consistent with postpartum clotting of uteroplacental arteries. Following placental separation, blood flow is slowed in the uterus by regular myometrial contractions that persist for several hours following delivery.⁵ Eventually, arteries throughout the myometrium clot; hours later the clot lyses and the myometrium is reperfused. The clot is not lysed in uteroplacental arteries. They scar and obliterate permanently.^{7,8} Remnant trophoblast at the base of the placental implantation site does not survive the clot-lysis cycle and over time it is sloughed into the uterine cavity. Epidemiologic studies have shown that the relative risk of myomas decreases with increasing parity;9,10 and magnetic resonance imaging (MRI) case reports after vaginal delivery and cesarean section illustrate that myomas that die in postpartum have an identical imaging appearance to myomas purposely infarcted by uterine artery embolization.^{11–13}

PREOPERATIVE SELECTION

Laparoscopic uterine artery occlusion can be used for patients who have qualified for hysterectomy or myomectomy indicated by symptomatic leiomyomas (menorrhaghia, pelvic pain-pressure). 14 Some of the patients object to resective surgery, medical treatment, or other minimally invasive procedures such as uterine artery embolization or myolysis. Since clinical response is dependent on effecting a decreased perfusion of fibroids, the criteria of selection include patients with >3 cm intramural fibroids that do not have ultrasound or MRI evidence of poor perfusion around the fibroid (calcifications, terminal degeneration, myomas with large submucosal position). Visualization is difficult in patients at or beyond a 20-week gestation uterine size. These patients are not candidates for this endoscopic procedure. When there is a large myoma suspended from a thin serosal pedicle, there is a concern that decreased flow could necrose the pedicle, causing intra-abdominal spill and separation of the fibroid. In this case, uterine artery occlusion is combined with removal of the pedunculated fibroid by morcellation. Patients with previous uterine artery embolization or uterine artery ligation during cesarean section bleeding events do not qualify for this procedure.

OPERATIVE TECHNIQUE

After general anesthesia is established, the patient is placed in the dorsolithotomy position. A Foley catheter is inserted into the bladder. After bimanual examination, hysteroscopy is performed and, if warranted, directed endometrial biopsies are performed. A uterine cannula is inserted to aid manipulation during the procedure. Using open technique, a 10 or 12 mm port is inserted in the subumbilicus. In patients with a large uterus or a short distance from pubic to umbilicus, a left upper quadrant abdominal port entry is used. Pneumoperitoneum is established under videolaparoscopic guidance and the patient is tilted in the Trendelenburg position to favor the viscera away from the pelvic cavity. Two additional ports — one 5 mm and the other 12 mm in diameter — are inserted under visualization on both sides above the inferior epigastric vessels.

Access to the peritoneum is safer when a lateral incision over the psoas muscle is used preventing direct trauma to the retroperitoneal vessels. This will also free periadnexal adhesions and release lateral anatomic displacement from myomas.

Applying uterine countertraction on the ipsilateral side, the round ligament is identified. The peritoneum is elevated and incised laterally next to the round ligament over the psoas muscle (Figure 33.1) The cut edges of the peritoneum are grasped and pulled laterally away from each other. The dissection is carried lateral to the uterus and below the round ligament. The lateral umbilical ligaments are vestigial obliterated umbilical arteries that reflect from the anterior peritoneum and become retroperitoneal as they pass below the round ligament through an avascular deep perivesical area (Figure 33.2). This white fibrous ligament is now traced backwards until it ends at the internal iliac artery (Figure 33.3). The ligament is then pulled laterally, allowing origin of the uterine artery to be seen (Figure 33.4). The first 2-3 cm of this artery has a straight tract and can be seen consistently pulsating; in its more medial tract, it becomes tortuous and surrounded by multiple veins as it travels crossing above the ureter. The artery has a diameter of 1-5 mm; it is extensible and tolerates significant manipulation. One or two preloaded 10 mm vascular clips are applied on the uterine artery at its origin. Some surgeons prefer bipolar or ultrasonic coagulation of the vessels. Once both



Figure 33.1 Right peritoneum incised laterally next to the round ligament over the psoas muscle.



Figure 33.2 Obliterated umbilical artery becomes retroperitoneal as it passes under the round ligament.

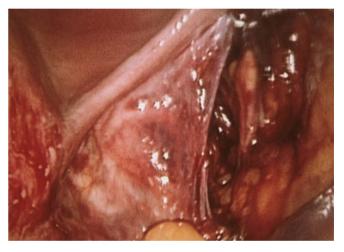


Figure 33.3 The fibrous white element (obliterated umbilical artery) ends at the internal iliac artery.



Figure 33.4 Proximal uterine artery.



Figure 33.5 Bilateral uterine artery occlusion produces blanching of the uterus.

uterine arteries are occluded, the uterus undergoes ischemia and blanches progressively (Figure 33.5). In 1–2% of women, one or both uterine arteries are hypoplastic and a communicating artery connects the ovarian artery to the uterus. When the uterine arteries are occluded in this patient, the uterus doesn't blanch. In this unusual finding, the utero-ovarian ligament is coagulated and only then does the uterus undergo blanching.

POSTOPERATIVE CARE

Depending on the their immediate postoperative assessment; patients are discharged home in less than 23 hours. Pain is managed with non-steroidal analgesics and occasionally with oral controlled medication. Antibiotic is continued for 5–7 days. The patient is seen in the office at weekly intervals for the first 3 weeks, then monthly. At 3 months, the follow-up continues every 3 months for the first year, then bianually. Imaging studies are ordered within the first 3 months, then every 3–6 months. Special attention is given to pain, menses diary, vaginal discharge, menopausal symptoms and laboratory testing if anemia is present.

IN-VIVO AND CLINICAL STUDIES

Treatment of intractable menorrhaghia by bilateral uterine vessel interruption was reported in 1964.¹⁵ This was a series of seven patients with and without fibroids who suffered from menorrhaghia. Uterine vessel interruption was performed via laparotomy. All seven patients had symptomatic improvement; one required simultaneous

hormonal treatment. No perioperative complications were reported.

Transcatheter uterine artery occlusion by radiologic embolization was used as a presurgical measure to reduce blood loss during and after subsequent hysterectomy or myomectomy. When uterine artery embolization was used to treat life-threatening bleeding in patients with myomas, it was noticed that bleeding resolved and myomas decreased in size. The procedure was then popularized as an alternative to surgical resective therapy. In a review of 200 patients with symptomatic leiomyomas, treated with radiologic uterine artery embolization, a reduction in dominant fibroid volume by 58% at 12 months after treatment was reported. Menstrual bleeding improved 90% and bulk symptoms improved in 95% of the patients at 1 year after treatment.

Laparoscopic bilateral occlusion of the uterine arteries to treat symptomatic leiomyomas was advanced as a minimally invasive alternative to radiologic uterine artery embolization. Using a laparoscopic bipolar coagulation technique, of the 87 patients evaluated, 89% experienced symptomatic improvement, and 76% had sonographic evidence of dominant fibroid reduction.^{20,21} We reported laparoscopic uterine artery occlusion with coated ligature and endovascular clips using a lateral retroperitoneal technique on eight women suffering from menorrhaghia and/or pelvic pressure or pain and anemia related to leiomyomata.¹⁴ At 3-month follow-up, seven patients reported complete resolution of pain, and the remaining patient reported mild pain. Five patients with previous menorrhaghia reported eumenorrhea; however, none became amenorrheic, and anemia was corrected in three patients. Average decrease in uterine volume at 3 months was 39-40%. (Table 33.1)¹⁴ There were no perioperative complications, the average operating time was 35 minutes, and estimated blood loss was less than 25 dl in all cases. Postoperative pain was managed by non-steroidal anti-inflammatory drugs (NSAIDS) in all patients. One requested parenteral narcotic analgesia in the recovery room. All the patients were managed as outpatients. Continuous monitoring of myometrial pH suggested a pattern similar to the physiologic response after uterine artery occlusion. Thirteen patients underwent continuous myometrial pH monitoring for several hours before and after uterine artery occlusion. The pH was used as a proxy for hypoxia and lactic acidosis from uterine ischemia. The results showed that the uterine pH returned to baseline (reperfusion) in all patients by 660 minutes.²²

MRI studies of uptake contrast media suggest that clot forms more rapidly in myomas than in the myometrium,²³ and that the myoma remains unperfused while the rest of the myometrium has normal perfusion at 1, 2, 3, 4, 6 months, and 1 year after uterine artery embolization.²⁴ An expanded review of our first 100 consecutive cases of

Table 33.1 Change in uterine volume by ultrasonography (eight patients)

Volume before occlusion (cm³)	Volume after occlusion (cm³)	% Percent decrease
4385	2063	52.9
411	300	27.0
670	420	37.0
3870	2100	45.7
850	420	50.0
630	429	31.9
671	329	32.9
1170	721	38.3
Average		
1582	719	39.4

laparoscopic bilateral uterine artery occlusion with a follow-up of 1 year or more showed a consistent 40% sonographic uterine volume decrease and 80% symptom resolution.

The procedure has also been used during laparoscopic myomectomy as a blood-sparing preliminary step, in conjunction with endometrial ablation, and to control massive postpartum bleeding not responding to medical therapy.

COMPLICATIONS

More than 2000 laparoscopic uterine artery occlusions have been performed worldwide. No serious complications have been reported. The procedure has possible complications: serious abdominal entry injuries have been calculated at a rate of 3/1000.²⁵ Anesthetic complications during retroperitoneal laparoscopic procedures have not been studied but are known to be extremely uncommon. Entering the retroperitoneum in a more lateral site of the posterior broad ligament circumvents uterine expansive and periadnexal anatomic alterations. The peritoneum is accessed directly above the psoas muscle, preventing direct trauma to the more medial retroperitoneal vessels.¹⁴

Prolapse and vaginal expulsion of necrotic tissue and myomas has been reported. ^{14,21} In most of the cases the tissue or myoma is passed within 3 months of the procedure and in the majority of the patients expulsion did not translate into infection. It has been theorized that it could be a further step in uterine restoration. ²⁶ Review of the first 100 consecutive procedures in our series disclosed: one return to the operating room, a patient with port site

Table 33.2 Laparoscopic uterine artery occlusion (100 consecutive patients)

Complications		
Return to the operation room		
Lower extremity neuropathy		
Post-occlusion syndrome		
Postoperative menopausal symptoms or amenorrhea		
Vaginal expulsion of myoma		
Endometrial hyperplasia		
Clinical failure		
Unhappy with degree of shrinkage		
Vaginal hemorrhage (emergency hysterectomy)		
Persistent pelvic pain (elective hysterectomy)		

bleeding secondary to undiagnosed von Willebrand's disease; one patient suffered lower extremity neuropathy that resolved completely with physical therapy by 3 months; spontaneous expulsion of a vaginal myoma in two patients; in two cases, we found mild endometrial hyperplasia from tissue obtained on the day of the procedure. Multiple follow-up biopsies were negative for hyperplasia in both patients. One patient was unhappy with the degree of shrinkage; two patients underwent subsequent hysterectomy, one who presented with a vaginal hemorrhage and one with persistent pelvic pain (Table 33.2). One patient became pregnant 4 years after laparoscopic occlusion. She underwent elective cesarean section at 38 weeks with no complications.

Cessation of uterine perfusion has been accomplished successfully by uterine artery embolization and laparoscopic uterine artery occlusion. ^{14,19} Serious complications after uterine artery embolization have been reported in approximately 1% of patients, ¹⁹ since both procedures share a similar mechanism of action after occlusion laparoscopists need to be aware of major complications reported after radiologic embolization: embolization in an undiagnosed sarcoma^{27,28} misembolization to non-target organs (buttock pain, ovarian failure), ^{29,30} pyometra requiring hysterectomy that ended in death, ³¹ and radiation exposure that has been measured at 100 times higher than that of traditional diagnostic procedures and 12–30 times lower than that during radiation therapy for Hodgkin's lymphoma. ³²

COST

Laparoscopic uterine artery occlusion requires the use of operative endoscopic instrumentation, which is already

available in most hospitals. In our experience it has been difficult to calculate hospital and physician reimbursement since there is a myriad of insurance companies with different individual contract arrangements. The average reimbursement for the gynecologist performing the procedure has ranged from US\$400 to US\$2000 and average hospital cost from US\$5000 to US\$7000.¹⁴

CONCLUSIONS

Laparoscopic bilateral uterine artery occlusion offers a minimally invasive surgical option for the gynecologist that causes transient uterine ischemia and subsequent relief of leiomyoma symptoms. It should be practiced by surgeons with operative laparoscopic training and privilege.

References

- Kjerolff KH, Erickson AB, Langerberg PW. Chronic gynecologic conditions reported by US women: findings from the National Health Interview Survey, 1984–1992. AM J Public Health 1996; 86: 195–6.
- 2. Cramer SF, Patel A. The frequency of uterine leiomyomata. Am J Clin Pathol. 1990; 94(4): 435–8.
- Callahan TL, Caughey AB, Heffner LJ. Blueprints in Obstetrics & Gynecology, 2nd edn. Malden, MA: Blackwell Publishing, 2001: 30.
- Burbank F, Hutchins FLJr. Uterine artery occlusion by embolization or surgery for the treatment of fibroids: a unifying hypothesis transient uterine ischemia. J Am Assoc Gynecol Laparosc 2000; 7(4 Suppl): 51–549.
- Cunningham FG, Gant MF, Leveno KJ et al. Williams Obstetrics, 21st edn. New York: McGraw-Hill/Medical Publishing Division, 2001.
- 6. Gerbasi FR, Bottoms S, Farag A et al. Changes in hemostasis activity during delivery and the immediate postpartum period. Am J Obstet Gynecol 1990; 162: 1158–63.
- Williams JW. Disappearance of the placental site during the puerperium. JAMA 1931; 97: 523–9.
- Williams JW. Regeneration of the uterine mucosa after delivery with especial reference to the placental site. Am J Obstet Gynecol 1931; 22: 664–96, 793–6.
- 9. Ross RK, Pike MC, Vessey MP et al. Risk factors for uterine fibroids: reduced risk associated with oral contraceptives. Br Med J (Clin Res Ed) 1986; 293: 359–62.
- Day Baird D, Dunson DB. Why is parity protective for uterine fibroids?. Epidemiology 2003; 14: 247–50.
- Boni RA, Hebisch G, Hugh A et al. Multiple necrotic uterine leiomyomas causing severe puerperal fever: ultrasound, CT, MR, and histological findings. J Comput Assist Tomogr 1994; 18: 828–31.
- 12. Murase E, Siegelman ES, Outwater EK et al. Uterine leiomyomas: histopathologic features, MR imaging findings, differential diagnosis, and treatment. Radiographics 1999; 19: 1179–97.
- 13. Lin YH, Hwang JL, Huang LW et al. Pyomyoma after a Cesarean section. Acta Obstet Gynecol Scand 2002; 81: 571–2.
- Lichtinger M, Hallson L, Calvo P, Adeboyejo G. Laparoscopic uterine artery occlusion for symptomatic leiomyomas. J Am Assoc Gynecol Laparosc 2002; 9: 191–8.
- Bateman W. Treatment of intractable menorrhaghia by bilateral uterine vessel interruption. Am J Obstet Gynecol 1964; 89(6): 825–7.
- Ravina JH, Merland JJ, Herbreteau D et al. Preoperative embolization of uterine fibroma. Preliminiary Result (10 cases). Presse Medi 1994; 23: 1540. [In French.]

- 17. Goodwin SC. New horizons in gynecologic embolotherapy. J Vasc Interv Radiol 1998; 9(suppl): 53–59.
- Ravina JH, Herbreteau D, Civaru-Vignevon N et al. Arterial embolization to treat uterine myomata. Lancet 1995; 346: 671–2.
- 19. Spies JB, Ascher SA, Roth AR et al. Uterine artery embolization for leiomyomata. Obstet Gynecol 2001; 98(1): 29–34.
- Liu WM. Laparoscopic bipolar coagulation of uterine vessels to treat symptomatic leiomyomas. J Am Assoc Gynecol Laparosc 2000; 7: 125–9.
- 21. Liu WN, Ng HTWUYC et al. Laparoscopic bipolar coagulation of uterine vessels: a new method for treating symptomatic fibroids. Fertil Steril 2001; 75(2): 417–22.
- 22. Lichtinger M, Burbank F, Hallson L et al. The time course of myometrial ischemia and reperfusion after laparoscopic uterine artery occlusion theoretical implications. J Am Assoc Gynecol Laparosc 2003; 10(4): 553–566.
- 23. DeSouza NM, Williams AD. Uterine arterial embolization for leiomyomas: perfusion and volume changes at MR imaging and relation to clinical outcome. Radiology 2002; 222: 367–4.
- 24. Jha RC, Imaoka I, Ascher SM et al. MR Imaging of uterine artery embolization for leiomyomas: morphological changes and features predictive of response (abstr). Radiology 1999; 213: 347.
- 25. Jansen FW, Kapiteyn K, Trimbos-Kemper T et al. Complications of laparoscopy: a prospective multicentre observational study. Br J Obstet Gynaecol 1997; 104: 595–600.
- Felemban A, Stein L, Tulandi T. Uterine restoration after repeated expulsion of myomas after uterine artery embolization. J Am Assoc Gynecol Laparosc 2001; 8(3): 442–4.
- 27. A1-Badr A, Faught W. Uterine artery embolization in an undiagnosed uterine sarcoma. Obstet Gynecol 2001: 97: 836–7.
- 28. Holub Z, Eim J, Tabor A et al. Complications and myoma recurrent after laparoscopic uterine artery occlusion for symptomatic myomas. J Obstet Gynecol Res 2006; 32: 55–62.
- Worthington-Kirsch RL, Smith SJ, Berkowitz RP. Transient buttock pain after uterine artery embolization for the management of fibroids. Minim Invasive Ther Allied Technol 1999; 8: 425–7.
- 30. Bradley EA, Reidy JF, Forman RG et al. Transcatheter uterine artery embolization to treat large uterine fibroids. Br J Obstet Gynaecol 1998; 105: 235–240.
- 31. Vaghisht A, Studd J, Carey A et al. Fatal septicemia after fibroid embolization. Lancet 1999; 354: 307–308.
- Nikolic B, Spies JB, Lundsten MJ et al. Patient radiation dose associated with uterine artery embolization. Radiology 2000; 214: 121–125.

Temporary occlusion of uterine artery for the treatment of fibroids

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INTRODUCTION

Traditional operative treatments for symptomatic fibroids are laparotomy with hysterectomy or myomectomy, involving considerable morbidity. Myomectomy involves the shelling out of fibroids from the myometrium, and in the case of submucosal fibroids these can be removed surgically via hysteroscopic procedures. Although morbidity is reduced with endoscopic surgery, this technique is not widely available and has limitations.

NEW TREATMENT OPTIONS

A number of minimally invasive treatments options are now available for the treatment of symptomatic fibroids. Surgical treatments with endoscopic technique include hysterectomy, myomectomy, and myolysis.⁴ Multiple fibroids pose a significant problem for treatment. When myomectomy or myolysis is performed and all clinically identified fibroids are removed or 'killed', in approximately half of the patients fibroids are seen at a later time.⁵

Non-surgical treatments include medical therapy and treatments interfering with the blood supply to the uterus or the fibroids, uterine artery embolization performed by the interventional radiologist, or laparoscopic uterine artery occlusion by the gynecologist. An even simpler treatment is the non-incision temporary uterine clamp, which is placed in the side fornices in the vagina, directed with Doppler ultrasound.

The continuous therapeutic goal for symptomatic fibroids must take into consideration the needs and desires of the patients: i.e. length of hospital stay, time to return to work, adverse events, and childbearing plans. Hysterectomy continues to be costly in terms of the billions of dollars spent annually, as well as in the more fundamental terms of morbidity and mortality when compared with the less-invasive alternatives.⁶

UTERUS CIRCULATION

The uterus has a very rich blood supply through two extrinsic arterial systems, the uterine and ovarian arteries. Intrinsic uterine arteries consist of ascending uterine, arcuate, radial, and peripherial arteries implicating free flow through the uterus. Fibroids receive their blood supply from the intrinsic arteries, primarily from branches of arcuate arteries, and the vessels are located in the pseudocapsule around the fibroids. The ipsilateral uterine and ovarian arteries are connected by communicating branches. In addition to its primary (uterine artery) and secondary (ovarian artery) extrinsic blood supply, the uterus enjoys a vast network of lesser known arterial collaterals. If the blood supply from the right or left uterine artery is occluded, blood from the left or right artery will supply the myometrium by communications through arcuate arteries. Finally, if both uterine arteries are occluded, blood flow to the myometrium will develop from the ovarian arteries through communicating arteries. In addition to the primary and secondary blood flow, the uterus has a vast network of collateral arterial communication from the aorta external iliac and femoral artery branch.8

FIBROID LIFE CYCLE

Fibroid degeneration is the physiologic way of terminating further growth of fibroids. Fibroids are particularly susceptible to degeneration because their rapid growths need increased blood supply. Fibroids have unsubstantiated connection to the uterine blood supply and, as a consequence, they frequently outgrow their blood supply, and thus two-thirds of fibroids show degeneration. Larger fibroids are more frequently associated with degenerative changes compared to the smaller ones. The different types of degenerative changes are hyaline or myxoid

degeneration (75%), calcification (10%), cystic degeneration (10%), fatty degeneration, and red degeneration during pregnancy.

IMPLICATIONS OF UTERINE ISCHEMIA

When the uterine circulation is interrupted, unperfused myometrium quickly becomes hypoxic, which creates pain. During ischemia, myometrial energy is derived anaerobically from the breakdown of glycogen through the glycolytic pathway.¹¹ After the uterine arteries are occluded, most blood stops flowing in myometrial arteries and veins, and the uterus becomes ischemic. It is postulated that myomas are killed by the same process that kills trophoblasts – transient uterine ischemia.¹²

Over time, stagnant blood in these arteries and veins clots. Then, tiny collateral arteries in the broad ligament, including communicating arteries from the ovarian arteries, open, and cause clots within the myometrium to lyse and the uterus to reperfuse. Fibroids, however, do not survive this period of ischemia. This is a unique organ response to clot formation and ischemia. After the uterine arteries are bilaterally occluded, either by uterine artery embolization or by laparoscopic obstruction, women with fibroids experience symptomatic relief after some time.

PRACTICAL ASPECTS OF THE PROCEDURE: UTERINE ARTERY OCCLUSION

In 1964 Bateman reported the successful treatment of menorrhagia in four patients with fibroids and three with functional uterine bleeding. ¹⁴ This was the first published article to demonstrate that uterine artery occlusion by ligation, division, or excision is an effective treatment for menorrhagia associated with fibroids and in patients without pathology.

Laparoscopic bipolar coagulation of uterine arteries and anastomotic sites of uterine arteries with ovarian arteries represents another modality of avoiding hysterectomy in some women. 15,16 This procedure was first described in 2000 in three women with symptomatic fibroids who required conventional surgical treatment. Uterine size and dominant fibroid size were assessed by ultrasonography before and after surgery. Both uterine arteries, as well as the anastomosis zone of uterine arteries with ovarian arteries, were occluded in all three women. Surgery was uneventful, and the patients were hospitalized for only 2 days. All women experienced improvement in symptoms with no complications. Postoperative

ultrasound showed progressive reduction in the size of the dominant fibroid.¹⁷

In our institution, we studied 46 premenopausal women, average age 43 years old (range 34-51 years old) with symptomatic uterine fibroids, undergoing radiologic embolization (n = 24) or laparoscopic closure of the uterine arteries (n = 22). The laparoscopic technique reduced the pictorial blood loss assessment chart (PBAC) score after 6 months by 50% in both groups. The uterus volume was also reduced by 35-40% in both groups. Postoperative pain and use of pain relief differed significantly, as patients required more pain medication after embolization: ketobemidon 38 mg compared with 16 mg in the laparoscopic group (p = 0.008). In conclusion, we found that laparoscopic occlusion of uterine vessels is a promising new method for treating fibroid-related symptoms, with less postoperative pain than embolization and comparable effects on symptoms.

DESCRIPTION OF TECHNOLOGY: TEMPORARY ARTERY OCCLUSION

A new exciting device, utilizing the principle of interference with the blood circulation, has recently been developed (Vascular Control Systems, Inc., San Juan Capistrano, CA) (FlowStat) for the treatment of fibroids with non-incision, only compression.

The system consists of a guiding cervical tenaculum, a transvaginal vascular clamp with integrated doppler ultrasound crystals, and a small, battery powered transceiver that generates audible doppler sound (Figure 34.1). The clamp slides along the guiding tenaculum to the level of the lateral vaginal fornices at the 9:00 and the 3:00 cervical positions. When the crystals on the arms of the clamp contact the vaginal mucosa, they return audible signals from the right and left uterine arteries. When the clamp is further advanced along the guiding tenaculum, the clamp displaces the uterine arteries superior to their points of insertion into the uterus. When closed, the clamp occludes the uterine arteries bilaterally by squeezing them against the lateral borders of the uterus, and the clamp is kept in place for 6 hours (see Figure 34.1).

IN-VITRO AND IN-VIVO STUDIES

After uterine artery occlusion, the pH falls and, when the clot lyses and reperfusion occurs, the pH returns to baseline. This has been investigated and monitored continuously before, during, and 24 hours after laparoscopic occlusion of uterine arteries.¹³ In patients with symptomatic fibroids, the pH was measured with a catheter

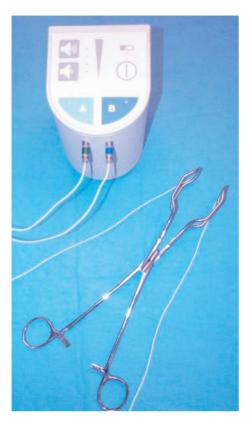


Figure 34.1 The transvaginal vascular clamp with integrated Doppler ultrasound crystals and Doppler receiver.

electrode embedded in the endometrium and in others in the myometrium. In 62% of the patients, the pH dropped 0.4–0.8 units, while in 38% the drop was greater, and the minimum was reached between 5 and 73 minutes. The return back to baseline was on average 5 hours. After the uterine artery is occluded, blood reaches the myometrium by secondary pathways and, for most women, these vascular pathways are insufficient to maintain aerobic metabolism. Until clotting occurs, blood continues to flow and supply oxygen to the myometrium, although at a new and slower speed.

CLINICAL STUDIES

We first published an account of this new technique in 2004, where a 43-year-old woman with menorrhagia, dysmenorrhea, and pelvic pain of several years' duration, with the uterus enlarged by fibroids to the size of a 16-week pregnancy, was treated.²⁰ Her uterine arteries were non-invasively transvaginally identified and occluded for 6 hours with a clamp that was guided by audible Doppler ultrasound. Following removal of the clamp, blood flow in the uterine arteries returned immediately. Three months following treatment, the uterine volume had

decreased by 49% and the dominant fibroid volume by 54% (Figure 34.2).

A study of 30 patients treated with this technique was presented in 2006 at the American Association of Gynecological endoscopy meeting in Las Vegas. Two options for analgesia were chosen (paracervical and epidural block were utilized in 17 and 13 patients, respectively). Menorrhagia was reduced in both groups; however, in the paracervical group, fibroid reduction was 12–24% and in the epidural group it was 24–45%. Two cases of hydronephrosis were observed and they were treated successfully with a stent.²¹ The explanation of additional fibroid reduction in the epidural group could be related to a more stable tenaculum placement, lesser pain, and consequently, constant compression of the uterine artery during the treatment time.

COMPLICATIONS

A disadvantage of the non-invasive transvaginal clamping technique is for fibroid location close to the cervix, in which case there are some difficulties in applying the clamp location correctly. In addition, the possibility of clamping the ureters, with subsequent hydronephrosis and possible damage of the renal function, is of concern. Currently, a multicenter study is planned which will hopefully answer many of the questions of this technique before it can be fully applied into clinical practice and for FDA (Food and Drug Administration) approval.

Another possible application of the temporary artery uterine clamp is during and after myomectomy operations. Thereby, we can reduce peri- and postoperative bleeding. In addition, the clamping may act as adjuvant therapy for possible residual fibromas. However, few results exist so far, and further studies of this therapeutic approach are needed to prove its long-term value.

USE AND INDICATION OF UTERINE ARTERY TECHNIQUES

The application of techniques such as uterine artery occlusion is primarily for women who wish to avoid hysterectomy. Many women do not wish to undergo an operative procedure, as they may not accept the associated risks of the operation, and therefore prefer the less-invasive procedures. Both radiologic and laparoscopic occlusion techniques are potential treatment options for fibroids. However, insufficient long-term follow-up results do not exist at present. Furthermore, both techniques are associated with a high level of skill, and consequently they should be performed only in special centers with

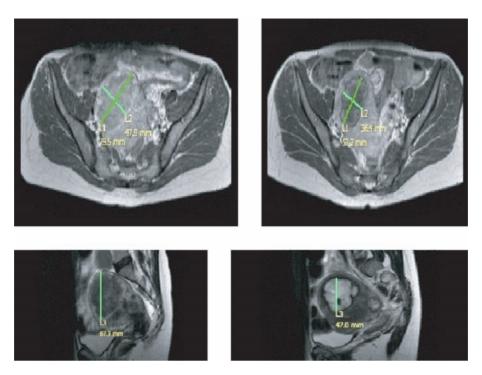


Figure 34.2 MRI showing major fibroid reduction of 54%. Images to left – pre-procedure = 82 cc. Images to right – post-procedure = 38 cc.

interest in this field. Anyhow, counseling of patients is of utmost importance before they make their own treatment choice.¹⁸

CONCLUSIONS

Fibroids present with different symptoms in different patients – i.e. infertility, bleeding problems, pressure and pain, single or multiple, different ages – and should be treated differently. In bleeding problems, an important issue is the location of the fibroid, and in cases with submucosal fibroids hysteroscopic resection is the method of

choice. In cases with intramural, subserosal, and even multiple fibroids, uterine artery therapy with embolization or laparoscopy seem to achieve good results on both bleeding problems and pressure symptoms. The temporary uterine clamp performed by a general gynecologist without incision may replace the more complicated procedures such as embolization performed by a radiologist and laparoscopic uterine artery closure performed by a skilled endoscopist.

In infertility patients, the single fibroid should be removed, whereas when multiple fibroids are present, medical or circulation therapy may be the only option for uterus-saving therapy.

References

- 1. Guarnaccia MM, Rein MS. Traditional surgical approaches to uterine fibroids: abdominal myomectomy and hysterectomy. Clin Obstet Gynecol 2001; 44: 385–400.
- Dicker RC, Greenspan JR, Strauss LT et al. Complications of abdominal and vaginal hysterectomy among women of reproductive age in the United States. The Collaborative Review of Sterilization. Am J Obstet Gynecol 1982; 144: 841–8.
- Fernandez H, Sefrioui O, Virelizier C et al. Hysteroscopic resection of submucosal myomas in patients with infertility. Hum Reprod 2001; 16: 1489–92.
- Dubuisson JB, Chapron C, Fauconnier A, Kreiker G. Laparoscopic myomectomy and myolysis. Curr Opin Obstet Gynecol 1997; 9: 233–8.
- Nezhat FR, Roemisch M, Nezhat CH, Seidman DS, Nezhat CR. Recurrence rate after laparoscopic myomectomy. J Am Assoc Gynecol Laparosc 1998; 5: 237–40.
- Goldfarb HA. Myoma coagulation (myolysis). Obstet Gynecol Clin North Am 2000: 27: 421–30.
- 7. Burbank F, Hutchins FL Jr. Uterine artery occlusion by embolization or surgery for the treatment of fibroids: a unifying

- hypothesis-transient uterine ischemia. J Am Assoc Gynecol Laparosc 2000; 7: S1–S49.
- 8. Chait A, Moltz A, Nelson JH Jr. The collateral arterial circulation in the pelvis. An angiographic study. Am J Roentgenol Radium Ther Nucl Med 1968; 102: 392–400.
- Huang SC, Yu CH, Huang RT et al. Intratumoral blood flow in uterine myoma correlated with a lower tumor size and volume, but not correlated with cell proliferation or angiogenesis. Obstet Gynecol 1996; 87: 1019–24.
- Cramer SF, Horiszny J, Patel A, Sigrist S. The relation of fibrous degeneration to menopausal status in small uterine leiomyomas with evidence for postmenopausal origin of seedling myomas. Mod Pathol 1996; 9: 774–80.
- Laudanski T. [Energy metabolism of the myometrium in pregnancy and labor]. Zentralbl Gynakol 1985; 107: 568–73 [in German].
- Burbank F. Childbirth and myoma treatment by uterine artery occlusion: do they share a common biology? J Am Assoc Gynecol Laparosc 2004; 11: 138–52.
- Lichtinger M, Burbank F, Hallson L et al. The time course of myometrial ischemia and reperfusion after laparoscopic uterine artery occlusion – theoretical implications. J Am Assoc Gynecol Laparosc 2003; 10: 554–63.
- Bateman W. Treatment of intractable menorrhagia by bilateral uterine vessel interruption. Am J Obstet Gynecol 1964; 89: 825–7.

- Liu WM. Laparoscopic bipolar coagulation of uterine vessels to treat symptomatic leiomyomas. J Am Assoc Gynecol Laparosc 2000; 7: 125–9.
- Liu WM, Ng HT, Wu YC, Yen YK, Yuan CC. Laparoscopic bipolar coagulation of uterine vessels: a new method for treating symptomatic fibroids. Fertil Steril 2001; 75: 417–22.
- Liu WM. Laparoscopic bipolar coagulation of uterine vessels to treat symptomatic leiomyomas. J Am Assoc Gynecol Laparosc 2000; 7: 125–9.
- Hald K, Langebrekke A, Klow NE et al. Laparoscopic occlusion of uterine vessels for the treatment of symptomatic fibroids: initial experience and comparison to uterine artery embolization. Am J Obstet Gynecol 2004; 190: 37–43.
- 19. Hald K, Klow NE, Qvigstad E, Istre O. Laparoscopic occlusion compared with embolization of uterine vessels: a randomized controlled trial. Obstet Gynecol 2007; 109: 20–7.
- 20. Istre O, Hald K, Qvigstad E. Multiple myomas treated with a temporary, noninvasive, Doppler-directed, transvaginal uterine artery clamp. J Am Assoc Gynecol Laparosc 2004; 11: 273–6.
- Vilos GA, Hollett-Caines J, Burbank F. Uterine artery occlusion: what is the evidence? Clin Obstet Gynecol 2006; 49: 798–810.

Hysterectomy rate variations

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INTRODUCTION

Hysterectomy is the most common surgical intervention in gynecology.¹ The vast majority of hysterectomies are performed for benign indications. Specifically, in 90% of the cases, hysterectomy is indicated for benign disorders and addresses function symptoms such as pelvic pain (17%), bleeding (42%), or both (40.3%).²

One of the main issues of debate and controversy is the hysterectomy rate variations. In fact, the rates of hysterectomy vary considerably between countries, and even between regions within the same country. Surprisingly, the incidence of hysterectomy is essentially stable over time, showing a poor clinical impact of the various and new medical and surgical treatments. In addition, a great change in the different routes for performing hysterectomy has been observed during recent years by the diffusion of the laparoscopic approach.

Several opinion leaders have tried to give explanations for these figures, even if nothing is obvious and clear.

In this chapter, we describe the main contradictory data regarding hysterectomy rate variations and, then, the clinical and scientific experience for defining the 'right', if possible, hysterectomy rate.

HYSTERECTOMY RATE VARIATIONS IN DIFFERENT GEOGRAPHIC AREAS

The total incidence of hysterectomy varies considerably between geographic areas. In particular, it is possible to observe a significant change in hysterectomy rate not only between but also within countries.

To date, literature is widely available on epidemiologic findings regarding the hysterectomy rate variations between different countries, whereas no clear data are available on the differences in the rate of this surgical procedure between different regions of the same country.

Hysterectomy rate variations between countries

Each year about 600 000 hysterectomies are performed in the USA, representing the most common non-pregnancy-related surgical procedure performed.^{3,4} About 100 000 hysterectomies are performed yearly in the UK,⁵ 69 000 in Italy,⁶ 60 000 in France,⁷ 30 000 in Australia, 10 000 in Finland,⁸ and more than 5 000 in Denmark.⁹

In the developed countries, marked national differences in the prevalence rates were reported from a high of 5.4 per 1000 women in the USA ⁴ through intermediate rates such as 3.7/1000 in Italy ¹⁰ to a low of 1.2/1000 in Norway. ¹¹ On the other hand, in developing countries, the rate of hysterectomy is poorly documented but is likely to be much lower than that in the more economically developed parts of the world. ¹²

There is no reason to suppose that women in different countries suffer different rates of menstrual disturbance, such as menorrhagia (the presenting symptom in the majority of cases of hysterectomies), yet there are widely different hysterectomy rates across the world.¹³

Currently, it is not possible to give an ideal hysterectomy rate or to know what factors influence the different rates. Thus, doubts remain if women in countries with lower hysterectomy rates are undertreated, or if women in countries with higher rates are unnecessarily subjected to a major operation in the presence of equally, or more, effective alternative treatments. In fact, excluding the case of malignancies, hysterectomy is a surgical procedure performed to improve the woman's quality of life rather than to save her life.

Hysterectomy is indicated when it is considered that medical or conservative treatments have failed or are unlikely to succeed. In these cases, hysterectomy is effective not only in inducing a definitive resolution of the symptoms without possibility of recurrence but also in terms of satisfaction rates, ^{13,14} quality of life, ^{15,16} and sexual functioning. ¹⁸ Furthermore, hysterectomy is a major

operation in relation to surgical complications and longterm risks.

In this view, effective alternatives to hysterectomy have been continuously searched. In order to be considered as acceptable, these alternatives treatments must provide at least comparable quality of life and satisfaction rates, and they must be safe and cost-effective.

Hysterectomy rate variations within countries

Despite it being commonly accepted that in different regions of the same country it is possible to observe big hysterectomy rate variations, few data at have been published.

In the USA hysterectomy rates were found to differ by geographic regions, ¹⁹ with the lowest rate for women in the Northeast and the highest for women in the South. In fact, the average annual rates are 3.9 and 6.8 hysterectomies per 1000 women in the Northeast and South, respectively, whereas the average annual rates for women in the Midwest and West are 5.5 and 4.9 per 1000 women, respectively.

Differences in hysterectomy rate are also reported for small areas of Ontario.²⁰ The regions with hysterectomy rates higher than the mean tended to have small populations and to be located mainly in northern, south-western, and north-eastern Ontario, whereas those with rates significantly lower than the provincial mean rates were primarily located in southern Ontario. It was found²⁰ that regions with teaching hospitals had lower overall rates of hysterectomy than other regions, lower rates of the procedure for non-objective indications, and higher rates for cancer and leiomyoma. This phenomenon can be explained by the major diffusion of ideas and technology from teaching hospitals, which are presumably at the forefront of medical knowledge, in comparison with more remote areas. New technologies, such as same specific procedures for endometrial destruction, are not widely available except in teaching centers.

Thus, several variables influence the choice to perform hysterectomy, such as cultural background (surgical or medical), availability of services, and community characteristics, and it is very difficult to define the main factor influencing the hysterectomy rate between different regions.

HYSTERECTOMY RATE VARIATIONS OVER THE TIME

The origins of hysterectomy are lost in the mists of antiquity, as historians say 'we don't know when'. First, the Greek physician Soranus of Ephesus (98–138 BC) ²¹ dis-

cussed the problem of uterine prolapse and, while acknowledging that this does not usually require surgical treatment, he advised: 'If the whole uterus has become black, one must cut it off in its entirety'.

There are several references to vaginal excision of the uterus in the 16th and 17th centuries. The first vaginal hysterectomy for uterine prolapse was reported by the Italian Giacomo Berengario in 1571.²² However, the first successful vaginal hysterectomy was performed in 1813 by Conrad Langenbeck, who reported the case only after 4 years.²³

Later, in 1843, Charles Clay performed the first subtotal abdominal hysterectomy in a patient with a large fibroid uterus that was excised through a great incision, which he was unable to repair.²⁴

During the mid 1800s the mortality rates for both vaginal and abdominal hysterectomy were so high that few cases were attempted. In particular, the operative mortality for abdominal hysterectomy exceeded 70%. With the development of anesthesia, antisepsis, and surgical instruments, the figure had slowly improved by the latter part of the 19th century. In fact, by the 1920s there was a significant reduction of the operative mortality of both abdominal and vaginal hysterectomy (~2–3%), and further improvements occurred with the development of asepsis, antibiotics, blood transfusion, and the refinement of anesthesia and perioperative care.²⁵

The first reports describing personal series of hysterectomies were published by the 1930s, and the first safety and efficacy data were given. ^{26–36}.

From 1940, hysterectomy became a surgical procedure that was widely diffused in clinical practice. From 1940 to 1980, a significant increase in hysterectomy rate was observed.²⁵

A national report on hysterectomy surveillance¹⁹ in the USA during the period 1980–1993 covered an estimated 8588 000 women aged ≥15 years old who underwent a hysterectomy in a non-Federal short-stay hospital in which an annual average of 613 000 hysterectomies were performed.

During 1980–1987, the average annual rate of hyster-ectomy was 6.9 per 1000 women. In 1980, the hysterectomy rate was 7.1 per 1000 women; whereas in 1987 it decreased to 6.6 per 1000 women. From 1988 through 1993, the average annual rate remained curiously stable at 5.5 hysterectomies per 1000 women, and that trend was maintained until to the present. In fact, in 1988, about 5.7 per 1000 women in the USA had a hysterectomy, and 10 years later the rate was still the same, showing a poor influence of several time-related variables on that rate.

This variation over the time in hysterectomy rate also reflects the trend reported in Italy.³⁷ In fact, a similar stability in the rate of hysterectomies was observed from the 1990s.³⁷

These data are more surprising also in consideration of the new minimally invasive approaches (medical and surgical) for treating several gynecologic diseases that in the past would have required an hysterectomy. In particular, number of less-invasive but effective therapeutic options, alternatives to hysterectomy, were researched and then introduced in the clinical practice for the treatment of fibroids and dysfunctional uterine bleeding. These alternatives to hysterectomy are going to be more acceptable, if they prove to be at least comparable in efficacy, safety, cost-effectiveness, quality of life, and satisfaction rate to hysterectomy.

Recent data³⁸ have demonstrated that hysterectomy is significantly superior to an expanded medical treatment regimen for health-related quality of life measures. In addition, several new surgical or parasurgical procedures, such as laparoscopic cryomyolysis,^{39,40} laparoscopic uterine artery occlusion,⁴¹ MRI (magnetic resonance imaging) guided or ultrasound focused thermal ablation of uterine fibroids,^{42–45} and laparoscopic/percutaneous radiofrequency thermal ablation of uterine fibroids ^{46,47} are experimental and, to date, little more than feasibility data are available. Other alternative procedures, such as uterine artery fibroid embolization,^{48,49} have failed to replace hysterectomy, as demonstrated in robust clinical trials.

To date, the useful alternatives in clinical practice are

- hysteroscopic surgery (including hysteroscopic myomectomy or endometrial destruction techniques)⁵⁰
- the levonorgestrel intrauterine device.⁵¹

In this regard, some reports have suggested that the levonorgestrel intrauterine device, ³⁸ and endometrial resection and ablation ⁵² could and should be employed widely in clinical practice as alternative techniques to hysterectomy in women with menorrhagia. Endometrial ablation reduces menstrual blood flow, but its benefits relative to hysterectomy are reduced over time; ⁵² indeed, no large-scale and adequately powered studies have compared the other alternative techniques to hysterectomy. Finally, satisfaction, health-related quality of life and psychosocial well-being rates are similar between hysterectomy and the levonorgestrel intrauterine device, ³⁸ but the latter has the advantage of reduced cost. ⁵³

Perhaps the advent of these alternatives has not reduced hysterectomy rates, but merely increased treatment options and interventions for excessive menstrual blood loss. There are several possible explanations:

- the fast development of innovative techniques does not allow the production of wide scientific data regarding their feasibility, safety, and efficacy
- a deeper knowledge of predictive factors is necessary for an optimal selection of patients to be treated

and an adequate learning curve of surgeons is mandatory in order to apply these procedures in clinical practice.

On the other hand, in the last few years, we have assisted to an affirmation, in an evidence-based surgery view, of hysterectomy as gold standard procedure for the therapy of uterine fibroids and abnormal uterine bleeding.¹ Finally, the laparoscopic route for hysterectomy, thanks to its minimally invasive approach, is easily accepted by patients and clinicians, and it is widely proposed and used in clinical practice.

VARIATIONS IN ROUTES FOR HYSTERECTOMY

A change in the proportion of different types of hysterectomy over time has been observed.

Abdominal hysterectomy is the most frequent procedure reported, representing ~63% of all interventions. The frequency of abdominal hysterectomy decreased to its lowest level in 1994, but then plateaued.⁴

The vaginal approach to hysterectomy varied from 10 to 20% of all hysterectomies, and its primary indication is for uterovaginal prolapse.⁵ In a different series, the vaginal to abdominal hysterectomy ratio ranged from 1:3 to 1:4.^{54–56} However, these frequencies were dependent on the surgeon and the country. In this regard, experienced vaginal surgeons have reported frequencies >50%, reaching a rate of 60–90%.^{56–58}

Of interest, significant differences were observed for hysterectomies using the abdominal and vaginal routes between and within countries. In particular, the abdominal route predominates in the USA and the UK, whereas the vaginal route is commoner in Europe.⁵⁹

Geographical variation in the use of abdominal and vaginal approaches is also observed in different regions of the same country. ^{60,61} In particular, in the UK, regional variations in the utilization rate of vaginal and abdominal hysterectomies were reported at different times. ^{60,61} There is a greater propensity to use the vaginal route in older women, particularly in Northern Ireland, and to a lesser extent in young women, especially in Yorkshire and the NW Thames area. ^{60,61} The interpretation of these data is very difficult. However, the choice of surgical route for hysterectomy is based upon physician practice style and is variably related to physician preoperative assessment, and, certainly, physicians from the same regions have similar clinical views, arising from the same regional meetings and postgraduate teaching.

In 1989, Reich et al.⁶² first described the laparoscopic approach to hysterectomy. During the 1990s, the rate of

laparoscopic hysterectomy increased more than exponentially. In particular, there was a 30-fold increase in the frequency of laparoscopic hysterectomy from 1990 to 1997, representing about 10% of all procedures in 1997.²

The percentage of laparoscopic hysterectomies varies widely according to surgeon or institute, region or country, and most importantly according to pathology and individual patients. In particular, the higher variations seem to be demonstrated even for uterine fibromatosis and/or abnormal uterine bleeding.⁶³

The introduction of laparoscopic hysterectomy has played an important role in reducing the incidence of abdominal hysterectomies. Moreover, isolated experiences seem to demonstrate that the introduction of the laparoscopic approach has paradoxically increased the use of the vaginal route. Gynecologists who had previously been only familiar with vaginal hysterectomy for prolapse began to realize that the vaginal step of laparoscopic-assisted vaginal hysterectomy was easer, safer, and quicker than using a laparoscope. Thus, many gynecologists have found that they were able to perform a high percentage of vaginal hysterectomy. Section 25

Another important point of debate, poorly addressed in almost all studies comparing surgical techniques, is the pivotal role of the practice style and personal preference of the surgeon in determining the choice for hysterectomy route. In fact, the large variations in practice indicate that the surgical route is more dependent on the clinical preference of the gynecologist than on medical conditions. ⁶⁴ Thus, a consensus on using optimal surgical techniques and on ensuring adequate surgical training for all gynecologists is needed.

VARIATION IN TOTAL/SUBTOTAL HYSTERECTOMY RATE

For centuries there has been an ongoing debate as to whether subtotal hysterectomy confers benefits over total hysterectomy. In the latter part of the 20th century there was a re-emergence of subtotal hysterectomy. ^{65,66} Specifically, it tripled from 1990 to 1997 in the USA population. ⁴ Despite this increase, the total rate of subtotal hysterectomy represented only 2% of all procedures. ⁴

Few data have suggested that subtotal hysterectomy offers any real advantages over total hysterectomy. In particular, it was shown that cervix preservation enhances the female sexual function and protects the integrity of the pelvic floor. 65,66 To the contrary, evidence from randomized studies demonstrated significant disadvantages of subtotal hysterectomy, such as continued vaginal bleeding, cervical mucus discharge, cervical hypertrophy, and prolapse (and potential risk of cervical cancer). 67 However, long-term results are awaited.

STRATEGY FOR TAILORING THE RIGHT INDICATION TO HYSTERECTOMY

Few data are available comparing different approaches and driving the best choice between several surgical and non-surgical options for menorrhagia. In our opinion, there is little clinical utility in comparing the efficacy of different techniques in a general population. On the contrary, data evaluating eventual predictors for treatment response could be applicable in a clinical setting in order to tailor the right indication to hysterectomy or other treatments. In particular, we performed a recent retrospective study that aimed to evaluate potential predictors of success for various approaches in the treatment of menorrhagia. 68

Demographic, anthropometric, ultrasonographic, and biochemical data of patients who had surgical or nonsurgical interventions for menorrhagia using the database of an academic department were recorded and analyzed according to the received interventions. Using the general linear model, which provides regression analysis and analysis of variance for one dependent variable by one or more factors and/or variables, the authors demonstrated that chronological age, 3-day follicle-stimulating hormone (FSH), levels and preantral count are strong predictors for efficacy in minimally invasive procedure. Specifically, advanced age and high 3-day FSH levels are associated with a better success rate of endometrial destruction. These data suggest that, in these patients, options to hysterectomy should always be considered. On the other hand, in younger patients with menometrorrhagia, we always prescribe, in the absence of intrauterine pathology, a levonorgestrel intrauterine device as the first step of treatment.

These findings are routinely applied in our experience in order to reduce the hysterectomy rate for menorrhagia and the hospital surgical waiting list, giving a high priority to the treatment of neoplastic diseases. In this regard, the hysterectomy rate for benign conditions in our department is very low and significantly lower when compared with the average hysterectomy rate in Italy.

In addition, a significant trend in hysterectomy rate reduction was recorded in our department throughout the last 7 years (Figure 35.1). In particular, the maximum reduction was observed in the last 3 years. At the same time, an increase of alternative techniques was recorded in our population. In fact, in about 85% of cases, women with menorrhagia having high 3-day FSH levels were successfully treated endometrial destruction, whereas younger women with menometrorrhagia, in the absence of intrauterine pathology, were successfully treated with the levonorgestrel intrauterine device. On the other hand, we consider hysterectomy only in selected cases of women with multiple submucosal fibroids, for patients in whom

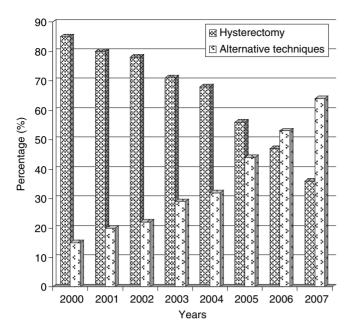


Figure 35.1 Rates of hysterectomy and alternative techniques (levonorgestrel intrauterine system alone and/or endometrial destruction techniques) performed for menorrhagia during the last 7 years in the Department of Obstetrics and Gynecology of the University 'Magna Graecia' of Catanzaro.

the levonorgestrel intrauterine device and/or endometrial ablation has already failed, in the case of supposed adenomyosis, and when patients specifically request hysterectomy, mainly because they have already been unsuccessfully treated by other options for a long time.

The efficacy of this strategy is further confirmed by the low and stable rate of patients who refer to our department – i.e. outpatient and emergency services – for abnormal uterine bleedings or complications related to the treatments.

CONCLUSIONS

In conclusion, the aim of gynecologists should be – more than the absolute reduction of hysterectomies – to avoid the uncorrected over- or underuse of hysterectomies for benign female diseases.

From this point of view, it is also very important that the evidence-based results can rapidly spread from the clinical setting close to academic centers to more peripheral health services.

Our clinical experience demonstrates that the 'right' hysterectomy rate is really lower than those observed in several countries, and that it is feasible to reduce it without worsening the patient's quality of life using, appropriately and timely, the new minimally invasive approaches, such as the levonorgesterel intrauterine system and endometrial destruction techniques, without patients tiring of unsuccessful medical attempts.

Thus, it is not important to decide which is the best approach but to employ appropriately and timely the different evidence-based effective treatments. In this regard, more scientific consensus for the right indications to the different therapeutic options should be obtained in the near future but also for evaluating predictive factors in order to select more responsive subpopulations.

References

- Lefebvre G, Allaire C, Jeffrey J et al. Clinical Practice Gynaecology Committee and Executive Committee and Council, Society of Obstetricians and Gynaecologists of Canada. SOGC clinical guidelines. Hysterectomy. J Obstet Gynaecol Can 2002; 24: 37–61.
- Clark TJ, Daniels J, Khan KS et al. Hysterectomy with bilateral salpingo-oophorectomy: a survey of gynecological practice. Acta Obstet Gynecol Scand 2001; 80: 62–4.
- Wilcox LS, Koonin LM, Pokras R et al. Hysterectomy in the United States, 1988–1990. Obstet Gynecol 1994; 83: 549–55.
- Farquhar CM, Steiner CA Hysterectomy rates in the United States 1990–1997. Obstet Gynecol 2002; 99: 229–34.
- Maresh MJ, Metcalfe MA, McPherson K et al. The VALUE national hysterectomy study: description of the patients and their surgery. BJOG 2002; 109: 302–12.
- Condizioni di salute, fattori di rischio e rischio ai servize sanitari. Istituto Nazionale di Statistica. Dati 1998.
- Cosson M, Lambaudie E, Boukerrou M et al. Vaginal, laparoscopic, or abdominal hysterectomies for benign disorders: imme-

- diate and early postoperative complications. Eur J Obstet Gynecol Reprod Biol 2001; 98: 231–6.
- 8. Makinen J, Johansson J, Tomas C et al. Morbidity of 10110 hysterectomies by type of approach. Hum Reprod 2001; 16: 1473–8.
- Moller C, Kehlet H, Utzon J et al. Hysterectomy in Denmark. An analysis of postoperative hospitalisation, morbidity and readmission. Dan Med Bull 2002; 49: 353–7.
- Materia E, Rossi L, Spadea T et al. Hysterectomy and socioeconomic position in Rome, Italy. J Epidemiol Community Health 2002; 56: 461–5.
- 11. McPherson K, Wennberg JE, Hovind OB et al. Small-area variations in the use of common surgical procedures: an international comparison of New England, England, and Norway. N Engl J Med 1982; 307: 1310–14.
- Garry R. Health economics of hysterectomy. Best Pract Res Clin Obstet Gynaecol 2005; 19: 451–65.
- Vessey MP, Villard-Mackintosh L, McPherson K et al. The epidemiology of hysterectomy: findings in a large cohort study. Br J Obstet Gynaecol 1992; 99: 402–7.

- Dwyer N, Hutton J, Stirrat GM. Randomised controlled trial comparing endometrial resection with abdominal hysterectomy for the surgical treatment of menorrhagia. Br J Obstet Gynaecol 1993; 100: 237–43.
- Weber AM, Walters MD, Schover LR et al. Functional outcomes and satisfaction after abdominal hysterectomy. Am J Obstet Gynecol 1999; 181: 530–5.
- Thakar R, Ayers S, Georgakapolou A et al. Hysterectomy improves quality of life and decreases psychiatric symptoms: a prospective and randomised comparison of total versus subtotal hysterectomy. BJOG 2004; 111: 1115–20.
- Rannestad T, Eikeland OJ, Helland H et al. The quality of life in women suffering from gynecological disorders is improved by means of hysterectomy. Absolute and relative differences between pre- and postoperative measures. Acta Obstet Gynecol Scand 2001; 80: 46–51.
- Rhodes JC, Kjerulff KH, Langenberg PW et al. Hysterectomy and sexual functioning. JAMA 1999; 282: 1934–41.
- Lepine LA, Hillis SD, Marchbanks PA et al. Hysterectomy surveillance United States, 1980–1993. MMWR CDC Surveill Summ 1997; 46: 1–15.
- Hall RE, Cohen MMVariations in hysterectomy rates in Ontario: does the indication matter?. CMAJ 1994; 151: 1713–19.
- Soranus' Gynecology. Traslated by Owsei Temkin. Baltimore: Johns Hopkins University Press, 1956: 13–207
- 22. Garrison FH. An Introduction to the History of Medicine, 4th edn. Philadelphia: WB Saunders 1929: 226–508
- Langeneck CJM. Geschichte einer von mir glucklich verichteten extirpation der ganger gebärmutter. Biblioth Chir Ophth Hanover 1817:I:557
- Bellinger J. Operations for the removal of abdominal tumors.
 J South Med Pharm 1847; 2: 241.
- Baskett TF. Hysterectomy: evolution and trends. Best Pract Res Clin Obstet Gynaecol 2005; 19: 295–305.
- Baskett TF. On the Shoulders of Giants: Eponyms and Names in Obstetrics and Gynaecology. London: RCOG Press, 1996
- Mathieu A. The history of hysterectomy. West J Surg Obstet Gynecol 1934; 42: 1–13.
- 28. Sutton C. Hysterectomy: a historical perspective. Clin Obstet Gynaecol 1997; 11: 1–22.
- Willughby P. In: Blenkinsop H ed. Observations in Midwifery.
 Warwick: Shakespeare Printing Press, 1863
- Benrubi GI. History of hysterectomy. J Fla Med Soc 1988; 75: 533–8.
- 31. Ricci JV. The Development of Gynaecological Surgery and Instruments. Philadelphia: Blakiston, 1949: 375, 386, 389–391, 487, 502–507
- Blundell J. Two cases in which extirpation of the uterus was performed. Lond Med Gaz 1828;2: 733.
- Editorial: extirpation of the uterus. Lond Med Chir Rev 1825;
 264–7
- 34. McDowell E. Three cases of extirpation of diseased ovaria. Eclectic Repertory Anal Rev Philadelphia 1817; 7: 242–244.
- Shaw WF. Charles Clay: the father of ovariotomy in England.
 J Obstet Gynaecol Br Emp 1951; 58: 930–40.
- 36. Clay C. Observations on ovariotomy, statistical and practical. Also, a successful case of entire removal of the uterus, and its appendages. Trans Obstet Soc Lond 1863; 5: 58–74.
- Parazzini F, La Vecchia C, Negri E et al. Determinants of estrogen replacement therapy use in northern Italy. Rev Epidemiol Sante Publique 1993; 41: 53–8.

- Marjoribanks J, Lethaby A, Farquhar C. Surgery versus medical therapy for heavy menstrual bleeding. Cochrane Database Syst Rev 2006; 2: CD003855
- Zupi E, Piredda A, Marconi D et al. Directed laparoscopic cryomyolysis: a possible alternative to myomectomy and/or hysterectomy for symptomatic leiomyomas. Am J Obstet Gynecol 2004; 190: 639–43.
- Zupi E, Marconi D, Sbracia M et al. Directed laparoscopic cryomyolysis for symptomatic leiomyomata: one-year follow up. J Minim Invasive Gynecol 2005; 12: 343–6.
- 41. Volkers NA, Hehenkamp WJ, Birnie E et al. Uterine artery embolization versus hysterectomy in the treatment of symptomatic uterine fibroids: 2 years' outcome from the randomized EMMY trial. Am J Obstet Gynecol 2007; 196: 519, e1–11
- 42. Stewart EA, Gedroyc WM, Tempany CM et al. Focused ultrasound treatment of uterine fibroid tumors: safety and feasibility of a noninvasive thermoablative technique. Am J Obstet Gynecol 2003; 189: 48–54.
- 43. Tempany CM, Stewart EA, McDannold N et al. MR imaging-guided focused ultrasound surgery of uterine leiomyomas: a feasibility study. Radiology 2003; 226: 897–905.
- 44. McDannold N, Tempany CM, Fennessy FM et al. Uterine leiomyomas: MR imaging-based thermometry and thermal dosimetry during focused ultrasound thermal ablation. Radiology 2006; 240: 263–72.
- Chapman A, Ter Haar G. Thermal ablation of uterine fibroids using MR-guided focused ultrasound – a truly non-invasive treatment modality. Eur Radiol 2007; May 1 [Epub ahead of print].
- Bergamini V, Ghezzi F, Cromi A et al. Laparoscopic radiofrequency thermal ablation: a new approach to symptomatic uterine myomas. Am J Obstet Gynecol 2005; 192: 768–73.
- 47. Ghezzi F, Cromi A, Bergamini V et al. Midterm outcome of radiofrequency thermal ablation for symptomatic uterine myomas. Surg Endosc 2007; May 19 [Epub ahead of print].
- 48. Manyonda I, Sinthamoney E, Belli AM. Controversies and challenges in the modern management of uterine fibroids. BJOG 2004; 111: 95–102.
- Edwards RD, Moss JG, Lumsden MA et al. Committee of the Randomized Trial of Embolization versus Surgical Treatment for Fibroids. Uterine-artery embolization versus surgery for symptomatic uterine fibroids. N Engl J Med 2007; 356: 360–70.
- 50. Garry R. Hysteroscopic alternatives to hysterectomy. Br J Obstet Gynaecol 1990; 97: 199–202.
- 51. Barrington JW, Bowen-Simpkins P. The levonorgestrel intrauterine system in the management of menorrhagia. Br J Obstet Gynaecol 1997; 104: 614–16.
- Lethaby A, Shepperd S, Cooke I et al. Endometrial resection and ablation versus hysterectomy for heavy menstrual bleeding. Cochrane Database Syst Rev 2000; 2: CD000329.
- 53. Lethaby AE, Cooke I, Rees M. Progesterone or progestogen-releasing intrauterine systems for heavy menstrual bleeding. Cochrane Database Syst Rev 2005; 4: CD002126.
- Bezdek J, Grigarova H, Kleisl R. Vaginal hysterectomy technique and results in the last 19 years. Sb Ved Pr Lek Fak Karlovy Univerzity Hradci Kralove 1985; 28: 31–7.
- 55. Kovac SR. Decision-directed hysterectomy: a possible approach to improve medical and economic outcomes. Int J Gynaecol Obstet 2000; 71: 159–69.
- Querleu D, Cosson N, Parmentier D et al. The impact of laparoscopic surgery on vaginal hysterectomy. Gynecol Endosc 1993; 2: 89–91.

- 57. Brown DA, Frazer MI. Hysterectomy revisited. Aust NZ J Obstet Gynecol 1991; 31: 148.
- Cosson M, Querleu D, Subtil D et al. The feasibility of vaginal hysterectomy. Eur J Obstet Gynecol Reprod Biol 1996; 64: 95–9.
- Straus IK. In: You Don't Need a Hysterectomy. Reading, MA: Addison Wesley, 1993
- Bottle A, Aylin P. Variations in vaginal and abdominal hysterectomy by region and trust in England. BJOG 2005; 112: 326–8.
- 61. Mulholland C, Harding N, Bradley S et al. Regional variations in the utilization rate of vaginal and abdominal hysterectomies in the United Kingdom. J Public Health Med 1996; 18: 400–5.
- 62. Reich H, De Cripo J, McGlynn F. Laparoscopic hysterectomy. J Gynecol Surg 1989; 5: 213–15.
- Claerhout F, Deprest J. Laparoscopic hysterectomy for benign diseases. Best Pract Res Clin Obstet Gynaecol 2005; 19: 357–75.

- Dorsey JH, Steinberg EP, Holtz PM. Clinical indications for hysterectomy route: patient characteristics or physician preference? Am J Obstet Gynecol 1995; 173: 1452–60
- Kilkku P. Supravaginal uterine amputation versus hysterectomy with reference to subjective bladder symptoms and incontinence. Acta Obstet Gynecol Scand 1985; 64: 375–9.
- Kilkku P, Gronroos M, Hirvonen T et al. Supravaginal uterine amputation vs. hysterectomy. Effects on libido and orgasm. Acta Obstet Gynecol Scand 1983; 62: 147–52.
- Gimbel H. Total or subtotal hysterectomy for benign uterine diseases? A meta-analysis. Acta Obstet Gynecol Scand 2007; 86: 133–44
- Palomba S, Zullo F. Can ovarian age drive the choice of different strategies for treating menorrhagia? A 3-year retrospective review. J Minim Inv Gyn 2007, in press

Total abdominal hysterectomy

Isaac T Manyonda and Essam Hadoura

INTRODUCTION

Hysterectomy is the most frequently performed major gynecologic operation in both the USA and the UK. It remains the only definitive cure for dysfunctional uterine bleeding and, compared to the myriad of alternative treatments now available, hysterectomy rates highest in satisfaction scores. Recent research has shown that it improves quality of life, an important consideration, since the vast majority of these procedures are performed for benign disease rather than to save lives. The vast majority of hysterectomies are performed by the abdominal route, despite strong research evidence showing that the vaginal route is superior in many respects, including recovery rates and complications. The laparoscopic approach is confined to centers with the requisite expertise, and the place of this approach remains to be fully evaluated. Uterine fibroids are the most common indication for hysterectomy. The longstanding debate on total vs subtotal hysterectomy has been resolved by recent large trials showing no major advantage for one operation over the other. Overall mortality rates are 0.5-2 per 1000, and rates of visceral damage are 0.5-2%. Complications are most common in women treated for uterine fibroids, and overall rates of complications decrease with increasing age of the woman. Although trends show that hysterectomy rates may be falling, such a fall as a result of conservative alternatives (endometrial ablative techniques, the Mirena IUS, and uterine artery embolization for fibroids) has not been as dramatic as might have been anticipated, and therefore abdominal hysterectomy is likely to remain the pre-eminent gynecologic operation for the foreseeable future. Hysterectomy rates vary widely between regions, and within the same geographical area, and the reasons for this are yet to be adequately researched.

PREVALENCE OF ABDOMINAL HYSTERECTOMY

Hysterectomy is the commonest major gynecologic operation in the UK, where it is estimated that over 100 000 are

performed annually,1 as well as in the USA, where the corresponding figure is 600 000.2 However, there are widely and wildly differing hysterectomy rates across the world.3 This is so even if one considers developed countries with comparable resources. Thus, in Denmark, a woman's lifetime risk of hysterectomy is estimated at a low 10.4%, 4, whereas in the USA, it is more than double, at 25%,5 Differences in hysterectomy rates are to be found even between regions within the same country,6 and between gynecologists within the same hospital. The factors influencing these differing rates are unknown, a problem compounded by the fact that the ideal hysterectomy rate is unknown. It is highly unlikely that women in different countries suffer different rates of menstrual disturbance such as menorrhagia (the presenting symptom in the majority of women who undergo hysterectomy) to explain the differing rates. Thus, it remains an enigma whether women in countries with high rates are being overtreated, or those in countries with lower rates are being denied treatment with a highly effective intervention - hysterectomy: the only definitive cure for dysfunctional uterine bleeding which has the highest satisfaction scores compared to any other alternative.

All large-scale surveys of hysterectomy practice show that 70–80% of hysterectomies are performed by the abdominal route, 2 except when there is uterovaginal prolapse, when the vaginal route is utilized. This is despite extensive data showing that the perioperative morbidity with the vaginal route is less and, in addition, associated with a shorter hospital stay and earlier return to work. 8 In recent years, effective alternatives to hysterectomy have emerged, and these include both medical and surgical options. However, a dramatic reduction in hysterectomy rates has yet to materialize, perhaps bearing testimony to the efficacy of hysterectomy and/or the fact that habits die hard among gynecologists.

INDICATIONS FOR ABDOMINAL HYSTERECTOMY

By far the vast majority of hysterectomies are performed for benign disease rather than malignancy: therefore, most hysterectomies are performed to improve quality of life rather than to save lives, and this should be borne in mind when offering this treatment to women. Thus, the majority of hysterectomies are performed for symptomatic fibroids, disorders of menstruation especially menorrhagia, pelvic pain, adenomyosis, and genital prolapse with or without stress incontinence (Figure 36.1). Fibroids remain the most frequent indication, surpassing all the other indications combined. The contribution of gynecologic malignancies as an indication is minuscule, and beyond the scope of this chapter.

Fibroids

Fibroids are the most common tumors in women of reproductive years, indeed in all women. Approximately 50% are asymptomatic. The most common symptom is abnormal uterine bleeding. In published series of myomectomies, 30% of women suffered from menorrhagia. The mechanism of fibroid-associated menorrhagia is unknown. Vascular defects, submucous tumors, and impaired endometrial hemostasis have been offered as possible explanations. Pelvic pain is rare with fibroids and it usually signifies degeneration, torsion, or, possibly, associated adenomyosis. Pelvic pressure, bowel dysfunction, and bladder symptoms such as urinary frequency and urgency may be present. Urinary symptoms should be investigated prior to surgical management of fibroids to exclude other possible causes. In the postmenopausal woman presenting with pain and fibroids, leiomyosarcoma should be considered.9 In women who do not wish to preserve fertility and who have been counseled regarding the alternatives and risks, hysterectomy may be offered as the definitive treatment for symptomatic uterine

fibroids and is associated with a high level of satisfaction.⁹ However, it should always be borne in mind that, apart from conventional myomectomy, there are now a variety of effective alternative treatments for fibroids, including uterine artery embolization,^{10,11} MRI (magnetic resonance imaging) guided focused ultrasound ablation,^{12,13} and promising reports on medical treatments are also now in the literature.¹⁴

Abnormal uterine bleeding

While abnormal uterine bleeding – either menorrhagia, persistent irregular, or intermenstrual bleeding - is a common indication for hysterectomy, it will be assumed here that appropriate investigations will have been undertaken, and non-surgical treatments tried prior to embarking on a hysterectomy. There are now numerous guidelines on the management of abnormal bleeding published by the Royal College of Obstetricians and Gynaecologists (RCOG) and/or the National Institute for Clinical Excellence (NICE), and hysterectomy is almost the last resort where more conservative measures have failed. 16 However, there is a need to strike the right balance: a 42-yearold woman whose family is complete, whose life is ruined by severe menorrhagia, who has tried one or two options without success, and now requests hysterectomy based on informed choice should not be denied early recourse to this very effective treatment.

Pelvic pain

Pelvic pain as an indication for hysterectomy warrants special consideration. The patient with chronic pelvic pain requires a thorough work-up to determine if there is

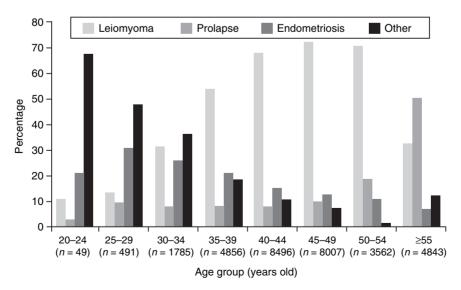


Figure 36.1 Relative proportions of hysterectomy by indication for each age group, 1994–2003. (Reproduced from Jacobson et al, 15 with permission.)

organic pathology amenable to other forms of therapy. Chronic pelvic inflammatory disease, for example, may respond to high doses of rotating antibiotics with or without laparoscopic adhesiolysis, and endometriosis may respond to surgical and/or medical treatment. For women who do not desire fertility and for whom hormonal or conservative surgery has failed, hysterectomy is usually the definitive treatment. However, careful counseling is mandatory in women with chronic pelvic pain, as sometimes hysterectomy does not effect the desired cure and pain persists. Gynecologists should take heart from a study of 228 women from New Zealand, which found that of 98 women in whom pain was the sole or most predominant reason for the hysterectomy, 87% were still satisfied with the operation at 1-year postoperatively.¹⁷

Indication for hysterectomy by route

While the above has dealt with indications for hysterectomy in general terms, rather than specifically for 'total abdominal hysterectomy', there are those who would argue that every hysterectomy should be considered for the vaginal approach unless there is a contraindication to this route. The vast majority of hysterectomies are performed via the abdominal route, and it is more likely that there may be a contraindication to the vaginal or laparoscopic route than to the abdominal route – if a hysterectomy is deemed possible, then it can always be performed via the abdominal route.

PREOPERATIVE PREPARATION FOR ABDOMINAL HYSTERECTOMY

Psychological preparation

In contemporary medical practice in the Western world, patients increasingly question treatments they are offered, and this is especially so in gynecologic practice. Women will often research their disease and the treatment options extensively, and present to the gynecologist with extensive printouts from the internet. What is clearly of fundamental importance is that women are allowed time and space to have their queries and concerns about hysterectomy fully answered, additional information in the form of leaflets supplied, and be allowed time to consider the treatment option offered. For many women the decision to go ahead with a hysterectomy is a momentous one, and the need to explain and reassure cannot be overstated. Fortunately, in most situations, hysterectomy is offered after failure of more conservative measures, or where the indication is obvious (e.g. a >40-year-old woman with massive fibroids, a complete family, and intractable menorrhagia), and in some situations the woman herself may well have decided that a hysterectomy is the appropriate treatment to improve her quality of life. The bottom line is that the woman must be furnished with all the information that enables her to make informed choices, especially in situations where the indication for the hysterectomy is benign pathology, which is the vast majority of instances. The indications for surgery must be explained clearly in language the patient can understand. The risks, benefits, and side effects must be reviewed. It is necessary to discuss all the ancillary points that patients will bring up, including details about the operation, hospital stay, and postoperative recovery period, and whether or not normal ovaries should be conserved, and if not, whether hormone replacement therapy will be appropriate and the implications of such treatment. Such preoperative assessment and careful counseling will help to identify cultural, religious, and personal beliefs, and other factors that may cause depression or other difficulties in posthysterectomy adjustment. One of the factors that affects a woman's experience with hysterectomy is the relationship and support from her friends, relatives, and especially her partner. There is ample evidence for the need to ensure that both the woman and her partner have accurate information, and research has highlighted misconceptions about hysterectomy;19,20 US research has shown that African-American men, in particular, hold more negative perceptions about hysterectomy than their white counterparts.²¹ Equipped with appropriate information and support, the woman should be allowed to participate in decision making about her treatment, and it has been shown that where women have been thus empowered, satisfaction rates with the treatment modality given are highest.²²

The ovaries – to remove or conserve the ovaries at abdominal hysterectomy

Given just how long gynacologists have been performing hysterectomies, it is quite surprising that the issue of when (age), and if, and whether both, ovaries should be removed or conserved at the time of hysterectomy remains unresolved.^{23–28} Yet many women are anxious about this, and do ask for the best advice. A recent study reported that 35% of women undergoing abdominal hysterectomy and unilateral oophorectomy had impaired function in the remaining ovary.²³ Other research has suggested that hysterectomy itself accelerates the decline in ovarian function, detectable even within as early as 6 months of the hysterectomy.²⁸ Ovarian cancer is very common and, in a woman with no obvious risk factors, routine oophorectomy at the time of hysterectomy and based on age alone may not be justified. In the younger woman having oophorectomy, hormone replacement therapy has to be considered.

Prophylactic antibiotics

Evidence for the benefits of prophylactic antibiotics in reducing the incidence and severity of postoperative infection during abdominal hysterectomy has come from many randomized, prospective double-blind studies. Such evidence is so overwhelming that routine use of prophylactic antibiotics should be considered good and standard practice. For the sake of clarity and completeness, two studies will be cited here. Eason et al. demonstrated that prophylactic antibiotic use was associated with decreases in abdominal wound infection (odds ratio [OR] = 0.45; 95% confidence interval [CI] 0.30-0.66) and pelvic infection (OR = 0.49; 95% CI 0.26-0.92), and concluded that prophylactic antibiotics should be recommended for all women undergoing total obdominal hysterectomy (TAH), including women considered at low risk of infection.²⁹ A prospective Spanish study by Rodriguez et al. on 878 patients who underwent total abdominal hysterectomy found that only 2.3% of patients who received antibiotic prophylaxis suffered infection, despite having more risk factors, compared with a 10.1% infection rate in those who did not receive antibiotics.³⁰

A variety of antibiotics have been used in different studies, and the exact choice does not appear to be that important: the choice should perhaps be guided by a combination of cost, simplicity of application, and surgeon preference. A combination of a cephalosporin and metronidazole would tend to cover the full range of potential pathogens. A single dose given perioperatively appears to be just as efficacious as giving antibiotics for 24–48 hours. Women known to have bacterial vaginosis require special attention, as they appear to be at added risk: in a study which compared preoperative treatment vs no treatment, there was an incidence of 27% vaginal cuff infection in the untreated group compared to 0% in the treated group.³¹

Bowel preparation

Traditionally, it has been standard practice to carry out bowel preparation prior to abdominal hysterectomy, especially where bowel injury is anticipated (previous extensive surgery, known adhesions, extensive endometriosis). However, recent studies have demonstrated that bowel preparation is not necessary to avoid colostomy in the event of intentional or incidental bowel entry. In a randomized prospective study, Ram et al. evaluated 329 patients who underwent colorectal surgery for cancer (81.5%) or benign disease (18.5%) and documented no statistically significant difference between the number of postoperative wound infections, dehiscence, or other complications between patients who did or did not have preoperative bowel preparation. However, they noted

that bowel preparation may be beneficial in patients who require a very low rectal anastomosis or when palpation of a colonic mass is required for resection.³²

Thromboprophylaxis

As with antibiotics, the benefits of thromboprophylaxis are proven, and failure to administer thromboprophylaxis should really be considered substandard practice. This should combine the mechanical effects of fitted thromboembolic disease (TED) stockings, applying pneumatic calf compression during (and occasionally as well as after) the operation, and the administration of low-molecular-weight heparin, usually Fragmin (dalteparin sodium) at a dose of 2500 U 2 hours preoperatively and continued every 12 hours until the patient has established full mobility at 4–5 days postoperatively. The expense of low-molecular-weight heparin means that in some settings fractionated heparin may have to be used, but the efficacy is similar.

Anemia preoperatively

Preoperative transfusion with packed red cells is seldom necessary and should be reserved for those patients with severe anemia associated with symptoms of hypovolemia. The administration of gonadotropin-releasing hormone (GnRH) agonist 2–3 months prior to hysterectomy for non-myomatous uteri has not been shown to reduce operative blood loss,³³ but in women with intractable menorrhagia the eradication of menses would allow the woman to build up her hemoglobin level prior to surgery, and thereby avoid the hazards of blood transfusion, and render the surgery that much safer.

TECHNIQUES OF ABDOMINAL HYSTERECTOMY

The intrafascial technique, originally described in 1929 by EH Richardson,³⁴ is the preferred method in the USA, while in the UK, the extrafascial technique of hysterectomy is more commonly used. There are few studies that have compared the two techniques of abdominal hysterectomy. Reyna Hinojosa et al. compared 150 hysterectomies performed with the extrafascial technique to 150 performed with intrafascial technique. The overall morbidity rate was 38% for the extrafascial technique and 32% for intrafascial technique.³⁵

Examination under anesthesia and bladder catheterization

With the patient placed in the dorsal lithotomy position, a pelvic examination is performed. The value and importance of this examination cannot be overstated. Adequate examination in the clinic is often difficult when the patient is alert and tense, and this examination enables the surgeon to assess pelvic pathology and mobility of pelvic organs, and therefore may influence the choice of incision — where there is limited mobility of the uterus and/or suspected adhesions, a midline vertical incision may be the wiser choice, but even with large (20-week size) myomas a transverse incision would be appropriate if the uterine mass were freely mobile. This is also an opportunity to teach a medical student the art of pelvic examination, since in current practice it is often difficult to do so on ward rounds or in the clinic. Patient consent to such an examination must be obtained and documented in the notes during the preoperative ward round.

Following the examination, the vagina and urethral meatus are cleaned with appropriate antiseptic, and a Foley catheter on free drainage is inserted into the bladder. The authors prefer to ensure that the bladder is completely empty by using an 'in-and-out catheter' first, followed by instillation of an antiseptic gel (Instillagel) into the bladder prior to insertion of the Foley catheter: this may further minimize the risk of urinary tract infection.

Skin preparation and draping

Preparation of the skin before surgery includes removing soil and bacteria from the skin, and it would seem teleologically sound to suppose that such practice would contribute towards a reduction in the risk of wound infection. In a meta-analysis, Edwards et al. reported that the incidence of wound infections can be decreased by reducing the number of common skin flora such as staphylococci, diphtheroid organisms, and Pseudomonas. The methods for accomplishing this task include patient showering before surgery, preoperative cleansing, and hair removal.³⁶ However, a meta-analysis by Tanner et al. found no difference in surgical site infection among patients who had hair removed prior to surgery and those who had not. If it is necessary to remove hair, both clipping and depilatory creams result in fewer surgical site infections than shaving using a razor.³⁷ It would appear that there is no difference in surgical site infection when patients are shaved or clipped 1 day before surgery or on the day of surgery.³⁷

Recent Cochrane meta-analysis of six randomized controlled trials evaluating preoperative antiseptics found significant heterogeneity in the comparisons and the results could not be pooled.³⁸ Only one study by Berry et al.³⁹ compared povidone-iodine (PI) 10% in alcohol vs chlorhexidine 0.5% in 371 people undergoing clean surgery: 28/176 (15.9%) people cleaned with PI developed an infection compared with 8/195 (4.1%) of people

cleaned with chlorhexidine, the difference being statistically significant.³⁹ There was no evidence of a benefit in four trials associated with the use of iodophor-impregnated drapes. Edwards et al., concluded that there is insufficient research examining the effects of preoperative skin antiseptics to allow conclusions to be drawn regarding their effects on postoperative surgical wound infections.³⁸

Skin incision and entry

For benign disease, the transverse suprapubic incision is the preferred incision for esthetic reasons, as well as the fact that it provides adequate access while minimizing the risk of wound dehiscence. For malignant disease, midline vertical incisions are preferred as they facilitate adequate staging of the tumor. Where extensive adhesions are anticipated, especially following previous myomectomy, it would be prudent to adopt the vertical midline incision also, initially subumbilical, but to be extended cephalad around and above the umbilicus should this be required. Bowel is often adherent to the uterus, especially where incisions were made on the posterior aspect of the uterus during the myomectomy, and a midline vertical incision affords better access than a transverse suprapubic one.

Following entry into the abdomen, the abdominal viscera are thoroughly examined, including the liver, gall-bladder, stomach, kidneys, and aortic lymph nodes.

The intrafascial hysterectomy

The following is a description of the intrafascial hysterectomy which, in a nutshell, is performed by entering the fascial planes between the bladder and uterus/vagina (i.e. the vesico-uterine space) and the rectum and uterus/vagina (i.e. the recto-uterine space) as follows. The basic steps are described, but in reality the precise sequence will vary from surgeon to surgeon, and indeed there are also variations even on some of the basic steps:

- (1) To provide traction to the uterus, a 0 Vicryl (polyglactin 910) suture is placed in the figure-of-eight fashion through the uterine fundus. With the uterus pulled upward and downwards by an assistant, the intestines are packed out of the operating field using warm, moist abdominal gauze pads. A ring retractor, or an equivalent self-retaining retractor, is placed into the abdomen and the urinary bladder is isolated by means of a bladder retractor.
- (2) The uterus is then deviated to the patient's left, placing the right round ligament on stretch. The latter is then grasped at approximately mid-point with two Zeppelin clamps, and cut between the clamps (Figure 36.2). The distal stump of the round

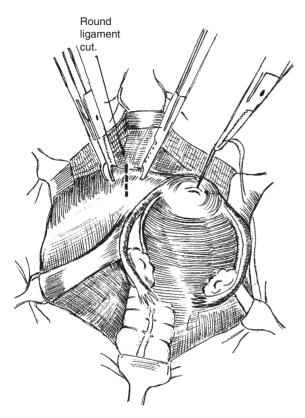


Figure 36.2

- ligament is ligated with 0 Vicryl suture, while the proximal stump is held with the clamp. This is done is identical fashion on the left side.
- (3) Normal saline (0.9%) is injected from a 20 ml syringe using a 22-gauge needle beneath the vesico-uterine peritoneal reflection. This is not dissimilar to the hydrodissection technique utilized during laparoscopic hysterectomy and facilitates the sharp dissection of the vesico-uterine space, but not all surgeons utilize this step. The vesico-peritoneal fold is elevated and the filmy attachments of the bladder to the pubocervical vesical fascia are seen and cut, and the bladder is gently separated from the corpus and cervix and mobilized inferiorly by sharp of blunt dissection. (Figure 36.3).
- (4) The peritoneum between the round ligament and infundibulopelvic ligament is opened by means of Metzenbaum scissors. The ovarian vessels are separated from the ureter, which lies posterior and medial to the ovarian vessels. The former are then doubly clamped with curved Zeppelin clamps and are severed with either scalpel or scissors between the applied clamps (Figure 36.4). Two suture ligatures secure the ovarian vessels. If the ovary is to be



Figure 36.3

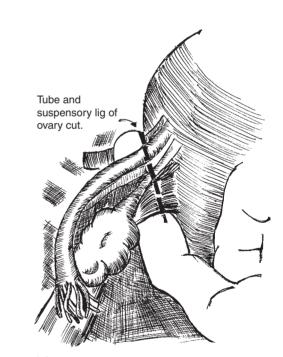


Figure 36.4

- preserved, the tube and ovarian ligament are clamped and doubly suture ligated.
- (5) The vessels to be ligated next are the uterine arteries: the vessels are skeletonized, triply clamped, cut and suture ligated with 0-vicryl. Two important points to remember here are the importance of securing good hemostasis, and the proximity of the ureters.

- The curved Zepplin clamps must therefore be juxtaposed to the uterus at the approximate point where the cervix joins the corpus, an important maneuver which avoids injury to the ureter (Figure 36.5).
- (6) The next maneuver it to cut the upper portions of the cardinal ligaments: straight Zeppelin clamps are applied parallel and immediately proximate to the side of the cervix. A sharp knife is used to cut the connective tissue medial to the applied clamp, and the pedicle ligated with a vicryl suture (Figure 36.6). Using the scalpel handle the space lying between the bladder, cervix and vagina is developed, and in this way it is ensured that the bladder and ureters will always be external to any clamps applied within the space (intrafascial).
- (7) The uterosacral ligaments are clamped close to the cervix. A transverse incision is made through the serosa of the uterus between the take-off points of the uterosacral ligaments (Figure 36.7). The scalpel handle is then used to develop the recto-uterine (rectovaginal) space as already described above. The lower portion of the cardinal ligament is now clamped by means of straight Zeppelin clamps. All clamps are applied intrafascially between the rectovaginal and vesico-uterine and vesicovaginal spaces. The cardinal ligamentous attachments to the uterus and cervix have now been cut, and 0 vicryl sutures are placed to secure these pedicles. The uterosacral ligaments are cut close to the

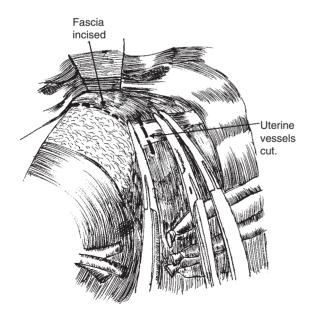


Figure 36.5

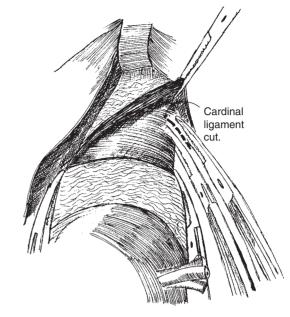


Figure 36.6

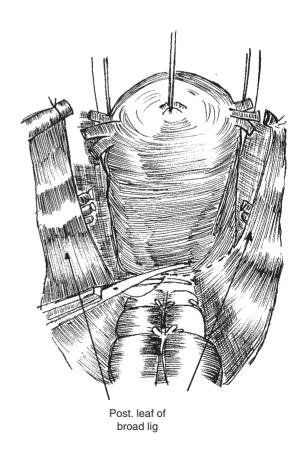


Figure 36.7

- cervix and suture ligated with 0 Vicryl sutures (Figure 36.8).
- (8) The 0 Vicryl suture at the uterine fundus is now used to pull the uterus sharply upwards. At this stage the cervix should be free of cardinal and uterosacral ligamentous support, but this should be confirmed by pinching the lateral margin of the vagina between thumb and index finger. The bladder is further mobilized inferiorly to free it from the vagina. Curved Zeppelin clamps are placed across the lateral aspect of the vagina below the cervix intrafascially. The vagina is entered by means of a scalpel cut made above the vaginal angle clamp. The vagina is cut free from the cervix and the free edges of the vagina are grasped with long Allis clamps.
- (9) The uterine specimen has now been removed and is handed over to be immersed into formal saline. Some surgeons have the habit of cutting open the uterus using a midline vertical incision from fundus to cervix to inspect the uterine cavity and exclude any obvious endometrial mitotic lesion. There may

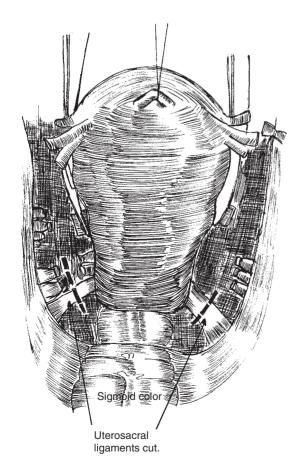


Figure 36.8

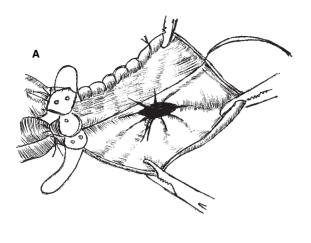
- be instances where this is indicated, but if preoperative preparation has been adequate this should not be necessary. The vaginal angles are secured with figure-of-eight suture ligatures of 0 Vicryl. The suture ends are held with artery forceps for traction.
- (10) The final step is to deal with the vaginal vault. Some surgeons routinely close the vaginal vault, while others never do so, arguing that an open vault decreases febrile morbidity and abscess formation. Those who close the vault usually do so with interrupted figureof-eight sutures of 0 Vicryl or by reefing with a running lock stitch of 0 Vicryl (baseball stitch). The cut ends of the cardinal and uterosacral ligaments are sutured into the vaginal cuff posteriorly in order to reinforce the vagina's support within the pelvis. Those who leave the vault open suture the edges of the vaginal mucosa with a running No. 1 vicryl suture, starting at the midpoint of the vagina underneath the bladder and proceeding around to the stumps of the cardinal and uterosacral ligaments which are sutured into the angle of the vagina (Figure 36.9). Studies comparing open vs closed vaginal vault in the prevention of postoperative morbidity after abdominal hysterectomy have failed to show benefit in favor of either of the two surgical policies. A careful surgical technique and antibiotic prophylaxis seem to remain the most important factors in the prevention of postoperative morbidity. 40,41 The field is irrigated with normal saline solution and checked for bleeding.
- (11) The visceral peritoneum may be closed with 2-0 vicryl (Figures 36.10 and 36.11). The authors recognize that research evidence does not show any benefits for closure of visceral peritoneum, but they prefer to carry out this procedure to close off raw areas minimize generalized ooze from the raw surfaces. Theoretically this may minimize small clot formation and possibly mild postoperative febrile mobility.

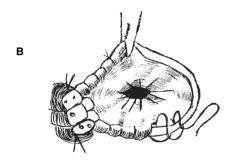
The extrafascial hysterectomy

In the extrafascial technique of hysterectomy, the clamps are placed directly on the uterine vessel and the cardinal and uterine ligaments without entering the vesico-uterine and recto-uterine space; otherwise, the rest of the basic steps are essentially similar.

The vagina vault

Some surgeons routinely close the vaginal vault, either with a figure-of-eight suture or a continuous stitch on





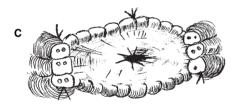


Figure 36.9

approximately the anterior and posterior edges. Other surgeons never close the vault, arguing that an open vault decreases febrile morbidity and abscess formation; they suture the edges of the vaginal mucosa with a running No. 1 Vicryl suture, starting at the midpoint of the vagina underneath the bladder and carried around to the stumps of the cardinal and uterosacral ligaments, which are sutured into the angle of the vagina.

Studies comparing open vs closed vaginal vault in the prevention of postoperative morbidity after abdominal hysterectomy have failed to show benefit in favor of either of the two surgical policies. A careful surgical technique and antibiotic prophylaxis seem to remain the most important factors in the prevention of postoperative morbidity. 40,41

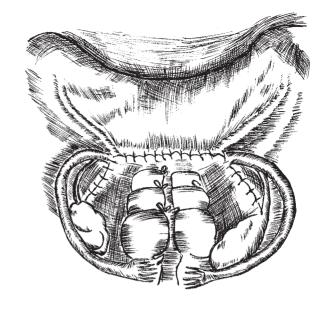


Figure 36.10

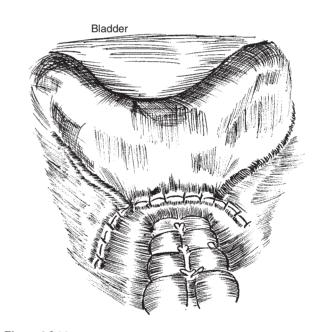


Figure 36.11

Peritoneal closure

Gupta et al. concluded that peritoneal closure at abdominal hysterectomy provides no immediate postoperative benefits while unnecessarily lengthening surgical time and anesthesia exposure. ⁴² They will often close the visceral peritoneum as a way of reducing oozing from raw

areas following removal of the uterus, and thereby reduce febrile morbidity consequent upon small hematomas which might otherwise form. There is no evidence to support this view. If the visceral peritoneum is to be closed, this is accomplished with a running 2/0 Vicryl suture from the anterior to the posterior leaf of the broad ligament. The stumps of the pelvic ligaments are buried retroperitoneally. There are no benefits, theoretical or proven, from closure of the parietal peritoneum following abdominal hysterectomy.

POSTOPERATIVE CARE FOLLOWING ABDOMINAL HYSTERECTOMY

Pain

Pain reduces deep breathing, thus impairing oxygenation and compounding the process of atelectasis that starts as a result of general anesthesia. Patient-controlled analgesia (PCA) was introduced to individualize pain control and minimize the delay in assessing pain and administering analgesia. It is administered in the first and second post-operative day. The main side effects are nausea and vomiting, which can be reduced by regular antiemetic injections.

Catheter

The in-dwelling urinary catheter is usually left in situ for 24–48 hours. The aim of the urinary catheter is to reduce the risk of bladder injury during surgery, and for patient comfort in the acute recovery phase. The authors usually leave the catheter in situ for no more than 24 hours, removing it once the patient is able to get out of bed: leaving it longer not only predisposes to urinary tract infection but also may hinder mobilization. Bladder drainage should be continued for 7–10 days if the bladder was entered and repaired during surgery. In radical hysterectomy, where the bladder may have been mobilized extensively and some of the innervation to the bladder disrupted, a suprapubic catheter is frequently used, and confers the advantage of residual urine volume measurements, thus aiding in deciding when the catheter should be removed.

Recent research has studied the issue of immediate vs delayed removal of the urinary catheter. ^{43,44} In a prospective, randomized study Dunn et al. ⁴³ found no decrease in fever, urinary tract infection, or incidence of recatheterization in women who had the Foley catheter removed immediately (compared to the delayed group) following hysterectomy. However, there was significantly less pain in the early removal group.

Wound care

Wound care begins in theater with careful hemostasis. The wound is kept covered with a sterile bandage for 48 hours, by which time the incision has sealed itself. After the bandage has been removed, the incision should be cleaned daily with water and kept dry.

On discharge, the patient is instructed to avoid heavy lifting, thereby minimizing stress on the fascia to allow full healing. Sexual intercourse is not recommended until 6 weeks after surgery, when the vaginal cuff is fully healed. Patients are instructed to avoid driving until full mobility returns because postoperative pain and tenderness may hinder sudden breaking or steering maneuvers in emergency situations. A follow-up appointment is traditionally given for 6–8 weeks from the operation, although in the UK patients are increasingly seen for their follow-up review in their general practitioner's surgery rather than in the hospital setting if the operation was entirely without complications.

COMPLICATIONS OF TOTAL ABDOMINAL HYSTERECTOMY

In good surgical hands, complications following total abdominal hysterectomy should be rare. Hemorrhage and infection are infrequent, if important, complications, while other complications include atelectasis, urinary complications, anorectal complications, and even rarer complications such as cervical stump carcinoma following subtotal hysterectomy, or vaginal evisceration.

Hemorrhage

A large Finnish study of 10110 hysterectomies reported a 2.1% incidence of severe hemorrhage in association with abdominal hysterectomy, while the incidence in association with laparoscopic and laparoscopic-assisted hysterectomy was 2.7%, and a somewhat higher rate of 3.1% with vaginal hysterectomy. Based on a study involving 867 women, it has been reported that intrafascial abdominal hysterectomy has an average blood loss of 286 ± 112 ml, and an incidence of significant hemorrhage of 0.2 - 1.0%.

Infections

Infectious morbidity associated with abdominal hysterectomy relates mainly to urinary tract infections associated with bladder catheterization, vaginal cuff infections by vaginal flora, and infections involving hematomas. A large Swedish study reported an overall infections rate of 23%, which subdivided into 13% urinary tract, 9.4% wound cuff deep infections, and 0.6% other.⁴⁷ In the

group with wound cuff deep infections, bacterial vaginosis accounted for 25%, compared with 8% for non-vaginosis patients. The While other studies have reported surgical site infections ranging from 7% to 11% following abdominal hysterectomy, ti is unfortunate that such figures may reflect sloppy practices. Prophylactic antibiotics are of proven value in reducing postoperative infections, yet in one study 71% of patients were not given antimicrobial prophylaxis, and in another with a febrile morbidity rate of 14% only 50% of the 686 women undergoing hysterectomy had received antibiotic prophylaxis.

Urinary tract

With regard to urinary tract complications, it is often difficult to know whether to include as complications the increase in urinary symptoms, including frequency, urgency, and urge and stress incontinence, that has been well documented in the literature.^{51–53} Based on data from a Finnish report, the total incidence of ureteral injuries after all hysterectomies was 1/1000 procedures, divided as follows: 13.9/1000 after laparoscopic hysterectomy; 0.4/1000 after total abdominal hysterectomy; 0.3/1000 after supracervical abdominal hysterectomy; and 0.2/1000 after vaginal hysterectomy.⁵⁴ In this same report,⁵⁴ the incidence of bladder injury was 1.3/1000, divided as follows: 2.2/1000 after laparoscopic hysterectomy; 1.0/1000 after total abdominal hysterectomy; 0.0/1000 after supracervical abdominal hysterectomy; and 0.2/1000 after vaginal hysterectomy. Of the bladder injuries, 65% were fistulas (incidence 0.8/1000).

Anorectal

As with de-novo urinary symptoms developing after hysterectomy, there are anorectal symptoms that women report for the first time after hysterectomy, and it is difficult to know whether to classify them as complications. There are numerous publications dealing with constipation, incomplete evacuation, and fecal incontinence following hysterectomy, and as part of the debate on total subtotal hysterectomy. ^{55–57} This issue is beyond the scope of this chapter, and is dealt with elsewhere in the book. Suffice to say that the general consensus would seem to be that anorectal complications are rare following abdominal hysterectomy.

In summary, as with any operation, hysterectomy can be associated with complications. It has a mortality rate in the range 0.38–1/1000;^{58,59} severe complications occur in 3% of women,⁵⁹ and minor morbidity (mainly fever and infection) in up to 30% of women. In the longer term, hysterectomy may be associated with urinary

incontinence many years after the procedure⁶⁰ and may cause early ovarian failure.⁶¹

CONCLUDING REMARKS

There is great emphasis in contemporary practice on the importance of evidence-based clinical practice, yet habits appear to die hard in gynecologic practice. Research indicates that hysterectomy remains the definitive cure for dysfunctional uterine bleeding, and improves quality of life. Although this should mean that hysterectomy will for the foreseable future remain an important weapon in the gynecologist's armamentarium, nevertheless there are highly effective surgical and non-surgical alternatives to hysterectomy,62 including tranexamic acid, the intrauterine system (IUS), endometrial ablative techniques, and uterine artery embolization, to name but a few: yet the advent of these options has had little impact on hysterectomy rates. There are robust data showing that the vaginal route is superior to the abdominal approach with respect to perioperative morbidity, postoperative hospital stay, and earlier return to work: 8,63-65 yet in most reports from North America and the UK, 60-80% of all hysterectomies for benign disease are still performed by the abdominal route.7,66

The recently published prospective, randomized multicenter trials, 67-69 which compared total against subtotal hysterectomy, all found that, at least in terms of pelvic organ function, subtotal hysterectomy failed to show any advantages over the total procedures. However, there can be no doubting that the subtotal procedure is quicker, and irrespective of the seniority of the surgeon, the safer option with respect to bladder and ureteric injury. At a time of rampant litigation, it might be supposed that gynecologists might reconsider their negative views of subtotal hysterectomy, especially as the argument for the total procedure based on the risk of cervical carcinoma is no longer tenable. In a woman whose smears have always been normal, the risk is less than 0.1%, 70 and this is likely to be even further reduced with the advent of vaccine against the human papillomavirus. Yet, currently, there is no indication that the rates of subtotal hysterectomy are increasing.

A disturbing issue, difficult to research but clammering nevertheless for the research to be done, is the varying hysterectomy rates between countries, between regions within the same country, and indeed between gynecologists even in the same hospital! Could it be that where rates are low, women are being denied a highly effective operation? Conversely, where rates are high, are women being subjected to unnecessary operations? What is the ideal hysterectomy rate anyway? These are urgent issues

that require careful research protocols to attempt to resolve the controversies. In the meantime, the gynecologist will do well to involve the woman in the decision making with regard to her management. The woman who, having been furnished with adequate information, requests a hysterectomy, will usually do well. The one who feels herself coerced into an operation she does not want will be resentful and may not reap the benefits she might otherwise have. The empowerment of women in this regard will go a long way to optimizing care and improving satisfaction with whatever treatment modality is administered.²²

References

- Hospital Episode Statistics (1998–1999) database. London: Department of Health.
- Lepine LA, Hillis SD, Marchbanks PA et al. Hysterectomy surveillance United States, 1980–1993. MMWR CDC Surveill Summ, 1997; 46(4): 1–15.
- Vessey MP, Villard–Mackintosh L, McPherson K et al. The epidemiology of hysterectomy: findings in a large cohort study. Br J Obstet Gynaecol 1992; 99: 402–7.
- 4. Settnes A, Jorgensen T. Hysterectomy in Danish cohort. Prevalence, incidence and socio-demographic characteristics. Acta Obstet Gynecol Scand 1996; 75(3): 274–280.
- Keshavarz H, Hillis SD, Kieke BA, Marchbanks PA. Hysterectomy surveillance: United States, 1994–1999. MMWR CDC Surveill Summ 1902; 51(SS-5): 1–8.
- Dwyer N, Hutton J, Stirrat GM. Randomised controlled trial comparing endometrial resection with abdominal hysterectomy for surgical treatment of menorrhagia. Br J Obstet Gynaecol 1993; 100: 237–43.
- Bachman GA. Hysterectomy: a critical review. J Reprod Med 1990; 35: 839–862.
- Campbell ES, Xiao H, Smith MK. Types of hysterectomy: a comparison of characteristics, hospital costs, utilization and outcome. J Reprod Medicine 1903; 48: 943–9.
- Lefebvre G, Allaire C, Jeffrey J et al. The management of uterine leiomyomas. J Obstet Gynaecol Can. 2003; 25(5): 396–418.
- Ravina JH, Herbreteau D, Ciraru-Vigneron N et al. Arterial embolisation to treat uterine myomata. *Lancet* 1995; 346: 671–672.
- 11. Edwards RD, Moss JG, Lumsden MA et al. Uterine artery embolization versus surgery for symptomatic uterine fibroids. N Engl J Med 1907; 356: 360–70.
- Hindley J, Gedroyc WM, Regan L et al. MRI guidance of focused ultrasound therapy of uterine fibroids: early results. AJR Am J Roentgenol 1904; 183: 1713-19.
- Stewart EA, Rabinovici J, Tempany CMC et al. Clinical outcomes of focused ultrasound surgery for the treatment of uterine fibroids. Fertil Steril 1906; 85: 22–29.
- Fiscella K, Eisinger SH, Meldrum S et al. Effect of Mifepristone for symptomatic leiomyomata on quality of life and uterine size. Obstet Gynecol 1906; 108: 1381–7.
- Jacobson GF, Shaber RE, Armstrong MA, Hung YY. Hysterectomy rates for benign indications. Obstet Gynecol 1906; 107(6): 1278–83.
- Royal College of Obstetricians and Gynaecologists. The initial management of menorrhagia. Evidence-based clinical guidelines, No. 1. London: RCOG, 1998.
- 17. Tay SK, Bromwich N. Outcome of hysterectomy for pelvic pain in premenopausal women. Aust NZ J Obstet Gynaecol 1998; 38(1): 72–76.

- 18. Sheth SS. The scope of vaginal hysterectomy. Eur J Obstet Gynecol Reprod Biol 1904; 115: 224–231.
- Harlow BL, Barbieri RL. Influence of education on risk of hysterectomy before age 45 years. Am J Epidemiol 1999; 150: 843–847.
- Richter DL, McKeown RE, Corwin SJ et al. The role of male partners in women's decision making regarding hysterectomy. J Womens Health Gend Based Med 1900; 9: 551–61.
- Galavotti C, Richter DL. Talking about hysterectomy: the experiences of women from four cultural groups. J Womens Health Gend Based Med 1900; 9: 563–7.
- Drife JO. Conserving the cervix at hysterectomy. Br J Obstet Gynaecol 1994: 101: 563–4.
- Bukovsky I, Halperin R, Schneider D et al. Ovarian function following abdominal hysterectomy with and without unilateral oophorectomy. Eur J Obstet Gynecol Reprod Biol 1995; 58(1): 29–32.
- 24. Zalel Y, Lurie S, Beyth Y et al. Is it necessary to perform a prophylactic oophorectomy during hysterectomy? Eur J Obstet Gynecol Reprod Biol 1997; 73(1): 67–70.
- Gross CP, Nicholson W, Powe NR. Factors affecting prophylactic oophorectomy in postmenopausal women. Obstet Gynecol 1999; 94(6): 962–8.
- 26. Kay VJ, Das N, Mahmood TA et al. Current practice of hysterectomy and oophorectomy in the United Kingdom and Republic of Ireland. J Obstet Gynaecol 1902; 22(6): 672–680.
- 27. Loft A, Lidegaard O, Tabor A. Incidence of ovarian cancer after hysterectomy: a nationwide controlled follow-up. Br J Obstet Gynaecol 1997; 104(11): 1296–301.
- Nahas E, Pontes A, Traiman P et al. Inhibin B and ovarian function after total abdominal hysterectomy in women of reproductive age. Gynecol Endocrinol 1903; 17(2): 125–31.
- Eason EL, Wells GA, Garber GE, Hopkins ML. Vaginal Antisepsis for Abdominal Hysterectomy Study Group. Prophylactic antibiotics for abdominal hysterectomy: indication for low-risk Canadian women. J Obstet Gynaecol Can. 1904; 26(12): 1067–72.
- Rodriguez JF, Trobo AR, Garcia MV et al. The effect of performance feedback on wound infection rate in abdominal hysterectomy. Am J Infect Control 1906; 34(4):182–7.
- Larsson PG, Carlsson B. Does pre- and post-operative metronidazole treatment lower vaginal cuff infection rate after abdominal hysterectomy among women with bacterial vaginosis? Infect Dis Obstet Gynecol 1902; 10(3): 133–40.
- Ram E, Sherman Y, Weil R et al. Is mechanical bowel preparation mandatory for elective colon surgery? A prospective randomized study. Arch Surg. 1905; 140(3): 285–8.
- Weeks AD, Duffy SRG, Walker JJ. A double-blind randomised trial of leuprorelin acetate prior to hysterecomy for

- dysfunctional uterine bleeding. Int J Obstet Gynaecol 1900; 107(3): 323–8.
- Richardson EH. A simplified technique for abdominal panhysterectomy. Surg Gynaecol Obstet 1929; 48: 248–51.
- Reyna Hinojosa R, Esparza Arechiga MA, Hernandez Aguilera C. [Extra-fascial vs subfascial abdominal hysterectomy. A comparative study]. Ginecol Obstet Mex 1986; 54: 236–40 [in Spanish].
- Edwards PS, Lipp A, Holmes A. Preoperative skin antiseptics for preventing surgical wound infections after clean surgery. Cochrane Database Syst Rev. 1904; (3): CD003949.
- Tanner J, Woodings D, Moncaster K. Preoperative hair removal to reduce surgical site infection. Cochrane Database Syst Rev 1906; 19(2): CD004122.
- Edwards PS, Lipp A, Holmes A. Preoperative skin antiseptics for preventing surgical wound infections after clean surgery. Cochrane Database Syst Rev 1904; (3): CD003949.
- 39. Berry A, Watt B, Goldacre M, Thomson J, McNair T. A comparison of the use of povidone-iodine and chlorhexidine in the prophylaxis. J Hosp Infect 1982; 3(1): 55–63.
- Colombo M, Maggioni A, Zanini A et al. A randomized trial of open versus closed vaginal vault in the prevention of postoperative morbidity after abdominal hysterectomy. Am J Obstet Gynecol 1995; 173(6): 1807–11.
- Aharoni A, Kaner E, Levitan Z et al. Prospective randomized comparison between an open and closed vaginal cuff in abdominal hysterectomy. Int J Gynaecol Obstet. 1998; 63(1): 29–32.
- Gupta JK, Dinas K, Khan KS. To peritonealize or not to peritonealize? A randomized trial at abdominal hysterectomy. Am J Obstet Gynecol. 1998; 178(4): 796–800.
- 43. Dunn TS, Shlay J, Forshner D. Are in-dwelling catheters necessary for 24 hours after hysterectomy? Am J Obstet Gynecol 1903; 189(2): 435–7.
- 44. Alessandri F, Mistrangelo E, Lijoi D, Ferrero S, Ragni N. A prospective, randomized trial comparing immediate versus delayed catheter removal following hysterectomy. Acta Obstet Gynecol Scand 1906; 85(6): 716–20.
- 45. Makinen J, Johansson J, Tomas C et al. Morbidity of 10110 hysterectomies by type of approach. Hum Reprod 1901; 16(7): 1473–8.
- Conde-Agudelo A. Intrafascial abdominal hysterectomy: outcomes and complications of 867 operations. Int J Obstet Gynaecol 1900; 68(3): 233–9.
- 47. Persson E, Bergstrom M, Larsson PG et al. Infections after hysterectomy: a prospective nation-wide Swedish study. Acta Obstet Gynecol Scand 1996; 75(8): 757–761.
- 48. Soper DE, Bump RD, Hurt WG. Wound infection after abdominal hysterectomy: effect of the depth of subcutaneous tissue. Am J Obstet Gynecol 1995; 173(2): 465–9.
- Taylor G, Herrick T, Mah M. Wound infections after hysterectomy: opportunities for practice improvement. Am J Infect Control 1998; 26(3): 254–7.
- Peipert JF, Weitzen S, Cruickshank C et al. Risk factors for febrile morbidity after hysterectomy. Obstet Gynecol 1904; 103(1): 86–91.
- 51. Neumann G, Olesen PG, Hansen V et al. The short-term prevalence of de novo urinary symptoms after different modes of hysterectomy. Int Urogynecol J 1904; 15(1): 14–19.

- Roovers JP, van der Bom JG, Huub van der Vaart C et al. Does mode of hysterectomy influence micturition and defecation? Acta Obstet Gynecol Scand 1901; 80(10): 945–51.
- Morgan JL, O'Connell HE, McGuire EJ. Is intrinsic sphincter deficiency a complication of simple hysterectomy? J Urol 1900; 164(3 Pt 1): 767–79.
- 54. Harkki-Siren P, Sjoberg T, Tiitinen A. Urinary tract injuries after hysterectomy. Obstet Gynecol 1998; 92(1): 113–18.
- Kelly JL, O'Riordain DS, Jones E et al. The effect of hysterectomy on ano-rectal physiology. Int J Colorectal Dis 1998; 13(3): 116–18.
- Goffeng AR, Andersch B, Antov S et al. Does simple hysterectomy alter bowel function? Ann Chir Gynaecol 1997; 86(4): 298–303.
- van Dam JH, Gosselink MJ, Drogendijk AC et al. Changes in bowel function after hysterectomy. Dis Colon Rectum 1997; 40(11): 1342–7.
- McPherson K, Metcalfe MA, Herbert A et al. Severe complications of hysterectomy: the Value study. BJOG 1904; l11: 688–94.
- Wingo PA, Huezo CM, Rubin GL et al. The mortality risk associated with hysterectomy. Am J Obstet Gynecol 1985; 152: 803–8.
- van der Vaart CH, van der Bom JG, de Leeuw JR, Roovers JP, Heintz AP. The contribution of hysterectomy to the occurrence of urge and stress urinary incontinence symptoms. BJOG 1902; 109: 149–154.
- Riedel HH, Lehmann-Willenbrock E, Semm K. Ovarian failure phenomena after hysterectomy. J Reprod Med 1986; 31: 597– 600.
- 62. Banu NS, Manyonda IT. Alternative medical and surgical options to hysterectomy. Best Pract Res Clin Obstet Gynaecol 1905; 19(3): 431–449.
- Dicker RC, Greenspan JR, Strauss LT et al. Complications of abdominal and vaginal hysterectomy among women of reproductive age in the United States. Am J Obstet Gynecol 1982; 144: 841–8.
- Basket TF, Clough H. Peri-operative morbidity of hysterectomy for benign gynaecological disease. J Obstet Gynaecol 1901; 21: 496–8.
- Sculpher M, Manca A, Abbott J et al. Cost effectiveness analysis
 of laparoscopic hysterectomy compared with standard hysterectomy: results from a randomised trial. BMJ 1904; 328: 134–7.
- Vessey MP, Villard-Mackintosh L, McPherson Ket al. The epidemiology of hysterectomy: findings in a large cohort study. Br J Obstet Gynaecol 1992; 99: 402–7.
- Thakar R, Ayers S, Clarkson P, Stanton S, Manyonda I. Outcomes after total versus subtotal abdominal hysterectomy. N Engl J Med 1902; 347(17): 1318–25.
- Learman LA, Summitt RL Jr, Varner RE et al. A randomized comparison of total or supracervical hysterectomy: surgical complications and clinical outcomes. Obstet Gynecol 1903; 102(3): 453–62.
- 69. Gimbel H, Zobbe V, Andersen BM et al. Randomized controlled trial of total compared with subtotal hysterectomy with one-year follow-up results. Br J Obstet Gynaecol 1903; 110: 1088–98.
- 70. Kilkku P, Gronoos M. Peroperative electrocoagulation of the endocervical mucosa and later carcinoma of the cervical stump. Acta Obstet Gynecol Scand 1982; 61: 265–7.

Vaginal hysterectomy

Henri Clavé

INTRODUCTION

The first vaginal hysterectomy was performed by Joseph Récamier at the Hôtel Dieu Hospital in Paris on July 26, 1829. The procedure became widely popular at the end of the 19th century.

In the 20th century, thanks to progress in general anesthesia, asepsis, and instrumentation, abdominal hysterectomy was developed to the detriment of the vaginal approach.

The current success of vaginal approach at the beginning of 21th century is the result of laparoscopic surgery. Indeed, since the 1980s, the development of laparoscopic surgery has given way to a minimally invasive, non-hemorrhagic approach which required a new series of tools that appeared with the modernization of electrosurgery.

Paradoxically enough, at the turn of the 20th century, the celioscopic approach led to the vaginal approach in the treatment of abnormal uterine bleeding, a less-invasive and safer option.

Indeed, what stopped gynecologic surgeons from choosing the vaginal approach were essentially the technicality of the procedure, the control of hemostases at the bottom of the vagina, as well as the impressive bleeding of the operative piece. The advent of safe hemostatic thermic forceps at the beginning of 2000 has radically changed this approach by simplifying the gestures and allowing for a bloodless and stressless surgery. Moreover, the vaginal approach allows for the performance of a multimodal anesthesia; this softer anesthesia is accompanied by much lower doses, as would have been required with an abdominal approach (laparotomy or laparoscopy). Thus, a vaginal hysterectomy will be followed by a 'fast post-operative recovery which is less painful, shorter and has the advantage of leaving no visible scars'. Those aspects are important because they concern a procedure whose objective is to improve quality of life through the preservation of the body image as well as the psychological balance of the patient.

DESCRIPTION OF THE TECHNOLOGY: MODERN THERMAL HEMOSTASIS

Mode of operation

The new forceps which facilitate the modern thermal hemostasis use two different effects to ensure a safe and definitive occlusion of the vessels:

- a mechanical effect flattening and compression of the two sides of the vessel and displacement of the blood
- a thermal effect the thermal effect from one branch of the forceps to the other leads to an increase in temperature, which results in (1) dehydration of tissue, which is recognizable by the white discoloration of the tissue and the generation of water vapor, and (2) destruction of the proteins and melting of the collagen.
- The hardening of the collagen gives the vessels their final shape and occludes them. Clinically, the tissue has a parchment-like coagulation surface. After severing with the scissors, this area feels as though it were made of plastic.

The high-frequency generators (Table 37.1)

High-frequency (HF) generators provide a high-frequency current with a higher peak amperage (4) than that of classic bipolar current. With the best generators, this current is modulated and pulsed; i.e. the variable energy depends on the change in impedance of the target tissue. This means that the heating of the tissue occurs in controlled dosages, which help to prevent carbonization. No carbonization means no scabbing and therefore no danger of the dreaded sloughing-off of scabs which occurs after conventional thermal hemostasis procedures.²⁻⁴

There are two types of generator:

 generators that deliver this type of current only: it is therefore necessary to have another classic generator in the operating room

	Manufacturer			
	ERBE	Gyrus	LAMIDEY	Valleylab
Name of the THF	BiClamp	Seal Open forceps	***	LigaSure
Reusable forceps	+	-	+	Single-use electrode
Name of the generator	VIO	PK workStation	SURGILEC SEAL	Force Triad
Multifunction generator	+	+	+	+

Table 37.1 Example of devices and products now available for thermal hemostasis in the vaginal approach

THF, thermal hemostatic forceps.

 multitask generators that offer all the potentialities of a modern electric bistoury (cutting, coagulation, vaporization).

Figure 37.1 shows the ERBE VIO 300 generator, which has a large monitor and different programs that are easy to operate. There is an 'Auto Stop' function which interrupts the flow of current and indicates to the operating physician that the hemostasis procedure is complete.

Thermal hemostatic forceps

Thermal hemostatic forceps (THF) look like a Faure or Heaney forceps. They are handled in the same way, so that it is not necessary to learn a new set of movements. All forceps have an integrated electric system: the two branches of the forceps work like the two electrodes of a bipolar forceps. They allow larger tissue areas to be coagulated with no need to dissect the different tissue structures. The structure of the jaws depends on the manufacturer; the surface varies depending on the respective models. They can be smooth, steel-coated, corrugated, or waffle-shaped; the smoothness of the coating can help to prevent the tissue from sticking to the forceps. The corrugated or ridged surface helps to prevent the tissue from slipping away and offers a better grip, but it also results in increased thermal injury to adjacent tissue with a concomitant risk of tissue trauma (ureter, bladder).

The branches of the ERBE BiClamp are coated with a ceramic layer that decreases the risk of collateral thermic damage and ensures a longer life to the instrument, which can be used more than 50 times (Figure 37.2). Indeed, some models are single use and other can be sterilized and are available in different lengths.

Impact on pain

Thermal hemostasis reduces inflammatory and painful events. The pedicles along the ligature are not crushed so



Figure 37.1 Modern HF multifunction generator with a large monitor and programs easy to operate.



Figure 37.2 Thermal hemostatic forceps (THF) with ceramic coating and smooth jaws.

that there is no tissue necrosis. The absence of necrotic tissue and foreign bodies (sutures) results in a reduction of the resorption process and of phagocytosis. This has already been noted by physicians carrying out endoscopic surgery and using bipolar coagulation for hysterectomy procedures for many years.

Purohit and Pattnaik have reported a decrease in the amount of analgesics required in 88% of cases if the vaginal hysterectomy was carried out with laparoscopic bipolar forceps.⁵

In a short comparative series, Zubke et al. were also able to confirm this distinct decrease in the amount of analgesic medications required when using the THF.⁶

PRACTICAL ASPECTS OF THE PROCEDURE

Preoperative stage

Positioning

The patient The patient is placed in the dorsosacral position with a slightly elevated pelvis; the lower legs are fixed in stirrups. The pubic hair is not shaved, as the removal of pubic hair increases the risk of infection and the shaving of pubic hair is unpleasant for the patient. The bladder is not catheterized: the patient should empty her bladder immediately prior to the operation. The catheterization of the bladder is the most common cause of nosocomial bladder infections and should therefore be avoided. In addition, due to the short duration of the operation and the absence of spinal analgesia, catheterization is useless. Catheterization also poses an additional risk, as injuries to the bladder may remain undetected. The skin and vagina are disinfected as usual.

The surgeon The surgeon is seated in front of the patient's legs on a high seat.

The two assistants They stand on either side of the physician. No scrub nurse is required for instruments, as few instruments are used and the individual steps of the operation are fairly simple.

The instrument table (Figure 37.3)

Basic instruments Six basic instruments are laid out on the table:

- one short-handled scalpel, No. 11 blade
- one small-toothed forceps, 18 cm
- one pair of Mayo scissors, 18 cm
- one bullet forceps or one Museux forceps



Figure 37.3 Very few and cheap instruments are necessary.

- one needle holder 18 cm
- one Bengolea-type forceps.

In addition, the following instruments are available:

- the THF
- one set of Breisky retractors
- · one vaginal weighted speculum
- one suction tube
- 10 compresses
- · one long gauze
- instruments for the local anesthetic (two 20 ml syringes, two long needles for infiltration).

The HF generator The generator should be positioned in such a way that it is clearly visible to the surgeon, allowing him to monitor the changes in power output on the display. The volume of the alarm and the Auto Stop signal must be adjusted so that the signals can be heard clearly and unmistakably by the operating team.

Multimodal anesthesia

Multimodal anesthesia combines general anesthesia with a local anesthetic making it possible to use a 'light' general anesthesia. The local anesthetic with a long-term effect prevents postoperative pain and allows the patient to wake up softly without experiencing pain from the operation.⁷

The local anesthetic For local anesthesia we combine a pudendal anesthetic with a paracervical block:⁸

 The following solution is used for local anesthesia: 30 ml of ropivacaine (Naropin) 7.5 mg/ml, combined

- with clonidine (Catapressan) at a ratio of 1 γ /kg, to prolong the effect for a period of at least 10 hours.
- For the pudendal anesthetic, 10 ml of this solution are injected in the vicinity of the Alcock's canal on either side near the ischium, using a 100 mm long 22-G cannula with a 20 ml syringe. The needle is positioned 3 cm laterally to the vulva and in the direction of the inner side of the ischiadic tuber. Two fingers of the contralateral hand are placed in the vagina to control this procedure. Prior to injecting the anesthetic, a brief aspiration is carried out with the tip of the syringe to ensure that no vessel has been punctured.
- For the paracervical block, the remaining 10 ml are injected paracervically at the 5 o'clock and the 7 o'clock positions. This anesthesia covers the entire paracervical area of the hypogastric plexus. This injection is carried out submucosally; it has an additional beneficial vasoconstrictive effect (in contrast to Naropin, which is used here, Xylocaine (lidocaine) has a vasodilative effect).

General anesthesia General anesthesia is carried out using a laryngeal mask. The same medication is used as that used for small gynecologic operative procedures. Propofol (Disoprivan) is administered using an automatic, preprogrammed infusion pump for the intravenous concentrated administration of medications. Remifentanil (Ultiva) is administered using a special automatic infusion pump.

Operative stage

General principles (Figure 37.4)

This operative procedure follows the classic steps of conventional vaginal hysterectomies; however, three new principles must be taken into account:

- Only two other instruments are present in the vagina in addition to the speculum:
 - the bullet forceps to properly fix the area, which will require hemostasis
 - either the THF or the scissors.
- (2) Hemostasis must always be carried out as close to the middle of the vaginal canal as possible; here it is important to make good use of the concave or convex shape of the instrument to ensure an optimal application of the THF on the edge of the uterus. It may be necessary to carry out two coagulations with the THF to ensure that the cut area is really dry.
- (3) No traction should be used and there should be no attempt to pull out the uterus in order to work

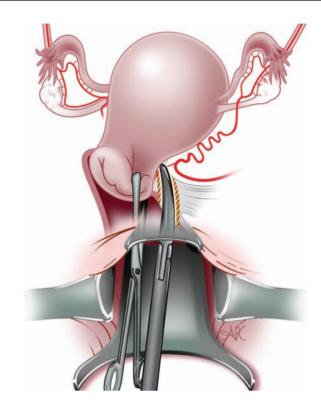


Figure 37.4 General principles for a true intravaginal and soft surgery. (Courtesy of Annaik Perron.)

'outside' the vagina. This helps to prevent postoperative pain and unwanted bleeding.

Vaginal circumferential cut around the cervix

The operation begins with a circumferential incision around the cervix carried out with a sharp scalpel. It may be advisable to infuse 10 ml of an epinephrine solution at the beginning (0.25 mg in a 40 ml physiologic infusion solution) to reduce bleeding in the frontal part of the vagina during the operation and to improve visibility. The bullet forceps are used to pull the cervix downwards, the anatomic forceps lift the edge of the front part of the vaginal wall, and the front speculum pushes the bladder in a ventral direction. Now the supravaginal septum can be incised: not too high, so as not to perforate the bladder; not too low, so as not to cut into the uterus.

Using the weighted speculum, the posterior fornix of the vagina is arranged so that there is a view of the sacrouterine arch and the caudal wall of the Douglas pouch.

The bullet forceps are positioned on the posterior lip of the cervix and luxated ventrally. At the same time, using the toothed forceps, the posterior vaginal edge of the incision is pulled dorsally. The Douglas pouch is opened using scissors. If there are intestinal adhesions, these can now be prepared and detached.

Palpation of the pericervical tissue using two fingers before the introduction of the self-locking speculum.

Hemostasis around the cervix (Figure 37.5)

With the THF, the exposed structures of the paracervix can be coagulated, either in one go or in smaller steps, and then severed with the scissors. The severing of the sacrouterine ligaments in particular improves the mobility of the uterus.

The technique is simple if the uterus is mobile. If mobility of the uterus is restricted, then the THF offers an important advantage – particularly if the paracervical tissue is very firm, very short, or if the sacrouterine ligaments are located at the end of a narrow vagina.

The cardinal ligaments and the columns of the bladder are severed caudally to the curve of the uterine arteries; it is important to ensure that the bladder is elevated using the front retractor. We avoid opening the peritoneum at this stage.

Amputation of the cervix (Figure 37.6)

If one does not pull the uterus or luxate it in front of the vulva, the cervix will be in the way of an operation carried out through the vagina. A pear-shaped uterus is difficult to turn or to move sideways. For this reason, the cervix is amputated with a scalpel; at this stage, it is simpler to open up the front of the peritoneum and to introduce a broader retractor under the bladder. This amputation of the cervix turns a pear-shaped uterus into an apple-shaped uterus.

Apple-shaped uterus (Figure 37.7)

Such a uterus has a rounder shape: it can be moved more easily and can be gradually turned without unnecessary pulling or traction. It is very simple to apply the curved

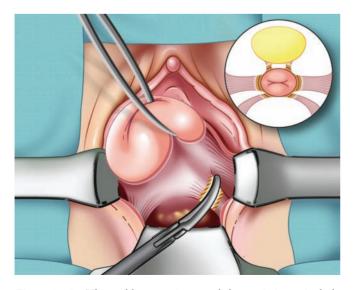


Figure 37.5 Thermal hemostasis around the cervix is particularly easier in the case of a narrow vagina. (Courtesy of Annaik Perron.)

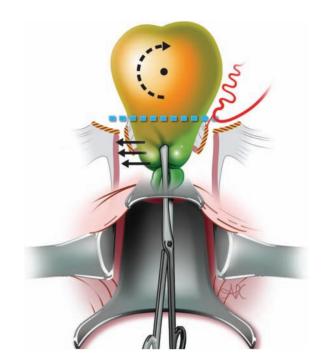


Figure 37.6 Amputation of the cervix: because a pear-shaped uterus is difficult to move sideways. (Courtesy of Annaik Perron.)

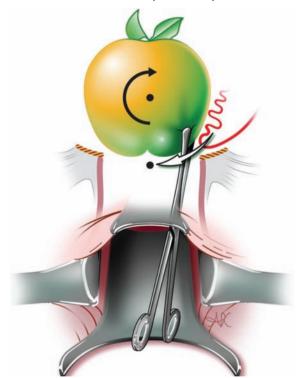


Figure 37.7 An apple-shaped uterus can be gradually turned without pulling. (Courtesy of Annaik Perron.)

branches of the THF to the concave or convex side of the uterus: the so-called 'cheek to cheek surgery'.

After the excision of the cervix, a gauze pack is placed in the Douglas pouch:

to protect the intestinal loops in this area from thermal damage

to offer better visibility of the posterior operative area.

Hemostasis and severing of the uterine vessels (Figure 37.8)

The bullet forceps are used to grasp the edge of the isthmus where coagulation and dissection should be carried out.

The forceps are used to pull the uterus slightly downwards. At the same time, one of the assistants places a suitable speculum beneath the bladder, pushes it away ventrally, and thereby distances the uterine artery from the ureter.

The THF can then be placed in the center of the vagina on the lateral edge of the isthmus.

Using the THF, the branches of the uterine vessels are coagulated twice: one coagulation is placed next to the other. The coagulated area will turn white; the cut should not be made in the middle of this area, but with one-third of the coagulated area on the side of the uterus that will be removed and two-thirds on the side of the remaining uterine artery. Afterwards, the bullet forceps are used to grasp the contralateral side of the isthmus to cut the uterine vessels in the same manner.

It is not necessary to prepare or to dissect the arch of the uterine artery any further. This method differs from the classic technique with clamp and purse-string sutures or ligatures.



Figure 37.8 The safest hemostasis of the uterine vessels. (Courtesy of Annaik Perron.)

Amputation of the uterus at the adnexa (Figure 37.9)

If the adnexa are to be left in place, the uterus must be grasped directly where it is attached to the adnexa; the adnexa have to be coagulated once or twice with the THF, after which they can be severed with scissors. Depending on the anatomy, it is possible to make use of either the concave or the convex shape of the instrument. It is not necessary to pull out the uterus or to tilt it to carry out hemostasis outside the vulva. If necessary, it is always possible to halve the uterus or morcellate it in order to reach the end of the adnexa with as little traction as possible.

It is important to ensure that the end of the THF is always clearly visible and that the intestinal loops have been securely pushed up and back with gauze strips.

Occlusion of the vaginal stump

At this stage the uterus has already been removed, either in one piece or after morcellation.

The operative area must be inspected to ensure that there is no bleeding at all. The gauze strip is removed to allow for inspection of the area. If it shows extensive traces of blood, the source of the bleeding must be found. In exceptional cases, it may be necessary to carry out an additional or repeat coagulation of a small area.

If necessary, fixation of the vagina can also be carried out. This is unproblematic, as with this technique all structures remain unchanged.

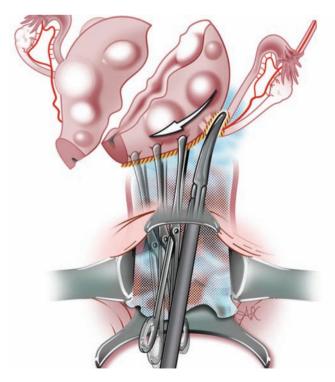


Figure 37.9 The 'cheek to cheek' intravaginal progression leads to the adnexa. (Courtesy of Annaik Perron.)

The vaginal occlusion is carried out using a single Monocryl 0 suture: only one suture is required for this operation, decreasing risks of injuries and blood contamination with hepatitis or HIV (human immunodeficiency virus) for surgeons, assistants and nurses.

The suture joins both the dorsal and ventral vaginal walls, as well as the dorsal and the ventral peritoneum, to prevent bleeding in this interstice, which is otherwise a frequent occurrence.

The knot of the absorbable monofilament suture will have dissolved within 3–4 weeks. This will ensure that scarring of the vaginal stump remains soft, regular, and without granulated tissue formation. This will allow sexual activities to be resumed without any dyspareunia.

Adnexectomy procedures with the THF (Figure 37.10)

This procedure can be carried out more easily with the THF than with the classic technique.

Coagulation of the round ligament as close to the pelvic wall as possible is essential as a first step.

The bullet forceps are positioned on the uterine horn to distance it from the pelvic wall. The uterine horn, which is thereby positioned in the middle of the vagina, attracts the infundibulopelvic ligament and leaves the ureter close to the pelvic wall.

The ovary and the fallopian tubes are grasped with a fenestrated clamp; the gauze strips are placed behind the vascular pedicle to protect the bowels and show the way for hemostasis.

The THF is used to coagulate the infundibulopelvic ligament in one or two steps. No traction is exerted during the procedure and it is important that the tip of the THF always remains visible; actually, vaginal adnexectomy

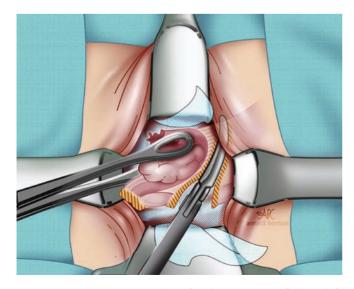


Figure 37.10 Easier and safer hemostasis of the left infundibulopelvic ligament. (Courtesy of Annaik Perron.)

procedures with the THF are safer than those using conventional ligatures. Due to the location of the infundibulopelvic ligament and the placing of the axis of the THF in the middle of the axis of the vagina, the coagulation cut can also be carried out at an angle.

With the classic technique it is imperative that the ligature used for hemostasis is knotted at right angles to the axes of the vessels in order to prevent a decrease of hemostasis when the ligament retracts.

Hemisection or morcellation

With a large uterus or if the mobility of the uterus is restricted, it is easier to carry out hemisection or morcellation than with the classic technique: as there is no retrograde bleeding, the operative area remains clean and dry and visibility is good. It is important to avoid any unintentional or strong traction and any forcible pulling out of the uterus. It is better to remove the uterus in several pieces than to extract it forcibly, as this has a negative impact on postoperative pain and on hemostasis.

Other interventions

There is no reason why additional interventions which are indicated cannot be carried out:

- prolapse therapy
- introduction of a mesh
- treatment of incontinence
- treatment of an ovarian cyst.

Postoperative stage

Prevention of postoperative pain

In the first few hours after the intervention, the patient can be given acetaminophen (Perfalgan 1 g every 8 hours) and AINS (Ketoprofen 100 mg every 12 hours), as required. An anticipated suspension of the analgesic effect can be prevented by the administration of painkillers; the patient can take the tablets herself, as required. On discharge, the patient can be given painkillers upon request.

The stay in hospital

Ideally, the patient will come to the hospital on the day of the operation without having eaten. After a shower and after having emptied her bladder, she will be given premedication and wheeled into the operating room. The patient will not be shaved, her bladder will not be catheterized, and she will not be given an enema or purgative. After the operation and a stay in the recovery room, the patient is brought to her room and, as a precautionary measure, she is given analgesics via an infusion. After the operation she can empty her bladder in the toilet as long as she is accompanied there. Eating may also be resumed on the same day, as soon as the patient wishes to do so. The discharge from hospital can be planned for the day after the intervention, after prior agreement with the patient.¹⁰

Postoperative check-up

The postoperative check-up is done 4 weeks after surgery. It allows us to note down and assess the pain the patients has endured, her feelings, and the quality of the scar at the end of the vagina. We can then allow her to have intravaginal intercourse and take baths. This consultation is a good opportunity to inform the patient again of the advantages of this procedure in terms of quality of life: no more periods; elimination of the risk of cervical and endometrial cancers; simplification of the clinical and paraclinical follow-up; no more contraception issues; improvement of her sex life; and allowing her to practice sports.

INDICATIONS AND CONTRAINDICATIONS

The vaginal approach is not linked only to prolapsed uteri.

Vaginal approach

In the interest of all patients, the vaginal approach is the best option when hysterectomy is required.¹¹ By taking the patient's history and performing a minutely clinical examination, the gynecologic surgeon has to make sure that the diagnosis, the ultrasound, as well as the anatomic state allow for this type of surgery.

The vaginal approach is even better for obese patients, and patients in poor health, especially those who have been deemed 'unoperable'.

A narrow vagina

The use of thermal hemostasis rather than traditional techniques allows us to operate on patients who present with narrower vaginas, thanks to threads and a needle holder. Nulliparity is not a contraindication if the vagina is supple and the uterus mobile. Surgery is generally feasible if – under anesthesia – we can introduce two fingers into the vagina and mobilize them. ^{12,13}

Disorders of the hips

It is preferable not to use the vaginal approach if, in the course of the clinical examination and before any anesthesia, the surgeon cannot get the patient to bend forward at 90° or if it is painful for the patient to do so.

Suspicious or malignant adnexal pathology

When the nature of a clinical or ultrasound adnexal lesion looks suspicious, the surgeon should perform a primary laparoscopy, which will then guide him or her, through the rest of the procedure.

Very big uterus

It is usually preferable not to use the vaginal approach with a uterus bigger than a 16-week pregnancy uterus. However, it also depends on the mobility of the uterus, the accessibility of the vagina, and the location of fibroids in the uterus. 14 Thermal hemostasis prevents bleeding from the uterus, thus presenting a dry operative area, which allows for the cutting down of big fibroids without any major risk of hemorrhage and in reasonable time. It is therefore important to have a good assessment of the size and the location of the fibroids through medical imagery (ultrasound or magnetic resonance imaging [MRI]) before choosing the approach. To reduce uterine volume, it was suggested to resort to chemical castration through gonadotropin-releasing hormone (GnRH) analogues for 2 months by associating it with a vaginal estrogenotherapy.

Severe endometriosis

Severe endometriosis of the Douglas pouch, pelvic peritoneum, or rectovaginal septum should be dealt with as a primary medical treatment and a celioscopic approach to assess the nature of the lesion, more particularly at the level of the adnexes and the peritoneum.

Previous laparotomy

A past history of a single or multiple cesarean sections¹⁵ or adnexal surgery (infertility, cysts, ligating of the Fallopian tubes) is not a contraindication. In the case of a previous cesarean section, the surgeon should pay particular attention to the section of the supracervical septum. In all cases, potential adhesions will be managed easily in the vaginal approach thanks to the descent of the operative piece. Those adhesions are less disturbing than in the laparoscopic approach. However, in case of a history of hysteropexy of a promontofixation type, a primary laparoscopy is definitely required.

CLINICAL STUDIES

The pain

The use of this technique has allowed us to reduce postoperative pain considerably,¹⁶ the latter being one of the reasons for the negative reputation of the procedure. The reduction of pain is the result of:

- good psychological preparation of the patient prior to the intervention
- the vaginal approach¹⁷
- multimodal anesthesia
- the non-aggressive operative technique, with no forcible pulling of the pedicles and the ligaments
- the principle of ensuring hemostasis through thermofusion and without ligatures.

Reduction of morphine

The prevention of postoperative pain by using a long-term local anesthetic results in a substantial decrease in the use of opiates, and thereby also avoids side effects. It could be shown that a substantial part of the postoperative discomfort experienced – such as nausea, vomiting, drowsiness, and urine retention – was due more to the administration of morphine than to the procedure itself.

Duration of hospital stay

This innovative technique allows the hysterectomy procedure to be carried out on a purely outpatient basis, ¹⁸ particularly in favorable cases (small mobile uterus, well-adjusted psychological profile, no additional stress, favorable social conditions).

Hospital stays of 1 day or <24 hours account for more than 85% of the indications, although patients may extend the duration of their stay if they wish to do so.¹⁹

Duration of the procedure

A thermal hemostasis procedure may sometimes appear to be rather long, particularly if the operating physician performs the hemostasis twice. In fact, the thermal hemostasis consists of only three steps, compared to the six steps necessary for classic hemostasis with sutures, which requires switching between numerous instruments. The three steps of the thermal hemostasis are:

- Positioning of the THF.
- (2) Removal of the THF after the generator has shut down automatically.

(3) Cutting with scissors.

The classic hemostasis with sutures requires:

- (1) Positioning of the Heaney clamp.
- (2) Severing of the pedicle using scissors.
- (3) Placing of the suture with a needle holder.
- (4) Knotting.
- (5) Removal of the forceps.
- (6) Cutting of the suture with scissors.

Thermal hemostasis of both edges of the pedicles prevents a flowing back of blood, so that there is no need for suctioning off of blood and frequent swabbing with compresses. The visibility in the operative area is also better and shortens the duration of the intervention.

COMPLICATIONS

Burns

The prevention of burns must be a guiding principle for the physician. Owing to the simplicity of the technique and the similarity of the THF to other commonly used forceps, mistakes or accidents may occur if a physician is unduly hasty.

Skin/mucosal burns

These are caused by prolonged contact of the forceps with the skin or vaginal wall. They are not electric burns but are first-degree thermal burns (caused by the heating of the forceps during hemostasis). They are a result of negligence on the part of the team when placing a 45° forceps against the wall of the vagina in order to reach the ligaments and to place a suture. Preventive measures include:

- positioning the forceps as close as possible to the center of the vagina
- entrusting an assistant with the dual task of suctioning off the surgical steam plume created during coagulation with the THF and monitoring to ensure that the forceps does not touch the vaginal wall.

Thermal necroses of the ureter

Every laparoscopic or vaginal hysterectomy procedure carries the risk of injuring the ureter, a serious complication of this procedure. It is important to remember that the uterine artery must not be clamped as with the classic technique, because if the artery is grasped too far laterally, there is quite a danger of burns to the ureter with immediate or secondary effects. If only one assistant is present, this danger is greater.

Thermal wounds to the digestive tract

These are created by the tip of the THF coming into contact with an intestinal loop or with the wall of the colon during vessel sealing. Preventive measures include:

- the use of a gauze strip to push away the intestinal loops and pad them
- constant direct visual monitoring during vessel sealing.

Bleeding

Immediate bleeding

To prevent immediate bleeding, it is necessary to be extremely cautious when applying the instrument. It is particularly important to react to the Auto Stop signal. The flow of current should not be interrupted too early. If necessary, coagulation must be repeated to ensure that only properly white, dry and parchment-like tissue is severed.

In addition, it is important to stick to an essential principle of electrosurgical procedures: namely, that no coagulation should be carried out in tissue which is under traction. If this precaution is not observed, there is the risk that the tissue will tear before proper hemostasis has been achieved.

In endoscopic surgery we have learnt to comply with these principles.

Secondary bleeding

This hemostasis procedure does not create any scabbing, so no secondary bleeding due to the sloughing-off of scabs will occur. Secondary bleeding can affect the vaginal incision and, for this reason, this cut must be carefully sutured using a hemostatic suture that will only dissolve very slowly.

Psychological troubles

In general, hysterectomy procedures have a very bad reputation among the general public, sometimes even among gynecologists. It is therefore very important to explain to patients how the operation is carried out and what the results of the procedure will be.

The course of the operation, the reduction of pain, and the decrease in impediments to daily activities and sexual activities should be particularly emphasized.

To reassure and prevent unnecessary fear, the surgeon should provide the patient with a comprehensive brochure describing her stay in hospital and the sequence of events.

COST

All recent publications have clearly shown that the vaginal approach was by far the least-expensive procedure²⁰ to perform a hysterectomy, with a reduction of 25% in costs, compared with the abdominal approach.²¹

The use of THF, especially when reusable, contributes to a further decrease in costs. The modern vaginal approach makes it the best economic choice over the short or long term.

Short-term costs

- Sturdy, low-cost, reusable instrument.
- Easy maintenance and storage.
- Short operating room stay for patient (easy installation, fast waking up).
- Short hospital stay or outpatient procedure.
- Decrease in nursing time.
- Low-cost medications.
- Very low rate of serious complications.

Long-term costs

- Patient is totally and definitively cured.
- · No recurrence.
- No clinical or imagery follow-up.
- No uterine cancer (endometrium or cervix).
- Cheaper hormone replacement therapy.

CONCLUSION

Vaginal hysterectomy is the best approach when a hysterectomy has to be performed. It is the solution patients prefer because it is transparent; it does not present with the risks of laparotomy (abscess, hematomas, hernias, occlusion) and those of a laparoscopy (trocart accident, deep anesthesia, hypercapnia, burns, elevated costs).

This surgical method benefits from the improvements of modern electrosurgery and the advantages of a multimodal anesthesia. The technical gesture – non-aggressive – and the operative follow-up – only slightly painful – are not comparable with those of the old-fashioned techniques. The old-fashioned vaginal approaches have stopped people from learning vaginal surgery.

The revival of this surgery in the modern management of abnormal uterine bleeding and the revival of the vaginal approach in the treatment of pelvic floor disorders requires it be part of the basic training of gynecologic surgeons.

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References

- Dargent D, Querleu D, Plante M, Reynolds K. Vaginal and Laparoscopic Vaginal Surgery. London: Taylor & Francis, 2004: 1.
- Peterson SL, Stranahan PL, Schmaltz D, Mihaichuk C, Cosgriff N. Comparison of healing process following ligation with sutures and bipolar vessel sealing. Surg Technol Int 2002; 10: 55–60
- Sigel B, Dunn MR. The mechanism of blood vessel closure by high frequency electrocoagulation. Surg Gynecol Obstet 1965; 121: 823–31.
- 4. Kennedy JS, Stranahan PL, Taylor KD et al. High-burst-strength, feedback-controlled bipolar vessel sealing. Surg Endosc 1998; 12: 876–8.
- Pattnaik KK, Purohit RK. Vaginal hysterectomy by electrosurgery (an extraperitoneal approach). J Obstet Gynecol India 2001; 51: 162–4.
- Zubke W, Becker S, Wallwiener D. Vaginal hysterectomy: a new approach using bicoagulation forceps. Gynecol Surg 2004; 1: 179–82.
- Kehlet H. Multimodal approach to control postoperative pathophysiology and rehabilitation. Br J Anaesth 1997; 78: 606.7
- O'Neal MG, Beste T, Shackelford DP. Utility of preemptive local analgesia in vaginal hysterectomy. Am J Obstet Gynecol 2003; 189: 1539–41.
- Kehlet H. Acute pain control and accelerated postoperative surgical recovery. Surg Clin North Am 1999; 79: 431–43.
- Ottesen M, Sorensen M, Rasmussen Y et al. Fast track vaginal surgery. Acta Obstet Gynecol Scand 2002; 81: 138–46.
- Cosson M, Querleu D, Dargent D. Traité de Chirurgie Vaginale. Paris: Masson, 2003: 200–1.

- Boukerrou M, Lambaudie E, Narducci F, Crepin G, Cosson M. [Hysterectomy for benign lesions: what remains for the abdominal route] J Gynecol Obstet Biol Reprod (Paris) 2001; 30: 584–9 [in French].
- 13. Martin X, Gjata A, Golfier F, Raudrant D. [Hysterectomy for a benign lesion: can the vaginal route be used in all cases?] J Gynecol Obstet Biol Reprod (Paris) 1999; 28: 124–30 [in French].
- Kovac S. Clinical opinion: guidelines for hysterectomy. Am J Obstet Gynecol 2004; 191: 635–40.
- Unger JB, Meeks GR. Vaginal hysterectomy in women with history of previous caesarean delivery. Am J Obstet Gynecol 1998; 179: 1473–8.
- Clavé H, Niccolaï P. [Painless hysterectomy: an innovative technique]. J Gynecol Obstet Biol Reprod 2003; 32: 375–80 [in French].
- Miskry T, Magos A. Randomized, prospective, double bind comparison of abdominal and vaginal hysterectomy in women without uterovaginal prolapse. Acta Obstet Gynecol 2003; 82: 351–8.
- 18. Clavé H, Baar H, Niccolaï P. Painless vaginal hysterectomy with thermal hemostasis (results of a series of 152 cases). Gynecol Surg 2005; 2: 101–5.
- 19. Easton K, Read MD, Woodman NM. Influence of early discharge after hysterectomy on patient outcome and GP workloads. Br J Obstet Gynaecol 2003; 23: 271–5.
- Campbell ES, Xiao H, Smith MK. Types of hysterectomy: comparison of characteristics, hospital costs, utilization and outcomes. J Reprod Med 2003; 48: 943–9.
- Levy BL, Luciano DE, Emery LL. Outpatient vaginal hysterectomy is safe for patients and reduces institutional costs. J Minim Invasive Gynecol 2005; 12: 494–501.

Laparoscopic hysterectomy – historical perspective

Harry L Reich

INTRODUCTION

Laparoscopic hysterectomy, defined as the laparoscopic ligation of the uterine vessels, is a substitute for abdominal hysterectomy, with more attention to ureteral identification. Laparoscopic hysterectomy (LH) is rarely indicated for the treatment of abnormal uterine bleeding (AUB) from a normal-sized uterus with no other associated pathology! Most of these cases can be done vaginally without the use of a laparoscope.¹

BACKGROUND

Laparoscopic hysterectomy evolved from my commitment in the early 1980s to minimize abdominal incisions in all cases, usually by a combination of vaginal and laparoscopic surgery. This choice was facilitated by my discovery in 1976 that bipolar desiccation of infundibulopelvic ligaments was possible to control hemostasis from the ovarian blood supply. Since 1983, I have done fewer than 20 laparotomies.

I started my private practice in 1976, and vaginal surgery was my major area of interest. That year, I was the consultant for an infertility clinic that had over 100 active patients who had never been laparoscoped. I was trained to do a diagnostic laparoscopy and, when indicated, laparotomy surgery for excision of ovarian endometriosis and separation of tubal adhesions usually 2 months later. Before that year was out, I realized that many of these operations could be done at the time of diagnostic laparoscopy.

In 1983 I began photodocumenting all of my operations using an Olympus OM2 camera with CLEF light source system, after a visit to Bob Hunt during Boston Marathon week. I began using the laparoscope as a part of total vaginal hysterectomy (TVH) before 1983, whenever uncomfortable with an exclusively vaginal approach. Thus, by 1988, I had done many laparoscopic oophorectomies and lysis of adhesions procedures with TVH. Today these cases would be called laparoscopic-assisted vaginal hysterectomy (LAVH).²⁻⁴

I consider 1976–1983 to be my learning curve years. I prepared myself to be a successful laparoscopic surgeon. In 1985 I presented laparoscopic treatment of pelvic abscess at the American College of Obstetricians and Gynecologists (ACOG) and both laparoscopic endometrioma excision and laparoscopic electrosurgical oophorectomy at the American Association of Gynecologic Laparoscopists (AAGL). I began teaching these techniques soon thereafter and taught an advanced laparoscopic course at AAGL for the next 20 years. One year earlier Ron Levine presented laparoscopic oophorectomy using endoloop sutures after visiting Kurt Semm in Kiel, Germany. Ron then put together the first US freestanding laparoscopic surgery course in April 1986 in Louisville and invited me as part of the faculty, along with Semm, Hulka, and Hasson.

Please realize that these operations were done with the operating surgeon visualizing the operative field with his right eye with minimal assistance before 1986. Throughout the rest of the 1980s, I operated using my eye and with a beam splitter to the video monitor so my assistant surgical technician and my students could see.

FIRST LAPAROSCOPIC HYSTERECTOMY AND DEVELOPMENT OF TOTAL LAPAROSCOPIC HYSTERECTOMY CONCEPT

The first laparoscopic hysterectomy recorded in the literature was done in January 1988. This was called a laparoscopic hysterectomy, as the major blood supply to the uterus was secured laparoscopically. The only difference between this operation and total laparoscopic hysterectomy (TLH) is that the vaginal cuff was closed vaginally.^{5–8}

At that time, a group of residents and staff from Baystate Medical Center, Springfield, MA, under the direction of Larry Lundy and Percy Wadman, a former president of the Massachusetts Medical Society, would visit Kingston, PA, every month to learn laparoscopic surgical techniques. On their visit that week, the case involved a 14-week size symptomatic fibroid uterus. A 3 mm and a 5 mm lower quadrant trocar site was used. Rectosigmoid to left ovary adhesions were divided. I dissected, desiccated, and divided the left infundibulopelvic ligament and the right utero-ovarian ligament. I exposed the ureter and uterine vessels on each side. I decided to ligate the uterine vessels using bipolar desiccation instead of completing the operation from below vaginally, as was my usual custom. The uterine artery and vein on each side had been skeletonized. Each ureter had been exposed to demonstrate their distance from the area of the bipolar desiccation energy. An ammeter was used to monitor current flow to determine the endpoint of the bipolar desiccation process. In that operation I opened the vagina anteriorly and posteriorly before going vaginally to complete the procedure. Operation time was 3 hours. All instruments used were reusable, including the trocars.

Soon thereafter in 1988, the next problem was tackled: TLH. It was cumbersome and time consuming to change from operating laparoscopically to a vaginal position and then back again. And I worried about a position change with the patient asleep. I decided that the laparoscopic view was so good that the vagina could be opened circumferentially in most cases laparoscopically. I used a CO₂ laser through the operating channel of the operating laparoscope or electrical scissors to open the cervicovaginal junction posteriorly over a sponge forceps and anteriorly over a narrow Deaver in the anterior vagina and then connect the two incisions, usually with much lateral bleeding from ascending vaginal vessels and thick cardinal and uterosacral ligaments. The major problem, of course, was loss of pneumoperitoneum. We went through 2 years using wet packs, balloon catheters, and surgical gloves filled with air or fluid to maintain pneumoperitoneum during cuff suturing. It was always a struggle.

In December 1990 at the first meeting of the Society for Minimally Invasive Therapy (SMITS) in London, England, I met Professor Gerhart Buess from Germany who was suturing the rectum through a large anoscope manufactured by Wolf Instruments. This instrument was what I needed to be able to maintain pneumoperitoneum during the culdotomy incision of laparoscopic hysterectomy and to suture repair the vaginal cuff afterwards. Richard Wolf Instrument Company modified it for me. The concept was simple: the instrument had to be made longer than an anoscope and be approximately 4 cm in diameter. (There was too much leakage at 3.5 cm diameter in most women.) When applied to the cervix, the surgeon could see the junction of the anterior and the posterior vagina with the cervix. The posterior rim is longer than the anterior, so that the posterior fornix can be entered first. Thereafter, the anterior fornix is entered and the lateral vagina on each side is pushed upward and outward away from the ureters to complete the incision on each side without losing pneumoperitoneum. I believe most of the vaginal delineators that are now available on the market are modifications of the original idea that was developed in the early 1990s.^{7–9}

I have always emphasized that laparoscopic hysterectomy is a substitute for abdominal hysterectomy and not for vaginal hysterectomy. Since 1987, no patient was denied a vaginal or laparoscopic approach to hysterectomy except when advanced cancer was suspected. Uterine size and extent of endometriosis were not considered contraindications; rather, they were the reasons to do a laparoscopic approach. Less than 15% of my hysterectomy patients had surgical castration.

My early results were great. Between April 1983 and September 1991, 94 women underwent either LH or LAVH. Their average age at time of surgery was 46 years old, and the age range was 30–79 years old. The most common reason for surgery was a symptomatic fibroid uterus. The average operation lasted less than 3 hours. The average length of hospital stay was less than 2 days, and recuperation was rapid. There was one conversion to laparotomy following extensive adhesiolysis with incidental enterotomies.

The concept of laparoscopic hysterectomy along with the video was presented at US Surgical Corporation head-quarters in Norwalk, CT, January 1988, soon after it was done. Among the small group present were Victor Gomel, Ron Levine, Steve Corson, Clifford Wheeless, Camran Nezhat, and Steve Kaali. The company swiftly adopted the concept that surgeons would much rather use techniques other than electricity to ligate the uterine arteries. The development of a laparoscopic clip followed by a laparoscopic stapler were in the works in 1988 because of this presentation of laparoscopic hysterectomy to this small group in Norwalk, CT.

Unfortunately, big business goes into new fields for big business. Clinical trials were not necessary for the clip applier because of the huge demand for it from general surgeons using makeshift instrumentation. The same was true for the ENDO GIA, a great device for general surgery but with few gynecologic applications. So LAVH was born!

LAVH is not LH. It is an expensive vaginal hysterectomy. Gynecologists were encouraged to use the ENDO GIA device to do the easy upper pedicle part of a vaginal hysterectomy. Hospital administrators soon calculated that the cost of laparoscopic hysterectomy was exorbitant. Expensive disposable trocars followed by multiple firings of a stapling device cost more than the reimbursement from the managed care or other insurer at that time. Unlike cholecystectomy where the surgeon could operate using a disposable clip device with one or two firings from

a single instrument, laparoscopic hysterectomy required at least four firings of a surgical stapler. The operation cost too much. And remuneration from insurance companies for laparoscopic skills was poor. This, I believe, destroyed the option of having a laparoscopic hysterectomy operation for most women in the USA. The rest of the world rarely took to staples, and laparoscopic hysterectomy is thriving there.

The ENDO GIA was released in late 1990 early 1991. After it received Food and Drug Administration (FDA) permission, I used it for a laparoscopic appendectomy in the summer of 1990. On August 29, 1990, as a visiting surgeon and lecturer at Rochester General Hospital in Rochester, NY, I did the first two TLHs using the ENDO GIA stapler. Through much of 1991 I used the ENDO GIA for laparoscopic hysterectomy, always after ureteral dissection. Ureteral dissection was done in some cases after application of the GIA, and its broad distal tip was too close to the ureter for comfort. OK, so I went from bipolar desiccation to the ENDO GIA stapler. What was next? The acceptance level of laparoscopic hysterectomy had not improved. Hospitals did not want to pay for the expensive disposable instruments used by gynecology in contrast to their attitude towards general surgery operations.

At that time I felt that the best way to progress was to go back to a technique that we all knew from laparotomy, i.e. suture ligation of the uterine vessels. While I had only a 30-year experience with bipolar desiccation of large vessels, suture has been around for centuries! When one looks at the evolution of laparoscopic hysterectomy and laparoscopic surgery in general, one of the major obstacles to adoption was the perception that too much expensive gimmickry was used. The simple solution was to use sutures for ligation for the major vessels, similar to what was done during major laparotomy surgery. I believe that suture ligation of the uterine and ovarian vessels is the safest technique near the ureter. Adhesions from living tissue distal to a tie still bother me as they may be more prevalent than after bipolar desiccation.

More about suturing. When I met Kurt Semm in 1986 he observed desiccation of the ovarian blood supply with reserve. He encouraged me to learn how to suture. For that I thank him very much. I think that he was right: the ability to suture defines a laparoscopic surgeon. In the early days, 1986–1988, I used a small Keith needle and a slip knot like Kurt and Lisolotte Mettler. The persistence of Courteney Clarke led to my adopting his knot pusher to do extracorporeal ties by 1989. Soon thereafter, I developed my technique to get large curved needles into the peritoneal cavity using a 5 mm trocar, and from then on, I felt that I could operate as well or better than most laparotomy surgeons. ¹⁰

Why ligate the uterine arteries with suture instead of bipolar? If suture is used, it can be removed if a problem is suspected afterwards. Unless the surgeon is absolutely sure that the uterine arteries are a reasonable distance away from the ureters, suture is the best technique. Of course this means that the surgeon has to have some suturing skill. I've learned over the years that most general surgeons think it's very easy to suture from their right side from 3 o'clock to 6 o'clock or 6 o'clock to 9 o'clock but have difficulty suturing from 9 o'clock to 12 o'clock. This makes no sense. If the surgeon grasps the suture with his left hand instead of his right hand, it should be easy to accomplish suturing from 9 o'clock to 12 o'clock by rotating the wrist in a backhand motion.

So we have three events in the evolution of laparoscopic hysterectomy. First, the discovery that bipolar desiccation was possible for large-vessel hemostasis made the operation possible. Secondly, industry's recognition that staples could be used; disposable staples brought them into the ballgame. Thirdly, the safest technique is suture: usually, what you see is what you get with suture, with no danger of energy spread. In most cases where the vessels are isolated and separated from the ureter, bipolar desiccation works fine. Most gynecologists will not dissect the ureter. Thus, I believe that when the gynecologist sees the pulsation of the uterine artery, it is much safer to use the technique of ligation of the uterine vessels with suture and at the end of operation check the ureters by cystoscopy after indigo carmine dye intravenous push to be sure that dye flows out of the ureteral orifices. If it does not, it is simple to look back with the laparoscope and undo the suture to release a potential ureteral injury. 11,12

As we knew then and know today, TLH and related procedures can be done with reusable instrumentation. In fact most of the procedures that have been developed over the last 20 years in laparoscopic surgery can be done using reusable instrumentation available in most operating rooms. This knowledge really helps when teaching the technique around the world, as most countries where I introduced TLH (Chile, Spain, Australia, Italy, Russia, and Ireland) had no disposable instrumentation.

Finally, please realize that publication of laparoscopic gynecologic operations was very difficult in the 1980s, as few of the pioneers were in academic positions. Laparoscopic hysterectomy was unpublishable in 1988 and before. This has been a major struggle. In fact, many papers of substance on laparoscopic surgery in the early 1990s were in a journal that never got Index Medicus acceptance: *Gynecological Endoscopy*. This travesty in our system prevented over a decade of great work from many pioneers in laparoscopic surgery being quoted. I remember, with bitterness, my struggles to get bipolar oophorectomy and cul-de-sac dissection for deep fibrotic endometriosis published in the 1980s, despite teaching

these techniques to the professors. My paper on laparoscopic treatment of ovarian cancer received a harsh reaction in 1988 in the USA but not in Europe. 13,14

The ACOG committee on quality assurance released a statement in October 1995 describing the indication for LAVH as follows: 'to assist in the performance of a vaginal hysterectomy in situations in which an abdominal approach might otherwise be indicated'. This opinion persists to this day. TLH is not yet considered a separate procedure by the ACOG.

I believe that most hysterectomies can be done using a laparoscopic approach. It is certain that if the problem is bleeding, especially from a large fibroid uterus, it can be solved by TLH and the woman will be very pleased. Why are there so few laparoscopic hysterectomies done today? It is a major problem! Gynecologists today are not trained to do laparoscopic surgery. *Unfortunately they are not trained to do vaginal surgery, either.* The truth of the matter is that the very low payments for gynecologic surgery make it much more cost-effective to stay in the office and to avoid surgery if possible. The major problem for LH from its birth to the present remains inappropriate reimbursement for the work and the extra training involved in developing the appropriate expertise.

In the USA we continue avoid LH because of lack of training and the concept that laparoscopic surgery just takes too long. In our specialty, in-vitro fertilization (IVF) took off and laparoscopic surgery did not. Just look at the remuneration.

TOTAL LAPAROSCOPIC HYSTERECTOMY TECHNIQUE

My technique for a TLH is described, since other types of laparoscopic hysterectomy are simply modifications of this more extensive procedure. These steps are designed to prevent complications. Very little has changed in this technique since its publication in 1993, except for the incorporation of cystoscopy. In the original paper, TLH is a substitute for abdominal hysterectomy and not for vaginal hysterectomy. In the original paper laparoscopic vaginal vault closure with suspension with McCall culdoplasty was described. Uterine vessel ligation was also described. Curved needles were used, and pulled through the 5 mm incision using my technique.

Since hysterectomy is usually an elective procedure, the patient is counseled extensively regarding the range of currently available options appropriate to her individual clinical situation. In 2007, it is clearly not acceptable to advocate hysterectomy without detailing the risks and benefits of other intermediary procedures, such as myomectomy and/or excision of endometriosis with uterine preservation.

Whereas conversion to laparotomy when the surgeon becomes uncomfortable with the laparoscopic approach has never been considered a complication, conversion rates should be monitored to safeguard the consumer's right to have this procedure performed by a competent laparoscopic surgeon. Surgeons who do more than 25% of their hysterectomies with an abdominal incision should not taut their ability and degree of expertise with a laparoscopic approach to their patients. Perhaps, conversion to laparotomy should be considered a complication!

Preoperative preparation

The patient is optimized medically for coexistent problems. Patients are encouraged to hydrate on clear liquids the day before surgery. Fleet Phospho-soda 3 oz. divided into two doses is given at 3:30 pm and 7:30 pm to evacuate the lower bowel. If the patient is prone to nausea, Phenergan (promethazine) 25 mg orally is taken 25 minutes before the bowel prep. Lower abdominal, pubic, and perineal hair is not shaved. All laparoscopic procedures are done using general endotracheal anesthesia with orogastric tube suction to minimize bowel distention. The patient's arms are placed at her side and shoulder braces are positioned at the acromioclavicular joint. Trendelenburg position up to 40° is available. I use one dose of prophylactic antibiotics after induction of anesthesia.

Incisions

Three laparoscopic puncture sites, including the umbilicus, are used. Pneumoperitoneum to 25–30 mmHg is obtained before primary umbilical trocar insertion and reduced to 15 mmHg afterwards. The lower quadrant trocar sleeves are placed under direct laparoscopic vision lateral to the rectus abdominis muscles and just beside the anterior superior iliac spines in patients with large fibroids. The left lower quadrant puncture is my major portal for operative manipulation as I stand on the patient's left.

Reduction in wound morbidity and scar integrity as well as cosmesis are enhanced using 5 mm sites. The use of 12 mm incisions when a 5 mm incision will suffice is not an advance in minimally invasive surgery.

Vaginal preparation

Every year, new innovations for uterine and vaginal manipulation appear. The Valtchev uterine manipulator (Conkin Surgical Instruments, Toronto, Canada) has been around for more than 15 years and allows anterior, posterior, and lateral manipulation of the uterus and permits the surgeon to visualize the posterior cervix and vagina. Newer devices are currently available developed

by Pelosi, Wattiez, Hourcabie, Koninckx, Koh, McCartney, Donnez, and myself. I still use the Valtchev and the Wolf tube.

Exploration

The upper abdomen is inspected, and the appendix is identified. Clear vision is maintained throughout the operation using the I.C. Medical smoke evacuator (Phoenix, AZ). Endometriosis is excised before starting TLH. Bleeding is controlled with microbipolar forceps.

Retroperitoneal dissection

The peritoneum is opened early with scissors in front of the round ligament to allow CO₂ from the pneumoperitoneum to distend the retroperitoneum. The tip of the laparoscope is then used to perform 'optical dissection' of the retroperitoneal space by pushing it into the loosely distended areolar tissue parallel to the uterus to identify the uterine vessels, ureter, or both. The uterine artery is often ligated at this time, especially in large uterus patients.

Ureteral dissection (optional)

The ureter is identified medially, superiorly, or laterally (pararectal space). Stents are not used, as they may cause hematuria and ureteric spasm. The laparoscopic surgeon should dissect (skeletonize) either the ureter or the uterine vessels during the performance of a laparoscopic hysterectomy.

Bladder mobilization

The round ligaments are divided at their midportion, and scissors or a spoon electrode is used to divide the vesicouterine peritoneal fold starting at the left side and continuing across the midline to the right round ligament. The upper junction of the vesicouterine fold is identified as a white line firmly attached to the uterus, with 2–3 cm between it and the bladder dome. The initial incision is made below the white line while lifting the bladder. The bladder is mobilized off the uterus and upper vagina using scissors or bluntly until the anterior vagina is identified. The tendinous attachments of the bladder in this area may be desiccated or dissected.

Upper uterine blood supply

When oophorectomy is indicated or desired, the peritoneum is opened on each side of the infundibulopelvic ligament with scissors and a 2/0 Vicryl (polyglactin 910)

free ligature passed through the window created and tied extracorporeally using the Clarke–Reich knot pusher. This maneuver is repeated until two proximal and one distal ties are placed, and the ligament divided. This maneuver helps develop suturing skills. The broad ligament is divided to the round ligament just lateral to the utero-ovarian artery anastomosis using scissors or cutting current through a spoon electrode. I rarely desiccate the infundibulopelvic ligament as it results in too much smoke early in the operation.

When ovarian preservation is desired, the utero-ovarian ligament and fallopian tube are compressed and coagulated until desiccated with bipolar forceps, at 25–35 W cutting current, and then divided. Alternatively, the utero-ovarian ligament and fallopian tube pedicles are suture ligated adjacent to the uterus with 2/0 Vicryl, using a free ligature passed through a window created around the ligament. Stapling devices are rarely used.

If the ovary is to be preserved and the uterus large, the utero-ovarian ligament/round ligament/fallopian tube junction may be divided with a 30 or 45 mm GIA type stapler. This may be time saving for this portion of the procedure, thus justifying its increased cost.

Many complications are related to the use of staplers: although operative time is decreased, the risk for post-operative hemorrhage and injury to the ureter is increased. Ligation or coagulation of the vascular pedicles is safer.

Uterine vessel ligation

The uterine vessels may be ligated at their origin, at the site where they cross the ureter, where they join the uterus, or on the side of the uterus. Most surgeons use bipolar desiccation to ligate these vessels, but this author prefers suture because it can be removed if ureteral compromise is suggested at cystoscopy.^{11,12}

In most cases, the uterine vessels are suture ligated as they ascend the sides of the uterus. The broad ligament is skeletonized to the uterine vessels. Each uterine vessel pedicle is suture ligated with 0 Vicryl on a CTB-1 blunt needle (Ethicon JB260) (27 inch), as a blunt needle reduces surrounding venous bleeding. The needles are introduced into the peritoneal cavity by pulling them through a 5 mm incision. 15 A short, rotary movement of the needle holder brings the needle around the uterine vessel pedicle. This motion is backhand if done with the left hand from the patient's left side and forward motion if using the right hand from the right side. In some cases, the vessels can be skeletonized completely and a 2-0 Vicryl free suture ligature passed around them. Sutures are tied extracorporeally using a Clarke-Reich knot pusher.

In large uterus patients, selective ligation of the uterine artery without its adjacent vein is done to give the uterus a chance to return its blood supply to the general circulation. It also results in a less voluminous uterus for morcellation.

Division of cervicovaginal attachments and circumferential culdotomy

The cardinal ligaments on each side are divided. Bipolar forceps coagulate the uterosacral ligaments. The vagina is entered posteriorly over the uterovaginal manipulator near the cervicovaginal junction. A 4 cm diameter reusable vaginal delineator tube (R. Wolf, Vernon Hills, IL) is placed in the vagina to prevent loss of pneumoperitoneum and to outline the cervicovaginal junction circumferentially as it is incised using the CO_2 laser to complete the circumferential culdotomy with the delineator as a backstop. The uterus is morcellated, if necessary, and pulled out of the vagina.

Morcellation (laparoscopic and vaginal)

Morcellation can be done laparoscopically or vaginally. Vaginal morcellation is done with a No. 10 blade on a long knife handle to make a circumferential incision into the uterus while pulling outwards on the cervix and using the cervix as a fulcrum. The myometrium is incised circumferentially parallel to the axis of the uterine cavity with the scalpel's tip always inside the myomatous tissue and pointed centrally, away from the surrounding vagina.

Morcellation through anterior abdominal wall sites is done when vaginal access is limited or supracervical hysterectomy requested. Reusable electromechanical morcellators are motorized circular saws. Using claw forceps or a tenaculum to grasp the fibroid and pull it into contact with the fibroid, large pieces of myomatous tissue are removed piecemeal until the myoma can be pulled out through the trocar incision. With practice, this instrument can often be inserted through a stretched 5 mm incision without an accompanying trocar. The new Sawalhe morcellator from Karl Storz (Karl Storz Endoscopy-America, Inc., Culver City, CA) comes with 12 mm, 15 mm, and 20 mm diameter circular saws.

Laparoscopic vaginal vault closure and suspension with Mccall culdeplasty¹⁶

The vaginal delineator tube is placed back into the vagina for closure of the vaginal cuff, occluding it to maintain pneumoperitoneum. The uterosacral ligaments are identified by bipolar desiccation markings or with the aid of a rectal probe. The first suture is complicated as it brings the uterosacral and cardinal ligaments as well as the rectovaginal fascia together. This single suture is tied extracorporeally, bringing the uterosacral ligaments, cardinal ligaments, and posterior vaginal fascia together across the midline. It provides excellent support to the vaginal cuff apex, elevating it and its endopelvic fascia superiorly and posteriorly toward the hollow of the sacrum. The rest of the vagina and overlying pubocervicovesicular fascia are closed vertically with one or two 0 Vicryl interrupted sutures.

Cystoscopy^{11,12}

Cystoscopy is done after vaginal closure to check for ureteral patency in most cases, after intravenous administration of indigo carmine dye. This is necessary when the ureter is identified but not dissected and especially necessary when the ureter has not been identified. Blue dye should be visualized through both ureteral orifices. The bladder wall should also be inspected for suture and thermal defects.

Underwater examination

At the close of each operation, an underwater examination is used to detect bleeding from vessels and viscera tamponaded during the procedure by the increased intraperitoneal pressure of the CO₂ pneumoperitoneum. The CO₂ pneumoperitoneum is displaced with 2–4 L of Ringer's lactate solution, and the peritoneal cavity is vigorously irrigated and suctioned until the effluent is clear of blood products. Any further bleeding is controlled underwater using microbipolar forceps to coagulate through the electrolyte solution, and 2 L of lactated Ringer's solution are left in the peritoneal cavity.

Skin closure

The vertical intraumbilical incision is closed with a single 4-0 Vicryl suture opposing deep fascia and skin dermis, with the knot buried beneath the fascia. This will prevent the suture from acting like a wick, transmitting bacteria into the soft tissue or peritoneal cavity. The lower quadrant 5 mm incisions are loosely approximated with a Javid vascular clamp (V. Mueller, McGraw Park, IL) and covered with Collodion (AMEND, Irvington, NJ) to allow drainage of excess Ringer's lactate solution.

CONCLUSION

Laparoscopic hysterectomy was first performed in January 1988. The sine qua non for laparoscopic hysterectomy is

the laparoscopic ligation of the uterine vessels either by electrosurgical desiccation, suture ligature, or staples. Although hysterectomy is not the most difficult laparoscopic procedure, it can be long and tedious because four very well-defined vascular pedicles must be ligated.

In 1988 no one was thinking about doing hysterectomy by laparoscopy. The major centers in the world doing laparoscopic surgery were in Clermont Ferrand, France and in Kiel, Germany. I acknowledge that Kurt Semm, Maurice Bruhat, and Hubert Manhes were great influences because they also knew no boundaries. However, most of my thinking was original.

The type of laparoscopic hysterectomy is usually defined by the extent of laparoscopic dissection performed during the procedure. The recently published Cochrane review of the surgical approach to hysterectomy uses the description of different techniques detailed by Reich and Roberts, which is based on the definitions published by Garry et al.

Recent papers by Clayton and the Cochrane database reviewed evidence-based hysterectomy studies and conclude that vaginal hysterectomy (VH) is preferable to abdominal hysterectomy (AH). There is no evidence to support the use of LH if VH can be done safely. Compared to AH, LH is associated with less blood loss, shorter hospital stay, and a speedier return to normal activities, but it takes longer, costs more, and urinary tract injuries are more likely. Vaginal hysterectomy should be the preferred route when applicable. Laparoscopic hysterectomy should be considered as an alternative to abdominal hysterectomy. 15,19,20

It took 5 years for laparoscopic cholecystectomy to be universally adopted! Laparoscopic hysterectomy has been available for the last 20 years with sporadic acceptance. TLH has no billing code in the USA!

Remuneration at a low level for laparoscopic skills in gynecology has curbed the enthusiasm for training in minimally invasive surgery in our specialty in the USA. Practitioners faced with shrinking reimbursement and rising costs must spend more time in the office and less in surgery. Abdominal hysterectomy is the preferred method of treatment based on training and economics, and, this poses an ethical dilemma. Are we offering the best choices to our patients? We, as specialists, need to answer this question. Why would physicians take time to learn a new technique if they are going to be poorly reimbursed?

So, how can we train the specialists of tomorrow in minimally invasive and vaginal surgery? Unfortunately, I do not know, but the answer has a strong financial component.

Laparoscopic hysterectomy is clearly beneficial for patients in whom vaginal surgery is contraindicated or cannot be done. When indications for the vaginal approach are equivocal, laparoscopy can be used to determine if vaginal hysterectomy is possible. With this philosophy, patients avoid an abdominal incision with resultant decrease in length of hospital stay and recuperation time. The laparoscopic surgeon should be aware of the risks and how to minimize them, and, when they occur, how to repair them laparoscopically.

References

- 1. Reich H. Hysterectomy as treatment for dysfunctional uterine bleeding. In: Smith SK, ed. Baillière's Clinical Obstetrics and Gynecology. Dysfunctional Uterine Bleeding. London: Harcourt Health Sciences, 1999; 13: 251–69.
- Reich H, McGlynn F. Laparoscopic oophorectomy and salpingo-oophorectomy in the treatment of benign tuboovarian disease. J Reprod Med 1986; 31: 609.
- Reich H. Laparoscopic oophorectomy and salpingo-oophorectomy in the treatment of benign tuboovarian disease. Int J Fertil 1987; 32: 233–6.
- Reich H. Laparoscopic oophorectomy without ligature or morcellation. Contemp Ob/Gyn 1989; 34: 34.
- Reich H, DeCaprio J, McGlynn F. Laparoscopic hysterectomy. J Gynecol Surg 1989; 5: 213–6.
- Reich H. Laparoscopic hysterectomy. Surgical Laparoscopy Endoscopy. New York: Raven Press, 1992; 2: 85–8.
- Reich H, McGlynn F, Sekel L. Total laparoscopic hysterectomy. Gynecol Endosc 1993; 2: 59–63.
- Garry R, Reich H. Laparoscopic Hysterectomy. Oxford: Blackwell Scientific, 1993.

- 9. The role of laparoscopy in hysterectomy. In: Rock JA, Faro S, Gant NF, Horowitz IR, Murphy A, eds. Advances in Obstetrics and Gynecology, Vol 1. St Louis: Mosby Year Book, 1994.
- Reich H, Clarke HC, Sekel L. A simple method for ligating in operative laparoscopy with straight and curved needles. Obstet Gynecol 1992; 79: 143–7.
- 11. Ribeiro S, Reich H, Rosenberg J. The value of intra-operative cystoscopy at the time of laparoscopic hysterectomy. Hum Reprod 1999; 14: 1727–9.
- 12. Reich H. Letters to the Editor. Ureteral injuries after laparoscopic hysterectomy. Hum Reprod 2000; 15: 733–4.
- Reich H, McGlynn F, Wilkie W. Laparoscopic management of Stage I ovarian cancer. J Reprod Med 1990; 35: 601–5.
- Reich H, McGlynn F, Wilkie W. Laparoscopic management of stage I ovarian cancer: a case report. Obstet Gynecol Surv 1990; 45: 772–4.
- 15. Clayton RD. Hysterectomy: best practice and research. Clin Obstet Gynecol 2006; 20: 1–15.
- Reich H, Orbuch I, Seckin T. Reich modification of the McCall culdeplasty to prevent and/or repair prolapse during total

- laparoscopic hysterectomy. In: Jain N, ed. Complete Manual & Atlas of Laparoscopic Suturing. New Delhi, India: Jay Pee Brothers, 2006: 78–82.
- 17. Garry R, Reich H, Liu CY. Laparoscopic hysterectomy definitions and indications. Gynecol Endosc 1994; 3: 1–3.
- 18. Reich H, Roberts L. Laparoscopic hysterectomy in current gynecological practice. Rev Gynecol Pract 2003; 3: 32–40.
- 19. Johnson N, Barlow D, Lethaby A et al. Surgical approach to hysterectomy for benign gynecological disease. Cochrane Database Syst Rev 2005; (1): CD003677.
- Johnson N, Barlow D, Lethaby A. Methods of hysterectomy: systematic review and meta-analysis of randomized controlled trials. BMJ 2005; 330: 1478–81.

Charles E Miller

INTRODUCTION

No one can argue that the ultimate treatment of abnormal uterine bleeding is hysterectomy. Since the first lap-aroscopic hysterectomy was reported by Reich et al.¹ in 1989, the laparoscopic approach was meant to replace total abdominal hysterectomy whenever possible, not vaginal hysterectomy. However, as will be discussed later in this chapter, quality of life data now exist giving credence to performing a laparoscopic hysterectomy instead of total vaginal hysterectomy.²

Munro and Parker have classified laparoscopic hysterectomy into four different categories.³ In this chapter, type III laparoscopic hysterectomy, i.e. total laparoscopic hysterectomy, is discussed. In the total laparoscopic hysterectomy, the entire procedure is performed via the laparoscope. This includes treatment of ancillary pathology prior to the initiation of the hysterectomy, ureterolysis as necessary, detachment of the uterus from its ligamentous support structure, securing the vascularity to the uterus, mobilization of the bladder off the cervix, and amputation of the cervix and uterus from the vagina. Ultimately, the specimen is removed via the vagina, and the cuff repaired laparoscopically, or the cuff repaired via the laparoscope prior to morcellation of the uterus and cervix if the uterus is too large to be delivered into the vagina.

Particularly when vaginal access is limited, as in the case of nulliparity, pelvic adhesions/frozen pelvis, a narrow pubic arch, or large uterine fibroids, it is advantageous to perform total laparoscopic hysterectomy.

TECHNICAL CONCEPTS AND CONCERNS

Fundamentally, total laparoscopic hysterectomy involves a series of steps that can be grouped into specific surgical techniques. Instrumentation ultimately must be available that allows the surgeon to proceed safely with minimal risk to nearby structures (ureters, rectum, bladder). In a total laparoscopic hysterectomy, the surgeon must be comfortable with the following techniques.

Dissection

Whether the adnexa are mobilized off the pelvic sidewall, endometriosis excised, adhesions are excised in the culde-sac to free an adherent uterus, ureterolysis performed, the bladder mobilized off the cervix, the uterine vessels skeletonized, or the cervix amputated from the vagina, dissection is involved. Instrumentation for this endeavor must enable cutting with some hemostasis. Desiccation and deep thermal damage can prove to be harmful, especially near the bowel, bladder, or ureter.

Desiccation/vessel sealing

Vascular pedicles, the infundibulopelvic ligament, uteroovarian ligament, and the uterine vessel complex require desiccation of tissue prior to transection. Even with the need for desiccation, lateral spread of energy must be considered to keep vital structures out of harm's way. Newer instrumentation enables less lateral spread of energy through vessel sealing: Harmonic ACE (Ethicon Endo-Surgery, Cincinnati, OH); EnSeal (SurgRx, Rodwood city, CA); LigaSure (Valleylab, Boulder, CO); and PlasmaKinetic (Gyrus, ACMI, MN) (Figures 39.1 and 39.2).

Suture repair

At present the vaginal cuff must be repaired with suture. If a total laparoscopic hysterectomy is to be performed, the step must be completed via a laparoscopic route. Excellent support and vaginal cuff repair can be gained with a continuous suture, mattress-style suturing, or interrupted sutures incorporating the cuff, uterosacral ligament, and cardinal ligament. Nevertheless, for most, the ability to suture the vaginal cuff is the rate-limiting step, and often times the 'deal breaker'.

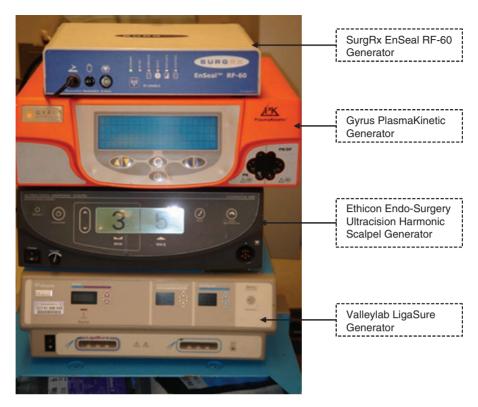


Figure 39.1 Instrumentation for total laparoscopic hysterectomy.



Figure 39.2 Instrumentation for total laparoscopic hysterectomy.

Morcellation of Specimen

Whereas, most of the time, the uterus (with or without the ovaries and tubes) can be removed prior to closure of the uterine cuff by placing the specimen in the vagina, at times, due to a large myomatous uterus, the specimen must be morcellated via an abdominal route. Although a knife can be used, specific instrumentation is available and safer: Morcellex (Ethicon Women's Health and Urology, (Cincinatti, OH); Sawalhe Morcellator (Karl Storz, Tuttlingen, Germany); Serrated Edge Macro-Morcellator (WISAP, Munich, Germany).

INSTRUMENTATION

The fact is that no surgical instrument offers perfect cutting and coagulation ability – the single dissector/desiccator does not exist for every case. Therefore, it is incumbent upon gynecologic surgeons to understand and avail themselves of state-of-the-art instrumentation.

Whereas monopolar electrosurgery can be used for cutting and thus tissue dissection, and bipolar electrosurgery used for tissue desiccation, these techniques must be used prudently. In both cases, energy effects follow the path of least resistance, and therefore, lateral destruction of tissue can occur.

To reduce the risk of deep tissue necrosis and potential damage to adjacent structures, vessel sealing devices can be used. The LigaSure, the PlasmaKinetic, and the EnSeal are all smart generators which utilize bipolar energy, but are associated with far less lateral distribution of energy. Unfortunately, all are disposable instruments and, therefore, the procedure cost is increased. In addition, these instruments are all poor cutting devices; each utilizes a sharp blade to cut through tissue after it has been desiccated.

It would appear that ultrasonic energy, in particular the Harmonic ACE offers the best ability to dissect, seal, and desiccate vessels with minimal lateral tissue destruction. Electrical energy is converted to mechanical energy. The tip of the Harmonic ACE moves in a 'to and fro' motion 55500 times per second: at level 1, the blade excursion is 50 µm, at level 3, the blade excursion is 70 µm and at level 5, it is 100 µm. Greater blade excursion translates into better cutting, while shorter blade movement yields more desiccation. To enhance cutting, tissue should be put on stretch, whereas tissue is relaxed if desiccation and coagulation are desired. Even though the Harmonic ACE has been designed to coagulate vessels up to 7 mm in size, its use over uterine vessels is, at times, inadequate. In this case, bipolar electrosurgery or a vessel sealing instrument is utilized.

SURGICAL APPROACH FOR TOTAL LAPAROSCOPIC HYSTERECTOMY

Step 1

Place the Foley catheter inside the bladder.

Step 2

Perform the examination under anesthesia.

Step 3

Place the uterine manipulator deep into the uterus. The device must be placed deep enough in the uterus to allow anterior, posterior, and lateral movement of the uterus. Consider use of a uterine manipulator with a cup to place around the cervix: VCare (ConMed, Corporation, Utica, NY) and Koh Colpotomizer (CooperSurgical, Lake Forest, CA). Ultimately, the vagina is entered by cutting over the cup. Moreover, the cup is helpful in maintaining the pneumoperitoneum.

Step 4

Place the laparoscope through the 5 mm umbilical port. Consider a 'supra' umbilical port for visualization, if the uterus is ≥16 weeks' size.

Step 5

Place bilateral 5 mm ports above and lateral to the uterus. Depending on the uterus size, place ports above the umbilicus (Figure 39.3).

Step 6

Prior to hysterectomy, normalize the pelvis; i.e. perform adhesiolysis, resection of endometriosis, ovarian cystectomy, appendectomy, etc. The uterus and adnexae must be mobile.

Step 7

At the very least, identify the course of each ureter through the peritoneum. If the ureter cannot be visualized, scarring is noted over the pelvic sidewall, endometriosis is noted over the ureter, or a culdoplasty is to be performed at the end of the procedure, perform ureterolysis. Ureterolysis should begin at the pelvic brim and continue until the ureter dives underneath the uterine vessels.

Step 8

If the adnexa cannot be visualized, secondary to uterine myomata, perform myomectomy (see Chapter 31). Only a one-layer closure is necessary to bring the uterus edges together.



Figure 39.3 Ports are placed above the umbilicus secondary to the large uterus with fibroids.

Step 9

If ovaries are to be conserved, transect the proximal fallopian tube and the utero-ovarian ligament with the Harmonic ACE at level 3 or desiccate, then transect with the bladed LigaSure, PlasmaKinetic, or EnSeal. If the adnexa is to be removed, transect the infundibulopelvic ligament with the Harmonic ACE at level 3 or desiccate and transect with the bladed EnSeal, LigaSure, or PlasmaKinetic. Make sure to take the infundibulopelvic ligament off stretch as it is sealed and transected (Figure 39.4).

Step 10

Continue peritoneal dissection to the mid portion of the round ligament. If using the Harmonic ACE, simply transect at level 5. If one of the 'smart' generators is utilized, continue the desiccation and cutting technique. Do not venture too close to the uterus, as vessels cascade and risk of bleeding increases (Figure 39.5).

Step 11

Open the medial posterior broad ligament to the level of the uterosacral ligament. Use the Harmonic ACE at level 5 or the smart generators using the blade to cut.

Step 12

Similarly open up the cervicovesicouterine peritoneum (Figure 39.6).

Step 13

Mobilize the bladder off cervix.



Figure 39.4 Transection of right utero-ovarian ligament with Harmonic ACE.

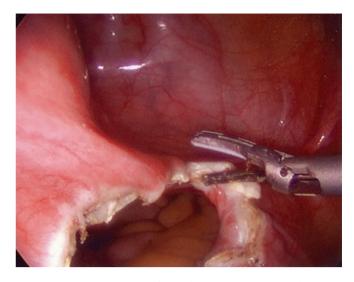


Figure 39.5 Transection of round ligament with EnSeal.



Figure 39.6 Harmonic ACE has been utilized to open up the medial posterior broad ligament and the cervicovesicouterine peritoneum.

Step 14

Skeletonize the uterine vessels (Figure 39.7).

Step 15

Transect the uterine vessels. Remember to relax the uterus. Use the Harmonic ACE at level 2 or the smart generators using the bladed instruments (Figure 39.8).

Step 16

Similarly transect the remaining cardinal ligament and uterosacral ligament.

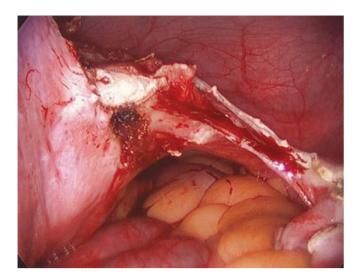


Figure 39.7 Skeletonized uterine vessels.

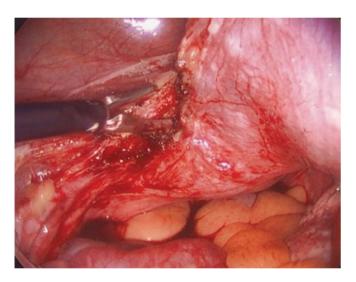


Figure 39.8 Sealing uterine vessels prior to transection with the PlasmaKinetic Lyons forceps.

Step 17

Repeat on the opposite side.

Step 18

If a uterine manipulator has a Koh Colpotomizer cup or a VCare system with a cup, cut around the cup to amputate the cervix and uterus from the vagina. If not, enter the vagina at the uterosacral ligament. If the pneumoperitoneum is lost, place a Kerlex in a surgical glove and place this in the vagina (Figure 39.9).

Step 19

Remove the specimen through the vagina.

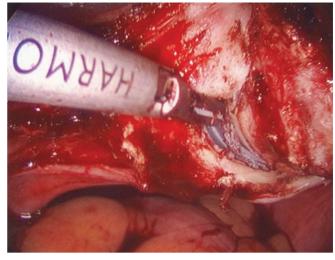


Figure 39.9 Amputating the cervix from vagina utilizing the VCare cup.

Step 20

Backload 0 PDS (polydioxanone suture) on a CT1 needle and place through lateral 5 mm port sight.

Step 21

Place 'angle' sutures bilaterally, incorporating the respective uterosacral ligaments and remainder of the cardinal ligament.

Step 22

Place one or two 'mattress' sutures midline to finish the cuff closure (Figure 39.10).



Figure 39.10 Repaired uterus cuff.

DISCUSSION

As Parker⁴ stated in *Obstetrics and Gynecology Clinics of North America*, in 2000, few randomized prospective studies that involve large numbers of patients have compared the risks and benefits of laparoscopic hysterectomy with standard hysterectomy.

Nevertheless, total laparoscopic hysterectomy appears to be a safe surgical procedure. As reported in *Human Reproduction*⁵ in 1996, Chapron et al. noted an overall complication rate of 10% in 222 total laparoscopic hysterectomy patients. Only two patients required reoperation (vesicovaginal fistula, vaginal cuff separation).

Wattiez et al.⁶ compared the frequency of complications of total laparoscopic hysterectomy based on years of experience with the procedure. When comparing complications with total laparoscopic hysterectomies in the periods 1989 to 1995 (695 cases) and 1996–1999 (952 women), substantial decreases in major complications were noted (5.6 % vs 1.3%), hemorrhage (1.9% vs 0.1%), blood transfusion (2.2% vs 01.%), and urinary complications (2.2% vs 0.9%). Conversions to laparotomy were greater in the first 6 years (4.7% vs 1.4%), nine patients requiring reoperations in 1989–1995, whereas three reoperations were required in 1996–1999. This despite the fact that uterine size significantly increased (179.5 g vs 292 g) and operating time decreased (179.5 minutes vs 90 minutes).

In 2002, Seracchioli et al.⁷ prospectively compared total laparoscopic hysterectomy with abdominal hysterectomy in the presence of a uterus >14 weeks' gestation. Sixty women underwent total laparoscopic hysterectomy and 62 patients had total abdominal hysterectomy. Operating time and hemoglobin drop were the same in both groups. One patient required conversion secondary to bowel injury, whereas one patient in the total abdominal hysterectomy group had a bladder injury. Febrile morbidity was also greater in the laparotomy group.

Recently, a prospective randomized study comparing laparoscopic supracervical hysterectomy and total laparoscopic hysterectomy was published by Morelli et al.⁸ One hundred and forty-one patients who complained of symptomatic uterine leiomyomata, abnormal bleeding refractory to hormonal treatment, or both were randomly assigned to receive a laparoscopic supracervical hysterectomy (71 patients) or total laparoscopic hysterectomy (70 patients). No statistical significant differences in the rate of complications, degree of symptomatic improvement, or activity limitation was noted.

In 2007, Ng and Chern⁹ retrospectively reported on their 5-year experience of total laparoscopic hysterectomy, using the Rumi Uterine Manipulator with the Koh Colpotomizer System. Of 512 women converted for total laparoscopic hysterectomy, 503 women had successful completion (98.2%); mean blood loss was 309 ml, and 20 patients required transfusion. Twenty-three patients (4.5%) suffered major complications.

In 2006, a Cochrane review evaluated 27 randomized controlled trials involving 3643 patients in an attempt to determine the desired approach to hysterectomy. While supracervical hysterectomy was excluded, all trials compared at least one hysterectomy approach to another for patients undergoing surgery for benign gynecologic disease. Ultimately, 16 trials compared laparoscopic with abdominal hysterectomy, four compared laparoscopic with vaginal hysterectomy. Major outcomes were as follows:

- Urinary tract injuries appear to be more likely in patients undergoing laparoscopic hysterectomy, no differences were found between vaginal hysterectomy and laparoscopic hysterectomy with respect to intraoperative injury or bleeding, conversion to laparotomy, duration of hospital stay, or return to normal activity.
- When comparing a laparoscopic approach with abdominal and vaginal hysterectomy, no differences were noted in occurrences of pelvic hematoma, vaginal cuff infection, urinary tract infection, pneumonia, or thromboembolic events. No differences were found for long-term fistula formation, urinary dysfunction, sexual dysfunction, or patient satisfaction.
- Return to work activities were slower post abdominal hysterectomy vs laparoscopic or vaginal hysterectomy.
- Total laparoscopic hysterectomy was associated with the longest operating room time, when compared to laparoscopic-assisted vaginal hysterectomy, abdominal or vaginal hysterectomy.

The single largest randomized trial cited by the Cochrane Database was the eVALuate trial. This consisted of a conglomerate of multicenter randomized controlled trials that evaluated the relative role of vaginal hysterectomy, abdominal hysterectomy, and laparoscopic hysterectomy. In one study, 292 women were assigned to abdominal hysterectomy, while 584 women were assigned to laparoscopic hysterectomy. The second study involved 504 women: one in three were assigned to vaginal hysterectomy, and two in three underwent laparoscopy. The studies only allowed women with benign disease with a uterus 12 weeks' size or less. Excluded were women with second- or third-degree prolapse, patients undergoing bladder or pelvic support surgery, and women unable to

undergo laparoscopy. The authors noted the following findings:

- Major complications were more likely to be noted in the laparoscopy vs abdominal hysterectomy group (11% vs 6%). Minor complications were virtually the same (25% vs 27%).
- Laparoscopic hysterectomy required longer operating time than abdominal hysterectomy (84 minutes vs 50 minutes).
- Laparoscopic hysterectomy took longer to perform than vaginal hysterectomy (72 minutes vs 39 minutes).
- Patients undergoing a laparoscopic hysterectomy were noted to have less pain in the postoperative state than the patients undergoing an abdominal hysterectomy. In addition, laparoscopic hysterectomy was associated with shorter hospitalization and a better quality of life at 6 weeks.
- Unexpected pathology was more likely to be recognized with the laparoscopic hysterectomy group than with either of the other two groups.

Finally, in quality of life and surgical outcome comparisons of total laparoscopic hysterectomy and total abdominal hysterectomy for benign disease, Kluivers et al. 12 noted that the laparoscopic approach resulted in 'more postoperative vitality'. This randomized controlled trial included 27 women allocated to the laparoscopic arm and 32 patients undergoing total abdominal hysterectomy. A significant treatment effect favoring laparoscopic hysterectomy was noted in the RAND 36 Item Health Survey for vitality. Furthermore, laparoscopic hysterectomy performed better on all other scales of the RAND 36, but these differences were not statistically significant.

CONCLUSION

Laparoscopic hysterectomy is a safe surgical procedure. It represents the ultimate treatment for abnormal uterine bleeding. Prior to surgery, it is important to properly work-up the patient. Moreover, technique minimizing risk to bladder, ureter, and rectum is essential. Besides safety, another advantage of laparoscopic hysterectomy appears to be a quick return to normal activity.

References

- Reich H, DeCaprio J, McGlynn F, Wilkie WL, Longo S. Peritoneal trophoblastic tissue implants after laparoscopic treatment of tubal ectopic pregnancy. Fertil Steril 1989; 52(2): 337–9.
- 2. Morelli M, Caruso M, Noia R et al. [Total laparoscopic hyster-ectomy versus vaginal hysterectomy: a prospective randomized trial]. Minerva Ginecol 2007; 59(2): 99–105 [in Italian].
- Munro MG, Parker WH. A classification system for laparoscopic hysterectomy. Obstet Gynecol 1993; 82(4 Pt 1): 624–9.
- 4. Parker WH. Total laparoscopic hysterectomy. Obstet Gynecol Clin North Am 2000; 27(2): 431–40.
- Chapron C, Dubuisson J, Ansquer Y. Is total laparoscopic hysterectomy a safe surgical procedure? Human Repro 1996; 11(11): 2422–4.
- 6. Wattiez A, Soriano D, Cohen SB, Nervo P et al. The learning curve of total laparoscopic hysterectomy: comparative analysis of 1647 cases. J Am Assoc Gynecol Laparosc 2002; 9(3): 339–45
- Seracchioli R, Venturoli S, Vianello F et al. Total laparoscopic hysterectomy compared with abdominal hysterectomy in the presence of a large uterus. J Am Assoc Gynecol Laparosc 2002; 9(3): 333–8.

- 8. Morelli M, Noia R, Chiodo D et al. [Laparoscopic supracervical hysterectomy versus laparoscopic total hysterectomy: a prospective randomized study]. Minerva Ginecol 2007; 59(1): 1–10 [in Italian].
- Ng CC, Chern BS. Total laparoscopic hysterectomy: a 5-year experience. Arch Gynecol Obstet May 17, 2007 [Epub ahead of print].
- Johnson N, Barlow D, Lethaby A et al. Surgical approach to hysterectomy for benign gynecological disease. Cochrane Database Syst Rev 2006; (2): CD003677.
- Garry R, Fountain J, Mason S et al. The eVALuate study: two parallel randomized trials, one comparing laparoscopic with abdominal hysterectomy, the other comparing laparoscopic with vaginal hysterectomy. BMJ 2004; 328(7432): 129.
- Kluivers KB, Hendriks JC, Mod BW et al. Quality of life and surgical outcome after total laparoscopic hysterectomy versus total abdominal hysterectomy for benign disease: a randomized, controlled trial. J Minim Invasive Gynecol 2007; 14(2): 145–52.

Laparoscopic supracervical hysterectomy

Thomas L Lyons and Wendy K Winer

INTRODUCTION

Hysterectomy as a procedure has developed in a predominately antisurgical environment as an effective and efficient procedure that has been of benefit to those women who have undergone the procedure. All surgical procedures currently in widespread use have been subjected to thorough clinical evaluation and have met the basic criterion required by ethical physicians for continued usage. Hysterectomy, as stated by Finley in 1943, must be used to (1) save life, (2) correct deformity, or (3) eliminate suffering.

Historically, this procedure dates meaningfully only to the turn of the century when it was used predominately to treat large tumors of the uterus (usually fibroids by description) and to treat catastrophic uterine bleeding. The largest number of these procedures was performed in a subtotal or supracervical manner, and morbidity and mortality (M&M) was significant. The reasons for this high rate of M&M were poor anesthesia techniques, absence of antibiotic therapy, and lack modern blood banking procedures. Thus, if a patient had a prolonged surgical procedure, bleeding of significance, or infection, there was a real chance of loss of life. During the first half of the 20th century gradual progress was made in the technical aspects of the procedure such that by the mid 1940s, when anesthesia was improving and antibiotics became available, mortality rates decreased rapidly. The procedure became safe enough to be warranted even to treat such benign conditions as pelvic floor prolapse.

In addition, another influence was present at that time. The existing mortality rate from cervical carcinoma was high, making this disease the third most common killer of women in the USA. For all of these reasons a change was destined to come about. Between 1940 and 1955 the rate of total vs subtotal hysterectomy was reversed. Whereas the subtotal rate was 85–95% in the early 1940s, by 1955 the subtotal rate was less than 5%. The stated reason for this shift was to lower the death rate from cervical cancer. This stated goal was not accomplished until Papanicolaou (Pap) smears became routine in the USA in 1958. However, the wholesale extirpation

of cervices continued for the next 40 years, with over one million total hysterectomies being performed in 1975.

In the late 1980s a revolution was about in the USA with laparoscopic cholecystectomy being introduced, rapid technological development, and surgeons grasping the concept of the lowered morbidity of minimally invasive surgery. Although gynecologists were the leaders in this revolution, the movement into more advanced procedures by the generalist OB/Gyn seemed to be mired. Reich first reported laparoscopic-assisted vaginal hysterectomy (LAVH) in 1989 and the push began.¹

It is imperative to emphasize that the goal of all minimally invasive procedures should be to accomplish the surgical task in an efficient manner while lowering the morbidity for the patient. This was the goal of LAVH and it is a goal which, when studied carefully, has been accomplished. Reich, Liu, and others have expanded the indications for this procedure to the point where if a patient has indications for hysterectomy and cannot have a total vaginal hysterectomy (TVH), then LAVH should be considered.^{1,2}

After a careful examination of the procedure and the needs of the patients involved, and, as always with the directive of lowering morbidity, in 1990 this author began a series of trials of laparoscopic supracervical hysterectomy (LSH). We felt that this was warranted because of the known lower morbidity of the supracervical procedure. Furthermore, the possibility of maintaining the procedure as a totally laparoscopic procedure offered a potential simplification to the average operator. After completing a series of these procedures and comparing them to a group of demographically similar patients undergoing LAVH, we found that LSH was a significantly lower morbidity procedure. Over the next 10 years we performed approximately 750 procedures with continued low morbidity, while treating uteri up to 2400 g, stage IV endometriosis, severe pelvic inflammatory disease (PID), ovarian cancer, leiomyosacoma, and total pelvic floor prolapse.³⁻⁵ These patients continued to have a remarkable recovery, with lower than normal morbidity despite the increased complexity of the procedures. Of course, the learning curve played a role in these statistics, but the clinical results were sufficient to warrant the continuation of the LSH procedure.

INDICATIONS

The LSH procedure can be the procedure of choice for most of those patients in whom hysterectomy is indicated. There are of course some specific contraindications which will be emphasized. Therefore, the list of indications is as follows:

- (1) Dysfunctional uterine bleeding.
- (2) Symptomatic uterine leiomyomata.
- (3) Pelvic pain.
- (4) Endometriosis.
- (5) Pelvic floor prolapse.
- (6) Ovarian cancer.
- (7) PID.

The absolute contraindications for the procedure are:

- (1) Endometrial cancer.
- (2) Invasive cervical cancer.
- (3) Pelvic floor relaxation in a patient with a retroverted uterus and a short anterior wall (<7 cm).
- (4) Any patient who cannot be expected to continue cytologic surveillance.

The real risk of cervical disease is no greater than in that patient with an intact uterus, but the patient should be counseled regarding continued Pap smears. The discussion should include an explanation of not only the potential benefits of maintenance of the cervix but also the possible liabilities of the cervix in situ.

TECHNIQUE

LSH is performed by this author as described in Telinde, with the exception that laparoscopic incisions are substituted for the midline or Pfannenstiel incision. First, the patient is consented for LSH and laparotomy. A discussion is held regarding continued cytologic surveillance and is documented in the chart. Bowel preparation with GoLYTELY or magnesium citrate is advised and preoperative antibiotics are prescribed (usually 1 g of cephalosporin intravenously 1 hour prior to surgery). Bowel

prep and antibiotic use may vary but should correspond to the prep that is desired by the gynecologist's consulting general surgeon. Simplification of the procedure and emphasis on preoperative preparation must be stressed.

The room set-up is critical to the efficiency of the procedure. The patient is placed in the modified dorsal lithotomy position in low stirrups. Allen stirrups or a similar device are recommended, as positioning is critical for the safety and success of the procedure. The surgeon should be present for and monitor this positioning until s/he is comfortable that the operating room (OR) team is totally comptetent in this activity. In the end it will be the operator's responsibility medicolegally and, therefore, it is imperative to assure that this is done properly. To this point, it is important to acknowledge the need for a team approach to this type of surgery. In order to become efficient, team members should be well schooled in their role; in the procedure and the importance of the role. This area has been addressed by Winer, 6 and cannot be overemphasized.

The devices used to complete the procedure are much to the prerogatives of the surgeon. Vascular pedicles must be isolated and occluded. Laparoscopically, this may be accomplished using suture, staples, clips, Harmonic Scalpel, bipolar electrosurgery, monopolar electrosurgery, or some form of laser energy. All of these energy forms have strengths and weaknesses, but it is wise for the operator to have working knowledge of all of these modalities and use those that best suit the particular style of that operator. In this book we descibe the use of bipolar energy for larger-vessel occlusion and the use of the contact Nd:YAG laser as a cutting device. We favor the Harmonic Scalpel as a cutter/coagulator and monopolar electrosurgery as a primary cutting device. We also use suture in selected cases as a large-vessel occlusive device.

The procedure begins with careful positioning of the patient. The monitors are placed at or toward the foot of the table, so that the operator can operate into the monitors, thus eliminating the need to work in a 'mirror image'. Any time the operator works at an angle of ≥90° (into or toward the laparoscope), the 'mirror image' is created, reversing the directions needed within the operative field.

After the sterile prep is complete, the uterine manipulator is placed. The use of an effective manipulator is critical. We have used both the Valchev and the Pelosi manipulators with success, but we favor the Pelosi. The manipulator is critical as a retractor and definitely aids in efficient completion of this task. Whatever the uterine size, the manipulator is key. There are advantages to the use of either the Valchev or the Pelosi, which enable both anteversion and retroflexion as well as rotation and lateral displacement, all using only one hand. Furthermore, the fact that the device is fixed to the cervix is of critical importance in the physics of the stated task.

The next step involves placement of trocars. The trocar scheme used by the present authors is based upon experience from several thousand cases but should not be considered as fixed in stone. Several key points should, however, be noted. First, the subumbilical trocar is placed using the open or Hasson technique and is 10/12 mm. The open technique is used because of the frequent treatment of women with very large uteri and/or multiple prior abdominal procedures. Other primary trocar techniques can certainly be considered, but the operator should select a technique that he is familiar with and suits the clinical situation. Next, the distribution of the lateral trocars is well lateral on the abdominal wall. This lateral placement, as well the need to place the trocars above the pathology, particularly in the large uterus, is again helpful to facilitate adequate retraction and access to the vascular pedicles. When possible, 5 mm trocars are used, particularly in the lateral sites. The lower midline trocar is 10/11 mm and is used later for suturing and for morcelpation of the specimen. In the very large uterus, the primary subumbilical trocar becomes the lower midline trocar and two 5 mm trocars are placed laterally on each side to accomplish the procedure. We currently use disposable trocars from Ethicon Endo-Surgery, but reusable devices may be used. The trocars should be threaded or gripped to the skin/fascia, as otherwise unwanted pullout can occur, which makes the procedure more difficult as well as lengthier. All secondary trocars should be placed under direct visualization with the laparoscope A 10 mm operating laparoscope is placed through the upper midline port and the contact Nd:YAG (neodynium: yttrium-aluminum-garnet) laser scalpel (Surgical Laser Technologies, Philadelphia, PA) is passed through the operating channel of the laparoscope. A 45° 10 mm scope is also kept on hand, particularly for the large uterus, as this can be very helpful if the fibroid obscures a straight-on view of the operative field. The BiCoag bipolar dissector/grasper (Everest Medical Corp, Minneapolis, MN) is used first through the left lower lateral port. An atraumatic grasper is used through the right lateral port and the suction irrigation device is placed in the midline lower portal.

The procedure then proceeds by exploration, adhesiolysis, and restoration of anatomy. At this point in the procedure, when possible, we perform ureterolysis. In this procedure, an incision is made medial to the ureter, beginning in the midpelvic area, and this incision is extended down to the level of the uterosacral ligaments. This serves two purposes. First, the ureter is identified and marked so that it is easily found later. Therefore, if bleeding occurs, and control of this bleeding is necessary, the potential for injury to the ureter is decreased. Secondly, this allows for aggressive support of the vault using a high McCall's culdoplasty at termination of the procedure without ureteral kinking or compromise.

Then the round ligaments, tubes, and utero-ovarian pedicle are desiccated on the specimen side to decrease back-bleeding. The round ligament is divided and the anterior uterovesical fold is scored with the laser scalpel and the bladder flap developed. The posterior leaf of the broad ligament is also scored down the specimen side and the vasculature is skeletonized. If the adnexa are to be taken, the infundibulopelvic ligament is desiccated and divided in typical fashion. The ureter is constantly in view due to the ureterolysis incision. Once the uterine vessels are skeletonized, these vascular pedicles can be taken with the bipolar placed in the ipsilateral lower lateral port with good countertraction being applied from the contralateral port and the uterine manipulator. The bipolar is placed at a right angle/perpendicular to the lateral uterus, which allows for a better occlusion of the spiral uterine vascular pedicle and allows the heat energy from the bipolar to displace into the specimen rather than away from the uterus and toward the ureter. The manipulator is pushed inward toward the patient's contralateral shoulder, thus increasing the distance from the lateral uterine wall and the ureter, which has been released by the ureterolysis incision further creating a safe margin for this desiccation process. Once these vascular pedicles are occluded, the uterus will become cyanotic, indicating that it is devascularized.

From this point, the procedure is very straightforward, with amputation of the cervix coring well down into the endocervical canal. This amputation should begin at the level of the internal os or at the level of entry into the uterus of the uterine vessels, and an aggressive attempt to core downward into the cervix should be used while pushing upward with the manipulator. Endocervical mucus is almost always visualized during this amputation, assuring that the operator is low enough and that no lower uterine segment is being left behind. Ablation of the remaining endocervical canal using bipolar is performed and then the cervical stump is closed using a 0 Vicryl (polyglactin 910) suture on a CT2 needle. The vault is then supported with ipsilateral McCall's sutures of 0 Ethibond suture.

The final portion of the procedure is specimen removal. We now use the mechanical morcellator from Gynecare. This device, which is called the DIVA, has been very useful and requires the use of a 10 mm single-toothed tenaculum to work at maximum efficiency. The device will fit through the lower trocar site and requires minimal practice to obtain proficiency. Other morcellators (Storz, WISAP) are available, but the DIVA has been the most efficient that we have found to date.

After all the specimen is removed, the abdomen is thoroughly irrigated, the fluid is removed, and the lower 10/11 mm site is closed using the Carter–Thomason fascial closure device. The larger sites receive a subcuticular closure and the 5 mm sites are steri-stripped. All sites

are injected with 0.25% Marcaine (bupivacaine) with epinephrine and dressings are applied.

Postoperative care allows the patient to be discharged from the surgical facility within 24 hours. The Foley catheter is removed in the recovery room and ambulation is encouraged. The patient is allowed to perform all activities in which she is comfortable. Individuals are able to return to normal activity within a few days and are able to return to work within 1–2 weeks.

CLINICAL EXPERIENCE, DATA, AND COMPLICATIONS

Various authors have reported retrospective series of the LSH procedures. The largest series was described by Donnez, with over 500 procedures.⁷ In this, as well as a 500 case series reported by Daniell,⁸ the morbidity was extremely low again, justifying the continuance of the procedure. The present author's series is now at >1800 procedures with continuing low morbidity and clinical outcomes based on patient satisfaction surveys and morbidity statistics. Data are given in Table 40.1.

There is more information on a form of supracervical hysterectomy called the CISH (classic intrafascial supracervical hysterectomy) procedure. This procedure was first reported by Semm in 1991. 10 Although technically this is also a supracervical hysterectomy, it differs sufficiently from LSH to separate the data and not include it in this discussion. Data from this literature are shown in Table 40.2.

Garry et al's meta-analysis (eVALUate study) of all forms of laparoscopic hysterectomies clearly shows that unless laparotomy is considered a 'complication', laparoscopic hysterectomy is the lowest morbidity procedure, although a cost analysis suggests that vaginal hysterectomy is the most cost-efficient. There have been other studies by Simon et al, Zupi, and others that demonstrate LSH to be the preferred procedure with reference to cost as well as other factors. He present author has demonstrated clearly over a >5 year period that M&M data in patients with large (>300 g) and very large (>500 g) was superior with LSH as compared with other traditional methods of hysterectomy. Bojahr et al have demonstrated similar low morbidity and complication rates associated with LSH in a large series (1706) of patients in a single clinical setting. Is

Table 40.1 Series of LSH procedures

Donnez (1997) ⁷	500 patients	60–810 g	0.6% complications
		30–135 minutes	
Daniell (1999) ⁸	500 patients	Size?	<1% complications
		90 minutes (mean)	
Lyons (1995) ⁹	294 patients	65–2180 g	< 1% complications
		55–224 minutes	

 Table 40.2
 The CISH procedure

Semm (1996) ¹¹	90 patients	Weight ?	0% complications!
		90 minutes (mean)	
Mettler (1995) ¹²	200 patients	50–250 g	'Minimal complications'
		120-240 minutes	
Levine (1996) ¹³	100 patients	27–950 g	3% complications
		105–240 minutes	
Vietz (1996) ¹⁴	60 patients	Weight?	0% 'major complications'
		90 minutes (mean)	

DISCUSSION

Hysterectomy is an effective procedure when used in appropriate patients requiring uterine extirpation. There are adequate data to support the use of this procedure for the treatment of abnormal uterine bleeding, symptomatic uterine leiomyoma, endometriosis, PID, atypical adenomatous hyperplasia, endometrial cancer, ovarian cancer, adenomyosis, and pelvic pain. Although the procedure has in the past been overused at times, the safety and efficiency of the surgery has not been questioned. In this era of attempts to control both the medical and economic morbidity of surgical procedures, minimally invasive alternatives have been developed. Such was the case with laparoscopic cholecystectomy in 1988 and such is the case with laparoscopic hysterectomy since its inception in 1989. LSH was proposed by the present author in 1990 as a possible alternative with further decreased morbidity and possible extended applications. Simon et al have evaluated the economic morbidity of the LSH procedure as compared with total abdominal hysterectomy in a community hospital setting.16 This study concluded that LSH was a costeffective alternative in those patients with indications for hysterectomy. This author's experience is now nearing 2000 patients. In this single surgeon's experience, three laparotomies have occurred, there have been no transfusions, no deaths, and all morbidity categories have remained well under a fraction of 1%. Satisfaction rates have remained

over 95% and recurrent symptomology (particularly with persistent cyclic bleeding <0.1%) has been minimal.

LSH has as its most positive attributes decreased overall morbidity, application to virtually any size uterus, probable improved overall pelvic floor support secondary to the intact pericervical ring, and intact neurovascular supply. In addition, the subtotal approach in virtually all cases adequately addresses the pathology associated with the admitting diagnosis.

Many women in today's world are concerned with destructive surgeries to the reproductive anatomy and the associated psychosocial effects of these procedures. LSH is a legitimate alternative for these individuals, offering a less-invasive and less-destructive procedure that can still eliminate the symptom complex which brings them to the surgical theater. Kilku has addressed these concerns in a series of articles in the mid 1980s. 19–21 Hasson also discussed this issue in an excellent review of subtotal hysterectomy in 1995. 22

The final factor is choice. Today's woman is an intelligent and well-informed consumer who is willing to get sufficient opinions until satisfied with her physician's recommendations. She is informed of the issues and the medical alternatives available and will demand these alternatives. Those surgeons who are willing to discuss these options and apply them to appropriate patients may find greater success and a less litigious atmosphere than those who attempt to patronize their clientele.

References

- 1. Reich H, DiCaprio J, McGlynn F. Laparoscopic hysterectomy. J Gynecol Surg 1989; 5: 213–16.
- 2. Liu CY. Laparoscopic hysterectomy. Report of 215 cases. Gynecol Endosc 1992; 1: 73–7.
- 3. Lyons TL. Laparoscopic supracervical hysterectomy a comparison of morbidity and mortality results with laparoscopically assisted vaginal hysterectomy. J Reprod Med 1993; 38: 763–7.
- Lyons TL. Subtotal hysterectomy. In: Diamond MP, Daniell JF, Jones HA, eds. Hysterectomy. Cambridge, MA: Blackwell Science, 1995: 84–98.
- Lyons TL. Laparoscopic supracervical hysterectomy. In: Wood C, Maher PJ, eds. Ballière's Clinical Obstetrics and Gynecology. London: Ballière & Tindall, 1997: 167–81.
- 6. Winer WK. Operating room personnel. In: Sanflippo JS, Levine RL, eds. Operative Gynecologic Endoscopy, 2nd edn. New York: Springer-Verlag, 1996: 412–22.
- 7. Donnez J, Nisolle M, Smets M et al. Laparoscopic supracervical (subtotal) hysterectomy: a first series of 500 cases. Gynecol Endosc 1997; 6: 73–6.
- 8. Daniell
- 9. Lyons

- Semm K. [Hysterectomy via laparotomy or pelviscopy. A new CASH method without culpotomy]. Geburtshilfe Frauenheilkd 1991; 51: 996–1003 [in German].
- Semm K. Endoscopic subtotal hysterectomy without culpotomy: classic intrafascial SEMM hysterectomy. A new method of hysterectomy by pelviscopy, laparotomy, per vaginam or functionally by total uterine mucosal ablation. Int Surgery 1996; 81: 362–70.
- Mettler L, Semm K, Lehmann-Willenbrode L et al. Comparative evaluation of classic intrafascial-supracervical hysterectomy (CISH) with transuterine mucosal resection as performed by pelviscopy and laparotomy – our first 200 cases. Surg Endosc 1995; 9: 418–23.
- 13. Levine DJ, Botney K. The classic intrafascial SEMM hysterectomy as an alternative to abdominal hysterectomy. J Am Assoc Gynecol Laparosc 1996; 3: 545–8.
- 14. Vietz PF, Ahn TS. A new approach to hysterectomy without culpotomy: pelviscopic intrafascial hysterectomy. Am J Obstet Gynecol 1994; 170: 609–13.
- Garry R, Fountain J, Brown J et al. EVALUATE hysterectomy trial: a multicentre randomised trial comparing abdominal,

- vaginal and laparoscopic methods of hysterectomy. Health Technol Assess 2004; 8: 1–154.
- Simon NV, Laveran RL, Cavanaugh S et al. Laparoscopic supracervical hysterectomy vs abdominal hysterectomy in a community hospital. A cost comparison. J Reprod Med 1999; 44: 339–45.
- 17. Zupi E, Zullo F, Marconi D et al. Hysteroscopic endometrial resection versus laparoscopic supracervical hysterectomy for menorrhagia: a prospective randomized trial. Am J Obstet Gynecol 2003; 188: 7–12.
- Bojahr B, Raatz D, Schonleber G, Abri C, Ohlinger R. Perioperative complication rate in 1706 patients after a standardized laparoscopic supracervical hysterectomy technique. J Minim Invasive Gynecol 2006; 13: 183–9.
- 19. Kilkku P. Supravaginal amputation versus hysterectomy with reference to bladder symptoms and incontinence. Acta Obstet Gynecol Scand 1985; 64: 375–9.
- Kilkku P, Hirvonen T, Gronoos M. Supracervical uterine amputation vs abdominal hysterectomy: the effects in urinary symptoms with special reference to pollakisuria, nocturia, and dysuria. Maturitas 1981; 3: 197.
- Kilkku P, Gronoos M, Hirvonen T et al. Supravaginal uterine amputation vs hysterectomy. Effects on libido and orgasm. Acta Obstet Gynecol Scand 1983; 62: 147–52.
- 22. Hasson

Further reading

- Anderson TL, Lindsay JH, Daniell JF. Performing laparoscopic supracervical hysterectomy. OBG Management 1999; January: 15–32.
- Brown RL. Iatrogenic endometriosis caused by uterine morcellation during a supracervical hysterectomy. Obstet Gynecol 2004; 103: 583; author reply 583–4.
- Chang WC, Li TC, Lin CC. The effect of physician experience on costs and clinical outcomes of laparoscopic-assisted vaginal hysterectomy: a multivariate analysis. J Am Assoc Gynecol Laparosc 2003; 10: 356–9.
- The Danish Hysterectomy Group. Randomized controlled trial of total compared with subtotal hysterectomy with 1 year follow up. Br J Obstet Gynaecol 2003; 110: 1088–98.
- Decenzo JA. Iatrogenic endometriosis caused by uterine morcellation during a supracervical hysterectomy. Obstet Gynecol 2004; 103: 583; author reply 583–4.
- El-Mowafi D, Madkour W, Lall C et al. Laparoscopic supracervical hysterectomy versus laparoscopic-assisted vaginal hysterectomy. J Am Assoc Gynecol Laparosc 2004; 11: 175–80.
- Ghomi A, Hantes J, Lotze EC. Incidence of cyclical bleeding after laparoscopic supracervical hysterectomy. J Minim Invasive Gynecol 2005; 12: 201–5.
- Hasson HM. Cervical removal at hysterectomy for benign disease. J Reprod Med 1993; 38: 781–90.
- Hilger WS, Magrina JF. Removal of pelvic leiomyomata and endometriosis five years after supracervical hysterectomy. Obstet Gynecol 2006; 108: 772–4.
- Hoffman CP, Kennedy J, Borschel L et al. Laparoscopic hysterectomy: the Kaiser Permanente San Diego experience. J Minim Invasive Gynecol 2005; 12: 16–24.
- Huang JY, Ziegler C, Tulandi T. Cervical stump necrosis and septic shock after laparoscopic supracervical hysterectomy. J Minim Invasive Gynecol 2005; 12: 162–4.
- Jenkins TR. Laparoscopic supracervical hysterectomy. Am J Obstet Gynecol 2004; 191: 1875–84.
- Kim DH, Lee YS, Lee ES. Alteration of sexual function after classic intrafascial supracervical hysterectomy and total hysterectomy. J Am Assoc Gynecol Laparosc 2003; 10: 60–4.
- Kim DH, Lee ES, Park SD. A safer, simpler, classic intrafascial supracervical hysterectomy technique. JSLS 2005; 9: 159–62.

- Lieng M, Istre O, Langebrekke A et al. Outpatient laparoscopic supracervical hysterectomy with assistance of the lap loop. J Minim Invasive Gynecol 2005; 12: 290–4.
- Lyons TL, Adolph AJ, Winer WK. Laparoscopic supracervical hysterectomy for the large uterus. J Am Assoc Gynecol Laparosc 2004; 11: 170–4.
- Mettler L, Ahmed-Ebbiary N, Schollmeyer T. Laparoscopic hysterectomy: challenges and limitations. Minim Invasive Ther Allied Technol 2005; 14: 145–59.
- Morrison JE, Jacobs VR. Outpatient laparoscopic hysterectomy in a rural ambulatory surgery center. J Am Assoc Gynecol Laparosc 2004; 11: 359–64.
- Morrison JE, Jacobs VR. Classic intrafascial supracervical hysterectomy (CISH): 10-year experience. JSLS 2006; 10: 26–9.
- Parker WH. Total laparoscopic hysterectomy and laparoscopic supracervical hysterectomy. Obstet Gynecol Clin North Am 2004; 31: 523–37, viii.
- Pasic R, Scobee J, Tolar B. Ectopic pregnancy months after laparoscopic supracervical hysterectomy. J Am Assoc Gynecol Laparosc 2004; 11: 94–5.
- Sarmini OR, Lefholz K, Froeschke HP. A comparison of laparoscopic supracervical hysterectomy and total abdominal hysterectomy outcomes. J Minim Invasive Gynecol 2005; 12: 121–4.
- Sepilian V, Della Badia C. Iatrogenic endometriosis caused by uterine morcellation during a supracervical hysterectomy. Obstet Gynecol 2003; 102(5 Pt 2): 1125–7.
- Thakar R, Ayers S, Clarkson P, Stanton S, Manyonda I. Outcomes after total vs subtotal abdominal hysterectomy. N Engl J Med 2002; 347: 1318–25.
- Thompson JD, Warsaw J. Hysterectomy. In: Rock JA, Thompson JD, eds. Telinde's Operative Gynecology, 8th edn. New York: Lippincott-Raven, 1996: 771–854.
- Total or Supracervical Hysterectomy Research Group. A randomized comparison of total versus supracervical hysterectomy: surgical complications and clinical outcomes. Obstet Gynecol 2003; 102: 453–62.
- Washington JL. Laparoscopic supracervical hysterectomy compared with abdominal, vaginal, and laparoscopic vaginal hysterectomy in a primary care hospital setting. JSLS 2005; 9: 292–7.

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Laparoscopic-assisted vaginal hysterectomy and abnormal uterine bleeding

Melissa Cameron and Peter J Maher

INTRODUCTION

Despite an increasing number of medical and surgical options for management of abnormal uterine bleeding, hysterectomy remains the definitive treatment. It has been shown to be associated with greater improvement in general health, particularly when compared with endometrial destruction techniques.¹

Questions remain regarding long-term data which compare hysterectomy with medical therapies. Overall quality of life is significantly better with major surgical intervention when compared with long-term medication and is at least equal in the short term when compared with the levonorgestrel intrauterine system (LNG-IUS; Mirena).² Additionally, hysterectomy has the obvious advantage over all other treatments in that it provides permanent relief from the symptoms of abnormal uterine bleeding.

This surgical procedure, of course, goes back many hundreds of years with evidence of vaginal hysterectomy (VH) occurring before the coming of Christ. Abdominal hysterectomy (AH), on the other hand, was first performed by Charles Clay in England in 1843. It was a further 10 years before the first successful procedure was performed in America, when, in fact, the patient survived. Since those early days, the route chosen to remove the uterus has been dictated by the skill and preference of the surgeon, which in turn is often dictated by the pathology present.

Little changed in the surgical techniques adopted until the late 1970s and early 1980s when Kurt Semm in Germany (Kiel) and Harry Reich in the USA independently developed techniques whereby the hysterectomy was performed with the assistance of the operating laparoscope and relatively crude laparoscopic instruments. This alternative to AH avoided the need for a large, painful abdominal incision and prolonged recuperation. It was not developed with the intent of replacing VH. Harry Reich then went on to perform the world's first total laparoscopic hysterectomy (TLH) in 1988, which was subsequently published the following year.³

Other doctors, keen to be seen to be adopting these new techniques, pursued a modification of the (TLH) and performed only part of the procedure laparoscopically. In fact, many of them performed diagnostic laparoscopy and then went on to finish the procedure vaginally while others performed small procedures laparoscopically, such as division of the top of the broad ligament, including the round ligament, before transferring to the vaginal approach.

The term that covers this approach, 'laparoscopic-assisted vaginal hysterectomy' (LAVH), encompasses a broad spectrum of approaches and is open to individual interpretation. Laparoscopic occlusion of the uterine vessels is considered the definitive step that distinguishes 'laparoscopic-assisted vaginal' from 'laparoscopic-assisted' hysterectomy. Table 41.1 illustrates the wide variety of specifications of the laparoscope and hysterectomy.

The uptake of laparoscopic-assisted hysterectomy (LAH) has, to say the least, been disappointing over the last 15 years. The reasons for this we are sure are many, with time concerns often quoted as the main reason for lack of interest in perfecting this procedure. The impact of a concurrent busy obstetric practice, as is the case with many gynecologists, is also prohibitive. Reich, in his original manuscript, described suture ligation of the uterine vessels laparoscopically, together with laparoscopic bladder reflection, colpotomy, and laparoscopic suture of the vaginal vault once the uterus had been removed. All of these techniques did and still do take time and skill and it would seem few surgeons are prepared to involve themselves in protracted surgical sessions.

INSTRUMENTATION FOR THE LAPAROSCOPIC APPROACH

Actual instrumentation required to perform laparoscopic hysterectomy has changed very little over the last 15–20 years. During the early days of advanced laparoscopic

Table 41.1 Classification of laparoscopic hysterectomy

- (1) Diagnostic laparoscopy with vaginal hysterectomy
- (2) Minor operative laparoscopy with vaginal hysterectomy
- (3) Laparoscopic-assisted vaginal hysterectomy (LAVH)
- (4) Laparoscopic-assisted hysterectomy LAH (uterine vessels only taken laparoscopically)
- (5) Total laparoscopic hysterectomy (TLH)
- (6) Laparoscopic-assisted minilaparotomy hysterectomy
- (7) Laparoscopic hysterectomy with lymph node dissection
- (8) Laparoscopic radical hysterectomy

Source: H Reich – pers comm.

surgery, a plethora of instruments adorned the instrument table in the operating theater. With experience, most gynecologists realize that very few instruments are required. Special instruments may be necessary in certain circumstances, but in most cases plain and toothed forceps, bipolar and monopolar power and suction irrigation, together with a camera, telescope, and instruments for the vaginal portion are all that is necessary. Reusable instruments will assist in limiting the cost of the procedure. There have been advances in the type and number of uterine manipulators present. The authors still use the Valtchev or Pelosi uterine stabilizer as standard, particularly when LAVH is contemplated. In some instances, for anatomic reasons, complete laparoscopic hysterectomy is performed, and in these circumstances some form of vaginal cup is necessary to prevent loss of pneumoperitoneum when the vagina is opened. Since its introduction, the McCartney Tube (Tyco Healthcare, Inc., Sydney Australia) has been the device of choice.

Many power sources have been tried through recent years, with personal preference of the surgeon dictating whether the Harmonic Scalpel (Ethicon Endo-Surgery, Inc., Cincinnati, OH), Ligasure (Tyco), PK System SEAL (Gyru International Ltd, Berkshire, UK) or Enseal Sealing Systems or the standard reusable Kleppinger-type forceps are chosen.

PATIENT SUITABILITY

When counseling a patient on the place of LAVH, it is also important to discuss alternatives such as medical treatment (tranexamic acid or progesterones) or the levonorgestrel-containing intrauterine device (Mirena) and the various endometrial ablation techniques that are available.

A precise medical history and adequate physical examination will alert the surgeon to underlying medical problems and physical contraindications to the usual placement of trocars. Any medical condition that is considered a contraindication to prolonged Trendelenburg positioning of the patient during surgery will influence the choice of treatment best suited to the patient.

Careful vaginal examination may detect pouch of Douglas nodularity or uterosacral thickening, which together may be considered diagnostic of severe endometriosis and a contraindication to the laparoscopic approach in particular for the less-experienced surgeon. Office ultrasound will provide clarification of the uterine size, presence of fibroids, and the existence of ovarian pathology before the route of hysterectomy is chosen.

All of this information is essential when, in consultation with the patient, the surgeon decides to proceed with the laparoscopic approach.

Garry, Reich, and Liu suggested a scoring symptom which would help the surgeon assess the suitability of the patient for laparoscopic hysterectomy (Table 41.2). Vaginal hysterectomy is likely to be successful in patients with scores <10. Laparoscopic or abdominal approaches were suggested for patients scoring >10. These criteria probably have little place today in the assessment of a patient's suitability, but were important at a time when the laparoscopic approach hysterectomy was very much under the microscope.⁴

Well-accepted criteria that were overlooked in this early publication, which have always been considered important in determining the route of hysterectomy (abdominal vs vaginal), are the mobility of the uterus and the vaginal access. These criteria are important in determining whether LAVH can replace the abdominal route in cases not suitable for vaginal hysterectomy.

Obesity

Surgery on obese patients presents several challenges for the operator and the anesthetist, regardless of the type of surgery or the approach chosen. An abdominal approach to hysterectomy is associated with increased perioperative complications such as infection and wound breakdown.^{5,6} The laparoscopic approach, however, has been shown to be associated with fewer such complications⁷ and may therefore be an advantage.

Despite these purported advantages, difficulties specific to the laparoscopic approach remain and must be taken into consideration during the planning process. Access to the pouch of Douglas may be hampered by increased mesenteric and pericolic fat. Retroperitoneal structures such as the ureter and inferior epigastric arteries can be difficult to identify and may therefore be at greater risk of injury.⁸

Table 41.2 Scoring system for suitability of the laparoscopic approach to hysterectomy

Parameter	Points
Uterine size	
Grade I: <8 weeks	1
Grade II: 8–12 weeks	3
Grade III: 12–16 weeks	5
Grade IV: >16 weeks	8
Mobility of adnexa as judged by stretched length of infundibulopelvic ligament	
Good: >5 cm	1
Moderate: 2–5 cm	3
Poor: <2 cm	5
Adhesion of adnexa	
None/mild: no significant paratubal or periovarian adhesions	1
Moderate: periovarian and/or paratubal adhesions without fixation; minimal cul-de-sac adhesions	3
Severe: dense pelvic or adnexal adhesions with fixation of ovary and tube to either broad ligament, pelvic wall, omentum, and/or bowel; severe cul-de-sac adhesions	5
Status of cul-de-sac	
Accessible	0
Obliterated	5
Rectal nodule	8
Endometriosis (American Fertility Society Classification)	
Stage I	1
Stage II	2
Stage III	3
Stage IV	4

From Reich et al. 4

It is extremely important to have a complete medical assessment of the obese patient prior to the commencement of surgery. Anesthetic considerations are paramount and a preoperative consultation with the anesthetist is an important aspect of risk management in these circumstances. When the hysterectomy is performed for a benign gynecologic condition, consideration should be given to postpone the procedure until the patient has lost weight. Professional dietary advice and an appropriate exercise regimen will be beneficial in achieving this goal.

Surgeon factors

The skill of the surgeon is of paramount importance. Appropriate training in units specializing in advanced endoscopic surgery is the only safe way for those interested in upskilling themselves to achieve a satisfactory level of expertise in laparoscopic surgery. The Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG), in conjunction with the Australian Gynaecological Endoscopy Society (AGES), have established guidelines for the performance of advanced laparoscopic procedures. These guidelines recommend attainment of Level 4 skills in order to perform an LAVH. If the operator does not have Level 4 or an equivalent skill level, adequate supervision or preceptoring by an experienced person is mandatory. Other societies around the world have similarly introduced levels of proficiency regarded as necessary to perform this type of surgery. Surgical assistants and operating room nursing

staff should also have adequate training in gynecologic laparoscopic techniques.

Consent

Special attention should be given to all the complications peculiar to laparoscopic surgery as well as those known to be associated with other types of hysterectomy. Informed consent should involve discussion of the risks and benefits of the procedure, and also information should be provided of the various alternative medical and surgical treatments available.

OPERATIVE CARE

Instrumentation and set-up

Laparoscopic hysterectomy is a cost-effective procedure when performed with reusable instruments. There are a plethora of instruments available to perform laparoscopic surgery, but there are very few required to successfully perform this procedure in the majority of cases. The following instruments should constitute the standard set required for performing this procedure:

- Veress needle or Hasson cannula (totally dependent on surgeon's choice)
- laparoscopic atraumatic forceps × 1
- laparoscopic grasping forceps × 2
- monopolar diathermy with spatula
- bipolar coagulation forceps
- laparoscopic curved scissors
- 0° or 30° laparoscope 5/10 mm (surgeon's preference)
- suction–irrigation device
- laparoscopic needle holders × 2
- · knot pusher
- uterine manipulator (Valtchev or Pelosi).

Completion of the procedure via the vagina will require those instruments traditionally used for vaginal hysterectomy.

Description of technique

A number of techniques for performing laparoscopic hysterectomy in all its forms have been described. The main differences, as previously mentioned, are concerned with

whether the uterine vessels are ligated laparoscopically or through the vagina. Other variations involve use of stapling devices vs suture, Harmonic Scalpel or electrocoagulation. Table 41.1 shows the diversity in techniques that have been reported since the introduction of this surgery.

Patient positioning

The positioning of the patient is all-important. The procedure is performed with the patient in dorsal lithotomy with the legs in flexion and abduction. The arms should be placed across the chest or by the sides to prevent any nerve complications with abduction of the upper arm. There is no place for the use of shoulder supports. This positioning of the limbs will also allow correct position of the surgeon and the surgical assistant on each side of the patient.

After creation of the pneumoperitoneum, the patient is placed in sufficient Trendelenburg to allow adequate visualization and access to the pelvic organs. An examination under anesthesia should be performed to allow further assessment and determination of the most appropriate surgical approach to remove the uterus. The uterus should be instrumented to allow manipulation. Although a curette may provide adequate manipulation for many laparoscopic procedures, we find that for advanced procedures such as an LAVH, a more sophisticated instrument such as the Valtchev or Pelosi uterine manipulator is required. Depending on the type of laparoscopic hysterectomy to be performed, other devices such as those developed by Wattiez, Hourcabie, Koninckx, Koh, Reich, and McCartney can be used.

All patients in our unit receive prophylactic intravenous antibiotics at induction of anesthesia and prophylaxis against deep vein thrombosis.

Trocar positioning

The size and number of trocars will be dependent upon the surgeon's technique, but there is always a minimum of three (a central umbilical and two lateral) with a possible fourth placed in the lower midline region. In our unit it is customary to use 1×5 mm trocars with the 5 mm intraumbilical site for use with a 0° 5 mm telescope.

Placement of the lower midline trocar should take into account access to the pelvis (especially in the situation of a large or unusually shaped uterus) and surgical ergonomics. It is ergonomic nonsense for the surgeon to be leaning forward slightly rotated to the patient's left side so as to be able to use an instrument in the right hand. We find that placing the midline trocar more cephalad addresses both of these situations.

Following establishment of the pneumoperitoneum and insertion of the telescope, an exploratory laparoscopy

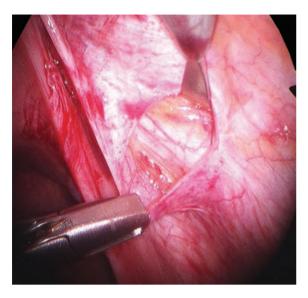


Figure 41.1 Formation of a window over the ureter.

should be performed. Adhesions from previous surgery are divided until the surgeon can visualize all the pelvic organs. Particular note can then be taken of access to the lateral aspects of the uterus, position of the ureters, and margins of the bladder. A final decision regarding the appropriate mode of hysterectomy can then be made. Once the decision to proceed with a laparoscopic hysterectomy is made, the first step in the procedure is to isolate the ureter on both pelvic walls (Figure 41.1). The longer the delay in identifying the path of the ureter as it traverses the pelvis, the more difficult the task becomes due to increasing edema and opacity of the overlying peritoneum. If the ureter cannot be identified in the base of the broad ligament when it passes under the uterine artery, it must be followed from where it crosses the pelvic brim to this site. Failure to isolate the ureter will increase the chance of injury later in the procedure. Although ureteric stents have been advocated in difficult circumstances, routine use should be avoided, as they have been associated with hematuria and even anuria.10

Upper uterine blood supply

When ovarian preservation is required, the broad ligament is opened following coagulation of the round ligament with bipolar forceps at 40 W current, followed by transection using a spatula with monopolar current at 80 W pure cutting current or scissors (Figure 41.2). The incision in the anterior leaf of the broad ligament is extended towards the vesicouterine fold to later facilitate reflection of the bladder. A window is then created in the posterior leaf of the broad ligament using either scissors or the spatula with cutting current. Great care must be taken at this point to

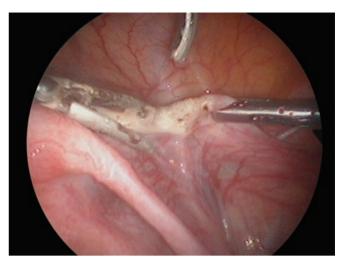


Figure 41.2 Division of the right round ligament.

make sure that there is no bowel in the vicinity of the posterior leaf. The ureter must be clearly visualized even at this early stage of the procedure and clear of the pedicle to be divided. The section of ureter previously exposed may be repeatedly identified throughout the course of the procedure. The tissue distal to the ovary containing the vessels and the ovarian ligament can then be desiccated with bipolar current, or suture ligated, depending on preference (Figure 41.3). We find that use of electrosurgery in this step is both effective, and time efficient, and new technologies such as pulsed bipolar have been shown to be just as efficacious. 11,12 The choice of electrosurgical instruments will be based upon availability, cost and most importantly surgeon preference.

An alternative to the use of electrosurgery in the formation of the upper pedicles is to use an endoscopic stapling device. Care must be taken in ascertaining the

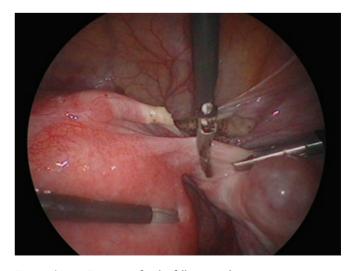


Figure 41.3 Division of right fallopian tube.

margins when using such a device. The staple line is 6 mm wide but the ureter has been shown to be as close as 6–10 mm from the side of the uterus.

When oophorectomy is required, the anterior and posterior leaves of the broad ligament are opened with scissors proximal to the ovary following medial traction on this organ from the contralateral side. The gonadal vessels are then skeletonized and either suture ligated or desiccated with the bipolar forceps and then divided. If there is any concern at this stage as to the integrity of the seal on the proximal cut end of the gonadal vessels, then one or two Endoloops (Vicryl; Ethicon, Somerville, NJ) can be placed over the vessel.

Bladder reflection and mobilization

Once the anterior sheath of the broad ligament has been opened, the bladder can be reflected. Various techniques have been described to assist in this step. The simplest method involves division of the loose peritoneum from the left anterior leaf of the broad ligament and following down across and just below the vesicouterine fold and up the right side in a similar fashion (Figure 41.4). The peritoneum is attached to the uterus and the area of attachment is identified as a white line across the cervix. There is an area of safety between this line and the dome of the bladder of between 2 and 3 cm. Care must be taken in patients who have undergone previous cesarean section, as scarring may render this area undefinable and thereby increase the risk of inadvertent bladder injury. 13 The bladder is mobilized off the cervix and vagina using sharp or blunt dissection. If a peanut swab is used on a laparoscopic forcep to mimic the action of the sponge forcep in open surgery used to achieve bladder mobility, it is essential to pass a suture through the peanut and have one end outside of the body, allowing ease of retrieval if the peanut should come loose.

Uterine vessel ligation

Laparoscopic ligation of the uterine vessels during LAVH has been shown to significantly reduce blood loss when compared with when this procedure is performed transvaginally. The vessels can be occluded at a number of places along their path, from their origin from the hypogastric vessels to when they intersect with the ureter or when the meet the uterus or on the side of the uterus. The vessels can be divided using several methods, but our preference is for bipolar desiccation (Figure 41.5). Prior to desiccation, the uterine arteries should be prepared by skeletonizing them. This process is made easier by manipulating the uterus away from the site of surgery. Once skeletonized, the pedicles can be coagulated and divided. Vascular clips or suture ligation with extraperitoneal knot tying may also be used.

An alternative is to utilize the lateral approach, as previously reported. 15,16 The uterus is displaced to the contralateral side and a pelvic side wall triangle is identified, comprising the infundibulopelvic ligament medially, the external iliac artery laterally, and the broad ligament as the base. The peritoneum in the middle of the triangle is opened and the combination of the CO₂ pneumoperitoneum and blunt dissection allows dissection into the loose areolar tissue of the retroperitoneum (Figure 41.6). The ureter can be identified on the undersurface of the pelvic side wall peritoneum. Although the ureter and the uterine artery have an intimate relationship as they course across the pelvic side wall, identification of the artery can be a challenge. A helpful maneuver is to identify the obliterated umbilical artery and trace it off the abdominal wall in a

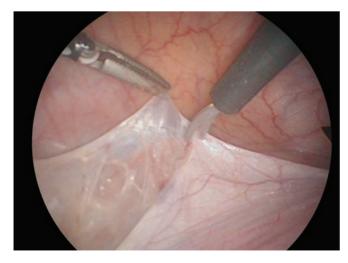


Figure 41.4 Reflecting the bladder.



Figure 41.5 Ligation of the left uterine vessels.

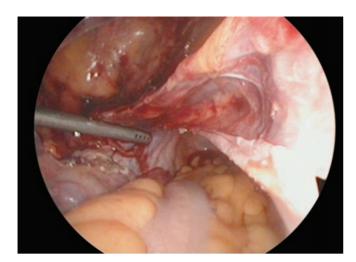


Figure 41.6 Retroperitoneal dissection to identify the left uterine artery.

retrograde manner. Gentle pulling on this structure will be reflected in movement of its origin, the terminal portion of the hypogastric artery. Once the hypogastric artery is identified, it can be followed until the uterine artery is identified coming from it. Once identified and isolated, the uterine artery may be ligated using sutures, clips, or electrosurgery. The surgeon should be mindful of the close proximity of the vessels to the ureter and steps taken to minimize direct injury or damage secondary to thermal spread. Such a procedure is particularly useful in reducing blood loss with large adenomyotic or multifibroid uterus when access to the side of the uterus can be difficult.¹⁷

Completion of the hysterectomy from the vagina

The vaginal component of a LAVH is similar to performing a vaginal hysterectomy, and techniques vary widely amongst gynecologists. The uterosacral—cardinal ligament pedicle is usually obtained vaginally. Depending upon the preference and skill of the surgeon and the extent of laparoscopic access in the pelvis, the uterine artery pedicles may also be secured vaginally. The laparoscopic ports should be left in place until completion of the vaginal part, so that the pelvis can be reassessed and hemostasis of all pedicles guaranteed.

After infiltrating the cervix with a vasoconstrictor agent, a circumferential incision is made around the cervix distal to the bladder reflection. The vaginal skin is then reflected, allowing access to the uterosacral ligaments, which can subsequently be suture ligated and transected. The bladder is further reflected, and anterior and a posterior colpotomy performed. Further pedicles are taken as required, the final number depending upon the size of the uterus. In a case where the uterus is large,

morcellation may be required to facilitate removal. Care must be taken to ensure that the pedicles formed vaginally are medial to those secured laparoscopically.

After removal of the uterus (and adnexae), the vaginal vault is closed longitudinally with an absorbable suture. The uterosacral—cardinal ligament complex may be incorporated into this closure in order to strengthen vault support.

Anecdotal evidence shows that packing of the vagina after VH or LAVH is associated with increased discomfort and analgesia requirements with no real benefits on reducing blood loss. The authors do not routinely pack the vagina following LAVH. An indwelling catheter is inserted postsurgery only when additional vaginal corrective surgery is performed.

Cystoscopy

It is our policy to perform cystoscopy at the completion of every hysterectomy, regardless of the operative approach. Visualization of ureteric jets is reassurance that there has been no immediate ureteric occlusion secondary to, for example, inappropriately placed sutures. Visualization of the ureteric jets may be enhanced by the intravenous administration of indigo carmine dye (Figure 41.7). Cystoscopy allows complete inspection of the bladder wall to insure that its integrity is maintained.

The risk of urinary tract injury during hysterectomy and the benefits of routine cystoscopy have been widely reported. Cystoscopy has been shown to detect up to 90% of unsuspected ureteral injuries and 85% of unsuspected bladder injuries. 18–21

Prompt intraoperative management of such complications will usually prevent the serious sequelae of an unrecognized injury. It is a cost-effective measure and adds little in the way of time to the operation.

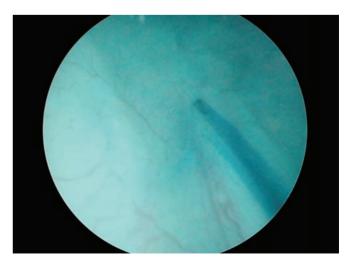


Figure 41.7 Ureteric jet at cystoscopy.

Checking for hemostasis

One of the advantages of LAVH over VH alone is the ease with which hemostasis can be checked.²² After completion of the vaginal component of the procedure, the pedicles are inspected laparoscopically (Figure 41.8). Hemostasis is secured using bipolar coagulation where necessary. Again, care must be taken to monitor the position of the ureter during this phase of the procedure.

Special considerations

Prior abdominal surgery

The potential for subumbilical adhesions should be considered in patients who have undergone prior open abdominal surgery or open laparoscopic entry. The entry point for creation of pneumoperitoneum should be adjusted accordingly. Left upper quadrant (Palmer's point) entry or an open Hasson procedure may reduce the incidence of inadvertent bowel injury.

Enlarged or fibroid uterus

In the past it has been accepted that an AH is the treatment of choice for the enlarged uterus, commonly defined as that >12 weeks' gestation size or >280 g. With the development of instruments such as uterine manipulators and electromechanical morcellators, the large uterus is no longer considered an absolute contraindication to LAVH. It is our experience that uterine shape is more crucial to success than size, as shape determines lateral access and therefore ability to secure the lateral pedicles. Similarly, if the uterus is enlarged due to the presence of fibroids, the size and position of these will need to be considered when determining the procedure to be undertaken.

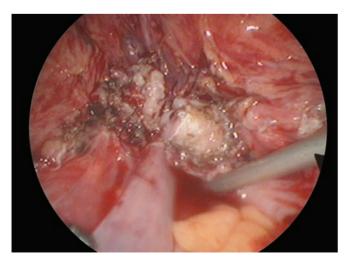


Figure 41.8 Checking for hemostasis after vault closure.

Several techniques have been described to assist in the mobilization and removal of large uteri at the time of LAVH. Laparoscopic coagulation of the uterine vessels followed by supracervical amputation and morcellation of the uterine body have been shown to result in less blood loss and shorter operating time compared with securing the vessels and cardinal–uterosacral complex from the vagina. Variations of this procedure, such as bisection/morcellation or myometrial coring, have also been described. Preoperative treatment with gonadotropin-releasing hormone (GnRH) agonists has been shown to decrease leiomyoma size and uterine volume and thus may facilitate the ease of performing an LAVH. 25,26

Studies investigating the outcomes of LAVH in uteri weighing >500 g have consistently shown a high incidence of perioperative blood transfusions ranging from 10% to as high as 35%. ^{17,27,28} The incidence of blood transfusion is less in cases where the uterus removed is small. Techniques to decrease blood loss include intraoperative administration of oxytocins^{29,30} and laparoscopic coagulation of the uterine vessels prior to completion of the procedure through the vagina. ^{12,14}

Rates of conversion to laparotomy vary depending on uterine size, operator experience, and surgical technique. ^{17,24,27} Surgical expertise in morcellation techniques appears to result in a lower rate of conversion. In our opinion, conversion to laparotomy does not constitute a complication but rather a judicious surgical decision.

Associated pathology

One of the advantages of the laparoscopic approach to hysterectomy is that it allows the surgeon to treat any coexisting pathology such as ovarian cysts, endometriosis, or adhesions. Salpingo-oophorectomy may also be performed with relative ease when compared with the vaginal route.

POSTOPERATIVE CARE

There is nothing in postoperative care that is peculiar to LAVH. Early ambulation and return to normal diet are mandatory if early discharge is to be achieved. Routine postoperative care, such as regular observations and analgesia, should be instituted. Additional antibiotics are not routinely administered unless clinically indicated. We advocate for the early removal of indwelling catheter if used, usually on the first postoperative day, to facilitate patient mobilization and reduce the risk of urinary tract infection. Deep vein thrombosis prophylaxis in the form of low-molecular-weight heparin and antiembolic stockings should be considered.

CLINICAL STUDIES

The role of laparoscopic-assisted vaginal hysterectomy in the treatment of abnormal uterine bleeding

Few studies have directly compared LAVH with other treatments for abnormal uterine bleeding. The Cochrane Collaboration has established that, when compared with medical therapies, hysterectomy is associated with a greater improvement in mental health than many treatments and is at least comparable to the LNG-IUS with regards improvement in quality of life in the short term. Long-term comparisons are lacking. When compared with endometrial destruction techniques, hysterectomy has the advantage of providing a permanent solution to menorrhagia, at the expense of increases in recovery time, procedure-related costs, and complications. The satisfaction rates for both treatments are high in the short term, again with long-term data lacking. 1,31

As it is well established that hysterectomy offers the only permanent solution to abnormal uterine bleeding, investigation has been concentrated on comparing the different approaches to hysterectomy and the relative virtues of each technique.

Laparoscopic-assisted vaginal hysterectomy vs abdominal hysterectomy

Several randomized trials have demonstrated that LAVH has clear clinical advantages over AH. The consensus from such trials is that, compared with abdominal hysterectomy, LAVH is associated with less pain, less blood loss, a significantly shorter stay in hospital, and a quicker convalescence and return to normal function.^{32–35} This also appears to be the case for the treatment of the large uterus using LAVH.³⁶ Several authors report comparative overall complication rates between the two procedures; however, the type of complications among the procedures is different. Abdominal hysterectomies are more likely to be associated with wound complications, whereas ureteric and bladder injuries are more frequent with LAVH. However, the eVALuate study,³⁷ the largest randomized study to compare abdominal vs laparoscopic hysterectomy, found a two times greater rate of major complications in patients undergoing laparoscopic hysterectomy. However, the laparoscopic arm of the trial included LAVH total and subtotal laparoscopic hysterectomies and was not stratified for the various types of laparoscopically assisted hysterectomy. It is therefore difficult to attribute the complication rate due to LAVH alone. Johnson et al., in a subsequent meta-analysis, stratified the procedures and reported the risk of urinary tract injury during LAVH as being roughly equivalent to that of AH. When the LAVH includes laparoscopic securing of the uterine artery pedicle, the risk of urinary tract complication is increased (odds ratio [OR] = 2.81), and AH is therefore the favored procedure.³⁸

Laparoscopic-assisted vaginal hysterectomy vs vaginal hysterectomy

Repeated studies have not consistently demonstrated a clear benefit of LAVH over VH. In fact, some authors have concluded that VH should be the procedure of choice if able to be done safely.^{37,39}

The eVALuate study was inconclusive on the differences between the two procedures with regard to complication rates, pain, and hospital stay. However, although underpowered to detect such differences, it remains one of the largest prospective studies to compare the two approaches. The only significant difference found between the two procedures was that VH was associated with a shorter operative time compared with laparoscopic hysterectomy. This finding is consistent with the results of previous randomized studies, with the earlier studies suggesting that LAVH takes almost twice as long as VH. ^{39,40} Later studies show a lesser time differential, presumably reflecting the advancement in laparoscopic skills.

It has been suggested that LAVH allows identification of pelvic disease that otherwise may lead to complications during VH, and that the laparoscopic approach allows for careful attention to hemostasis and therefore may reduce postoperative bleeding complications and vault hematomas. In the eVALuate study, more unexpected pathology was detected in the laparoscopic arm; however, the clinical consequences of this were not evaluated. The more recently published meta-analysis by Johnson et al.³⁸ also found no evidence supporting the benefit of detecting such pathology.

Neither has it been clearly established that LAVH has advantages over VH with regards to management of enlarged uteri. Soriano et al. failed to find LAVH advantageous for this clinical scenario and recommended a vaginal approach to be appropriate in most circumstances.⁴¹

Laparoscopic-assisted vaginal hysterectomy vs total laparoscopic hysterectomy

Fewer studies have compared LAVH with TLH. A randomized trial by Ghezzi et al. found TLH to be significantly quicker than LAVH, particularly in obese patients. Estimation of blood loss was similar between the two procedures and, although there was a slight increase in complications in the LAVH group, this was not found to be statistically significant. There was no difference in the rates of postoperative complications. Non-randomized

comparisons of LAVH with TLH have produced similar results. Long et al. reported similar complication rates, length of hospital stay, and blood loss between the two groups. 43 They found TLH to be a significantly longer operation, although the TLH group had significantly more patients who had undergone previous abdominal surgery and therefore the likelihood of need for adhesiolysis may explain the differences found. A retrospective analysis by Cook et al. found TLH to be a quicker procedure, associated with less blood loss and similar complication rates to LAVH. 44

COMPLICATIONS

Many studies comparing LAVH with other forms of hysterectomy are underpowered to detect differences in complication rates as such events are rare. However, from the existing data, the rate of major complications with LAVH appears to range from 3% to 17%. 45–47 These studies suggest that this rate is dependent upon surgeon experience – the more experienced the surgeon in performing the procedure, the fewer the complications. This has important implications for training, accreditation, and mentoring programs. Other factors such as prior surgery, concomitant pelvic pathologies, and patient obesity are also influencing factors.

Urinary tract injuries

The major criticism of LAVH is the increased incidence of ureteric injuries when compared with other surgical routes for hysterectomy. One review of ureteric injuries after gynecologic surgery indicated that such injury is more frequently associated with LAVH than with any other gynecologic procedure. 48 Incidence of ureteric injuries varies from 0.3% to 4%.37,46 In most studies it is unclear whether these injuries have occurred during the laparoscopic or vaginal components of the procedure; however, the incidence is higher in LAVH where the uterine vessels are secured laparoscopically. Intraoperative cystoscopy may detect some injuries, although injury from thermal damage may not be obvious for several days. Patients with such injuries typically present with increasing loin pain, fever, or peritonitis, symptoms of incontinence suggesting ureterovaginal fistula or, in the rare case of bilateral ureteric injury, anuria. Investigations may include intravenous pyelogram, ultrasound, and cystoscopy with ureteric catheterization. The repair technique will obviously depend upon the injury, but should always be performed in conjunction with urologic colleagues.

Damage to the bladder is more common than that to the ureter, occurring in around 1% of cases, primarily because the bladder must always be reflected from the uterus. Previous surgery, especially repeated cesarean section, is associated with a higher risk of bladder injury. Simple cystotomy, if recognized intraoperatively, may be managed by single-layer closure with an absorbable suture, followed by prolonged catheterization. Routine intraoperative cystoscopy, as previously described, will increase the likelihood of detection of such an injury. However, like the ureter, thermal injuries will not be immediately recognized and may present days to weeks after the initial surgery. A high index of suspicion should be adopted if an abnormal postoperative course is encountered.

Bowel injuries

Injury to the bowel during LAVH is rare, occurring in 0.2–0.5% of cases. 44,46,47 The incidence is increased if extensive adhesiolysis is required or endometriosis is resected from the pouch of Douglas. Care must be taken when using electrosurgical instruments, as inadvertent burns may occur, either due to electrical shorting or faulty insulation. Thermal injuries most often present in the postoperative period and, again, a high index of suspicion must be maintained. Management will often need to be in conjunction with a general surgeon.

Vascular injuries

Blood loss is difficult to estimate and amounts vary between studies. Most studies report a higher loss with LAVH compared with other approaches, but this does vary according to uterine size. Despite this, blood transfusion requirements are low, with most reports estimating a transfusion rate of between 1 and 3%. Similar rates are seen with AH and VH. Major vascular injuries are extremely rare and not necessarily increased in LAVH compared with other gynecologic laparoscopic procedures.

Conversion to laparotomy

We do not view conversion to laparotomy as a true surgical complication, rather that it reflects prudent decision making on behalf of the surgeon. Conversion rates vary, but are generally around 2–5%.^{37,46} Unintended intraoperative laparotomy may be more frequent in the presence of an enlarged uterus, fibroids, or severe endometriosis, yet still the rate remains low.

Other surgical complications

Other surgical complications such as pulmonary embolus, wound infection, and ileus are rare events and do not appear to be increased with LAVH.

COST

Most healthcare systems in the world are straining under burgeoning costs. One of the major challenges to modern health care is to provide effective and safe treatment while minimizing cost.

A major criticism of laparoscopic hysterectomy is that it is costly to perform. Compared with vaginal hysterectomy, LAVH is consistently found to be associated with higher theater costs, with no advantage in reduced hospital stay. ^{49,50} A large proportion of the high intraoperative cost may be due to the use of disposable instrumentation. Such instrumentation is not essential to performing the procedure, and thus costs could be contained by using reusable equipment such as the usual monopolar and bipolar instruments. Compared with abdominal hysterectomy, LAVH has distinct financial advantages, mainly due to reduced hospital stay and analgesia requirements.

Whereas it is relatively easy to account for the costs of the procedure and hospitalization, it is more difficult to estimate overall costs with respect to loss of productivity due to inability to perform usual duties or return to work. It is accepted that LAVH and VH result in quicker return to normal function compared with AH and one could therefore presume that there may therefore be further economic benefits to these procedures although they are difficult to quantify.

CONCLUSION

LAVH is an appropriate, permanent treatment for abnormal uterine bleeding and should be considered if medical treatment has failed or is unacceptable to the patient.

It represents an important step in the evolution from traditional abdominal and vaginal hysterectomy to total laparoscopic hysterectomy. Current evidence supports vaginal hysterectomy as the procedure of choice if vaginal access and uterine descent allows. However, LAVH remains a practical alternative for some patients, particularly those who may otherwise undergo AH. With appropriate training and attention to surgical detail, complication rates should remain low and costs may be contained by sensible choice of equipment.

References

- Lethaby A, Shepperd S, Cooke I, Farquhar C. Endometrial resection and ablation versus hysterectomy for heavy menstrual bleeding. Cochrane Database Syst Rev 1999; (2): CD000329.
- Marjoribanks J, Lethaby A, Farquhar C. Surgery versus medical therapy for heavy menstrual bleeding. Cochrane Database Syst Rev 2006; (2): CD003855.
- 3. Reich H, DeCaprio J, McGlynn F. Laparoscopic hysterectomy. J Gynecol Surg 1989; 5: 213–15.
- 4. Reich H, Garry R. Laparoscopic hysterectomy definitions and indications. Gynaecol Endosc 1994; 3: 1–3.
- 5. Isik-Akbay E, Harmanli O, Panaganmamula U et al. Hysterectomy in obese women: a comparison of abdominal and vaginal routes. Obstet Gynecol 2004; 104: 710–14.
- 6. Rasmussen K, Neumann G, Ljungstrom B et al. The influence of body mass index in the prevalence of complications after vaginal and abdominal hysterectomy. Acta Obst Gynecol Scand 2004; 83: 85–8.
- Obermair A, Manolitsas T, Leung Y et al. Total laparoscopic hysterectomy versus total abdominal surgery for obese women with endometrial cancer. Int J Gynecol Cancer 2005; 15: 319– 24.
- Holub Z, Jabor A, Klimiet D et al. Laparoscopic hysterectomy in obese women. Eur J Obstet Gynecol Reprod Biol 2001; 98: 77–82.
- Guidelines for performing advanced operative laparoscopy. RANZCOG College Statement 2005 (cited 10th June 2006). available from: www.ranzcog.edu.au/publications/statements/ C-trg2.pdf

- Wood E, Maher P, Pelosi M. Routine use of ureteric catheters at laparoscopic hysterectomy may cause unnecessary complications. J Am Assoc Gynecol Laparosc 1996; 3: 393–7.
- Wang C, Yen C, Lee C, Soong Y. Comparison of the efficacy of laparoscopic coagulating shears and electrosurgery in laparoscopically assisted vaginal hysterectomy. Int Surg 2000; 85: 88–91.
- 12. Wang C, Yeung L, Yen C et al. Comparison of the efficacy of the pulsed bipolar system and conventional bipolar electrosurgery in laparoscopically assisted vaginal hysterectomy. J Laparoendosc Adv Surg Tech 2005; 15: 361–4.
- Rooney C, Crawford A, Vassalio B et al. Is previous caesarean section a risk factor for incidental cystotomy at the time of hysterectomy? A case-controlled study. Am J Obstet Gynecol 2005; 193: 2041–4.
- 14. Kohler C, Hassenbein K, Klemm P et al. Laparoscopic coagulation of the uterine blood supply in laparoscopic-assisted vaginal hysterectomy. Eur J Gynecol Oncol 2004; 25: 453–6.
- Chang W, Torng P, Huang S. Laparoscopic-assisted vaginal hysterectomy with uterine artery ligation through retrograde umbilical ligament tracking. J Minim Invasive Gynecol 2005; 12: 336–42.
- Kadar N. A laparoscopic technique for dissecting the pelvic retroperitoneum and identifying the ureters. J Reprod Med 1995; 40: 116–22.
- Salmanli N, Maher P. Laparoscopically-assisted vaginal hysterectomy for fibroid uteri weighing at least 500 grams. Aust NZ J Obstet Gynaecol 1990; 39: 182

 –4.

- Gilmour D, Dwyer P, Carey M. Lower urinary tract injury during gynaecologic surgery and its detection by intraoperative cystoscopy. Obstet Gynecol 1999; 94(5 Pt 2): 883–9.
- Ribeiro S, Reich H, Rosenberg J et al. The value of intraoperative cystoscopy at the time of laparoscopic hysterectomy. Hum Reprod 1999; 14: 1727–9.
- 20. Vakili B, Chesson R, Kyle B et al. The incidence of urinary tract injury during hysterectomy: a prospective analysis based on universal cystoscopy. Am J Obstet Gynecol 2005; 192: 1599–604.
- 21. Visco A, Taber K, Weidner A et al. Cost effectiveness of universal cystoscopy to identify ureteral injury at hysterectomy. Obstet Gynecol 2001; 97(5 Pt 1): 685–92.
- Wood C, Maher P, Hill D. Bleeding associated with vaginal hysterectomy. Aust NZ J Obstet Gynaecol 1997; 37: 257–60.
- Yen Y, Liu W, Yuan C, Ng H. Comparison of two procedures for laparoscopically-assisted vaginal hysterectomy of large myomatous uteri. J Am Assoc Gynecol Laparosc 2002; 9: 63–9.
- 24. Nazah I, Robin F, Jais J et al. Comparison between bisection/ morcellation and myonetrial coring for reducing large uteri during vaginal hysterectomy or laparoscopically assisted vaginal hysterectomy: results of a randomized prospective study. Acta Obstet Gynecol Scand 2003; 82: 1037–42.
- Broekmans F. GnRH agonists and uterine leiomyomas. Hum Reprod 1996; 11(Suppl 3): 3–25.
- Lethaby A, Vollenhoven B, Sowter M. Pre-operative GnRH analogue therapy before hysterectomy or myomectomy for uterine fibroids. Cochrane Database Syst Rev 2001; (2): CD000547.
- Pelosi M, Kadar N. Laparoscopically assisted hysterectomy for uteri weighing 500g or more. J Am Assoc Gynecol Laparosc 1994; 1: 405–9.
- Wang C, Yen C, Lee C et al. Laparoscopically assisted vaginal hysterectomy for a large uterus: a comparative study. Eur J Obstet Reprod Biol 2004; 115: 219–23.
- 29. Chang F, Yu M, Ku C et al. Effect of uterotonics on intraoperative blood loss during laparoscopically-assisted vaginal hysterectomy. BJOG 2006; 113: 47–52.
- Wang C, Yuen L, Yen C et al. A simplified method to decrease operative blood loss in laparoscopically-assisted vaginal hysterectomy for the large uterus. J Am Assoc Gynecol Laparosc 2004; 11: 370–3.
- 31. Tapper A, Heinonen P. Comparison of hysteroscopic endometrial resection and laparoscopically assisted vaginal hysterectomy for the treatment of menorrhagia. Acta Obstet Gynecol Scand 1998; 77: 78–82.
- 32. Falcone T, Paraiso M, Mascha E. Prospective randomised trial of laparoscopically assisted vaginal hysterectomy versus total abdominal hysterectomy. Am J Obstet Gynecol 1999; 180: 955–62.
- Marana R, Busacca M, Zupi E et al. Laparoscopically assisted vaginal hysterectomy versus total abdominal hysterectomy: a prospective, randomised, multicentre study. Am J Obstet Gynecol 1999; 180: 270–5.
- Ollson J, Ellstrom M, Hahlin M. A randomised prospective trial comparing laparoscopic and abdominal hysterectomy. BJOG 1996; 103: 345–50.

- 35. Summit R, Stovall T, Steege J, Lipscomb G. A multicentre randomised comparison of laparoscopically assisted vaginal hysterectomy and abdominal hysterectomy in abdominal hysterectomy candidates. Obstet Gynecol 1998; 92: 321–6.
- Ferrari M, Berlanda N, Mezzopane R et al. Identifying the indications for laparoscopically assisted vaginal hysterectomy: a prospective, randomised comparison with abdominal hysterectomy in patients with symptomatic uterine fibroids. BJOG 2000; 107: 620–5.
- Garry R, Fountain J, Mason S et al. The eVALuate study: two parallel randomised trials, one comparing laparoscopic with abdominal hysterectomy, the other comparing laparoscopic with vaginal hysterectomy. BMJ 2004; 328: 134.
- Johnson N, Barlow D, Lethaby A et al. Methods of hysterectomy: systematic review and meta-analysis of randomized controlled trials. BMJ 2005; 330: 1478.
- Richardson R, Bournas N, Magos A. Is laparoscopic hysterectomy a waste of time? Lancet 1995; 345: 36–41.
- 40. Summit R, Stovall T, Lipscomb G, Ling F. Randomised comparison of laparoscopically-assisted hysterectomy in an outpatient settting. Obstet Gynecol 1992; 80: 895–901.
- 41. Soriano D, Goldstein A, Lecuru F, Darai E. Recovery from vaginal hysterectomy compared with laparoscopically-assisted hysterectomy: a prospective randomized, multicenter study. Acta Obst Gynecol Scand 2001; 80: 337–41.
- 42. Ghezzi F, Cromi A, Bergammi V et al. Laparoscopic-assisted vaginal hysterectomy for the management of endometrial cancer: a randomized clinical trial. J Minim Invasive Gynecol 2006; 13: 114–20.
- Long C, Fang J, Chen W et al. Comparison of total laparoscopic hysterectomy and laparoscopically assisted vaginal hysterectomy. Gynecol Obstet Invest 2002; 53: 214–19.
- Cook J, O'Shea R, Seman E. Laparovaginal hysterectomy: a decade of evolution. Aust NZ J Obstet Gynaecol 2004; 44: 111–16.
- 45. Davies A, Hart R, Magos A et al. Hysterectomy: surgical route and complications. Eur J Gynecol Oncol 2002; 104: 148–51.
- Harkki P, Kurki T, Sjoberg J, Tiitinen A. Safety aspects of laparoscopic hysterectomy. Acta Obst Gynecol Scand 2001; 80: 383–91.
- Makinen J, Johansson J, Tomas C et al. Morbidity of 10100 hysterectomies by type of approach. Hum Reprod 2001; 16: 1473–8.
- 48. Ostrzenski A, Radolinski B, Ostrzenska K. A review of laparoscopic ureteral injury in pelvic surgery. Obstet Gynecol Surv 2003; 58: 794–9.
- 49. Ellstrom M, Ferraz-Nunes J, Hahlin M, Ollson J. A randomised trial with a cost-consequence analysis after laparoscopic and abdominal hysterectomy. Obstet Gynecol 1998; 91: 30–4.
- 50. Schulpher M, Manca A, Abbott J et al. Cost effectiveness analysis of laparoscopic hysterectomy compared with standard hysterectomy: results from a randomised trial. BMJ 2004; 328: 134–40.

Laparoscopic hysterectomy for the large uterus

Pascale Jadoul and Jacques Donnez

INTRODUCTION

The development of new accessories and improved technology has enabled gynecologists to perform hysterectomy by laparoscopy. Reich and colleagues¹ described the technique of laparoscopic hysterectomy for the first time in 1989.

There are many surgical advantages to laparoscopy, particularly magnification of the anatomy and pathology, access to the uterine vessels, vagina, and rectum, and the ability to achieve complete hemostasis and clot evacuation. Patient advantages are multiple and are related to the avoidance of a painful abdominal incision. They include a shorter hospitalization and recuperation time and an extremely low rate of infection and ileus.

A number of trials and reviews have recently tried to identify the most beneficial and least harmful surgical approach to hysterectomy (for benign diseases) in a comparison of abdominal hysterectomy (AH), vaginal hysterectomy (VH), and laparoscopic hysterectomy (LH).^{2,3} In these papers, laparoscopic hysterectomy was found to be associated with a higher rate of major complications than abdominal hysterectomy.

In this chapter, we set out to describe the different techniques for laparoscopic hysterectomy and to assess their safety and efficiency compared to abdominal and vaginal hysterectomy, even in the case of large uteri.

LAPAROSCOPIC HYSTERECTOMY: TECHNIQUES

Several classifications of laparoscopic hysterectomy have been proposed.⁴⁻⁷ At least four types must be considered:

- (1) LAVH laparoscopic-assisted vaginal hysterectomy, involving an initial laparoscopic surgical procedure after which vaginal hysterectomy is carried out.
- (2) LH laparoscopic hysterectomy, with laparoscopic dissection to free the uterus of all its attachments in the peritoneal cavity.

- (3) TLH total laparoscopic hysterectomy, with suture of the vagina by laparoscopy.
- (4) LASH laparoscopic subtotal hysterectomy.

All procedures start in the same way. A Foley catheter is inserted during surgery to empty the bladder. Four laparoscopic puncture sites, including the umbilicus, are used: 10 mm umbilical, 5 mm right, 5 mm medial, and 5 mm left lower quadrant, just above the pubic hairline; lateral incisions are made next to the deep epigastric vessels. A cannula is placed in the cervix for appropriate uterine mobilization.

Abdominal and adnexal adhesions, if present, are lysed to mobilize the uterus, and the ureters are identified. When adnexectomy is required, the adnexa are freed first. The infundibulopelvic ligament is identified and exposed by applying traction to the adnexa with opposite forceps. Bipolar forceps are used to compress and desiccate the vessels, which are then cut with scissors. Bipolar coagulation is used to coagulate the pedicle, but staples or sutures may be applied. Scissor division is carried out close to the line of desiccation to ensure that the pedicle remains compressed. The peritoneum between the infundibulopelvic ligament and the round ligament is cut. The round ligaments are then desiccated and cut with scissors. When adnexectomy is not required, the surgical procedure starts by grasping, coagulation, and section of the round ligament. The vesicouterine peritoneum is then opened with scissors to expose the posterior leaf of the cardinal ligament. This posterior leaf is coagulated and cut with scissors.

A window is thus created, allowing easy grasping, coagulation, and section of the proximal part of the fallopian tube and the utero-ovarian ligament. The same procedure is subsequently performed on the opposite side.

The peritoneum of the vesicouterine space is then grasped and elevated with forceps, while scissors are used to dissect the vesicouterine space. Aquadissection may be applied to separate the leaves of the broad ligament, distending the vesicouterine space and defining the tendinous attachments of the bladder in this area, which are

coagulated and cut. Sharp dissection can also be used to divide the peritoneum down to the uterosacral ligaments.

In the case of LAVH, the procedure continues with normal VH at this point. When LH, TLH, or LASH is performed, the procedure is as follows. The uterine vessels are identified and skeletonized using aquadissection. When these are well identified, and after confirming the position of the ureters, the uterine vessels are desiccated with bipolar coagulation and cut. The same procedure is performed on the opposite side. In some departments, staples or specialized equipment (like ultrascissors) are used, but this is very expensive. Some authors prefer suture ligation of the vascular bundle.

When LASH is performed, the unipolar knife or unipolar scissors are used to cut the cervix below the level of the internal os and separate the cervix from the corpus. In our department, until November 1993, longitudinal (vertical or horizontal) posterior colpotomy was performed either by laparoscopy or through the vagina to remove the uterus. Since then, however, the uterus has been removed through a 12 mm trocar after morcellation using a morcellator.

When TLH is performed, a vaginal incision is made over a sponge placed between the anterior vaginal wall and the cervix or on a uterine mobilizer equipped with a vaginal cupula. The vagina is entered using a unipolar cutting current or scissors. The same procedure is performed posteriorly, exposing the area in the cul-de-sac where an incision can be made. The completely freed uterus is then pulled into the vagina. The vagina may be sutured from below or laparoscopically with three sutures. The first suture joins the uterosacral ligaments across the midline. The second brings the cardinal ligaments and underlying vagina across the midline. The third closes the anterior vagina and its fascia. A running suture can also be used, but care must be taken to incorporate the uterosacral ligaments into the suture.

The pelvis is rinsed with saline solution. Blood clots are removed. A drainage catheter can be left in the pelvic cavity. Antibiotics (Zinacef [cefuroxime] 2 g/day, Flagyl [metronidazole] 2 g/day) are given preoperatively (one shot).

COMPARISON OF THE DIFFERENT TECHNIQUES

The most appropriate surgical technique for hysterectomy is that which is most beneficial and least harmful. With this in mind, we should compare the different techniques with respect to different primary and secondary outcomes:

- (1) Primary outcomes
 - Intraoperative complications: bowel injury, bladder or ureteral injury, vascular injury, mortality, conversion to laparotomy.

- Duration of hospital stay.
- Return to normal activities.
- Long-term complications: urinary dysfunction or sexual dysfunction.

(2) Secondary outcomes

- Operating time.
- Minor complications: wound or abdominal infections, febrile episodes, need for blood transfusion.

Johnson et al. recently conducted a review of all existing randomized trials comparing abdominal, vaginal, and laparoscopic techniques in the context of the Cochrane Collaboration.³ They reviewed 27 trials involving 3624 hysterectomies.

The benefits of VH over AH included a shorter hospital stay (weighted mean difference [WMD] = 1.0 day, 95% confidence interval [CI] CI 0.7–1.2 days), speedier return to normal activities (WMD = 9.5 days, 95% CI 6.4–12.6 days), and fewer unspecified infections or febrile episodes (odds ratio [OR] = 0.42, 95% CI 0.21–0.83).

There was no evidence of any benefit of LH over VH and the operating time was increased (WMD = 41.5 minutes, 95% CI 33.7–49.4 minutes).

The benefits of LH over AH included less intraoperative blood loss (WMD = 45.3 ml, 95% CI 17.9–72.7 ml) with a smaller drop in hemoglobin levels (WMD = 0.55 g/L, 95% CI 0.28–0.82 g/L), shorter hospital stay (WMD = 2.0 days, 95% CI 1.9–2.2 days), speedier return to normal activities (WMD = 13.6 days, 95% CI 11.8–15.4 days), fewer wound or abdominal wall infections (OR = 0.32, 95% CI 0.12–0.85), fewer unspecified infections or febrile episodes (OR = 0.65, 95% CI 0.49–0.87), balanced against a longer operating time (WMD = 10.6 minutes, 95% CI 7.4–13.8 minutes) and more urinary tract (bladder or ureter) injuries (OR = 2.61, 95% CI 1.22–5.60).

This increased risk of urinary tract injuries was essentially seen in the eVALuate study published by Garry et al. in the *British Medical Journal* in 2004.² Twentynine of the 53 urinary tract injuries in Johnson's review occurred in Garry's eVALuate study. Garry et al. conducted two parallel randomized trials, involving 1380 patients, to evaluate the effects of LH compared to AH and VH. We believe considerable bias in their method unfortunately led them to the wrong conclusions.

Their primary endpoint was the occurrence of major complications, which was as high as 11.1% and 9.8% in the LH groups of the two trials (Table 42.1). This rate is totally unacceptable, but may well be explained by the major bias encountered.⁸

First, 43 gynecologists from 30 centers took part. The mean number of LHs (n = 920) per gynecologist was

	Abdomin	al trial	Vaginal trial		
	AH (n = 292)	LH (n = 584)	VH (n = 168)	LH (n = 336)	
Major hemorrhage	7 (2.4)	27 (4.6)	5 (2.9)	17 (5.1)	
Bowel injury	3 (1)	1 (0.2)	0	0	
Ureteral injury	0	5 (0.9)	0	1 (0.3)	
Bladder injury	3 (1)	12 (2.1)	2 (1.2)	3 (0.9)	
Intraoperative conversion	-	23 (3.9)	7 (4.2)	9 (2.7)	
At least one major complication	18 (6.2)	65 (11.1)	19 (9.5)	33 (9.8)	

Table 42.1 Major complications in the eVALuate study²

Values are numbers (percentages) of participants.

AH, abdominal hysterectomy; VH, vaginal hysterectomy.

Table 42.2 Hysterectomy techniques in our department between 1994 and 2005

Procedure	199	4–95	1990	6–97	199	8–99	200	00–01	200.	2–03	200-	4–05	To	tal
	n	%	n	%	n	%	n	%	n	%	n	%	n	%
LASH	236	46	240	41.5	248	43.5	205	38	179	30	252	40.5	1360	39.9
LAVH/LH ^a	130	26	127	22	177	31	203	37.5	294	50	306	49.3	1236	36.3
VH	82	16	159	27.5	111	19.5	102	19	94	16	53	8.5	601	17.6
AH	60	12	52	9	32	6	31	5.5	24	4	11	1.7	210	6
Total	508		578		568		541		591		622		3407	

LASH, laparoscopic subtotal hysterectomy; LAVH, laparoscopic-assisted vaginal hysterectomy; LH, laparoscopic hysterectomy (*in 2000, we switched from LAVH to LH); VH, vaginal hysterectomy; AH, abdominal hysterectomy.

therefore 21 over 4 years. Secondly, the experience of the 43 gynecologists most certainly differed from center to center. The rate of complications is not analyzed according to the gynecologists' experience. Thirdly, the learning curve greatly exceeds 25 cases. A conversion rate from laparoscopy to laparotomy of 3.5% (32/920), in the knowledge that the mean uterine size was 6 weeks of pregnancy (0–12), seems very high to us.

In our series of more than 3400 hysterectomies (Table 42.2), the rate of major complications was 0.8% after LASH and 1.5% after LH (Table 42.3). All but four of the complications occurred from 1990 to 1995 (LASH, n = 295; LH, n = 136). Later, the rate of major complications was exactly the same as that observed after AH. In our series of 2596 laparoscopic hysterectomies, there was only one conversion to laparotomy.

The conclusions reached by Garry et al. are therefore not admissible because of all the bias identified. The high complication rates are probably due more to the relative inexperience of surgeons in laparoscopic hysterectomy than the technique of itself.

Moreover, because Garry's eVALuate patients represent 38% of the patients (1380/3624) in Johnson's Cochrane Review, we believe the same bias explains Johnson's, in our opinion erroneous, conclusions.

We therefore believe that, taking into account primary and secondary outcomes, laparoscopy clearly emerges as the most appropriate technique for a number of reasons:

- Hospital stay after hysterectomy in our department is just 1–4 days.
- Resumption of normal activities is very quick.
- There are fewer wound or abdominal wall infections, and fewer unspecified infections or febrile episodes.
- One of our papers in the New England Journal of Medicine demonstrated that the laparoscopic approach is not expensive if non-disposable material is used.

Table 42.3	Complications in ou	r series of 2596 lapa	aroscopic hysterectomic	es (1994–2005)

Complications (n)	LAVH/LH/TLH (n = 1236)	LASH (n = 1360)
Fever >38.5°C (after day 2) requiring 5–7 days of antibiotic therapy	9 (0.7%)	3 (0.2%)
Hemorrhage	1 (0.1%)	1ª (0.1%)
Bladder incision (sutured by laparoscopy)	3 (0.2%)	3 (0.2%)
Vesicoperitoneal fistula diagnosed by CT scan (treated by a Foley catheter for 14 days)	1 (0.1%)	0
Ureteral lesion (four cases treated by a JJ stent, two cases by ureteral reimplantation	3 (0.2%)	3 (0.2%)
Rectal perforation	1 (0.1%)	0
Conversion to laparotomy	0	1ª (0.1%)
Late complications: iatrogenic adenomyomas ^b	-	9 (0.6%)
Total	18/1236 (1.5%)	20/1360 (1.5%)

^aExternal iliac artery lesion during section of the cervix with monopolar scissors, treated by emergency laparotomy.

LAVH, laparoscopic-assisted vaginal hysterectomy; LH, laparoscopic hysterectomy; TLH, total laparoscopic hysterectomy; LASH, laparoscopic subtotal hysterectomy; CT, computed tomography.

- Operating time depends on the surgeon's experience. In our department, the median operating time for laparoscopic hysterectomy is 45 minutes (35–120 minutes).
- In experienced hands, laparoscopic hysterectomy is safe, with major complications occurring in only 1.5% of cases
- Recently, El-Toukhy et al.¹¹ compared urinary and sexual function after AH, VH, TLH, and LASH. No adverse effects on sexual function were observed with any of these techniques 6 months after surgery.
- Compared to VH, laparoscopy allows us to diagnose and treat other pelvic diseases such as endometriosis, carry out adnexal surgery, including removal of the ovaries, and secure hemostasis.

No randomized studies have been conducted to compare the different laparoscopic techniques, but we believe there is a place for all these techniques.

LAPAROSCOPIC HYSTERECTOMY FOR THE LARGE UTERUS

Three prospective randomized studies were published in 2002 comparing different approaches to hysterectomy in

the case of large uteri. In Schutz et al's study, ¹² patients were randomized for LAVH or AH, Seracchioli et al. compared LH and AH, ¹³ while Hwang et al. ¹⁴ evaluated VH, LAVH, and AH. No significant differences in complication rates were found between the different groups in any of the studies. In Seracchioli et al's report, ¹³ there were no significant differences in operating time or blood loss. Schutz et al. ¹² observed no difference in operating time, but less blood loss with LAVH. In Hwang et al's study, ¹⁴ LAVH took longer than VH and AH.

Overall, laparoscopy was associated with shorter hospitalization, a decreased pain index, and quicker resumption of normal activities.

Prospective studies comparing laparoscopic hysterectomy for normal uteri and large uteri (>500 g) have shown a linear relation between uterine weight and intraoperative blood loss. ^{15,16} In Wang et al's study, ¹⁶ 35% of patients with uteri >500 g required blood transfusion, compared to 4.8% in the <500 g group. In Chang et al's report, ¹⁵ although bigger uteri are associated with increased blood loss, no differences in transfusion rates were found.

In our opinion, laparoscopic hysterectomy is feasible for large uteri and probably not associated with an increase in major complication rates, but might be accompanied by increased blood loss and involve a longer operating time. It is therefore important to optimize some steps of the surgical technique to reduce these risks.

^bSpecimen of myometrium and endometrium left behind after morcellation.

Preoperative treatment with gonadotropin-releasing hormone agonists

Gonadotropin-releasing hormone (GnRH) agonists have been shown to reduce uterine myoma size. 17 Although expensive and with adverse side effects, a 3-month preoperative course of GnRH agonists in women with very enlarged uteri may facilitate or indeed allow laparoscopic hysterectomy by decreasing uterine size and improving preoperative hemoglobin levels. 18 On the other hand, this treatment induces vaginal atrophy, making vaginal extirpation and morcellation of the uterus more difficult.

Trocar placement

There is a physical limit to the maneuverability of instruments and to the angle of vision, represented by the space between the distended abdominal wall and the uterus. To increase maneuverability, the trocar insertion sites can be changed. The optic trocar can be placed up to 10 cm above the umbilicus. The other trocars are placed according to uterine size and myoma location. The higher the uterus, the higher the trocars should be inserted. This will allow easier coagulation and section of the infundibulopelvic ligaments in the case of radical hysterectomy, and of the utero-ovarian ligament and fallopian tube in the case of non-radical hysterectomy.

It should be noted that not only is the uterine volume important but so also is the uterine shape. When the transverse diameter of the uterus is increased, we cannot see its isthmic part, even if we try to push or pull the uterus by means of a uterine manipulator. Therefore, a short but wide uterus ('pear-shaped') may be more challenging than a much bigger one that allows easy access to the uterine vessels ('inverse pear-shaped').

In the case of very large uteri, it may be necessary to increase the number of operative trocars, allowing an additional instrument to be used for traction and manipulation, so as to have the operating field always accessible with three basic instruments (bipolar coagulation forceps, grasping forceps, and scissors).

Identification of the ureters

Three approaches have been used for laparoscopic ureteral identification: namely, medial, superior, and lateral.¹⁹ The laparoscopic surgeon should identify and dissect (skeletonize) either the ureter or the uterine vessels during the performance of a laparoscopic hysterectomy procedure.

The medial approach

If the uterus is anteverted using a uterine manipulator, the ureter can usually be easily visualized in its natural position on the pelvic side wall (posterior leaf of the broad ligament), provided no significant cul-de-sac or adnexal abnormality is present. This maneuver allows the peritoneum immediately above the ureter to be incised to create a 'window' in the peritoneum, to make division of the infundibulopelvic ligament or adnexal pedicle safer. The ureter and its overlying peritoneum are grasped deep in the pelvis below and caudal to the ovary, lateral to the uterosacral ligament. Scissors are used to divide the peritoneum overlying the ureter. The ureter and its surrounding longitudinal endopelvic fascia sheath are dissected together from the peritoneum without compromising its blood supply. This dissection is continued deep into the pelvis where the uterine vessels cross the ureter, lateral to the point of cardinal ligament insertion into the cervix. Connective tissue between the ureter and the vessels is separated with scissors. Bleeding is controlled with bipolar forceps or hemostatic clips. The uterine artery can be ligated or clipped at this time.

The superior approach

The superior approach entails dissecting the colon (rectosigmoid on the left; cecum on the right) from the pelvic brim and freeing the infundibulopelvic ligament vessels from the roof of the broad ligament to allow the ureter that lies below to be identified. The ureter is discerned as it crosses the iliac vessels (or below them between the hypogastric and superior rectal vessels on the left). The ureter is then reflected off the broad ligament and traced into the pelvis.

The lateral approach

The lateral approach makes use of the pararectal space to identify the ureter, and the ureter does not need to be peeled off the broad ligament for its entire pelvic course to be visible.

After displacing the uterus to the contralateral side, a pelvic side wall triangle is identified, formed of the round ligament, laterally bordered by the external iliac artery, and medially bordered by the infundibulopelvic ligament. The peritoneum in the middle of the triangle is incised with scissors and the broad ligament opened by bluntly separating the extraperitoneal areolar tissues. The infundibulopelvic ligament is pulled medially with grasping forceps to expose the ureter at the pelvic brim where it crosses the common or external iliac artery. The operator then searches for the ureter distal to the pelvic brim

and lateral to the infundibulopelvic ligament. Blunt dissection is carried out beneath and caudal to the round ligament, until the obliterated hypogastric artery is identified extraperitoneally. The obliterated hypogastric artery is traced proximally to where it is joined by the uterine artery, and the pararectal space is opened by blunt dissection proximal and medial to the uterine vessels, which lie on top of the cardinal ligament. After the pararectal space has been opened, the ureter can be easily identified on the medial leaf of the broad ligament (actually posterior leaf), which forms the medial border of the pararectal space. The uterine artery and cardinal ligament at the distal (caudal) border of the space, and the internal iliac artery on its lateral border, also become clearly visible.

Securing the uterine vessels to decrease the risk of hemorrhage

Difficult exposure can increase the risk of hemorrhage. Therefore, it is sometimes appropriate to start the procedure by ligation of the uterine arteries. Identification of the umbilical ligament and dissection of this ligament exposes the uterine artery at its origin in the internal iliac artery. At this point, the artery can be sutured or clamped using vascular clips before it crosses the ureter. Ligation of both uterine arteries at the beginning of the procedure will decrease intraoperative blood loss¹⁵ (Figures 42.1–42.3).

Uterine morcellation (laparoscopic and vaginal)

Several techniques of vaginal morcellation of a freed uterus have been described. A No. 10 blade on a long knife handle is used to incise the uterus and remove it in pieces. Whichever technique is used, care must be taken



Figure 42.1 Initial view of a large uterus.



Figure 42.2 After identification of the ureter, the uterine artery is clipped at its origin in the internal iliac artery. (A) Umbilical ligament. (B) Internal iliac artery. (C) Uterine artery. (D) Ureter.



Figure 42.3 After clipping both uterine arteries and coagulation and section of the utero-ovarian ligaments, the uterus turns bluish in color. Hysterectomy can be performed without risk of hemorrhage.

to avoid lesions to the bladder, rectum, and surrounding vagina.

When vaginal access is limited or when a subtotal hysterectomy is performed, the uterus can be morcellated through a 10–20 mm trocar. We use the Rotocut morcellator (Karl Storz GmbH, Tuttlingen, Germany), a motorized circular saw, using claw forceps or a tenaculum to grasp the uterus and pull it into contact with the saw.

CONCLUSION

We firmly believe that laparoscopic hysterectomy offers multiple advantages over abdominal hysterectomy and vaginal hysterectomy. The increased risk of major complications during laparoscopic hysterectomy reported by both Garry and Johnson results from serious bias.

The results from our series of 2596 patients clearly show that LASH and LH are safe procedures. Do we really need randomized trials to tell us that laparoscopic hysterectomy is as valuable as or more valuable than other techniques, after encountering only 1.5% of major complications out of 2596 laparoscopic hysterectomies?

There is no doubt that laparoscopic hysterectomy requires greater surgical expertise and that the complication rate is related to the surgeon's skill. Such surgical expertise is surely required for laparoscopic hysterectomy in case of large uteri, as this type of surgery may well be accompanied by increased blood loss and a longer operating time. It is therefore important to optimize certain steps of the surgical technique in order to reduce these risks. In experienced hands, laparoscopic hysterectomy is totally feasible for large uteri and not associated with any increase in major complication rates.

References

- Reich H, De Caprio J, MacGlynn F. Laparoscopic hysterectomy. J Gynecol Coll Surg 1989; 5: 213.
- Garry R, Fountain J, Mason S et al. The eVALuate study: two
 parallel randomised trials, one comparing laparoscopic with
 abdominal hysterectomy, the other comparing laparoscopic with
 vaginal hysterectomy. BMJ 2004; 328: 129.
- Johnson N, Barlow D, Lethaby A et al. Methods of hysterectomy: systematic review and meta-analysis of randomised controlled trials. BMJ 2005; 330: 1478.
- Reich H. New techniques in advanced laparoscopic surgery. Clin Obstet Gynecol 1989; 3: 655–81
- Mage G, Wattiez A, Chapron C et al. [Laparoscopic hysterectomy, Results in 44 cases]. J Gynecol Obstet Biol Reprod (Paris) 1992; 21: 436–44 [in French].
- Donnez J, Nisolle M, Squifflet J, Smets M. Laparoscopy-assisted vaginal hysterectomy and laparoscopic hysterectomy in benign diseases. In: Donnez J, Nisolle M, eds. An Atlas of Operative Laparoscopy and Hysteroscopy. Carnforth, UK: Parthenon, 2001: 251–60.
- Johns A. Laparoscopic assisted vaginal hysterectomy (LAVH).
 In: Sutton C, Diamond D, eds. Gynecologic Endoscopy for Gynecologists. London: WB Saunders, 1993: 179–86.
- 8. Donnez J, Squifflet J, Jadoul P, Smets M. Results of eVALuate study of hysterectomy techniques: high rate of complications needs explanation. BMJ 2004; 328: 643.
- 9. Wattiez A, Soriano D, Cohen SB et al. The learning curve of total laparoscopic hysterectomy: comparative analysis of 1647 cases. J Am Assoc Gynecol Laparosc 2002; 9: 339–45.
- Donnez J, Nisolle M, Smets M et al. LASH: laparoscopic subtotal hysterectomy. In: Donnez J, Nisolle M, eds. An Atlas of Operative Laparoscopy and Hysteroscopy. Carnforth, UK: Parthenon, 2001: 243–50.
- 11. El-Toukhy TA, Hefni M, Davies A et al. The effect of different types of hysterectomy on urinary and sexual functions: a prospective study. J Obstet Gynaecol 2004; 24: 420–5.

- Schutz K, Possover M, Merker A et al. Prospective randomized comparison of laparoscopic-assisted vaginal hysterectomy (LAVH) with abdominal hysterectomy (AH) for the treatment of the uterus weighing >200g. Surg Endosc 2002; 16: 121–5.
- Seracchioli R, Venturoli S, Vianello F et al. Total laparoscopic hysterectomy compared with abdominal hysterectomy in the presence of a large uterus. J Am Assoc Gynecol Laparosc 2002; 9: 333–8.
- 14. Hwang JL, Seow KM, Tsai YL et al. Comparative study of vaginal, laparoscopically assisted vaginal and abdominal hysterectomies for uterine myoma larger than 6 cm in diameter or uterus weighing at least 450g: a prospective randomised study. Acta Obstet Gynecol Scand 2002; 81: 1132–8.
- Chang WC, Torng PL, Huang SC et al. Laparoscopic-assisted vaginal hysterectomy with uterine artery ligation through retrograde umbilical ligament tracking. J Minim Invasive Gynecol 2005; 12: 336–42.
- Wang CJ, Yen CF, Lee CL et al. Laparoscopically assisted vaginal hysterectomy for large uterus: a comparative study. Eur J Obstet Gynecol Reprod Biol 2004; 115: 219–23.
- Donnez J, Nisolle M, Smets M, Squifflet J. Hysteroscopic myomectomy. In: Donnez J, Nisolle M, eds. An Atlas of Operative Laparoscopy and Hysteroscopy. Carnforth, UK: Parthenon, 2001: 483–93.
- Seracchioli R, Venturoli S, Colombo FM et al. GnRH agonist treatment before total laparoscopic hysterectomy for large uteri. J Am Assoc Gynecol Laparosc 2003; 10: 316–19.
- Reich H, Seckin T, Reich JM. Laparoscopic hysterectomy including for advanced endometriosis with rectosigmoid disease.
 In: Donnez J, ed. An Atlas of Operative Laparoscopy and Hysteroscopy, 3rd edn. Oxon, UK: Informa Healthcare, 2006: 93–112.

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Robotics: an evolving option in the management of abnormal uterine bleeding

Arnold P Advincula

INTRODUCTION

Technological advancements in minimally invasive surgery have greatly impacted the field of gynecology and how pathology is treated. It was only 70 years ago that Boesch described tubal sterilization via laparoscopy. By the early 1970s, laparoscopy had revolutionized gynecology. Since then, minimally invasive surgery has become increasingly popular and demanded by both surgeons and patients in the field of gynecologic surgery.

Within the past 25 years, minimally invasive surgery has again evolved with the introduction of robotics. Historically, the concept of robotic technology was born through the collaborative efforts of the Stanford Research Institute (SRI), the Department of Defense, and the National Aeronautics and Space Administration (NASA).¹ The impetus for this concept was the need to be able to provide immediate operative care to wounded soldiers on the battlefield. Initial prototypes involved robotic arms that could be mounted on an armored vehicle in order to facilitate remote battlefield surgery. Soon thereafter, this technology became commercialized and robots were no longer just passive devices in surgery but ones that could be actively controlled in civilian operating rooms. It wasn't long before these developments were applied to various surgical disciplines.

The first application of a robot in surgery was in neurosurgery.² The original model, known as the PUMA 560, was used for neurosurgical stereotactic maneuvers under computed tomography (CT) guidance. Soon, other disciplines such as orthopedic surgery were utilizing a device called ROBODoc to aid in total hip replacements.³ A common theme to these early designs was the fact that these robots were developed to function autonomously with a preoperative plan or in a supervisory role. This passive role was soon going to evolve into a more active one, with an immersive environment that became known as robotic telepresence technology.

ROBOTICS IN GYNECOLOGY

Technical advancements such as improved hand instrumentation and electrosurgical devices have clearly brought about improvements to modern-day laparoscopy. This technology has continued to grow by leaps and bounds in the area of minimally invasive gynecologic surgery. Although a laparotomy may seem advantageous for the surgeon at first, the large abdominal incision, prolonged hospitalization, increased postoperative analgesic requirements, and increased morbidity are disadvantages for the patient. The days of a surgeon only obtaining access to the abdomen by laparotomy have long passed. Studies have clearly shown that laparoscopic surgery allows faster recovery with shorter hospitalization, improved cosmesis, decreased blood loss, and less postoperative pain.^{4,5} Despite these technological advancements and proven benefits, gynecologic conditions such as abnormal uterine bleeding and endometriosis and more complex procedures such as myomectomy and sacrocolpopexy are typically still managed by laparotomy.

One major obstacle to the more widespread acceptance and application of minimally invasive surgical techniques to gynecologic surgery has been the steep learning curve for surgeons that are associated with many of these advanced procedures. Other limitations encountered with conventional laparoscopy include counterintuitive hand movement, two-dimensional visualization, and limited degrees of instrument motion within the body as well as ergonomic difficulty and tremor amplification. In an attempt to overcome these obstacles, robotics has been incorporated into the gynecologic armamentarium. In this chapter we review the evolving data surrounding the application of robotics to the management of abnormal uterine bleeding.

The da Vinci Surgical System

Robotics is not new to the field of gynecologic surgery. Evidence of its early use in gynecologic surgery can be seen with two early predecessors, a voice-activated robotic arm known as Aesop (Computer Motion Inc., Goleta, CA) and a three-armed remotely controlled robot known as Zeus (Computer Motion Inc., Goleta, CA). The use of robotic technology to facilitate laparoscopic procedures such as tubal reanastomosis is clearly evident with these two early systems.^{7,8} The use of robotics in gynecology has only continued to increase over the past 5 years, particularly with the introduction of the latest and only FDA (Food and Drug Administration) approved platform in surgical robotics, the da Vinci Surgical System (Intuitive Surgical, Sunnyvale, CA). In fact, the da Vinci surgical system is the only actively produced robotic surgical system incorporating an immersive telepresence environment. In numerous studies across various surgical disciplines, it has been shown to be a safe and effective alternative to conventional laparoscopic surgery, particularly when dealing with complex pathology. In the area of gynecology, there are multiple reports of robot-assisted laparoscopy with the da Vinci Surgical System that involve a wide range of procedures and pathologic conditions, including abnormal uterine bleeding.

Prior to discussing the evolving gynecologic applications to abnormal uterine bleeding, it is important to understand the three technological components of the da Vinci Surgical System (Figure 43.1). The first component is the surgeon console, which is located remotely from the patient bedside. The surgeon seated at this console is able to control robot-assisted instruments within the patient with the aid of a stereoscopic viewer, hand manipulators, and foot pedals.

The second component of the da Vinci Surgical System is the *InSite* Vision System which provides three-dimensional imaging through a 12 mm endoscope. A newer model, the da Vinci S, provides the option of high

Figure 43.1 Photograph of the da Vinci Robotic System. From left to right: surgeon's console, patient-side surgical cart, and InSite Vision System. (Photo courtesy of Intuitive Surgical, Inc.)

definition in addition to telestration. Although a 5 mm endoscope is available, this only provides two-dimensional imaging.

The third component of the da Vinci Surgical System is the patient-side cart with robotic arms and *EndoWrist* instruments. Currently the System is available with either three or four robotic arms. One of the arms holds the endoscope while the other two to three arms hold the various *EndoWrist* instruments, which come in either 8 mm or 5 mm sizes. A newer model, the da Vinci S, functions on the same platform as its predecessor; however, it provides surgeons with an additional range of motion from longer instruments and increased pitch.

The *EndoWrist* instruments are unique in that they possess a wrist-like mechanism that allows seven degrees of movement, thereby replicating the full range of motion of the surgeon's hand, and in turn eliminating the fulcrum effect seen with conventional laparoscopy. A series of *EndoWrist* instruments, such as needle drivers, scissors, and graspers, can be interchanged on either of the lateral robotic arms (Figure 43.2). Although disposable, these *EndoWrist* instruments typically last for 10 uses and cost approximately \$2500 each. The actual da Vinci Surgical System itself retails for around \$1300000 to \$1500000.

Robotic myomectomy

Leiomyomata are often implicated in cases of abnormal uterine bleeding, particularly when submucosal in location. The primary surgical management of symptomatic leiomyomata for women desiring future fertility or uterine conservation is through a myomectomy. Today, many cases of intramural and subserous leiomyomata are managed with laparoscopic myomectomy, while select cases of submucosal leiomyomata are managed with hysteroscopic myomectomy. When submucosal leiomyomata approach



Figure 43.2 Photograph of an Endowrist instrument.

a size deemed unsafe and too large to address by hysteroscopy, a transabdominal route is necessary for extraction. Despite the fact that two prospective trials have shown postoperative morbidity to be less and recovery faster with laparoscopic myomectomy, the majority of cases are still performed via laparotomy.^{9,10}

The management of leiomyomata endoscopically is one of the more challenging procedures in minimally invasive surgery and requires a skilled surgeon. Because the various steps can be difficult with conventional laparoscopy, many concerns exist. In particular, the ability to enucleate leiomyomata and perform a multilayer closure requires advanced laparoscopic skills. The ability to suture is considered fundamental and, although pregnancy rates for leiomyomata managed endoscopically are similar to those after laparotomy, a major worry continues to be the risk of uterine rupture. The risk is essentially unknown.

Also, the risk of recurrence seems to be higher after laparoscopic myomectomy compared with laparotomy.¹¹ These factors and the associated learning curve may contribute to the reluctance to shift to a laparoscopic approach to myomectomy.

Senapati and Advincula recently described their surgical technique with robot-assisted laparoscopic myomectomy as a means to overcome the difficulties encountered with hysterotomy, enucleation, repair, and extraction during conventional laparoscopy. ¹² In their technical description, the advantages that robotic technology provided to a laparoscopic myomectomy were highlighted not only by the ability to perform a hysterotomy in both the horizontal and vertical plane but also with the ease of completing a multilayer sutured closure of the uterine defect (Figures 43.3 and 43.4). As an example, a three-layer closure modeled after traditional open surgical technique







Figure 43.3 (A) Serosal incision over leiomyoma with Endowrist permanent cautery hook. (B) Fibroid being enucleated robotically with countertraction provided by bedside surgical assistant using the Endowrist tenaculum.



Figure 43.4 Intracorporeal instrument tying with Endowrist instruments (DeBakey forceps and needle driver) during multilayer sutured closure of uterine defect: (A) deep myometrial layer, (B) running baseball stitch on serosal layer.

was utilized. Interrupted sutures of 0 Vicryl (polyglactin 910) on CT-2 needles were used to close the first two layers with interrupted figure-of-eight stitches followed by a running baseball stitch of 3-0 Vicryl on an SH needle for the serosa. All knots were tied intracorporeally.

The only published series of robot-assisted laparoscopic myomectomy is from Advincula et al.¹³ In this series of 35 cases, the mean myoma weight was 223.2 \pm 244.1 g (95% confidence interval [CI] 135.8–310.6). The mean number of myomas removed was 1.6 (range 1–5) and the mean diameter was 7.9 \pm 3.5 cm (95% CI 6.6–9.1). The average estimated blood loss was 169 \pm 198.7 ml (95% CI 99.1–238.4). No blood transfusions were necessary. The mean operating time was 230.8 \pm 83 minutes (95% CI 201.6–260.0). Median length of stay for these patients was 1 day; however, currently at our institution, this procedure is performed on an outpatient basis.

Of these cases, two were converted to laparotomy secondary to an absence of haptic (tactile) feedback, which made enucleation of the leiomyomas difficult. The third conversion was a result of cardiogenic shock secondary to the vasopressin used as an adjunct to hemostasis, an event unrelated to the robotic approach.

Recently, Advincula et al. compared surgical outcomes and costs between traditional abdominal myomectomy and the robot-assisted laparoscopic myomectomy through a retrospective case-matched analysis of 58 patients with symptomatic leiomyomata.¹⁴ An equal number of casematched patients based on age, body mass index (BMI), and fibroid weight were analyzed in each group (29 vs 29). Among these three variables, there were no statistically significant differences between the robotic and laparotomy groups. Mean age was 36.6 vs 35.9 years old, mean BMI was 25.2 vs 28.3 kg/m², and mean fibroid weight was 227.9 vs 223.8 g, respectively. Interestingly, robot-assisted laparoscopic myomectomy patients had decreased estimated blood loss (mean 195.7 vs 364.7 ml) and length of stay (mean 1.48 vs 3.62 days) when compared to the laparotomy group. Both of these differences were statistically significant at p < 0.05. Operative times were significantly longer in the robotic group (mean 231.4 vs 154.4 minutes, p < 0.05). Complication rates were higher in the laparotomy group.

Professional charges (mean US\$5946.48 vs US\$4664.48, p < 0.0002) and hospital charges (mean US\$30 084.20 vs US\$13 400.62, p < 0.0001) were statistically higher for the robotic group. Although professional reimbursement was not significantly different between the two groups (mean US\$2263.02 vs US\$1841.99, p = 0.2831), mean hospital reimbursement rates for the robotic group were significantly higher (mean US\$13 181.39 vs US\$7015.24, p = 0.0372). The authors

concluded that it was not unexpected that a robotic approach to myomectomy costs more than a traditional laparotomy given the new technology. On the other hand, the decreased estimated blood loss, complication rates, and length of stay with the robotic approach in the end may prove to have a significant societal benefit that will outweigh the upfront financial impact after further investigation is conducted.

Robotic hysterectomy

Hysterectomy remains the treatment of choice for patients with refractory abnormal uterine bleeding, despite conservative medical and/or surgical attempts at management, who also no longer desire fertility preservation. Traditionally, this is approached by either an abdominal or vaginal route; however, with the evolution of surgical technology, the approaches by which a hysterectomy is performed have also evolved. This is seen in the transformation of hysterectomy to laparoscopic-assisted vaginal hysterectomy and, eventually, to laparoscopic supracervical and total laparoscopic hysterectomy. 15-17 As a result, a definite trend toward laparoscopic hysterectomy has been seen since the 1990s. Despite these advancements in surgical technique, in 2002, Farquhar and Steiner reported that only 10% of hysterectomies were performed minimally invasively with the assistance of laparoscopy. 18

One major obstacle to the more widespread acceptance and application of minimally invasive surgical techniques to hysterectomy has been the limitations encountered with conventional laparoscopy. These include counterintuitive hand movement, two-dimensional visualization, and limited degrees of instrument motion within the body. Another explanation for this slow acceptance has been the learning curve with conventional laparoscopy and its associated complications. Advanced pathology such as pelvic adhesions or an altered surgical anatomy field has also often been a limiting factor to applying conventional laparoscopic techniques to gynecologic procedures.

Additional challenges have been the issues surrounding the surgeon's skill level as well as the training and acquisition of advanced skills. As a result of these obstacles, gynecologic surgeons have begun to apply robotic technology to their endoscopic armamentarium, particularly to help facilitate hysterectomy.

In the gynecologic literature, several authors have evaluated robot-assisted laparoscopic hysterectomy and patient outcomes. Diaz-Arrastia and colleagues in 2002 reported one of the earliest experiences with robot-assisted laparoscopic hysterectomy. This series included 16 patients, ranging in age from 27 to 77 years old. Operative times ranged from 270 to 600 minutes and blood loss

ranged between 50 and 1500 ml, with an average of 300 ml.¹⁹ Average hospital stay was 2 days, with a range of 1 to 3 days. Although their approach was labeled a laparoscopic hysterectomy, all cases in that series were Type IIB according to the American Association of Gynecologic Laparoscopists (AAGL) classification system for laparoscopic hysterectomy, meaning that the posterior culdotomy and ligation of the cardinal and uterosacral ligament complexes were performed vaginally in order to complete the hysterectomy.²⁰

Beste et al. described their initial hysterectomy experience with 10 robot-assisted AAGL Type IVE cases. The AAGL Type IVE hysterectomy is defined as totally laparoscopic removal of the uterus and cervix, including vaginal cuff closure. They found their operative results were similar to those of conventional laparoscopic hysterectomy.²¹

Recently, Fiorentino and colleagues published the largest series of AAGL Type IVE hysterectomy. Eighteen out of twenty women presenting with benign gynecologic conditions underwent a successful robot-assisted total laparoscopic hysterectomy. Two patients were converted to laparotomy with subsequent abdominal hysterectomy because of poor visualization during robot-assisted surgery.²² Reynolds and Advincula reported the first series of 16 consecutive patients who underwent either an AAGL Type IVE or LSH III hysterectomy. In contrast to the Type IVE, the LSH III hysterectomy is defined as a totally laparoscopic supracervical procedure with removal of the uterine corpus, including division of the uterine arteries. The mean uterine weight was 131.5 g, with a range of 30-327 g. There were no conversions to laparotomy in this series. Specifically, they noted the advantage of robotic technology in the patient with scarred or obliterated surgical planes, since 13 of the 16 patients had prior pelvic surgery and required intraoperative management of pelvic adhesions in order to complete the hysterectomy.²³ This same advantage was also described by Advincula and Reynolds in a robotic series of six patients undergoing successful hysterectomy who had a scarred or obliterated anterior cul-de-sac as a result of prior cesarean deliveries.²⁴ A description of the robotic technique was published in 2006.²⁵ Robotics played a critical role in the safe and successful completion of a robot-assisted hysterectomy by facilitating adherence to the principles of open surgery, which included proper development of avascular planes and skeletonization of vascular pedicles prior to ligation either by suture or radiofrequency current. Procedural steps such as vaginal cuff closure were more readily accom-



Figure 43.5 Closure of vaginal cuff with interrupted sutures of 0 Vicryl on CT-2 needles.

plished as a result of the increased instrument dexterity afforded by the *EndoWrist* technology (Figure 43.5).

Despite significant advantages seen with the robotic approach for hysterectomy, Nezhat et al described disadvantages with their very early robotic experience. They found the absence of haptic (tactile) feedback, bulkiness of the system, lack of vaginal access, and costs to be limiting factors; however, their experience included only three robotic hysterectomies.²⁶

CONCLUSION

The evolution of surgical technology has brought about many more options for managing abnormal uterine bleeding. The current literature demonstrates that myomectomy and hysterectomy can be approached successfully with robot-assisted laparoscopy. The benefits of a laparoscopic approach are maintained while gaining the advantages of improved instrument precision and dexterity coupled with three-dimensional imaging. Although these improvements seem to overcome many of the limitations seen with conventional laparoscopy, there are also drawbacks. The absence of haptic (tactile) feedback and costs remain limitations. While evolving robotic technology may further improve patient outcomes and overcome current limitations, prospective studies will need to be conducted to determine appropriate applications and delineate advantages and disadvantages when compared to conventional laparoscopic techniques.

References

- Satava RM. Robotic surgery: from past to future a personal journey. Surg Clin North Am 2003; 83: 1–6.
- Kwoh YS, Hou J, Jonckheere EA, Hayati S. A robot with improved absolute positioning accuracy for stereotactic brain surgery. IEEE Trans Biomed Eng 1988; 35: 153–60.
- Bauer A, Borner M, Lahmer A. Clinical experience with a medical robotic system for total hip replacement. In: Nolte LP, Ganz R, eds. Computer Assisted Orthopedic Surgery. Bern: Hogrefe & Huber, 1999: 128–33.
- Yuen PM, Yu KM, Yip SK et al. A randomized prospective study of laparoscopy and laparotomy in the management of benign ovarian masses. Am J Obstet Gynecol 1997; 177: 109– 14.
- Lo L, Pun TC, Chan S. Tubal ectopic pregnancy: an evaluation of laparoscopic surgery versus laparotomy in 614 patients. Aust NZ J Obstet Gynecol 1999; 39: 185–7.
- Stylopoulos N, Rattner D. Robotics and ergonomics. Surg Clin North Am 2003; 83: 1–12.
- Mettler L, Ibrahim M, Jonat W. One year of experience working with the aid of a robotic assistant (the voice-controlled optic holder AESOP) in gynecologic endoscopic surgery. Hum Reprod 1998; 13: 2748–50.
- 8. Falcone T, Goldberg JM, Margossian H, Stevens L. Robotically assisted laparoscopic microsurgical anastomosis: a human pilot study. Fertil Steril 2000; 73: 1040–2.
- Seracchioli R, Rossi S, Govoni F et al. Fertility and obstetric outcome after laparoscopic myomectomy of large myomata: a randomized comparison with abdominal myomectomy. Hum Reprod 2000; 15: 2663–8.
- Mais V, Ajossa S, Guerriero S et al. Laparoscopic versus abdominal myomectomy: a prospective randomized trial to evaluate benefits in early outcome. Am J Obstet Gynecol 1996; 174: 654–8.
- 11. Doridot V, Dubuisson JB, Chapron C et al. Recurrence of leiomyomata after laparoscopic myomectomy. J Am Assoc Gynecol Laparosc 2001; 8: 495–500.
- Senapati S, Advincula AP. Surgical techniques: robot-assisted laparoscopic myomectomy with the daVinci® surgical system. J Robotic Surg 2007; Epub ahead of print.

- Advincula AP, Song A, Burke W, Reynolds RK. Preliminary experience with robot-assisted laparoscopic myomectomy. J Am Assoc Gynecol Laparosc 2004; 11: 511–8.
- Advincula AP, Xu X, Goudeau S, Ransom S. Robot-assisted laparoscopic myomectomy versus abdominal myomectomy: a comparison of surgical outcomes and costs. American Association of Gynecologic Laparoscopists Annual Meeting, Las Vegas, NV, November 2006.
- Reich H, Decaprio J, McGlynn F. Laparoscopic hysterectomy. J Gynecol Surg 1989; 5: 213–6.
- Donnez J, Nisolle M. Laparoscopic supracervical (subtotal) hysterectomy (LASH). J Gynecol Surg 1993; 9: 91–4.
- Reich H, McGlynn F, Sekel L. Total laparoscopic hysterectomy. Gynecol Endosc 1993; 2: 59–63.
- Farquhar CM, Steiner CA. Hysterectomy rates in the United States 1990–1997. Obstet Gynecol 2002; 99: 229–34.
- Diaz-Arrastia C, Jurnalov C, Gomez G, Townsend C. Laparoscopic hysterectomy using a computer-enhanced surgical robot. Surg Endosc 2002; 16: 1271–3.
- Olive DL, Parker WH, Cooper JM, Levine RL. The AAGL classification system for laparoscopic hysterectomy. J Am Assoc Gynecol Laparosc 2000; 7: 9–15.
- Beste TM, Nelson KH, Daucher JA. Total laparoscopic hysterectomy utilizing a robotic surgical system. JSLS 2005; 9: 13–5.
- Fiorentino RP, Zepeda M, Goldstein BH et al. Pilot study assessing robotic laparoscopic hysterectomy and patient outcomes. J Minim Invasive Gynecol 2006; 13: 60–3.
- Reynolds RK, Advincula AP. Robot-assisted laparoscopic hysterectomy: technique and initial experience. Am J Surg 2006; 191: 555–60.
- Advincula AP, Reynolds RK. The use of robot-assisted laparoscopic hysterectomy in the patient with a scarred or obliterated anterior cul-de-sac. JSLS 2005; 9: 287–91.
- Advincula AP. Surgical techniques: robot-assisted laparoscopic hysterectomy with the daVinci® surgical system. Int J Med Robotics Comput Assist Surg 2006; 2: 305–11.
- Nezhat C, Saberi NS, Shahmohamady B, Nezhat F. Roboticassisted laparoscopy in gynecological surgery. JSLS 2006; 10: 317–20.

Complications and clinical outcomes of hysterectomy

Craig Skidmore and Caroline E Overton

INTRODUCTION

Hysterectomy remains the definitive treatment for uterine bleeding, carrying with it the risk of serious complications.1 Medical and surgical advances in gynecologic practice now offer several alternative treatments to be considered before hysterectomy. Symptoms can be controlled by less-invasive, less-risky, less-painful, and often less-costly approaches, and hysterectomy is now less common. There has been a decline by two-thirds in the number of hysterectomies performed for menorrhagia in the UK over the last decade, attributed to the increased use of the levonorgestrel-releasing intrauterine device and endometrial ablative techniques.2 Interestingly, this may lead to an increase in the operative difficulty of hysterectomy.³ Over half a million hysterectomies are performed annually in the USA, 4 although there is evidence from regional reports that the rate of hysterectomy for benign conditions is on the decline.⁵ Nevertheless hysterectomy has a firmly established place. As alternative therapies to hysterectomy have developed, so too have methods for hysterectomy advanced. Abdominal, abdominal via mini-laparotomy, laparoscopic (in part or total), laparoscopic robotic, and vaginal hysterectomy are available. Whereas bias, experience, and skill may partly determine the route taken, the method of hysterectomy should be selected on safety and the most satisfactory outcome for the patient.

A discussion of complications and clinical outcomes of hysterectomy will compare and review significant and serious complications. It is the doctor's responsibility to ensure that alternative treatments that carry less morbidity have been considered prior to hysterectomy. It must also be acknowledged that abnormal uterine bleeding is not the only benign gynecologic indication for hysterectomy, and that much of the published data on hysterectomy outcomes include surgery for a number of benign indications. Concomitant endometriosis, fibroids, symptomatic uterine prolapse, adenomyosis, dysmenorrhea, chronic pelvic pain, endometrial hyperplasia, or coincident severe cervical dysplasia are examples of conditions

that may weigh towards hysterectomy. Authors of the VALUE⁶ trial reported that the indication for hysterectomy was dysfunctional uterine bleeding in 40% of cases. The data were collected for the period 1994–1995, and there is evidence that the frequency of hysterectomy is declining.

INFORMING PATIENTS OF CHOICES AND RISKS

Whereas individual patients have different priorities, we must understand and ourselves be informed about the absolute and relative intraoperative, short- and long-term risks of the surgical approaches, the likelihood of a satisfactory outcome, and the impact of short- and long-term complications, side effects, and positive outcomes for our patients. Such information should also include guidance on recovery time, as well as the likelihood of long-term psychological, physical, and sexual well-being.

That said, despite research, audit, and experience, we are limited in our knowledge of these and many other relevant factors in preparing a patient for hysterectomy. Importantly, we must integrate what we do know with the individual's perception of risk and benefit. This is the process of risk communication, and it is vital that all clinicians are competent in accurate and meaningful risk conveyance.

The evidence needs to be applied appropriately to the individual woman. Vaginal hysterectomy is the best choice *when it is achievable*, but in real practice, we don't always know until intraoperative assessment, that this route is achievable. It is no longer considered reasonable to perform an abdominal hysterectomy solely because pathology is suspected. Guidelines have been produced to assist clinicians in making more objectively based decisions on the route of hysterectomy,⁷ and there is evidence that practice is changing.⁸ Surgical feasibility thus alters the balance of information we convey, although patients report that it is important that they know the options and the reasons why one route is offered over another.

TYPES OF HYSTERECTOMY

Total hysterectomy results in complete amenorrhea with rare exceptions (e.g. vaginal endometriotic implants). Subtotal hysterectomy is also extremely effective in treating heavy menstrual bleeding, although minor bleeding can occur, even if the endocervical canal is ablated. Studies report continued cyclical bleeding in 7–20%^{9,10} of patients after supracervical hysterectomy, the average reported incidence being around 11%.¹¹

Surgical approaches to hysterectomy are vaginal hysterectomy (VH), open abdominal hysterectomy (AH), and three laparoscopic approaches, as proposed by Reich and Roberts¹² (other nomenclatures have been proposed) that define the extent of surgery that is undertaken laparoscopically: Laparoscopic-assisted vaginal hysterectomy (LAVH) involves partial laparoscopic hysterectomy, but not division of the uterine arteries; laparoscopic hysterectomy (LH) includes laparoscopic uterine artery ligation; and total laparoscopic hysterectomy (TLH) describes a procedure where all surgery including vault closure is achieved laparoscopically. Any of the techniques may include adnexectomy (unilateral or bilateral). Any form of hysterectomy can preserve the cervix, although it is most commonly undertaken in the subtotal abdominal hysterectomy (sAH) and subtotal laparoscopic hysterectomy (sLH) procedures.

WHICH SURGICAL APPROACH?

The literature suggests that VH should be the operation of choice for benign abnormal uterine bleeding. The decision to carry out LH or AH over VH may be swayed by a variety of factors: ¹³ prophylactic removal of the ovaries, previous cesarean section, suspected pelvic pathology (palpable endometriosis), uterine size greater than 14–16 weeks, nulliparity, inadequate descent, or inadequate access. Melis and coauthors ¹⁴ reported a retrospective series of hysterectomies. Significant factors that determined the type of hysterectomy were uterine weight/volume, nulliparity, narrow vagina, and planned salpingo-oophorectomy. AH may be preferred over all other techniques when the uterus is very large, and certainly remains the intraoperative default when it is recognized that any other method cannot be completed safely.

Patient preference, along with the surgeon's bias and experience, remain significant determinants of hysterectomy approach. ¹⁵ Other determinants, such as availability of assisting devices such as a laparoscopic morcellator, may also alter the feasibility of a route of operation.

The evidence on outcomes and complications of hysterectomy needs to be interpreted in two key ways:

• If any route of hysterectomy is possible, which is the safest method with the best outcome?

 When a particular method is selected, what are its specific rates of complications, and expected outcome(s)?

Evidence from randomized controlled trials (RCTs) is the soundest method for addressing the first of these questions (if the trials are sufficiently large and the incidence of complications is high enough). Inclusion and exclusion criteria determine the pool of patients who are randomized, and different methods of hysterectomy are compared. The best operation can then be recommended for the individual patient.

However, the real world is not this simple. A patient with known extrauterine pathology and a large (>16-week size) uterus would not meet the criteria for inclusion in most trials that have assessed vaginal hysterectomy. Thus, it is not appropriate to look in isolation at the LH arm of VH vs LH RCTs to get outcome data for counseling this patient. Some RCTs comparing LH with AH also exclude patients with this size uterus (e.g. Garry et al. ¹⁶). We must therefore carefully select the RCTs to ascertain the likely complications and outcomes, and look towards evidence from studies with different methodologies when suitable RCTs have not been undertaken.

Unless patient numbers are very large, RCTs are not suitable for determining the true rate of complications when complications are rare. Meta-analysis may partly improve this by pooling data. Large cohort studies, or published audit, are of value in determining rates of complication, although comparison of risks of techniques may be less valid.

THE EVIDENCE AND RESEARCH

The Cochrane Collaboration concentrates on evidence from selected RCTs to perform meta-analyses from which the authors draw conclusions. In 2006, the surgical approaches to hysterectomy for benign gynecologic disease were subject to review and comparison in two separate publications: one review compared outcomes between VH, AH, and LH; the other review compared outcomes of total vs subtotal AH.^{11,17} All the hysterectomy trials included were for benign disease. Some details of the studies essential for the interpretation of results are discussed below.

The Cochrane meta-analysis of the surgical approaches to hysterectomy for benign gynecologic disease¹⁸ drew its results from 27 RCTs. Sixteen studies compared LH vs AH. Selection criteria varied between studies. Most (11/16 studies) had inclusion criteria of planned AH or some contraindication to VH. Enlarged uterine size was also an exclusion criterion in 11 of these 16 trials, varying between >12–18 weeks, or a width of >10–11 cm. Four

RCTs compared LH and VH, two of these excluded patients if uterine size was >16 weeks, and two included patients if the uterus was enlarged (>280 g). Three trials looked at LH and VH vs AH, and a single RCT trial was identified comparing LAVH vs LH. The final trial compared LH to AH and VH. Data from over 3500 patients were combined for analysis. A separate meta-analysis¹¹ of subtotal AH vs AH included three RCT trials primarily comparing subtotal to total AH (733 patients).

SHORT-TERM OUTCOMES AND COMPLICATIONS

Operating time

The Cochrane group identified two RCTs^{18,19} that indicate an 11.41 minute (95% confidence interval [CI] 6.6–16.3) shorter operating time for subtotal AH vs AH. The two RCTs included in the Cochrane review comparing VH vs AH had discordant results regarding operating time (VH shorter in one, AH shorter in the other). LAVH appeared to take less time than AH (7.6 minutes, 95% CI 3.0–12.2 minutes). Further analysis suggested that operating time for LH overall was significantly longer, while the finding that LAVH was shorter than AH was not statistically significant (Figure 44.1). LAVH operating time was shorter than LH (25 minutes, CI 95% 10–40 minutes), and VH shorter than LH (41.5 minutes, CI 95% 33.7–49.5 minutes).

Other intraoperative factors

Aside from operating time, various intraoperative factors were assessed in the Cochrane analysis of surgical

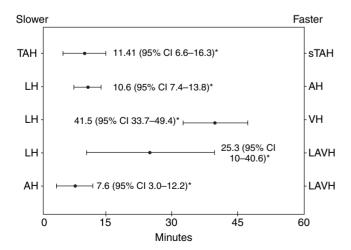


Figure 44.1 Comparison of route of hysterectomy operating times. Data assembled from results of two Cochrane Collaborative reviews. 11,17

approaches to hysterectomy for benign gynecologic disease. 18 Importantly, apart from overall urinary tract injuries, intraoperative complications were not found to be significantly increased in the laparoscopic procedures, and VH was not shown to reduce the urinary tract injury rate compared to AH. Intraoperative complications were thoroughly assessed by most of the RCTs included. Looking at all urinary tract injuries, complications were more likely during LH vs AH (odds ratio [OR] = 2.61, 95% CI 1.22-5.60), but not LH vs VH, or LH vs LAVH. In the meta-analysis, when complications were analyzed separately, there were no detectable differences in the incidence of bladder, ureteric, or bowel injury.¹⁸ No difference was seen in the rate of vascular injury; neither was there an increase in unintended laparotomy when the surgical approaches LH vs LAVH or VH were compared. Intraoperative complications other than operating time and blood loss were not reported or were not subject to comparison in the Cochrane analysis of subtotal vs total AH.¹¹

Early postoperative outcomes

Infections, wound infections, and postoperative fever

The majority of trial subjects in both Cochrane group collaborations^{11,18} received prophylactic antibiotics, and had their surgery performed under general anesthesia. VH and LH compared favorably to AH, both having less unspecified febrile illnesses or infections – VH: OR = 0.42, 95% CI 0.21–0.83; LH: OR = 0.65, 95% CI 0.49–0.87. There were fewer abdominal wall or wound infections in the LH group compared to the AH group (OR = 0.32, 95% CI 0.12–0.85). These data suggest that a patient is about half as likely to get a postoperative fever or infective illness if they have a VH or LH as compared an AH.

In all three trials 9,10,18 included in the Cochrane groups report comparing sTAH with AH, 11 postoperative fever was less common, overall being less than half as likely to occur in subtotal rather than total abdominal hysterectomy (OR = 0.43, 95% CI 0.25–0.75).

Blood loss (measured loss and hemoglobin [Hb] drop) and the need for transfusion were not significantly different for VH vs AH, or LH vs LAVH. Whilst transfusion rate was no less for LH vs AH, blood loss and mean hemoglobin drop were less in the LH group: weighted mean difference (WMD) was blood loss 43.3 ml, 95% CI 17.9–72.7ml; Hb: WMD = 0.55 g/L, 95% CI 0.28–0.82 g/L.

The incidence of vault hematoma, urinary tract infection, chest infection, and venous thromboembolic events did not differ between groups compared in the Cochrane review of the surgical approaches to hysterectomy for benign gynecologic disease. Whilst 1% of sAH patients

got a pelvic hematoma or abscess compared with 5% in the AH group in the Cochrane sAH vs AH review,¹¹ this did not reach significance (p = 0.06).

Hospital stay and return to normal activity

The Cochrane review¹⁸ reported that length of hospital stay was reduced if hysterectomy was achieved by VH (1 day less, 95% CI 0.7–1.2 days) or LH (2 days less, 95% CI 1.9–2.2 days) when compared to AH.

Return to normal activities is a rough method to compare techniques. It depends on local postoperative guidelines, social factors, and probably only acts as a marker of true complete recovery. RCTs should control for most of these variables reasonably, and findings are reported below from the two recent Cochrane reviews.^{11,18}

Overall, time to return to normal activities was significantly reduced in the VH (9.5 days faster return to normal activity, 95% CI 6.4–12.6 days) and LH (13.6 days faster, 95% CI 11.8–15.4 days) groups compared to AH patients. Return to normal activities was commonly judged by follow-up questioning of time from operation until return to work. LAVH vs LH, and LH vs VH were studied, but hospital stay and time to return to normal activities were not found to be different.

Hospital costs

Overall hospital costs between LH and AH were not found to be different in the five RCTS that addressed this question. However, VH was found to be less expensive than LH in the one RCT that assessed this.²⁰ No difference in return to normal activities was detected in the review that compared RCTs of sTAH vs AH.

Bleeding after subtotal abdominal hysterectomy and total abdominal hysterectomy

The Cochrane Collaboration review of total vs subtotal hysterectomy for benign gynecologic conditions¹¹ reported that ongoing cyclical vaginal bleeding was 11 times more likely to occur in the sAH group compared to the AH group (OR = 11.31, 95% CI 4.1–41.2): 11.9% of woman at 1 year who were treated in the sAH group had ongoing cyclical bleeding (compared to 0.98% of the AH recipients).

Learning curve and safety factors

LH and LAVH are subject to a learning curve. Rosen et al²¹ suggested that 10 cases should be supervised by an experienced laparoscopic surgeon to minimize the complications and reduce operating times, and 16 cases by a trainee. They report that the rate of complications plateaus after

this, although the trial was small (33 patients and three complications). A well-designed RCT by Perino and colleagues²² observed that the operating time plateaued after approximately 12 LH cases. While these trials have reported great improvements in operating time and competency after relatively few cases, the case numbers were small for the study of relatively infrequent events. It is generally regarded that true competency in LH procedures is achieved after far more cases than these numbers suggest.

The incidence of major complications is a topic of much debate. Garry et al¹⁶ reported an 11.1% rate of major complications in the largest multicenter RCT to date comparing LH with AH. Major complications in their series included major hemorrhage, hematoma requiring drainage or transfusion, bowel, ureteric or bladder injury, pulmonary embolus, major anesthetic problems, wound dehiscence, and unintended laparotomy. They concluded that this was clinically relevant when compared to a complication rate of 4.9% in AH (p = 0.02, 95% CI 0.9%-9.1%). They advocated further development of training and methods to reduce this rate. Their eVALuate trial was criticised for the high rate reported. It was suggested that the study was undertaken too early in the collective experience(s) of the surgeons performing LH.²³ Certainly, the complication rate is far higher than that reported by other surgeons, who reported their rates after experience of several hundreds of cases.²⁴

Most would agree that unplanned or conversion to laparotomy is not as consequential as the other major complications, and that any hysterectomy is performed with the understanding that AH may be necessary to safely complete the procedure. Reanalysis of comparative complication rates after excluding the 'unintentional laparotomy' from major complications in the eValuate trial has been undertaken, and it revealed no significant difference between LH and AH. ²⁵ This resulted in a complication rate of 7.8%, not dissimilar to Waittez and colleagues' rates in their first 695 LHs (5.6%). ²⁴

LONGER-TERM OUTCOMES AND COMPLICATIONS

High-quality research into long-term outcomes after hysterectomy is lacking.

Based on anatomic knowledge, it is likely that disruption and removal of sections of the pelvic plexus may occur in both routine and complicated hysterectomy. The pelvic plexus innervates the vagina, cervix, uterus, bladder, urethra, and bowel. Results overall suggest that presumed damage to the pelvic plexus does not cause clinically relevant side effects.

Bladder function

Overall, hysterectomy for benign disease does not appear to negatively impact on urinary function. It may even lead to an overall improvement in bladder function, although the mechanism for such improvement has not been elucidated.

Retrospective studies initially suggested a worsening of urinary incontinence, although prospective studies did not confirm this. The only RCT identified compared bladder function at 2 years in a group of patients who underwent hysterectomy vs endometrial ablation. A total of 79% of patients responded to subjective questionnaire review and 50% had objective follow-up (bladder cystometry). There were no significant differences between the treatment groups in terms of reported or measured bladder dysfunction.²⁶ Systematic review by Brown and colleagues²⁷ suggested that hysterectomy increased the risk of developing bladder dysfunction, although the studies were predominantly retrospective and observational (most did not adjust for parity, age, or weight), only one was randomized, and follow-up was short. The largest prospective study which addressed urinary incontinence compared woman having a hysterectomy and concurrent stress incontinence surgery with those having hysterectomy.²⁸ The study findings supported other prospective findings that urinary incontinence was overall not worsened or caused by hysterectomy in the interval of follow-up. Kjerulff et al²⁸ found that women with severe and moderate incontinence showed persistent improvement at 2 years following hysterectomy alone. In the same treatment group (hysterectomy only), about 10% of women with no or mild urinary incontinence developed symptoms that persisted at 2 years. They concluded: women with significant incontinence symptoms may benefit from hysterectomy; women with no or mild symptoms should be warned that symptoms could develop, with a de-novo incidence of about 10%.

Methods of hysterectomy and urinary function

There are no published RCTs that compare methods of hysterectomy and urinary function at 1 or 2 years after surgery. Evidence from the meta-analysis of three trials comparing sAH with AH¹¹ found that one trial reported increased incontinence after AH compared to sAH (Gimbel, 2003),¹⁰ a finding not supported by the other two included RCTs.^{9,18} Thakar and colleagues thoroughly assessed urinary incontinence, including reporting of symptoms and urodynamic studies, repeated at 12 months after sAH and AH.¹⁹ Women were found to report less symptoms of urinary stress incontinence, urgency, frequency, nocturia, interrupted stream, and incomplete

emptying in both groups. Urodynamic stress incontinence was also decreased in both groups at 12-month follow-up compared to preoperatively, and the urodynamic test indices 'first' and 'strong' desire to void mean values were increased. Overall improvement in urinary function at 2 years was also reported by Learman et al.¹⁸ They reported less bladder or pelvic pressure, less urgency, less sensation of incomplete emptying, and less stress and urge incontinence.

It would seem that there is no robust evidence supporting the historic notion that hysterectomy of any type for benign disease worsens urinary function. Older, retrospective, or non-randomized studies must be questioned for validity. There is a need for further robust research with long-term outcomes, and the suggested improvement in urinary function also warrants further study.

Sexual function

The recent Cochrane review of RCTs comparing subtotal with total abdominal hysterectomy showed no significant differences in frequency of orgasm, incidence of dyspare-unia, vaginal lubrication, and sexual satisfaction. The concept of 'sexual satisfaction' was addressed differently in the trials included in the meta-analysis, and data could not be combined. Keeping or removing the cervix thus seems not to influence sexual function in patients after hysterectomy (see Chapter 46).

Pelvic prolapse

No significant difference was demonstrated in the two RCTs included in the Cochrane collaboration¹¹ that assessed the odds of pelvic prolapse in subtotal vs total AH. There was a trend towards greater prolapse in the subtotal group which did not reach statistical significance. No RCT has been identified that assessed pelvic organ prolapse from studies comparing LH, VH, and AH methods.

Overall mortality

There is no evidence that undergoing hysterectomy increases overall long-term mortality. The longest follow-up trial with a large sample size (nested cohort of 7410 woman, average follow-up more than 20 years)²⁹ reported non-significant protective trends, possibly greater in women who underwent the procedure at a younger age. The authors emphasize that this does not endorse routine hysterectomy as a public health measure, but does allow the clinician to reassure their patients they are not putting themselves at increased long-term mortality if the operation is necessary.

PREVENTING AND MINIMIZING THE IMPACT OF COMPLICATIONS

Having now looked at the clinical outcomes and complications of the various types of hysterectomy, we will look at the ways in which such complications can be minimized and managed.

Principles of management

Management of postoperative complications requires recognition that the injury has occurred and repair, best completed at the time of the operation. Consult intraoperatively with the appropriate specialist if you have any reservations about performing the repair or determining the best management. Patients are least satisfied with surgical care if they need to be readmitted, and litigation is more costly with a delay in diagnosis.

Prevention of intra- and postoperative complications

'Prevention is better than cure.' Selection of the safest operation, detailed knowledge of pelvic anatomy, and how pathology alters it are the key principles to injury prevention.

Does bowel preparation help?

In cases of known endometriosis or altered anatomy, consider bowel preparation. An enema to clear the rectum allows greater access laparoscopically and during laparotomy. There is now evidence that mechanical bowel preparation does not affect the postoperative course in either planned or unplanned large bowel injury repair or anastomosis. The absence of a prepped bowel is no longer a contraindication for immediate primary repair.

DIAGNOSIS AND REPAIR OF INTRA- AND POSTOPERATIVE COMPLICATIONS

Diagnosis

Table 44.1 depicts hysterectomy-type specific tests for detection of suspected visceral injury.

Management and repair of bowel injury

The colon and rectum

Repair can be undertaken vaginally, laparoscopically (if skilled with suturing techniques), or abdominally. Any approach is acceptable, as long as the full extent of the

injury is accessible and assessable. Clean and irrigate the area and cover intraoperatively with prophylactic antibiotics. Repair in two layer(s) (mucosa and seromuscular) with interrupted, rapidly absorbable monofilament 3/0 sutures, minimizing tension; Postoperatively, use stool softeners. Anticipate an excellent outcome.

Small bowel

Clean and irrigate the area and give prophylactic antibiotic cover. Inspect adjacent bowel and mesentery to exclude other injury. Laparoscopic trocar injuries normally require laparotomy to fully assess for other injuries. If the full extent of the injury is assessable and accessible, 1–2 cm long injuries can be repaired via any route when competency allows. Repair in one layer (serosa and muscularis, but excluding the mucosa) with an absorbable monofilament 2/0 or 3/0 suture, repairing across, rather than along the length of the small bowel. If there is mesenteric bleeding, tie off as close as possible to bleeder, rather than higher in arcade system. For larger-size injuries, involve surgical expertise.

Blood vessels

Control of the bleeding is required. If bleeding is catastrophic, laparotomy and aortic/iliac compression is required and urgent attendance of the vascular team.

Bladder and ureteric injury

The ureter is most at risk at the pelvic brim, as it crosses the uterine vessels and lateral vaginal vault. Safe electrocautery and surgical techniques, and a well-hydrated patient (better ureteric flow = less thermal injury) helps prevent ureteric injury. Prophylactic stenting of the ureters has its supporters, and may be indicated in some cases. It is time consuming and would be required over 200 times to potentially identify an injury more easily intraoperatively.³⁴ Neither has urography been shown to decrease the risk of ureteric injury in prospective trials.

Surgeons should have a low threshold for cystoscopy if urinary tract injury is suspected. Ureteric integrity can at this time be assessed with intravenous indigo carmine (5–10 ml) administration prior to cystoscopy. Flow may be increased with diuretics or repositioning the patient. Look for efflux that is both present (rules out complete ligation or breaching of ureteric lumen) and equal bilaterally (partial obstruction or ligature 'kinking'). Intraoperative identification and repair reduces postoperative complications, return to theatre, impaired renal function, and nephrostomy.³⁵ Intravenous indigo carmine is particularly useful for identification of bladder and ureteric

Table 44.1 Intraoperative techniques for immediate diagnosis of complications

Location	Vaginal hysterectomy	Laparoscopic hysterectomy	Abdominal hysterectomy
Large bowel	Direct visualization or digital rectal examination. Injury should be suspected if difficult posterior colpotomy or obliterated pouch of Douglas	Direct visualization (including thermal whitening) or digital rectal examination. Fill the pelvis with saline and force gas into rectum. Bubbles appearing suggests injury	Direct visualization or digital rectal examination. Fill the pelvis with saline and force gas into rectum. Bubbles appearing suggests injury
Small bowel	Direct visualization. Injury should be suspected if unrecognized enterocoele present or bowel adhesions to the uterus	Direct visualization (including thermal whitening). Injury more common if there are bowel adhesions to the uterus	
Blood vessels	Direct or indirect visualization. Clamp and ligate the bleeding vessel by any approach (abdominally if bleeding heavily)	Direct visualization. Blood from the Verress needle at insertion. Laparoscopic control by clip/diathermy/ ligation. Laparotomy and aortic/iliac compression if large vessel injury + urgent attendance of vascular team	Direct visualization. Clamp and ligate the bleeding vessel by any approach
Bladder	Fluid leak seen during anterior colpotomy. Test with sterile milk or Methylene blue (infuse via urethral catheter). Cystoscopy	Diathermy or dissection injury. Exposure of bladder mucosa in the plane of dissection. Catheter visible. Fluid leak. Gas in catheter bag. ³² Test with sterile milk or methylene blue (infuse via urethral catheter). Cystoscopy	Diathermy or dissection injury. Exposure of bladder mucosa in the plane of dissection. Catheter visible. Fluid leak. Test with sterile milk or methylene blue (infuse via urethral catheter). Cystoscopy
Ureter	Suspect if lateral bleeding and deep sutures placed. In prolapse cases, 1 cm ureteric descent per 3 cm cervical descent. ³³ Cysto/ureteroscopy intraoperatively ± indigo carmine intravenous	Suspect if lateral bleeding and deep sutures placed, especially at the vaginal cuff angles. Also suspect in cases with lateral adnexal pathology and dissection/diathermy	Suspect if lateral bleeding and deep sutures placed, especially at vaginal cuff angles. Also suspect in cases with lateral adnexal pathology and dissection/ diathermy

injury at VH, as it can obviate the need for laparotomy if injury can be excluded.

A small puncture or hole to the bladder dome, anterior or lateral aspects will heal spontaneously in non-irradiated, non-septic patients (think of a suprapubic catheter removal and healing). This type of injury does not require prolonged catheterization. Cystoscopy is indicated to visualize the injury and confirm ureteric efflux. Exclude other damage. If the injury is >0.5 cm and is more >1 cm from ureteric orifices, repair the bladder in three layers (mucosa and two adventitial layers). The knots should be placed outside the bladder. Monocryl 3/0 is an ideal suture. Martius or fat pad techniques are not required in benign surgery. Repeat cystoscopy and leakage test after repair to

ensure bladder wall integrity. An indwelling catheter for 10 days to 3 weeks is required postoperatively. Injury to trigone or the posterior wall of the bladder requires repair and a urologist should be involved. The defect should be closed horizontally rather than vertically.

DELAYED DIAGNOSIS

If not recognized at the time, diagnosis of injury can be delayed, adding to morbidity. Thermal injury to bowel may be delayed in its presentation. After LH, the signs may be subtle. The requirement for opiate analgesia after 24 hours, a tachycardia >90 beats/min, or postoperative

fever >37.5°C should prompt a careful review. Carbon dioxide is extremely soluble and there will be no carbon dioxide under the diaphragm after 24 hours. Rarely, bowel damage will present as dyspnea,³⁶ and clinicians must have a high index of suspicion in all cases where a patient's recovery is atypical.

Ureteric or bladder damage should be suspected if urine output is low, but renal function normal. There may be flank or back pain. There may be hematuria. An ultrasound scan may show hydronephrosis or free fluid within the pelvis (uroperitoneum). An intravenous pyelo-

gram (IVP) may show de-novo hydronephrosis; a retrograde contrast-filled bladder combined with computer tomography (CT) is sensitive in identifying bladder trauma as well as free fluid intra-abdominally if ureteric leakage has occurred.

Vessel damage, if significant, is usually diagnosed at the time of injury. Postoperatively, there may be a tachycardia or blood pressure drop. Anemia may be an incidental finding on the postoperative blood count. Ultrasound scanning of the vaginal vault for detecting a hematoma is seldom helpful in assisting management.

References

- Marjorbanks J, Lethaby A, Farquar C. Surgery versus medical therapy for heavy menstrual bleeding. Cochrane Database Syst Rev 2006; (2): CD003855.
- Reid PC, Mukri F. Trends in number of hysterectomies performed in England for menorrhagia: examination of health episode statistics, 1989 to 2002-3. BMJ 2005; 330: 938–9.
- 2007 National Collaborating Centre for Women's and Children's Health. Heavy Menstrual Bleeding.
- Keshavarz H, Hillis SD, Kieke BA, Marchbanks PA. Hysterectomy surveillance United States, 1994–1999. MMWR Morb Mortal Wkly Rep Surveill Summ 2002; 51: 1–8.
- Jacobson GF, Shaber RE, Armstrong MA, Hung YY. Hysterectomy rates for benign indications. Obstet Gynecol 2006; 107: 1278–83.
- 6. Maresh MJ, Metcalfe MA, McPherson K et al. The VALUE national hysterectomy study: description of the patients and their surgery. BJOG 2002; 109: 302–12.
- National Guideline Clearinghouse. Guideline synthesis: guidelines for determining the route of hysterectomy for benign conditions. In: National Guidelines Clearinghouse (NGC) website: Rockville, MD; [cited 2000 Mar 1].
- 8. Kovac RS. Clinical opinion: guidelines for hysterectomy. Am J Obstet Gynecol 2004; 191: 635–40.
- Thakar R, Ayers S, Clarkson P et al. Outcomes after total versus subtotal abdominal hysterectomy. N Engl J Med 2002; 347: 1318–25.
- Gimbel H, Zobbe V, Andersen BM et al. Randomised controlled trial of total compared with subtotal hysterectomy with one-year follow up results. BJOG 2003; 110: 1088–98.
- Lethaby A, Ivanova V, Johnson NP. Total versus subtotal hysterectomy for benign gynaecological conditions. Cochrane Database Syst Rev 2006; (2): CD004993.
- Reich H, Roberts L. Laparoscopic hysterectomy in current gynaecological practice. Rev Gynecol Pract 2003; 3: 32–40.
- Garry R, Reich H, Liu CY. Laparoscopic hysterectomy definitions and indications. Gynecol Endosc 1994; 3: 1–3.
- Melis A, Buisson S, Lutz JM, Salvat J. Factors considered to choose type of a hysterectomy for benign uterus lesions (excluding prolapsus and obstetrical indications). J Gynecol Obstet Biol Reprod (Paris) 2005; 34(3 Pt 1): 241–51 [in French].
- Johns DA, Carrera B, Jones J et al. The medical and economical impact of laparoscopically assisted vaginal hysterectomy in a

- large, metropolitan, not-for-profit hospital. Am J Obstet Gynecol 1995; 172: 1709–15.
- 16. Garry R, Fountain J, Mason S et al. The eVALuate study: two parallel randomised trials, one comparing laparoscopic with abdominal hysterectomy, the other comparing laparoscopic with vaginal hysterectomy. BMJ 2004; 328: 129.
- Johnson N, Barlow D, Lethaby A et al. Surgical approach to hysterectomy for benign gynaecological disease. The Cochrane Database of Systematic Reviews 2006, Issue 2. Art. No. CD003677.
- Learman LA, Summitt RL, Varner RE et al. A randomized comparison of total or supra-cervical hysterectomy: surgical complications and clinical outcomes. Obstet Gynecol 2003; 102: 453–62.
- Thakar R, Ayers S, Georgakapolou A et al. Hysterectomy improves quality of life and decreases psychiatric symptoms: a randomised comparison of total versus subtotal hysterectomy. BJOG 2004; 111: 1115–20.
- Summitt RL Jr, Stovall TG, Lipscomb GH, Ling FW. Randomized comparison of laparoscopy-assisted vaginal hysterectomy with standard vaginal hysterectomy in an outpatient setting. Obstet Gynecol 1992; 80: 895–901.
- Rosen DM, Cario GM, Carlton MA et al. An assessment of the learning curve for laparoscopic and total laparoscopic hysterectomy. Gynecol Endosc 1998; 7: 289–93.
- 22. Perino A, Cucinella G, Venezia R et al. Total laparoscopic hysterectomy versus total abdominal hysterectomy: an assessment of the learning curve in a prospective randomized study. Hum Reprod 1999; 14: 2996–9.
- 23. Donnez J, Squifflet J, Jadoul P, Smets M. Results of eVALuate study of hysterectomy techniques: high rate of complications needs explanation. BMJ 2004; 328: 643.
- Wattiez A, Soriano D, Cohen SB et al. The learning curve of total laparoscopic hysterectomy: comparative analysis of 1647 cases. J Am Assoc Gynecol Laparosc 2002; 9: 339–45.
- Chien P, Khan K, Mol BW. How to interpret the findings of the eVALuate study. BJOG 2005; 112: 391–3.
- Bhattacharya S, Mollison J, Pinion S et al. A comparison of bladder and ovarian function two years following hysterectomy or endometrial ablation. Br J Obstet Gynaecol 1996; 103: 898–903.
- Brown JS, Sawaya G, Thom DH, Grady D. Hysterectomy and urinary incontinence: a systematic review. Lancet 2000; 356: 535–9.

- 28. Kjerulff KH, Langenberg PW, Greenaway L et al. Urinary incontinence and hysterectomy in a large prospective cohort study in American women. J Urol 2002; 167: 2088–92.
- Iversen L, Hannaford PC, Elliott AM, Lee AJ. Long term effects of hysterectomy on mortality: nested cohort study. BMJ 2005; 330: 1482.
- Sasaki LS, Allaben RD, Golwala R et al. Primary repair of colon injuries: a prospective randomized study. J Trauma 1995; 39: 895–901.
- 31. Zmora O, Mahajna A, Bar-Zakai B et al. Colon and rectal surgery without mechanical bowel preparation: a randomized prospective trial. Ann Surg 2003; 237: 363–7.
- 32. Classi R, Sloan PA. Intraoperative detection of laparoscopic bladder injury. Can J Anaesth 1995; 42(5 Pt 1): 415–6.

- DeLancey JOL, Strohbehn K, Aronson MP. Comparison of ureteral and cervical descents during vaginal hysterectomy for uterine prolapse. Am J Obstet Gynecol 1998; 179(6 Pt 1): 1405–10.
- Preston JM. Iatrogenic ureteric injury: common medicolegal pitfalls. BJU Int 2000; 86: 313–7.
- 35. Kim JH, Moore C, Jones JS et al. Management of ureteral injuries associated with vaginal surgery for pelvic organ prolapse. Int Urogynecol J Pelvic Floor Dysfunct 2006; 17: 531–5.
- Cooper MJ, Reid GD, Kaloo P. Respiratory symptoms as an indicator of undiagnosed bowel perforation following laparoscopic surgery – an observation. Aust NZ J Obstet Gynaecol 2002; 42: 545–7.

Comparison of hysterectomy techniques and cost-benefit analysis

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INTRODUCTION

The first description of the removal of gangrenous and inverted uteri goes back to the third century ad. However, it was not until 1813 when a German surgeon Conrad Langenbeck described the first intentional complete vaginal hysterectomy in which the patient survived. In those days the operative mortality rate was close to 90%. The first reports of abdominal hysterectomies were accidental hysterectomies at the time of ovariectomy, mostly with conservation of the cervix. The first abdominal hysterectomy where the patient survived was reported by an American surgeon, Walter Burnham, in the *American Lancet* in 1854.² Another American surgeon, Harry Reich, reported the first laparoscopic-assisted vaginal hysterectomy in 1989.³

Hysterectomy is now the most frequently performed major gynecologic operation, with millions of procedures annually performed throughout the world.⁴ Abdominal hysterectomy has traditionally been the surgical approach for gynecologic malignancy, in cases where pelvic pathology such as endometriosis or adhesions is suspected and in the presence of a large uterus. Abdominal hysterectomy remains the 'fallback option' if the uterus cannot be removed by another approach. The vaginal approach was originally used for prolapse, but has become more widely used for abnormal uterine bleeding when the uterus is of fairly normal size with or without a small degree of descent. Compared to abdominal hysterectomy, successful vaginal hysterectomy is considered as less invasive and can be performed under spinal anesthesia, whereas abdominal and laparoscopic hysterectomy will mostly require general anesthesia.

In women with an enlarged uterus, where vaginal hysterectomy is not feasible, laparotomy can be avoided by performing a laparoscopic hysterectomy. If oophorectomy is needed, a laparoscopic approach may also be preferred over the vaginal approach. Laparoscopic hysterectomy usually refers to a hysterectomy where at least part of the operation is undertaken laparoscopically.

Laparoscopic hysterectomy (LH) is further subdivided into three categories (Table 45.1):

- laparoscopic-assisted vaginal hysterectomy (LAVH), where vaginal hysterectomy is assisted by prior laparoscopy and the laparoscopic procedure does not include the occlusion of the uterine arteries
- laparoscopic hysterectomy (LH(a)), where the laparoscopic part of the hysterectomy includes the occlusion of the uterine arteries
- total laparoscopic hysterectomy (TLH), where the vaginal part of the operation is restricted to the removal of the laparoscopically freed uterus and all other operative manipulations, including vaginal vault closure, are undertaken laparoscopically.⁵

This classification causes some confusion, as the term 'laparoscopic hysterectomy' is used for the overall laparoscopic hysterectomy (LH), as well as for LH(a), which refers to one of the three categories.

A total hysterectomy is the removal of the entire uterus and cervix. When the cervix is preserved, this is known as a subtotal hysterectomy. Other terms used for subtotal hysterectomy are supracervical and supravaginal hysterectomy. The procedure may be advantageous in the case of dense pelvic adhesions or emergency obstetric hysterectomy for atonic bleeding.

OUTCOMES OF HYSTERECTOMY

In common with the overall hysterectomy rate, the proportion of hysterectomies currently being performed by different approaches varies markedly across countries, within countries, and even between individual surgeons working within the same unit. Each gynecologist will have different indications for the approach to hysterectomy for benign disease, based largely on his own array of surgical skills and patient characteristics such as uterine size and descent, extrauterine pelvic pathology, previous

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Table 45.1	Categories	of Japai	rosconic	hysterectomy	v

Category	Laparoscopic content
LAVH	Laparoscopic content does not involve division of the uterine vessels, which is performed vaginally
LH(a)	Laparoscopic content includes ligation of the uterine vessels, where there is a vaginal component in the procedure
TLH	Entire operation is performed laparoscopically, including suturing vaginal vault

pelvic surgery, and other features such as obesity, nulliparity, and the need for oophorectomy. Even though vaginal hysterectomy has been widely considered to be the operation of choice for abnormal uterine bleeding, the VALUE study has shown that in 1995 in the UK, 67% of the hysterectomies performed for this indication were abdominal hysterectomies.⁶ Previous cesarean section is often considered as a contraindication for vaginal hysterectomy. However, this is not supported by evidence, as the retrospective trials available have not reported a clinically relevant increase in complication rate in hysterectomy patients following cesarean section.^{7–10} Encouraging vaginal surgery amongst gynecologists has been shown to be an effective method of increasing the vaginal hysterectomy rates. Finland had a vaginal hysterectomy rate as low as 7% in the 1980s. Following annual meetings on gynecological surgery where vaginal and laparoscopic surgery was encouraged, the vaginal hysterectomy rate increased to 39% in 2004.11

Following the introduction of laparoscopic hysterectomy in 1989, research on hysterectomy received a new impetus. A systematic review summarizes the results of all randomized controlled trials on the subject, assessing the potential role of the three approaches to hysterectomy for benign indications. The meta-analysis provided adequate estimates on blood loss, operation times, complication rates, and return to normal activities. However, estimates on posthysterectomy quality of life, pelvic organ function, and psychosocial effects could still not be given owing to a lack of heterogeneous data. Both LAVH and LH(a) are frequently evaluated in trials, whereas TLH has only been studied in two randomized controlled trials.

Although much has been written in the scientific literature about various outcomes of hysterectomy, no discussion has been had over what outcomes are of key importance. Surgeons wish to minimize operative complications, healthcare managers wish to minimize costs, but what do patients want? Complications are often uncommon, and existing studies do not capture each one

of them individually and powerfully. Therefore, researchers tend to pool them together into composite outcomes, an approach that is not scientifically sound. More importantly, when comparing different types of hysterectomies, laparotomy can be a complication of vaginal and laparoscopic hysterectomy, but cannot be a complication of abdominal hysterectomy. This leads to asymmetry in the comparison of complication rates. We have proposed that quality of life is likely to be the most key outcome, as it captures the benefit the patient experiences from treatment and takes into account the effects of complications on patients' lives. ¹³ The choice should therefore weigh this outcome when decision making.

In the following sections the comparable oucomes of approaches to hysterectomy are described, mainly based on the results achieved in the meta-analysis.¹² Available quantitative data from the meta-analysis can be found in table

Operating time

Operating time was longer for laparoscopic as compared to either abdominal or vaginal hysterectomy. However, LAVH had a significantly shorter operating time than both abdominal hysterectomy and LH(a), thus suggesting that the operating time is governed by the proportion of the surgery performed laparoscopically. The greater the proportion performed laparoscopically, the lengthier the operation.¹²

Hemorrhage

Although there was no significant difference in the need for blood transfusions between laparoscopic hysterectomy and abdominal hysterectomy, laparoscopic hysterectomy was associated with significantly less blood loss and a smaller drop in hemoglobin. The need for blood transfusion, the mean blood loss, and hemoglobin drop for comparisons between abdominal and vaginal hysterectomy, as well as between laparoscopic and vaginal hysterectomy, were not significantly different.¹²

Infections

There was significantly less infectious morbidity for vaginal hysterectomy as compared to abdominal hysterectomy. For laparoscopic hysterectomy vs abdominal hysterectomy, there were significantly fewer wound infections as well as other infectious morbidity. No significant differences were found between vaginal and laparoscopic hysterectomy. Thus, avoidance of abdominal hysterectomy appears to be important in the avoidance of postoperative infectious morbidity. 12

Parameter	AH vs VH	LH vs AH	LH vs VH
Operating time (minutes)	NR	10.6 (7.4;13.8)	41.5 (33.7;49.4)
Blood loss (ml)	NR	-45.3 (-72.7;-17.9)	9.7 (-50.2;69.7)
Drop in hemoglobin (g/L)	NR	-0.6 (-0.8;-0.3)	0.2 (-0.3;0.6)
Infection unspecified	0.4 (0.2;0.8) ^a	$0.7 (0.5;0.9)^a$	0.8 (0.5;1.3) ^a
Wound infections	NR	$0.3 (0.1;0.9)^a$	3.1 (0.1;77.8) ^a
Urinary tract injury	NR	3.0 (1.3;6.9) ^a	1.0 (0.4;2.8) ^a
Hospital stay (days)	1.0 (0.7;1.2)	-2.0 (-2.2;-1.9)	0.3 (-0.1;0.8)
Return to normal activities (days)	12.3 (4.8;19.9)	-13.6 (-15.4;-11.8)	-1.1 (-4.2;2.1)

Table 45.2 Differences between approaches to hysterectomy¹²

AH, abdominal hysterectomy; LH, laparoscopic hysterectomy; VH, vaginal hysterectomy; NR, not reported. Data presented as weighted mean difference (95% confidence interval) or ^aodds ratio (95% confidence interval).

Urinary tract injury

A study amongst 37 295 women undergoing hysterectomy in the UK has shown that bladder injury was the most frequent visceral injury, with an incidence of 1 in 200 hysterectomies.¹⁴ Although no significant difference between the three different approaches has been found, the occurrence of ureteric injury remains the major concern in relation to the laparoscopic approach. Meta-analysis has shown that in laparoscopic hysterectomy the risk of urinary tract injury was 2.6-fold increased as compared to abdominal hysterectomy. 12 Moreover, there was a tendency to increased ureteric injury, which occurred in 1 in 78 women having laparoscopic hysterectomy and in 1 in 492 women having abdominal hysterectomy. Although it could be speculated that laparoscopic uterine artery ligation is the maneuver most likely to increase the risk of ureteric injury, this was not confirmed by evidence, as no statistically significant difference has been found in urinary tract injury for LH(a) vs LAVH.

Unintended laparotomy

As the abdominal approach is the 'fallback option' in case of difficult and complicated hysterectomies, unintended laparotomies or conversions are inherent to the laparoscopic and vaginal approach. Sometimes these conversions are prudent rather than the result of a complication. As calculated from randomized controlled trials, conversions occurred in 8.7% of laparoscopic hysterectomy patients and 2.6% of vaginal hysterectomy patients. The possibility of the need for conversion should be discussed with the patient prior to surgery.¹²

Other complications

There were no significant differences in the occurrence of bowel injury between any of the approaches to hysterectomy, with an overall incidence of 0.2%. The same holds true for the occurrence of thromboembolic events, number of severe bleedings, blood transfusions, and pelvic hematoma, as well as for vaginal cuff infections, urinary tract infections, and chest infections as separate entities.¹²

Although it has been suggested that LAVH does little more than to combine the complications of laparoscopic surgery with those of vaginal surgery, ¹⁵ this has not been supported by evidence. The concepts that laparoscopic hysterectomy allows identification of pelvic disease such as adhesions and endometriosis and that the meticulous hemostasis achievable with 'final-look' laparoscopy might reduce pelvic hematomas or vaginal cuff infections¹⁶ have not been borne out by improved outcomes following laparoscopic vs abdominal hysterectomy in the meta-analysis of randomized trials.¹²

Pain, hospital stay, and return to normal activities

Avoidance of abdominal hysterectomy appears to be important to minimize postoperative pain. Recovery from surgery favored vaginal hysterectomy and laparoscopic hysterectomy as compared to abdominal hysterectomy in terms of shorter hospital stay and return to normal activities. There were no significant differences in hospital stay and return to normal activities between laparoscopic hysterectomy and vaginal hysterectomy or between LH(a) and LAVH. Thus, the speed of postoperative recovery

seems to be determined by the avoidance of an abdominal procedure; abdominal hysterectomy is associated with lengthier recovery as compared to the other approaches to hysterectomy.¹²

Psychosocial effects and quality of life

A further report of the systematic review of randomized trials of surgical approach to hysterectomy arbitrarily identified three primary outcomes: time to return to normal activities, major operative complication, and major lasting problem. 16 As long-term outcomes were not reported in any of the 27 randomized trials included in this review, no information was available for the latter outcome. Indeed, approximately 90% of hysterectomies are performed for benign indications, which are rarely life-threatening.¹⁷ Thus there is a strong argument that psychosocial effects and changes in quality of life should be considered as the outcomes of paramount importance in the comparison of techniques. Surprisingly, few studies assessing laparoscopic techniques address these issues. The available evidence does not support any broad adverse effects of hysterectomy on psychosocial functioning. 18 As far as quality of life is concerned, there are various reports on the enhancement after hysterectomy. 19 Randomized controlled trials using validated quality of life methods have shown that the enhancement of quality of life is equal or greater in vaginal as well as laparoscopic hysterectomy when compared to abdominal hysterectomy, 15,20-24 whereas no differences have been found amongst vaginal and laparoscopic hysterectomy. 15,23

Pelvic organ dysfunction

In the early 1980s advantages, as far as postoperative urinary incontinence and sexuality were concerned, were claimed from a prospective observational study on subtotal hysterectomy and total abdominal hysterectomy. This has now been challenged by a meta-analysis of three randomized controlled trials where no advantages of subtotal hysterectomy were found. ²⁷

In the short term there does not seem to be a negative effect from non-radical hysterectomy on the incidence of urinary, bowel, and sexual dysfunctions.²⁸ An improvement of urinary incontinence and sexual problems has even been found and de-novo problems were rare. The roles of the different approaches still needs further establishment, but thus far there is no evidence of superiority of one of the approaches. No prospective long-term data are available up to date, although large epidemiologic studies have shown an increased risk of urinary incontinence in posthysterectomy women.²⁹

RESOURCE USE IN HYSTERECTOMY RELATIVE TO OUTCOME

There are several types of economic analysis available for the evaluation of healthcare technology.³⁰ Costs or resource use for different treatment options can be compared without considering a (potential) difference in treatment outcome. In cost-effectiveness analysis however, costs are related to the effect of a particular treatment. A difference in effectiveness between two strategies is expected and the analysis aims to express additional costs of the additional health gain. Alternatives to costeffectiveness analysis are cost-utility analysis and costbenefit analysis. In cost-utility analysis, the outcome of medical interventions is expressed in utilities: e.g. life years that are adjusted for the quality of life of these years. In cost-benefit analysis, not only the costs but also the potential benefits of interventions are expressed in financial terms. Since there is no uniform extrapolation of women having had hysterectomy into financial terms, cost-benefit analysis is only rarely applied. Where the difference in effectiveness or quality of life has not been assessed, and the analysis is limited to the difference in costs, assuming a similar medical outcome, the analysis is a cost-minimization analysis.

When hysterectomy is compared to other interventions, such as ablation or a levonorgestrel intrauterine device (IUD), a difference in effect on menorrhagia is expected, which makes a cost-effectiveness analysis appropriate. When comparing various approaches to hysterectomy, a difference in recovery can be expressed in quality-adjusted life years (QALYs), making cost-utility analysis possible.

PubMed searches for economic analyses were performed using the key words 'cost\$, combined with menorrhagia, uterine bleeding, hysterectomy, endometrial ablation (fibroid or myom\$ and emboli\$), and myomectomy'. Data on economic analyses from reviews and randomized controlled trials on comparisons of approaches to hysterectomy and comparisons of hysterectomy to other treatments were extracted.

Hysterectomy vs medical treatment as well as endometrial ablation has been subject to randomized studies comparing the costs or resource use. Tormal costutility analysis has been performed for hysterectomy as compared to the levonorgestrel IUD and for laparoscopic hysterectomy as compared to both vaginal and abdominal hysterectomy.

The applicability of randomized studies to the economic impact of different treatment options for abnormal uterine bleeding is limited, as endometrial ablation and hysterectomy are not options for women wishing to retain their fertility, and as hormonal treatment is

inappropriate for women wishing to become pregnant. Furthermore, a sufficiently long follow-up period is required to include all costs of retreatments in the group where a less-effective strategy has initially been applied. These costs will increase over time, whereas hysterectomy is more expensive in the short term, but has a long-lasting effect.

Resource use in different approaches to hysterectomy

Operating time, hospital stay, and return to normal activities are obviously the most important factors in potential differences in resource use amongst approaches to hysterectomy. As derived from randomized controlled studies summarized in the meta-analysis, 12 in laparoscopic hysterectomy the difference in operating time was 11 minutes as compared to abdominal hysterectomy and 42 minutes as compared to vaginal hysterectomy, both detrimetal to laparoscopic hysterectomy. On the other hand, hospital stay was 2 days longer in abdominal hysterectomy as compared to laparoscopic hysterectomy and 1 day longer in abdominal hysterectomy as compared to vaginal hysterectomy. Furthermore, in abdominal hysterectomy the difference in time taken until return to normal activities was 14 days as compared to laparoscopic hysterectomy and 12 days as compared to vaginal hysterectomy. There were no statistically significant difference amongst laparoscopic hysterectomy and vaginal hysterectomy as far as hospital stay and return to normal activities were concerned.

Six randomized controlled trials^{21-23,39-41} have compared the resource use in laparoscopic vs abdominal hysterectomy, from which one performed a formal cost-utility analysis.23 None of the studies found a significant difference in overall costs. However, hospital costs were significantly higher for the laparoscopic approach in two of these studies, 21,22 caused by the longer operation times and higher costs of disposables in laparoscopic hysterectomy. When including society costs due to productivity loss, this difference was wiped out.²¹ Until now, the resource use for basic equipment in laparoscopic hysterectomy, which is extremely variable, has not been taken into account. The least expensive will be a simple uterine manipulator and reusable bipolar coagulation forceps and scissors, although many surgeons regard an optimal vaginal delineator as an essential safety feature in total laparoscopic hysterectomy. However, many varieties of more expensive equipment are now available for therapeutic laparoscopy. These costs should be carefully recorded in future studies to get a more thorough picture of comparable costs of laparoscopic and abdominal hysterectomy.

Resource use in hysterectomy as compared to alternative treatments

Medical treatment

Both endometrial ablation and hysterectomy have been shown to be more effective in the resolution of abnormal uterine bleeding and the enhancement of quality of life, as compared to medical treatment.^{31,32} However, at the end of a 2-year follow-up period, the total resource use was significantly higher (51%) in women randomized to hysterectomy as compared to women randomized to expanded medical treatment, i.e. combinations of prostaglandin synthase inhibitors, tranexamic acid, and hormonal treatment. Fifty-three percent of the women in the medical treatment group had undergone hysterectomy as a subsequent treatment within these 2 years.

Furthermore, in a randomized controlled trial comparing the levonorgestrel IUD with hysterectomy, 42% of the women in the levonorgestrel IUD group eventually underwent hysterectomy in the 5-year follow-up period. Nonetheless, a cost–utility analysis at 1-year follow-up and a cost comparison at 5-year follow-up both favored the levonorgestrel IUD group. Five years after randomization, the resource use was 65% higher in the hysterectomy group. 33,38

Endometrial ablation

In three randomized controlled trials, costs were calculated for endometrial ablation vs hysterectomy^{34–37} and all showed that the costs were lower in the endometrial ablation group. However, with longer-term follow-up periods this difference had narrowed due to the costs of further treatments in the endometrial ablation groups.³⁷

Myomectomy

Myomectomy is associated with a high recurrence rate. Following hysteroscopic myomectomy, 25% of the women needed additional surgical treatment at the end of an 8-year follow-up period. Comparable data have been reported following laparoscopic and abdominal myomectomy. However, myomectomy may bring relief to women suffering abnormal uterine bleeding due to myoma and wishing to preserve the uterus. Short-term costs of abdominal myomectomy will be comparable to those of hysterectomy, which makes cost-effectiveness of abdominal myomectomy less likely, although no studies are available to date.

Uterine artery embolization

In two randomized controlled trials uterine artery embolization was compared to hysterectomy, but costs were

not considered as clinical endpoints.^{46,47} In a prospective observational study comparing hysterectomy with uterine artery embolization, women >40 years old were followed until menopause.⁴⁸ This study suggested that the costs in the embolization group were lower.

Cost-utility analysis in hysterectomy

The first analysis in gynecologic surgery on resource use in relation to outcome was published by Grover et al. in 1996.⁴⁹ They reported positive cost-effectiveness of concomitant elective hysterectomy at the time of adnexectomy in women >45 years old.

In the cost-utility analysis published in 2004 by Sculpher et al., the costs for laparoscopic hysterectomy as compared to vaginal and abdominal hysterectomy were calculated in a secondary analysis of the eVALuate study data.²³ One QALY when performing a laparoscopic hysterectomy instead of abdominal hysterectomy would cost the British National Health System (NHS) £26571 (US\$46893 or €37813). Provided that the outcome, including operation time, would not change when exchanging disposables for reusable instruments, these costs would decrease 2.5-fold. In the parallel trial on laparoscopic vs vaginal hysterectomy, it was shown that laparoscopic hysterectomy was not cost-effective.²³ No other randomized studies have been performed on the financial implications of abdominal vs vaginal hysterectomy. However, as vaginal hysterectomy is associated with a shorter operation time and hospital stay, it is expected to be less expensive.

One randomized controlled study has reported a similar resource use over a 2-year period after subtotal abdominal hysterectomy as compared to total abdominal hysterectomy. Furthermore, the conclusion from a study on cost-effectiveness of the application of preoperative gonadotropin-releasing hormone (GnRH) agonists in women with fibroids undergoing hysterectomy was that the benefits do not justify the costs. A cost-effectiveness analysis of oophorectomy at the time of hysterectomy has not yet been undertaken.

As has already been remarked in the section on resource use, a cost–utility analysis at 1-year follow-up favored the levonorgestrel IUD as compared to hysterectomy.³⁸

OTHER CONSIDERATIONS ON HYSTERECTOMY

Learning curve

Mäkinen et al. have reported a prospective study on the learning curve in 10110 hysterectomies for benign indications, of which 5875 were abdominal, 1801 were vaginal, and 2434 were laparoscopic hysterectomies. ⁵² As far as injuries to adjacent organs were concerned, the surgeons' experience significantly correlated inversely with the occurrence of urinary tract injuries in laparoscopic hysterectomy and the occurrence of bowel injuries in vaginal hysterectomy. Still, randomized controlled trials frequently do not report the experience of the surgeon(s), which hampers interpretation of the results. However, in the two largest trials incorporated in the meta-analysis on hysterectomy, thus having the highest impact on the outcome, surgeons had performed at least 25 and 50 interventions, respectively, by either approach. ^{15,22}

All gynecologists tend to become thoroughly trained in abdominal hysterectomy techniques, but there is huge variation in their learning curve position in relation to vaginal and laparoscopic hysterectomy techniques.⁵³ Total laparoscopic hysterectomy requires the highest degree of surgical skill, and currently only a very small proportion of newly trained gynecologists will be able to perform this type of surgery. However, some gynecologists who have not received specific training have acquired the skills to perform laparoscopic hysterectomy. One important benefit of the introduction of laparoscopic hysterectomy into gynecologic training has been to increase surgeons' confidence and skills with vaginal and overall laparoscopic surgery.

CONCLUSIONS

In conclusion, when technically feasible, vaginal hysterectomy should be performed in preference to laparoscopic and abdominal hysterectomy. There are no significant disadvantages of vaginal hysterectomy compared with any other surgical approach to hysterectomy, provided it can be accomplished safely. Compared with the abdominal approach, successful vaginal hysterectomy has a shorter operation time, is less painful, and there are fewer febrile episodes postoperatively, and it is associated with earlier discharge from hospital and return to normal activities. Where vaginal hysterectomy is not feasible, laparoscopic hysterectomy offers some benefits of avoiding abdominal hysterectomy, including less operative blood loss, less pain, and less infectious morbidity, as well as a shorter hospital stay and more rapid return to normal activities. These advantages are offset by longer operating time and more urinary tract injuries. No advantages of laparoscopic hysterectomy over vaginal hysterectomy could be found, whereas the disadvantages are a longer operating time, greater use of pain medication, and higher cost.

In women undergoing hysterectomy, vaginal hysterectomy is cost-effective compared to laparoscopic hysterectomy and is likely to be cost-effective compared to

abdominal hysterectomy. The difference in cost-effectiveness between laparoscopic and abdominal hysterectomy is more balanced, especially when avoiding the use of disposable instruments.

Cost-effectiveness of the levonorgestrel IUD over hysterectomy has been reported in women suffering menorrhagia. Although other medical treatments are less expensive, cost-effectiveness is less likely, due to their lower effectiveness. The costs of endometrial ablation and uterine artery embolization are lower as compared to hysterectomy, although the difference decreases over time

due to the higher costs of retreatments in the non-hysterectomy groups.

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References

- Bachmann GA. Hysterectomy. A critical review. J Reprod Med 1990; 35: 839–62.
- Sutton C. Hysterectomy: a historical perspective. Baillière's Clin Obstet Gynecol 1997; 11: 1–22.
- Reich H, DeCaprio J, McGlynn F. Laparoscopic hysterectomy. J Gynecol Surg 1989; 5: 213–16.
- Garry R. Health economics of hysterectomy. Best Pract Res Clin Obstet Gynecol 2005; 19: 451–65.
- Reich H, Roberts L. Laparoscopic hysterectomy in current gynecological practice. Rev Gynecol Pract 2003; 3: 32–40.
- 6. Maresh MJ, Metcalfe MA, McPherson K et al. The VALUE national hysterectomy study: description of the patients and their surgery. BJOG 2002; 109: 302–12.
- Boukerrou M, Lambaudie E, Collinet P et al. A history of cesareans is a risk factor in vaginal hysterectomies. Acta Obstet Gynecol Scand 2003; 82: 1135–9.
- Poindexter YM, Sangi-Haghpeykar H, Poindexter AN III et al. Previous cesarean section. A contraindication to vaginal hysterectomy? J Reprod Med 2001; 46: 840–4.
- 9. Sheth SS, Malpani AN. Vaginal hysterectomy following previous cesarean section. Int J Gynecol Obstet 1995; 50: 165–9.
- Unger JB, Meeks GR. Vaginal hysterectomy in women with history of previous cesarean delivery. Am J Obstet Gynecol 1998; 179(6 Pt 1): 1473–8.
- Härkki P. Finland has not turned her back on laparoscopy. Gynecol Surg 2006; (3 Suppl 1): S6.
- Johnson N, Barlow D, Lethaby A et al. Surgical approach to hysterectomy for benign gynecological disease. Cochrane Database Syst Rev 2006; (2): CD003677.
- Chien P, Khan K, Mol BW. How to interpret the findings of the eVALuate study. BJOG 2005; 112: 391–3.
- McPherson K, Metcalfe MA, Herbert A et al. Severe complications of hysterectomy: the VALUE study. BJOG 2004; 111: 688–94.
- Garry R, Fountain J, Mason S et al. The eVALuate study: two parallel randomised trials, one comparing laparoscopic with abdominal hysterectomy, the other comparing laparoscopic with vaginal hysterectomy. BMJ 2004; 328: 129.
- Johnson N, Barlow D, Lethaby A et al. Methods of hysterectomy: systematic review and meta-analysis of randomised controlled trials. BMJ 2005; 330: 1478.
- Garry R. Health economics of hysterectomy. Best Pract Res Clin Obstet Gynecol 2005; 19: 451–65.

- Flory N, Bissonnette F, Binik YM. Psychosocial effects of hysterectomy: literature review. J Psychosom Res 2005; 59: 117–29.
- Rannestad T. Hysterectomy: effects on quality of life and psychological aspects. Best Pract Res Clin Obstet Gynecol 2005; 19: 419–30.
- Silva-Filho AL, Werneck RA, de Magalhaes RS et al. Abdominal vs vaginal hysterectomy: a comparative study of the postoperative quality of life and satisfaction. Arch Gynecol Obstet 2006; 274: 21–4.
- Ellstrom M, Ferraz-Nunes J, Hahlin M, Olsson JH. A randomized trial with a cost-consequence analysis after laparoscopic and abdominal hysterectomy. Obstet Gynecol 1998; 91: 30–4.
- Lumsden MA, Twaddle S, Hawthorn R et al. A randomised comparison and economic evaluation of laparoscopic-assisted hysterectomy and abdominal hysterectomy. BJOG 2000; 107: 1386–91.
- 23. Sculpher M, Manca A, Abbott J et al. Cost effectiveness analysis of laparoscopic hysterectomy compared with standard hysterectomy: results from a randomised trial. BMJ 2004; 328: 134.
- Kluivers KB, Johnson N, Chien P et al. Comparison of laparoscopic and abdominal hysterectomy in terms of quality of life; a systematic review. Eur J Obstet Gynecol 2007; (in press).
- 25. Kilkku P, Hirvonen T, Gronroos M. Supra-vaginal uterine amputation vs. abdominal hysterectomy: the effects on urinary symptoms with special reference to pollakisuria, nocturia and dysuria. Maturitas 1981; 3: 197–204.
- Kilkku P. Supravaginal uterine amputation vs. hysterectomy. Effects on coital frequency and dyspareunia. Acta Obstet Gynecol Scand 1983; 62: 141–5.
- 27. Lethaby A, Ivanova V, Johnson NP. Total versus subtotal hysterectomy for benign gynecological conditions. Cochrane Database Syst Rev 2006; (2): CD004993.
- 28. Thakar R, Sultan AH. Hysterectomy and pelvic organ dysfunction. Best Pract Res Clin Obstet Gynecol 2005; 19: 403–18.
- Vierhout ME. Influence of nonradical hysterectomy on the function of the lower urinary tract. Obstet Gynecol Surv 2001; 56: 381–6.
- Gold MR, Siegel JE, Russel LB, Weinstein MB. Cost-Effectiveness in Health and Medicine. Oxford: Oxford University Press, 1996.
- Cooper KG, Jack SA, Parkin DE, Grant AM. Five-year follow up of women randomised to medical management or transcervical resection of the endometrium for heavy menstrual loss: clinical and quality of life outcomes. BJOG 2001; 108: 1222–8.

- Showstack J, Lin F, Learman LA et al. Randomized trial of medical treatment versus hysterectomy for abnormal uterine bleeding: resource use in the Medicine or Surgery (Ms) trial. Am J Obstet Gynecol 2006; 194: 332–8.
- 33. Hurskainen R, Teperi J, Rissanen P et al. Clinical outcomes and costs with the levonorgestrel-releasing intrauterine system or hysterectomy for treatment of menorrhagia: randomized trial 5-year follow-up. JAMA 2004; 291: 1456–63.
- 34. Gannon MJ, Holt EM, Fairbank J et al. A randomised trial comparing endometrial resection and abdominal hysterectomy for the treatment of menorrhagia. BMJ 1991; 303: 1362–4.
- Sculpher MJ, Dwyer N, Byford S, Stirrat GM. Randomised trial comparing hysterectomy and transcervical endometrial resection: effect on health related quality of life and costs two years after surgery. Br J Obstet Gynecol 1996; 103: 142–9.
- 36. Cameron IM, Mollison J, Pinion SB et al. A cost comparison of hysterectomy and hysteroscopic surgery for the treatment of menorrhagia. Eur J Obstet Gynecol Reprod Biol 1996; 70: 87–92.
- A randomised trial of endometrial ablation versus hysterectomy for the treatment of dysfunctional uterine bleeding: outcome at four years. Aberdeen Endometrial Ablation Trials Group. Br J Obstet Gynecol 1999; 106: 360–6.
- Hurskainen R, Teperi J, Rissanen P et al. Quality of life and cost-effectiveness of levonorgestrel-releasing intrauterine system versus hysterectomy for treatment of menorrhagia: a randomised trial. Lancet 2001; 357: 273–7.
- 39. Falcone T, Paraiso MF, Mascha E. Prospective randomized clinical trial of laparoscopically assisted vaginal hysterectomy versus total abdominal hysterectomy. Am J Obstet Gynecol 1999; 180: 955–62.
- Raju KS, Auld BJ. A randomised prospective study of laparoscopic vaginal hysterectomy versus abdominal hysterectomy each with bilateral salpingo-oophorectomy. Br J Obstet Gynecol 1994; 101: 1068–71.
- Summitt RL Jr, Stovall TG, Steege JF, Lipscomb GH. A multicenter randomized comparison of laparoscopically assisted vaginal hysterectomy and abdominal hysterectomy in abdominal hysterectomy candidates. Obstet Gynecol 1998; 92: 321–6.

- 42. Emanuel MH, Wamsteker K, Hart AA et al. Long-term results of hysteroscopic myomectomy for abnormal uterine bleeding. Obstet Gynecol 1999; 93(5 Pt 1): 743–8.
- Rossetti A, Sizzi O, Soranna L et al. Long-term results of laparoscopic myomectomy: recurrence rate in comparison with abdominal myomectomy. Hum Reprod 2001; 16: 770–4.
- 44. Fauconnier A, Chapron C, Babaki-Fard K, Dubuisson JB. Recurrence of leiomyomata after myomectomy. Hum Reprod Update 2000; 6: 595–602.
- 45. Lefebvre G, Vilos G, Allaire C et al. The management of uterine leiomyomas. J Obstet Gynecol Can 2003; 25: 396–418.
- 46. Pinto I, Chimeno P, Romo A et al. Uterine fibroids: uterine artery embolization versus abdominal hysterectomy for treatment a prospective, randomized, and controlled clinical trial. Radiology 2003; 226: 425–31.
- 47. Hehenkamp WJ, Volkers NA, Donderwinkel PF et al. Uterine artery embolization versus hysterectomy in the treatment of symptomatic uterine fibroids (EMMY trial): peri- and postprocedural results from a randomized controlled trial. Am J Obstet Gynecol 2005; 193: 1618–29.
- Beinfeld MT, Bosch JL, Isaacson KB, Gazelle GS. Cost-effectiveness of uterine artery embolization and hysterectomy for uterine fibroids. Radiology 2004; 230: 207–13.
- Grover CM, Kuppermann M, Kahn JG, Washington AE. Concurrent hysterectomy at bilateral salpingo-oophorectomy: benefits, risks, and costs. Obstet Gynecol 1996; 88: 907–13.
- Showstack J, Kuppermann M, Lin F et al. Resource use for total and supracervical hysterectomies: results of a randomized trial. Obstet Gynecol 2004; 103(5 Pt 1): 834–41.
- 51. Farquhar C, Brown PM, Furness S. Cost effectiveness of preoperative gonadotrophin releasing analogues for women with uterine fibroids undergoing hysterectomy or myomectomy. BJOG 2002; 109: 1273–80.
- 52. Màkinen J, Johansson J, Tomas C et al. Morbidity of 10110 hysterectomies by type of approach. Hum Reprod 2001; 16: 1473–8.
- 53. Miskry T, Magos A. A national survey of senior trainees surgical experience in hysterectomy and attitudes to the place of vaginal hysterectomy. BJOG 2004; 111: 877–9.

Analysis of sexual activity after hysterectomy

Sahana Gupta and Isaac Manyonda

INTRODUCTION

Few operations raise more passion and controversy than hysterectomy, and undoubtedly one of the most contentious issues is whether the operation adversely affects pelvic organ function: namely, bladder, bowel, and sexual. Contrary to popular belief and despite some adverse publicity as a result of poorly designed studies, there is now considerable and robust research evidence that simple abdominal hysterectomy does not adversely affect pelvic organ function and subtotal hysterectomy does not confer advantage over total hysterectomy with respect to bladder, bowel, or sexual function. This also appears to be true for vaginal hysterectomy, although the evidence is mainly in the form of retrospective and prospective observational studies, whereas evidence from randomized controlled trials is lacking. Such trials are not easy to conduct because of the difference in indications for the two routes. By contrast, as radical hysterectomy involves more extensive dissection of the pelvic organs and their innervation, some degree of pelvic organ dysfunction might be expected. The evidence from mainly small prospective trials is inconclusive, although major sexual problems after radical hysterectomy appear to be transient. Debilitating effects on sexuality after treatment for cervical cancer seem to be a problem associated with the radiotherapy component of the treatment rather than the surgery. An additional issue of debate is whether concomitant oophorectomy contributes adversely towards sexual function.

The issue of the impact of hysterectomy on sexual function is of fundamental importance, given that hysterectomy is the most common major gynecologic operation performed in the UK and the USA. Perhaps gynecologists and their patients can take comfort from the fact that hysterectomy provides the highest satisfaction scores compared to all other modalities of treatment for dysfunctional uterine bleeding, suggesting that adverse sequelae (on pelvic organ function) do not occur as frequently as might be feared.

In this chapter we consider the anatomic and physiologic consequences of hysterectomy that could impact on

sexual function, and then evaluate the research evidence available, focusing on psychological factors, total vs subtotal hysterectomy, the route of the hysterectomy (abdominal vs vaginal vs laparoscopic), radical vs simple hysterectomy, and the impact of concurrent oophorectomy. We acknowledge that the study of human sexual function is highly complex, as both physical and psychological factors influence sexuality in a way that is both varying and difficult to quantify.

ANATOMIC/PHYSIOLOGIC CONSIDERATIONS

Hysterectomy disrupts the anatomic and spatial relationships in the pelvis, and sometimes includes the removal of ovaries: it is therefore teleologically sound to suppose that the function of the pelvic organs could be adversely affected, although where organic pathology such as endometriosis is also removed this could have a positive impact.

Innervation of the pelvic organs

The surgical anatomy of the autonomic pelvic nerves and their importance in the neurophysiology of the female sexual response has recently been fully elucidated.1 The fibers of the superior hypogastric plexus (SHP) exit the spinal cord at thoracic level 10 to lumbar level 2. The SHP is connected to the inferior hypogastric plexus (IHP or pelvic plexus) by the hypogastric nerves, which exit bilaterally from the inferior poles of the SHP. The IHP receives input from the sacral roots S2-S4 via the pelvic splanchnic nerves. Its end supplies the uterus, vagina, and the cervix. Studies on sexual functioning in women after spinal cord injuries as well as radical hysterectomy provide strong evidence that the IHP plays an important role in female sexual arousal. The sympathetic pathways originating from the spinal levels T10-T12 play an essential role in lubrication and sensation of the internal genitalia in the sexual response cycle.2 On the other hand, the

pudendal nerve, which is a somatosensory nerve, supplies the labia and clitoris and reaches the external genitalia through the pudendal canal, which is not at risk during hysterectomy.

During total hysterectomy the IHP is at risk of damage at four areas:

- the main branches of the plexus running beneath the uterine arteries may be damaged during the division of the cardinal ligaments
- the major part of the vesical innervation, which enters the bladder base before spreading throughout the detrusor muscle, may be damaged during the blunt dissection of the bladder from the uterus and the cervix
- extensive dissection of the paravaginal tissue may disrupt the pelvic neurons passing from the lateral aspect of the vagina
- removal of the cervix results in the loss of a large segment of the plexus that is intimately related to it, with the remaining portion of the plexus being inadequate to deal with afferent impulses from the bladder and the rectum, possibly causing sexual, bowel, and bladder dysfunction. This nerve disruption theory has been the basis of the long-standing debate on whether subtotal hysterectomy, which minimizes disruption and damage to pelvic innervation, could be advantageous over total hysterectomy with regard to pelvic organ function.^{3,4}

On the other hand, radical hysterectomy (RH) for cervical cancer is associated with a greater degree of nerve damage than simple hysterectomy, and this has been confirmed by immuohistochemical studies.⁵ In order to ensure adequate surgery, a radical procedure involves the removal of the uterus and cervix together with its lateral, anterior, and posterior ligaments. This can cause major disruption of the pelvic autonomic nerves for which these ligaments serve as the anatomic pathways. Therefore, RH for cancer is expected to be associated with more severe sexual dysfunction than simple hysterectomy for benign disease. Recently, surgical techniques have been introduced in which the autonomic nerves are identified and spared during RH, with the aim of preventing postoperative pelvic organ dysfunction. 6-8 The data from such studies have led to the conclusion that disruption of specific components of the autonomic nerve supply during RH could lead to specific sexual disturbance. Thus, disruption of the sympathetic innervations would be expected to lead to impaired lubrication and sensation of the female internal genital organ, while the motor component of the orgasm would be severely affected. Injury to the parasympathetic nerve supply would lead to impaired

vasocongestion. Therefore, needless to say, surgical preservation of the pelvic autonomic nerves either in laparoscopic or traditional RH deserves consideration in the quest to improve both cure and quality of life in patients with cancer of the cervix. Theoretically, clitoral orgasm should not be damaged in such an operation.³ A recent study objectively quantified a significant sensory loss in the vagina after RH coupled with preservation of clitoral sensation.⁹

Spatial relationships

From the point of view of spatial relationships, removal of the cervix can shorten the vagina, and this could cause dyspareunia and altered sensation during coitus. ¹⁰ Scar tissue in the vaginal vault could also cause dyspareunia. ¹¹ Orgasm is a neurologic genital reflex in which the uterus and cervix appear to play a crucial role: at the beginning of orgasm there is a biphasic motor response involving the non-striated smooth muscles of the fallopian tubes, uterus, and the paraurethral glands of Skene in the first phase and the striated muscles of the pelvic floor, perineum, and anal sphincter in the second phase. The appreciation of the sensory stimuli from the contraction of the smooth muscles of the uterus, cervix, and vagina probably leads to the sensation of orgasm, ¹² and their removal could therefore affect orgasm adversely.

Hormonal influences

The physiologic ovarian failure that takes place in postmenopausal women results in the marked decrease in estrogen and androgen levels. The decline in estrogen level is thought to cause reduced vaginal lubrication and dyspareunia, while androgen deficiency is thought to be the cause of decreased libido and sexual arousability. While estrogen and androgen levels do not change in postmenopausal woman after hysterectomy with concurrent oophorectomy because of the existing physiologic ovarian failure, the situation is entirely different in the premenopausal woman, where removal of the ovaries (surgical castration) causes a marked and rapid decline in the levels of both hormones, which would be expected to have an even more dramatic effect on sexual function than the gradual physiologic ovarian failure of the menopause. An issue of contention is whether the procedure of premenopausal hysterectomy with ovarian conservation could lead to ovarian failure occurring earlier than would otherwise have been the case. There are theoretical reasons for supposing that this could happen: the ovarian arteries, after reaching the ovaries, continue upwards along the fallopian tube to supply the upper part of the uterus; ligation of the fallopian tubes, an essential step

during hysterectomy, will include ligation of this continuation, and this might lead to a change in the blood flow dynamics in the artery and damage the ovarian microcirculation.¹³ In a retrospective study, Siddle et al. found that the mean age of ovarian failure in women who had undergone premenopausal hysterectomy with ovarian conservation was 45.5 years old which is significantly lower than the mean age of 49.5 years old in the control group.14 However, many of these hysterectomies were performed due to dysfunctional uterine bleeding and, because of the retrospective design of the study, it is difficult to say whether these women already had premature ovarian failure to account for the abnormal bleeding or indeed if hysterectomized women were more perceptive of their climacteric symptoms. Coppen et al., using a prospective follow-up design, failed to find any effect of hysterectomy without oophorectomy on estrogen, luteinizing hormone (LH), or follicle-stimulating hormone (FSH) levels. 15 Thus, the evidence for a causal relationship between hysterectomy, with conservation of the ovaries, and premature ovarian failure remains equivocal.

SEXUAL FUNCTION FOLLOWING HYSTERECTOMY: THE EVIDENCE

The psychological aspects

Perhaps in part because of the central role it plays in the propagation of the species, the uterus is often imbued in all kinds of myths in the human psyche. The Greeks thought of it as the source of madness (hysteria) in women, with the monthly bleeds being seen as necessary to avoid insanity. Then again, it has been given a more edifying role, regarded as the regulator and controller of important physiologic functions, a sexual organ, a source of energy and vitality, and a maintainer of youth and attractiveness. With such ideas on the role of the womb, its removal might be expected to alter a woman's perception of self, especially with regard to femininity, attractiveness, sexual desire, and ability to respond sexually. While the subject of sexuality might once upon a time have been taboo, in contemporary practice women are encouraged to participate in decision making about their treatment, and the impact of hysterectomy on subsequent sexual function is a major issue of concern for many women.16

Research suggests that a wide range of patient characteristics influence posthysterectomy sexual function. For instance, poor knowledge of reproductive anatomy, prehysterectomy negative expectation of sexual recovery, preoperative psychiatric morbidity, depression, and unsatisfactory preoperative sexual relations were all associated

with poor outcome. ^{16–18} Conversely, frequency of coitus, frequency of desire, orgasmic response, healthy relationship with a partner, good general health of both partners, freedom from severe life stresses, and absence of major financial worries are prehysterectomy factors associated with positive postsurgery sexuality. ^{17–19} A recent Danish study²⁰ concurred, reporting that satisfaction with sexual life preoperatively, relationship with the partner, chronic disease, and use of hormone replacement therapy (HRT) were predictors of satisfaction with sexual life after hysterectomy. Therefore, those women who retain an overall desire for sexual activity and were presumably hampered by negative physical symptoms may be expected to experience an improvement in their sexual function following hysterectomy.

Early studies tended to report a decrease in sexual activity, desire, and pleasure from sexual intercourse and an increase in sexual dysfunction in the form of vaginismus, dyspareunia, and low frequency of orgasm after hysterectomy. 16,21,22 This of course was consistent with the prevailing attitudes about the role of the uterus, the loss of which was thought to affect a woman's feminine self-concept, including sexual attractiveness, 22,23 as well causing depression and other sexual problems. 16,22-24 A prospective cohort study up to 5 years postsurgery for dysfunctional uterine bleeding comparing transcervical resection with hysterectomy with or without bilateral salpingo-oophorectomy reported an increase in psychosexual problems such as loss of libido, difficulty with sexual arousal, and vaginal dryness amongst women who had undergone hysterectomy with odds particularly high amongst women who had undergone concurrent oophorectomy.25 However, most recent studies, using more robust tools, but presumably also reflecting contemporary views on the perceived role of the uterus, have found more favorable outcomes. 26,27 The relief from preoperative gynecologic complaints was the most important reason for improvements in sexuality and sense of well-being.²⁶⁻²⁹ Alexander et al. performed a randomized trial comparing hysterectomy with endometrial ablation using validated measures of psychological and sexual function both pre- and postoperatively and found no difference in postoperative sexuality after 12 months.³⁰ It seems highly likely that the conflicting data reported on the impact of hysterectomy may be due to the methodological differences among the studies, such as mixed samples (e.g. patients with both benign and malignant conditions), different measures used to assess sexuality, the use of prospective vs retrospective methods, and diverse medical indications for different types of surgery.31 In a recent systematic review, Farrell and Kieser reported that research in this area was largely retrospective and failed to use validated outcome measures.³² Most recent studies show either no change or an enhancement of sexuality

following hysterectomy. Theoretically, removal of the uterus should increase pleasure because it removes fear of pregnancy and uterine disease and relieves dysmenorrhea and dyspareunia. The Maryland Women's Health Study demonstrated that patients who had undergone hysterectomy had an improvement (increased frequency) in sexual relations and less dyspareunia without a change in orgasmic frequency.¹⁸ However, this study did not explore patients' expectations of sexual relations after hysterectomy. Dragisic and Milad sought to rectify this deficiency by conducting a prospective observational study assessing sexual function and patients' expectations of sexual functioning after hysterectomy, and they used the same validated questionnaire about sexual function adapted from the Maryland Study.³³ To assess expectations, patients were asked the five questions in Table 46.1, adapted from a previous study.²⁶

Dragisic and Milad did not find significant changes in sexual desire and frequency, orgasmic frequency, or orgasmic strength after hysterectomy.³³ There was, however, a significant improvement in sexuality for patients who underwent hysterectomy for pelvic pain and dyspareunia. Interestingly, most of the patients expected to have no change in desire (53%), orgasmic frequency (76%) or orgasmic strength (67%) after hysterectomy. However, this study had limited power in testing for association between sexual function and indications or types of hysterectomy (the latter issue is dealt with later in this chapter). This study also did not examine any measures of psychological status. Rhodes et al. found that women with prehysterectomy depression experienced less improvement in sexual functioning after hysterectomy compared to those with no depression.¹⁸ Intuitively, it might be expected that patients suffering from depression and/or pain before surgery may be at high risk for poor operative outcomes such as slow recovery, persistent pain, or development of new symptoms. Dissatisfaction with the surgical outcomes may be related to subjective factors such as quality of life, which of course are beyond the control of the surgeon. Such intuition has been confirmed in a large prospective study by Hartman et al., which found that women with both pelvic pain and depression at the time of hysterectomy fare less well during the subsequent 24 months than their counterparts.³⁴ However, these women nevertheless had substantial improvement from their preoperative baseline status in all areas of quality of life and sexual function. The magnitude of improvements is consistent with individually meaningful and clinically relevant improvements in quality of life and sexual function, across domains like physical activity, social contacts, mental health, self-perception of health status, and enjoyment of intercourse. The consistency of improvements across multiple interrelated areas suggests that overall no harm is rendered to these complex patients when they undergo

Table 46.1 Questions about expectations of sexual function

Question	Responses
How do you expect your desire for sex to compare after hysterectomy?	Less
How do you expect your pain with sexual relations to change?	No change
How often do you expect to have sexual relations after your hysterectomy?	More
How often do you expect to have orgasms after your hysterectomy?	Don' know
How do you expect your orgasms to change after your hysterectomy?	Poorer
	Better

hysterectomy. This is no cause for complacency, as research may well show that preoperative strategies could further improve outcomes. For example, should depressed women scheduled for hysterectomy receive treatment for depression prior to the surgery? If so, what would be the appropriate time frame before surgery? In women with chronic pelvic pain, should ancillary pain treatment modalities precede surgery? The scope for further research is immense, but in the meantime gynecologists might do well to modify their counseling of these complex patients, with emphasis on describing the hysterectomy as only one component of a multidisciplinary approach in restoring their patients' quality of life and sexual activity.³⁴

Total abdominal hysterectomy (TAH) vs subtotal abdominal hysterectomy (STAH) – an enduring debate resolved

The early abdominal hysterectomies were all subtotal. Leading up to and after the Second World War the advent of antibiotics, blood transfusion, better anesthesia, and improvements in surgical techniques emboldened surgeons to perform total hysterectomy. The 1% chance of developing cancer in the cervical stump was a strong clinical argument against subtotal hysterectomy, and of course in those years there were no cervical screening programs. Total hysterectomy became the standard procedure, while performing STAH was considered a sign of surgical inexperience. Even today, STAH is much less frequently performed, accounting for less than 5% of abdominal hysterectomies in the UK.

In the early 1980s an enduring debate was ignited when reports from Scandinavia suggested that retaining the cervix enhanced the female sexual response and protected against bladder and bowel dysfunction. 11,35,36 The anatomic consideration discussed earlier in the chapter provided a theoretical basis for these arguments, since STAH minimizes the anatomic disruption of hysterectomy, rendering the procedure quicker and safer (a reduced risk of damage to bladder and the ureter;35,37 a reduced risk of postoperative pelvic hematoma³⁸). With dramatically falling rates of invasive cervical cancer and the imminent introduction of vaccines against the human papillomavirus, the risk of cervical stump carcinoma can be regarded as virtually negligible, at present in women whose smears have always been normal, and in the future in women who have been immunized. The risk of cervical stump carcinoma in a woman with previously normal smears at the time of STAH is less than 0.3%.³⁹ Moreover, the litigious atmosphere in which gynecologists currently practice (ureteric or bladder injury can rarely ever be successfully defended in court) might persuade them to consider whether it is always necessary to perform TAH in situations where STAH is an option. However, many gynecologists remained sceptical of the claims from Scandinavia, and on close scrutiny the studies left a lot to be desired. Some of the key criticisms of the Kilkku studies include the fact they were not randomized controlled trials but retrospective analyses which did not use validated questionnaires. Moreover, subsequent studies by Virtanen et al. in the same institute did not concur with Kilkku's reports, 40 although in fairness the study designs were significantly different. Nonetheless, an enduring debate had been ignited, and it is only in recent years that at least three robust studies 41-43 have resolved the issues of whether STAH confers benefits over TAH with respect to pelvic organ function.

There were significant, if subtle, differences in the design between the different studies. For example, while frequency of orgasm and multiple orgasm were measured on a 4-point scale in all studies, sexual satisfaction (the proportion of women who were satisfied with their sexual life, if sexually active) was measured by questionnaire in two trials. Thakar et al. asked whether women had good sexual relations with their partner, while Gimbel et al. asked if women were satisfied with their sexual life (either with or without a partner) - these are sufficiently different questions to render a meta-analysis difficult or impossible.⁴⁴ However, all of three trials assessed the effect of surgical technique on a number of factors that are considered to be related to sexual function, and all three failed to demonstrate an unequivocal difference in outcomes between TAH and STAH. The broad findings were similar: women in both groups in all three trials experienced significant improvements in sexual function and quality of life following hysterectomy, i.e. women who underwent STAH did not fare any better than those who had TAH.

So what is the bottom line? Arguments can be made for performing a STAH as opposed to TAH (the former being a simple and safe operation which minimizes the risk from litigation), but the arguments cannot be based on any presumed advantage with regard to pelvic organ function, and specifically with regard to sexual function.

Surgical techniques – do they influence outcomes?

While the vast majority of hysterectomies the world over are performed via the abdominal route, the vaginal and laparoscopic approaches are viable alternatives. Despite good evidence that vaginal hysterectomy (VH) confers advantages over the abdominal approach in almost all parameters, vaginal hysterectomy accounts for no more than 20% of all cases, and most gynecologists reserve this route for cases where there is prolapse. Laparoscopic hysterectomy boasts less bleeding, less pain, less cost, and rapid recovery advantages, 45-47 but requires expertise and equipment which confine its practice to a limited number of centers, so that it accounts for a minuscule proportion of the total number of hysterectomies. Nevertheless, it is pertinent to explore whether the route of hysterectomy influences sexual function postprocedure.

In a retrospective study in which patient self-appraisal of sexual responsiveness after hysterectomy was studied (61 TAH, 22 STAH, 42 VH), Roussis et al. found that neither self-image nor sexuality diminished after any type of hysterectomy. 48 Gayler et al. compared 30 women who had undergone hysterectomy (20 TAH, 10 VH) with 10 women who had undergone non-gynecologic surgery using validated questionnaires and found no difference in sexual desire. 49 Gutl et al. conducted a prospective study which evaluated and compared the impact of vaginal (46) and abdominal hysterectomy (44) on women's sexual behavior, body image, sexual dysfunction, and satisfaction with surgical outcomes by collecting data prior to surgery, and 3 months after surgery using self-reported questionnaires.⁵⁰ The results showed significant differences in women's sexual behavior and sexual dysfunction before and after hysterectomy, independent of the procedure performed. Women in both groups reported improvements in sexual desire, sexual activity, and sexual intercourse 3 months and 2 years after surgery. Sexual dysfunction such as dyspareunia, vaginismus, and lack of orgasm and loss of sexual interest diminished significantly after surgery. Regression analyses in this study revealed that postmenopausal status, severity of gynecologic complaints, and frequency of sexual intercourse were the most important factors for improved sexual outcomes. Recently, Roovers et al., in a prospective observational study over 6 months in which they compared the effects of vaginal, subtotal, and total abdominal hysterectomy on sexual

well-being, concluded that sexual pleasure significantly improved in all patients independent of the type of hysterectomy.⁵¹ The prevalence of bothersome sexual problems 6 months after VH, STAH, and TH was 43%, 41%, and 39%, respectively (differences not significant), while new sexual problems developed in 23% of patients after VH, 24% after STAH, and 19% after TAH. Unfortunately, this study did not use a validated questionnaire, and normative clinical data from non-clinical women from the local population were not available. The prevalence of bothersome sexual problems appears high, and comparison of study group outcome with outcome values of the normal population would have given more insight into the severity of sexual problems in women both before and after hysterectomy as opposed to those in the normal population.⁵²

A prospective observational study by Ayoubi et al. on the respective consequences of abdominal, vaginal, and laparoscopic hysterectomies on women's sexuality suggested that the impact of vaginal and laparoscopic hysterectomy may be milder than that of the abdominal route.⁵³ In contrast, two studies which addressed psychological well-being and sexuality after laparoscopic and abdominal surgery^{54,55} both concluded that psychosexual well-being was unaffected by the surgical approach used. The latter study⁵⁵ emphasized the fact that sexuality is one of the most important aspects when evaluating quality of life after gynecologic surgery, and that it is also one of the most difficult aspects to monitor. In semistructured interviews with prospective design exploring sexual life, women have evaluated the socioemotional aspects as at least as important as quantitative variables, such as frequency of coitus, when judging the total concept of sexuality. One of the advantages of the McCoy scale used in this study is that it emphasizes sexual cognition rather than sexual behavior. Sexual behavior can be influenced by other factors (e.g. partner's erectile dysfunction). Another factor of importance is the patient's relationship with her partner and this has been touched on before in this chapter. When asked an open question about the meaning of sexuality, the majority of women defined this as expressions of a partner relationship, sometimes contradicting the questionnaire on frequency of desire.⁵⁶

Effect of radical hysterectomy on sexuality

The diagnosis of gynecologic cancer is a major blow for any woman, and just the diagnosis itself generates fear and anxiety that are bound to have a significant psychosexual impact, even before treatment issues are considered. Even when treatment is thought to have been successful, women have to live with the persistent fear of recurrence. The focus on the overwhelming implications of the diagnosis, and the meticulous attention often paid to treatment modalities, means that issues of sexuality more often than not are neglected. While early-stage endometrial and ovarian cancers may be 'cured' by surgery that often has no more negative impact on sexual function than simple hysterectomy for benign disease, this is not so for cervical cancer. Moreover, unlike the other gynecologic cancers, cervical cancer often affects the younger, more sexually active woman,⁵⁷ so that both its diagnosis and treatment (radical surgery alone for earlystage disease, or radiotherapy for advanced disease) are more likely to adversely affect sexual function. It does not help that the causal agent of carcinoma of the cervix is a sexually transmitted virus, so that for the poorly counseled woman there might be issues of guilt and regret associated with the diagnosis, and linked directly to sexual behavior. All these issues mean that studies of sexual function after diagnosis and radical hysterectomy are fraught with methodological difficulties and confounding variables.

There is extensive evidence in the literature indicating that outcome of treatment for cervical cancer entails adverse effect on sexual function.⁵⁸⁻⁶¹ But most of these studies report on mixed samples of patients undergoing surgery, radiotherapy, or combined treatment.⁶¹ Radiotherapy as primary or adjuvant treatment has been reported to result in more severe disruption of sexual functioning than hysterectomy alone. 62-64 According to the literature, a considerable proportion of patients treated for gynecologic cancer either do not resume sexual intercourse or cease to have intercourse within the first year of treatment, 65,66 particularly those undergoing intracavitary irradiation. 67,68 Patients treated surgically alone seem to overcome the adverse outcomes on sexual functioning more quickly and regain their full sexual capacity and satisfaction more frequently than women treated by radiotherapy alone or a combination.⁶⁹ Frumovitz et al. recently compared quality of life and sexual functioning in cervical cancer survivors treated with either radiotherapy or radical hysterectomy and lymph node dissection.⁷⁰ At least 5 years after initial treatment, survivors treated with the former had worse sexual function than the latter group. This data also suggest that cancer cervix-treated survivors treated with surgery alone can expect overall quality of life and sexual function not unlike that of peers without a history of cancer.

Bergmark et al. compared 256 women who had undergone RH for early cancer cervix and 350 controls. Their findings suggest that the resulting changes in vaginal anatomy and function exert negative effects on sexual function. These changes include decreased lubrication and genital swelling during arousal and reduction in perceived vaginal length and elasticity during intercourse.

Dyspareunia was more frequent in the cancer cervix group. However, frequency of coitus, orgasmic frequency, and pleasure did not differ significantly between the two groups, indicating that the physical changes induced by cervical cancer do not affect this aspect of sexuality. Interestingly, Jensen et al. also reported that in their cohort of patients with early-stage cervical cancer undergoing RH, surgery had a persistent negative impact on patients' sexual interest and vaginal lubrication, whereas the majority of other sexual and vaginal problems disappeared over time.⁷²

Grumann et al. prospectively investigated whether RH for stage IB cancer cervix without adjuvant treatment entails short- or long-term sexual difficulties.⁷³ Twenty patients in stage IB undergoing RH, 18 women treated with hysterectomy for benign gynecologic conditions, and 20 gynecologically healthy women were studied. At 0, 4, and 8 months postoperatively, data were prospectively collected using standardized questionnaires and specifically developed scales. Sexual functioning was covered in 15 specifically designed items and analyzed using Fisher's exact tests. For all other variables, group comparisons were computed using analysis of variance (ANOVA) or non-parametric statistical equivalents. Nonsignificant trends, consistent across time and groups, resulted for most of the sexual variables. Preoperatively, cancer patients exhibited slightly better sexual functioning than the other two groups, which can be explained by the fact that they were younger, most often asymptomatic, and diagnosed accidentally during a routine Papanicolaou (Pap) smear, but over time this decreased slightly. Conversely, sexual functioning among the patients with benign disease showed steady improvement. These results indicate that radical hysterectomy for stage IB cervical cancer does not entail major sexual sequelae. Because of the limited sample size of the study, caution must be exercised in interpreting these findings. While this is encouraging, the minor decrements in frequency and responsiveness need to be addressed. Dyspareunia is a complaint raised by some of the patients undergoing radical hysterectomy.

RH can also entail transient ovarian dysfunction even if the ovaries are conserved, and some patients experience a total loss of their ovarian function for reasons not entirely understood,⁷⁴ although this is more likely to happen if the ovaries have been transposed to the paracolic gutters. Reduced vaginal congestion, lubrication, and expansion are characteristic outcomes. In concert with this, cancer patients in the Grumann trial⁷³ also complained of vaginal dryness at 4 and 8 months postoperatively, although only 15% underwent oophorectomy, and most of these patients were put on HRT afterwards. In cancer patients vaginal dryness could not be attributed to

psychological factors such as increased apprehension about sexual intercourse, given that their level of self-reported sexual anxiety was stable across the time of study. Unfortunately, menopausal problems and difficulties resulting from pelvic denervation in patients following RH are often neglected because of the welter of medical and psychosocial problems to be considered in this point in time.⁶⁴

Maas et al. objectively assessed sexual arousal in women after RH (n=12), TAH (n=12), and 17 age-matched controls by photo-plethysmography (an objective measure of the vaginal pulse amplitude which measures vaginal blood flow during sexual arousal using erotic films).⁵¹ They hypothesized that damage to the autonomic nerves results in disrupted vaginal blood flow response during sexual stimulation. Subjective sexual response was recorded after each erotic stimulus condition. Women after RH had a lower maximum response than controls but an equally strong subjective sexual response similar to that in young women without sexual problems. After simple hysterectomy, there was an intermediate maximum vaginal pulse impulse, but these women had a weaker sexual response compared to the other two groups. It was suggested that although RH appears to be associated with a disturbed blood flow after sexual response, larger studies are needed for confirmation. Overall, it seems that although RH affects some aspects of sexuality, the majority of these appear to be transient and may be influenced by other overriding issues related to the diagnosis of cancer.

Impact of concurrent oophorectomy on sexual function

Ovaries are the source of the female sex hormones estrogen, testosterone, and progesterone. Apart from the obvious role of estrogen and progesterone in the reproductive cycle, there can be no doubting the important role these hormones play in the female sexual response. The role of testosterone is often overlooked. When a woman undergoes a normal menopause, there is ample evidence that there is often a profound decline in all aspects of sexual function, including libido, coital frequency, coital enjoyment, frequency of orgasm, intensity of orgasm, and vaginal lubrication. It would seem to stand to reason that oophorectomy in the premenstrual woman, which catapults the woman into the menopausal state, might impair sexual function in an even more dramatic way than the natural menopause, since in the latter there is often a gradual decline in hormonal levels. Yet the real picture is far from crystal clear. The fundamental question for the purposes of this chapter is whether concomitant oophorectomy causes the expected decline in sexual function in the

premenopausal woman, whether this is obviated by hormone replacement, and also what the impact of oophorectomy in the postmenopausal woman might be. There is a great deal of literature on this matter, but the waters are very muddy indeed, not only because of the poor design of the published studies but also because of the inherent difficulty of designing robust protocols in studies of human sexual function alluded to earlier. In addition, there is some evidence that even when ovaries are conserved at hysterectomy, these women experience an earlier menopause, by about 2 years, than they might otherwise have experienced had they not had a hysterectomy. ^{13,14} So what is the research evidence with regard to the impact of oophorectomy on sexual function?

Many premenopausal women undergo hysterectomy with concomitant oophorectomy (total abdominal hysterectomy and bilateral salpingo-oophorectomy - TAH/ BSO)75,76 and clinical guidelines for prophylactic oophorectomy have been published.⁷⁷ Oophorectomy is often recommended in the hope of improving outcomes for women with pelvic pain, endometriosis, and premenstrual symptoms. 78-80 In older premenopausal women, oophorectomy is often advised because of concerns about ovarian carcinoma risk. However, there are concerns that oophorectomy may in fact lead to new health problems, and a recently published decision analysis suggested no improvement in long-term survival for women undergoing oophorectomy.81 With regards to sexuality, the studies have so far yielded conflicting evidence. In a review of the psychosocial outcomes of hysterectomy, Flory et al. reported that although hysterectomy appears to reduce pain, there is not much to be gained in terms of psychosocial or psychosexual effects, and in fact, there may be a subgroup of women (about 10-20%), mostly undergoing concomitant oophorectomy, who report negative psychosexual outcomes such as reduced sexual interest, arousal, and orgasm as well as elevated depressive symptoms and impaired body image.82 Kuscu et al. found significantly lowered sexual desire and frequency of sexual attempts after a TAH but, surprisingly, the presence of adequate estrogen replacement therapy in the postoperative period did not make any positive difference.83

Kraamiaat and Veeninga found that oophorectomized women reported more physical complaints and more frequent loss of sexual interest than a control group of chole-cystectomized women, but there were no difference between the groups with regards to general discomfort, anxiety, and depression. ⁸⁴ In both oophorectomized and cholecystectomized women, life stress contributed to general discomfort, anxiety and physical complaints. Nathorst-Boos et al. interviewed 678 women about psychological reactions and sexual adjustments after TAH with or without simultaneous oophorectomy. ⁸⁵ A more

positive attitude towards the operation was found in the group of women whose ovaries had been preserved. Oophorectomized women experienced deterioration in sexual life compared to those with preserved ovaries. Importantly, this was observed regardless of age and in different parameters of sexual function such as coital frequency and experience of intercourse. In a separate study, ⁸⁶ the same group of authors also investigated the effect of estrogen replacement on sexual life and psychological well-being in women who had undergone concurrent oophorectomy during hysterectomy. Three age-matched hysterectomized groups of women were investigated:

- Group A (n = 33): oophorectomized, not receiving estrogen replacement therapy (ERT).
- Group B (*n* = 33): oophorectomized and receiving ERT.
- Group C (*n* = 35): ovaries preserved and not receiving ERT.

The McCoy Sexual Rating Scale and the Psychological General Well-Being Index as well as a semistructured interview were used to assess postoperative experience with respect to libido, vaginal lubrication, ability of getting pleasure from intercourse, and ability to achieve orgasm. In oophorectomized women, sexual life was impaired as compared to those with intact ovaries, and these women complained of less pleasure from coitus, and impaired libido and lubrication. Regardless of whether estrogen was administered or not, a similar pattern was found, indicating that estrogens are of little value in treating these specific aspects of sexual dysfunction. Oophorectomized women receiving ERT reported less anxiety and depression and a greater sense of well-being, similar to women whose ovaries were preserved. Interestingly, no correlation was found between psychosexual variables and biochemical androgen markers such as total and free testosterone and dehydroepiandrosterone sulfate (DHEAS).

In a prospective study, Aziz et al. evaluated psychological well-being and sexuality 1 year after hysterectomy—oophorectomy compared to hysterectomy alone. ⁸⁷ In 217 women the ovaries were preserved, while 106 women underwent concomitant oophorectomy. Psychological well-being was studied by the Psychological Well-Being Index and sexuality by the McCoy's sex questionnaire. The prevalence of climacteric symptoms was reported by the modified Kupperman Index. Postoperatively, all oophorectomized women and those with climacteric symptoms with ovaries conserved were recommended ERT. The two groups did not differ in psychological well-being, either before surgery or at 1-year postoperatively. Most of the sexual parameters showed positive correlation

to psychological well-being parameters. The correlation was strong regarding parameters of overall sexual satisfaction, weak regarding sexual motivation and relationship to partner, while absent regarding coital frequency. The authors concluded that prophylactic oophorectomy at elective hysterectomy does not negatively affect general well-being in adequately estrogenized perimenopausal women, and that most aspects of sexuality are correlated to aspects of psychological well-being.⁸⁸

But why should ERT fail to improve sexuality in oophorectomized women? It is likely that the answer lies in the role of testosterone. The ovaries produce at least half of the circulating testosterone in premenopausal women, and it should therefore not be surprising that after surgery many women report impaired sexual functioning despite ERT: loss of the physiologic testosterone milieu could account for a decrease in libido, sexual pleasure, and sense of well-being. As alluded to above, removal of the uterus, even when ovaries are conserved, may compromise ovarian function and lead to an earlier menopause. In a review, Cutler et al. stressed that estrogen, progesterone, and androgen levels all tend to be altered by hysterectomy, with a potential subsequent negative impact on the cardiovascular system, bone metabolism, cognitive function, sexual response, and sexual attractiveness.⁸⁹ This is of course contradicted by the prospective observational study by Aziz et al. mentioned earlier,88 which concluded that perimenopausal androgen decline after oophorectomy does not influence sexuality or psychological wellbeing; it was supported by the study of Nathorst-Boos et al., who found that although elective ovarian removal had a negative impact on women's sexuality, there was no correlation between psychosexual variables and biochemical androgen markers like total and free testosterone and dehydroepiandrosterone sulfate (DHEAS).86

With such conflicting evidence from research, what advice can be given to the gynecologist? The decision to remove the ovaries at the time of simple hysterectomy should not be taken lightly in the premenopausal woman: there may be little benefit with regard to primary pathology, and the potential health hazard may be considerable. The risk of ovarian cancer subsequent to hysterectomy is extremely low, and therefore oophorectomy in the perimenopausal woman should not be routine practice. Hormone replacement in the premenopausal woman should be routine, unless there are specific contraindications. Where HRT is being considered in the pre- and perimenopausal woman, testosterone as well as estrogen replacement should be considered, since estrogen alone may be insufficient. It seems teleologically sound that many women would benefit from having the HRT administered as implants at the time of the oophorectomy, with women being counseled about what to expect as the estrogen and testosterone levels gradually decline over a 6-month period, and therefore being given plenty of time to decide on future HRT, including the administration of further implants. There is clearly a need for further research in this area.

General conclusions

Despite the passions and controversies generated by hysterectomy, it is nevertheless a highly successful operation. It rates highest in satisfaction scores when compared to all other treatment modalities for dysfunctional uterine bleeding, which is just as well, since it is the most frequently performed major gynecologic operation in the UK and the USA, and the vast majority of cases are performed for benign rather than lifesaving indications. Historically it had been supposed that hysterectomy could adversely affect sexual function, but recent robust research using validated and other sophisticated tools suggests the contrary, with the vast majority of women who undergo simple hysterectomy reporting improved sexual function, presumably in part due to the removal of pathology along with the uterus. This is of course consistent with the high satisfaction scores. Elegant recent research utilizing immunohistochemical techniques and studying interruptions to the innervation of pelvic organs also now explains why simple hysterectomy preserves sexual function, while radical hysterectomy does indeed compromise it. However, such knowledge is leading to novel nerve-sparing surgical innovations in radical hysterectomy which are designed to minimize the negative impact of the operation on sexual and other pelvic organ function. The controversy over total vs subtotal hysterectomy has largely been resolved, with the current consensus being that the subtotal procedure confers no benefits over total hysterectomy with respect to sexual function, although there may be other good reasons to choose the former procedure, not least the simplicity and safety of the procedure. A small minority of women (some 10-15%) report sexual dysfunction developing for the first time after simple hysterectomy: this area is little researched, and the vast majority of women can and should be reassured about this highly efficacious operation.

Future research

Whereas it is generally accepted that hysterectomy brings about anatomic changes and is associated with psychological sequealae which could change the female sexual response, it remains unclear whether these psychophysiologic changes have clinical significance. Future research should therefore approach these issues from a variety of angles and employ a variety of tools: e.g. objective measures such

as vaginal pulse amplitude^{90,91} can reliably measure increased vaginal blood flow during sexual arousal, while data from such studies need to be complemented by studies that utilize validated or standardized self-report measures on sexual functioning, depression, anxiety, and quality of life issues, including relationship parameters. Self-report questionnaires should be validated in non-clinical samples. Whenever possible, studies should be prospective, multicenter, randomized, and powered to answer clearly defined questions, with pre- and post-hysterectomy assessment.

Clinical implications

In a web-based survey by Berman et al. of 3807 women, 40% of the women reported that they did not actively seek

help from a physician for sexual functioning complaints, but 54% indicated that they would have liked to have done so. 92 Only 39% of those surveyed felt that the physician addressed their concerns seriously. Despite the advent of effective alternatives to hysterectomy, this operation remains a frequently performed and highly effective treatment modality which is likely to continue to be offered to many women for the foreseeable future. Sexual functioning will always remain a central issue of concern for women undergoing this procedure. Therefore, medical professionals should not hesitate to address the psychological and physiologic aspects of female sexuality when counseling women both pre- and posthysterectomy, even when the women do not themselves actively seek information. Generally speaking, women should be reassured of positive outcomes on the basis of the available robust research evidence.

References

- Maas K, Moriya Y, Kenter G et al. A plea for preservation of pelvic autonomic nerves. Lancet 1999; 354: 772–3.
- Bérard EJ. The sexuality of spinal cord injured women: physiology and pathophysiology. A review. Paraplegia 1989; 27: 99–112.
- Hasson HM. Cervical removal at hysterectomy for benign disease: risks and benefits. J Reprod Med 1993; 38: 781–90.
- Maas CP, DeRuiter MC, Kenter GC, Trimbos JB. The inferior hypogastric plexus in gynecologic surgery. J Gynecol Tech 1999; 5: 55–62
- Butler-Manuel SA, Buttery LDK, A'Hern RP et al. Pelvic nerve plexus trauma at radical hysterectomy and simple hysterectomy: the nerve content of uterine support ligaments. Cancer 2000; 89: 834-41
- 6. Houeckel M, Konerding MA, Heussel CP. Liposuction-assisted nerve-sparing extended radical hysterectomy: oncologic rationale, surgical anatomy, and feasibility study. Am J Obstet Gynecol 1998; 178: 971–6.
- Possover M, Stober S, Plaul K, Schneider A. Identification and preservation of the motoric innervation of the bladder in radical hysterectomy type III. Gynecol Oncol 2000; 79: 154–7.
- 8. Trimbos JB, Maas CP, DeRuiter MC et al. A nerve-sparing radical hysterectomy: guidelines and feasibility in Western patients. Int J Gynecol Cancer 2001; 11: 180–6.
- Lowenstein L, Yarnitsky D, Gruenwald I et al. Does hysterectomy affect genital sensation? Eur J Obstet Gynecol Reprod Biol 2005; 119: 242–5.
- Jewett J. Vaginal length and incidence of dyspareunia following total abdominal hysterectomy. Am J Obstet Gynecol 1952; 63: 400–7.
- Kilkku P, Gronroos M, Hirvonen T, Rauramo L. Supravaginal uterine amputation vs. hysterectomy. Effects on libido and orgasm. Acta Obstet Gynecol Scand 1983; 62: 147–52.
- Segraves RT, Segraves KB. Medical aspects of orgasm disorders. Handbook of Sexual Dysfunction. Assessment and Treatment. Boston: Allyn and Bacon, 1993: 225–52.

- 13. Cattanach J. Oestrogen deficiency after tubal ligation. Lancet 1985; 1: 847–9.
- 14. Siddle N, Sarrel P, Whitehead M. The effect of hysterectomy on the age at ovarian failure: identification of a subgroup of women with premature loss of ovarian function and literature review. Fertil Steril 1987; 47: 94–100.
- 15. Coppen A, Bishop M, Beard RJ et al. Hysterectomy, hormones and behaviour. A prospective study. Lancet 1981; 1: 126–8.
- Dennerstein L, Wood C, Burrows GD. Sexual response following hysterectomy and oophorectomy. Obstet Gynecol 1977; 49: 92–6.
- 17. Helstrom L, Lundberg PO, Sorborm D, Backstrom T. Sexuality after hysterectomy: factor analysis of women's sexual lives before and after subtotal hysterectomy. Obstet Gynecol 1993; 81: 357–62.
- 18. Rhodes JC, Kjerullf KH, Langenberg PW, Guzinsky G. Hysterectomy and sexual function. JAMA 1999; 282: 1934–41.
- Darling CA, McKay-Smith YM. Understanding hysterectomies: sexual functioning and quality of life. J Sex Res 1990; 30: 324–35.
- Zobbe V, Gimbel H, Andersen BM et al. Sexuality after total vs subtotal hysterectomy. Acta Obstet Gynecol Scand 2004; 83: 191–6.
- 21. Richards DH. A post-hysterectomy syndrome. Lancet 1974; 2: 983–5.
- 22. Kaltreider NB, Wallace A, Horowitz MJ. A field study of the stress response syndrome: young women after hysterectomy. JAMA 1979; 242: 1499–503.
- Lalinec-Michaud M. Depression after hysterectomy. Psychosomatics 1988; 3: 307–14.
- Bernherd LA. Consequences of hysterectomy in the lives of women. Health Care Women Int 1992; 13: 281–91.
- 25. McPherson K, Herbert A, Judge A et al. Psychosexual health 5 years after hysterectomy: population-based comparison with endometrial ablation for dysfunctional uterine bleeding. Health Expectations 2005; 8: 234–43.

- Helstrom L. Sexuality after hysterectomy: a model based on quantitative and qualitative analysis of 104 women before and after hysterectomy. J Psychosom Obstet Gynecol 1994; 15: 219–29.
- Filiberti A, Regazzoni M, Garavoglia M et al. Problems after hysterectomy. A comparative content analysis of 60 interviews with cancer and non-cancer hysterectomized women. Eur J Gynecol Oncol 1991; 12: 445–9.
- Barensten R, Foekema HA, Bezemer W et al. The interview of women aged 45–65 and their partners on aspects of climacteric phase of life. Eur J Obstet Gynecol 1994; 57: 95–101.
- Oldenhave A, Jaszmann LJB, Everaerd TAM et al. Hysterectomised women with ovarian conservation report more severe climacteric complaints than do normal climacteric women of similar age. Am J Obstet Gynecol 1993; 168: 765–71.
- Alexander AD, Naji AA, Pinion SB et al. A randomised trial of hysterectomy vs endometrial ablation for dysfunctional uterine bleeding: psychiatric and psychosocial outcome. BMJ 1996; 312: 280–312.
- Bernherd LA. Methodological issues with hysterectomy. Health Care Women Int 1992; 13: 218–22.
- Farrell SA, Kieser K. Sexuality after hysterectomy. Am J Obstet Gynecol 2000; 95: 1045–51.
- Dragisic KG, Milad MP. Sexual functioning and patient expectations of sexual functioning after hysterectomy. Am J Obstet Gynecol 2004; 190: 1416–8.
- 34. Hartmann KE, Ma C, Lamvu GM et al. Quality of life and sexual function after hysterectomy in women with preoperative pain and depression. Obstet Gynecol 2004; 104: 701–9.
- Kilkku P. Supravaginal uterine amputation vs. hysterectomy. Effects on coital frequency and dyspareunia. Acta Obstet Gynecol Scand 1983; 62: 141–5.
- Kilkku P, Hirvonen T, Gronroos M. Supra-cervical uterine amputation vs. hysterectomy; the effects on urinary symptoms with special reference to pollakiuria, nocturia and dysuria. Maturitas 1981; 3: 197–204.
- 37. Parys BT, Haylen BT, Hutton JL. Urodynamic evaluation of lower urinary tract function in relation to hysterectomy. Aus NZ J Obstet Gynecol 1990; 30: 161–5.
- Nathorst-Boos J, Fuchs T, von Schoultz B. Consumers attitude to hysterectomy: the experience of 678 women. Acta Obstet Gynecol Scand 1992; 71: 230–4.
- Storm HH, Clemmensen IH, Manders T et al. Supra-vaginal uterine amputation in Denmark 1978–88 and risk of cancer. Gynecol Oncol 1992; 45: 198–201.
- Virtanen H, Makinen J, Tenho T et al. Effects of abdominal hysterectomy on urinary and sexual symptoms. Br J Urol 1993; 72: 868–72.
- Thakar R, Ayers S, Clarkson P et al. Outcomes after total vs subtotal hysterectomy. N Engl J Med 2002; 347: 1318–25.
- Gimbel H, Zobbe V, Andersen BA et al. Randomised controlled trial of total compared with subtotal hysterectomy with one-year follow up results. BJOG 2003; 110: 1088–98.
- Learman LA, Summitt RL, Varner RE et al. A randomised comparison of total or supracervical hysterectomy: surgical complications and clinical outcomes. Obstet Gynecol 2003; 102: 453–62.
- 44. Lethaby A, Ivanova V, Johnson NP. Total vs subtotal hysterectomy for benign gynecologic conditions. Cochrane Database Syst Rev 2006; (2): CD004993.
- 45. Munro MG, Deprest J. Laparoscopic hysterectomy: does it work? A bicontinental review of literature and clinical commentary. Clin Obstet Gynecol 1995; 38: 401–25.

- Frazee RC, Roberts JW, Okeson GC et al. Open vs laparoscopic cholecystectomy. A comparison of postoperative pulmonary function. Ann Surg 1991; 213: 651–4.
- Olsson JH, Ellstrom M, Hahlin M. A randomised prospective trial comparing laparoscopic and abdominal hysterectomy. Br J Obstet Gynecol 1996; 103: 345–50.
- Roussis NP, Watrous L, Kerr A et al. Sexual response in the patient after hysterectomy: total abdominal vs supra-cervical vs vaginal procedure. Am J Obstet Gynecol 2004; 190: 1427–8.
- Gayler KT, Conaglen HM, Hare A et al. The effect of gynecologic surgery on sexual desire. J Sex Marital Ther 1999; 25: 81–8
- Gutl P, Greimel ER, Roth R, Winter R. Women's sexual behaviour, body image and satisfaction with surgical outcomes after hysterectomy: a comparison of vaginal and abdominal surgery. J Psychosom Obstet Gynecol 2002; 23: 51–9.
- 51. Roovers J-PWR, van der Bom JG, van der Vaart CH et al. Hysterectomy and sexual well-being: prospective observational study of vaginal hysterectomy, sub-total abdominal hysterectomy and total hysterectomy. BMJ 2003; 327: 774–8.
- Maas CP, Weijenborg PT, ter Kuile MM. The effect of hysterectomy on sexual functioning. Ann Rev Sex Res 2003; 14: 83–113.
- 53. Ayoubi JM, Fanchin R, Monrozies X et al. Respective consequences of abdominal, vaginal, and laparoscopic hysterectomies on women's sexuality. Eur J Obstet Gynecol Reprod Biol 2003; 111: 179–82.
- 54. Strauss B, Jakel I, Koch-Dorfler M et al. Psychiatric and sexual sequelae of hysterectomy a comparison of different surgical methods. Geburtshilfe Frauenheilkd 1996; 56: 473–83.
- 55. Ellstrom MA, Astrom M, Moller A et al. A randomized trial comparing changes in psychological well-being and sexuality after laparoscopic and abdominal hysterectomy. Acta Obstet Gynecol Scand 2003; 82: 871–5.
- Helstrom L, Sorbom D, Backstrom T. Influence of partner relationship on sexuality after subtotal hysterectomy. Acta Obstet Gynecol Scand 1995; 74: 142–6.
- Coates M, Day P, McCredie M et al. Cancer in New South Wales. Incidence and Mortality 1993. Sydney, NSW, Cancer Registry. Sydney: NSW Cancer Council, 1996.
- Van de Weil HBM, Weijmar Schultz WCM, Hallensleben A et al. Sexual functioning following treatment of cervical cancer. Eur J Gynecol Oncol 1988; 9: 275–81.
- Schover LR, Fife M, Gershenson DM et al. Sexual dysfunction and treatment for early stage cervical cancer. Cancer 1989; 63: 204–12.
- Horton B. Sexual outcomes arising from the diagnosis and treatment of cervical cancer and cervical intra-epithelial neoplasia: a review of the literature. Sex Mar Ther 1991; 6: 29–39.
- 61. Weijmar Schultz WCM, Bransfield DD, Van de Weil HBM et al. Sexual outcomes following female genital cancer treatment: a critical review of methods, investigations and results. Sex Mar Ther 1992; 7: 29–64.
- 62. Andersen BL, Jochimsen PR. Sexual functioning among breast cancer, gynecologic cancer, and healthy women. J Consult Clin Psychol 1985; 53: 25–32.
- 63. Seibel MM, Freeman MG, Graves WL. Carcinoma of the cervix and sexual function. Obstet Gynecol 1980; 55: 484–7.
- 64. Auchincloss SS. After treatment. Psychosocial issues in gynecologic cancer survivorship. Cancer 1995; 76(Suppl): 2117–24.
- Andersen BL, Anderson B, deProsse C. Controlled prospective longitudinal study of women with cancer: I. Sexual functioning outcomes. J Consult Clin Psychol 1989; 57: 683–91.

- 66. Andersen BL. Quality of life for women with gynecologic cancer. Curr Opin Obstet Gynecol 1995; 7: 69–76.
- Abitol MM, Davenport JH. Sexual dysfunction after therapy for cervical carcinoma. Am J Obstet Gynecol 1974; 119: 181–9.
- 68. Bertelsen K. Sexual dysfunction after treatment for cervical cancer. Dan Med Bull 1983; 30(Suppl): 31–4.
- 69. Thranov I, Klee M. Sexuality among gynecologic cancer patients
 a cross-sectional study. Gynecol Oncol 1994; 52: 14–9.
- Frumovitz M, Sun CC, Schover LR et al. Quality of life and sexual functioning in cervical cancer survivors. J Clin Oncol 2005; 23: 7428–36.
- Bergmark K, Avall-Lundqvist E, Dickman PW et al. Vaginal changes and sexuality in women with history of cervical cancer. N Engl J Med 1999; 340: 1383–89.
- 72. Jensen PT, Groenvold M, Klee MC et al. Early-stage cervical carcinoma, radical hysterectomy and sexual function. Cancer 2004; 100: 97–106.
- Grumann M, Robertson R, Hacker NF, Sommer G. Sexual functioning in patients following radical hysterectomy for stage IB cancer of the cervix. Int J Gynecol Cancer 2001; 11: 372–80.
- Moadel AB, Ostroff JS, Lesko LM et al. Psychosexual adjustment among women receiving hormone replacement therapy for premature menopause following cancer treatment. Psychooncology 1995; 4: 273–82.
- Keshavarz H, Hills SD, Kjeke BA et al. Hysterectomy surveillance – United States, 1994–1999. MMWR CDC Surveill Summ 2002; 51: 1–8.
- 76. Kjerulff KH, Langenberg PW, Rhodes JC et al. Effectiveness of hysterectomy. Obstet Gynecol 2000; 95: 319–26.
- American College of Obstetrics and Gynecology. Prophylactic oophorectomy. ACOG Practice Bulletin No.7. Washington, DC: ACOG, 1999.
- Beard RW, Kennedy RG, Gangar KF et al. Bilateral hysterectomy and oophorectomy in the treatment of intractable pelvic pain associated with pelvic congestion. BJOG 1991; 98: 988–92.
- Cronje WH, Vashisht A, Studd JW. Hysterectomy and bilateral oophorectomy for severe premenstrual syndrome. Hum Reprod 2004; 19: 2152–5.

- Namnoum AB, Hickman TN, Goodman SB et al. Incidence of symptom recurrence after hysterectomy for endometriosis. Fertil Steril 1995; 64: 898–902.
- Parker W, Broder M, Liu Z et al. Ovarian conservation at the time of hysterectomy for benign disease. Obstet Gynecol 2005; 106: 219–26.
- 82. Flory N, Bissonnette F, Binik YM. Psychosocial effect of hysterectomy: literature review. J Psychosom Res 2005; 59: 117–29.
- 83. Kuscu NK, Oruc S, Ceylan E et al. Sexual life following total abdominal hysterectomy. Arch Gynecol Obstet 2005; 271: 218–21.
- 84. Kraaimaat FW, Veeninga AT. Life stress and hysterectomy-oophorectomy. Maturitas 1984; 4: 319–25.
- 85. Nathorst-Boos J, von Schoultz B. Psychological reactions and sexual life after hysterectomy with or without oophorectomy. Gynecol Obstet Invest 1992; 34: 97–101.
- 86. Nathorst-Boos J, von Schoultz B, Carlstrom K. Elective ovarian removal and estrogen replacement therapy effects on sexual life, psychological well-being and androgen status. J Psychosom Obstet Gynecol 1993; 14: 283–93.
- 87. Aziz A, Bergquist C, Nordholm L et al. Prophylactic oophorectomy at elective hysterectomy. Effects on psychological well-being at 1-year follow-up and its correlations to sexuality. Maturitas 2005; 51: 349–57.
- 88. Aziz A, Brannstrom M, Bergquist C et al. Perimenopausal androgen decline after oophorectomy does not influence sexuality or psychological well-being. Fertil Steril 2005; 83: 1021–8.
- Cutler WB, Genovese-Stone E. Wellness in women after 40 years of age: the role of sex hormones and pheromones. Dis Mon 1998; 44: 421–546.
- 90. Laan E, Everaerd W, Evers A. Assessment of female sexual arousal: response specificity and construct validity. Psychophysiology 1995; 32: 476–85.
- 91. Rosen RC. Assessment of female sexual dysfunction: review of validated methods. Fertil Steril 2002; 77: 89–93.
- 92. Berman L, Berman J, Felder S et al. Seeking help for sexual function complaints: what gynecologists need to know about the female patient's experience. Fertil Steril 203; 79: 572–6.

Non-invasive surgery using magnetic resonance-guided focused ultrasound surgery technology

Richard Chudacoff

Described as the ideal surgery, 1 magnetic resonance (MR)guided focused ultrasound surgery (MRgFUS) completely destroys targeted tissue without causing structural or functional damage to adjacent tissue. Magnetic resonance imaging (MRI) identifies targeted tissue and detects suitable access routes for the acoustic waves. The ultrasound energy penetrates normal tissue with minimal interference, reaching targeted tissue in sufficiently high energy levels, inducing cell death. MRI contrast scans then verify effective therapeutic treatment. Thus, an effective, safe, non-invasive, closed-loop procedure eradicates circumscribed tissue with minimal discomfort and recovery time. So effective and novel, the first table approved for MRg-FUS (ExAblate 2000) topped the list of the US FDA's (Food and Drug Administration's) Office of Device Evaluation Annual Report Fiscal Year 2005 for new devices approved the previous year.2

Since 1935, researchers have known thermal energy created by focused ultrasound acoustic beams results in localized heating.^{3,4} This thermal ablation causes a coagulative necrosis, destroying all structural and enzymatic proteins sensitive to short-term temperatures >54°C. All mammalian cells, regardless of function and structure, are destroyed above this temperature.

Early trials ablating intracranial lesions in Parkinson's disease patients noted therapeutic effects.^{3,5} Problems with localization of the ultrasound focus and measuring the heat generated limited this technique as a viable treatment modality. This absence of localization and temperature-sensitive imaging methods prevented further exploration. Contemporary treatment of prostate cancer with ultrasound-guided focused ultrasound surgery ran into similar roadblocks. Focused ultrasound destruction of adjacent nerve-bearing tissue results in a high (>50%) rate of impotency.⁶ Without precise placement of ultrasound thermal spots, collateral structural and functional damage occurs. Additionally, diagnostic ultrasound lacks temperature sensitivity, prohibiting identification of focally heated spots within the treatment zone. Lack of real-time monitoring

and control without identifying appropriately heated areas of treatment lessens treatment efficacy and sensitivity.

The concept of MR-guided focused ultrasound surgery was demonstrated in 1991 when the acoustic ultrasound generator was integrated with MRI temperature-sensitive technology to facililate monitoring and control of thermal ablations. This coupling permits quantification and localization of acoustic-generated energy. Accurate thermal monitoring detects and maps areas that achieved thermal necrosis.

Along with thermal dosimetery, MR's excellent imaging defines tissue characteristics. All surgery requires precise visualization of tissue margins, regardless of technique: open, minimally invasive, or non-invasive ultrasound or MR guided. The highly sensitive imaging of MR guides numerous therapeutic interventions and outperforms all other modalities in bulk tumor detection, tumor deposits, tumor infiltrations, and postoperative debulking residuals. Certain brain and breast tumors cannot be completely identified during open procedures and require diagnostic MRI-determined surgical margins. Real-time MRI has recently been introduced intraoperatively. As we become more comfortable with pelvic MR images, the differentiation of intrauterine masses, most notably leiomyomas and adenomyomas, becomes easier and more critical in therapeutic planning.

Localization of thermal ablation sites, whether by open, minimally invasive, or non-invasive techniques, and regardless of energy modality (radiofrequency, cryotherapy, microwave, laser, or electrotherapy) requires visualization of anatomic boundaries for targeted applications. This is true for single- or multiple-dose procedures. Open or minimally invasive procedures benefit from direct, realtime visualization, patient positioning, retractors, and, in the case of the former, packing. Planning the best route for closed procedures requires real-time imaging. In MRg-FUS, real-time MRI assists with trajectory planning of the ultrasound beam, safely directing the penetrating acoustic waves through near-field tissue unfocused, and then focusing on the targeted tissue without collateral damage.

Visualization of the anatomic structures, such as skin, surgical clips, bowel, bladder, fibroid, bone, and nerves, is essential to safe and effective treatment. Since sound waves penetrate and are absorbed differently by different tissue types, identification of tumor and surrounding anatomy is required before tissue can be treated. Potential damage to vital adjacent structures may require less than complete, but acceptable, tumor ablation.

MRI detects thermal changes best using the magnetic resonance shift of water, a sensitive and reliable process.⁹ Thermally sensitive MRI time sequences verify heating location, three-dimensional tissue effects, and the magnitude and time course of heating and cooling. This combination can be calculated and consolidated into a thermal dose map of tissue to achieve the predicted thermal dose necrosis, adding to the planning of the next or future foci.^{10,11} Image-based dosimetry assures efficient treatment by detecting non-thermally damaged foci. The surgeon then has an opportunity to increase energy parameters (watts, time) or frequency to achieve an adequate thermal dose.

Denatured tissue, which achieves a temperature of 54°C for >1 second, becomes avascular. Coagulative necrotic tissue no longer accepts contrast uptake. When compared to the preplanning MRI, the surgeon can see the total non-perfused volume achieved during surgery.

Thus, the non-invasive surgeon can control spot placement, size, and energy, insuring adequate energy deposition, prevent non-intended collateral damage, and confirm treatment in one sitting.

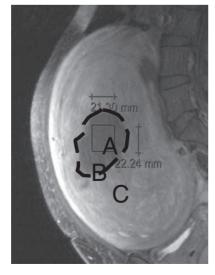
Stewart et al. demonstrated the safe treatment of leiomyoma in her feasibility study. ¹² Fifty-five women with clinically significant uterine leiomyomata, as determined by

their perceived symptoms and a gynecologic review board, were chosen for the study. All patients were treated as outpatients, and no patients required prolonged observation or readmission after discharge. Only five patients required postprocedure pain medication, one using non-steroidal anti-inflammatory drugs (NSAIDs). Twenty-five percent of patients complained of generalized discomfort, and 14% reported fibroid tenderness. Two subjects were found to have 1 cm first-degree burns that the subjects had not noticed prior to their 72-hour postoperative evaluation.

The average volume treated in this feasibility study was 12.1 ml, although post-treatment contrast studies noted a larger than expected non-perfused volume. Twenty-seven women underwent surgery under a hysterectomy protocol. An extension of the effective treatment volume was confirmed by gross and histiologic specimens in the women who underwent hysterectomy between 2 and 31 days post-FUS treatment (Figures 47.1 and 47.2). Confined to the margins of the treated myoma a three-fold increase in histologically documented necrosis volume was noted, as compared to the treatment volume. In only one instance was thermal damage noted in normal surrounding myometrium, and in this case bladder filling caused movement of the targeted tissue.

Of the patients that underwent hysterectomy, there was a significant incidence of postoperative adverse events. However, most of these patients received either no therapeutic sonications or minimally delivered energy. Febrile morbidity was the most often seen complication.

The outcome of this feasibility study proved the safety of the procedure and the effectiveness of MRgFUS in producing coagulative necrosis in the targeted tissue.



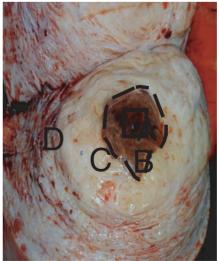


Figure 47.1 Treated region in MR image correlates with the 'coagulative necrosis' region. (A) Thermal dose volume; (B) Non-perfused volume; (C) Undamaged fibroid; (D) Normal uterine muscle.

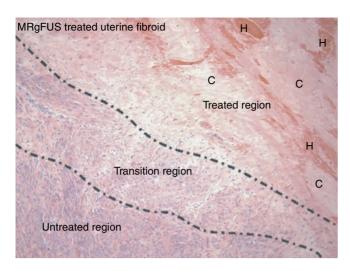


Figure 47.2 Histology analysis shows a sharp demarcation between treated and nontreated regions. H, hemorrhage; C, coagulative necrosis.

Stewart et al. followed up the feasibility study with a pivotal clinical trial assessing 6- and 12-month outcomes of MRgFUS treatment to uterine fibroids:¹³ 109 perimenopausal women with no plans for future fertility were treated with MRgFUS to determine efficacy and safety of MRgFUS.

The study used a symptom severity score (SSS) generated by the Uterine Fibroid Symptom and Quality of Life (UFS-QOL) instrument, originally developed by Spies, ¹⁴ to assess response to uterine artery embolization. This instrument asks eight questions related to fibroid-specific symptoms – pain, bleeding, and bulk – and 29 health-related quality of life questions with six subscales. It is the only validated tool for assessing quality of life related to leiomyomata, discriminating between women with and without fibroids. Assessing symptoms on a 100-point scale, higher scores represent worse symptoms. Whereas women without fibroids have an SSS around 21, and the average woman with fibroids has an SSS near 42, the average woman in this study had an SSS of 62.

Of these 109 patients, the mean decrease in SSS was almost 24 points, averaging 37. Seventy-seven (70%) patients had a decrease >10 points and 25 (23%) had a decrease of >40 points, mimicking those patients without fibroids, and essentially becoming asymptomatic. Ten patients were considered unchanged, but of these patients nine were considered unavailable to follow-up. Twelve patients noted worsening of symptoms. Thus, 89% of patients responded favorably to MRgFUS.

The pivotal study treatment was limited to 33% of prescribed myomas, 100 cm³ per myoma, and 150 cm³ per treatment for safety optimization. Treatment also lasted 120 minutes from first to last sonication, had to maintain

a minimum distance of 1.5 cm from the myometrium and serosa, was restricted to 0.5 cm on the side closest to the serosa, and patients could only have one treatment.

A later, FDA-approved, expanded guideline treated up to 50% of the prescribed volume, other than subserosal myomas (33%), maximized treatment to 150 cm³ regardless of the number of treatments, lengthened treatment to 180 minutes from first to last sonication, removed the restriction of endometrial and serosal side tumor, but kept the distance from the serosa to 1.5 cm. Two treatments could be performed if both treatments were within a 2-week period. By determining the percentage of patients with a >10 point improvement in SSS, an average of 92% of treated patients under the expanded protocols had symptom improvement at all time points, while over 84% of treated patients had symptom improvement in all groups/protocols at all time points. An overall larger percentage of patients had symptom improvement under expanded treatment guidelines.

Expanded treatment guidelines enabled larger treatable regions, thus larger non-perfused volumes. ¹⁵ Postprocedure non-perfuced volume (NPV) had a significant effect on the SSS at the 3-month point, and beyond. In patients with greater than 20% NPV, there was an average of 6 points greater decrease in the SSS than if the NPV was 20% or less NPV. Moreover, the group with greater than 20% NPV maintained and even slightly improved on their SSS, with significant improvement up to 24 months. The more fibroids treated, the greater chance of symptom improvement.

The second aspect of the pivotal study compared the safety of MRgFUS to prior documented hysterectomy cases as a definition of significant clinical complications. 13 No deaths, life-threatening events, unintended second procedures, separate interventional treatment, or patients discharged with urinary catheters were documented at the 6-month mark. Nor were any thrombotic events experienced by these patients. There was a low number of patients with antibiotic-requiring postprocedure febrile morbidity, mostly for urinary tract infections. Three percent of patients required postprocedure transfusions and 7% required hospitalization within 6 months of treatment; however, none of these were related to MRgFUS but rather their underlying disease. One patient was admitted for nausea and required intravenous (IV) fluids overnight. Skin burns were confined to the abdominal wall, secondary to inadequate hair removal.

The most serious complication occurred in a woman with a posterior myoma who refused to report substantial pain during treatment. The development of a sciatic nerve palsy by far field bone absorption resolved completely by her 12-month follow-up. An ultra-marathon runner, she competed in a 100-mile event within 6 months after her

treatment. While the nerve was not directly sonicated, heat transfer from the adjacent pelvic bones led to this indirect injury.

The expanded guideline studies also noted that patients had an improved safety profile (adverse event/patient), as compared to the pivotal study patients, owing to improved training, learning curve, and portability of knowledge from one site to another, such as removing all abdominal hair and lotions, and improved patient selection. Although there was one serious adverse event in the pivotal study, no serious adverse events were reported in the 160 patients participating in the expanded protocol group. The total number of adverse events (AE) dropped from 2.5 AE/patient in the pivotal group to 1.8 AE/patient in the expanded protocol group. Twenty-three percent of patients had no AE in the expanded group vs 19% in the pivotal group, had each group had approximately 81% of patients with only 1 AE.

Economically, the pivotal study noted a lower rate of medical resource use by MRgFUS patients vs TAH. Only 1% of MRgFUS patients had length of stay greater than 5 hours post treatment, and MRgFUS patients had 83% fewer provider encounters, 66% fewer additional procedures, and 66% fewer additional diagnostic tests in the first 30 days after treatment.

The later, expanded guideline studies corroborated the decreased need for additional treatments for leiomyomas in patients with >20% NPV after the first year of treatment. With minimal treatment, >50% of patients required additional treatment for their fibroids within 24 months, but this decreased significantly in patients who achieved >20% NPV. There is a direct correlation between the postprocedure NPV and the probability of intervention-free survival.¹⁵

Recent studies have clarified the relationship between fibroid image intensity on T2-weighted MRIS and the effectiveness of MRgFUS.¹⁶ Three types of fibroid were described:

- type 1 fibroids are very low intensity images comparable to skeletal muscle
- type 2 fibroids have an image intensity lower (darker) than that of myometrium but higher (brighter) than skeletal muscle
- type 3 fibroids are brighter, or have a higher image intensity than myometrium.

The studies showed that type 1 fibroids had the greatest shrinkage, and mean percentage of area covered by the target thermal dose, followed by type 2 fibroids. Type 3 fibroids had the least amount of shrinkage, treated area ratio, and required the most energy for thermal ablation. This increased energy demand may have also accounted for

the increased usage of the patient-controlled 'panic button' for external or internal pain during treatment sessions.

The 6-month follow-up noted a markedly significant decrease in the size of type 1 and type 2 fibroids, while some type 3 fibroids actually increased in size. Findings showed that the type 3 fibroids were the least responsive to MRgFUS, had the smallest treated volume, and shrunk less that the type 1 and type 2 fibroids. Nonetheless, the nonperfused volume stayed the same, regardless of the fibroid type.

Type 3, 'white' or 'bright' fibroids with higher signal intensity, suggests an increase in fluid-rich and vascular tissue, and a higher cell proliferative activity.¹⁷ Energy requirements for thermal ablation increase in these fibroids, as the blood flow acts as a heat sink, transporting the energy away from the intended target.

Gonadotropin-releasing hormone (GnRH) agonists reduce the diameter of intramyometrial arteries up to 24%¹⁸ and decrease blood flow by 21%,¹⁹ reducing this heat sink. Decreased cell proliferation and increased cell apoptosis have been demonstrated after a 3-month treatment with GnRH agonists.²⁰ Pretreatment with GnRH agonist has been shown to increase the thermal lesions in all fibroids. A documented volume of 44.5% of the uterus and 36% volume reduction of the targeted fibroid was noted after 3 months of GnRH agonist therapy.²¹ Based on this result, one might assume that type 3 fibroid signal intensity could decrease after treatment with a GnRH agonist, thus making fibroids more responsive to MRgFUS treatments. These studies have yet to be published.

Whereas MRgFUS is approved for treatment of leiomyomata, there is one case report of treatment for symptomatic adenomyosis. ²² This patient had symptoms of dysmenorrhea, menometrorrhagia, distended abdomen, dyspareunia, and fatigue. MRI noted an enlarged junctional zone and no discrete capsule. Using standard MRgFUS techniques, at post-treatment a 39% non-perfused volume was described. Within 6 weeks, the patient described a decrease in her dysfunctional bleeding and ultrasound noted a marked decrease in the adenomyoma's size. The woman's dyspareunia decreased and she was able to engage in normal sexual relations. Three cycles after treatment, she spontaneously conceived, eventually delivering a full-term infant vaginally.

MRgFUS is not currently approved by the FDA for patients desiring future fertility. As of this writing, there has been a total of 25 pregnancies in 23 patients.²³ The mean age was 36, ranging from 28–44 years old. The average time to conception was 10 months after treatment. Thirty percent of pregnancies went to the third trimester, with 64% of patients delivering vaginally and 36% delivering via cesarean section. Thirteen percent of patients had spontaneous abortions and 30% terminated

their pregnancies. Complications of delivery include excessive bleeding during a cesarean section when the surgeon performed a myomectomy.

In one case report of pregnancy after treatment, a patient underwent standard protocol MRgFUS for a $9 \times 10 \times 10$ cm solitary myoma. She had been fully counseled prior to the procedure regarding the lack of studies in patients who have conceived after MRgFUS. She spontaneously conceived 18 months after her treatment. While the myoma did enlarge significantly during her pregnancy, the fetal vertex was able to descend below the mass. She underwent induction of labor for maternal–fetal indications and delivered a full-term infant at 39 weeks via vacuum-assisted vaginal delivery. 24

Leiomyosarcoma is always a worry when performing minimally and non-invasive surgery. Leiomyosarcomas can be diagnosed on MRI based on T1 and T2 signal intensities. These tumors present on MRI as heterogeneous type 3 myomas; therefore, caution must be emphasized before attempting MRgFUS, or any other conservative treatment, on these tumors. In one case report, a patient underwent MRgFUS for a presumed myoma.25 Four months after the successful procedure, a high signal intensity mass was discovered within the myoma, and 2 months later decreased non-perfused volume was documented. This was accompanied by an atypical increase in the size of an intermediate signal intensity mass. A laparoscopic myomectomy was performed and an early leiomyosarcoma was detected within the leiomyoma. While rare, leiomyosarcomas can be detected on pre- and postoperative MRgFUS patients by MRI.

The MRgFUS procedure is as follows. The approved candidate is fully counseled regarding the risks and benefits of the procedure, including postprocedure pregnancy desires. Prior to treatment, the patient is asked to fast for at least 6–8 hours, similar to most preoperative protocols. Depending on the findings on her diagnostic studies, she may be asked to use a bowel prep. An IV line is placed and an IV solution is started. A Foley catheter is placed. During the procedure, the patient receives a light conscious sedation of fentanyl, midazolam, and ketorolac, as tolerated. She is monitored throughout the procedure with an electrocardiogram and pulse oximetry. A nurse or anesthesiologist trained for conscious sedation is usually in the room or by the control panel at all times.

The patient is place on a specially modified MRI table containing a concave, multi-element phased array transducer. She is prone, with the targeted area laying in a water bath over the transducer. She is then placed into the MRI magnet, with her head outside the coil. Either a 1.5 or 3 tesla magnet can be used. The patient has a self-controlled 'panic button' to stop treatments at any time, usually for external or internal pain. Constant two-way



Figure 47.3 Patient on ExAblate 2000 modified MRI table prior to placement into the magnet.

communication occurs between the patient and the gynecologist via microphones (Figure 47.3).

An MR technician performs T2 planning images in the coronal, axial, and sagittal planes and the operating surgeon determines if a clear acoustical pathway, devoid of scar, surgical clips, and bowel exists. If bowel is noted between the anterior abdominal wall and the uterus, a bladder fill may be required. If the area of sonication is out of range, a bowel fill may be required. A combination of the two may be needed in other unique circumstances. To prevent unintended injury to these tissues, the positions of peripheral bowel, bone, and nerves are marked. The targeted tissue is demarcated, followed by geometric and dose verification.

Once the pathway, focus, and energy dose are assured, sonications are placed by the gynecologist. The gynecologist can change the length, width, or energy of these sonications, depending on the absorptive qualities of the tumors. Each sonication is mapped that reaches the predicted thermal dose to denature structural and enzymatic proteins. Multiple, adjacent foci fill up the targeted tissue volume, often overlapping to increase efficacy of treatment.

An MRI image is taken every 3 seconds during each sonication. The first image taken before the ultrasound activation determines the baseline temperature of the target. Ultrasound activation is usually 20 seconds, but this can be modified by the surgeon or the computer program, depending on energy levels and spot size selected. Successive 3 second images are performed up to and right after ultrasound activation. This real-time continuous

monitoring with three-dimensional dose accumulation and thermometry determines whether treatment can proceed as planned or has to be changed. The interactive process continues until the entire region of treatment has been ablated.

Once the region of treatment is ablated, or the patient has reached 4 hours on the table, a contrast scan is performed. Three-dimensional images are taken and the total non-perfused volume is calculated. The patient is then removed from the table, taken to a recovery room, and observed for 45 minutes to 1 hour. Post-treatment discomfort usually requires only the use of over-the-counter NSAIDs. A follow-up 6-month contrast MRI scan can be performed at the discretion of the surgeon.

Future applications for MRgFUS seem endless. The treatment for metastatic bone cancer in non-weightbearing bone has been approved in Europe.²⁶ Studies show a rapid decrease in the need for chronic pain medication and in increase in activities of daily living after only a few treatments.²⁷ Since there is no residual radiation, treatments can

occur daily as needed, unlike traditional radiation therapy. Open-skull treatments for brain tumors have been performed successfully in Israel, and studies are currently underway for closed-skull treatment of tumors using a specially designed helmet. Sentinel lymph node negative breast cancer tumors have been treated with this excisionless surgery in Japan. Prostate cancer, liver cancer, and in fact almost every soft tissue tumor should be accessible to MRg-FUS in the future.

Gynecologists can easily be trained to read MRIs and perform focused ultrasound surgery on their patients, giving them a safe and effective non-invasive option for the treatment in symptomatic uterine fibroids. Approved in the USA since October 2004, MRgFUS is an available, safe, and effective option for treating the appropriate candidate for symptomatic uterine fibroids. Preoperative screening MRIs and 6-month postoperative MRIs should be evaluated by a radiologist trained in pelvic floor anatomy, to rule out pathology outside the uterus or to determine the likelihood of a leiomyosarcoma.

References

- Jolesz JA, Hynynen K. Magnetic resonance image-guided focused ultrasound surgery. Cancer J 2002; 8(Suppl 1): 100– 12
- 2. http://www.fda.gov/cdrh/annual/fy2005/ode/part1.html.
- Chan A. Image guided high intensity focused ultrasound treatment for uterine leiomyomata. PhD dissertation, University of Washington, Department of Bioengineering, 2003.
- Gruetzmacher J. Piezoelektrischer kristall mit ultraschallkonvergenz. Z Phys 1935; 96: 342–9.
- Meyers R, Fry W et al. Early experiences with ultrasonic irradiation of the pallidofugal and nigral complexes in hyperkinetic and hypertonic disorders. J Neurosurg 1959; 16: 32–54.
- Blana A, Walter B, Rogenhofer S, Wieland WF. High-intensity focused ultrasound for the treatment of localized prostate cancer: 5-year experience. Urology 2004; 63: 297–300.
- Jolesz FA, Jakab PD. Acoustic pressure wave generation within an MR imaging system: potential medical applications. J Magn Reson Imaging 1991; 1: 609–13.
- 8. Peters TM. Image-guidance for surgical procedures. Phys Med Biol 2006; 51: R505–40.
- Ishihara Y, Calderon A, Wantanabe H et al. A precise and fast temperature mapping using water proton chemical shift. Magn Reson Med 1995; 34: 814–23.
- Chung A, Jolesz FA, Hynynen K. Thermal dosimetry of a focused ultrasound beam in vivo by MRI. Med Phys 1999; 26: 2017–26.
- 11. Hynynen K, Freund W, Cline JE et al. A clinical noninvasive MRI monitored ultrasound surgery method. Med Phys 1999; 16: 185–95.
- 12. Stewart EA, Gedroyc WM, Tempany CM et al. Focused ultrasound treatment of uterine fibroid tumors: safety and feasibility

- of a noninvasive thermoablative technique. Am J Obstet Gynecol 2003; 189: 48–54.
- 13. Stewart EA, Rabinovici J, Tempany CM et al. Clinical outcomes of focused ultrasound surgery for the treatment of uterine fibroids. Fertil Steril 2006; 85: 22–9.
- Spies JB, Coyne K, Guaou N et al. The UFS-QOL, a new disease-specific and health-related quality of life questionnaire for leiomyomata. Obstet Gynecol 2002; 99: 290–300.
- Stewart EA, Gostout B, Rabinovici J et al. Sustained relief of leiomyoma symptoms by using focused ultrasound surgery. Obstet Gynecol 2007; 110: 279–87.
- Funaki K, Fukunishi H, Funaki T et al. Magnetic resonanceguided focused ultrasound surgery for uterine fibroids: relationship between the therapeutic effects and signal intensity of preexisting T2-weighted MR images. Am J Obstet Gynecol 2007; 196: 184.e1–6.
- 17. Oguchi O, Mori A, Kobayashi Y et al. Prediction of histopathologic features and proliferative activity of uterine leiomyoma by magnetic resonance imaging prior to GnRH analogue therapy: correlation between T2-weighted images and effect of GnRH analogue. J Obstet Gynaecol 1995; 21: 107–7.
- Rutgers JL, Spong CY, Sinow R, Heiner J. Leuprolide acetate treatment and myoma arterial size. Obstet Gynecol 1995; 86: 386–8.
- Reinsch RC, Murphy AA, Morales J, Yen SS. The effects of RU 486 and leuprolide acetate on uterine artery blood flow in the fibroid uterus: a prospective, randomized study. Am J Obstet Gynecol 1994; 170: 1623–8.
- Mizutani T, Sugihara A, Nakamuro K, Terada N. Suppression of cell proliferation and induction of apoptosis in uterine leiomyoma by gonadotropin-releasing hormone agonist (leuprolide acetate). J Clin Endocrinol Metab 1998; 83: 1253–5.

- Smart OC, Hindley JT, Regan L, Gedroyc WM. Magnetic resonance guided focused ultrasound surgery of uterine fibroids the tissue effects of GnRH agonist pre-treatment. Eur J Radiol 2006; 59: 163–7.
- 22. Rabinovici J, Inbar Y, Eylon SC et al. Pregnancy and live birth after focused ultrasound surgery for symptomatic focal adenomyosis: a case report. Hum Reprod 2006; 21: 1255–9.
- 23. Insightec correspondence.
- 24. Gavrilova-Jordan LP, Rose CH, Traynor KD et al. Successful term pregnancy following MR-guided focused ultrasound treatment of uterine leiomyoma. J Perinatol 2007; 27: 59–61.
- 25. Fukunishi H, Funaki K, Ikuma K et al. Unsuspected uterine leiomyosarcoma: magnetic resonance imaging findings before and after focused ultrasound surgery. Int J Gynecol Cancer 2007; 17: 724–8.
- InSightec receives european CE mark for ExAblate 2000 treatment of pain caused by bone metastases. http://www.insightec.com/490-2822-en-r10/CEMark-ExAblate.aspx.
- Catane R, Beck A, Inbar Y et al. MR-guided focused ultrasound surgery (MRgFUS) for the palliation of pain in patients with bone metastases – preliminary clinical experience. Ann Oncol 2007; 18: 163–7.

Future research in abnormal uterine bleeding

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INTRODUCTION

The term 'abnormal uterine bleeding' covers all vaginal bleeding other than regular menstrual bleeding <80 ml every 25–42 days. Premenopausal abnormal uterine bleeding can be divided into irregular bleeding (metrorrhagia) and abnormally heavy bleeding during regular menses (menorrhagia). In this chapter we discuss future research for women suffering from regular heavy menstrual bleeding.

A first important issue when discussing future research is the question who should determine the research agenda. In a postal questionnaire survey among members of the British Society of Gynaecological Endoscopy, 99% of respondents indicated that their society should play a proactive role in directing future research. There was substantial commitment to research, with 47% respondents actively involved in research projects at the time of the survey. However, there was no consensus about the agenda for research in menorrhagia, which will be explicated later.

In this chapter, we address future research topics by examining clinically relevant issues; basic research of the endocrine aspects of endometrial tissue will not be dealt with. We focus on studies of diagnostic strategies, quality of life assessment, and therapeutic effectiveness of existing and new treatment options. Finally, we discuss the role of studies on preference assessment.²

DIAGNOSTIC PROCESS

Establishing an accurate diagnosis is an important part of the clinical process. Incorrect diagnoses may put patients at unnecessary risks, as ineffective treatments will be started, patients will suffer longer from their complaints, and unnecessary costs will be generated. Available diagnostic methods for the evaluation of women with menorrhagia include endometrial biopsy, inpatient and outpatient hysteroscopy, transvaginal ultrasonography with or without color flow Doppler, three-dimensional ultrasonography, sonohysterography, computed tomography (CT),

and magnetic resonance imaging (MRI). These methods are used as individual strategies or in combination to assess the uterine cavity.

Many of the tests for endometrial assessment are yet to undergo rigorous clinical evaluation. Even tests that are routinely used, such as hysteroscopy and ultrasonography, have been poorly evaluated. In a survey of areas for the direction of future research in hysteroscopic diagnosis, 36% of the responders felt that research of diagnostic procedures was important. Although not all respondents specified particular research topics, those that did identified studies to determine the diagnostic accuracy of hysteroscopy in endometrial cancer and its diagnostic performance compared to ultrasonography (with or without saline contrast) to be of importance.1 However, when asked about their current research activity, relatively few respondents indicated that they were actually conducting diagnostic accuracy studies in gynecologic endoscopy. This may reflect a perceived lack of importance compared to developing new therapies or a lack of experience in designing diagnostic test studies.

Evaluation of test accuracy must start with the premise that diagnosis will be based on information acquired from a variety of sources: i.e. history, examination, and tests. The need to rigorously assess the accuracy of the clinical history and examination has been highlighted,³ but it has seldom been integrated in the evaluation of diagnostic tests.^{3,4} The whole clinical process should be borne in mind when conducting research to evaluate a diagnostic strategy, because test accuracy studies in isolation from the rest of the clinical context does not necessarily indicate how useful the test will be in practice. Estimates of diagnostic accuracy derived in this way can lead to erroneous inferences and may artificially inflate the value of diagnostic tests.⁵

To determine the real value of the tests listed above, evaluation within the context of contemporary clinical practice is essential. The clinical value of tests lies in the added information over and above what was already known from the history and examination. Recent evaluation of literature addressing the diagnostic accuracy of

ultrasound,^{6,7} hysteroscopy,⁸ and endometrial biopsy^{9,10} shows that only a limited number of existing studies consider the value of the test in the clinical context, whereas the majority of the studies evaluate the accuracy of the test in isolation. Multivariable analysis should be used to delineate the significance of diagnostic variables. Future diagnostic research should determine how the test adds value to the overall diagnostic process. When systematic reviews are used, this approach would require use of individual patient data.¹¹

QUALITY OF LIFE ASSESSMENT

One of the most important challenges in menorrhagia research in the near future is the development of disease-specific 'quality of life' instruments. 12,13 The overall aim of management of chronic benign conditions such as menorrhagia is to reduce the adverse health impact of the condition, thus improving the patient's quality of life. It is therefore apparent that the use of instruments to measure disease-specific life quality will be essential for the evaluation of the effectiveness of treatment, thus allowing a more objective assessment of the clinical condition. Although generic instruments have been available for many years, these instruments ignore aspects that are unique to menorrhagia. Thus, disease-specific instruments are required to obtain patient-focused measurements.

Numerous definitions of quality of life exist, each with a slightly different underlying theoretical emphasis. Generic quality of life instruments attempt to capture a broad range of aspects of life quality that are important to all patients. They allow comparison across different diseases. Disease-specific quality of life instruments, on the other hand, are expected to capture how specific aspects of the disorder interfere with quality of life. The two most important aspects of any type of quality of life instrument are clinical appropriateness (or face validity) and measurement properties. In order for an instrument to have clinical face validity it must include items that are of importance to patients and adequately reflect their experiences and concerns. Instruments with sound measurement properties are those instruments that have demonstrated reliability, validity, responsiveness, etc.

Evaluation of recent research on menorrhagia shows that in studies where quality of life instruments are employed, there is good compliance with the criteria for measurement properties but not with those for clinical face validity. ¹⁴ Therefore, the appropriateness of the quality of life measures used in menorrhagia research is questionable. The Short Form (SF-36) health survey questionnaire, the most commonly used instrument in menorrhagia, is seemingly reliable, valid, and responsive.

However, several of its questions are inappropriate or difficult to answer for women with menorrhagia, which is understandable as menstrual complaints have a cyclical character, and they are distressing but non-life threatening.15 Consequently, the SF-36 is inappropriate as a patient-based outcome measure in menorrhagia. The available disease-specific instruments^{16–19} have poor face validity because they do not use a more flexible questionnaire format incorporating global patient ratings, ratings of importance of constituents of quality of life and allowing supplemental patient comments. 16 It is disappointing that even recently developed disease-specific instruments do not show compliance with criteria for face validity.^{17–19} Thus, there is a need to develop methodologically sound diseasespecific quality of life instruments in menorrhagia focusing both on face validity and measurement properties.

THERAPEUTIC EFFECTIVENESS

Traditionally, medical treatment is the first-line intervention for women suffering from menorrhagia. Hysteroscopic treatment includes resection of polyps²⁰ and submucous myoma²¹ to resection or ablative procedures of the endometrium.^{22,23} These procedures may be carried out in the outpatient setting.²⁰ More recently, the levonorgestrel-releasing intrauterine system (LNG-IUS) has been used as an alternative to surgery.²⁴ Second-generation endometrial ablation also has a place in the treatment of menorrhagia.²⁵

Not only have systematic reviews of randomized controlled trials (RCTs) been able to plug gaps in available evidence of therapeutic effectiveness²⁶ but also, equally importantly, they have been able to identify gaps, where insufficient RCT evidence is available, even after systematic review and meta-analysis where appropriate, thus defining the research agenda for therapeutic interventions. Although three systematic reviews assessing interventions for abnormal uterine bleeding had clear-cut evidence of effectiveness,^{27–29} there were nine reviews where insufficient or conflicting evidence was found,^{30–38} including:

- (1) Oral contraceptive pills for heavy menstrual bleeding.³⁰
- (2) Antifibrinolytics for heavy menstrual bleeding.³¹
- (3) Danazol for heavy menstrual bleeding.³²
- (4) Preoperative endometrial thinning agents before endometrial destruction for heavy menstrual bleeding.³³
- (5) Endometrial destruction techniques for heavy menstrual bleeding.³⁴
- (6) Surgery vs medical therapy for heavy menstrual bleeding.³⁵

- (7) Uterine artery embolization (UAE) for symptomatic uterine fibroids.³⁶
- (8) Total vs subtotal hysterectomy for benign gynecologic conditions.³⁷
- (9) Uterine polypectomy for abnormal uterine bleeding.³⁸

A similar collation of information to that of Johnson et al;²⁶ 'Gaps in the evidence for fertility treatment' was undertaken for the reviews assessing interventions for abnormal uterine bleeding (Table 48.1) the number of trials available for meta-analysis, the total number of trial participants, and whether there was an answer to the primary clinical question – into which category from (A) to (C), below, the review fell:

- (A) Where there is evidence of effectiveness or harm from a meta-analysis of trial data.
- (B) Where there is insufficient evidence of effectiveness and the review authors have called for further research.
- (C) Where there is insufficient evidence for effectiveness and the review authors have not called for further research.
- (1)³⁰ Although the oral contraceptive pill is used widespread to regulate abnormal uterine bleeding, there is only one very small RCT. Placebo-controlled RCTs with adequate patient numbers, duration of at least three to six cycles, and adequate follow-up are required to establish whether or not the oral contraceptive pill is an effective treatment for menorrhagia.
- (2)³¹ Antifibrinolytic agents give a significant reduction in regular heavy menstrual bleeding, although it is uncertain if this objective reduction in blood loss is reflected in any significant improvement in subjective symptoms of heavy menstrual bleeding. Further research for the practical implications is necessary.
- (3)³² Danazol appears to be an effective treatment for heavy menstrual bleeding when compared to other medical treatments, although it is uncertain whether it is acceptable to women. Future trial design needs to include outcomes such as quality of life measures and a longer period of treatment (at least 6 months) to adequately evaluate adverse events and participant satisfaction.
- (4)³³ The use of gonadotropin-releasing hormone (GnRH) analogues or danazol prior to endometrial resection and ablation is effective in preparing the intrauterine operating environment and for improving short-term postoperative outcomes. Future trials should evaluate the benefits of these agents on treatment outcomes in the longer term. The results obtained with newer techniques

- could be influenced by the use of preoperative endometrial thinning and this should be evaluated in future trials as well.
- (5)³⁴ The existing evidence suggests that success rates and complication profiles of newer techniques of ablation compare favorably with transcervical resection of the endometrium (TCRE). Technical difficulties with new equipment need to be ironed out. The rapid development of a number of new methods of endometrial destruction has made systematic comparisons between methods and with the gold standard of TCRE difficult.
- Surgery, especially hysterectomy, reduces menstrual bleeding at 1 year more than medical treatments, but LNG-IUS appears equally effective in improving quality of life. Future research needs long-term follow-up. Three RCTs compared the levonorgestrel-releasing IUD with endometrial destruction techniques, but were underpowered.³⁹⁻⁴¹ New and larger RCTs are needed to compare second-generation techniques and LNG-IUS. Often, studies in this field present adverse events of a different nature as a composite outcome. 42,43 Such measures are usually seen with scepticism in clinical trials, as they invalidate inferences about effectiveness, particularly when there is insufficient power to discern an effect separately for any one of the individual events. Moreover, for a meaningful comparison, outcome measures have to be symmetrically applicable to all trial arms, e.g. when abdominal hysterectomy is compared with the LNG-IUS, it cannot have an unintended laparotomy as a complication.44
- (7)³⁶ UAE offers an advantage over hysterectomy with regards to a shorter hospital stay and a quicker return to routine activities. There is no evidence of benefit of UAE compared to surgery (hysterectomy/myomectomy) for satisfaction. Future research requires longer-term follow-up trials to comment on its effectiveness and safety profile.
- (8)³⁷ Subtotal hysterectomy offers no improved outcomes for sexual, urinary, or bowel function when compared with total abdominal hysterectomy. Larger randomized trials are needed with very long follow-up to get an idea about future chance of prolapse.
- (9)³⁸ There is a lack of evidence to inform clinical practice regarding the efficacy of intrauterine polypectomy in women with AUB. A large multicenter RCT, stratified by technique, setting, and pattern of AUB is necessary to resolve this.

It is not always easy to start an RCT. In the UK, the SMART study (Satisfaction with Mirena and Ablation: a Randomized Trial) was initiated as a randomized multicenter controlled trial. The aim of the study was to recruit 300 patients in 18 months. After 9 months, only 16 patients had been randomized, after which the study was

Table 48.1 Reviews of premenopausal abnormal uterine bleeding

Review title	No. of includea RCTs	No. of participants	Conclusion	Category	Gaps
Oral contraceptive pills (OCPs) for heavy menstrual bleeding ³⁰	1	45	One small study found no significant difference between groups treated with OCP, mefenamic acid, low-dose danazol, or naproxen.	В	Placebo-controlled RCTs with adequate patient numbers, duration of at least three to six cycles and adequate follow-up are required to establish whether or not the OCP is an effective treatment for menorrhagia
Non-steroidal anti- inflammatory drugs (NSAIDs) for heavy menstrual bleeding ²⁸	9	377	NSAIDs help reduce heavy menstrual bleeding but tranexamic acid or danazol work better	A	
Cyclical progestogens for heavy menstrual bleeding ²⁷	6	252	Progestogens administered from day 15 or 19 to day 26 of the cycle offer no advantage over other medical therapies such as danazol, tranexamic acid, NSAIDs, and the intrauterine system (IUS) in the treatment of menorrhagia in women with ovulatory cycles	A	
Endometrial resection and ablation vs hysterectomy for heavy menstrual bleeding ²⁹	n 5		Both procedures are effective and satisfaction rates are high. Although hysterectomy is associated with a longer operating time, a longer recovery period, and higher rates of postoperative complications, it offers permanent relief from heavy menstrual bleeding. The cost of endometrial destruction is significantly lower than hysterectomy but since retreatment is often necessary the cost difference narrows over time	A	
Antifibrinolytics for heavy menstrual bleeding (HMB) ³¹	7	273	Antifibrinolytic agents give a significant reduction in regular HMB, although it is uncertain if this objective reduction in blood loss is reflected in any significant improvement in subjective symptoms of HMB		Additional randomised controlled trials (RCTs) are needed to test the efficacy of antifibrinolytic agents compared to other medical therapies. Future trial design needs to include participant satisfaction, cost-effectiveness data and quality of life measures and a longer period of treatment to adequately assess adverse events

(Continued)

Table 48.1 (Continued)

Review title	No. of included RCTs	No. of participants	Conclusion	Category	Gaps
Danazol for heavy menstrual bleeding ³²	9	353	Danazol appears to be an effective treatment for HMB when compared to other medical treatments, although it is uncertain whether it is acceptable to women	В	Future trial design needs to include outcomes such as quality of life measures and a longer period of treatment (at least 6 months) to adequately evaluate adverse events and participant satisfaction
Preoperative endometrial thinning agents before endometrial destruction for heavy menstrual bleeding ³³	12	1139	Evidence from RCTs, supports the use of gonadotropin-releasing hormone (GnRH) analogues or danazol prior to endometrial resection and ablation in terms of their effect on the intrauterine operating environment and short-term postoperative outcomes	В	The benefits of these agents on treatment outcomes in the longer term is uncertain. The results obtained with newer techniques could be influenced by the use of preoperative endometrial thinning, and this should be evaluated in, future trials
Endometrial destruction techniques for heavy menstrual bleeding ³⁴	19	3285	The existing evidence suggests that success rates and complication profiles of newer techniques of ablation compare favourably with transcervical resection of the endometrium (TCRE)	В	Technical difficulties with new equipment need to be ironed out. The rapid development of a number of new methods of endometrial destruction has made systematic comparisons between methods and with the gold standard of TCRE difficult
Surgery vs medical therapy for heavy menstrual bleeding ³⁵	8	821	Surgery, especially hysterectomy, reduces menstrual bleeding at 1 year more than medical treatments but the levonorgestrel intrauterine system (LNG- IUS) appears equally effective in improving quality of life	В	Long-term follow-up. Comparison of second-generation techniques and LNG device.
Uterine artery embolization (UAE) for symptomatic uterine fibroids ³⁶	3	297	UAE offers an advantage over hysterectomy with regards to a shorter hospital stay and a quicker return to routine activities. There is no evidence of benefit of UAE compared to surgery (hysterectomy/ myomectomy) for satisfaction	В	The higher minor complications rate after discharge in the UAE group as well as the unscheduled visits and readmission rates require more longer-term follow-up trials to comment on its effectiveness and safety profile. There is currently an ongoing tria (REST, UK) and EMMY trial yet to report on the long-term follow-up, the results of which are awaited with interest
Total vs subtotal hysterectomy for benign gynecologic conditions ³⁷	3	733	Subtotal hysterectomy offers no improved outcomes for sexual, urinary, or bowel function when compared with total abdominal hysterectomy	В	Larger double-blind RCTs

stopped (2000). Clinicians from all centers involved reported a strong patient preference for treatment (usually endometrial ablation) and an almost universal refusal to accept a levonorgestrel-releasing IUD as the most common barrier for recruitment. The reason for this reluctance to be treated with a levonorgestrel-releasing IUD is unclear, and is contrary to a similar study in New Zealand⁴² and to the RCT comparing levonorgestrel-releasing IUD to hysterectomy. ^{42,43} Despite the failure of the SMART study, there is still a need for a large RCT. Today, there is the conviction that such a trial can successfully be carried out in order to assess the effectiveness of the levonorgestrel-releasing IUD compared to endometrial ablation (first or second generation).

There is sufficient evidence to suggest that endometrial surgery is efficacious but there is still uncertainty about its role in clinical practice. 35,45 At present, it is unknown whether endometrial ablation should be used as an intermediate procedure after failed medical treatment and prior to hysterectomy, or that it should be used as a first-line treatment instead of medical treatment? The promising results of endometrial ablation techniques made proponents predict that techniques aimed at ablating the endometrial tissue would probably replace hysterectomy, or would at least significantly reduce the number of hysterectomies. The clinical practice shows a decline in hysterectomy. In the Netherlands, there has been a decline in the number of hysterectomies for an increase in the number of ablations, thus providing an opportunity for the use of more ablative techniques. 46 In the USA 47 the ratio of hysterectomies to endometrial ablations decreased in each state. However, the total number of hysterectomies and endometrial ablations for women with benign uterine conditions increased by more than 10%. Endometrial ablation in the USA seems to be used as an additive medical technology, increasing the range of less-invasive treatment options available, rather than simply as a substitute for hysterectomy. In the UK, on the other hand, we notice an important reduction of the hysterectomies, probably due to both the introduction of second-generation ablations and the levonorgestrel-releasing IUD. 48,49

The majority of existing randomized trials in the treatment of menorrhagia used reduction in measured menstrual blood after treatment as the primary outcome measure. While such an outcome measure has the advantage of the need for a relatively small sample size to conduct the trial, its clinical relevance is limited.² It has been previously indicated that there is a need to develop and use quality of life instruments for assessing effectiveness of menorrhagia treatments.^{12,13}

The value of endometrial surgery has mainly been assessed in observational studies with a moderate follow-up period. Almost all of these studies have enrolled women from the gynecologic outpatient clinic after failure with some form of medical intervention administered prior to surgery. Such studies may be biased, as the study population is recruited exclusively from a hospital setting. Future studies may be targeted on a mix of women recruited from the general practitioners as well as from hospital outpatient clinics. Another problem with observational cohort studies that report on endometrial surgery is the fact that time to result is not taken into account. To control for differences in follow-up, statistical analyses should take into account time to event, e.g. by the use of Kaplan–Meier survival curves or Cox proportional hazard analysis. ^{50,51}

There is obviously a need to generate experimental (i.e. randomized) evidence to compare the effectiveness of the various treatment modalities for menorrhagia (see Table 49.1). The study populations should be followed for a long period of time in order to recognize complications and hysterectomy rates in the various groups. Preference assessment needs to be included in these trials. These trials should be robust and their design may take account of variation in current practice, and views of practitioners and consumers. Without them, the effectiveness and the place of endometrial surgical and therapeutical modalities will remain uncertain. Where systematic reviews of effectiveness are needed, decisionmaking would benefit from individual patient data metaanalyses, indirect comparisons, and use of their output in decision-analytic modeling.

NEW TREATMENT OPTIONS

The ideal ablation technique will be a safe and completely effective technique, without the need for premedication or timing of the treatment. The procedure should be fast, easy to perform, and require only local anesthesia. Although there are a number of second-generation ablation techniques claiming high success rates, none of these techniques has all of these features. Thus, there is still the need for improvement.

Several studies report on the acceptability of the office ablation procedure. 52-54 Unfortunately, not all women can be treated under these circumstances. 55 The fundal nerve in the uterus, coming from thoracal 12 cannot be blocked by paracervical analgesia; as a consequence, some women still experience pain during ablation. Intravenous sedation helps with this problem. Local infiltration in the fundal area with a needle passed through the working channel of the hysteroscope can potentially solve these problems, and would therefore be an issue for future research. Endometrial ablation performed as an office procedure will only be universally acceptable if clinicians can predict a painless procedure for all women.

Selective treatment of fibroids is a new field of research in women suffering from abnormal uterine bleeding. 56-59 One-third of all women will have fibroids. Investigation of women suffering from abnormal uterine bleeding will often show a uterus containing several fibroids. It is not always clear if these fibroids will be the underlying cause of the heavy menstrual bleeding. The reason why a uterus myomatosus will give abnormal uterine bleeding is still a matter of uncertainty and debate. An epidemiology study to evaluate the influence of fibroids on women's health is necessary to predict the effect of treatment of fibroids. It seems reasonable to stratify for women with type 0 and type I fibroids, women with type II fibroids, women with intramural fibroids, and subserosal fibroids. This trial should form a basis for all new treatment options that will be developed for the treatment of fibroids.

PREFERENCE ASSESSMENT

For the agenda of future research, it is of imminent importance to know what women suffering from menor-rhagia value as important. Preference assessment can demonstrate what is really important for women suffering from menorrhagia. A recent preference assessment study showed that women undergoing endometrial ablation accepted a 50% failure rate.² In the same study, women scheduled for hysterectomy answered that if they would undergo endometrial ablation they would accept a failure rate of 20%. A limitation of this study was that the choice of treatment had already been made before the woman was interviewed.² Of importance, however, is that a fail-

ure rate of 50% should be the minimum target for ablative techniques.

Traditional studies comparing two treatments are powered to detect a difference between the two treatments in any direction. A disadvantage of such an approach is that the comparison is made in only one direction, whereas other issues such as complications of the treatment and costs are not taken into account. If a treatment is inexpensive and has no side effects, the patient is likely to accept the treatment at a lower success rate as compared to more expensive treatments with more side effects. In our opinion, a preference assessment study should precede a power calculation. Preference assessment will be important for the design of studies in the treatment of menorrhagia. Examples of preference assessment studies are the preference for treatment in an office setting or in the operation room, the choice between laparoscopic hysterectomy and hysterectomy by laparotomy.

CONCLUSION

Rigorous, relevant, and timely research is essential for improvement in the quality of care we provide to our patients with menorrhagia. The conduct of such research requires a systematic appraisal of the existing evidence, an examination of current medical practice, and an appreciation of the whole clinical process. In addition, a multidisciplinary collaborative approach should be encouraged, incorporating the views of all stakeholders. In this way, increasingly effective diagnostic and therapeutic strategies for such a common condition as menorrhagia can be implemented in future clinical practice.

References

- Clark TJ, Khan KS, Gupta JK et al. Effect of paper quality on the response rate to a postal survey: a randomized controlled trial. ISRCTN 32032031. BMC Med Res Methodol 2001; 1:
- Bourdrez P, Bongers MY, Mol BW. Treatment of dysfunctional uterine bleeding: patient preferences for endometrial ablation, a levonorgestrel-releasing intrauterine device, or hysterectomy. Fertil Steril 2004; 82: 160–6.
- McAlister F, Straus S, Sackett D. Why we need large, simple studies of the clinical examination: the problem and a proposed solution. Lancet 1999; 354: 1721–4.
- Clark TJ, Bakour S, Gupta JK, Khan KS. Evaluation of outpatient hysteroscopy and ultrasonography in the diagnosis of endometrial disease. Obstet Gynecol 2002; 99: 1001–7.
- Bachmann LM, ter Riet G, Clark TJ et al. Probability analysis for diagnosis of endometrial disease in postmenopausal bleed-

- ing: an approach for a rational diagnostic workup. Acta Obstet Gynecol Scand 2003; 82: 564–9.
- Smith-Bindman R, Kerlikowske K, Feldstein VA et al. Endovaginal ultrasound to exclude endometrial cancer and other endometrial abnormalities. JAMA 1998; 280: 1510–17.
- 7. Dijkhuizen FP, De Vries LD, Mol BW et al. Comparison of transvaginal ultrasonography and saline infusion sonography for the detection of intracavitary abnormalities in premenopausal women. Ultrasound Obstet Gynecol 2000; 15: 372–6.
- Clark TJ, Voit D, Gupta JK et al. Accuracy of hysteroscopy in the diagnosis of endometrial cancer and hyperplasia: a systematic quantitative review. JAMA 2002; 288: 1610–21.
- Clark TJ, Mann CH, Shah N et al. Accuracy of outpatient endometrial biopsy in the diagnosis of endometrial cancer: a systematic quantitative review. Br J Obstet Gynecol 2002; 109: 313–21.

- Clark TJ, Mann CH, Shah N et al. Accuracy of outpatient endometrial biopsy in the diagnosis of endometrial hyperplasia: a systematic quantitative review. Acta Obstet Gynecol Scand 2001; 80: 784–93.
- 11. Khan KS, Bachmann LM, ter Riet G. Systematic reviews with individual patient data meta-analysis to evaluate diagnostic tests. Eur J Obstet Gynecol Reprod Biol 2003; 108: 121–5.
- Abbott JA, Hawe J, Garry R. Quality of life should be considered the primary outcome for measuring success of endometrial ablation. J Am Assoc Gynecol Laparosc 2003; 10: 491–5; discussion 495.
- Bongers MY, Bourdrez P, Heintz AP et al. Bipolar radio frequency endometrial ablation compared with balloon endometrial ablation in dysfunctional uterine bleeding: impact on patients' health-related quality of life. Fertil Steril 2005; 83: 724–34.
- Clark TJ, Khan KS, Foon R et al. Quality of life instruments in studies of menorrhagia: a systematic review. Eur J Obstet Gynecol Reprod 2002; 104: 96–104.
- 15. Jenkinson C, Peto V, Coulter A. Making sense of ambiguity: evaluation of internal reliability and face validity of the SF 36 questionnaire in women presenting with menorrhagia. Qual Health Care 1996; 5: 9–12.
- Guyatt GH, Cook DJ. Health status, quality of life, and the individual. JAMA 1994; 272: 630–1.
- 17. Lamping DL, Rowe P, Clarke A et al. Development and validation of the menorrhagia outcomes questionnaire. Br J Obstet Gynecol 1998; 105: 766–79.
- Shaw RW, Brickley MR, Evans L, Edwards MJ. Perceptions of women on the impact of menorrhagia on their health using multi-attribute utility assessment. Br J Obstet Gynecol 1998; 105: 1155-9
- Ruta DA, Garratt AM, Russell IT. Patient centred assessment of quality of life for patients with four common conditions. Qual Health Care 1999; 8: 22–9
- Clark TJ, Khan KS, Gupta JK. Current practice for the treatment of benign intrauterine polyps: a national questionnaire survery of consultant gynecologists in UK. Eur J Obstet Gynecol Reprod Biol 2002; 103: 65–7.
- Clark TJ, Mahajan D, Sunder P, Gupta JK. Hysteroscopic treatment of symptomatic submucous fibroids using a bipolar intrauterine system: a feasibility study. Eur J Obstet Gynecol Reprod Biol 2002; 100: 237–42.
- Kremer C, Duffy S. Endometrial ablation: the next generation. Br J Obstet Gynecol 2000; 107: 1443–52.
- 23. O'Connor H, Magos A. Endometrial resection for the treatment of menorrhagia. N Engl J Med 1996; 335: 151–6.
- Barrington JW, Bowen-Simpkins P. The levenorgestrel intrauterine system in the management of menorrhagia. Br J Obstet Gynecol 1997; 104: 614–16.
- Bongers MY, Bourdrez P, Mol BW et al. Randomised controlled trial of bipolar radio-frequency endometrial ablation and balloon endometrial ablation. Br J Obstet Gynecol 2004; 111: 1095–102.
- Johnson NP, Proctor M, Farquhar CM. Gaps in the evidence for fertility treatment – an analysis of the Cochrane Menstrual Disorders and Subfertility Group database. Hum Reprod 2003; 18: 947–54.
- Lethaby A, Irvine G, Cameron I. Cyclical progestogens for heavy menstrual bleeding. Cochrane Database Syst Rev 1998; (4): CD001016.
- 28. Lethaby A, Augood C, Duckitt K. Nonsteroidal anti-inflammatory drugs for heavy menstrual bleeding. Cochrane Database Syst Rev 1998; (3): CD000400.

- Lethaby A, Shepperd S, Cooke I, Farquhar C. Endometrial resection and ablation versus hysterectomy for heavy menstrual bleeding. Cochrane Database Syst Rev 1999; (2): CD000329
- Iyer V, Farquhar C, Jepson R. Oral contraceptive pills for heavy menstrual bleeding. Cochrane Database Syst Rev 1997; (2): CD000154.
- Lethaby A, Farquhar C, Cooke I. Antifibrinolytics for heavy menstrual bleeding. Cochrane Database Syst Rev 2000; (4): CD000249.
- 32. Beaumont H, Augood C, Duckitt K, Lethaby A. Danazol for heavy menstrual bleeding. Cochrane Database Syst Rev 2002; (2): CD001017.
- Sowter MC, Lethaby A, Singla AA. Pre-operative endometrial thinning agents before endometrial destruction for heavy menstrual bleeding. Cochrane Database Syst Rev 2002; (3): CD001124.
- Lethaby A, Hickey M, Garry R. Endometrial destruction techniques for heavy menstrual bleeding. Cochrane Database Syst Rev 2005; (4): CD001501.
- Marjoribanks J, Lethaby A, Farquhar C. Surgery versus medical therapy for heavy menstrual bleeding. Cochrane Database Syst Rev 2006; (2): CD003855.
- Gupta JK, Sinha AS, Lumsden MA, Hickey M. Uterine artery embolization for symptomatic uterine fibroids. Cochrane Database Syst Rev 2006; (1): CD005073.
- Lethaby A, Ivanova V, Johnson NP. Total versus subtotal hysterectomy for benign gynecological conditions. Cochrane Database Syst Rev 2006; (2): CD004993.
- Nathani F, Clark TJ. Uterine polypectomy in the management of abnormal uterine bleeding: a systematic review. J Minim Invasive Gynecol 2006; 13: 260–8.
- Crosignani PG, Vercellini P, Mosconi P et al. Levonorgestrelreleasing intrauterine device versus hysteroscopic endometrial resection in treatment of dysfunctional uterine bleeding. Obstet Gynecol 1997; 90: 257–63.
- Istre O, Trolle B. Treatment of menorrhagia with the levonorgestrel intrauterine system versus endometrial resection. Fertil Steril 2001; 76: 304–9.
- Busfield RA, Farquhar CM, Sowter MC et al. A randomised trial comparing the levonorgestrel intrauterine system and thermal balloon ablation for heavy menstrual bleeding. BJOG 2006; 113: 257–63
- 42. Hurskainen R, Teperi J, Rissanen P et al. Quality of life and cost-effectiveness of levonorgestrel-releasing intrauterine system versus hysterectomy for treatment of menorrhagia: a randomised trial. Lancet 2001; 357: 273–7.
- 43. Hurskainen R, Teperi J, Rissanen P et al. Clinical outcomes and costs with the levonorgestrel-releasing intrauterine system or hysterectomy for treatment of menorrhagia: randomized trial 5-year follow-up. JAMA 2004; 291: 1456–63.
- 44. Khan KS, Daniels J. Review: surgery is more effective than medical treatment for heavy menstrual bleeding but quality of life results are similar [Commentary on: Marjoribanks J et al. Cochrane Database Syst Rev 2006; 2: CD003855]. Evid Based Med 2006; 11: 182.
- 45. Chien PF, Khan KS, Garry R. Medical treatment or endometrial surgery for dysfunctional uterine bleeding? Acta Obstet Gynecol Scand 1998; 77: 587–90.
- Brolmann HA, Vervest HA, Heineman MJ. Declining trend in major gynecological surgery in The Netherlands during 1991– 1998. Is there an impact on surgical skills and innovative ability? BJOG 2001; 108: 743–8.

- 47. Farquhar CM, Naoom S, Steiner CA. The impact of endometrial ablation on hysterectomy rates in women with benign uterine conditions in the United States. Int J Technol Assess Health Care 2002; 18: 625–34.
- Bridgman SA, Dunn KM. Has endometrial ablation replaced hysterectomy for the treatment of dysfunctional uterine bleeding? National figures. Br J Obstet Gynecol 2000; 107: 531–4.
- Reid PC. Endometrial ablation in England coming of age? An examination of hospital episode statistics 1989/1990 to 2004/2005. Eur J Obstet Gynecol Reprod Biol 2006 Oct 11 [Epub ahead of print]
- Bongers MY, Mol BW, Dijkhuizen FP, Brolmann HA. Is balloon ablation as effective as endometrial electroresection in the treatment of menorrhagia? J Laparoendosc Adv Surg Tech A 2000; 10: 85–92.
- 51. Kleijn J, Bourdrez P, Mol BW, Bongers MY. Five-year follow up of a randomised controlled trial comparing NovaSure and ThermaChoice endometrial ablation. BJOG 2007 Jul 6 [Epub ahead of print]
- 52. Jack SA, Cooper KG, Seymour J et al. A randomised controlled trial of microwave endometrial ablation without endometrial

- preparation in the outpatient setting: patient acceptability, treatment outcome and costs. BJOG 2005; 112: 1109–16.
- Wallage S, Cooper KG, Graham WJ, Parkin DE. A randomised trial comparing local versus general anaesthesia for microwave endometrial ablation. BJOG 2003; 110: 799–807.
- Marsh F, Thewlis J, Duffy S. Randomized controlled trial comparing Thermachoice III in the outpatient versus daycase setting. Fertil Steril 2006 Nov 14.
- 55. Cooper KG. Outpatient endometrial ablation. Best Pract Res Clin Obstet Gynecol 2005; 19: 713–26.
- Vilos GA, Vilos EC, Hollett J, Abu B. Transvaginal Dopplerguided temporary uterine artery occlusion for the treatment of symptomatic fibroids. J Minim Invasive Gynecol 2006; S16.
- Bruno R, Dick AB, Briggs MH et al. Initial experience utilizing magnetic resonance guided focused ultrasound to treat fibroids. J Minim Invasive Gynecol 2006; S17.
- 58. Cowan BD, Sewell PE, Pansky M, Zimberg S. The evolution of fibroid cryotherapy. J Minim Invasive Gynecol 2006; S17.
- Jacoby AF, Grossman J. Development of an endoscopic radiofrequency ablation device for myomas. J Minim Invasive Gynecol 2006; S132.

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