Problem Solving in Women's Health

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Contents

Abbreviations

Abbreviation:	Chapter(s):	Definition:
ACOG	9,46	American College of Obstetricians and Gynecologists
ACS	41	American Cancer Society
ACTs	10	alternative and complementary therapies
AFC	18	antral follicle count
AIS	7	androgen insensitivity syndrome
AMH	18	anti-Müllerian hormone
ART	19	assisted reproduction treatment
BMD	5,13,24,25,44	bone mineral density
BMI	8,20	body mass index
BTX	37,39	botulinum toxin
BV	32	bacterial vaginosis
CAI	38	community acquired infection
CBT	33	cognitive behavioural therapy
CCCT	18	Clomiphene Citrate Challenge Test
CFU	38	colony-forming units
CI	5,16,21,23	confidence interval
CIN	41,48	cervical intraepithelial neoplasia
COC	1,5,11,16,23,25,29, 32,43	combined oral contraceptive
COX	1	cyclooxygenase
COX-1	1	cyclooxygenase-1
COX-2	1,3	cyclooxygenase-2
CPP	4	Chronic pelvic pain
CT	45,47,48,49	computed tomography
D&C	14,46	dilatation and curettage
DES	14	diethylstilbestrol
DEXA	13,44	dual-energy X-ray absorptiometry
DHEA	17,30	dehydroepiandrosterone
DMPA	24,25	depot medroxyprogesterone acetate
DSM-IV	31	Diagnostic and Statistical Manual of Mental Disorders–Fourth Edition
DVS	15	desvenlafaxine succinate
EA	2	endometrial ablation
EFORT	18	exogenous FSH ovarian reserve test
ERMD	7	exercise related menstrual dysfunction
ERPC	26	evacuation of retained products of conception
EUA	45	examination under anaesthesia
FDA	1,14,43,46	Food and Drug Administration
FIGO	45,46,48,49	International Federation of Gynaecology and Obstetrics
FSH	7,11,12,18,19,22,25	follicle-stimulating hormone
GAST	18	gonadotrophin agonist stimulation test
GnRH	1,4,5,6,7,19	gonadotrophin-releasing hormone
GnRHa	5	gonadotrophin-releasing hormone agonist

Abbreviation:	Chapter(s):	Definition:
GTD	28	gestational trophoblastic disease
hCG	19,26,27	human chorionic gonadotrophin
HERS	16	Heart and Estrogen/progestin Replacement Study
HGSIL	45	high-grade squamous intraepithelial lesion
HIV	34,35,41	human immunodeficiency virus
HNPCC	50	hereditary non-polyposis colorectal cancer
HPV	41,45	human papillomavirus
HRT	2,11,12,13, 14,15, 16,17,40,42,46,50	hormone replacement therapy
HSG	18	hysterosalpingogram
HSV	35	herpes simplex virus
IBS	4	irritable bowel syndrome
IC	4,39	interstitial cystitis
ICSI	19,21	intracytoplasmic sperm injection
Ig	22	immunoglobulin
IP	49	intraperitoneal (chemotherapy)
ISVD	48	International Society for the Study of Vulvar Disease
IU	18	international units
IUCD	29	intrauterine contraceptive device
IUI	19	intrauterine insemination
IUS	1	intrauterine system
IVF	5,19,27	*in vitro* fertilization
LACE	46	Laparascopic Approach to Cancer of the Endometrium
LAP2	46	Laparascopic Surgery or Standard Surgery in Treating Patients with Endometrial Cancer or Cancer of the Uterus
LBC	41	liquid-based cytology
LH	7,18,22	luteinizing hormone
LNG	1,29	levonorgestrel
LNG-IUS	1,6,11,12,25	levonorgestrel-releasing intrauterine system
LUNA	3	laparoscopic uterine nerve ablation
LVSI	45,46	lymphovascular space invasion
MEA	2	microwave endometrial ablation
MPA	46	medroxyprogesterone acetate
MRI	3,4,7,22,42,45, 46,48	magnetic resonance imaging
MSU	37,38	mid-stream urine
NAAT	35	nucleic acid amplification technique
NCI	43	National Cancer Institute
NICE	42	National Institute for Clinical Excellence
NIH-NIDDK	39	National Institutes of Health – National Institute of Diabetes and Digestive and Kidney Diseases
NSAID	1,3,5,6,20	non-steroidal anti-inflammatory drug
OAB	37	overactive bladder
OR	16,21	odds ratio
ORT	18	ovarian reserve test
OVVOL	18	ovarian volume
PCO	7	polycystic ovaries
PCOS	8,20,46	polycystic ovary syndrome
PEPI	42	Progestin Estrogen–Progestin Intervention
PET	45	positron emission tomography
PFMT	36	pelvic floor muscle training

Abbreviation:	Chapter(s):	Definition:
PGF2	10	prostaglandin F2
PID	18,35	pelvic inflammatory disease
PMB	14	post-menopausal bleeding
PSN	3	presacral neurectomy
PMS	9	premenstrual syndrome
POC	25	progesterone-only contraception
POF	12	premature ovarian failure
PTH	13	parathyroid hormone
PUFAs	10	polyunsaturated fatty acids
PVA	6	polyvinyl alcohol
PYC	10	pycnogenol
RANKL	13	receptor activator of nuclear factor-kappa B ligand
RCT	13	randomized controlled trial
REA	2	rollerball endometrial ablation
SD	44	standard deviations
SERM	13	selective oestrogen receptor modulator
SNRI	15,36	serotonin and noradrenaline reuptake inhibitor
SPRM	6	selective progesterone receptor modulator
SSRIs	9,15,30	selective serotonin reuptake inhibitors
STIs	24,25,29,32,35,40	sexually transmitted infections
T3	28	triiodothyronine
T4	28	thyroxine
TAHBSO	46,50	total abdominal hysterectomy and bilateral salpingo-oophorectomy
TCRE	2	transcervical endometrial resection
TOP	4,23,29	termination of pregnancy
TSH	28	thyroid-stimulating hormone
TVS	11,14,22,23,26,27,43	transvaginal ultrasound scanning
TVT	36	tension-free vaginal tape
UAE	6	uterine artery embolization
UK	24,29,35,42,44	United Kingdom
UPSI	29	unprotected sexual intercourse
US	10,35	United States
UTI	38	urinary tract infection
VAC	10	vitex agnus castus
VEGF	47	vascular endothelial growth factor
VIN	48	vulvar intraepithelial neoplasia
VTE	16	venous thromboembolism
VVC	34	vulvovaginal candidiasis
WHI	13,16,42	Women's Health Initiative
WHO	18,24,25	World Health Organization
WHOMEC	25	World Health Organization Medical Eligibility Criteria for Contraceptive Use

Preface

Problem solving in women's health aims to give health professionals an easily readable practical guide to deal with common gynaecological presentations. The evidence, where available, is presented. With the lifespan of women continuing to increase and many surviving into their 10th or even 11th decades the problems of postreproductive health are increasing. This book covers problems from the menarche until old age.

The book is in eight sections and covers menstrual problems, menopause, fertility and contraception, gynaecological emergencies, sexual problems, urogenital problems, prevention and screening and gynaecological cancer. Alternative and complementary therapies as well as standard pharmacopiea are discussed.

The cases are described in a format suitable both for a consultation and could also be used for teaching and training of medical postgraduates preparing for higher qualifications. The cases are based on common problems encountered by the authors in both primary care and hospital-based practice.

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Menstrual Problems

PROBLEM

01 Menorrhagia with Medical Management

Case History

A 35-year-old woman comes complaining that her periods have become increasingly heavy since her children were born. She stopped the pill, which in the past had made her periods lighter, and is now using condoms for contraception. She does not want surgery.

How do you assess her?

What are the non-hormonal treatment options?

What are the hormonal options?

Background

Menorrhagia is a complaint of heavy cyclical menstrual blood loss over several consecutive cycles without any intermenstrual or post-coital bleeding.[1] In objective terms it is a blood loss greater than 80 ml per period.[2] While various pathologies have been implicated in menorrhagia, in 50% of cases of objective menorrhagia no pathology is found at hysterectomy. Although 'unexplained' menorrhagia is a very appropriate term, the label dysfunctional uterine bleeding, which implies endocrine abnormalities, is often given. However most cases of menorrhagia are associated with regular ovulatory cycles, and anovular cycles tend mainly to occur soon after the menarche or in the peri-menopausal period. Management has changed over the past two decades with the introduction of the levonorgestrel-releasing intrauterine device. In the United Kingdom the number of hysterectomies for menorrhagia fell by 36% between 1989 and 2002/3.[3] Medical management is advocated as initial treatment in women without significant pelvic pathology.[2,4]

How do you assess her?

Patients with menorrhagia commonly complain of increased menstrual loss requiring more sanitary protection or the passage of clots and flooding. History and assessment are detailed in Table 1.1.

Table 1.1 History and assessment

What questions do you ask? ● Duration of the problem ● Flooding or passage of clots ● Length and frequency of periods ● Has there been any change ● Intermenstrual bleeding or post-coital bleeding ● Presence of pelvic pain or dyspareunia ● Contraception used ● Are cervical smears up to date (according to local screening programmes)
Assessment ● Undertake pelvic examination and cervical smear (according to local screening programmes) ● Haematology and biochemistry ● Imaging ● Endometrial sampling ● Hysteroscopy

In a woman of this age pelvic pathology is unlikely so if pelvic examination is normal and there are no other symptoms, one can proceed to treat her medically. It is essential to check that she is not anaemic but further tests such as thyroid function should only be undertaken if clinically indicated. However if she does not respond to treatment she will need further investigation starting with a transvaginal ultrasound scan.

What are the non-hormonal treatment options?

Non-steroidal anti-inflammatory drugs

The cyclooxygenase (COX) pathway, with its two enzymes cyclooxygenase-1 (COX-1) and cyclooxygenase-2 (COX-2), represents one of the major routes for oxidative

metabolism of arachidonic acid to prostaglandins. Cyclooxygenase inhibitors, commonly referred to as non-steroidal anti-inflammatory drugs (NSAIDs), can be chemically classified into two main groups: COX-1 inhibitors (salicylates [aspirin], indoleacetic acid analogues [indomethacin], aryl propionic acid derivatives [naproxen, ibuprofen] and fenamates [mefenamic acid, flufenamic acid, meclofenamic acid]) and COX-2 inhibitors (coxibs [celecoxib]).

Various NSAIDs have been evaluated in a number of randomized trials, which have to date been limited to COX-1 inhibitors. In a Cochrane review, five of seven randomized trials showed that mean menstrual blood loss was less with NSAIDs than with placebo, and two showed no difference.[5] Furthermore, there was no evidence that one NSAID (naproxen or mefenamic acid) was superior to the other. The fenamates (e.g. mefenamic acid) are the most extensively studied NSAIDs. They have the unique property of inhibiting prostaglandin synthesis as well as binding to prostaglandin receptors, whose concentrations are significantly increased in the uteri of women with menorrhagia.[1] The percentage of blood loss reduction varies from 25% to 47% depending on the agent and dosage used.[5] An additional beneficial effect is that these drugs will also alleviate symptoms of dysmenorrhoea.

Optimal doses and schedules are difficult to define. Most studies, however, analyzed regimens starting on the first day of menstruation and continuing for five days or until cessation of menstruation. Common side effects of NSAIDs are gastrointestinal irritation and inhibition of platelet aggregation. Specific inhibitors of COX-2 might also be effective in the treatment of menorrhagia, but there is great uncertainty about the safety of this class of drugs.

Antifibrinolytics

Plasminogen activator inhibitors have been promoted as a treatment for menorrhagia because of increased endometrial fibrinolytic activity in women with menorrhagia. Tranexamic acid 2–4.5 g/day for four to seven days reduces menstrual blood flow by between 34% to 59% over two to three cycles. The effect is superior to placebo, mefenamic acid, flurbiprofen, ethamsylate and oral luteal phase norethisterone at clinically relevant dosages.[6] Side effects are mainly limited to mild gastrointestinal complaints. Earlier theoretical concerns about thromboembolism caused by the antifibrinolytic action of tranexamic acid have been refuted by long-term studies.

Etamsylate

Etamsylate is thought to act by reducing capillary fragility, though the precise mechanisms are uncertain. Studies with objective menstrual blood loss measurement using the currently recommended doses show that it is ineffective.[4]

Hormonal treatments

Progestogens

The use of progestogens is based on the erroneous concept that women with menorrhagia principally have anovulatory cycles and that a progestogen supplement is required. Progestogens are a common prescription for women complaining of menorrhagia. Oral administration, intrauterine administration and intramuscular depot injections are employed. The latter are used mainly for contraception and there is little information regarding menorrhagia.

Intrauterine administration

Intrauterine administration, especially of levonorgestrel (LNG), is very effective. There are currently two progestogen-impregnated devices: the Mirena® intrauterine system (IUS), which delivers 20 μg of LNG over 24 hours for about five years and the Progestasert® IUS, which releases about 65 μg of progesterone over 24 hours for about 16 months. Other newer, so-called 'frameless' IUSs are currently being evaluated.

The Mirena® levonorgestrel-releasing intrauterine system (LNG-IUS) reduces menstrual blood loss by up to 96%, and 20% of women using the LNG-IUS are reported to be amenorrhoeic after one year.[7] The LNG-IUS also provides very effective contraception. Its effectiveness has been compared to cyclical progestogens, endometrial ablation and hysterectomy. The LNG-IUS is more effective than cyclical norethisterone (for 21 days). The LNG-IUS results in a smaller mean reduction in menstrual blood loss (as assessed by pictorial charts) than endometrial ablation but there is no evidence of a difference in the rate of satisfaction with treatment. Women with an LNG-IUS experience more progestogenic side effects compared to women having endometrial ablation but there is no evidence of a difference in their perceived quality of life. The LNG-IUS treatment costs less than hysterectomy but there is no evidence of a difference in quality of life measures between these groups. However one of the few randomized controlled trials using the LNG-IUS for five years found a 42% hysterectomy rate.[8] The main adverse effect associated with LNG-IUS is frequently occurring variable bleeding and spotting, particularly within the first few months of use. LNG-IUS is also sometimes associated with the development of ovarian cysts, but these are usually symptomless and show a high rate of spontaneous resolution.

The Progestasert® was the first hormonally impregnated device but prospective randomized studies in menorrhagia are lacking.[7] The main disadvantage of this device is its association with an increased risk of ectopic pregnancy.

Oral and intramuscular progestogens

Traditionally, oral progestogen administration was in the luteal phase. However studies with measured menstrual blood loss with luteal administration for seven days of norethisterone 5 mg twice daily show either a decrease or even an increase in flow.[9] However, norethisterone 5 mg three times daily from days 5 to 26 is effective. Side effects include weight gain, headache and bloatedness. Depo-Provera (intramuscular medroxyprogesterone acetate), despite being licensed as a contraceptive, is often used to treat menorrhagia as it can induce amenorrhoea. However, there are no randomized controlled trial data. There are also no data with progestogen-only pills.

Combined oestrogen/progestogen contraceptives

From clinical experience, combined oral contraceptives (COCs) are generally considered to be effective in the management of dysfunctional menstrual bleeding. However, there are few available data to support this observation.[10] There are no data with the contraceptive patch.

Others

Danazol is an isoxazol deivative of 17α-ethinyl-testosterone which acts on the hypothalamic–pituitary axis as well as on the endometrium to produce atrophy. Danazol reduces menstrual blood loss by up to 80% from baseline. Its clinical use is limited by androgenic side effects, which are experienced by up to three-quarters of patients.[4]

Gestrinone is a 19-nortestosterone derivative which has antiprogestogenic, anti-oestrogenic and androgenic activity. In a placebo-controlled study it reduced menstrual blood loss in 79% of patients with objective menorrhagia.[1] However, it also has androgenic side effects.

Gonadotrophin-releasing hormone (GnRH) agonists, administered continuously or in depot form, downregulate expression of GnRH receptors, which blocks gonadotrophin secretion from the anterior pituitary. This leads to ovarian suppression. GnRH agonists have been mainly used in fibroid-associated bleeding.[1] Concerns about the long-term effects of ovarian suppression such as osteoporosis generally limit use beyond six months, even when add-back therapy (oestrogen/progestogen hormone replacement therapy) is used in conjunction.

Recent Developments

1 The LNG-IUS is recommended by the UK National Institute for Health and Clinical Excellence as a first-line treatment provided long-term use (at least 12 months) is anticipated.[4] The use of the LNG-IUS for the management of menorrhagia in primary care (as opposed to women recruited to menorrhagia trials with a menstrual blood loss >80 ml, i.e. objective menorrhagia) is currently being evaluated in the ECLIPSE study (International Standard Randomised Controlled Trial Number 86566246).

2 The United States Food and Drug Administration (FDA) has recently approved the marketing of a monophasic levonorgestrel and ethinyl oestradiol COC in an extended regimen (Seasonale). A patient considered for this regimen would have to be assessed as to whether she had contraindications to COC use such as smoking. One could also consider continuous use without a break. However, neither regimen has been studied in menorrhagia.

Conclusion

Menorrhagia is a common condition. It is important that healthcare professionals should be aware that it is the woman herself who determines whether a treatment is successful for her. What is the first-line treatment for an individual depends on her contraceptive needs. If this woman's family were complete, one would suggest trying the LNG-IUS. This will also provide effective contraception.

Further Reading

1 Oehler MK, Rees MC. Menorrhagia: an update. *Acta Obstet Gynecol Scand* 2003; **82**: 405–22.

2 CKS. Clinical topic. Menorrhagia (heavy menstrual bleeding). www.cks.library.nhs.uk/menorrhagia (accessed 20 09 07)

3 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.

4 National Institute for Health and Clinical Excellence. Heavy menstrual bleeding: investigation and treatment. Clinical guideline 44. London: NICE, January 2007. www.nice.org.uk/guidance/CG44 (accessed 20 09 07)

5 Lethaby A, Augood C, Duckitt K. Nonsteroidal anti-inflammatory drugs for heavy menstrual bleeding. *Cochrane Database Syst Rev* 2007; CD000400.

6 Lethaby A, Farquhar C, Cooke I. Antifibrinolytics for heavy menstrual bleeding. *Cochrane Database Syst Rev* 2007; CD000249.

7 Lethaby AE, Cooke I, Rees M. Progesterone or progestogen-releasing intrauterine systems for heavy menstrual bleeding. *Cochrane Database Syst Rev* 2005; CD002126.

8 Hurskainen R, Teperi J, Rissanen P, Aalto AM, Grenman S, Kivelä A, Kujansuu E, Vuorma S, Yliskoski M, Paavonen J. 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.

9 Lethaby A, Irvine G, Cameron I. Cyclical progestogens for heavy menstrual bleeding. *Cochrane Database Syst Rev* 2007; CD001016.

10 Davis A, Godwin A, Lippman J, Olson W, Kafrissen M. Triphasic norgestimate-ethinyl estradiol for treating dysfunctional uterine bleeding. *Obstet Gynecol* 2000; **96**: 913–20.

PROBLEM

02 Menorrhagia with Surgical Management

Case History

A 43-year-old woman comes demanding surgical treatment for her menorrhagia. She has tried mefenamic acid and tranexamic acid and her levonorgestrel-releasing intrauterine device has fallen out with a particularly heavy bleed. Her family is complete. She has already been investigated and has no significant pelvic pathology. She cannot cope with the embarrassing flooding and has already ruined a white sofa.

What endometrial ablative techniques can you offer?

How is hysterectomy performed?

How do the different methods compare?

What is life after hysterectomy?

Background

Surgery is a more definitive treatment for menorrhagia and is appropriate for those in whom medical therapy has failed and whose families are complete.[1,2]

What endometrial ablative techniques can you offer?

Endometrial ablation (EA) aims to destroy the endometrium along with the superficial myometrium thus reducing endometrial shedding at menstruation and resulting in less bleeding.[3] Not all women are amenorrhoeic, with rates varying between 15% and 50%. Directed ablation/resection deals with removal of individual fibroids and polyps. Endometrial ablative techniques are often done as day cases, and a return to normal activities is usually possible within 3–4 days. There are two types of techniques: first generation requiring hysteroscopy, and second generation that do not (Table 2.1). The former are technically more difficult than the latter.

Table 2.1 Methods of endometrial ablation

First generation
Transcervical resection of the endometrium (TCRE)
Endometrial laser ablation (ELA)
Rollerball endometrial ablation (REA)
Second generation
Thermal balloons
Microwave endometrial ablation (MEA)
Circulating hot saline
Cryotherapy

Transcervical endometrial resection (TCRE) involves diathermic removal of the endometrium in strips, similar to a transurethral resection of the prostate. It has been exhaustively proven to be effective. It is the only ablative procedure that obtains endometrial material from the whole of the uterine cavity other than the cornual regions. This may suggest TCRE is more appropriate in peri-menopausal women who have a higher risk of endometrial cancer, though no evidence is available at present to substantiate this theory.

Pre-operative use of endometrial thinning agents, such as danazol or gonadotrophin-releasing hormone analogues, to improve success rates has been recommended for first-generation endometrial ablative techniques where optimum visualization of the cavity is required.

The complications of TCRE have been well documented. These include haemorrhage (2.38%–3.5%), perforation (1%) and fluid overload (0.5%–4%) similar to other first-generation methods of EA such as laser and rollerball endometrial ablation.

Second-generation methods require less operating time and bypass well-recognized first-generation complications by not using fluid with cutting apparatus. In some methods endometrial preparation is also not required, reducing costs and side effects. Although the thermal balloon method is reported to have few complications, it is

currently restricted to normal uterine cavities. In comparison, microwave endometrial ablation (MEA) can treat women with irregular uterine cavities in a similar way to TCRE.

In a comparison of the newer non-hysteroscopic techniques (second generation) with the gold-standard hysteroscopic ablative techniques (first generation), surgery was an average of 15 minutes shorter and local anaesthesia was more likely to be employed. Women undergoing newer ablative procedures were less likely to have fluid overload, uterine perforation, cervical lacerations and haematometra than women undergoing the more traditional type of ablation and resection techniques. However there was a higher probability of equipment failure with second-generation ablation techniques.

The main disadvantage of the second-generation endometrial ablative techniques is lack of endometrial material for histology. Although endometrial biopsy is essential prior to all ablations (or a strip of endometrium taken off pre-rollerball), this does not sample the whole uterine cavity and focal endometrial cancer or atypical hyperplasia can be missed.

How is hysterectomy performed?

Hysterectomy is the second most common major operation performed after Caesarean section in the Western world. Hysterectomy appears to be a more definitive operation than EA (Table 2.2), with women undergoing a hysterectomy being less likely to be re-admitted to hospital up to five years after their operation and significantly less likely to be re-admitted for reasons related to their operation, particularly for gynaecological reasons.[4] The three choices are abdominal, vaginal or laparoscopic hysterectomy.[5] Laparoscopic hysterectomy has three further subdivisions: laparoscopic-assisted vaginal hysterectomy, where a vaginal hysterectomy is completed with varying degrees of laparoscopic assistance; subtotal laparoscopic hysterectomy, where the uterine body is removed leaving the cervix in place; and total laparoscopic hysterectomy, where the uterus and cervix are removed and the vaginal vault is sutured laparoscopically. Total abdominal hysterectomy is useful in women with large uteri, fibroid uteri, adenomyosis, endometriosis and pelvic adhesions. Oophorectomy performed at the time of hysterectomy to reduce the risk of ovarian cancer is a controversial issue. In women at low risk and whose ovaries are healthy it is generally advised to retain the ovaries.

There is currently a vogue for subtotal hysterectomy conserving the cervix, with the understanding that sexual function is better preserved than with total hysterectomy. However this has not been confirmed with prospective studies. The downside is that cervical smears have to be continued. Also there may be some endometrium in the cervical stump and this has been reported in 7% of women.[6]

Table 2.2 Comparison of endometrial ablation and hysterectomy

Issues	Hysterectomy	Endometrial ablation
Amenorrhoea	100% if total	15%–50%
Contraception	Provided	Not provided
Cervical smears	No need unless subtotal	Need to continue
Hormone replacement therapy	Oestrogen only	Oestrogen plus progestogen
Fertility	Offered only if no fertility goals	Offered only if no fertility goals

How do the different methods of hysterectomy compare?

The United Kingdom VALUE study examined complications after hysterectomy.[7] The overall operative complication rate was 3.5%, and highest for the laparoscopic techniques. The overall post-operative complication rate was 9%. One per cent of these were regarded as severe, with the highest rate for severe in the laparoscopic group (2%). There were no operative deaths; 14 deaths were reported within the six-week post-operative period, a crude mortality rate soon after surgery of 0.38 per thousand (95% confidence interval 0.25–0.64). In the international eVALuate study, two parallel multicentre trials compared laparoscopic hysterectomy with abdominal hysterectomy, and laparoscopic hysterectomy with vaginal hysterectomy.[8] Laparoscopic hysterectomy was associated with a higher rate of major complications than abdominal hysterectomy (11.1% vs 6.2%). Laparoscopic hysterectomy also took longer to perform (84 minutes vs 50 minutes) but was less painful and resulted in a shorter stay in hospital after the operation (three days vs four days). There was no evidence of a difference in major complication rates between laparoscopic hysterectomy and vaginal hysterectomy (9.8% vs 9.5%). Again, laparoscopic hysterectomy took longer to perform than vaginal hysterectomy (72 minutes vs 39 minutes).

What is life after hysterectomy?

In the late 1970s it was believed from retrospective studies that hysterectomy increased psychiatric morbidity. Several prospective studies undertaken in the 1980s found a reduction of morbidity six months after surgery. This has been confirmed in a recent study of total versus subtotal hysterectomy.[9] All women showed an improvement in psychological symptoms following both operations and no difference was found between the two procedures.

Early ovarian failure may occur even if ovaries are conserved. These women will require oestrogen-only hormone replacement therapy (HRT). In women who have had a subtotal hysterectomy there may be a concern that there is a remnant of endometrium in the cervical stump.[6] If this is the case, empirically the presence or absence of bleeding induced by monthly sequential HRT may be a useful diagnostic test. If withdrawal bleeds occur, the woman will need oestrogen–progestogen combined HRT. If not, she can have oestrogen-only HRT.

Recent Developments

1 A systematic review found that the benefits of vaginal versus abdominal hysterectomy were shorter duration of hospital stay, speedier return to normal activities and fewer unspecified infections or febrile episodes.[5] The benefits of laparoscopic versus abdominal hysterectomy were lower intra-operative blood loss, shorter duration of hospital stay, speedier return to normal activities, fewer wound or abdominal wall infections and fewer unspecified infections or febrile episodes, at the cost of longer operating time and more urinary tract (bladder or ureter) injuries. There was no evidence of benefits of laparoscopic versus vaginal hysterectomy and the operating time was increased. The authors concluded that vaginal hysterectomy should be performed in preference to abdominal hysterectomy where possible.

2 In the UK, the National Institute for Health and Clinical Excellence states that endometrial ablation may be offered as an initial treatment for menorrhagia after full discussion with the woman of the risks and benefits and of other treatment options.[1] Women must be advised to avoid subsequent pregnancy and on the need to use effective contraception, if required, after endometrial ablation. Hysterectomy should not be used as a first-line treatment solely for menorrhagia. Hysterectomy should be considered only when:

- other treatment options have failed, are contraindicated or are declined by the woman;
- there is a wish for amenorrhoea;
- the woman (who has been fully informed) requests it;
- the woman no longer wishes to retain her uterus and fertility.

Conclusion

This patient has not responded to medical treatment and her family is complete. She elects to have an endometrial ablation.

Further Reading

1 National Institute for Health and Clinical Excellence. Heavy menstrual bleeding: investigation and treatment. Clinical guideline 44. London: NICE, January 2007. www.nice.org.uk/guidance/CG44 (accessed 20 09 07)

2 CKS. Clinical topic. Menorrhagia (heavy menstrual bleeding). www.cks.library.nhs.uk/menorrhagia (accessed 20 09 07)

3 Lethaby A, Hickey M, Garry R. Endometrial destruction techniques for heavy menstrual bleeding. *Cochrane Database Syst Rev* 2005; CD001501.

4 Clarke A, Judge A, Herbert A, McPherson K, Bridgman S, Maresh M, Overton C, Altman D. Readmission to hospital 5 years after hysterectomy or endometrial resection in a national cohort study. *Qual Saf Health Care* 2005; **14**: 41–7.

5 Johnson N, Barlow D, Lethaby A, Tavender E, Curr E, Garry R. Surgical approach to hysterectomy for benign gynaecological disease. *Cochrane Database Syst Rev* 2006; CD003677.

6 Thakar R, Ayers S, Clarkson P, Stanton S, Manyonda I. Outcomes after total versus subtotal abdominal hysterectomy. *N Engl J Med* 2002; **347**: 1318–25.

7 Maresh MJ, Metcalfe MA, McPherson K, Overton C, Hall V, Hargreaves J, Bridgman S, Dobbins J, Casbard A. The VALUE national hysterectomy study: description of the patients and their surgery. *BJOG* 2002; **109**: 302–12.

8 Garry R, Fountain J, Mason S, Hawe J, Napp V, Abbott J, Clayton R, Phillips G, Whittaker M, Lilford R, Bridgman S, Brown J. The eVALuate study: two parallel randomised trials, one comparing laparoscopic with abdominal hysterectomy, the other comparing laparoscopic with vaginal hysterectomy. *BMJ* 2004; **328**: 129.

9 Thakar R, Ayers S, Georgakapolou A, Clarkson P, Stanton S, Manyonda I. Hysterectomy improves quality of life and decreases psychiatric symptoms: a prospective and randomised comparison of total versus subtotal hysterectomy. *BJOG* 2004; **111**: 1115–20.

PROBLEM

03 Dysmenorrhoea

Case History

A 15-year-old girl attends with her mother asking for treatment for her painful periods. She has to take at least one day a month off school because of the pain and is concerned about how this will affect her examination results. She is not yet sexually active.

What specific areas should you explore in the history?

Is a pelvic examination indicated?

What first-line treatments would you recommend?

What non-pharmacological treatments exist?

Is surgery ever indicated?

Background

Dysmenorrhoea is defined as painful menstrual cramps and has been traditionally subdivided into primary (without any pathology) and secondary dysmenorrhoea (due to other pathology). It is very common, with estimates of prevalence ranging from 20% to 90%.[1] Most adolescents self-medicate rather than consult a doctor; however, dysmenorrhoea is the most common cause of recurrent school absenteeism in teenage girls. It is important, therefore, that it is identified and treated early.

What specific areas should you explore in the history?

Pain with menstruation will usually commence within a year of menarche, thus if it starts beyond this period it should alert to the possibility of other pathology (such as endometriosis or adenomyosis).[2] Therefore, age at menarche and age at which dysmenorrhoea began should be elicited. An attempt should be made to understand the bleeding pattern, as initial anovulatory cycles are often more irregular, heavier and more painful and this may improve as cycles become ovulatory and more regular. Associated symptoms may include radiation of pain to the back or thighs, nausea, vomiting or diarrhoea. However, cyclical rectal bleeding or other bowel symptoms may point to a diagnosis of rectal endometriosis or irritable bowel syndrome. The pain usually starts no more than a few hours before the onset of menstruation and settles after the first 24–36 hours. More prolonged pain or pain of a non-cyclical nature should raise the suspicion of other pathology. Dysmenorrhoea usually improves after childbirth and if parity is controlled for there is no relationship with age.[3] However, depression and anxiety, disruption of

social networks and smoking are all associated factors.[1] As many of the initial treatments are available over the counter, what treatments have been tried and whether or not they were successful at all should be established.

Is a pelvic examination indicated?

As long as nothing in the history suggests another pathology, there is no need for a pelvic examination prior to commencing empirical treatment, especially in girls who are not yet sexually active. Abnormal vaginal discharge or risk of sexually transmitted infections should prompt internal examination and appropriate swabs.

What first-line treatments would you recommend?

Dysmenorrhoea is thought to be due to increased prostaglandin production by the endometrium which causes stronger and more irregular uterine contractions, reducing uterine blood flow and causing painful, transient ischaemia. Prostaglandins are also likely to be responsible for the nausea, vomiting and diarrhoea which are often associated with the pain.[2] Thus first-line medical treatment is usually non-steroidal anti-inflammatory drugs (NSAIDs), such as ibuprofen and naproxen sodium, because of their action in reducing prostaglandin synthesis as well as a central analgesic action.[4] In order for them to be effective they need to be commenced at or just before the onset of menstruation and continued at regular intervals throughout the first two days, rather than waiting for the pain to increase. Their half-life is a few hours. NSAIDs have been shown to be significantly more effective at relieving dysmenorrhoea when compared to placebo, but there is insufficient evidence to recommend any one drug over another.[5] NSAIDs are not without side effects; however, if just taken for two days a month by otherwise healthy girls or women they are likely to be well tolerated. More recently, cyclooxygenase-2 (COX-2)-specific inhibitors have been shown to be similarly efficacious.[6] However, there are current safety concerns and thus they cannot be recommended over traditional NSAIDs.

Combined oral contraceptive pills induce endometrial atrophy and thus reduce menstrual fluid prostaglandins as well as reducing the amount of bleeding and pain. They are therefore also recommended as a first-line treatment, especially if contraception is required. Although they are effective clinically, the studies are small and of poor quality.[7] It would be prudent, however, to check whether contraception is needed and see the patient alone without her mother.

What non-pharmacological treatments exist?

A number of dietary supplements and modifications have been suggested to improve dysmenorrhoea, although convincing evidence does not exist for most of these in humans. Both fish oil and krill oil, however, were shown to have a significant effect.[2,4] Transcutaneous electrical nerve stimulation has been shown to be effective in both reducing dysmenorrhoea and reducing analgesia usage,[8] as has continuous low-level topical heat,[9] although neither of these are as easy to manage outside the home as simple analgesics. There is limited evidence that exercise reduces dysmenorrhoea.[2]

Is surgery ever indicated?

If dysmenorrhoea does not respond to first-line treatments then a laparoscopy may be justified to look for other causes of pain such as endometriosis or congenital uterine

abnormalities. Ultrasound and magnetic resonance imaging (MRI) scans pre-operatively may also help investigate the pain.

A few studies have looked at the role of laparoscopic uterine nerve ablation (LUNA) and presacral neurectomy (PSN) in women whose dysmenorrhoea is severe and refractory to other treatments. PSN appears to be effective in a small number of women whereas LUNA is not; however, the long-term benefits are not known.[10]

Recent Developments

Behavioural interventions for dysmenorrhoea have been examined in a systematic review.[11] Five trials involving 213 women were included. Behavioural intervention vs control: One trial of pain management training reported reduction in pain and symptoms compared to a control. Three trials of relaxation compared to control reported varied results, two trials showed no difference in symptom severity scores, however one trial reported that relaxation was effective for reducing symptoms in menstrual sufferers with spasmodic symptoms. Two trials reported less restriction in daily activities following treatment with either relaxation or pain management training compared to a control. One trial also reported less time absent from school following treatment with pain management training compared to a control. The authors concluded that there is some evidence from five RCTs that behavioural interventions may be effective for dysmenorrhoea, however results should be viewed with caution as they varied greatly between trials due to inconsistency in the reporting of data, small trial size, poor methodological quality and age of the trials.

Conclusion

It is essential that this patient is taken seriously. The pathophysiology of dysmenorrhoea needs to be explained and effective treatment instigated. If appropriate, further investigations should be undertaken, but many patients can be effectively managed with simple analgesics or the combined oral contraceptive pill.

Further Reading

1 French L. Dysmenorrhea. *Am Fam Physician* 2005; **71**: 285–91.

2 Dawood MY. Primary dysmenorrhea: advances in pathogenesis and management. *Obstet Gynecol* 2006; **108**: 428–41.

3 Sundell G, Milsom I, Andersch B. Factors influencing the prevalence and severity of dysmenorrhoea in young women. *Br J Obstet Gynaecol* 1990; **97**: 588–94.

4 Proctor M, Farquhar C. Diagnosis and management of dysmenorrhoea. *BMJ* 2006; **332**: 1134–8.

5 Marjoribanks J, Proctor ML, Farquhar C. Nonsteroidal anti-inflammatory drugs for primary dysmenorrhoea. *Cochrane Database Syst Rev* 2003; CD001751.

6 Daniels SE, Talwalker S, Torri S, Snabes MC, Recker DP, Verburg KM. Valdecoxib, a cyclooxygenase-2-specific inhibitor, is effective in treating primary dysmenorrhea. *Obstet Gynecol* 2002; **100**: 350–8.

7 Proctor ML, Roberts H, Farquhar CM. Combined oral contraceptive pill (OCP) as treatment for primary dysmenorrhoea. *Cochrane Database Syst Rev* 2001; CD002120.

8 Proctor ML, Smith CA, Farquhar CM, Stones RW. Transcutaneous electrical nerve stimulation and acupuncture for primary dysmenorrhoea. *Cochrane Database Syst Rev* 2002; CD002123.

9 Akin MD, Weingand KW, Hengehold DA, Goodale MB, Hinkle RT, Smith RP. Continuous low-level topical heat in the treatment of dysmenorrhea. *Obstet Gynecol* 2001; **97**: 343–9.

10 Proctor M, Latthe P, Farquhar C, Khan KS, Johnson N. Surgical interruption of pelvic nerve pathways for primary and secondary dysmenorrhoea. *Cochrane Database Syst Rev* 2005; CD001896.

11 Proctor M, Murphy P, Pattison H, Suckling J, Farquhar C. Behavioural interventions for primary and secondary dysmenorrhoea. *Cochrane Database Syst Rev* 2007; CD002248.

PROBLEM

04 Chronic Pelvic Pain

Case History

A 32-year-old woman presents with a ten-year history of pelvic pain which is present most days of the month but has cyclical exacerbations. She is nulliparous, although she underwent a surgical termination of pregnancy (TOP) at age 17 years. Currently she is not in a stable relationship. Previously she had two diagnostic laparoscopies, both of which were completely normal.

What areas should you explore in the history?

What are you looking for on examination?

Are any investigations justified?

What treatment might be appropriate?