

## CLINICAL REVIEW

## Managing unscheduled bleeding in non-pregnant premenopausal women

Mary Ann Lumsden *professor of gynaecology and medical education, honorary consultant gynaecologist*<sup>1</sup>, Ailsa Gebbie *consultant gynaecologist and clinical lead for family planning*<sup>2</sup>, Cathrine Holland *consultant gynaecological surgeon and oncologist*<sup>3</sup>

<sup>1</sup>Department of Reproductive and Maternal Medicine, University of Glasgow, Glasgow G4 0SF, UK; <sup>2</sup>NHS Lothian Sexual and Reproductive Health Service, Edinburgh, UK; <sup>3</sup>Department of Gynaecological Oncology, Central Manchester University Hospital Foundation Trust, Manchester, UK

Unscheduled vaginal bleeding—bleeding that occurs outside the normal menstrual period or the regular withdrawal bleed associated with the combined oral contraceptive pill—is a common reason for women of reproductive age to attend primary care. It is also referred to as intermenstrual bleeding. As well as intermenstrual bleeding, unscheduled bleeding also includes postcoital bleeding; it can be difficult to distinguish between the two because they often occur together. Because postcoital bleeding may have different implications, the causes of both need to be considered in a woman with unscheduled bleeding. Irregular bleeding associated with hormonal contraception is generally called breakthrough bleeding.

In a study of women presenting to primary care with menstrual problems, 36% of women reported intermenstrual bleeding or postcoital bleeding in addition to heavy menstrual loss.<sup>1</sup> Unscheduled bleeding causes anxiety and concern because it can be a presenting symptom for gynaecological cancer, particularly cervical and endometrial cancer. This symptom can also be associated with other menstrual disorders, such as heavy menstrual bleeding, particularly when caused by benign lesions such as fibroids or endometrial polyps, but also heavy menstrual bleeding of no known cause (formally called dysfunctional bleeding).

However, it also occurs with the use of hormonal and intrauterine contraception, particularly progestogen only methods, and results in many women discontinuing an otherwise highly effective method. This article reviews the causes of unscheduled vaginal bleeding and how to investigate and manage this problem after pregnancy has been excluded. Recent changes in cervical screening guidelines mean that women below the age of 25 years are not routinely offered cervical smears. This has led to concerns about the risk of missing a diagnosis of cervical cancer in women in this age group. We have included specific guidance on abnormal bleeding in very young women that cannot be attributed to contraceptive use to aid the general practitioner in light of these concerns.

### Who gets unscheduled bleeding?

Abnormal bleeding is common and accounts for 20% of referrals to gynaecological outpatient clinics.<sup>1</sup> The causes vary with age, although overlap occurs between the groups. For young women (<35 years), it is often related to contraceptive use, particularly progestogen only contraception, and malignant disease is uncommon. Data from the Office of National Statistics suggest that the likelihood of cervical or endometrial cancer increases with age,<sup>2</sup> as do other diseases such as uterine fibroids and polyps.<sup>3,4</sup>

### What causes unscheduled bleeding?

Unscheduled bleeding has many causes, some of which result in predominantly intermenstrual bleeding and others lead to postcoital bleeding, although there is a considerable overlap. For the purpose of this review, the causes are discussed below under the pattern of bleeding that they are most likely to bring about, but there is crossover between the two entities.

### Intermenstrual bleeding

Observational studies have found that uterine fibroids occur in over 25% of women of reproductive age and are more common in black women. About 50% cause symptoms,<sup>5</sup> with heavy or irregular bleeding (or both) being a common presentation. Fibroids are fibromuscular round growths found in the myometrium. Their size varies from a few millimetres to that of a full term pregnancy. Submucosal or pedunculated fibroids distort the endometrial cavity and may be covered with vessels that break down and bleed (fig 1⇓), leading to irregular bleeding or heavy bleeding. The risk of malignant transformation is low,<sup>6</sup> occurring in 0.5–3.3 cases per 100 000 symptomatic women a year, but the denominator cannot be estimated accurately because fibroids are often multiple or asymptomatic (or both). Endometrial polyps are another benign cause of intermenstrual bleeding. Polyps are mucosal outgrowths that can reach several

### Summary points

- Pregnancy must always be excluded in the presence of unscheduled vaginal bleeding
- Unscheduled bleeding is often seen with hormonal contraceptives, particularly progestogen only ones, in the first six months of use
- Unscheduled bleeding results in many women discontinuing an otherwise highly effective method of contraception
- Bleeding can result from benign lesions such as endometrial or cervical polyps, uterine fibroids, or adenomyosis, but consider concurrent disease of the endometrium and cervix in those at high risk
- Although uncommon, endometrial and cervical cancer may present with unscheduled bleeding
- The most important intervention in general practice is a vaginal speculum examination to visualise the cervix; the presence of bleeding should not defer this

### Sources and selection criteria

We used the search terms "abnormal bleeding," "unscheduled bleeding," "intermenstrual bleeding," and "postcoital bleeding." We searched PubMed, Medline, Embase, Cochrane reviews, reference lists in general articles, guidelines of the UK Faculty of Sexual and Reproductive Healthcare, and Department of Health evidence based guidance documents. Our personal reference collections were also consulted.

centimetres in length. They are associated with irregular and sometimes heavy menstrual bleeding (fig 2). A recent systematic review and meta-analysis of more than 10 000 women with endometrial polypectomy concluded that the incidence of cancer within a polyp in women of reproductive age was only 1.7%, compared with 5.4% in postmenopausal women. Although the malignant potential of polyps is generally low, women with polyps and abnormal bleeding are more likely to have a diagnosis of cancer than those with asymptomatic polyps.<sup>4 7</sup>

Some women will experience irregular bleeding during the perimenopause, probably because of hormonal fluctuation. A large population study found that the length of the menstrual cycle often decreases in women during their late 30s and early 40s, and longer, irregular cycles become common.<sup>8</sup> However, perimenopausal dysfunctional bleeding is a diagnosis of exclusion, and irregular bleeding between periods should be investigated. This is particularly so for women who are at higher risk of endometrial cancer, such as those from families affected by hereditary non-polyposis colorectal cancer, because abnormal uterine bleeding (prolonged or intermenstrual) can be a symptom of underlying endometrial cancer. Most women with endometrial cancer are postmenopausal, with peak incidence above age 55 years. However, endometrial cancer can occur in premenopausal women, and the incidence rises steeply after the age of 40. Overall, 7% of women with endometrial cancer are below the age of 50. There is a risk of delayed diagnosis in these women because increasingly heavy or irregular bleeding may be falsely attributed to hormonal factors or the perimenopause.

Intermenstrual bleeding can also be caused by the inflammatory endometrial response to a copper intrauterine device. Studies show that women using such devices experience more days of intermenstrual spotting and bleeding than non-users.<sup>9</sup> A malpositioned device (low lying or abnormally rotated in the uterine cavity), which can be detected by ultrasound, is associated with a higher chance of irregular bleeding and pain. Infection can also lead to intermenstrual bleeding. Sexually transmitted infections, particularly chlamydia, can cause endometritis, which is often associated with irregular bleeding and lower abdominal pain. Although most women with chlamydia are asymptomatic, intermenstrual bleeding can be the presenting symptom. Gonorrhoea can also cause bleeding but is much less prevalent than chlamydia in women in most populations.

### Postcoital bleeding

Postcoital bleeding is often reported in women who describe abnormal intermenstrual bleeding. Causes of postcoital bleeding reported in women referred to secondary care for evaluation are cervical polyp (5-13%), ectopy (34%), chlamydia infection (2%), cervical intraepithelial neoplasia (7-17%), and invasive cervical cancer (0.6-4%). No specific cause for bleeding is found in about 50% of women.<sup>10 11</sup> Cervical ectropion, which looks red on examination, can occur as a result of sex hormones (particularly oestrogen) that encourage the growth of columnar epithelium over the ectocervix. It is particularly common in women who are pregnant or taking the combined oral contraceptive pill. Cervical polyps can also bleed and can also normally be visualised on examination. Infection can cause cervicitis and lead to postcoital bleeding. Cervicitis is usually associated with vaginal discharge as well as bleeding. It may be due to sexually transmitted infections such as chlamydia or gonorrhoea and occasionally herpes.

Most invasive cancers that cause postcoital bleeding are clinically apparent on speculum examination, and the proportion of invasive cancers diagnosed in women who have had a recent normal smear is low (0.6%).<sup>10 11</sup> Although women can be counselled that serious disease is unlikely to be found, cervical cancer is more common in women with postcoital bleeding than in asymptomatic women. It is therefore important to perform a speculum examination and refer urgently to secondary care if there are concerns about the appearance of the cervix.

In the United Kingdom, cervical cancer most commonly affects women aged 25-64, with a peak incidence at 30-34 years.<sup>12</sup> It is less common than other cancers that affect women. In stark contrast, cervical cancer is a common cause of death in many developing countries. Oncogenic human papillomavirus subtypes cause cervical cancer. Women who have ever had sex are at risk, particularly immunocompromised women. It is a common misconception that women who are in same sex relationships are not at risk. A literature review of prevalence studies and case reports documented transmission of human papillomavirus between female sexual partners. In addition, 35% of homosexual women reported having had one to three male partners and 28% reported having four to 10 previous male partners.<sup>13</sup> Therefore all women eligible for screening (age 25-64) should be encouraged to attend for routine cervical screening regardless of sexual orientation.

## Breakthrough bleeding with hormonal contraception

Unscheduled vaginal bleeding is common when a new contraceptive method is started and often settles without intervention. Before the bleeding is attributed to the contraceptive method itself, pregnancy must be excluded. Infection must also be excluded in women using hormonal contraception.

Some women find breakthrough bleeding with hormonal contraception unacceptable and will discontinue the contraception, thus increasing the risk of unintended pregnancy. The table<sup>1</sup> outlines the expected bleeding patterns in the first three months and thereafter for a variety of contraceptive methods. The data come from observational studies. Data for combined hormonal contraception are for the combined oral contraceptive pill but can be extrapolated to other combined methods (transdermal patch and vaginal ring). Bleeding problems are more common with progestogen only methods. Women should be counselled about the risks of bleeding abnormalities before they start contraception.

Box 1 details the main causes of breakthrough bleeding in women taking oral contraceptives. The most common cause is missed pills. Regular pill taking should be encouraged and bleeding often settles completely when adherence improves.<sup>14</sup>

A systematic review showed that preparations containing 20 µg ethinylestradiol are more likely to be associated with breakthrough bleeding than those containing 30-35 µg.<sup>15</sup> Breakthrough bleeding seems to be linked to ovarian follicular development, oestradiol concentrations, and blood vessel fragility.<sup>16 17</sup> Sometimes—to avoid a withdrawal bleed at an inconvenient time or to prevent cyclical symptoms such as migraine—women do not take a break from combined oral contraception, and this often results in bleeding. “Tailored pill use” allows women to continue taking the pill until breakthrough bleeding develops, before stopping for a planned withdrawal bleed at that stage; thereafter, once the woman knows roughly when breakthrough bleeding will start, she can use this as a guide to when she should stop for a break in the future.<sup>18</sup> Several randomised trials have shown that breakthrough bleeding is significantly lower with the contraceptive vaginal ring than with the standard 30 µg combined oral contraceptive pill.<sup>19</sup>

Antibiotic use is no longer thought to decrease the effectiveness of combined oral contraceptives or cause breakthrough bleeding, other than enzyme inducing rifamycin preparations for treating tuberculosis.<sup>6</sup> Bleeding with progestogen only contraception is thought to be caused by abnormal vascular morphology in the endometrium.<sup>16</sup>

## How should I evaluate a woman with unscheduled bleeding?

In most situations, a careful history will identify the possible causes of unscheduled bleeding and guide the need for examination and further investigations. The questions that should be covered are straightforward. Box 2 provides a list women who should be referred to secondary care.

It is important to know the woman's age because causes tend to differ with age. The last menstrual period will give an indication of the likelihood of pregnancy, and cycle length is valuable in determining the probability of anovulation. The frequency, heaviness, and duration of the irregular bleeding and its association with menses are also relevant. Premenstrual and postmenstrual bleeding and midcycle bleeding are often related to cyclical changes in sex steroids and less likely than prolonged

bleeding to be associated with disease. Prolonged bleeding, particularly if associated with irregular (probably anovulatory) cycles, is more suggestive of endometrial cancer in a woman approaching the menopause.

The sexual history—for example, starting a relationship with a new partner or the presence of vaginal discharge—might suggest an infection, such as chlamydia.

Ask about use of hormonal contraception and adherence to the regimen because this is often the cause, particularly if started within the past three months. Bleeding of more than 3 months' duration, particularly when heavy, will require further evaluation.

Cervical disease is unlikely if the woman has a regular and up to date screening history. Cervical ectropion is also more likely with oestrogen containing hormonal contraception. A family history of cancers is rare but important, because serious endometrial disease is associated with some gene mutations that cause hereditary cancers.

## Examination

Note whether the woman is obese because obesity is associated with anovulatory cycles.

A pelvic mass on abdominal examination could suggest fibroids, particularly if the woman has heavy periods; this diagnosis is likely to be supported by bimanual examination.

Digital examination may identify cervical excitation (indicative of infection) or cervical cancer if there is a craggy irregular cervix.

The most important intervention is a vaginal speculum examination to visualise the cervix.<sup>20 21</sup> This is crucial for detecting cervical ectropion and cancer.

## Investigations

Some investigations can be performed in primary care before referral. A cervical smear should be performed if not in date. If the cervix looks abnormal on examination, urgent referral is indicated.<sup>22</sup>

If the woman is at risk of infection, take an endocervical or vaginal swab (depending on the locally available tests) to check for infection, usually chlamydia and gonorrhoea.

If the history is of heavy or prolonged bleeding, take a full blood count to check for anaemia. In the presence of heavy menstrual bleeding and a palpable pelvic mass, uterine fibroids are the most likely diagnosis, particularly in women aged 35-50 years. An ultrasound scan will then be required (see below).

Other investigations that may take place after referral include hysteroscopy, which will determine whether a fibroid distorts the cavity of the uterus and can also confirm the presence of an endometrial polyp. Figures 1-4<sup>23</sup> show examples of a normal and diseased endometrial cavity.

Magnetic resonance imaging is increasingly used in secondary care to provide good definition if the uterus is large, the ovaries are not easy to visualise, or doubt remains about the origin of a pelvic mass.

## What is the role of ultrasound?

Because it can be difficult to distinguish between an ovarian cyst and uterine fibroids on examination, if a patient has a pelvic mass, it is often helpful to have a pelvic ultrasound available for when the woman is seen in secondary care. If there is no pelvic mass and referral is being made to a “one-stop” clinic, ultrasound will automatically be repeated before any further

**Box 1 Checklist for causes of breakthrough bleeding related to use of combined oral contraception**

- Ask about adherence with regular pill taking
- Check for any possible drug interactions, including over the counter drugs, such as St John's wort
- If the woman smokes encourage her to stop because smokers have a higher risk of breakthrough bleeding
- Check for risk of sexually transmitted infections, particularly chlamydial infections
- Check cervical cytology history
- Exclude pregnancy
- Look for symptoms that suggest an underlying gynaecological cause such as pain, dyspareunia, or heavy menstrual bleeding

**Box 2 Who needs referral?**

- Women with an abnormal looking cervix, particularly in those without a recent smear test
- Women with a cervical polyp not easily removed in the surgery or that looks suspicious
- Women with a pelvic mass associated with heavy menses and intermenstrual bleeding, because these women are likely to have fibroids
- Women at high risk of endometrial cancer, such as those with a family history of hormone dependent cancer, those with prolonged and irregular cycles, and women on tamoxifen
- Women in whom irregular bleeding might lead to discontinuation of hormonal contraception. Such women are best referred to their local family planning centre where there will be clinics for complex contraceptive problems
- All women over 45 years with intermenstrual bleeding should have a biopsy and those under 45 with persistent symptoms or risk factors for endometrial cancer should also be referred

investigation, so may not be necessary in primary care. These clinics may have the facilities to carry out investigations, including hysteroscopy, and start treatment in one visit. However, local guidelines on carrying out an ultrasound before referral may be in place and should be checked.

Endometrial polyps can also be visualised with ultrasound and this may be facilitated by the infusion of saline into the cavity (saline infusion sonography).<sup>23</sup>

A systematic review of ultrasound found that its sensitivity and specificity for identifying the cause of abnormal bleeding (unscheduled bleeding and heavy menstrual bleeding) varied considerably, with a sensitivity of 48-100%.<sup>24</sup> Sensitivity probably depended on the quality of the study and also on the skill of the person doing the scan.

A randomised controlled trial found that fibroids are better detected by ultrasound than by hysteroscopy (generally considered the gold standard for diagnosis, although not usually performed in primary care). However, hysteroscopy is usually better at detecting intracavity disease, such as endometrial polyps.<sup>25</sup>

**When is endometrial biopsy indicated?**

The absence of a thickened endometrium on ultrasound does not totally exclude serious endometrial disease, such as atypical hyperplasia or invasive endometrial cancer. However, endometrial cancer is unlikely in women under 40 years, particularly if there is no family history. Referral for endometrial biopsy is therefore not indicated in these women unless the abnormal bleeding persists or the treatment provided fails to resolve the symptoms. Because the incidence of endometrial cancer starts to rise sharply at age 40, consider referral for endometrial biopsy in women between 40 and 45 years; referral is indicated for women aged 45 or more.<sup>26</sup>

Consider endometrial biopsy in all women over 40 known to have benign disease, such as fibroids or endometrial polyps, because endometrial cancer may also be present.<sup>27</sup>

**How should I investigate women aged 20-24 years not on hormonal contraception?**

Although abnormal bleeding is common in young women, it is rarely a sign of cancer (about 50 cases a year in the UK). However, these women are often referred to specialist services because they do not have routine cervical screening. Any woman in this age group who presents with postcoital bleeding or persistent intermenstrual bleeding must be offered an immediate speculum examination because about 80% of invasive cervical cancers are visible to the naked eye. The NHS Advisory Committee for Cervical Screening recommends urgent referral for colposcopy in the small number of young women with a cervix that looks abnormal and suspicious.<sup>22</sup> Do not wait for the result of a cervical smear, because smears are unreliable in the diagnosis of cervical cancer. Women who are found to have a benign lesion, such as a cervical polyp or ectropion, can be referred to a general gynaecological outpatient clinic rather than for colposcopy.

**How should women with abnormal bleeding while using hormonal contraception be investigated?**

Tell women of any age who are using progestogen only contraceptives to expect irregular bleeding in the early months of use. Unscheduled bleeding may not improve with some methods, but the woman may be happy to continue if reassured that there is no serious underlying cause. If abnormal bleeding patterns persist with any contraceptive method beyond the first six months of use or arise de novo, gynaecological investigations, including an ultrasound scan, are indicated.

**What treatment will be required?**

This will depend on the underlying cause of the bleeding. If anaemia is present secondary to bleeding, prescribe iron supplements. Minor disease, such as polyps or small fibroids, can be removed hysteroscopically. Larger fibroids can be removed by transcervical resection. New devices are available to facilitate hysteroscopic procedures under local anaesthetic. Cryotherapy for symptomatic cervical ectropion can also be performed in a general gynaecology clinic.

Women with larger fibroids can be treated with drugs, vascular embolisation, surgery, or a combination of these methods, with good resolution of bleeding disorders. Box 3 lists treatments for uterine fibroids that have been investigated in well performed randomised controlled trials. They have been assessed in review articles and a Cochrane review.<sup>28-30</sup>

Hormonal treatments such as oral progestogen or the levonorgestrel releasing intrauterine system can be useful, particularly in dysfunctional uterine bleeding, and long term randomised controlled trials report a decrease in the number of bleeding days.<sup>31 32</sup> A recent Cochrane review confirms the absence of good randomised trials to support the use of cyclical progestogens or oestrogen and progestogen in the treatment of irregular and intermenstrual bleeding.<sup>33</sup> Manipulation of sex steroid hormone levels will provide symptomatic relief and shrink fibroids, but the problems usually resume on stopping treatment.

Refer any cancer to the local gynaecological oncology team for specialist management. Hyperplasia can be reversed by progestogen, which is the treatment of choice in a woman wishing to retain her fertility.<sup>34</sup> Atypical hyperplasia and cancer are usually treated with surgery.

## How do I treat bleeding associated with contraception?

Unscheduled vaginal bleeding in association with hormonal contraception can be difficult to treat. Management is generally based on consensus expert opinion because the scientific evidence is of insufficient quality to provide evidence based recommendations.<sup>14</sup> The World Health Organization selected practice recommendations form the basis for this and have been adapted by many countries.<sup>35</sup> Treatment options are generally limited.

Small randomised trials show that non-steroidal anti-inflammatory drugs can shorten the duration of bleeding episodes when given continuously for three to four weeks but have limited clinical value. Tranexamic acid will help heavier bleeding. Although unlicensed for this indication, an oestrogen containing combined pill can provide temporary relief from breakthrough bleeding associated with the progestogen only implant, injectable preparation, or intrauterine system, probably through stabilisation of the endometrium. A three month course is usually given initially, but it will improve cycle control for as long and as often as it is continued. Its use is restricted to women with no contraindications to an oestrogen containing preparation. Box 4 summarises the available treatments for breakthrough bleeding in women who use progestogen only contraception.

If bleeding persists after three months of combined oral contraceptive use, increase the dose of ethinylestradiol up to a maximum of 35 µg to give the best cycle control.<sup>15</sup> There is no evidence that changing the type of progestogen or dose will improve the bleeding pattern, but anecdotally this may help individual women. Running more than one packet of combined pills together before having a break or continuous use of the pill may exacerbate the problems so should be stopped.<sup>14</sup> A woman could consider switching to the combined vaginal ring to improve cycle control if she wishes to continue a combined method.<sup>19</sup>

Other drugs that have shown some degree of efficacy in small studies are doxycycline and mifepristone; neither produces lasting benefit and they are unlicensed for this indication.

The UK Faculty of Sexual and Reproductive Healthcare has produced comprehensive evidence based guidelines on the

management of unscheduled bleeding in women using hormonal contraception.<sup>14</sup>

Contributors: All three authors contributed to the manuscript according to their area of specialist interest—AG contraception, CH cervical screening and pathology, MAL benign gynaecological disease. MAL finalised the manuscript and is guarantor.

Competing interests: We have read and understood the BMJ Group policy on declaration of interests and declare the following interests: None.

Provenance and peer review: Commissioned; externally peer reviewed.

- Warner P, Critchley HO, Lumsden MA, Campbell-Brown M, Douglas A, Murray G. Referral for menstrual problems: cross sectional survey of symptoms, reasons for referral and management. *BMJ* 2001;323:24-8.
- Office for National Statistics. Cancer statistics registrations. Registrations of cancers diagnosed in England 2003. ONS, 2005.
- Kjerulf KJ, Langenberg P, Seidman JD, Stolley PD, Guzinski GM. Uterine leiomyomas. Racial differences in severity, symptoms and age at diagnosis. *J Reprod Med* 1995;41:483-90.
- Dreisler E, Sorensen S, Ibsen PH, Lose G. Prevalence of endometrial polyps and abnormal uterine bleeding in a Danish population aged 20-74 years. *Ultrasound Obstet Gynecol* 2009;33:102-8.
- Buttram VC, Reiter RC. Uterine leiomyomata: etiology, symptomatology, and management. *Fertil Steril* 1981;36:433-45.
- Harlow BL, Weiss NS, Lafton S. The epidemiology of sarcomas of the uterus. *J Natl Cancer Inst* 1986;76:399-402.
- Lee SC, Kaunitz AM, Sanchez-Ramos L, Rhatigan RM. The oncogenic potential of endometrial polyps: a systematic review and meta-analysis. *Obstet Gynecol* 2010;116:1197-205.
- Treloar AE, Boynton RE, Behn BG, Brown BW. Variation of the human menstrual cycle throughout life. *Int J Fertil* 1967;12:77-126.
- Faculty of Sexual and Reproductive Healthcare Clinical Guidance. Intra-uterine contraception. 2007. [www.fsrh.org/pdfs/CEUGuidanceIntrauterineContraceptionNov07.pdf](http://www.fsrh.org/pdfs/CEUGuidanceIntrauterineContraceptionNov07.pdf).
- Rosenthal AN, Panoskaltis T, Smith T, Soutter WP. The frequency of significant pathology in women attending a general gynaecological service for postcoital bleeding. *Br J Obstet Gynaecol* 2001;108:103-6.
- Sahu B, Latheef R, Magd SA. Prevalence of pathology in women attending colposcopy for postcoital bleeding with negative cytology. *Arch Gynecol Obstet* 2007;276:471-3.
- Cancer Research UK. CancerStats—Cancer statistics for the UK. 2009. [www.cancerresearchuk.org/cancer-info/cancerstats/](http://www.cancerresearchuk.org/cancer-info/cancerstats/).
- Henderson HJ. Why lesbians should be encouraged to have regular cervical screening. *J Fam Plann Reprod Health* 2009;35:49-52.
- Royal College of Obstetricians and Gynaecologists. Faculty of Sexual and Reproductive Healthcare clinical guidance. Management of unscheduled bleeding in women using hormonal contraception. 2009. [www.fsrh.org/pdfs/UnscheduledBleedingMay09.pdf](http://www.fsrh.org/pdfs/UnscheduledBleedingMay09.pdf).
- Gallo MF, Nanda K, Grimes DA, Lopez LM, Schulz KF. 20 µg versus >30 µg estrogen combined oral contraceptives for contraception. *Cochrane Database Syst Rev* 2011;1:CD003989.
- Endrikat J, Gerlinger C, Plettig K, Wessel J, Schmidt W, Grubb G, et al. A meta-analysis on the correlation between ovarian activity and the incidence of intermenstrual bleeding during low-dose oral contraceptive use. *Gynecol Endocrinol* 2003;17:107-14.
- Hickey M, Fraser IS. Clinical implications of disturbances of uterine vascular morphology and function. *Baillieres Best Pract Res Clin Obstet Gynaecol* 2000;14:937-51.
- Szarewski A. Sisters doing it for themselves. *J Fam Plann Reprod Health Care* 2009;35:71-2.
- Oddsson K, Liefels-Fischer B, Wiel-Masson D, de Melo NR, Benedetto C, Verhoeven CHJ, et al. Superior cycle control with a contraceptive vaginal ring compared with an oral contraceptive containing 30 mcg ethinylestradiol and 150 mcg levonorgestrel: a randomized trial. *Hum Reprod* 2005;20:557-62.
- Public Health England. Colposcopy and Programme Management. Guidelines for the NHS cervical screening programme. No 20. 2010:15-6. [www.cancerscreening.nhs.uk/cervical/publications/nhsfsp20.html](http://www.cancerscreening.nhs.uk/cervical/publications/nhsfsp20.html).
- Public Health England. Clinical practice guidance for the assessment of young women aged 20-24 with abnormal vaginal bleeding. 2010. [www.cancerscreening.nhs.uk/cervical/publications/doh-guidelines-young-women.html](http://www.cancerscreening.nhs.uk/cervical/publications/doh-guidelines-young-women.html).
- National Institute for Health and Care Excellence. Referral guidelines for suspected cancer. CG27. 2005. <http://publications.nice.org.uk/referral-guidelines-for-suspected-cancer-cg27/guidance>.
- AAGL Practice Report. Practice guidelines for the diagnosis and management of endometrial polyps. *Journal of Minimally Invasive Gynaecology* 2012;19:3-10.
- Farquhar C, Ekeroma A, Furness S, Arroll B. A systematic review of transvaginal ultrasonography and hysteroscopy for the investigation of abnormal uterine bleeding in premenopausal women. *Acta Obstet Gynaecol Scand* 2003;82:493-504.
- Critchley HO, Warner P, Lee AJ. Evaluation of abnormal uterine bleeding: comparison of 3 outpatient procedures within cohorts defined by age and menopausal status. *Health Technol Assess* 2001;8:iii-iv, 1-139.
- National Institute for Health and Care Excellence. Heavy menstrual bleeding: investigation and management. CG44. 2007. [www.nice.org.uk/CG44](http://www.nice.org.uk/CG44).
- ESHRE Capri Workshop Group. Endometrial bleeding. *Hum Reprod Update* 2007;13:421-31.
- Lumsden MA. Modern management of fibroids. *Obstet Gynaecol Reprod Med* 2009;20:82-6.
- Donnez J, Tatarchuk T, Bouchard P, Puscasiu L, Zakharenko N, Ivanova T, et al. Ulipristal acetate versus placebo for fibroid treatment before surgery. *N Engl J Med* 2012;366:409-20.
- Gupta JK, Sinha A, Lumsden MA, Hickey M. Uterine artery embolisation for uterine fibroids. *Cochrane Database Syst Rev* 2012;5:CD005073.

**Box 3 Treatments for fibroids***Medical*

- Drugs that decrease oestrogen levels
- Gonadotrophin releasing hormone agonists (given subcutaneously or intramuscularly)
- Drugs that block progesterone
- Progesterone receptor modulators, such as ulipristal
- Progestogens may be used if the cavity is normal

*Surgical*

- Myomectomy, which may be performed by the open, laparoscopic, or combined laparoscopic and vaginal routes
- Small intracavity fibroids (<5 cm in diameter) can be removed by hysteroscopic resection; if larger, a gonadotrophin releasing hormone agonist or progesterone receptor modulator may be used to shrink the fibroid before removal
- Intramural or subserosal fibroids are removed abdominally
- Uterine artery embolisation is associated with relief of menstrual disorder and fibroid shrinkage
- High intensity focused ultrasound (guided by magnetic resonance imaging) is a precise treatment but is available in only a few centres

**Box 4 Options for managing unscheduled bleeding in users of progestogen only contraception***Progestogen only pill*

- No evidence that changing type or dose of pill (including desogestrel containing pills) improves the bleeding pattern
- No evidence that taking two types of progestogen only pill improves bleeding
- A non-steroidal anti-inflammatory drug (such as mefenamic acid 500 mg three times daily) may shorten the duration of the bleeding episode

*Subdermal implant and levonorgestrel releasing intrauterine system*

- Give a three month course of combined oral contraceptive (containing 30-35 µg ethinylestradiol), either continuously or in usual cyclical regimen. This can be repeated as often as needed
- A non-steroidal anti-inflammatory drug (such as mefenamic acid 500 mg three times daily) may shorten the duration of the bleeding episode

*Injectable preparations*

- No evidence that reducing the injection interval improves bleeding
- Give a three month course of combined oral contraceptive (containing 30-35 µg ethinylestradiol), either continuously or in usual cyclical regimen. This can be repeated as often as needed
- A non-steroidal anti-inflammatory drug (such as mefenamic acid 500 mg three times daily) may shorten the duration of the bleeding episode

**Tips for non-specialists**

- Perform a speculum examination and pelvic examination to exclude an obvious cervical or pelvic abnormality. Examination should not be deferred because of bleeding at the time of consultation because this can delay the diagnosis
- Do not wait for the results of a cervical smear before referral of a woman with suspected cervical cancer
- Irregular bleeding in the first three to six months of hormonal contraceptive use is to be expected and the woman should be warned about this
- Endometrial biopsy should be performed in women over 45 years with intermenstrual bleeding even in the presence of normal ultrasound findings and in younger women with persistent symptoms or risk factors for endometrial cancer

**Additional educational resources***Resources for healthcare professionals*

- NHS Cervical Screening Programme (<http://www.cancerscreening.nhs.uk/cervical/>)—Contains advice on onward referral to a gynaecologist or a colposcopy clinic for women with abnormal vaginal bleeding
- National Institute for Health and Care Excellence ([www.nice.org.uk/nicemedia/live/11514/32743/32743.pdf](http://www.nice.org.uk/nicemedia/live/11514/32743/32743.pdf))—Guidance on the use of liquid based cytology for cervical screening
- NHS ([www.cancerscreening.nhs.uk/cervical/publications/doh-guidelines-young-women.pdf](http://www.cancerscreening.nhs.uk/cervical/publications/doh-guidelines-young-women.pdf))—Specific recommendations for the assessment of young women aged 20-24 with abnormal vaginal bleeding
- National Institute for Health and Care Excellence ([www.nice.org.uk/CG027](http://www.nice.org.uk/CG027))—Information for GPs on appropriate referral for women with symptoms suggestive of cancer

*Resources for patients*

- Jo's Cervical Cancer Trust ([www.jostrust.org.uk/](http://www.jostrust.org.uk/))—UK charity providing information and support for women with regard to cervical abnormalities and cervical cancer
- Cancer Help UK ([cancerhelp.cancerresearchuk.org/](http://cancerhelp.cancerresearchuk.org/))—Patient information resource from Cancer Research UK

- 32 Abdel-Aleem H, d'Arcangues C, Vogelsong K, Gulmezoglu AM. Treatment of vaginal bleeding irregularities induced by progestin only contraceptives. *Cochrane Database Syst Rev* 2007;4:CD003449.
- 33 Hickey M, Higham H, Fraser I. Progestogens with or without oestrogen for irregular uterine bleeding associated with anovulation. *Cochrane Database Syst Rev* 2012;9:CD001895.
- 34 Orbo A, Arnes M, Hancke C, Vereide AB, Pettersen I, Larsen K. Treatment results of endometrial hyperplasia after prospective D-score classification—a follow-up study comparing effect of LNG-IUD and oral progestins versus observation only. *Gynecol Oncol* 2008;111:68-73.
- 35 WHO. Selective practice recommendations for contraceptive use. 2nd ed. 2004. Updated 2008. [www.who.int/reproductivehealth/publications/family\\_planning/9241562846index/en/index.html](http://www.who.int/reproductivehealth/publications/family_planning/9241562846index/en/index.html)

Cite this as: *BMJ* 2013;346:f3251

© BMJ Publishing Group Ltd 2013

## Table

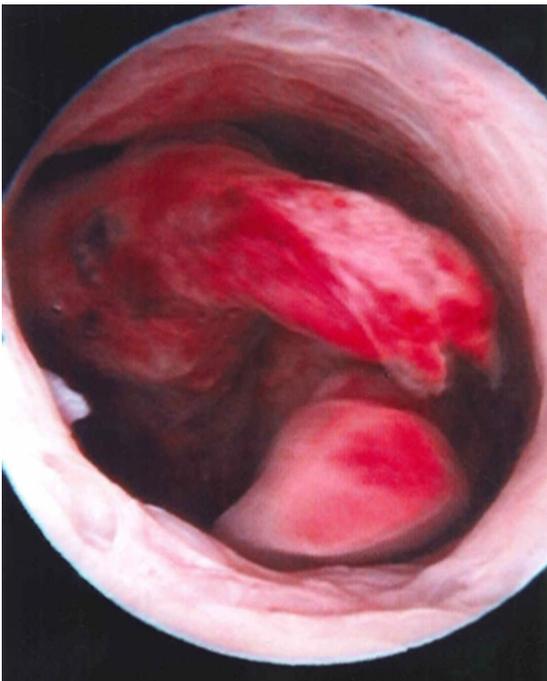
**Table 1 | Expected bleeding patterns in women using various contraceptive methods<sup>14</sup>**

Contraceptive method	Bleeding patterns in the first 3 months of use	Longer term bleeding patterns
Combined hormonal contraception (oral, transdermal patch, or vaginal ring)	20% of combined oral contraception users will have irregular bleeding; no significant differences between pill or patch use	Bleeding usually settles; ovarian activity is effectively suppressed
Progestogen only pill	A third of women have a change in bleeding and 1 in 10 has frequent bleeding	Bleeding may not settle with time because ovarian activity is incompletely suppressed; 10-15% of users are amenorrhoeic; 40-50% have a regular bleed; 30-40% have irregular bleeding
Progestogen only injectable preparation	Bleeding disturbances (spotting, light, heavy or prolonged bleeding) are common; 34-35% are amenorrhoeic at 3 months	70% of users are amenorrhoeic at 1 year
Progestogen only implant	Bleeding disturbances are common	20% are amenorrhoeic; 50% have infrequent, frequent, or prolonged bleeding, which may not settle with time
Levonorgestrel releasing intrauterine system	Irregular, light, or heavy bleeding is common (in the first 6 months)	65% have amenorrhoea or reduced bleeding at 1 year; a 90% reduction in menstrual blood loss has been shown over 12 months of use
Copper intrauterine contraceptive device	Spotting, light bleeding, heavier, or prolonged episodes of bleeding are common in the first 3-6 months	Bleeding patterns tend to improve after the first few months, but periods generally continue to be slightly heavier with more days of light bleeding and spotting compared with non-users
Barrier methods (condoms) and female barriers (diaphragm, condoms, cervical caps)	Unchanged	Unchanged

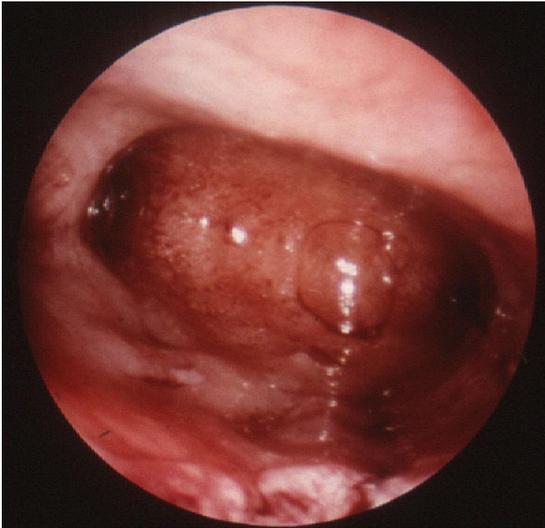
## Figures



**Fig 1** Hysteroscopic view of the endometrial cavity showing a submucous fibroid; provided with permission by Adam Magos, consultant gynaecologist, Royal Free Hospital, London



**Fig 2** Hysteroscopic view of the endometrial cavity showing an endometrial polyp; provided with permission by Susan Milne, Royal Infirmary, Edinburgh



**Fig 3** Hysteroscopic view of a normal endometrial cavity; provided with kind permission by Adam Magos, consultant gynaecologist, Royal Free Hospital, London



**Fig 4** Hysteroscopic view of the endometrial cavity in a patient with endometrial cancer; provided with kind permission by Adam Magos, consultant gynaecologist, Royal Free Hospital, London