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Intermenstrual and postcoital bleeding

Intermenstrual bleeding (IMB) refers to vaginal bleeding (other than postcoital) at any time during the menstrual cycle other than during normal menstruation. It can sometimes be difficult to differentiate true IMB bleeding from metrorrhagia (irregularly frequent periods).

Postcoital bleeding (PCB) is non-menstrual bleeding that occurs immediately after sexual intercourse.

Breakthrough bleeding is irregular bleeding associated with hormonal contraception.

IMB and PCB are both *symptoms*, rather than diagnoses, and warrant further assessment. They occur commonly and lead to worry in women and their doctors as they can be symptoms of cancer, although cancer is not the cause in most cases. Whilst genital tract malignancy is an uncommon cause of bleeding and a rare cause in young women, it must be considered in all patients.

The International Federation of Gynecology and Obstetrics (FIGO) proposed systems for terminology for normal and abnormal uterine bleeding (AUB) in the reproductive years in 2011, and updated this in 2018 ^[1]. The FIGO recommendation is that older terms such as oligomenorrhoea, menorrhagia, and dysfunctional uterine bleeding, for which there are no standard definitions, be discarded in favour of using simple terms to describe the nature of the abnormal uterine bleeding. It describes parameters for normal duration/frequency/loss, etc, and the 2018 update included the intermenstrual bleeding category. These relate only to bleeding coming from the uterus.

Epidemiology

 Around 14% of pre-menopausal women experience irregular or excessively heavy menstrual bleeding ^[2].

- It has been estimated that in those women who present to primary care with menstrual problems, around one third will have IMB or PCB in addition to heavy menstrual loss [3].
- Prevalence of PCB ranges from 0.7% to 9% of menstruating women [4].
- The two-year cumulative incidence of IMB has been shown to be 24% and that of PCB was around 8% in one UK-based study of perimenopausal women ^[5]. Rates of spontaneous resolution were 37% and 51% respectively and association with malignancy was weak.
- Unscheduled bleeding causes anxiety and concern because it can be a presenting symptom for gynaecological cancer.

Aetiology

The causes of abnormal bleeding typically vary with age and a malignant cause is very uncommon in younger women. In addition, the likelihood of uterine polyps and fibroids increases with age.

Many women will present with a combination of PCB and IMB.

Causes of PCB

- Infection.
- Cervical ectropion especially in those women taking the combined oral contraceptive (COC) pill.
- Cervical or endometrial polyps.
- Vaginal cancer.
- Cervical cancer usually apparent on speculum examination.
- Trauma or sexual abuse.
- Vaginal atrophic change.

NB: no specific cause for bleeding is found in about 50% of women [6].

Causes of IMB

- Pregnancy-related, including ectopic pregnancy and gestational trophoblastic disease.
- Physiological:
 - Vaginal spotting may occur at around the time of ovulation.
 - Hormonal fluctuation during the perimenopause (this should be a diagnosis of exclusion).
- Vaginal causes:
 - Adenosis.
 - Vaginitis (bleeding uncommon before the menopause).
 - Tumours.
- Cervical causes:
 - Infection chlamydia, gonorrhoea.
 - Cancer (but bleeding is most often postcoital).
 - Cervical polyps.
 - Cervical ectropion.
 - Condylomata acuminata of the cervix.
- Uterine causes:
 - Fibroids (occur in over 25% of women of reproductive age).
 - Endometrial polyps.
 - Cancer (endometrial adenocarcinoma, adenosarcoma and leiomyosarcoma).
 - Adenomyosis (usually only symptomatic in later reproductive years).
 - Endometritis.
- Oestrogen-secreting ovarian cancers.

- latrogenic causes:
 - Tamoxifen.
 - Following smear or treatment to the cervix.
 - Missed oral contraceptive pills.
 - Drugs altering clotting parameters eg, anticoagulants, selective serotonin reuptake inhibitors (SSRIs), corticosteroids.
 - Alternative remedies when taken with hormonal contraceptives
 eg, ginseng, ginkgo, soy supplements, and St John's wort.

Causes of breakthrough bleeding

Unscheduled vaginal bleeding is common when a new contraceptive method is started and often settles without intervention ^[3]. It is important to exclude pregnancy and also any underlying infection.

Bleeding problems are more common with progestogen-only methods. Smokers have a greater risk of breakthrough bleeding.

- COC pill:
 - Preparations containing 20 micrograms ethinylestradiol are more likely to be associated with breakthrough bleeding than those containing 30-35 micrograms ^[7].
 - In combination with an enzyme-inducing drug eg, rifampicin.
- Contraceptive progestogen-only pill (POP).
- Contraceptive depot injections.
- Intrauterine system (IUS) or implant.
- Emergency hormonal contraception.

Presentation

Given the wide differential for non-menstrual vaginal bleeding, a careful history and examination are paramount.

History

- Menstrual history:
 - Last menstrual period ask whether the last period was a 'normal' period.
 - Regularity and cycle length.
 - Duration of abnormal bleeding discuss prolonged versus recent change.
 - Presence of menorrhagia.
 - Timing of bleeding in the menstrual cycle.
 - Associated symptoms eg, abdominal pain, fever, vaginal discharge, dyspareunia.
 - Factors that aggravate bleeding eg, exercise, intercourse.
- Obstetric history:
 - Previous pregnancies and deliveries, including time since last delivery/miscarriage/termination.
 - Current breastfeeding.
 - Risk of current pregnancy increased, for example, with unprotected intercourse, forgotten pills or gastroenteritis.
 - Risk factors for ectopic pregnancy for example, a history of pelvic inflammatory disease or endometriosis, IVF treatment, use of an intrauterine contraceptive device (IUCD) or the POP.
- Gynaecological history:
 - Current use of contraception
 - Smears most recent test results, any previous smear abnormalities, colposcopy, treatment for abnormalities, etc.
 - Previous gynaecological investigations or surgery.

- Sexual history risk factors for sexually transmitted infection (STI) in those aged <25 years, or at any age with a new partner or more than one partner in the preceding year; past history of and treatment for STIs.
- Medical history eg, bleeding disorders, diabetes.
- Current medication (including unprescribed).

Examination

- Establish (by history and examination) that the bleeding is from the vagina, not the rectum or in the urine. Doubt could be eliminated by asking the patient to insert a tampon which will confirm presence of blood in the vagina.
- BMI high BMI is an independent risk factor for endometrial cancer.
- Abdominal examination noting the presence/absence of pelvic masses.

- PV examination (speculum and bimanual) looking for obvious genital tract pathology. Note whether any contact bleeding occurs, friability of tissue, cervical 'excitation' or tenderness, presence of ulceration, polyps or discharge and any other lower genital tract sites of bleeding. Common findings include:
 - Cervical ectropion (or erosion) appears as a red ring around the external os due to extension of the endocervical columnar epithelium over the ectocervix.
 - Cervical polyp mass arising from the endocervix, usually
 protruding through the external os into the vagina. They can be
 avulsed and sent to histology. Occasionally, endometrial polyps
 can be seen extruding through the cervix.
 - Cervicitis the cervix appears red, congested and sometimes oedematous. There may be purulent discharge and the cervix is usually tender to palpation. The most common cause of infection currently is *Chlamydia trachomatis*. *Neisseria gonorrhoeae* as a cause of cervicitis should not be forgotten. A rarer cause is *Trichomonas vaginalis* where the cervix is friable, with prominent papillae and punctate haemorrhages, and is commonly described as a 'strawberry cervix'. Herpetic cervicitis gives rise to multiple ulcerated regions.

Editor's note

Dr Sarah Jarvis, 11th February 2021

In September 2020 and again in January 2021, the National Institute for Health and Care Excellence (NICE) updated its guidance on suspected cancer recognition and referral. However, there are no changes in these updates which relate to IMB or PCB [8].

Investigations

Always exclude the possibility of pregnancy and STIs as a cause of bleeding:

- Pregnancy test have a low threshold for checking.
- Infection screen always consider STIs, in particular chlamydia, with IMB and PCB. The decision to test for N. gonorrhoeae will depend on the woman's individual sexual risk and the local prevalence of this infection.

Cervical smears should only be taken where a woman is due or overdue for her regular screening.

Blood tests may include:

- FBC.
- Clotting.
- TFT.
- FSH/LH levels (if onset of menopause is suspected).

Transvaginal ultrasound is the investigation of choice to look for structural abnormality. Ultrasound should ideally be done immediately postmenstrually, as the endometrium is at its thinnest and polyps and cystic areas tend to be more obvious. Evidence of endometrial thickening should prompt referral for biopsy.

Endometrial biopsy may be done as a surgical or clinic-based procedure, usually using the Pipelle® device.

NICE guidelines on *heavy* menstrual bleeding recommend hysteroscopy with endometrial biopsy as the investigation of choice for women with heavy menstrual bleeding with associated persisting IMB whose history is suggestive of fibroids, polyps or endometrial pathology ^[9].

For women with persistent PCB, colposcopy is often recommended because of its high sensitivity [10].

Who needs referral?

- Women with an abnormal-looking cervix suspicious of cervical cancer should have an urgent referral under the two-week wait pathway^[8].
- Women with a cervical polyp that is not easily removed in primary care or that looks suspicious.
- Women with a pelvic mass found on examination or a significant abnormality on ultrasound scan.
- Women at high risk of endometrial cancer:
 - Those with a family history of hormone-dependent cancer.
 - Those with prolonged and irregular cycles.
 - Those women taking tamoxifen.
- Women aged 45 years or over with IMB and women aged under 45 years with persistent symptoms or risk factors for endometrial cancer.
- Women with no cause found on examination for postcoital bleeding.

NB: bleeding of more than three months' duration, particularly when heavy, will require further evaluation.

Management

Management is dependent on the cause of the bleeding.

Suspected cancer

If gynaecological cancer is suspected, refer urgently for investigation. The most recent guidelines from NICE consider referral for postmenopausal bleeding rather than pre-menopausal abnormal bleeding as a sign of cancer ^[8]. Other than a finding of an appearance of the cervix that is suggestive of cancer, there are no recommendations in terms of referral for suspected cancer with regard to this kind of abnormal bleeding. Always bear in mind malignancy as a possible cause however.

Infection

- Antibiotic treatment will depend on the organism involved and local patterns of sensitivity.
- Contact tracing and treatment of sexual partners should be initiated.
- Electrocautery of secondarily infected Nabothian follicles is sometimes performed for chronic cervicitis.

Hormonal contraception [11]

- Warn women that unscheduled bleeding in the first three months
 after starting a new hormonal contraceptive method is common.
 This commonly continues to at least six months with the LNG-IUS and
 progestogen-only implants.
- A pregnancy test is advised in all women using hormonal contraception who have problematic bleeding. Those at risk of STIs should have chlamydia testing as a minimum and others considered.
- Check the method is being used correctly, and that there are no interacting medicines or absorption-altering illnesses.
- Examination may not be required provided there are no risks of STI, the woman's cervical smear is up to date, there are no concurrent symptoms and the hormonal contraception was started less than three months ago.
- For persistent bleeding beyond the first three months' use, or where there is a change in bleeding pattern, or where a woman has not participated in a National Cervical Screening Programme, a speculum examination should be performed.
- In women ≥45 with problematic bleeding on hormonal contraception lasting more than three months, or with a change in bleeding pattern on hormonal contraception, an endometrial biopsy should be considered. Women under the age of 45 who have risk factors for endometrial cancer should also be considered for an endometrial biopsy.

Strategies for treating unscheduled bleeding in those using hormonal contraception:

- For COC pill users:
 - Stick with the same pill for a trial of at least three months, as bleeding may settle.
 - Use a pill with a dose of ethinylestradiol sufficient to provide the best cycle control - consider increasing to a maximum of 35 micrograms.
 - A different COC pill may be tried, with a different dose of ethinylestradiol or a different dose or type of progestogen.
- For contraceptive POP users:
 - A different POP may be tried (although there is no evidence that changing the progestogen type or increasing the dose improves bleeding).
 - There is no evidence that desogestrel-only pills (eg, Cerazette®) have better bleeding patterns than traditional POPs.
 - There is no evidence that doubling to two pills per day improves bleeding.
- For progestogen-only implants, depots and IUS users:
 - A first-line COC pill (with 30-35 micrograms ethinylestradiol and LNG or norethisterone) may be considered for up to three months continuously or in the usual cyclical regimen. This can be repeated as often as needed.
 - There is no evidence that reducing the injection interval for depot progestogen injections improves bleeding, but the injection can be given from 10 weeks after the last one.
 - Mefenamic acid or tranexamic acid can be used to reduce the duration of bleeding for women, but have no long-term benefit.

Cervical ectropions

 These may resolve spontaneously if the COC pill is stopped, or following pregnancy.

- They can be treated conservatively or cauterised with silver nitrate.
- Other treatment options include thermal cautery and diathermy, cryosurgery, laser or microwave therapy.

Cervical and endometrial polyps

- Cervical polyps should be avulsed and sent for histology.
- A systematic review and meta-analysis found that the incidence of cancer within an endometrial polyp in women of reproductive age was only 1.7%, compared with 5.4% in postmenopausal women [12].

Fibroids

- Small fibroids can be removed hysteroscopically.
- Uterine artery embolisation can be effective.
- Medical management includes using drugs that reduce oestrogen levels.
- Women with larger fibroids can be treated with drugs, vascular embolisation, surgery, or a combination of these methods, with good resolution of their bleeding disorder.

NB: there is a high rate of spontaneous resolution of intermenstrual and postcoital bleeding in naturally menstruating women during the perimenopausal years. As mentioned earlier, one study demonstrated that the rates of spontaneous resolution without recurrence for two years were 37% for women with IMB and 51% in those with PCB ^[5].

Further reading

• Davis E, Sparzak PB; Abnormal Uterine Bleeding (Dysfunctional Uterine Bleeding)

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