# Intermenstrual and postcoital bleeding

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**Abstract**

Unexpected vaginal bleeding, whilst responsible for much anxiety amongst women, is rarely associated with any serious underlying pathology. Nevertheless, bleeding which occurs spontaneously in between menses or after intercourse is recognised as a 'red flag' symptom for gynaecological cancer. Infection, hormonal fluctuations, benign cervical and endometrial conditions are, however, more common causes of abnormal bleeding. The role of the generalist clinician is to diagnose and treat uncomplicated conditions, whilst also determining the likelihood of malignancy and referring for further investigations appropriately.

**Keywords** intermenstrual bleeding; postcoital bleeding

Intermenstrual bleeding, defined as any vaginal bleeding occurring outwith normally timed menstrual periods, may affect between 13 and 21% of naturally menstruating women. The prevalence varies significantly with age: intermenstrual bleeding is more frequently seen in perimenopausal women. Estimates of the prevalence of postcoital bleeding, which is vaginal bleeding provoked by intercourse, vary between 5 and 10% of naturally menstruating women. Postcoital bleeding does not appear to be related to age.

The positive predictive value of these 'red flag' symptoms is low. Of those who present to their GP with postcoital bleeding, only 1 in 44,000 women aged 20–24 and 1 in 2400 women aged 45–54 will have cervical cancer. Rates of endometrial cancer in women with intermenstrual bleeding, given the higher prevalence of this symptom, is even lower.

The majority of women with intermenstrual or postcoital bleeding will have a benign cause for their symptoms. These can be categorised broadly by the anatomical source of their bleeding (i.e. uterine, cervical, vaginal) and/or by cause (i.e. structural, infection, ovulatory dysfunction, iatrogenic, coagulopathy). This review aims to provide an outline of how to approach the management of a woman presenting with intermenstrual or postcoital bleeding and illustrate this using four clinical scenarios.

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## Who should be referred?

Given the rarity of malignancy in women with intermenstrual or postcoital bleeding, it is impractical to refer all women for investigations. A thorough history and examination should be performed to elicit risk factors and signs which may indicate pathology. The history should cover the patient's age, the duration, nature and frequency of symptoms, any associated features (including pain, bloating, changes in vaginal discharge, bleeding from other sites) menstrual history, contraceptive and other hormonal therapy use, smear history, past medical history, current medications (especially anticoagulants), family history and sexual history. Examination must include abdominal and pelvic examination to assess for uterine and pelvic masses and tenderness. Speculum examination will allow inspection of the ectocervix for evidence of cervicitis, ectropion, polyps or suspicious lesions. The assessment of such lesions will include assessing their propensity to bleed on contact and allow the clinician to take microbiological swabs.

### Case 1

A 20 year old woman presents to her GP with intermenstrual spotting and postcoital bleeding. She started a new relationship 6 months ago. She has not been using hormonal contraception and admits to having unprotected intercourse with her partner. Her mother was diagnosed with cervical cancer in her 30's after presenting with similar symptoms.

1 in 600 women between 20 and 24 will present with postcoital bleeding every year. Less than 1% will present per year with intermenstrual bleeding. It is firstly important to exclude pregnancy in any woman of reproductive age presenting with unscheduled bleeding. Approximately 1 in 6 pregnancies are unplanned, which equates to 1 in 60 women having an unplanned pregnancy each year. A woman is much more likely to bleed during early pregnancy than outside of pregnancy. Up to a quarter of pregnant women will report bleeding during the first trimester. Threatened miscarriage is common but there should also be a low index of suspicion for ectopic pregnancy.

This patient can be reassured that the likelihood of her bleeding being associated with cervical cancer is extremely low given her age. In 99.7% of cases cervical cancer is preceded by infection with human papillomavirus (HPV). Infection with HPV is the most common sexually transmitted infection, affecting approximately 70% of all women in their lifetime. The term HPV describes a group of approximately 150 small, non-enveloped DNA viruses. Over 40 subtypes have been associated with transmission through skin-to-skin contact during oral, anal and vaginal intercourse. These subtypes are classified as low risk and high risk depending on their oncogenic potential. Low risk HPVs, such as HPV 6 and 11, are associated with the development of genital warts. High risk HPVs, such as HPV 16 and 18 account for over 70% of all cervical cancers. Acute infection with high risk HPV is asymptomatic for the majority of women. Most women will clear the infection. Persistence of HPV DNA may lead to the development of cancer. Transformation of the cervical epithelium requires the integration of the viral genome into host DNA.

The latent period between initial infection and the development of cervical cancer is variable. The median latency period is estimated to be between 7 and 12 years with HPV 16. There are two peaks in age specific incidence of cervical cancer. The early peak, between 30 and 34, is associated with women becoming sexually active in their late teens and early twenties. The second is between 80 and 84.

The risk of cervical cancer in a woman whose mother or sister has had cervical cancer is twice that of a woman who has no family history of cervical cancer. Specific gene mutations only confer a slightly increased risk of cervical cancer. Much of the increased risk may, instead, be attributed to shared environmental factors between mother and daughter.

The number of women between 20 and 24 who develop cervical cancer is less than 50 per year in the UK. The recent introduction of HPV vaccination of girls aged 12–13 in the UK will reduce this further. In 2008, the immunisation programme comprised three doses of the bivalent HPV vaccine, Cervarix, which protects against HPV 16 and 18. A catch-up programme, offering immunisation to girls up to age 18 (i.e. those born on or after 1st September 1990), ran for 3 years until 2011. From September 2012, Cervarix was replaced by Gardasil, a quadrivalent vaccine, which protects against HPV 6 and 11, as well as HPV 16 and 18. A phase III clinical trial showed that Gardasil prevented 98% of persistent infections and cervical intraepithelial neoplasia (CIN) caused by HPV 16 and 18. Gardasil also prevents genital warts and may provide protection against neoplasia caused by other subtypes of HPV and from neoplasia at sites other than the cervix. Nonetheless, if examination reveals suspicious findings, the patient should be referred to colposcopy and not offered a smear test.

Bleeding in this case is much more likely to follow acute infection with other sexually transmitted organisms, particularly those causing cervicitis. Examination and collection of microbiological specimens for diagnosis are essential in this patient's management. Chlamydia is the commonest bacterial sexually transmitted cause of cervicitis. It is estimated to affect 3–7% of women under the age of 24. Risk factors for infection include: age under 25, a new sexual partner, more than one sexual partner in the preceding year and inconsistent use of barrier contraception. However, 70% of women with chlamydia are asymptomatic. Where symptoms occur, post-coital and intermenstrual bleeding, abnormal vaginal discharge, abdominal pain, dysuria and dyspareunia may be reported. Untreated infections persist for more than a year in over 50% of people, but 95% of infections will be cleared spontaneously over 4 years. Between 10 and 40% of untreated individuals will develop pelvic inflammatory disease.

Chlamydia can be detected using nucleic acid amplication techniques (NAATs) either from swabs or urine. Self-taken lower vaginal swabs are as sensitive as cervical swabs for detecting chlamydia. Both techniques are more reliable than a first-void urine sample. First line treatment for women with suspected or confirmed chlamydial infection is a 7-day course of doxycycline or a single 1 g dose of azithromycin. The latter is preferred where compliance is of concern. During this 7-day window, women should be advised to abstain from intercourse. Patients should be referred to Genitourinary medicine (GUM) for screening for other STIs and for partner notification. Test of cure is not usually required if first line treatment is used.

Gonorrhoea remains an important, but slightly less common cause of postcoital and intermenstrual bleeding. Gonorrhoeal infection co-exists with chlamydial infection in 41% of cases. It is asymptomatic in up to 50% of cases. The most common symptom when present is a change in vaginal discharge. Frequently on examination no abnormal findings are seen. Mucopurulent endocervical discharge is seen in less than 50% of women with gonorrhoea, but when present predicts an infection in 40% of cases. Detection is using NAATs in either vaginal or endocervical swab specimens. In contrast to the diagnosis of gonorrhoea in men, microscopy is not recommended due to low sensitivity. Urine specimens for NAATs are also not recommended for the diagnosis of gonorrhoea for similar reasons. First line treatment for women with gonorrhoea is with a single intramuscular dose of ceftriaxone 500 mg and a 1 g oral dose of azithromycin. Treatment with a high dose extended spectrum cephalosporin combined with azithromycin irrespective of the results of chlamydia testing has been proposed to try to limit the growing resistance and decreasing sensitivity to antibiotics of gonorrhoea in the UK. Test of cure is also now recommended to identify emerging resistance. A swab should be sent for NAATs two weeks following the completion of antibiotic therapy. If the specimen is positive, a further sample should be sent for culture. Untreated women are at risk of spread of the infection to the pelvis leading to pelvic inflammatory disease, tubo-ovarian abcesses, infertility and chronic pelvic pain or systemically leading to perihepatitis (Fitz-Hugh Curtis Syndrome) or disseminated gonococcal infection, which may present as skin lesions or a reactive arthritis (Reiter's syndrome). Given growing resistance, treatment and follow up should be within a GUM setting.

*N. gonorrhoeae* also commonly co-exists with other pathogens, such as *Trichomonas vaginalis* and *Candida albicans*. Infection with these organisms are rarer causes of postcoital bleeding. Bleeding is as a result of vulvovaginitis. Trichomonas is a protozoan which can infect the vagina, urethra, and paraurethral glands in women. It presents with a range of nonspecific symptoms including vaginal discharge, vulval itch, dysuria and abdominal pain. Up to 70% will have increased vaginal discharge. Classical signs of a frothy yellow discharge and a strawberry cervix are seen in 10–30% and 2% of patients respectively. Vulvovaginitis may also be apparent. NAATs are becoming rapidly adopted in place of culture as the gold standard for diagnosis. NAATs offer the highest level of sensitivity and can often be done on the same platform as NAATs for chlamydia and gonorrhoea. As trichomonas infects multiple sites in women, systemic rather than vaginal antibiotics are recommended. First line treatment is either with a single 2 g oral dose of metronidazole or 400 mg twice daily for 5–7days. Test of cure is not required unless symptoms persist.

Severe vulvovaginitis secondary to *Candida* can lead to bleeding as a result of excoriation, fissuring and oedema. These signs are usually accompanied by vulval itch, discharge, soreness and superficial dyspareunia. Severe vulvovaginitis is uncommon. Up to 10–20% of women in the reproductive age group will be colonised with *Candida* species. These asymptomatic women do not require treatment. Severe and recurrent symptoms are more common in women with diabetes or those who are immunocompromised. Severe vulvovaginitis can be treated with either extended topical therapy (10–14 days) or oral fluconazole 150