

ABNORMAL UTERINE BLEEDING IN THE NON-PREGNANT STATE

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Bleeding in the non-pregnant state may occur at the time of an expected menstrual period, between periods (intermenstrual bleeding; IMB), after intercourse (postcoital bleeding; PCB) or following the menopause (postmenopausal bleeding; PMB). Menopause is diagnosed in women who have not had a menstrual period after 12 months without the use of hormonal contraception. Vaginal bleeding may also occur after surgical instrumentation of the uterus and/or cervix, including insertion of an IUCD. The principal causes of uterine and vaginal bleeding in the non-pregnant state can be divided into structural and non-structural causes (Table 87.5) and their relationship to menses or coitus (Table 87.6). The mainstay of management is to identify and treat the associated pathology . Investigations include a pregnancy test and ultrasound assessment of the pelvic anatomy (two dimensional/three-dimensional ultrasound scan or saline the uterine sonogram) as well as an endometrial biopsy of cavity , performed either under direct vision at hysteroscopy or ® biopsy . Hysteroscopy combined with blindly with a Pipelle endometrial biopsy improves the sensitivity and specificity for detection of endometrial pathology compared with either performed alone (Figure 87.18). The indications for undertaking an endometrial biopsy are shown in Summary box 87.2 . A colonoscopy may also be indicated to exclude colorectal pathology as a potential cause for the bleeding. - Women taking tamoxifen, a selective oestrogen receptor modulator used in the treatment of breast cancer, represent a special group as the drug can induce uterine abnormalities in endometrial 10–40% of women, such as the development of polyps, hyperplasia, cancer and, rarely , uterine sarcomas, which are much more aggressive. Tamoxifen treatment results in a doubling of the risk of endometrial cancer after 1–2 years and has a quadrupling effect after 5 years. The relationship is time dependent but dose independent. The risk does not decrease on cessation of treatment. There is no consensus regarding the need for screening and which method to use; the alternative, more common approach is to investigate only those women who develop abnormal uterine bleeding with tamoxifen use. Aromatase inhibitors such as anastrozole, letrozole and exemestane are also used in the treatment of breast cancer, but their effects are not mediated via the oestrogen receptor tied with less endometrial pathology so they have been associated with less endometrial pathology than tamoxifen. They may also reverse abnormalities induced by tamoxifen use.

Figure 87.16 Ultrasound features of adenomyosis. Anechogenic myometrial tissue with acoustic shadowing posterior to it (arrow). Figure 87.17 Ultrasound features of adenomyosis. Fan-shaped

shadowing (arrow).

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Indications for an endometrial biopsy /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF
/uni25CF /uni25CF /uni25CF /uni25CF /uni25CF Erik Adolf von Willebrand , 1870–1949, physician,
Helsinki, Finland. Henry T Lynch , 1928–2019, Professor of Preventative Medicine, Creighton
University , Omaha, NE, USA, discovered familial susceptibility to certain kinds of cancer. Women
known to have Lynch syndrome (hereditary non - polyposis colorectal cancer) and those considered
at risk of inheriting a mismatch repair gene abnormality are another special group, as their lifetime
risk of developing endometrial cancer is as high as 60%. Unlike sporadic cases of endometrial
cancer, which are usually diagnosed during the sixth and seventh decades, the mean age at
diagnosis in Lynch syndrome is the fifth decade. However, it appears that the 5-year survival rate
in patients with Lynch syndrome-associated endometrial cancer is similar to that in women with
sporadic disease. International guidelines suggest that these women should be screened annually
from the age of 35 years with transvaginal ultrasound to measure the endometrial thickness and
an endometrial biopsy . Abnormal bleeding can also be caused by invasive carcinoma of the
cervix, the incidence of which has been reduced by screening programmes that aim to detect the
precancerous state, cervical intraepithelial neoplasia (CIN), using cervical cytology . The sample is
checked for high-risk serotypes of human papilloma virus (HPV) (16, 18, 31 and 33) that can cause
changes to the cervical cells. If these types of HPV are not identified on the sample, then no further
action is required. If, however, these high-risk HPV serotypes are identified, the sample is checked
for cervical cell changes, with the aim of treating these before they get a chance to turn into
cervical cancer. In the UK, this is carried out every 3 years in women aged 25–49 years, and every
5 years in women aged 50–64 years. In women aged 65 years or older, a cervical screen will be
conducted if one of the last three tests was abnormal or no test had been performed since the age
of 50 years. Abnormalities in cervical cytology are followed up by microscopic examination of the
cervix (colposcopy). CIN may be treated with local ablation (cryocautery , cold coagulation,
electrocoagulation or laser) or excision (large loop excision of the transformation zone [LLETZ]).

uterine and vaginal bleeding.
Structural Endometrial or
endocervical polyp Fibroids
(leiomyoma) Endometrial
hyperplasia Malignancy of the

genital tract Non

Endometriosis structural Adenomyosis Coagulopathy, e.g. thrombocytopenia, von Willebrand's disease Ovulatory dysfunction, e.g. polycystic ovary syndrome Endometrial, e.g. endometritis Iatrogenic, e.g. exogenous sex steroid administration, IUCD, hormonal contraceptive use Other, e.g. arteriovenous malformations, chronic renal/hepatic disease IUCD, intrauterine contraceptive device. TABLE 87.6 Uterine and vaginal bleeding in the non-pregnant state in relation to menstrual bleeding. a Menstrual Endometrial polyp/malignancy Fibroids a Intermenstrual Vaginal trauma/malignancy Cervical polyp/malignancy a Endometrial polyp/malignancy a Postcoital Vaginal malignancy Cervical ectropion/polyp/malignancy a These cancers occur principally in postmenopausal women. Endometrial biopsy should be considered in the following cases: Women with suspected endometrial pathology All women >45 years old in whom medical treatment has been unsuccessful Women with persistent intermenstrual bleeding Endometrial thickness >4 mm in postmenopausal women or persistently thickened or abnormal appearance of the endometrium in premenopausal women and endometrial thickness >7 mm in women with known polycystic ovarian syndrome Irregular or unscheduled bleeding while on hormone replacement therapy after the initial 3 months Younger women with major risk factors for endometrial hyperplasia/cancer: Polycystic ovarian syndrome Obesity Treatment with tamoxifen Irregular bleeding while on unopposed oestrogen Irregular bleeding in high-risk populations, such as family history of endometrial/colon cancer, especially hereditary non-polyposis colorectal cancer Figure 87.18 Hysteroscopic biopsy of endometrial cancer (cystic endometrium is visible at hysteroscopy).

Cervical cancer is one of the leading causes of mortality in the world. To improve the uptake of the cervical screening programme, testing for HPV in the comfort of a woman's own home is being investigated. Current vaccination programmes against HPV serotypes are aimed at reducing the incidence of cervical carcinoma. In the UK, the vaccination is currently offered to girls and boys aged 12–13 years with a repeat dose offered 6–24 months later, prior to becoming sexually active. The vaccine helps protect against mouth, throat, anal and genital cancers as well cervical cancer. Menstrual bleeding may be excessively heavy, irregular or frequent in the absence of pathology; this is known as dys-functional uterine bleeding. NICE guidance in the UK has suggested a three-step hierarchical treatment approach to the management of heavy menstrual bleeding (Table 87.7).

Investigations TVUS has high sensitivity and specificity; MRI may be indicated if the women declines Radiological imaging a TVUS or the findings are unclear. Identification of potential pathology such as polyps, fibroids Hysteroscopy and histology Direct visualisation of pathology with guided samples taken for histopathology Management Medical management Tranexamic acid, NSAIDs (off-label use) Oestrogen suppression with hormonal treatments (i.e. levonorgestrel IUS [after 1 year of use, there is a 71–95% reduction in menstrual blood loss with approximately 50% of women becoming amenorrhoeic], combined oral contraceptive pill [off-label use], progestogens, i.e. desogestrel [off-label use], GnRH agonists with or without add-back hormone replacement therapy) GnRH agonists aim to shrink fibroids by inducing a hypo-oestrogenic state. This class of

drug, however, is limited by its association with a loss in bone mineral density; in addition, *leiomyomas* tend to regrow to their original size when treatment is discontinued. Ulipristal acetate (Esmya) in whom surgical procedures (including uterine *leiomyoma* embolisation) are not appropriate or have not worked. This drug should be used with caution as it has been associated with severe liver injury and liver function should be monitored during its use. Radiological interventions/minimally invasive HIFU or MRgFUS: adverse effects include abdominal pain, skin burns and leg pain treatment options secondary to thermal injury of the sciatic nerve, intestinal perforation and temporary acute renal failure. UAE involves blocking the blood supply to the *leiomyomas* using a technique in which particles are embolised into each uterine artery via an angiographic catheter (87.19). This technique has shown more value in the presence of a single large *leiomyoma* than in a multi *leiomyoma* uterus. Postembolisation syndrome is reported, which consists of pelvic pain as a result of uterine ischaemia, nausea, fever secondary to necrosis and haematoma formation at the femoral artery puncture site. In addition, complications such as those associated with radiation exposure, haemorrhage, unplanned surgery, infection, thrombosis and an age-related impairment of ovarian reserve have also been reported. Surgical management (uterus preserving) Hysteroscopic polypectomy (risks include uterine perforation; damage to surrounding organs) Transcervical resection of *leiomyomas* (complications include hyponatraemic *fluid* overload and thermal injury to surrounding structures) Myomectomy (open or laparoscopic [bleeding and damage to surrounding structures, with the risk of conversion to a hysterectomy <1% secondary to excessive bleeding. Morcellation is described in further detail in Uterine *leiomyomas* (leiomyoma) Surgical management (non-uterine Endometrial ablation/resection (risks include thermal injury to surrounding organs and preserving) *fluid* overload; not recommended in women wishing to retain their fertility). The aim of ablative methods is to reduce the menstrual bleeding by ablating the endometrium down to the basalis layer using electrical, thermal or laser energy. More than 90% of women report a reduction in menstrual blood loss without the need for further treatment at 2 years of follow-up, with 25–35% experiencing amenorrhoea. The criteria for endometrial ablation are described in Hysterectomy: a total hysterectomy is preferred over a subtotal procedure as persistence of symptoms is reported within the cervical stump (risks include damage to surrounding organs and *leiomyoma* stula formation) GnRH, gonadotropin-releasing hormone; HIFU, high-intensity focused ultrasound; IUS, intrauterine system; MRgFUS, magnetic resonance- guided focused ultrasound; MRI, magnetic resonance imaging; NSAID, non-steroidal anti-in *flammation* drug; SPRM, selective progesterone receptor modulator; TVUS, transvaginal ultrasound scan; UAE, uterine artery embolisation. ®), an SPRM, is only licensed for use in premenopausal women Figure Figure 87.20]). Surgical complications include Table 87.8

leiomyoma The management plans are individualised for the patient, taking into account concomitant symptoms and fertility requirements. A hysterectomy can be carried out by three different routes: vaginally , abdominally or laparoscopically . The route of entry is dependent on a number of factors, including: uterine size; presence of other pathology; mobility and descent of the uterus; history of previous surgery; and skill of the operating surgeon. No difference in prolapse symptoms, sexual satisfaction or pelvic pain has been reported between a total or subtotal (conservation of the cervix) hysterectomy . Furthermore, it is now recommended that the fallopian tubes are removed in conjunction with the uterine body , whether the ovaries are conserved or not. The fallopian tubes have no continued functionality following a hysterectomy but can be a potential source of malignancy if retained. Conservation or removal of the stage, presence of coexisting ovaries is dependent on the woman's pathology and/or risk

factors for malignancy .

Figure 87.19 Pre-embolisation angiogram showing catheterisation of the left uterine artery and blood supply to a large fundal /f_i broid (courtesy of Dr Mark Bratby, Consultant Vascular and Interventional Radiologist, John Radcliffe Hospital, Oxford, UK). TABLE 87.8 Criteria for endometrial ablation. Uterus <10 /uni00A0 cm in length Absence of major intrauterine pathology that would distort the uterine cavity No history of previous endometrial ablation procedures No evidence of endometritis Family is complete Figure 87.20 Laparoscopic view of a uterine fundal /f_i broid. Pedunculated Intramural submucosal Fallopian tube Uterine cavity Pedunculated Subserosal subserosal Uterus Submucosal Cervix Vagina Figure 87.21 Uterine /f_i broids.