Approach to patient with Abnormal uterine bleeding

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Abnormal uterine bleeding (AUB)

- is a common problem encountered in general practice and refers to any change in the regularity, frequency, heaviness or length of menstruation.
- Heavy menstrual bleeding (HMB) is the most common presentation of AUB.
- A careful history is vital, as women who have always experienced heavy bleeding may consider this normal.

- The classification system for abnormal uterine bleeding uses nine basic categories, separated into structural and non-structural conditions:
- (PALM-COEIN) Polyp, Adenomyosis, Leiomyoma, Malignancy–Coagulopathy, Ovulatory disorders, Endometrium, Iatrogenic and Not otherwise specified.

Classification of abnormal uterine bleeding

Abnormal rhythm

- Irregularity of cycle
- Intermenstrual bleeding
- Postcoital bleeding
- Postmenopausal bleeding

Abnormal amount

- Increased amount = heavy menstrual bleeding (previously called menorrhagia)

Combination (rhythm and amount)

- Irregular and light periods = oligomenorrhoea
- Absence of periods = amenorrhea

Key facts and checkpoints

- Up to 25% of women of reproductive age experience abnormal uterine bleeding (AUB)..
- At least 4% of consultations in general practice deal with AUB.
- There is no pathology diagnosed in 50% of women with AUB.
- The possibility of pregnancy and its complications, such as ectopic pregnancy, miscarriage (threatened, complete or incomplete), hydatidiform mole or choriocarcinoma should be kept in mind.
- A menstrual record is a useful way to recognize patterns of blood loss.
- Heavy menstrual bleeding (HMB) accounts for 25–30% of iron-deficiency anemia.
- Two common organic causes of HMB are fibroids and adenomyosis (presence of endometrium in the uterine myometrium).
- Various drugs can alter menstrual bleeding (e.g. anticoagulants, cannabis, steroids).
- The possibility of genital tract malignancy should be considered in women who present with intermenstrual bleeding (IMB), postcoital bleeding (PCB) and postmenopausal bleeding.

Defining what is normal and what is abnormal

- This feature is based on a meticulous history, an understanding of the physiology and physiopathology of the menstrual cycle and a clear understanding of what is normal.
- Most girls reach menarche by the age of 13 (range 10–16 years).
- Irregular, painful and heavy periods are more common in the first 2–3 years after menarche and during perimenopause due to a higher number of anovulatory cycles.

- Once ovulation and regular menstruation are established the cycle usually follows a predictable pattern and any deviation can be considered as abnormal uterine bleeding

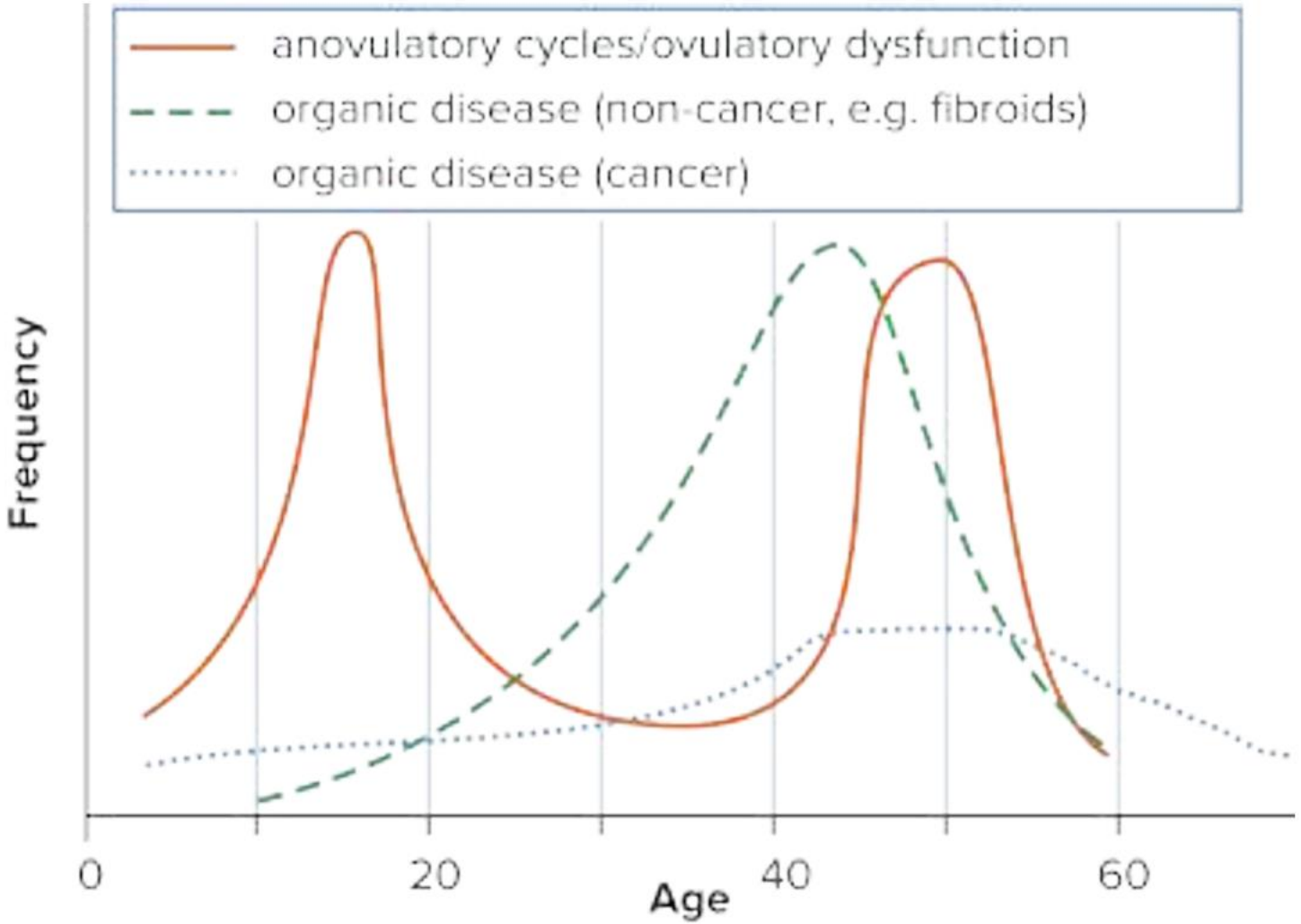
Normal menstruation in the reproductive age group

	Mean	Range
Length of cycle	26–28 days	21–35 days
Menstrual flow	3–4 days	2–7 days
Normal blood loss	30–40 mL	20–80 mL

- A normal endometrial thickness, as measured by ultrasound (best on days 4–7 of cycle), is between 6 and 12 mm in premenopausal women

- Relationship of bleeding to age Heavy menstrual bleeding (HMB) due to anovulatory cycles (ovulatory dysfunction) is more common at the extremes of the reproductive era .
- The incidence of malignant disease as a cause of bleeding increases with age, being greatest after the age of 45, while endometrial cancer is predicted to be less than 1 in 100 000 in women under the age of 35.

The relationship between age and various causes of abnormal uterine bleeding.



Heavy menstrual bleeding (HMB)

- Excessive menstrual blood loss which interferes with the woman's physical, emotional, social and material quality of life, and which can occur alone or in combination with other symptoms.
- (HMB) is the commonest cause of iron-deficiency anemia in the Western world.
- Causes of HMB are diverse and can be categorized into structural and non structural, with some women having more than one cause.
- The terms 'menorrhagia' and 'dysfunctional uterine bleeding' are no longer recommended.
- When no cause is found, the problem is considered a primary disorder of the endometrium, with disruption of mechanisms regulating endometrial hemostasis.

- The most common structural causes are leiomyomata (fibroids, 30%), endometrial polyps (10%), endometriosis, adenomyosis (‘endometriosis’ of the myometrium) and PID.
- 50% of women with HMB experience associated pain (dysmenorrhea) even in the absence of uterine pathology.
- Consider endometriosis and PID as other causes of pain with HMB.

HMB: diagnostic strategy model

Probability diagnosis

Ovulatory dysfunction

Fibroids

Complications of hormone therapy

Adenomyosis

Serious disorders not to be missed

Disorders of pregnancy:

- ectopic pregnancy
- abortion or miscarriage

NEOPLASIA

- CERVICAL CANCER.
- ENDOMETRIAL CANCER.
- Estrogen-producing ovarian tumor (cancer)
- Gestational trophoblastic disease
- Leukemia
- Benign tumors (polyps, etc.)
- Endometrial hyperplasia
- Severe infections:
- PID

Pitfalls (often missed)

- Genital tract trauma
- Copper IUD
- Adenomyosis/endometriosis
- SLE

Rarities:

- endocrine disorders (e.g. thyroid disease)
- bleeding disorder (e.g. von Willebrand disease, usually diagnosed in early
- teens)
- liver disease

- Seven masquerades checklist(COMMONLY MISSED)
- Depression (association)
- Diabetes
- Drugs
- Anemia (association)
- Thyroid disorder (hypothyroidism)
- Is the patient trying to tell me something?
- Consider associated anxiety and depression.

Important ‘not to be missed’ causes of irregular bleeding[6]

15–20	20–30	30–45	45–55	55+ (years)
Chlamydia/PID			Endometrial/ovarian cancer	
Pregnancy and pregnancy complications				
	Endometrial polyps Endometrial hyperplasia			

History

- A meticulous history should include details of the use of tampons, pads, frequency of changes and their degree of saturation.
- Ask about clotting, flooding and pain.
- A pictorial blood assessment chart can be a very useful guide.
- Enquire about contraceptive use and dyspareunia and take a sexual history.
- A history of smoking and psychosocial factors should also be checked.

- Questions need to be directed to rule out:
- Pregnancy or pregnancy complications (e.g. ectopic pregnancy)
- Trauma of the genital tract
- Medical disorders (e.g. bleeding disorder)
- Endocrine disorders
- Cancer of the genital tract
- Complications of hormonal contraception or replacement therapy(HRT)

Examination

- A general physical examination should aim at ruling out anaemia, evidence of a bleeding disorder and any other stigmata of relevant medical or endocrine disease.
- Specific examinations include:
- Speculum examination: ?ulcers (cervical cancer) or polyps
- Cervical screening test (if due)
- Abdominal examination (an enlarged fibroid uterus may be palpable)
- Bimanual pelvic examination: ?uterine or adnexal tenderness, size and regularity of uterus.

Investigations

- Abnormal pelvic examination findings, persistent symptoms, older patients and other suspicions

of disease indicate further investigation to confirm symptoms of menorrhagia and exclude pelvic or systemic pathology.

Consider foremost:

- Full blood count (to exclude anemia and thrombocytopenia)
- Iron studies: serum ferritin
- Pregnancy testing (β-hCG)

Special investigations (if indicated):

- First pass urine or vaginal swabs for STIs (chlamydia, gonorrhea, mycoplasma)
- Serum biochemical screen
- Coagulation profile screen
- Thyroid function tests, especially TSH
- Tests for SLE: antinuclear antibodies

Investigations

- Transvaginal ultrasound: should be used when structural causes are suspected, there is increased risk of malignancy or no response to 6 months of medical therapy.
- It is best performed in the first 5 to 10 days of the menstrual cycle when endometrial thickness is most easily assessed.
- An endometrial thickness >12 mm for premenopausal, ≥5 mm for perimenopausal and >4 mm in postmenopausal women requires endometrial biopsy.
- Note: Hysteroscopy and D&C remain the gold standard for abnormal uterine bleeding.

Medical and surgical management:

- Medical
- It is important to offer initial oral treatment at the first visit, even while waiting for investigations.
- Appropriate initial oral treatment is with fibrinolytic inhibitors or antiprostaglandin agents, given as soon as possible and throughout the menses.
- The agent of first choice is usually tranexamic acid, which reduces blood loss by about 50%.
- These agents are simple to use, generally very safe and can be used over long periods of time.

Table 94.5 Regimens used in management of HMB[10] (includes options)

Therapy	Mean reduction[9] in blood loss 80 mL/cycle %
52 mg levonorgestrel (LNG-IUD), Mirena	94
Oral progestogen: • norethisterone 5 mg tds on days 5–26 of cycle	83
Tranexamic acid 1 g (o) 6 hourly on days 1–4 of menstruation	47
Combined oral contraceptive pill	43
NSAIDs (oral): • ibuprofen 400 mg 3–4 times daily • naproxen 500 mg statim then 250 mg every 6–8 hours • mefenamic acid 500 mg tds	29

- The most effective medical treatment is the 52 mg levonorgestrel intra-uterine device (LNG IUD, Mirena), which has a mean reduction in blood loss of 94% and should be offered to women if clinically appropriate.
- It should be noted that the lower dose LNG-IUD (Kyleena) is not indicated for HMB.
- Alternative hormonal agents include oral progestogens, the combined oral contraceptive pill (COCP) and vaginal ring.
- Running hormone pills or vaginal rings together in an extended regimen may also be helpful.
- Oral progestins administered to women from day 5 to day 26 of their cycle result in a significant reduction in menstrual blood loss.
- Adverse side effects of oral progestins include weight gain, bloating, breast tenderness, headaches, acne and depressed mood, rendering it more suitable for short-term therapy.
- Intramuscular medroxyprogesterone acetate (Depo-Provera) will induce amenorrhea in approximately 50% of users within 1 year; however, studies for its use in HMB are limited.

Surgical treatment

- This is indicated if menorrhagia interferes with lifestyle despite medical treatments.
- Uterus preserving options should be offered initially.

Surgical treatment

- Options include:
- Myomectomy
- Polypectomy
- Uterine artery embolization
- Endometrial ablation (provided no contraindications)
- Hysterectomy (appropriate for women with increased endometrial cancer risk, e.g. endometrial hyperplasia)

Practice tip

Acute severe uterine bleeding:[10]

- tranexamic acid 1–1.5 g (o) 6–8 hourly until bleeding stops

  or

- norethisterone 5–10 mg (o) 4 hourly until bleeding stops

  or

- medroxyprogesterone 10 mg (o) 4 to 8 hourly until bleeding stops

  or

- ethinyloestradiol 30–35 mcg combined oral contraceptive pill, 6 hourly until bleeding stops, re-evalute after 48 hours

Uterine fibroids (leiomyoma) Fibroids

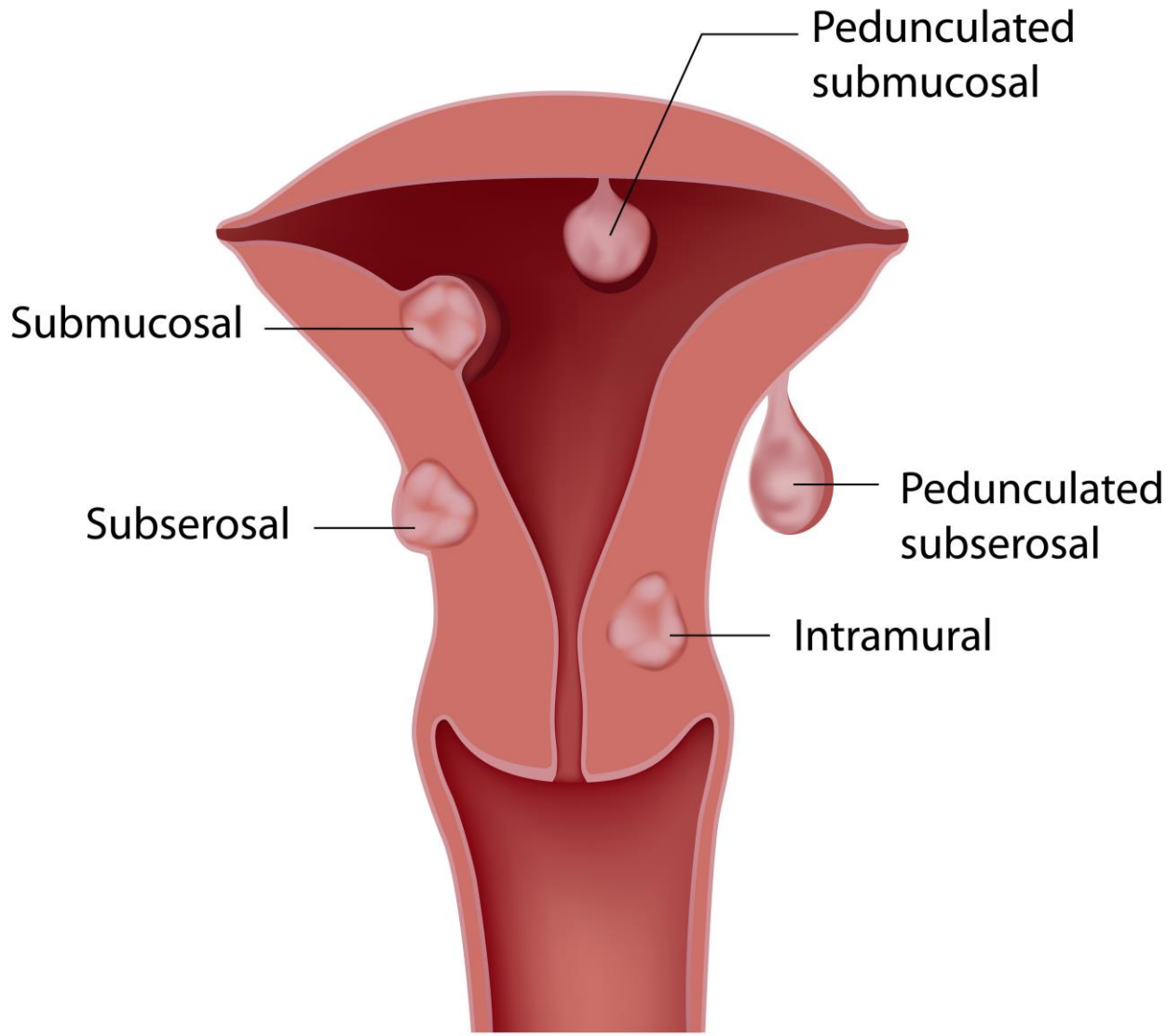
are benign tumors of smooth muscle of the myometrium.

- They are usually classified according to their location: submucosal, intramural, subserosal and cervical.
- They are estrogen dependent and shrink with the onset of menopause.

Clinical features

- Affects 40–80% of women by age 50 years
- Only 1 in 800 develop malignancy
- Usually asymptomatic

Uterine fibroids



Symptoms

- Often asymptomatic if small.
- Menorrhagia.
- Dysmenorrhea.
- Pelvic discomfort ± pain (pressure) including dyspareunia.
- Bladder dysfunction.
- Pain with torsion of pedunculated fibroid.
- Pain with ‘red degeneration’—only in pregnancy (pain, fever, local tenderness)

Uterine fibroids (leiomyoma) Fibroids

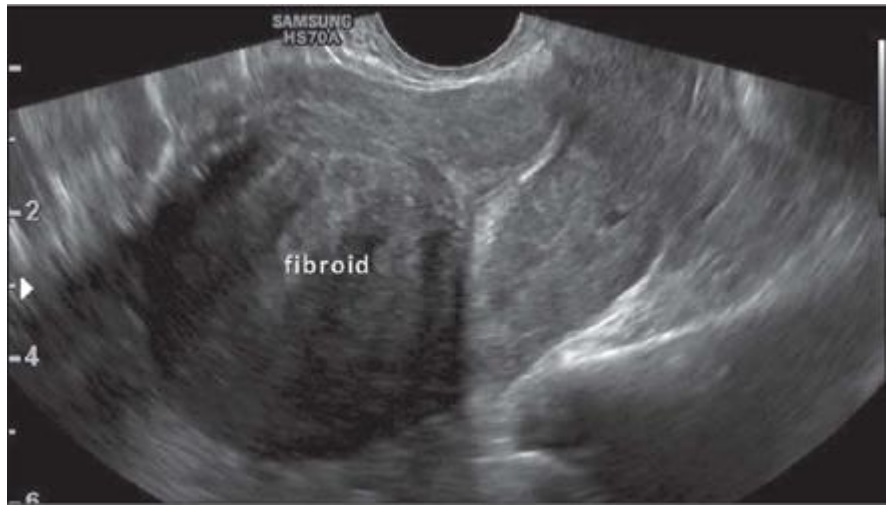
Other features

- Infertility (acts like IUCD if submucosal)
- Calcification

Examination

- Bulky uterus

Uterine fibroids (leiomyoma) Fibroids



Investigations

- Transvaginal ultrasound
- FBE ?anemia

Management

- Medical management the same as for HMB
- Levonorgestrel IUD has now largely taken over as the preferred treatment
- GnRH analogues—especially if >42 years can shrink fibroids (maximum 6 months)—use only immediately pre-operative

Uterine fibroids (leiomyoma) Fibroids

- Surgical options:
- Myomectomy (remove fibroids only, esp. child-bearing years)
- Hysteroscopic resection/endometrial ablation
- Hysterectomy
- Other options: uterine artery embolisation, Magnetic Resonance-guided Focused Ultrasound Surgery (MRgFUS)

Intermenstrual bleeding (IMB) and postcoital bleeding (PCB)

- It is important to note that genital tract malignancy is an uncommon cause of bleeding at any stage, but must be considered in all patients. In particular, postcoital bleeding (PCB) is regarded as a cardinal symptom of cervical cancer.

CAUSES

- Periovulatory bleeding (normal variant)
- Defective luteal phase (causes premenstrual spotting)
- Endometriosis (causes pre- and postmenstrual spotting)
- Hormonal contraceptives and copper IUD
- Menopausal hormone therapy
- Pregnancy—early loss or ectopic
- Cervical ectropion
- STIs causing cervicitis or PID (especially if PCB)
- Polyps—cervical, endometrial
- Uterine fibroids
- Cervical cancer
- Endometrial/myometrial hyperplasia and malignancy

Examination

Perform an abdominal, bimanual pelvic examination and speculum examination.

- Check for cervical ectropion, presence of polyps, vaginal discharge and cervical tenderness.
- Note any friability of the cervix.

Investigations

- Cervical cancer ‘co-test’ (i.e. HPV and liquid-based cytology)
- Transvaginal ultrasound (especially for IMB)
- Endocervical swabs for chlamydia and gonorrhea PCR
- Pregnancy test.

MANAGEMENT

- All women with persistent PCB require the cervical cancer co-test and gynecologist referral for colposcopy.
- Immediate referral is not required after a single episode, provided examination and the co-test are normal.
- A second episode mandates referral.
- If the suspected cause of PCB is a cervical ectropion, persistent bleeding still requires referral.
- Various ablative treatment methods are available, but are appropriate only once pathology has been excluded.
- Irregular bleeding while taking hormonal therapies should be investigated and referral considered if bleeding is excessively frequent, prolonged or new in onset.
- Consider ceasing hormonal therapy to assess whether symptoms resolve.
- Persistent IMB requires gynecologist referral for hysteroscopy with endometrial biopsy.

POST MENOPAUSAL BLEEDING

- Postmenopausal bleeding suggests cervical endometrial/myometrial cancer in up to 25% of cases.
- Other causes include polyps, atrophic vaginitis, menopausal hormone therapy, endometrial hyperplasia and urethral caruncle.
- It is worth noting that tamoxifen can increase the risk of endometrial cancer.
- Earlier referral is indicated for women on tamoxifen who present with PMB.
- Transvaginal ultrasound should be performed.
- Gynecologist referral is not immediately indicated if the ultrasound reveals an endometrial thickness ≤4 mm and there are no suspicious features.
- However, if endometrial thickness is >4 mm or there is persistent bleeding, referral is indicated with a view to a diagnostic procedure (hysteroscopy and D&C).

- Cervical cancer: This should be the diagnosis until proved otherwise for postcoital bleeding.

Clinical features

- Peak incidence in sixth decade
- 80% due to squamous cell carcinoma
- Risk factors: Risk factors for cancer progression include the grade of oncogenicity of the HPV type, immune status, the presence of other sexually transmitted infections, number of births, young age at first pregnancy, hormonal contraceptive use, and smoking.

Symptoms

- Postcoital bleeding
- Intermenstrual bleeding
- Vaginal discharge—may be offensive

Mainly diagnosed on routine screening.

Examination

- Ulceration or mass on cervix
- Bleeds readily on contact—may be friable

Management

- Urgent gynecological referral

- Endometrial cancer
- This is the diagnosis until proved otherwise in any woman presenting with postmenopausal bleeding.

Clinical features

- Peak incidence 50–70 years
- Risk factors:
- Age
- Obesity
- Nulliparity
- Late menopause
- Diabetes mellitus
- History of chronic anovulatory bleeding
- Polycystic ovarian syndrome
- Drugs (e.g. unopposed estrogen, tamoxifen)
- Family history—breast, ovarian, endometrial or colon cancer (Lynch syndrome)

- Symptoms:
- Ninety per cent present with abnormal bleeding, especially postmenopausal bleeding.
- Note: Intermenstrual bleeding or persistent bleeding in postmenopausal women should be treated with suspicion.

Examination

- Uterus usually feels normal, but may be bulky.

Investigations

- Cervical cytology—detects some cases. Endometrial cancer is not excluded by normal cervical cytology
- Transvaginal ultrasound/endometrial biopsy

Management

- Urgent gynecological referral.

AMENORRHEA

- Amenorrhea is classified as primary or secondary.
- Primary amenorrhea is the failure of the menses to start by 16 years of age.
- Secondary amenorrhea is the absence of menses for over 6 months in a woman who has had established menstruation.

Primary amenorrhea

- The main approach is to differentiate primary amenorrhea from delayed puberty, in which there are no signs of sexual maturation by age .

Causes include:

1.hypothalamic amenorrhea:

- Excessive exercise
- Low body mass
- Severe chronic illness
- Psychological stress

2. PCOS
3. Imperforate hymen
4. Congenital absence of uterus or vagina
5. Chromosomal anomalies (e.g. Kallmann syndrome, Turner syndrome)
6. Pituitary tumors.

Diagnostic tests include serum FSH, LH, prolactin, estradiol and also chromosome analysis. Early referral is appropriate.

Secondary amenorrhea

- The most common causes in general practice are :PCOS and hypothalamic amenorrhea.

❑Hypothalamic amenorrhea:

- Excessive exercise.
- Low body mass .
- Severe chronic illness.
- Psychological stress

- ❑PCOS
- ❑ Pregnancy
- ❑ Hyperprolactinemia
- ❑ Premature ovarian insufficiency
- ❑ Medication (e.g. hormonal contraception, antipsychotics, opiates, chemotherapy)
- ❑ Post-pill amenorrhea
- ❑ Thyroid dysfunction
- ❑ Adrenal disorders (e.g. Cushing disease, congenital adrenal hyperplasia)
- ❑ Asherman syndrome (following gynecological surgery)

Gynecological intervention is appropriate for women with prolonged amenorrhea due to the increased risk of endometrial cancer.

- Oligomenorrhoea:
- Infrequent and usually irregular periods, where the cycles are between 6 weeks and 6 months.
- PCOS is the most common cause.

- Premature ovarian insufficiency
- Apart from iatrogenic causes, this may be caused by idiopathic early menopause and autoimmune ovarian failure.
- Other genetic associations are Turner syndrome and Fragile X prem utation.
- It is considered a hormonal deficiency and requires hormonal therapy with either combined oral contraception or menopausal hormonal therapy

When to refer

- Women with persistent IMB and/or PCB
- Women with persistent postmenopausal bleeding
- Women with persistent increased endometrial thickness on transvaginal ultrasound
- Possibility of intra-uterine pathology
- The patient does not respond to initial therapy
- There is evidence of underlying disease (e.g. endometriosis, SLE)
- Surgery is indicated

- Practice tip
- Non-menstrual bleeding suggests cancer until proved otherwise: it may be postcoital (cervical cancer); intermenstrual (common with hormonal contraception); postmenopausal (endometrial cancer).