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ABNORMAL UTERINE BLEEDING

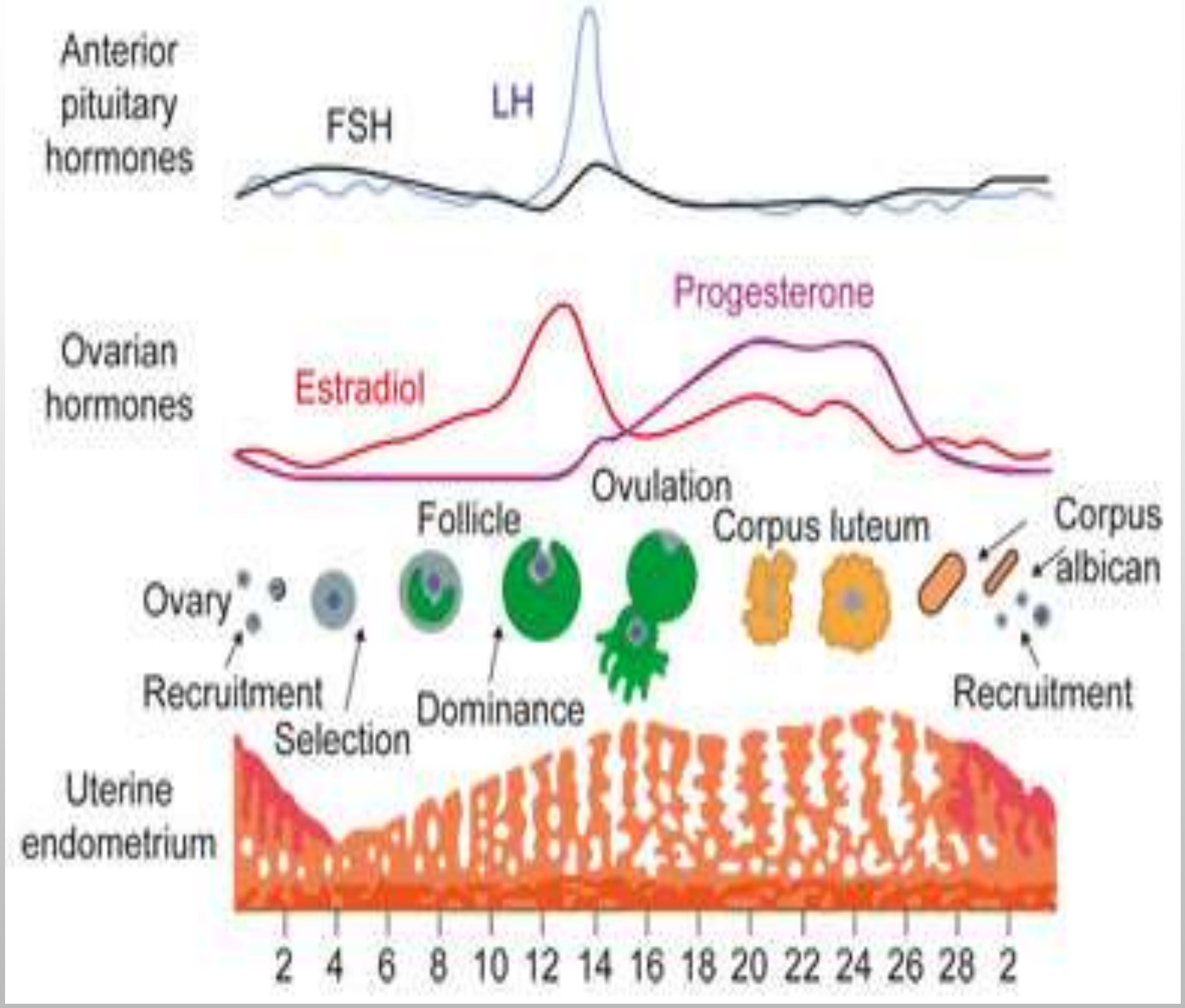
Dr.Ala'a Awees

MENSTRUATION

Menstruation is a woman's monthly bleeding from her reproductive tract induced by hormonal changes of the menstrual cycle. The length of a menstrual cycle is the time from the start of a period to the start of the next.

Beliefs derived from personal experience and cultural, social and educational influences determine whether she perceives the menstrual blood loss to be 'normal' for her. However, a 'normal' quantity of monthly blood loss (MBL) can be defined objectively for the whole population.

Due to difficulties in determining when a menstrual period begins (e.g. spotting, brown/pink discharge, continuous prolonged bleed), it is often difficult to differentiate between a menstrual period and an intermenstrual bleed (IMB). In the main, the aetiopathology and treatment of IMB differs from heavy menstrual bleeding (HMB).


Anterior pituitary hormones
FSH
LH
Ovarian hormones
Progesterone
Estradiol
Ovulation
Follicle
Corpus luteum
Corpus albican
Ovary
Recruitment
Selection
Dominance
Recruitment
Uterine endometrium
2 4 6 8 10 12 14 16 18 20 22 24 26 28 2

NORMAL MENSTRUAL CYCLE

- The Menstrual Cycle (As Well As AUB) Should Be Described According To Four Specific Symptomatic Components (Cycle Frequency, Duration, Volume, Regularity Of Cycle).
- **Frequency Of Menses (Or Length Of Menstrual Cycle)**
- Mean Is 28 Days (95% CI 24–38 Days); Frequent <24 Days, Infrequent >38 Days.
- As Age Increases, The Menstrual Cycle Tends To Shorten; Age 13–19 Years, Mean Cycle Length 35 Days (90th Centile Range: 28–44 Days), Age 35–52 Years, Mean Cycle Length 28 Days (90th Centile Range: 25–32 Days).
- As Age Increases, The Frequency Of Irregular Periods Reduces. The Frequency Of Irregular Periods Is Around 21% Between The Ages 15 And 19 Years And Reduces 11% Between Ages 40 And 44 Years.

- **Duration Of Menstruation**
- Normal 4.5–8.0 Days; Prolonged >8 Days, Shortened <4.5 Days.
- Mean Is 5 Days (95% Ci 4.5–8 Days).
- **Volume Of Monthly Menstrual Blood Loss (Ml)**
- Mean 40 Ml (95% CI 5–80 Ml); Heavy Is >80 Ml; Light Is <5 Ml.
- **Regularity Of Menstrual Cycle (Cycle To Cycle Variation Over 12 Months, Measured In Days)**
- Regular Cycle-to-cycle Variation Is Between 2–20 Days, Irregular Variation Is >20 Days.

DEFINITION OF HMB

- Heavy Menstrual Bleeding (HMB) Is Clinically Defined As Menstrual Blood Loss (MBL) That Is Subjectively Considered To Be Excessive By The Woman And Interferes With Her Physical, Emotional, Social And Material Quality Of Life.
- Quantifying Monthly Menstrual Blood Loss (Mbl) Does Not Improve Clinical Care And Is Not Undertaken In Modern Clinical Practice. MBL May Be Estimated Directly (E.G. By Collecting All Sanitary Protection And Eluting And Quantifying Blood By Laboratory Techniques Such As The Alkaline Haematin Test) Or Indirectly (E.G. Pictorial Blood Loss Assessment Chart [PBAC]; Subjective Measures).

- **Objective Assessment:** A Pbac Score Greater Than Or Equal To 100 Equates To A Sensitivity Of 86%–91% And A Specificity Of 82–89% In Predicting Mbl Greater Than 80 Ml By Alkaline Haematin Test (Gold Standard Reference Technique).
- **Subjective Assessment**: Subjective Assessment Of Mbl Combines Information Of Sanitary Protection Usage, Flooding, Clots, Duration Of Menstruation And The Woman's Personal Opinion Of Her Menstrual Loss. Although This Tends To Be Inaccurate, It Is Easy To Undertake In Clinical Practice And Is The Preferred Method Of Assessing HMB.

PREVALENCE OF HMB

- HMB Has A Major Adverse Effect On The Quality Of Life Of Many Women. Overall, 3% Of Premenopausal Women Experience HMB. However, This Absolute Risk Is Almost Doubled In Woman Aged 40–51. HMB Accounts For Around 15% Of All Secondary Care Gynaecological Referrals In The UK.

CAUSES OF HMB

- Between 40–60% Of Women With HMB Have No Uterine, Endocrine, Haematological Or Infective Pathology On Investigation. These Women Were Formerly Termed To Have Dysfunctional Uterine Bleeding (DUB) Of Ovulatory (Regular Cycle) Or Anovulatory (Irregular Cycle) Type.
- **Most Hmb Is Due To A Combination Of Coagulopathy, Ovulatory Or Endometrial Dysfunction That Does Not Require Secondary Referral** And Treatment Can Be Commenced In Primary Care. The Term DUB Should Be Discarded And PALM-COEIN Classification Adopted.
- Pathological Causes Of Hmb Include Uterine Fibroids (20–30%), Uterine Polyps (5–10%), Adenomyosis (5%); Endometriosis Rarely Presents As Aub, But Is Identified In <5% Of Cases Of Aub.
- Gynaecological Malignancy Rarely Presents As Hmb, But Can Present As Prolonged Intermenstrual Bleeding (Imb), Postcoital Bleeding (Pcb), Postmenopausal Bleeding (Pmb) And As A Pelvic Mass.

TERMINOLOGY USED TO DESCRIBE AUB

Terms To Be Kept In New Terminology

- **Abnormal Uterine Bleeding (Aub)**any Menstrual Bleeding From The Uterus That Is Either Abnormal In Volume (Excessive Duration Or Heavy), Regularity, Timing (Delayed Or Frequent) Or Is Non-menstrual (IMB, PCB Or PMB)
- **Heavy Menstrual Bleeding (HMB)** For Clinical Purposes, HMB Is Defined As Excessive Menstrual Blood Loss Leading To Interference With The Physical, Emotional, Social And Material Quality Of Life Of A Woman, And Which Can Occur Alone Or In Combination With Other Symptoms. Adverse Outcome Is Greater In Women With Total MBL That Exceeds 80 Ml Or Menses Duration >7 Days

- **Intermenstrual Bleeding (IMB)** Uterine Bleeding That Occurs Between Clearly Defined Cyclic And Predictable Menses. Such Bleeding May Occur At Random Times Or May Manifest In A Predictable Fashion At The Same Day In Each Cycle
- **Postmenopausal Bleeding (Pmb)**genital Tract Bleeding That Recurs In A Menopausal Woman At Least One Year After Cessation Of Cycles **Postcoital Bleeding (Pcb)**non-menstrual Genital Tract Bleeding Immediately (Or Shortly After) Intercourse
- **Chronic AUB** AUB Has Been Present For The Majority Of The Past 6 Months. In Most Cases, Chronic AUB Is Unlikely To Require Urgent Immediate Clinical Intervention
- **Acute AUB** Excessive AUB Bleeding That Requires Immediate Intervention To Prevent Further Blood Loss. Acute AUB May Present In The Context Of Existing Chronic AUB Or Might Occur Without Such A History

TERMS THAT SHOULD BE DISCARDED IN NEW TERMINOLOGY

- **Menorrhagia** Heavy Menstrual Bleeding That Occurs At Expected Intervals Of The Menstrual Cycle (Cycle Length Varying From 21 To 35 Days)
- **Oligomenorrhoea** Bleeding That Occurs At Intervals Of >35 Days And <6 Months, Usually Caused By A Prolonged Follicular Phase
- **Polymenorrhoea** Regular Bleeding At Intervals Of Less Than 3 Weeks, Which May Be Caused By A Luteal Phase Defect
- **Amenorrhoea** No Uterine Bleeding For At Least 6 Months
- **Menometrorrhagia** HMB At The Usual Time Of Menstrual Periods And At Other Irregular Intervals
- **Metrorrhagia** Uterine Bleeding At Irregular Intervals, Particularly Between The Expected Menstrual Periods
- **Dysfunctional Uterine Bleeding (Dub)**this May Be Ovulatory Or Anovulatory HMB. This Is Diagnosed After The Exclusion Of Pregnancy, Medications, Iatrogenic Causes, Genital Tract Pathology And Systemic Conditions

An Expert Consensus Panel On Menstrual Disorders Has Suggested That:

- Terms Such As Menorrhagia, Menometrorrhagia, Metrorrhagia And Dysfunctional Uterine Bleeding Be Discarded
- AUB Should Be Described According To Four Specific Symptomatic Components (Cycle Frequency, Duration, Volume And Regularity Of Cycle). For Example, Instead Of Stating This Woman Has Menorrhagia, One Would State She Has Normal Frequency, Prolonged Duration, Heavy Menstrual Bleeding (HMB) Without Any Variation Between Cycles. The Terminology Suggested By Fraser Et Al Advises Using Simple Universally Accepted Terminology To Describe The Four Cycle Components:
  - *Regularity* Should Be Specified As Irregular, Regular Or Absent
  - *Frequency* Should Be Specified As Frequent, Normal Or Infrequent
  - *Duration* Should Be Specified As Prolonged, Normal Or Shortened
  - *Volume* Should Be Specified As Heavy, Normal Or Light.
  - No Specific Guidance Has Been Issued For The Terms Oligomenorrhoea, Polymenorrhoea And Amenorrhoea. However, These Are Better Described Using Cycle Frequency And Regularity Of Cycle Components.

FIGO CLASSIFICATION OF THE CAUSES OF AUB

- FIGO Have Approved This New Classification System And Have Called It PALM-COEIN:

  • **Structural Causes** For AUB: **P**olyp; **A**denomyosis; **L**eiomyoma; **M**alignancy And Hyperplasia

  • **Non-structural Causes** For AUB: **C**oagulopathy; **O**vulatory Dysfunction; **E**ndometrial; **I**atrogenic; And **N**ot Yet Classified.

  Using The Full Notation 'PALM-COEIN' It Is Possible To Define Women With AUB Who Have One Or More Contributing Pathologies. In All Cases, The Presence Or Absence Of Each Criterion Is Noted Using 0 If Absent, 1 If Present, And ? If Not Yet Assessed.

Polyp

Adenomyosis

Leiomyoma

Malignancy & hyperplasia

→ **Submucosal**

→ **O**ther

Coagulopathy

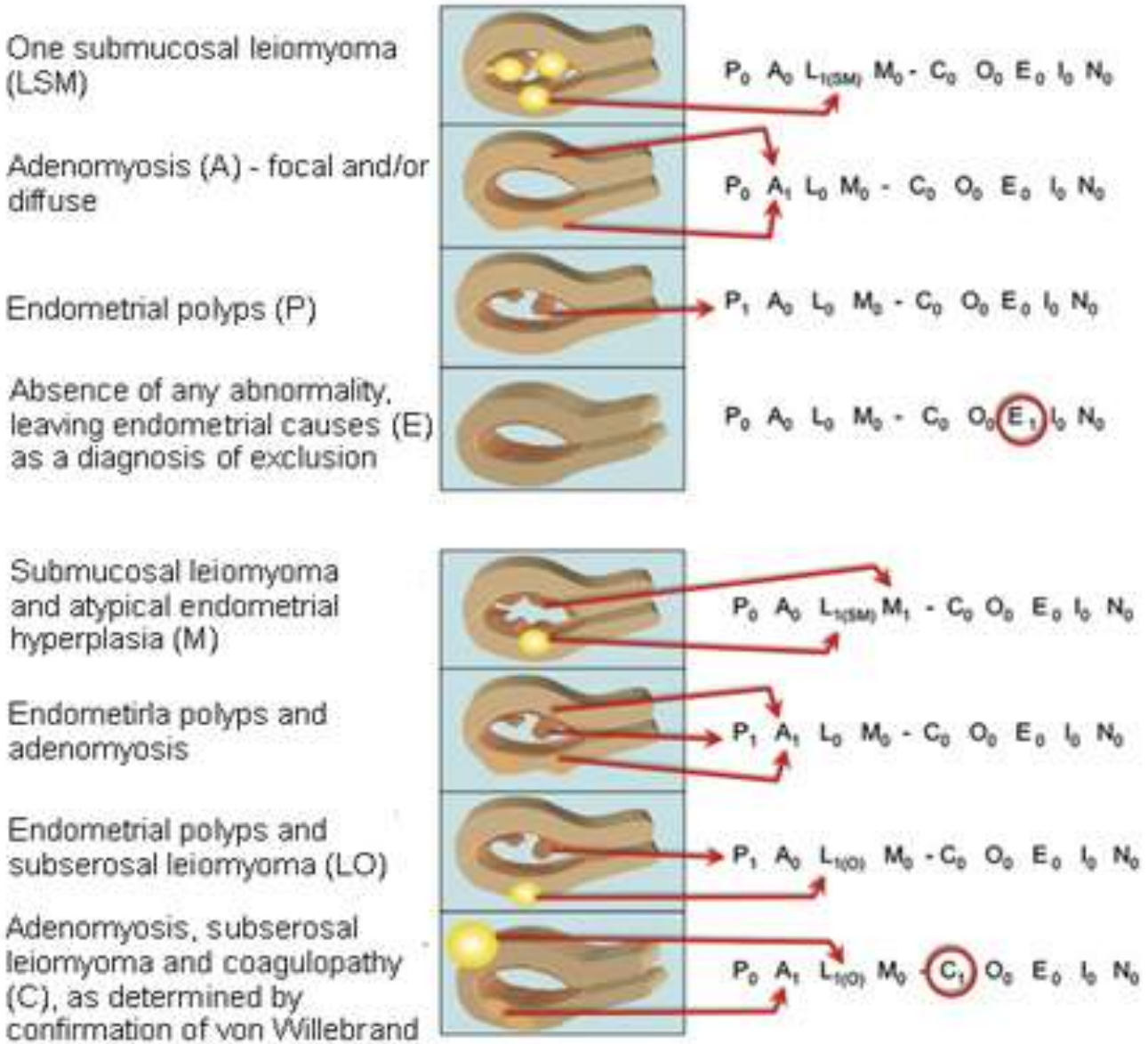
Ovulatory dysfunction

Endometrial

Iatrogenic

Not yet classified

- In General, The Components Of The PALM Group Are Discrete (Structural) Entities That Can Be Measured Visually With Imaging Techniques And/Or Histopathology, Whereas The COEIN Group Is Related To Entities That Are Not Defined By Imaging Or Histopathology (Non-structural).
- The Term 'Dysfunctional Uterine Bleeding' Which Was Previously Used As A Diagnosis For Aub That Occurs In The Absence Of Systemic Or Locally Definable Genital Tract Pathology, Should Be Discarded And Is Not Included In Palm-coein. Women Who Fit This Description Generally Have Any Combination Of Coagulopathy, Ovulation Or Primary Endometrial Disorder.
- The Following Illustrated Table Shows How Diagnosed Pathology Can Be Described Used Palm-coein Terminology

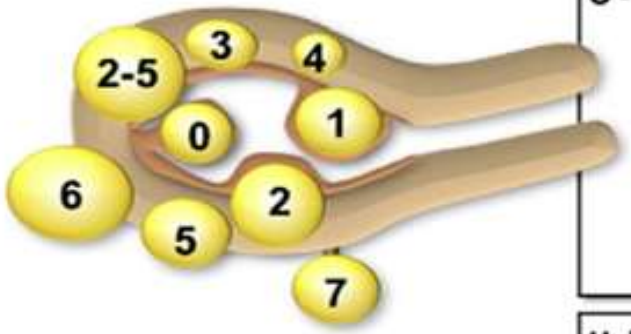

One submucosal leiomyoma (LSM)
Adenomyosis (A) - focal and/or diffuse
Endometrial polyps (P)
Absence of any abnormality, leaving endometrial causes (E) as a diagnosis of exclusion
Submucosal leiomyoma and atypical endometrial hyperplasia (M)
Endometirla polyps and adenomyosis
Endometrial polyps and subserosal leiomyoma (LO)
Adenomyosis, subserosal leiomyoma and coagulopathy (C), as determined by confirmation of von Willebrand disease
P0 A0 L1(SM) M0 - C0 O0 E0 I0 N0
P0 A1 L0 M0 - C0 O0 E0 I0 N0
P1 A0 L0 M0 - C0 O0 E0 I0 N0
P0 A0 L0 M0 - C0 O0 E1 I0 N0
P0 A0 L1(SM) M1 - C0 O0 E0 I0 N0
P1 A1 L0 M0 - C0 O0 E0 I0 N0
P1 A0 L1(O) M0 - C0 O0 E0 I0 N0
P0 A1 L1(O) M0 - C1 O0 E0 I0 N0

Polyp
Adenomyosis
Leiomyoma
Malignancy & hyperplasia

Submucosal
Other

Coagulopathy
Ovulatory dysfunction
Endometrial
Iatrogenic
Not yet classified

Leiomyoma subclassification system



SM - Submucosal	0	Pedunculated intracavitary
	1	<50% intramural
	2	≥50% intramural
O - Other	3	Contacts endometrium; 100% intramural
	4	Intramural
	5	Subserosal ≥50% intramural
	6	Subserosal <50% intramural
	7	Subserosal pedunculated
	8	Other (specify e.g. cervical, parasitic)

Hybrid leiomyomas (impact both endometrium and serosa)	Two numbers are listed separated by a hyphen. By convention, the first refers to the relationship with the endometrium while the second refers to the relationship to the serosa. One example is below	
	2-5	Submucosal and subserosal, each with less than half the diameter in the endometrial and peritoneal cavities, respectively.

The PALM-COEIN System Can Also Include The Type O, 1, 2 Submucosal Fibroid Classification System (Wamsteker 1993 And ESGE), And Expand This Further To Intramural And Subserosal Location Of Fibroids. This Is Depicted In The Figure.

- Type 8 Fibroids Are Leiomyomas That Do Not Relate To The Myometrium And Include Cervical Or Broad Ligament Fibroids Without Direct Attachment To The Uterus, As Well As Other So-called 'Parasitic' (Extra-pelvic) Lesions.

Structural	
P	Endometrial polyps, cervical polyps
A	Adenomyosis
L	Leiomyoma
M	Premalignancy (endometrial hyperplasia) Malignancy of the genital tract (cervical, endometrial, ovarian, vaginal, vulval, sarcoma of endometrium or myometrium)

Non-structural	
C	Systemic coagulopathy, e.g. thrombocytopenia, von Willebrand's disease, leukaemia, warfarin
O	Disorders of ovulatory function, e.g. polycystic ovary syndrome, congenital adrenal hyperplasia, hypothyroidism, Cushing's disease, hyperprolactinaemia
E	Primary endometrial disorders, e.g. disturbances of local endometrial haemostasis, vasculogenesis or inflammatory response (chronic endometritis)
I	Iatrogenic causes, e.g. exogenous sex steroid administration (combined oral contraceptives, progestins, tamoxifen), intrauterine contraceptive device, traumatic uterine perforation
N	Generally rare causes, e.g. arteriovenous malformations, myometrial hypertrophy, sex steroid secreting ovarian neoplasm, chronic renal or hepatic disease, endometriosis

- The Term ‘Dysfunctional Uterine Bleeding’ Which Was Previously Used As A Diagnosis For AUB That Occurs In The Absence Of Systemic Or Locally Definable Genital Tract Pathology, Should Be Discarded And Is Not Included In PALM-COEIN. Women Who Fit This Description Generally Have Any Combination Of Coagulopathy, Ovulation Or Primary Endometrial Disorder.
- If There Is Aub Before Menarche Then A Pelvic Examination (Usually Under Anaesthesia) Should Be Performed. In Cases Such As These, The Differential Diagnoses Would Be: Malignancy, Trauma, Sexual Abuse, Assault Or Congenital Malformations.

ASSESSMENT OF AUB

- Establish If Chronic AUB (>6 Months) Or Acute AUB (Urgent Intervention Required).
- Initial Step Should Be To Exclude Pregnancy.
- Understand The Differential Diagnosis Of Aub (I.E. PALM-COEIN Classification) And Accept The Concept That Women Could Be Affected By More Than One Component, But Not All Components May Be Causal To AUB.
- Undertake Relevant Gynaecological History And Examination.
- Screen For Coagulopathy (Such As Von Willebrand Disease) By Using A Specific Structured History. If Clinical History Screen Is Positive Then Undertake Coagulation Profile And Vwd Test.
- Recommendation For **Full Blood Count (Fbc), Cervical Smear, Pelvic Infection Swabs And Pelvic Ultrasound** (And Coagulation Screen If Clinical Question Screen Positive).

- Referral To Secondary Care (One-stop Or Rapid Access Clinic) If Malignancy Is Suspected, Endometrial Biopsy Is Required, Pathology Suspected/Identified Or Medical Treatment Deemed Unsuccessful; Collectively Termed ‘Red Flag’ Features.
- Most Hmb Is Due To A Combination Of Coagulopathy, Ovulatory Or Endometrial Dysfunction That Does Not Require Secondary Referral And Treatment Can Be Commenced (And Successfully Undertaken) In Primary Care.
- **Uterine/Endometrial Assessment**: Investigation Using Hysteroscopy With Endometrial Biopsy Or Ultrasound And Endometrial Biopsy Improves The Detection Rate Of Endometrial Pathology (Malignant And Benign) Compared With Hysteroscopy Or Ultrasound Alone.

HISTORY AND CLINICAL ASSESSMENT

1. Define The **Nature Of Bleeding:**
   - Age
   - Menstrual Or Non-menstrual (Intermenstrual Bleeding, Postcoital Bleeding, Postmenopausal Bleeding)
   - Subjective Assessment Of MBL (Sanitary Protection Usage, Flooding, Clots, Duration Of Menstruation) And The Woman's Personal Opinion
   - Alteration In The Menstrual Cycle
   - Pelvic Pain And Pressure Effects
   - Previous Medical Or Surgical Treatment For AUB
   - Up-to-date Smear Test
   - Family History Of Gynaecological Pathology.

2. Identify Symptoms That May Indicate **Pathology Or Need For Secondary Care Referral** .

Pathology May Include:

- Fibroids (Pelvic Pain, Pelvic Mass, Pressure/Obstructive GI/GUT Symptoms)
- Endometriosis/Adenomyosis (Cyclical And Non-cyclical Chronic Pelvic Pain, Dyspareunia, Dysmenorrhoea, Infertility)
- Inherited Or Acquire Haemostatic/Coagulopathy Disorder E.G. Von Willebrand Disease. See Table Below. The Presence Of All Three Domains On Clinical Questioning Is Highly Predictive For A Haemostatic Condition That Could Be Contributory/Causal To AUB And Indicates The Need To Perform Specific Haematological Screening Blood Tests.
- Secondary Care Referral Is Indicated If Pathology Is Suspected/Identified, Malignancy Is Suspected And/Or Failure Of Medical Treatment. Malignancy May Be Indicated By: PMB, IMB, PCB, Alteration In Menstrual Cycle, Pelvic Pain, Pelvic Mass, Pressure/Obstructive GI/GUT Symptoms, Weight Loss/Gain.

3. Identify **Pathological Effects** Such As:
Anaemia (Request FBC)
Pelvic Pain
Impaired Quality Of Life.

4. Identify **Treatment Expectations** Such As:
Concerns And Needs
Future Fertility And Contraception Wishes
Need For Definitive Treatment When Offered Treatment Alternatives.

Structured history to screen for coagulopathies (AUB-C)	
Domain	**Characteristic**
1	Heavy menstrual bleeding since menarche
2	One of the following: •postpartum haemorrhage •surgical-related bleeding •bleeding associated with dental work
3	Two or more of the following symptoms: •bruising 1–2 times per month •epistaxis 1–2 times per month •frequent gum bleeding •family history of bleeding symptoms

EXAMINATION, BASIC INVESTIGATIONS AND DIAGNOSIS

- If History Taking Reveals HMB Without The Presence Of Pathology, Then There Is No Need To Undertake A Physical Examination Prior To Initiating First-step Medical Treatment ?????.
- This Will Apply To The Vast Majority Of Cases. However, Some Clinicians Have Raised Concerns With This Approach And It Would Be Reasonable To Undertake A Clinical Examination Particularly If There Was:

  - Uncertainty Or Overdue **Routine Cervical Cancer Screening** Or Underlying **Pelvic/STI Infective Process**

  - **Structural Pathology** (I.E. PALM Part Of PALM-COEIN Classification): Given Severity Of Symptoms Or Co-existing Pelvic Pain And Other Symptoms Such As IMB, PCB And PMB, Weight Loss/Gain

  - **Suspected Coagulopathy**: HMB Or AUB Since Menarche, Tendency To Bruise Easily, And Family History Of Coagulopathy May Indicate An Inherited Or Acquired Coagulopathy

  - **Suspected Ovulatory Dysfunction**: Oligoamenorhoea, Obesity, Acne, Hirsutism, And Acanthosis Nigricans May Be Suggestive Of Polycystic Ovary Syndrome Or Diabetes Mellitus, Or Oligoamenorrhoea And Galactorrhoea, Which Could Suggest Hyperprolactinaemia

- Clinical Examination
- General Examination – Pallor (Anaemia)
- Abdominal Palpation
- Visualisation And Palpation Of The Cervix
- Bimanual (Internal) Pelvic Examination To Estimate Uterine Size And/Or Adnexal Masses

INVESTIGATIONS

- There Is No Agreed 'Gold Standard' As To Which Methods (Or Combinations Of Methods) Of Investigation Are Better At Identifying Certain Types Of Pathology Than Others And, As Such, A Comprehensive Evaluation Is Required For Women With A High Risk Of Benign Or Malignant Genital Tract Pathology.
- Full Blood Count
- Cervical Smear
- Pelvic Ultrasound (Structural Pathology)
- Pelvic Infection Screening (Genital Tract Swab Testing).
- Hysteroscopy (For Endometrial Pathology)

IN ORDER TO MAKE AN ASSESSMENT MORE ASSURED, THE ,PHYSICIAN HAS DEFINED 'HIGH RISK' WOMEN AS FOLLOWS.

- **Women With AUB Who Have:**
- Declined Or Failed An Adequate Trial Of Medical Treatment
- Aged >45 Years
- Pathology Suspected Based On History ± Physical Examination.
- **Where Aub Includes Women With:**
- Abnormal Menstrual Bleeding
  - HMB With Regular And Irregular Cycles
  - HMB And Dysmenorrhoea
  - ± Pelvic Pain
  - ± Pressure Effects On GIT/GU Tract
- Non-menstrual Bleeding
  - Intermenstrual Bleeding
  - Postcoital Bleeding
  - Postmenopausal Bleeding

WHEN TO CONSIDER TREATMENT BRFORE IVESTIGATION

- For Women With HMB Who Are Under 45 Years Of Age With No Obvious Pathology Based On Any Combination Of History, Physical Examination, GP Organised Investigations (Such As Cervical Smear, FBC, Pelvic Ultrasound), There Are Two Options For Treatment:
- Immediately Refer To Secondary Care For Evaluation
- Commence A 3–6 Month Trial Of Medical Therapy (E.G. COC, Mirena LNG-IUS) And If There Is No Improvement Refer The Woman To Secondary Care For Evaluation

PATHOLOGY NEEDS FURTHER INVESTIGATION OR SURGICAL TREATMENT

Pathology suspected before treatment		
1	Suspected gynaecological cancer	•PCB •PMB •IMB •pelvic mass •cervix lesion
2	Requires endometrial biopsy (to rule out endometrial hyperplasia or endometrial malignancy)	•Persistent IMB •>45 years with treatment failure •Irregular bleeding while on hormone-replacement therapy or tamoxifen

Pathology identified before/after treatment		
3	Enlarged uterus (clinically measures >10 weeks size or >10 cm uterine cavity length on uterine sounding)	Fibroids, adenomyosis
4	Moderate/severe anaemia on FBC	Usually benign pathology such as fibroids, endometriosis
	Uterine/ovarian pathology identified on pelvic ultrasound scan	
	Identification of coagulation/haemostatic disorder on clinical screening and testing	e.g. von Willebrand disease

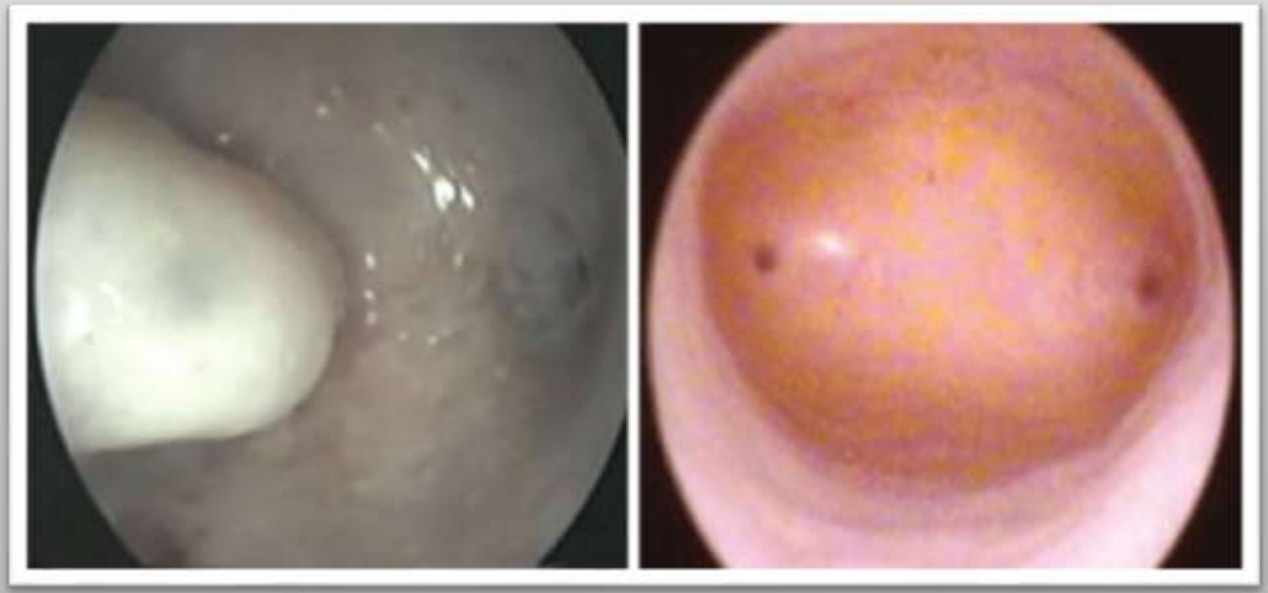
Pathology suspected after treatment		
5	Medical treatment has failed	At least 3 months of drug treatment (at least 6 months of Mirena) and failure is based on woman's own assessment
6	Patient wishes for surgery	Endometrial ablation, hysterectomy

UTERINE AND ENDOMETRIAL ASSESSMENT

- Assessment Of The Uterus And Endometrium Is Conducted In Women At High Risk Of Benign Or Malignant Genital Tract Pathology. This Essentially Comprises Of Three Components:
- Pelvic Ultrasound
- Hysteroscopy
- Endometrial Biopsy; Either Hysteroscopically Directed Or Through 'Blind' Global Uterine Cavity Pipelle® Sampling.

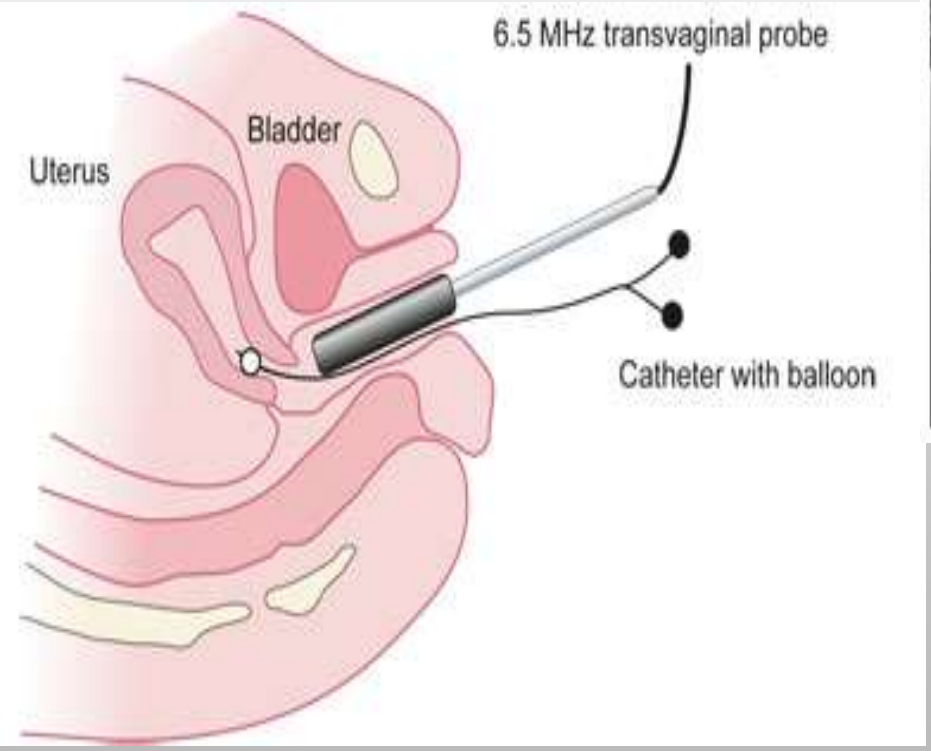
SALINE HYSTEROSCOPY

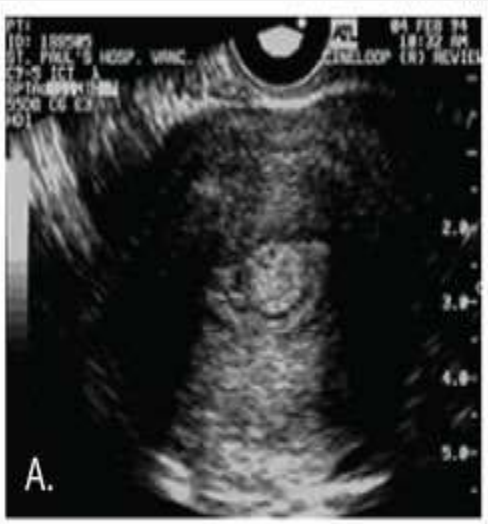
- Hysteroscopy Combined With Endometrial Biopsy Improves The Sensitivity And Specificity For Detection Of Endometrial Malignancy And Other Pathology Compared With Either Diagnostic Tests Performed Alone.
- Hysteroscopy Has A Sensitivity And Specificity For Identifying Endometrial Cancer Of 86% And 99%, Respectively. Endometrial Sampling Alone Has A Sensitivity And Specificity Of 68–81% And 99–100% For Identifying Endometrial Hyperplasia And Endometrial Cancer

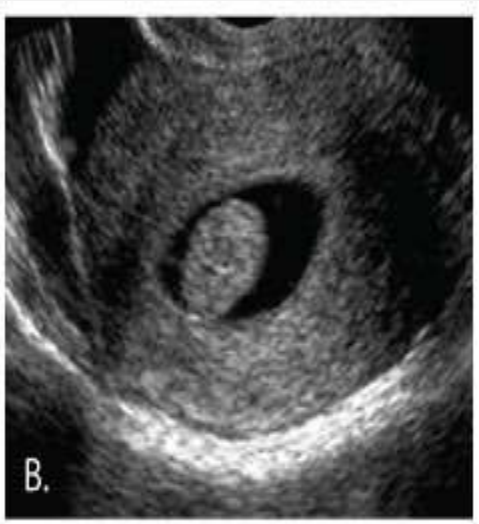


SALINE INFUSION SONOGRAPHY

- Saline Infusion Sonography (SIS) Provides Improved Visualisation Of Uterine And Endometrial Pathology. SIS Involves An Infusion Of Sterile Saline Through A Soft, Plastic Catheter Placed In The Cervix In Conjunction With Transvaginal Ultrasound. The Saline Infusion Distends The Uterine Cavity.







SIS outlines the intrauterine polyp (Figure B), which could not be easily seen with in the routine transvaginal pelvic ultrasound (Figure A).

ENDOMETRIAL PIPELLE SAMPLING

- The Pipelle© Biospy Instrument Is A Fine-bore Plastic Instrument With A Curette-like Tip And A Central Plunger, Which Creates A Vacuum When Pulled.
- The Pipelle Can Be Inserted With Or Without Local Anaesthesia And, When The Plunger Is Pulled Back, It Sucks A Sample Of Endometrium Into The Instrument. It Is Then Rotated And Removed Slowly While Keeping The Plunger Pulled Back In An Attempt To Sample All Anterior/Posterior/Lateral Surfaces Of The Uterine Cavity.
- It Is Then Inserted Into Formalin And The Plunger Replaced To Expel The Endometrial Biopsy.

SUPPLEMENTARY INVESTIGATIONS

Investigations supplementary to baseline set	
MRI and endometrial biopsy	Particularly for assessing suitability for UAE or surgical therapy for fibroids Particularly for advanced stage endometriosis or features suggestive of endometriosis recurrence
Sonohysterography (saline infusion sonography)	Routine pelvic ultrasound identifies more uterine fibroids than hysteroscopy but fewer polyps. Ultrasound will also assess for ovarian pathology
Pelvic infection screening	Particularly reproductive age groups or where sequelae of STI (sexually transmitted infection) are suspected
Von Willebrand's disease (vWD)	Around 5–20% of women with menorrhagia have an inherited bleeding disorder, most often vWD Indications to test for vWD include: menorrhagia since menarche, family history of idiopathic menorrhagia, easy bruising and/or personal history of easy bruising or dental bleeding

POSTMENOPAUSAL BLEEDING

- Unscheduled Bleeding In Postmenopausal Women Is Abnormal And May Indicate The Presence Of Endometrial Cancer.
- Nearly All Cases Of Endometrial Cancer (96%) Are Associated With A Thickened Endometrium (>4 Mm In Postmenopausal Women), Which Can Be Measured By Transvaginal Ultrasonography. If The Scan Shows A Thickened Endometrium >4 Mm, Then Histological Sampling Is Essential In The Diagnostic Evaluation Of Abnormal Bleeding In Postmenopausal Women.
- Hysteroscopy Combined With Endometrial Biopsy Improves The Detection Of Intrauterine Pathology And Has A High Specificity (Highly Unlikely Not To Detect Cancer). SIS Is A Sensitive Technique For The Detection Of Intrauterine, Intramural And Ovarian Pathology But Does Not Provide Histological Data.

Causes of vaginal bleeding in postmenopausal women	
Polyps	30%
Submucosal fibroids	20%
Endometrial atrophy	30%
Hyperplasia	8–15%
Endometrial carcinoma	8–10%
Ovarian, tubal, cervical malignancy	2%

PMB, HRT, TAMOXIFEN AND ENDOMETRIAL CANCER

- More Than 90% Of The Cases Of Endometrial Cancer Occur In Women Over 50 And This Cancer Is Associated With 10% Of The Cases Of Postmenopausal Vaginal Bleeding.
- To This End, Any Unscheduled Bleeding While On Hrt Should Be Referred To Secondary Care For Further Investigation. Manufacturers Of HRT Have Advised That Erratic Bleeding May Occur In The Intial 3 Months Of HRT Commencement, Or When Changing Preparations. However, Unscheduled Bleeding Persisting Beyond This Period Warrants Urgent Referral And Investigation.

  *Tamoxifen Usage, Like HRT, Also Increases The Risk Of Developing Endometrial Hyperplasia Or Cancer, But TVUS Can Be Misleading In These Patients.
- Tamoxifen Can Cause Subendometrial Cyst Development, Which Makes The Endometrium Appear Thickened In Transvaginal Sonograms. However, The Subendometrial Cystic Tissue Can Be Differentiated From The Endometrium Itself In SIS.

ENDOMETRIAL THICKNESS

- The Thickness Of The Endometrial Stripe Can Be Measured Accurately By Transvaginal Sonography And It Has Been Estimated That 96% Of Postmenopausal Women With Endometrial Cancer Will Have An Endometrial Thickness (ET) >4 Mm. At This Threshold, The False Positive Rate Is 50%.

  Women With PMB Whose ET Is <4 Mm Still Have A 1–2% Risk Of Having Endometrial Cancer. TVUS Can Also Show If The Endometrial Lining Is Very Thin. If So, The Bleeding May Be Due To Endometrial Atrophy.

  It Has, Therefore, Been Suggested That As A Minimum Screening Test An Endometrial Biopsy Is Required If ET Is:

- >4 Mm In Postmenopausal Women
- >16 Mm In Premenopausal Women
- And May Be Selectively Performed In Postmenopausal Women With ET <4 Mm If Other Historical, Clinical Or Sonographic Risk Factors Are Present.

TESTING FOR ENDOMETRIAL CANCER

- The Preferred Investigation Of Endometrial Cancer Is Hysteroscopy And Either Blind Endometrial Biopsy (Using Pipelle Sampler) Or Hysteroscopic-guided Endometrial Biopsy.
- This Diagnostic Test May Be Expanded In A 'Therapeutic Manner' By Performing Hysteroscopic Resection Of Any Identified Intrauterine Focal Lesions (Polyps, Submucous Fibroids), I.E. See-and-treat.
- This Test Has A 99% Specificity In Women With Pmb.
- If This Test Is Negative, Then Endometrial Cancer Is Highly Unlikely As The Post-test Probability Of Endometrial Cancer Is <0.5%.

INTERMENSTRUAL BLEEDING

- Intermenstrual Bleeding (IMB) Encompasses Any Bleeding Which Occurs Outside Of The Woman's Menstrual Period. It May Affect Between 13–21% Of Women. The Incidence In Perimenopausal Women Is As High As 24%. IMB Can Also Include Postcoital Bleeding. It Is A Symptom Which Although Largely Attributed To A Benign Cause, Can Result In Significant Distress To The Patient As It Is A Commonly Known And Accepted Symptom Of Cervical Cancer.

CAUSES

- Causes Of IMB Can Be Classified Based On Their Anatomical Site. Commencing At The Top Of The Reproductive Tract They Are:
- Ovarian Causes: 1–2% Of Women Will Spot At Ovulation. Estrogen Secreting Ovarian Tumours Can Also Cause IMB In Postmenopausal Women.
- Uterine Causes:
  - Iatrogenic – Irregular Bleeding Secondary To Hormonal Contraceptives (COC, POP, IUS [Mirena]) And Hormonal Implants. The Bleeding May Be Due To The Medication Itself, Its Misuse E.G Missed Pills, Or Interactions With Other Medications Like Enzyme Inducers. Other Medications Include Drugs Which Affect The Clotting Pathway E.G. Ssri's And Anticoagulants.
  - Infective – Endometritis
  - Structural Benign – Uterine Polyps And Fibroids, Adenomyosis
  - Structural Malignant – Endometrial Cancer.

- **Cervical Causes:**

  Iatrogenic – Following Examination/Smear Test

  - Infective – Cervicitis Secondary To Infection Usually Chlamydia Or Gonorrhoea
  - Structural Benign – Cervical Ectropion Can Occur Spontaneously Or In Response To Increased Estrogen Levels Secondary To Pregnancy Or The Combined Oral Contraceptive Pill. Cervical Polyps 1.5–10% Prevelance, Largely Benign (Malignancy 0.1% And Dysplasia 0.5%)
  - Structural Malignant – Cervical Cancer.

- **Vaginal Causes:**
  - Infective – Chlamydia And Gonorrhoea May Cause Cervicitis As Above. Vulvovaginitis Secondary To *Trichomonas Vaginalis* Or *Candida Albicans* Infection May Present With IMB In The Context Of Severe Vaginal/Vulval Oedema Or Excoriations.
  - Structural Benign – Adenosis (Metaplastic Cervical Or Endometrial Tissue On The Vaginal Wall)
  - Structural Malignant – Vaginal Cancer.

EXAMINATION AND INVESTIGATION

- As Outlined In The AUB Bleeding Section, Thorough Clinical History Taking And Examination Is Vital To Elicit And Identify The Possible Causes Of IMB. Undertaking Speculum Examination Should Allow Identification Of Any Cervical Or Vaginal Abnormalities. A Cervical Smear Should Be Taken Only If The Patient Is Due One Based On National Screening.
- Referral To Colposcopy Should Be Made If There Is An Obvious Abnormality Of The Cervix Or If There Are Symptoms Of Cervical Cancer (Persistent Postcoital Bleeding Or Persistent Vaginal Discharge Which Cannot Be Explained By Other Causes Such As Infection, Polyp Etc)
- Cervical Cytology With High Vaginal And Endocervical Swabs Should Be Obtained For The Diagnosis Of Sti’s

Note

- Uterine Polyps, Whether Endometrial Or Submucous Fibroid Polyps, Are A Common Cause Of Intermenstrual Bleeding (IMB).
- Once Diagnosed By Hysteroscopy, Uterine Polyps Are Easily Treated By Hysteroscopic Techniques With Highly Successful Results In The Vast Majority Of Women.

TREATMENT OF HMB - A THREE-STEP APPROACH

- In The Early 1990s, It Was Estimated That At Least 60% Of Women Presenting With HMB Would Have A Hysterectomy As The First-line Treatment. The Majority Of These Hysterectomies Occurred In Women Without Uterine Pathology.
- Step One Is Medical Treatment With Both Hormonal And Non-hormonal Treatment (When Assessed Over A 2-year Period, Lng-ius Was More Effective Than Usual Medical Treatments In Improving Heavy Menstrual Bleeding).
- Step Two Is Minimally Invasive Uterus Conserving Surgery E.G. Hysteroscopic Fibroid Resection, Endometrial Ablation, Transcervical Resection Of Endometrium And Laparoscopic Myomectomy.

- Step Three Involves Major Surgical Procedures E.G. Abdominal Myomectomy And Hysterectomy.
- For Women With Hmb And Large Fibroids And/Or Significant Symptoms, Such As Chronic Pelvic Pain Or Dysmenorrhoea (Pressure Symptoms), A Hysterectomy Or Uterine Artery Embolisation May Be Offered As First-step Therapy. Similarly, Women With Significant Diagnoses Like Endometriosis Can Also Be Offered Hysterectomies As Primary Treatments.

Treatment	Effect on fibroid size	Effect on HMB	Effect on fertility
First-step treatments (all medical)			
Tranexamic acid	No effect	Decrease 30–50%	No effect
NSAIDs (e.g. mefenamic acid)	No effect	Decrease 20–40%	No effect
Combined oral contraceptive (synthetic estrogen)	No data	Decrease 40%	Licensed contraceptive
Combined oral contraceptive Qlaira (natural estrogen)	No data	Decrease 30%	Licensed contraceptive
Oral progestogen (high-dose)	No effect	Decrease 60%	Contraceptive effect or licensed contraception
Intrauterine progestogen (LNG-IUS)	Decrease 30%	Decrease 70–100% (may also treat endometriosis and adenomyosis)	Licensed contraceptive
GnRH analogues (3–6 months with/without add-back HRT)	Decrease 30%	Decrease 60–100% (causes amenorrhoea in 80–90% of women)	Likely contraceptive but contraception is advised
Progestogen-only implant (Nexplanon) or Progestogen-only injectable (Depoprovera)	Unknown	Decrease 30–100% (causes amenorrhoea in 15–20%)	Licensed contraceptive

Second-step treatment (minimally invasive uterus-conserving surgery)			
Hysteroscopic myomectomy (hysteroscopic fibroid resection)	Excision and removal of intracavitary fibroids	Decrease 50–80%	Improved if excising submucous fibroid No effect if excising uterine polyp
Endometrial ablation	No effect	Decrease 80% (may also treat adenomyosis)	Likely contraceptive but contraception is advised following ablation
Transcervical resection of endometrium	Will be able to excise and removal intracavity fibroids	Decrease 80%-100%	Likely contraceptive but contraception is advised following ablation
Laparoscopic myomectomy	Excise subserosal and non-deeply embedded intramural fibroids	No effect or may decrease up to 30%	No effect or may increase

Second-step OR third-step treatment (established and newly developed minimally invasive uterus-conserving treatments)			
Focal fibroid treatment			
MRI-guided focused ultrasound therapy	Decrease 15–20%	Decrease 60%	May decrease, have no effect, or improve fertility
Radiofrequency ablation of fibroids (hysteroscopic system is VizAblate	Decrease 50-80%	Decrease 50%	Treatment still under trial
Global uterus treatment			
Uterine fibroid embolisation	Decrease 30%	Decrease 60–80%	May decrease, have no effect, or improve fertility
Laparoscopic uterine artery occlusion (with or without ovarian artery occlusion)	Decrease 20-30%	Decrease 50%-60%	Treatment still under trial
Doppler-guided transvaginal uterine artery occlusion	Decrease 20-30%	Decrease 40-60%	Treatment still under trial

Third-step treatments (major surgical procedures)			
Abdominal myomectomy	Excise subserosal, intramural and intracavitary lesions	Decrease 60–80%	Improved, particularly if uterine cavity is no longer distorted
Hysterectomy	Complete cure	Complete cure	Irreversible contraceptive