بسم الله الرحمن الرحيم

Abnormal uterine bleeding (AUB)

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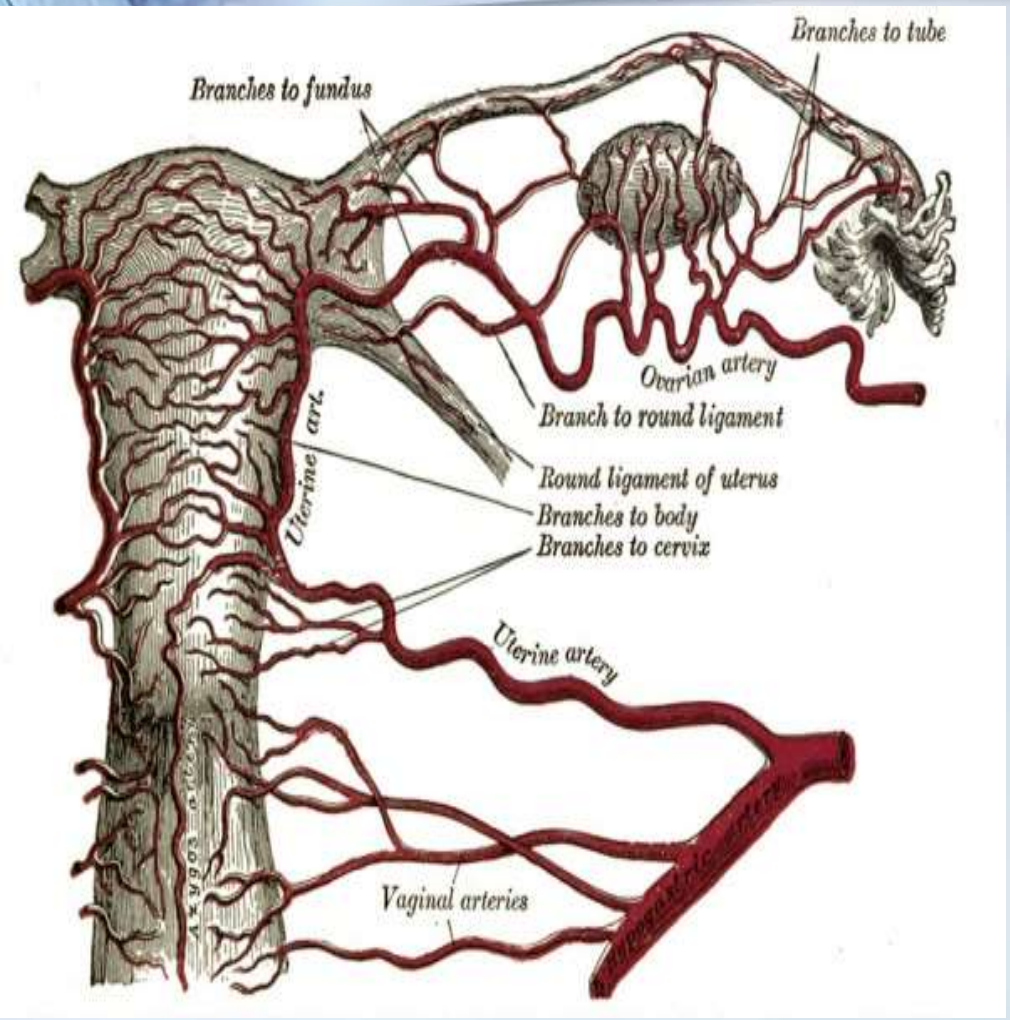
Definition

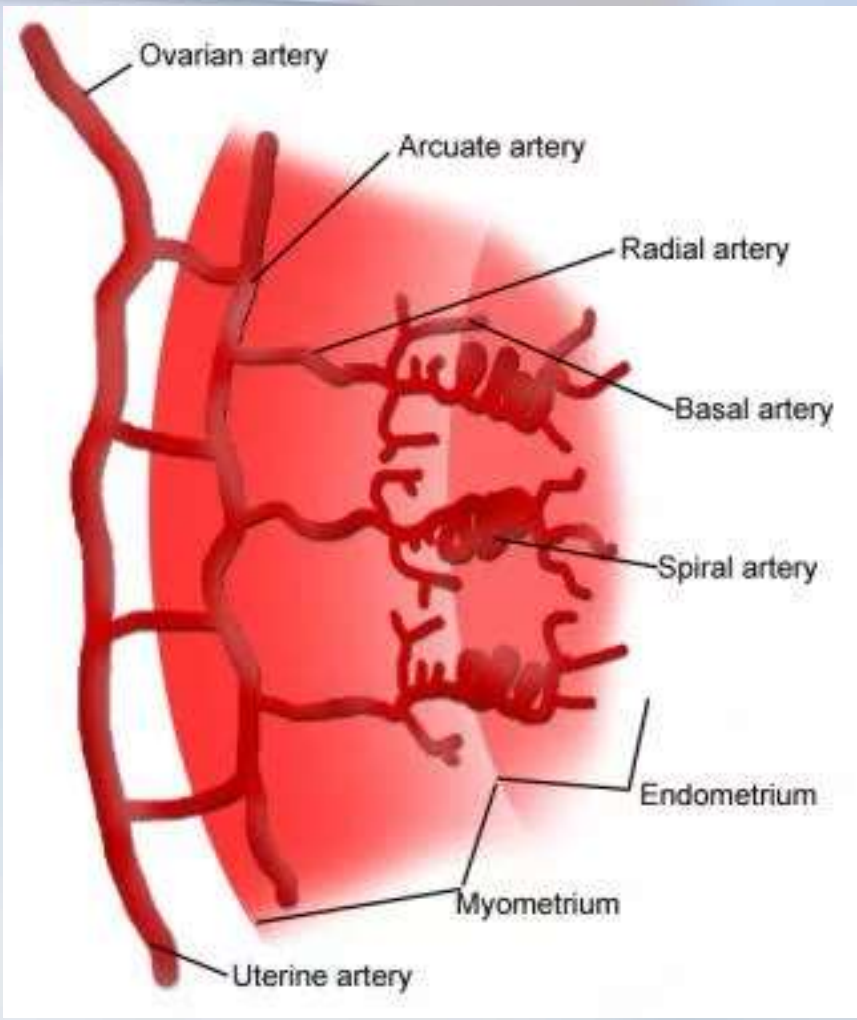
- **Abnormal uterine bleeding**
- Abnormal uterine bleeding in nonpregnant women of reproductive age is defined as menstrual bleeding of abnormal volume, duration, regularity, or frequency, and includes bleeding between cycles.
- Acute: refers to an episode of heavy bleeding that is of sufficient quantity to require immediate clinical intervention to stop further blood loss
- Chronic: defined as bleeding of abnormal volume, duration, regularity, or frequency that has been present for most of the previous 6 months

Scope of AUB

- AUB affects up to 30% of women throughout their reproductive lifetime
- 1/3 of outpatient visits to the Gynecologist
- Responsible for over one third of hysterectomies
- Effect on:
  - HRQoL
  - Anemia
  - Pain
  - Social impact
  - Surgery
  - Infertility

Uterine blood supply





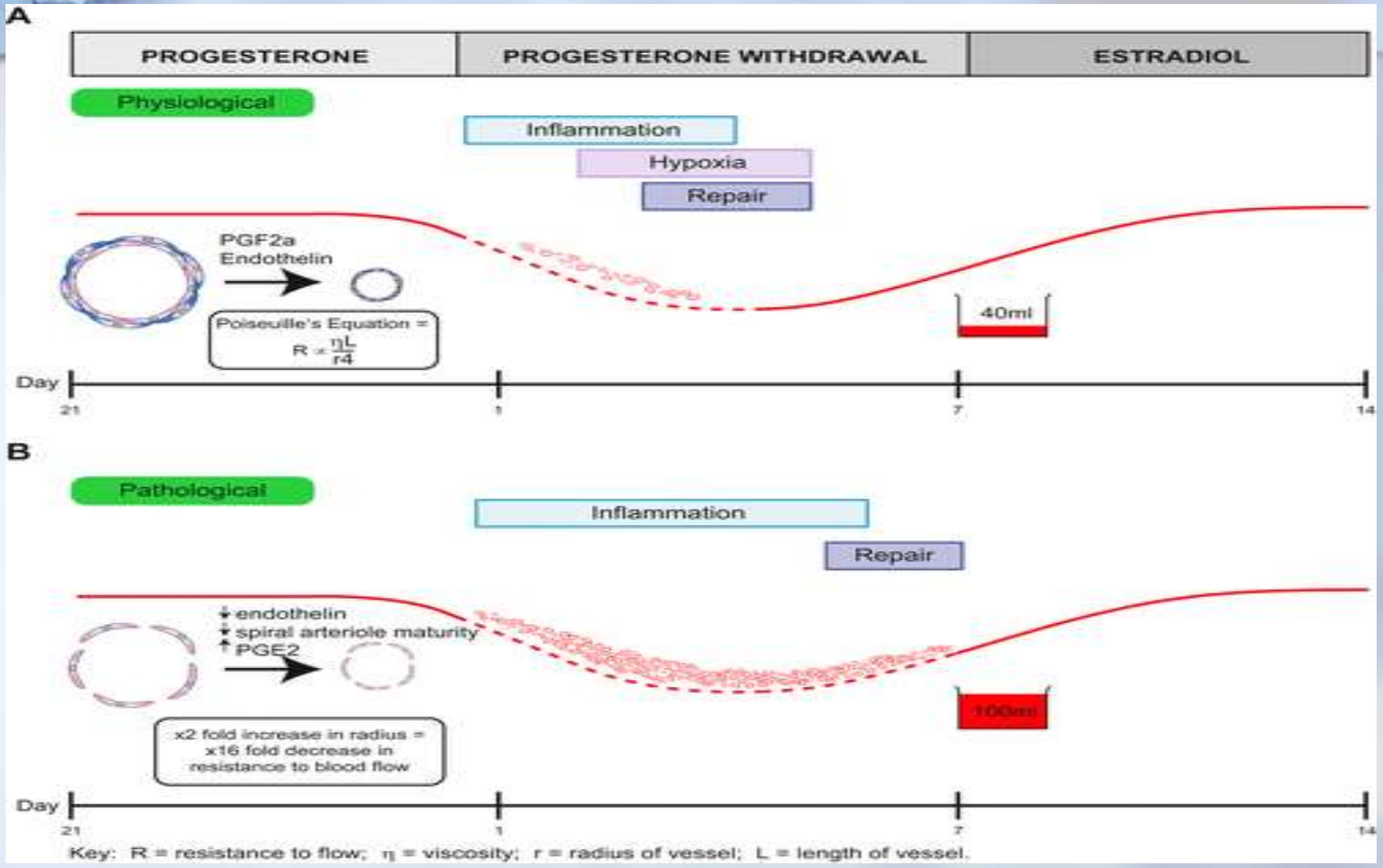
PATHOGENESIS OF AUB :

- Endometrium normally produces, prostaglandin from arachidonic acid which is a fatty acid.
- **PGE_2** and **PGI_4** are vasodilators and antiplatellet aggregates.
- **PGF_2** and thromboxane A_2 – vasoconstriction and platelet aggregates.

PATHOGENESIS OF AUB :

- Progesterone produces **PGF_2.**
- In anovulatory cycles, the absence of progesterone and therefore **PGF_2** causes AUB.
- In some cases tissue plasminogen activator (TPA) which is a fibrinolytic enzyme is increased leading to AUB.

PATHOGENESIS OF AUB :



AUB patterns based on symptoms

- Heavy menstrual bleeding: excessive menstrual blood loss that interferes with patient's quality of life; may occur alone or with other symptoms
- Irregular menstrual bleeding: Varying lengths of bleeding-free intervals of more than 20 days in one 90-day period
- Infrequent menstrual bleeding: Bleeding at intervals of more than 38 days apart
- Frequent menstrual bleeding: Bleeding at intervals of less than 24 days apart
- Prolonged menstrual bleeding: Menstrual bleeding lasting more than 8 days
- Shortened menstrual bleeding: Menstrual bleeding lasting less than 3 days
- Irregular no menstrual bleeding
- Intermenstrual bleeding: Irregular episodes of bleeding (often light and short) occurring between otherwise normal menstrual periods
- Postcoital bleeding: Bleeding after sexual intercourse
- Pre- or postmenstrual spotting
- Bleeding that regularly occurs 1 or more days before or after menstrual period

Menstrual cycle

- The mean interval between menses is 28 days (±7 days).
- Thus, if bleeding occurs at intervals of 21 days or less, it is abnormal.
- The mean duration of menstrual flow is 4 days.
- Few women with normal menses bleed more than 7 days, so bleeding for longer than 7 days is considered to be abnormally prolonged (menorrhagia).

Abnormal Menses—Terminology

Term	Interval	Duration	Amount
Menorrhagia	Regular	Prolonged	Excessive
Metrorrhagia	Irregular	±Prolonged	Normal
Menometrorrhagia	Irregular	Prolonged	Excessive
Hypermenorrhea	Regular	Normal	Excessive
Hypomenorrhea	Regular	Normal or less	Less
Oligomenorrhea	Infrequent or irregular	Variable	Scanty
Amenorrhea	Absent	No menses for 90 days	Absent

Menstrual Terminology

Cycle		Normal	
Regularity	Absent	Regular	Irregular
Frequency of menstruation	Infrequent	Normal	Frequent
Duration of menstrual flow	Shortened	Normal	Prolonged

Menstrual blood loss
MBL

- The average menstrual blood loss is 35 mL.
- The amount of MBL increases with parity but not age in the absence of disease.
- A MBL of 80 mL or greater is defined as menorrhagia, which occurs in 9% to 14% of women.

Measurements of MBL

- Direct measurement of MBL – alkaline haematin
- *Indirect measurement of MBL – pictorial blood loss assessment charts (PBAC)*
  - A chart for recording the level of menstrual loss based on appearance of sanitary pads.

Suggested Normal limits for menstrual parameters. Adapted from Fraser et al

Clinical Parameter	Descriptive term	Normal limits (5–95th percentiles)
Frequency of menses (days)	Frequent Normal Infrequent	<24 24–38 >38
Regularity of menses, cycle to cycle (Variation in days over 12 months)	Absent Regular Irregular	No bleeding Variation ± 2–20 days Variation >20 days
Duration of flow (days)	Prolonged Normal Shortened	>8.0 4.5–8.0 <4.5
Volume of monthly blood loss (mL)	Heavy Normal Light	>80 5–80 <5

Severity of MBL

- Clots greater than approximately 2.5cm in diameter
- Anemia or Low serum ferritin
- Changing a pad or tampon more than hourly
- Social embarrassment

Causes (old nomenclature)

- The causes of abnormal bleeding can be divided into:
- **Organic**:
  - systemic disease
  - reproductive tract disease.
- **Dysfunctional uterine bleeding** (DUB, hormonally related) is further divided into:
  - anovulatory bleeding
  - ovulatory bleeding.

Systemic disease
disorders of blood coagulation

1- von Willebrand disease
2- prothrombin deficiency,
3- leukemia, severe sepsis
4- idiopathic thrombocytopenic purpura
5- hypersplenism

- Routine screening for coagulation defects is mainly indicated for the adolescent who has prolonged heavy menses beginning at menarche, unless otherwise indicated by clinical signs such as petechiae or ecchymosis.

AUB in adolescence

- Coagulation disorders are found in:
  - 5-20% of adolescent girls who require hospitalization for abnormal uterine bleeding.
  - 25% of those whose hemoglobin levels fall below 10 g/100 mL,
  - in one third of those who require transfusions.
  - in 50% of those whose severe menorrhagia occurred at the time of the first menstrual period

VWF

- The gene for VWF is located on the short arm of chromosome 12.
- Synthesized in endothelial cells and megakaryocytes.
- VWF functions in primary hemostasis by:
  - forming an adhesive bridge between platelets and vascular subendothelial structures as well as between adjacent platelets at sites of endothelial injury.
  - plays a role in fibrin clot formation by acting as a protective carrier protein for factor VIII which has a greatly shortened half-life unless it is bound to VWF- The low factor VIII concentration in VWD is due to the decreased levels of VWF, since VWF normally protects factor VIII from proteolytic inactivation by activated protein C and its cofactor protein S

Acquired von Willebrand syndrome

- Caused by immune and non-immune mechanisms- Cardiovascular disease, SLE and other autoimmune disorders.
- VWF production in endothelial cells is increased by both estrogen and thyroid hormone, and increased estrogen levels during pregnancy lead to higher levels of VWF during the second and third trimesters.
- acquired reductions in VWF synthesis can occur in certain conditions such as hypothyroidism.
- Autoantibodies against VWF have been reported in autoimmune thyroiditis.
- Patients who have VWF levels below 20 international units (IU)/dL usually have increased bleeding, and those with levels of 20 to 30 IU/dL are at increased risk for bleeding

Specific test for VWF disease

- A CBC with platelet count and coagulation testing including a (PT) and (aPTT).
- These three tests, readily available in most larger hospitals:
  - VWF: Ag: measure the amount of VWF protein present in plasma
  - VWF: Rco: measures the function of the VWF protein that is present as ristocetin cofactor activity.
  - FVIII: measures the ability of the VWF to serve as the carrier protein to maintain normal FVIII survival.

Abnormal uterine bleeding in women of reproductive age

- The most common causes of are accidents of pregnancy such as:
  - threatened,
  - incomplete,
  - missed abortion
  - ectopic pregnancy
  - trophoblastic disease.
- A sensitive b-human chorionic gonadotropin (b-hCG) assay should be performed as part of the diagnostic evaluation.

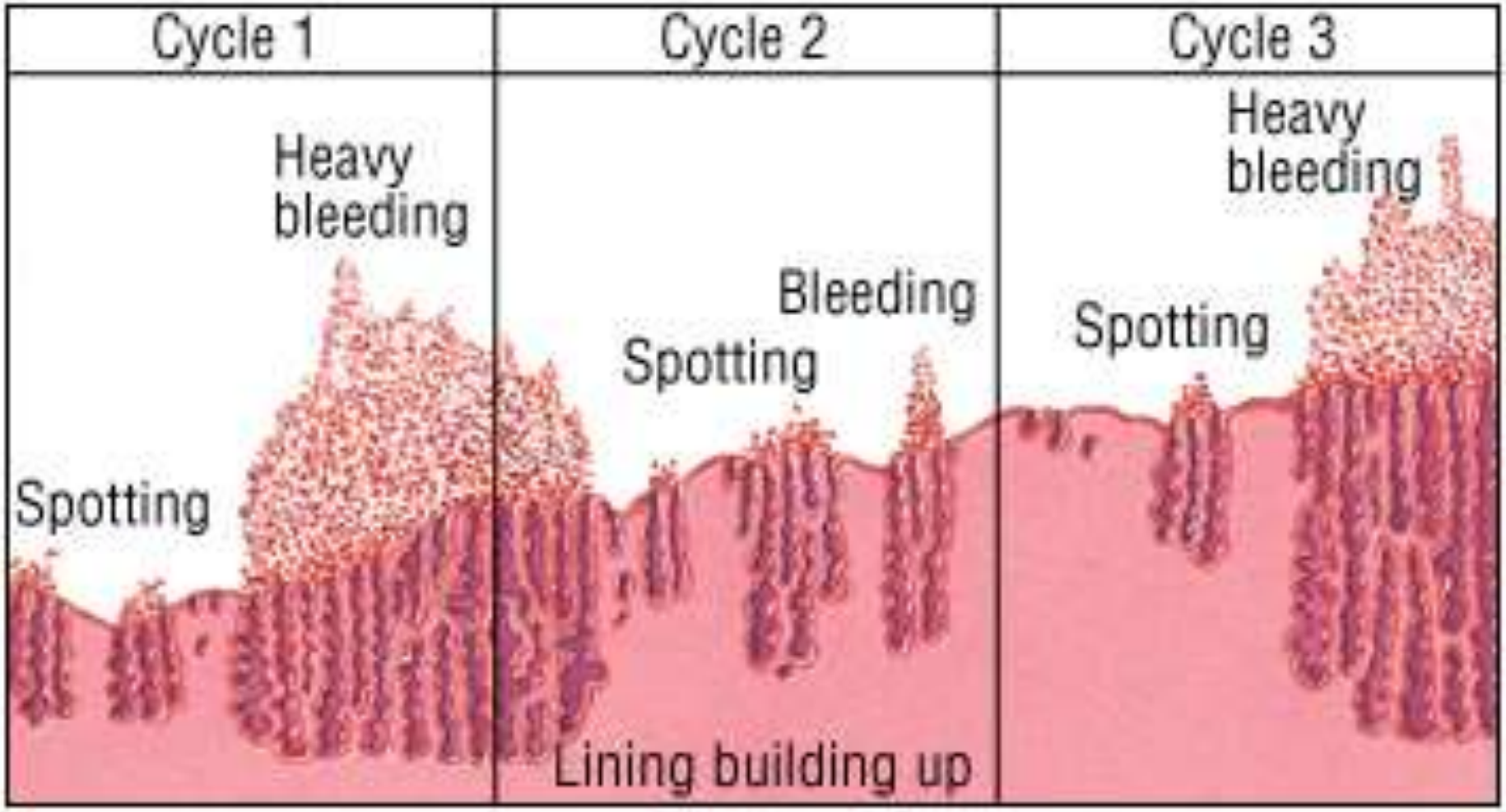
AUB causes not related to pregnancy

- Anatomic uterine abnormalities such as:
  - submucous myomas,
  - endometrial polyps,
  - adenomyosis frequently produce symptoms of prolonged and excessive regular uterine bleeding.
- Cervical lesions such as:
  - erosions,
  - polyps,
  - cervicitis may cause irregular bleeding, particularly postcoital spotting.
- These lesions can usually be diagnosed by visualization of the cervix.
- In addition, traumatic vaginal lesions, severe vaginal infections, and foreign bodies have been associated with abnormal bleeding.

Other less common causes of AUB

- Any malignancy of the genital tract,
  - Endometrial
  - cervical cancer,
  - vaginal, vulvar, and fallopian tube cancer
  - Ostrogen-producing ovarian tumors may become manifest by abnormal uterine bleeding.Thus, granulosa theca cell tumors may present with excessive uterine bleeding.
- Infection of the upper genital tract, particularly endometritis, may present as prolonged menses, although episodic intermenstrual spotting is a more common symptom.
- Endometriosis may also result in abnormal bleeding and frequently presents as premenstrual spotting.

Dysfunctional uterine bleeding



FIGO classification system (PALM-COEIN) for causes of abnormal uterine bleeding in nongravid women of reproductive age

- There are 9 main categories, which are arranged according to the acronym PALM-COEIN (pronounced “pahm-koin”):
- polyp;
- adenomyosis;
- leiomyoma;
- malignancy and hyperplasia;

Structural

- coagulopathy;
- Ovulatory dysfunction;
- endometrial;
- Iatrogenic; and
- not yet classified.

Non-structural

Polyp

Adenomyosis

Leiomyoma

Malignancy & hyperplasia

Submucosal

Other

Coagulopathy

Ovulatory dysfunction

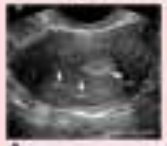
Endometrial

Iatrogenic

Not yet classified

P

Polyp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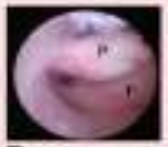

B

A

Adenomyosis


C


D

L

Leiomyoma


E

M

Malignancy


F


G

A: USS view of polyp
B: Hysteroscopic view of polyp
C: MRI of adenomyosis
D: USS of adenomyosis
E: Hysterectomy specimen containing fibroids
F: Hysterectomy specimen containing endometrial cancer
G: Histology of endometrioid carcinoma
H: Excessive bruising
I: USS of polycystic ovary
J: Progesterone receptor localisation in secretory phase
K: levonorgestrel-releasing intrauterine system (LNG-IUS)
L: Doppler USS of AV malformation
M: Doppler USS of endometrial pseudo-aneurysm

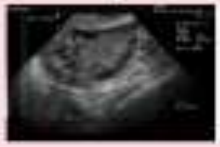
C

Coagulopathy


H

O

Ovulatory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E

Endometrial


J

I

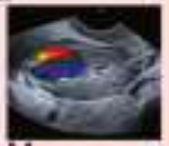
Iatrogenic


K

N

Not otherwise classified


L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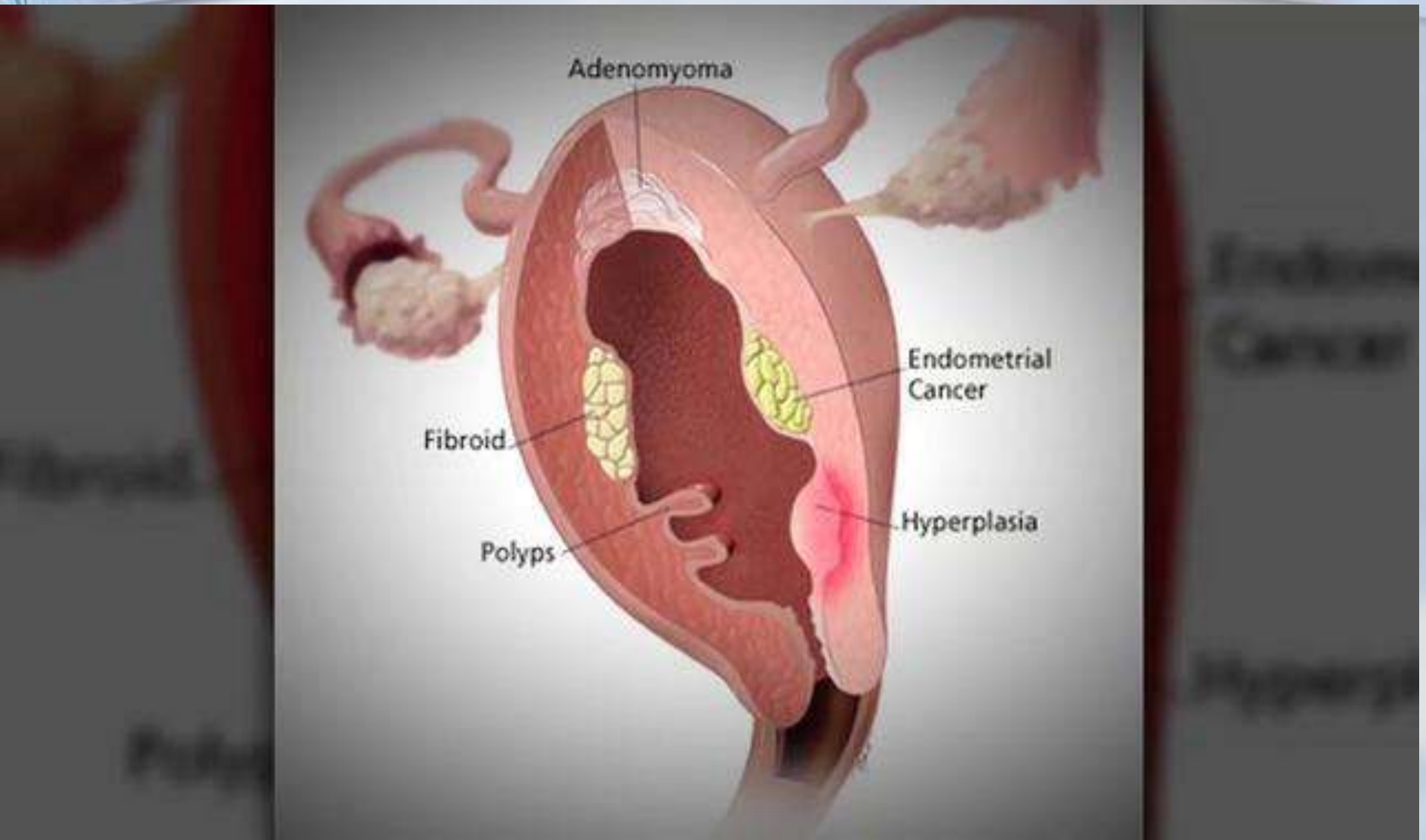
Structural and histological abnormalities

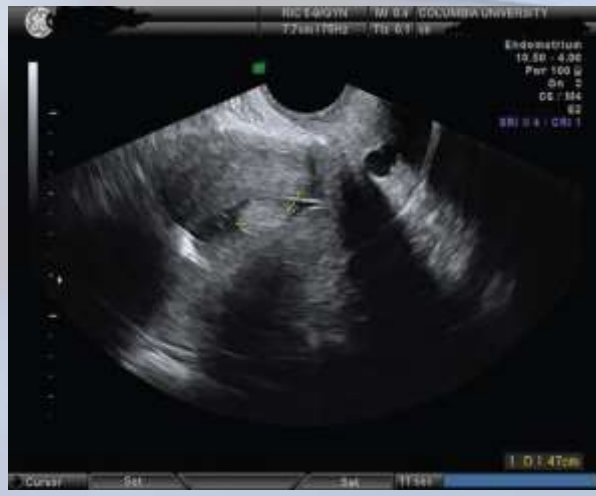


Dysfunctional uterine bleeding

- The term “DUB,” which was previously used as a diagnosis when there was no systemic or locally definable structural cause for AUB, is not included in the system and should be abandoned, per the agreement process

Polyp (AUB-P)

- Pre-menopausal polyps:
  - 64 – 88% have symptoms
- Present with HMB, IMB, or PCB
- Symptoms do NOT correlate with number, diameter & site
- Diagnosis: US, SIS, hysteroscopy
- These epithelial proliferations comprise a variable vascular, glandular, and fibromuscular and connective tissue component and are often asymptomatic, but it is generally accepted that at least some contribute to the genesis of AUB.
- The lesions are usually benign but a small minority may have atypical or malignant features



FULL TEXT ARTICLE

Novel finding of high density of activated mast cells in endometrial polyps

Moamar Al-Jefout M.D., Kirsten Black M.D., Lauren Schulke M.Sc., Marina Berbic B.Med.Sc., Georgina Luscombe Ph.D., Natsuko Tokushige Ph.D., Frank Manconi Ph.D., Robert Markham Ph.D. and Ian S. Fraser M.D.

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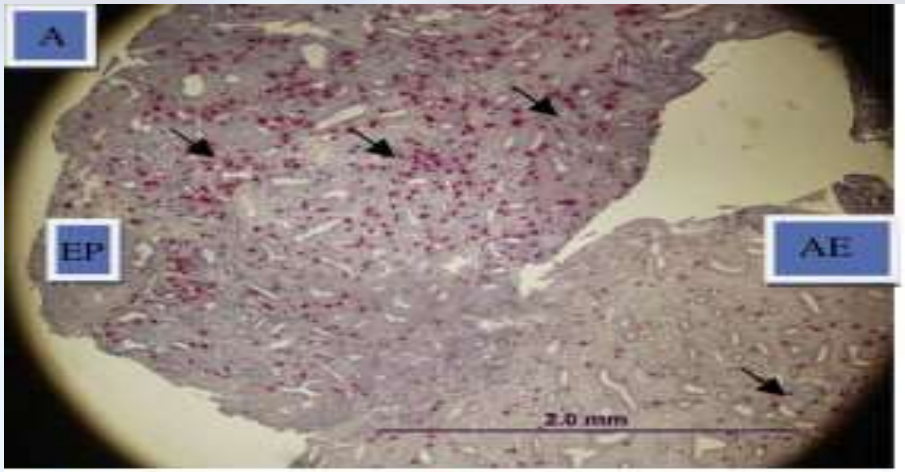
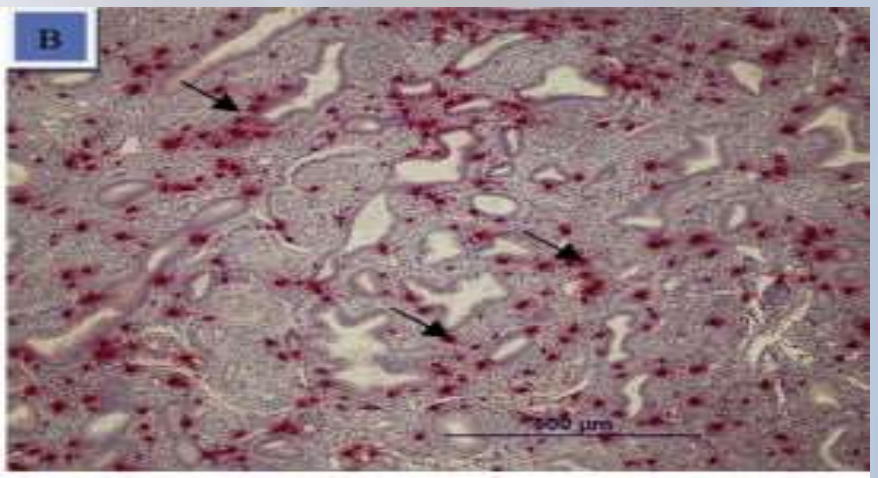
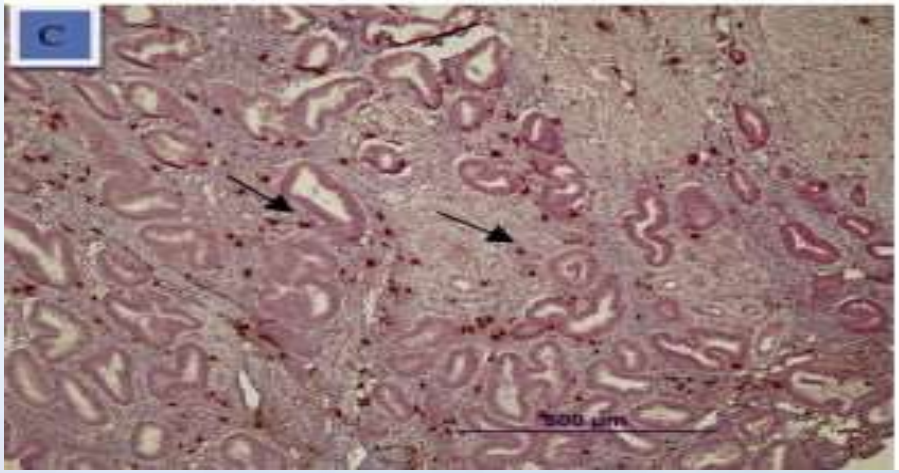
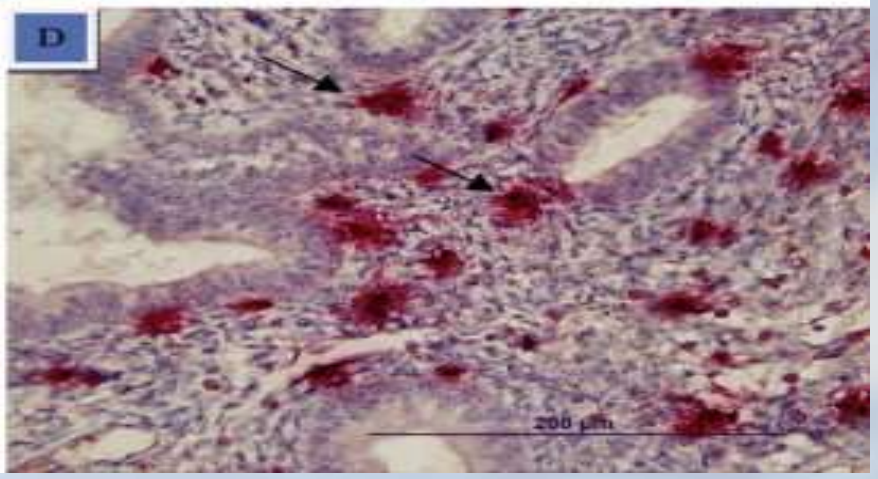
Fertility and Sterility









Adenomyosis (AUB-A)

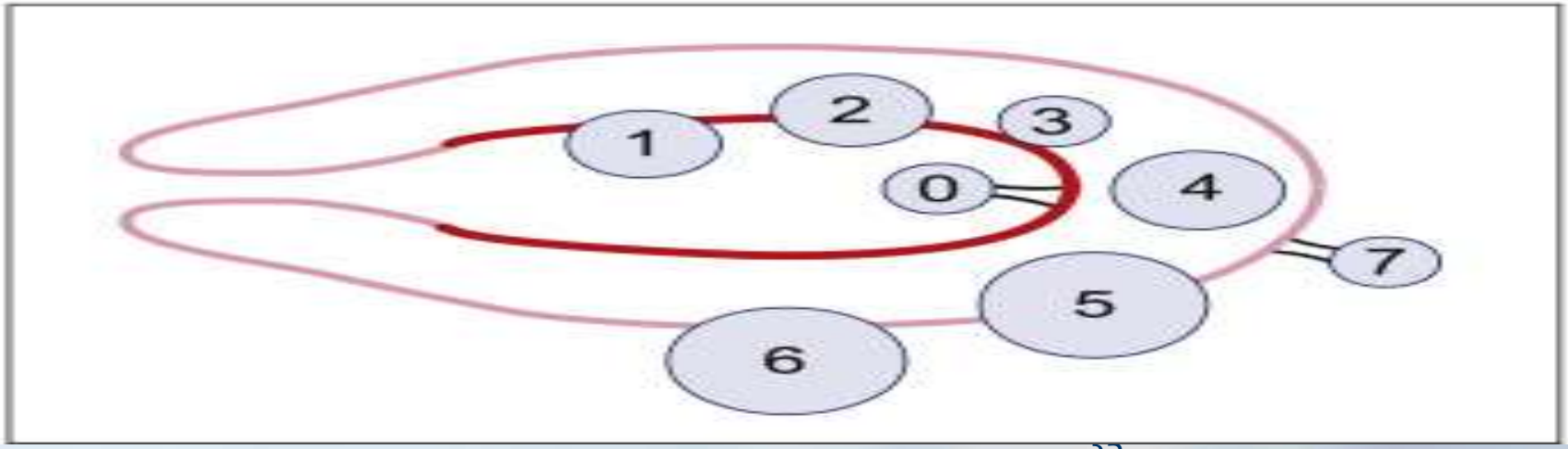
- The relationship between adenomyosis and the genesis of AUB is unclear, lending strength to the notion that extensive additional research is required.
- Estimates of the prevalence of adenomyosis vary widely, ranging from 5% to 70%

Leiomyoma (AUB-L)

- Benign fibromuscular tumors of the myometrium are known by several names, including “leiomyoma,” “myoma,” and the frequently used “fibroid.”
- “Leiomyoma” is generally accepted as the more accurate term and was selected for use in the present system.
- The prevalence of these lesions (up to 70% in Caucasians and up to 80% in women of African ancestry , their spectrum of size and location (subendometrial, intramural, subserosal, and combinations of these),
- Like polyps and adenomyosis, many leiomyomas are asymptomatic, and frequently their presence is not the cause of AUB.
- Furthermore, leiomyomas have widely varying rates of growth, even in a single individual

Wamsteker classification
Tertiary classification of AUB-L

Primary	Secondary	Tertiary
Absent	Submucosal	0 Pedunculated intracavity
		1 ≤50% intramural
OR	OR	2 ≥50% intramural
Present	Other	3 Contacts endometrium
		4 Intramural
		5 Subserosal >50% intramural
		6 Subserosal <50% intramural
		7 Subserosal pedunculated
		8 Other (eg cervical parasitic)



Symptoms			
	AUB only	AUB with pressure symptoms; family complete and no desire to retain fertility	AUB symptoms and fertility desire/subfertility
No cavity distortion	LNG-IUS Tranexamic acid Mefenamic acid UPA GnRH analogue P	UPA GnRH analogue	Tranexamic acid Mefenamic acid UPA (short course) GnRH analogue (short course)
	UAE EA Hysterectomy	UAE (MRgFUS) Myomectomy Hysterectomy	Myomectomy UAE (evidence here needed) (MRgFUS)
Cavity distortion	Tranexamic acid Mefenamic acid UPA GnRH analogue P	UPA GnRH analogue	Tranexamic acid Mefenamic acid UPA (short course) GnRH analogue (short course)
	TCRF UAE Hysterectomy	UAE Myomectomy Hysterectomy	TCRF Myomectomy UAE (evidence here needed)

Medical treatment
Surgical treatment

LNG-IUS	Levonorgestrel-releasing -intrauterine system
UPA	Ulipristal acetate
GnRH analogue	Gonadotrophin-releasing hormone analogue
P	Systemic progestogens • Medroxyprogesterone acetate • Norethisterone • Depo-Medroxyprogesterone acetate
EA	Endometrial ablation
UAE	Uterine artery embolisation
(MRgFUS)	MR-guided focused ultrasound – predominantly experimental at present
TCRF	Transcervical resection of fibroid

Malignancy and hyperplasia (AUB-M)

- Although relatively uncommon, atypical hyperplasia and malignancy are important potential causes of, or findings associated with, AUB and must be considered in nearly all women of reproductive age.
- The present classification system is not designed to replace those of WHO and FIGO for categorizing endometrial hyperplasia and neoplasia .
- Consequently, when a premalignant hyperplastic or malignant process is identified during investigation of women of reproductive age with AUB, it would be classified as AUB-M and then subclassified using the appropriate WHO or FIGO system.

Coagulopathy (AUB-C)

- The term “coagulopathy” encompasses the spectrum of systemic disorders of hemostasis that may be associated with AUB.
- Prevalence: 3% of women presenting with HMB
- Etiologies:
  - Von Willebrand’s disease (10%)
  - Platelet Dysfunction
  - Factor XI deficiency
  - Factor X deficiency
  - Category includes patient’s taking anti-coagulants

Coagulopathy (AUB-C)

- HMB since menarche
- One of the following:
  - PPH
  - Surgical related bleeding
  - Bleeding associated with dental work
- Two or more of the following:
  - Bruising 1-2 times/month
  - Epistaxis 1-2 times/ month
  - Frequent gum bleeding
  - Family history of bleeding problems

Ovulatory dysfunction (AUB-O)

- Mainly due to anovulatory bleeding
  - Age-related: peri-menarche, perimenopause
  - Estrogenic: unopposed exogenous or endogenous Estrogen
  - Androgenic: PCOS; CAH, acute stress
  - Systemic: Renal disease, liver disease
- Hyperthyroidism or hypothyroidism
- Luteal Phase Defect (LPD) dysfunction can contribute to the genesis of AUB, generally manifesting as a combination of unpredictable timing of bleeding and variable amount of flow (AUB), which in some cases results in HMB.

Endometrial causes AUB-E

- Etiology: diagnosed by exclusion
- Deficiencies of local production of vasoconstrictors
  - Endothelin-1
  - Prostaglandin F2a
- Excessive production of plasminogen activators
- Increased local production of vasodilators
  - Prostaglandin E2
  - Prostacyclin I2
- Inflammation (Endometritis)
  - Chlamydia

Iatrogenic (AUB-I)

- Breakthrough bleeding (BTB) using gonadal steroids is the major component of AUB-I :
  - Oral contraceptives
  - Continuous or cyclic progesterone
  - IUD or implant related bleeding
  - Implanon Subdermal implant
  - Selective oestrogen receptor modulators (SERMs) and more rarely selective progesterone receptor modulators (SPRMs)

Not otherwise classified (AUB-N)

- It is inevitable that there will be pathologies that are either rare or poorly defined that do not easily fit within the categories described earlier.
- Examples include:
  - arteriovenous malformations,
  - endometrial pseudoaneurysms,
  - myometrial hypertrophy
  - chronic endometritis (not precipitated by an IUD)

Abnormal Uterine Bleeding
Step 1: History

- When did the bleeding start?
- Were there precipitating factors, such as trauma?
- What is the nature of the bleeding (temporal pattern, duration, postcoital, quantity)
- Associated symptoms (pain, vaginal odor, changes in bowel/bladder function)
- Previous hx or FHx of bleeding disorder?
- PMH/Meds
- Sexually active?
- Weight changes; h/o excessive exercise; h/o eating disorder?

Abnormal Uterine Bleeding
Step 2: Physical Examination

- General PE to look for systemic illness, signs of hyperandrogenism
- Careful pelvic exam – focus on identifying site of bleeding (vulva, vagina, cervix, uterus, bladder, rectum)
- Assess size, contour and tenderness of the uterus

Abnormal Uterine Bleeding
Step 3: Initial Labs/Studies

- HCG
- Pap smear, biopsy of visible cervical lesions
- Determine ovulatory status
  - Menstrual cycle history
  - Basal body temperature monitoring
  - Serum progesterone
  - Urinary LH excretion
  - Ultrasound evidence of a periovulatory follicle

Laboratory tests

- A full blood count test should be carried out on all women with HMB. This should be done in parallel with any HMB treatment offered. [C]
- Testing for coagulation disorders (for example, von Willebrand disease) should be considered in women who have had HMB since menarche and have personal or family history suggesting a coagulation disorder. [C]
- A serum ferritin test should not routinely be carried out on women with HMB. [B]
- Female hormone testing should not be carried out on women with HMB. [C]
- Thyroid testing should only be carried out when other signs and symptoms of thyroid disease are present. [C]

Endometrial biopsy

- Endometrial biopsy may be indicated and, if obtained at the onset of bleeding, will show secretory changes.
- Transvaginal ultrasound can be helpful in ruling out pathology and helping to guide the need for endometrial biopsy.
- Women who are older (>35 years) and/or have a long history of excessive bleeding would benefit from an endometrial biopsy.
- It has been suggested that an endometrial lining of more than 8 mm has a greater sensitivity for picking up endometrial pathology.
- If bleeding has been prolonged and an ultrasound endometrial thickening is less than 4 mm, there is little benefit for a biopsy in this setting.
- A biopsy at the time of bleeding can also help determine whether the bleeding is caused by ovulatory function if it reveals a secretory endometrium.

Structural and histological abnormalities

- If appropriate, a biopsy should be taken to exclude endometrial cancer or atypical hyperplasia.
- Indications for a biopsy include, for example, persistent intermenstrual bleeding, and in women aged 45 and over treatment failure or ineffective treatment. [D(GPP)]
- Imaging should be undertaken in the following circumstances:
  - the uterus is palpable abdominally
  - vaginal examination reveals a pelvic mass of uncertain origin
  - pharmaceutical treatment fails. [D(GPP)]
- Ultrasound is the first-line diagnostic tool for identifying structural abnormalities. [A]

- Hysteroscopy should be used as a diagnostic tool only when ultrasound results are inconclusive, for example, to determine the exact location of a fibroid or the exact nature of the abnormality. [A]
- If imaging shows the presence of uterine fibroids then appropriate treatment should be planned based on size, number and location of the fibroids. [D(GPP)]
- Saline infusion sonography should not be used as a first-line diagnostic tool. [A]
- Magnetic resonance imaging (MRI) should not be used as a first-line diagnostic tool. [B]
- Dilatation and curettage alone should not be used as a diagnostic tool. [B]
- Where dilatation is required for non-hysteroscopic ablative procedures, hysteroscopy should be used immediately prior to the procedure to ensure correct placement of the device. [D(GPP)]

Medical options

- Traneximic acid-AMCA is administered in a dose of 6 g/day for 3 days, 4, 3, 2, and 1 g/day on successive days.
- Estrogens- for acute bleeding , oral conjugated equine estrogen (CEE) 10 mg/day, in four divided doses or 25 mg IV
- Progestogen oral rout: 3 weeks each month
- Progetogens injectable forms: every 3 months
- GnRh-a for 3 months markedly reduced MBL from 100 to 200 mL per cycle to 0 to 30 mL per cycle.
- Danazol- 200 and 400 mg daily
- OCCP: will reduce the blood loss by 50% in women with ovulatory DUB.
- NSAIDs: mefenamic acid (500 mg, three times daily), ibuprofen (400 mg, three times daily),
- Mirena IUS: levonorgestrel-releasing intrauterine system (LNG-IUS)

NSAIDs for acute AUB

- Prescribed for the first 3 days of menstruation each month for chronic heavy menstrual bleeding
- Ibuprofen: Ibuprofen Oral tablet; Adults: 400 mg PO q4—6h PRN.
- Naproxen: Naproxen Oral tablet; Adults: 500 mg PO, then 250 mg PO q6—8h PRN; use lowest effective dose for shortest possible duration; consider lower doses in geriatric patients. Max: 1250 mg on day 1 and 1000 mg/day thereafter.
- Mefenamic acid: Mefenamic Acid Oral capsule; Adult and Adolescent females >= 14 years: 500 mg PO at menses onset; then, 250 mg every 6 hours PRN for 2 to 3 days.

Antifibrinolytic agent

- Tranexamic acid (for chronic & acute heavy menstrual bleeding)
- Tranexamic Acid Oral tablet; Children and Adolescent females 12 to 17 years: 1,300 mg PO 3 times daily for 5 days during monthly menstruation.
- Tranexamic Acid Oral tablet; Adult females: 1,300 mg PO 3 times daily for 5 days during monthly menstruation

Pharmaceutical treatments for HMB (ACO&G)

- Treatments should be considered in the following order:

1. levonorgestrel-releasing intrauterine system (LNG-IUS) provided long-term (at least 12 months) use is anticipated [A]

2. tranexamic acid [A] or nonsteroidal anti-inflammatory drugs (NSAIDs) [A] or combined oral contraceptives (COCs) [B]

3. norethisterone (15 mg) daily from days 5 to 26 of the menstrual cycle, or injected long-acting progestogens. [A]

Progestogens	Progesto-genic	Anti-oestrogenic	Anti-androgenic	Androgenic	Glucocorticoid	Anti-Mineralocorticoid	Increased Risks
Progesterone	**+**	**+**	**(+)**	**-**	**(+)**	**+**	Hirsuitism,
Dienogest	**+**	**+**	**+**	**-**	**-**	**-**	Used with oestrogen, specific profile not available
Drospirenone	**+**	**+**	**+**	**-**	**-**	**+**	Used with oestrogen, specific profile not available, some speculation may be decreased cardiac risk due to anti-androgenic effects.
Nomegesterol acetate	**+**	**+**	**(+)**	**-**	**-**	**-**	Used with oestrogen, specific profile not available
Norethisterone	**+**	**-**	**-**	(+)	-	**-**	Very low risk of Thromboemolism, hepatic cancer, breast cancer
MPA	**+**	**+**	**-**	**(+)**	**(+)**	**-**	Very low risk of Breast cancer, lipid profile, coronary heart disease

Synthetic vasopressin analogue for patients with acute AUB due to von Willebrand disease

- Desmopressin Acetate Nasal spray, solution; Adolescents, Children, and Infants 11 months and older: A single 150 mcg intranasal spray into 1 nostril. Most patients respond to 1 to 2 doses; the second dose should be given 8 to 24 hours after the first. If used preoperatively, administer 2 hours before surgery.
- Desmopressin Acetate Nasal spray, solution; Adults weighing less than 50 kg: A single 150 mcg intranasal spray into 1 nostril.
- Most patients respond to 1 to 2 doses; give the second dose 8 to 24 hours after the first. If used preoperatively, administer 2 hours before surgery. NOTE: The parenteral form should be used in patients for whom the intranasal route is compromised or inappropriate.
- Desmopressin Acetate Nasal spray, solution; Adults weighing 50 kg or more: One spray (150 mcg/0.1 mL) in each nostril.
- Most patients respond to 1 to 2 doses; the second dose should be given 8 to 24 hours after the first. Following a 300 mcg intranasal dose, serum von Willebrand factor levels increase 3 to 5 times over baseline.
- If used preoperatively, administer 2 hours before surgery. NOTE: The parenteral form should be used in patients for whom the intranasal route is compromised or inappropriate.

Endometrial ablation

- In women with HMB alone, with uterus no bigger than a 10 week pregnancy, endometrial ablation should be considered preferable to hysterectomy. [A]
- Endometrial ablation should be considered where bleeding is having a severe impact on a woman's quality of life, and she does not want to conceive in the future. [C]
- Various endometrial ablation techniques achieve a 22% to 55% amenorrhea success rate at 1 year but an 86% to 99% satisfaction rate.
- Within 4 years after endometrial ablation, approximately 25% of women so treated will have a hysterectomy.
- This is the destruction or removal of the endometrium. It should be considered in women with a uterus under 10–12 week-size (depending on technique) or fibroids measuring < 3 cm in diameter, who do not wish to conceive in the future. Overall, the average rate of amenorrhoea at 12 months is around 40 %.

Endometrial ablation
First-generation techniques

- These involve resection or ablation of the endometrium under direct hysteroscopic vision using electro-cautery (monopolar or bipolar) and include TCRE (transcervical resection of endometrium), rollerball, and laser.
- The rollerball ablation to be safer than loop resection and a 4.4 % rate of significant complications including two deaths in just over 10 000 women.
- Potential complications are associated with dilutional hyponatraemia (cerebral oedema, seizures, and death) if excessive absorption of 1.5 % glycine which is used as a distention medium occurs.

Endometrial ablation
Second-generation techniques

- These are newer techniques which do not require hysteroscopic guidance, and are generally quicker. Some can be performed in the outpatient setting.
- Examples include:
  - microwave endometrial ablation (MEA),
  - fluid-filled thermal balloon endometrial ablation
  - impedance-controlled bipolar radiofrequency ablation.
- They should be used as first line where no structural or histological abnormality is present.
- The overall success rates and complication profile are reported to be favourable when compared to first generation techniques.
- The long-term hysterectomy rate post second-generation technique treatment is low at 16 %.
- RCT comparing various second-generation ablation techniques show no significant differences in complication rates, amenorrhoea rates, or quality of life post procedure. Therefore, choice of instrument will depend on operator experience and local availability of equipment.

Surgical Rx

- Dilatation and curettage should not be used as a therapeutic treatment. [C]
- Therefore, D&C is only indicated for women with acute bleeding resulting in hypovolemia and for older women who are at higher risk of having endometrial neoplasia

For women with large fibroids and HMB

- Referral for consideration of surgery or uterine artery embolisation (UAE) as first-line treatment can be recommended. [D(GPP)]
- Uterine Artery Embolization, myomectomy or hysterectomy should be considered in cases of HMB where large fibroids (greater than 3 cm in diameter) are present and bleeding is having a severe impact on a woman's quality of life. [C]
- When surgery for fibroid-related HMB is felt necessary then UAE, myomectomy and hysterectomy must all be considered, discussed and documented. [D(GPP)]
- Women should be informed that UAE or myomectomy will potentially allow them to retain their fertility. [C]

Uterine artery embolization UAE

- This is a minimally invasive procedure performed under moderate sedation and local anaesthesia by interventional radiologists.
- The femoral artery is canulated using 5F vascular sheath. The uterine arteries are then catheterized using micro catheters (2.7F) and micro embolic particles (350–900 micron) are injected in order to partially occlude the uterine arteries.
- Serious complications are uncommon although systemic infection due to septic fibroid degeneration is a recognized consequence and reported to be less than 1 %.
- UAE is an alternative treatment for women with AUB secondary to fibroids.
- Trials have demonstrated that UAE alleviates symptoms in 60–90 % of women, and that the effects last for an average of 5 years.
- The effects on fertility and pregnancy following UAE are unclear; therefore patients should be counselled appropriately prior to undertaking this procedure.

Hysterectomy

- Hysterectomy should not be used as a first-line treatment solely for HMB. Hysterectomy should be considered only when:
  - other treatment options have failed, are contraindicated or are declined by the woman
  - if there is a wish for amenorrhoea
  - the woman (who has been fully informed) requests it
  - the woman no longer wishes to retain her uterus and fertility. [C]

TAH route

- Taking into account the need for individual assessment, the route of hysterectomy should be considered in the following order: first line vaginal; second line abdominal. [A]

Case #1

- A 35-year-old G5 P5 woman complains of heavy prolonged periods with clots; changing 6 to 8 fully stocked pads during her periods lasting 8 to 10 days every 30 days causing her to develop anemia (recent Hb of 9 mg/L). She also c/o urinary frequency. She had no intermenstrual nor postcoital bleeding. A prior office endometrial sampling showed benign pathology. Abdominal examination reveals an irregular midline solid, mobile & tender mass approximately 18 weeks' size that is seemingly not contiguous with the cervix, no adnexal masses and confirmed by bimanual examination.
- What is the most likely diagnosis? What are your differential diagnoses?
- What modalities of treatment you will offer if it is benign mass?

Case #II

- A 18-year-old nulliparous woman complains of heavy prolonged periods with clots; changing 6 to 8 fully stocked pads during her periods lasting 8 to 10 days every 30 days causing her to develop anemia (recent Hb of 9 mg/L). She also c/o gum bleeding. She mentioned that been admitted for blood transfusion for a similar episodes twice during the last few years. U/S scan-normal.
- What is the most likely diagnosis? What are your differential diagnoses?
- What modalities of treatment you will offer if it is benign mass? Justify your answer please.

Case #III

- A 41-year-old Para 3 woman was referred to you. She presented with increasingly heavy periods over the past year. She continued to have a regular 28-day cycle, but was now bleeding for six days each month, four of which she felt were excessively heavy, such that her daily activities were interrupted. She was not experiencing any inter-menstrual or post-coital bleeding, but did describe a feeling of 'pressure' in the pelvis. She was otherwise fit and well. Her smear tests were up to date and had always been normal.
- Having had three caesarean sections (CS) in the past, she expressed a desire to retain her fertility, although she had no immediate plans to conceive. For the previous four months the patient had been using tranexamic acid as prescribed by her GP, but had not noted any significant improvement in her symptoms.
- A pelvic examination was performed. The patient was noted to have a slightly bulky uterus, of approximately 10/40 size. The cervix was normal and there were no adnexal masses. The patient was referred for a full blood count and pelvic ultrasound scan. A menstrual calendar was provided in order for the patient to record the duration and severity of her bleeding prior to her subsequent review. In the meantime she was advised to continue taking the tranexemic acid.

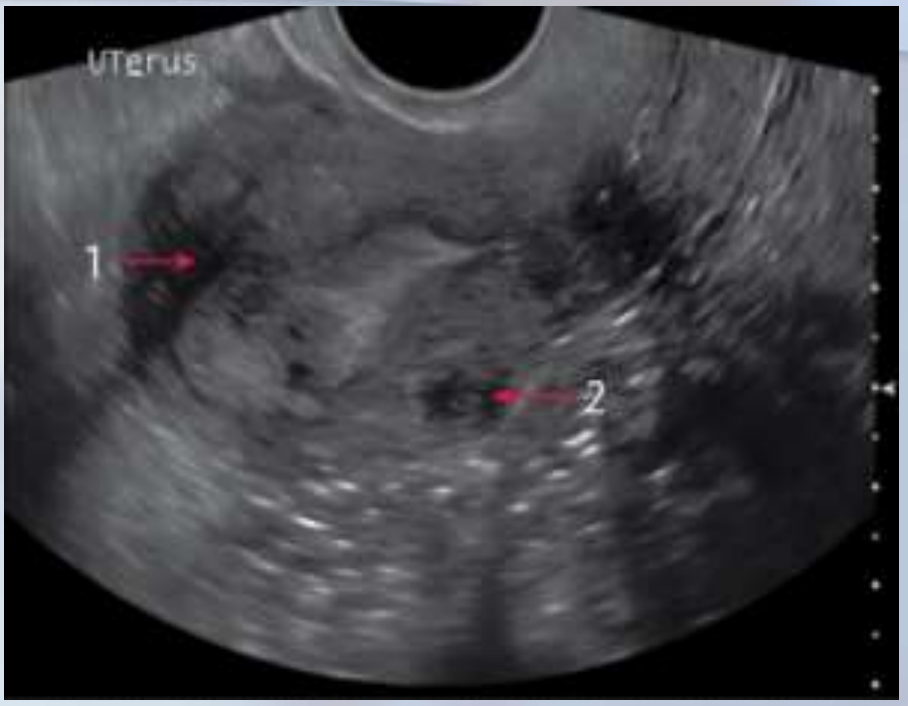
Case #III

She was reviewed in gynaecology clinic one month later. Her Hb was 10.2 g/dl (normal range 12.0-15.5 g/dl) and pelvic ultrasound demonstrated an enlarged fibroid uterus; one subserosal fibroid of 4 cm, one intramural of 3 cm, and one submucous fibroid of 3 cm diameter. No endometrial or adnexal abnormality was noted, what to do?

a. Hysteroscopy with trans-cervical resection of fibroid as appropriate, +/− insertion of Levornogestrel intra-uterine system (LNG–IUS)

b. Insertion of LNG–IUS without resection of fibroid

c. Uterine artery embolization



Case # IV

- A 27-year-old nulliparous female, c/o primary infertility for 3 years. Her periods every 35-40 days 5 days heavy and prolonged. On examination, she is 165 cm in tall and weighs 55 kg, waist circumference >85 cm. Her blood pressure is 120/88 mm Hg. mFG>12, Ludwig I, Acanthosis Nigricans ++. Her thyroid gland is normal. She has appropriate Tanner stage IV breast development, axillary and pubic hair, and female external genitalia are normal. U/S scan showed: thick endometrium, PCOM volume >13 cm3
- What are the key issues in her case
- What is your most likely diagnosis and your DD?
- Next step in diagnosis:
- If your primary diagnosis is right what is your plan of management?


Thank You!