



Abnormal Uterine Bleeding (AUB)

with 2018 FIGO updates on AUB

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Reference:

- **Comprehensive Gynecology 7th edition, 2017 (Lobo RA, Gershenson DM, Lentz GM, Valea FA editors) chapter 26, pp 621-633.**
- **Munro MG, Critchley HO, Fraser I, FIGO Menstrual Disorders Committee. The Two FIGO Systems for Normal and Abnormal Uterine Bleeding Symptoms and Classification of Causes of Abnormal Uterine Bleeding in the Reproductive Years: 2018 Revisions. Int J Gynaecol Obstet. 2018 Dec;143(3):393-408. doi: 10.1002/ijgo.12666. Epub 2018 Oct 10**



Outline: AUB

1. Definition : 2018 updates
 2. Classification and Pathophysiology
 3. Diagnosis
 4. Treatment of acute and chronic AUB
- 

Abnormal uterine bleeding (AUB)

- One of the most common health concerns of women
- can present in many ways, from infrequent episodes (oligomenorrhea) to excessive flow (heavy menstrual bleeding, or prolonged duration of menses and intermenstrual bleeding)
- *This lecture will focus only on heavy menstrual bleeding*



Ryntz T, Lobo R. Chapter 26. Abnormal Uterine Bleeding; In Comprehensive Gynecology 7th edition, 2017;Lobo RA, Gershenson DM, Lentz GM, Valea FA editors; pp 621-633.

Review: Normal Menstrual blood flow

- ▶ mean duration of the menstrual cycle is **24-38 days**
- ▶ Average menstrual blood loss (MBL) is **35 mL**. (normal range: 10-80ml)
- ▶ Average number of days of menses: **4 days** (normal : ≤ 8 days)



Abnormal uterine bleeding (AUB)

- **Bleeding is abnormal if:**
 - it occurs at intervals of less than 24 days, or more than 38 days;
 - Lasts longer than 8 days;
 - MBL of 80 mL or greater
- the term ***dysfunctional uterine bleeding (DUB)*** is no longer favored and should be discarded.



Heavy Menstrual Bleeding (HMB)

- ▶ FIGO 2018 update:
- ▶ Heavy menstrual bleeding is defined as excessive menstrual blood loss which interfere with the woman's physical, social , emotional and /or material quality of life



Munro MG, Critchley HO, Fraser I, FIGO Menstrual Disorders Committee. The Two FIGO Systems for Normal and Abnormal Uterine Bleeding Symptoms and Classification of Causes of Abnormal Uterine Bleeding in the Reproductive Years: 2018 Revisions
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Updated definitions: Acute vs chronic

- **Chronic nongestational AUB** in the reproductive years is defined as bleeding from the uterine corpus that is abnormal in duration, volume, frequency, and/or regularity, and has been present for the majority of the preceding 6 months.
- **Acute AUB** is defined as an episode of heavy bleeding that, in the opinion of the clinician, is of sufficient quantity to require immediate intervention to minimize or prevent further blood loss.
- **Acute heavy menstrual bleeding** may present in the context of existing chronic AUB or can occur in the absence of such a background history.

FIGO-AUB system 1

Revision of terminologies and definitions of symptoms of abnormal uterine bleeding

Parameter	Normal	Abnormal	<input checked="" type="checkbox"/>
Frequency	Absent (no bleeding) = amenorrhea		<input type="checkbox"/>
	Infrequent (>38 days)		<input type="checkbox"/>
	Normal (≥24 to ≤38 days)		<input type="checkbox"/>
	Frequent (<24 days)		<input type="checkbox"/>
Duration	Normal (≤8 days)		<input type="checkbox"/>
	Prolonged (>8 days)		<input type="checkbox"/>
Regularity	Normal or "Regular" (shortest to longest cycle variation: ≤7-9 days)*		<input type="checkbox"/>
	Irregular (shortest to longest cycle variation: ≥8-10 days)*		<input type="checkbox"/>
Flow Volume (patient determined)	Light		<input type="checkbox"/>
	Normal		<input type="checkbox"/>
	Heavy		<input type="checkbox"/>
Intermenstrual Bleeding (IMB) Bleeding between cyclically regular onset of menses	None		<input type="checkbox"/>
	Random		<input type="checkbox"/>
	Cyclic (Predictable)	Early Cycle	<input type="checkbox"/>
		Mid Cycle	<input type="checkbox"/>
		Late Cycle	<input type="checkbox"/>
Unscheduled Bleeding on Progestin ± Estrogen Gonadal Steroids (birth control pills, rings, patches or injections)	Not Applicable (not on gonadal steroid medication)		<input type="checkbox"/>
	None (on gonadal steroid medication)		<input type="checkbox"/>
	Present		<input type="checkbox"/>

Parameter	Change
Frequency	Amenorrhea is now part of the frequency category
Regularity	Refined definition of regularity Normal variation (shortest to longest) 7-9 d Slight variance depends on age
Duration	Now only two categories for duration Normal: ≤8 d Prolonged: >8 d
Volume	Definition of the symptom of HMB NICE definition ^{5,28} Bleeding volume sufficient to interfere with the woman's quality of life
Intermenstrual bleeding	Definition of the symptom of inter-menstrual bleeding Spontaneous bleeding occurring between menstrual periods Can be either cyclical, or random

Abbreviations: FIGO, International Federation of Gynecology and Obstetrics; HMB, heavy menstrual bleeding; NICE, National Institute of Care Excellence.

FIGO-AUB system 2

PALM-COIEN classification of causes of AUB

Anatomic causes

P olyp
A denomyosis
L eiomyoma
M alignancy & hyperplasia



C oagulopathy
O vulatory dysfunction
E ndometrial
I atrogenic
N ot otherwise classified

Non-anatomic causes



Diagnosis Notation

- ▶ the acronym AUB is followed by the letters PALM-COEIN and a **subscript 0 or 1** associated with each letter to indicate the absence or presence, respectively, of the abnormality.
- ▶ Example #1: A patient with abnormal bleeding due to a polyp :

AUB-P₁A₀L₀M₀-C₀O₀E₀I₀N₀

Diagnosis Notation

- ▶ Example #1: A patient with abnormal bleeding due to a polyp :

AUB-P₁A₀L₀M₀-C₀O₀E₀I₀N₀

or

AUB - P

Diagnosis Notation:

- ▶ Example #2: A patient with abnormal bleeding that is both irregular and heavy may have endometrial hyperplasia due to anovulation.

AUB- P₀A₀L₀M₁- C₀O₁E₀I₀N₀

or

AUB – M₁;-O

FIGO AUB system 2 diagnostic matrix

	Y	N	?
P			
A			
L			
M			

	Y	N	?
C			
O			
E			
I			
N			

	Y	N	?
P		X	
A		X	
L _o	X		
M		X	

	Y	N	?
C			X
O		X	
E			X
I		X	
N		X	

	Y	N	?
P		X	
A		X	
L _o	X		
M		X	

	Y	N	?
C		X	
O		X	
E	X		
I		X	
N		X	



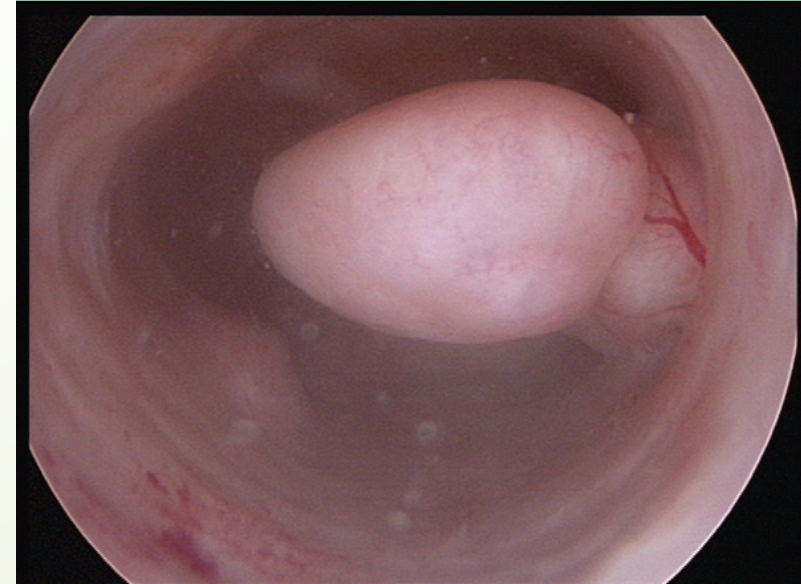
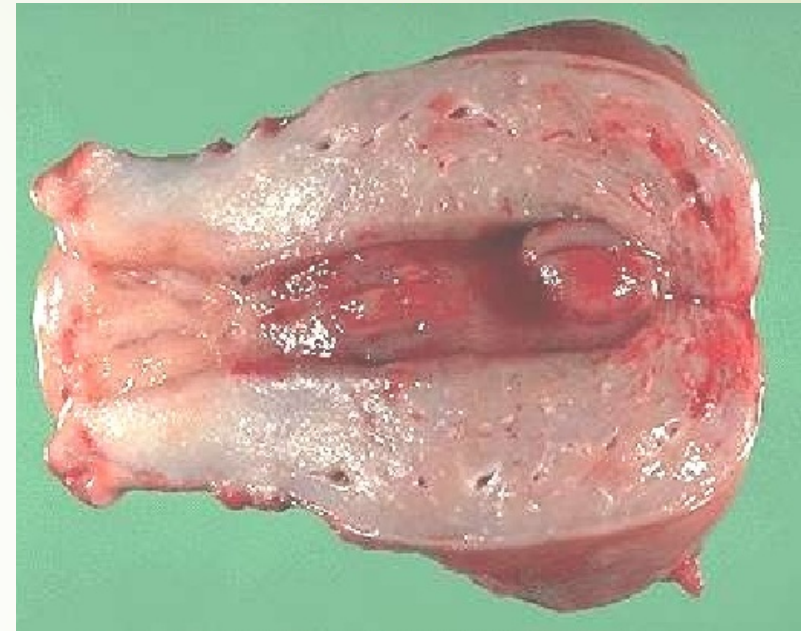
Pathophysiology

ENDOMETRIAL POLYPS (AUB-P)

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- ▶ localized overgrowths of endometrial tissue, containing glands, stroma, and blood vessels, covered with epithelium.
- ▶ Most commonly found in reproductive-age women
- ▶ estrogen stimulation is thought to play a key role in their development.
- ▶ Usually benign.
- ▶ Women with symptomatic polyps can be treated safely and effectively with operative hysteroscopy

Ryntz T, Lobo R. Chapter 26. Abnormal Uterine Bleeding; In Comprehensive Gynecology 7th edition, 2017;Lobo RA, Gershenson DM, Lentz GM, Valea FA editors; pp 621-633.



ADENOMYOSIS (AUB-A)

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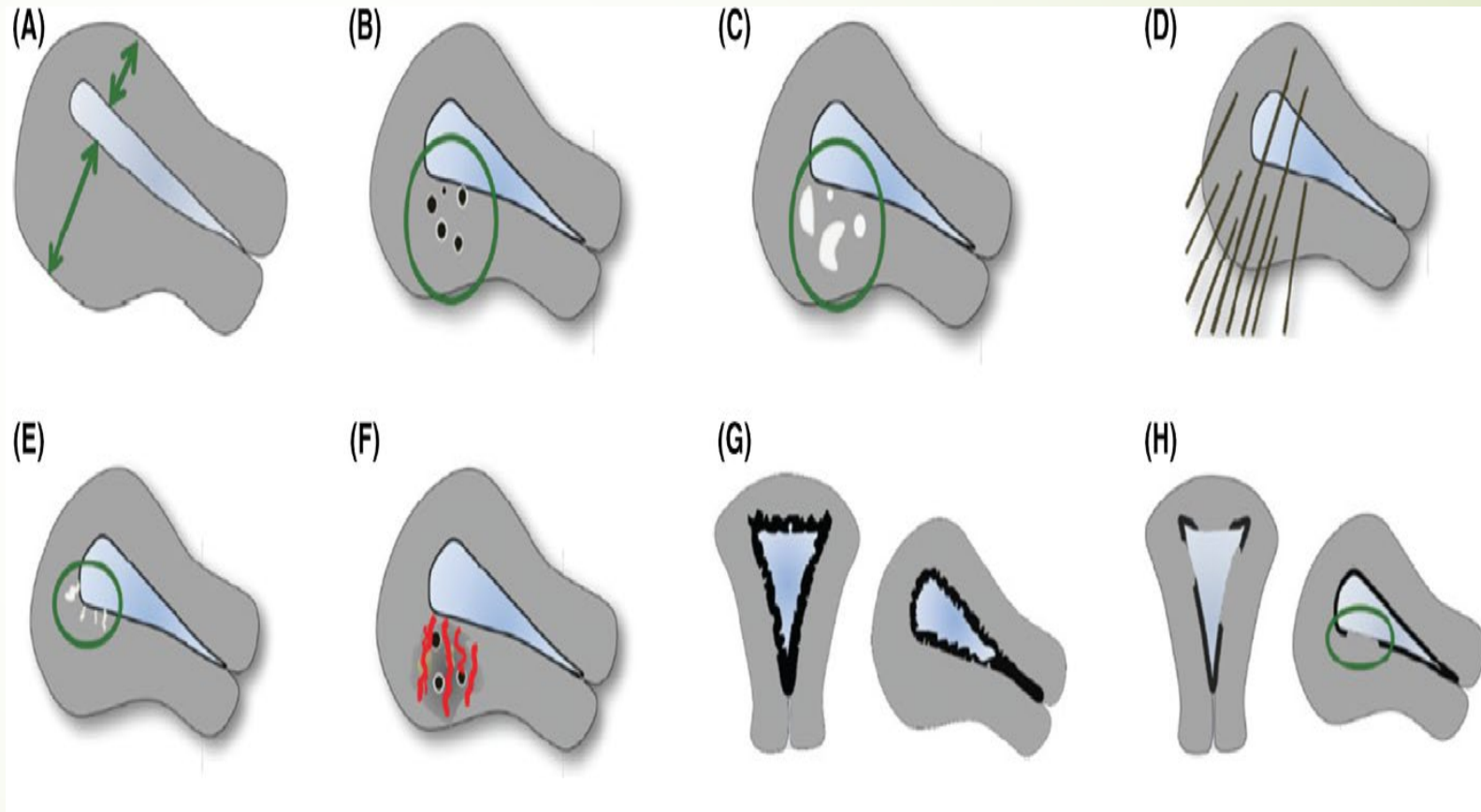
- presence of endometrial glands and stroma in the uterine myometrium. → ectopic endometrial tissue leads to hypertrophy of the surrounding myometrium.
- Risk factors: **Multiparity (most significant)** and any process that allows for penetration of endometrial glands and stroma past the basalis layer (e.g., dilation and curettage, cesarean delivery, spontaneous abortion)
- **Enlarged, asymmetric uterus** on ultrasound
- Abnormal bleeding due to adenomyosis is thought to be a result of altered uterine contractility and is associated with **profound dysmenorrhea**.

Ryntz T, Lobo R. Chapter 26. Abnormal Uterine Bleeding; In Comprehensive Gynecology 7th edition, 2017;Lobo RA, Gershenson DM, Lentz GM, Valea FA editors; pp 621-633.



Adenomyosis: diagnostic criteria

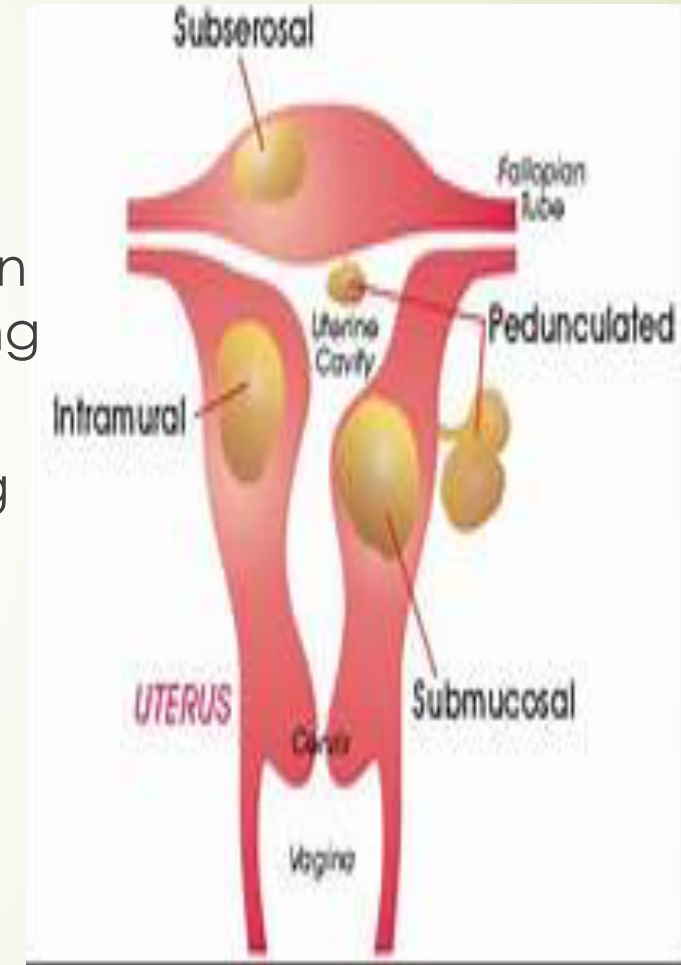
- A. Asymmetrical myometrial thickening
- B. myometrial cysts
- C. hyperechoic islands
- D. fan shaped shadowing
- E. echogenic subendometrial lines and buds
- F. translesional vascularity where present
- G. irregular junctional zone
- H. interrupted junctional zone



LEIOMYOMA (AUB-L)

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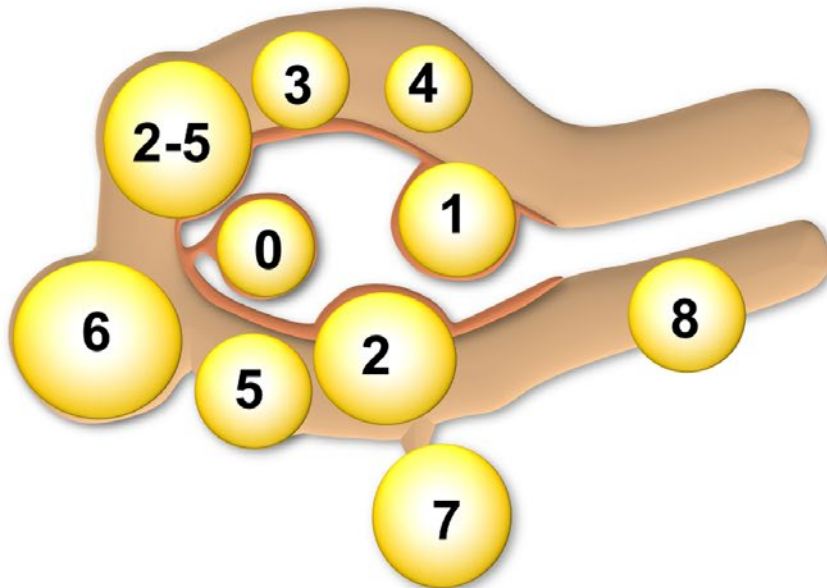
- Also called fibroids, are benign tumors of the uterine myometrium.
- pathogenesis : myometrial injury leading to cellular proliferation, decreased apoptosis, increased production of extracellular matrix, and overexpression of transforming growth factor beta that leads to fibrosis of these tumors.
- Mechanisms by which fibroids cause abnormal bleeding are varied and depend on size, location, and number:
 - **Intracavitary/submucous fibroids**
 - intramural fibroids
 - Subserous fibroids
- Management:
 - Medical management
 - Surgical : hysterectomy, myomectomy



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FIGO Leiomyoma subclassification system

FIGO Leiomyoma Subclassification System



Polyp
Adenomyosis
Leiomyoma
Malignancy & hyperplasia

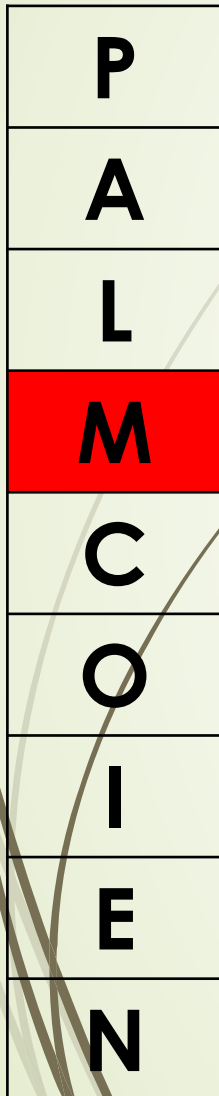
Submucous
Other

Coagulopathy
Ovulatory dysfunction
Endometrial
Iatrogenic
Not otherwise classified

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

Hybrid (contact both the endometrium and the serosal layer)	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	Submucous and subserous, each with less than half the diameter in the endometrial and peritoneal cavities, respectively.

MALIGNANCY (AUB-M)



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- vulvar, vaginal, cervical, endometrial, uterine, and adnexal (ovarian or fallopian tube) cancers.
- Bleeding from cervical malignancy classically presents as **coital bleeding or intermenstrual bleeding**
- Endometrial cancer is mostly secondary to prolonged exposure to hyperestrogenic state (chronic anovulation, PCOS, obesity, nulligravidity, etc)
- **Lynch syndrome**, or hereditary nonpolyposis colorectal cancer, is an autosomal dominant disease caused by a disruption in the mismatch repair (MMR) genes → carries a 40% to 50% lifetime risk of endometrial cancer (mostly before the age of 45.)
- estrogen-producing ovarian tumors (ex. Granulosa theca cell tumors)

COAGULOPATHY (AUB-C)

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- disorders of blood coagulation such as **von Willebrand disease** (most common), prothrombin deficiency, hemophilia, leukemia, severe sepsis, idiopathic thrombocytopenic purpura, and hypersplenism
- Routine screening mainly indicated for the **adolescent who has prolonged heavy menses beginning at menarche**.
- In adults, screening for these disorders indicated by clinical signs such as bleeding gums, epistaxis, or ecchymosis.
- Other disorders that produce platelet deficiency, such as Chronic anticoagulation as a result of heparin, low-molecular-weight heparin, direct thrombin inhibitors, and direct factor Xa inhibitors

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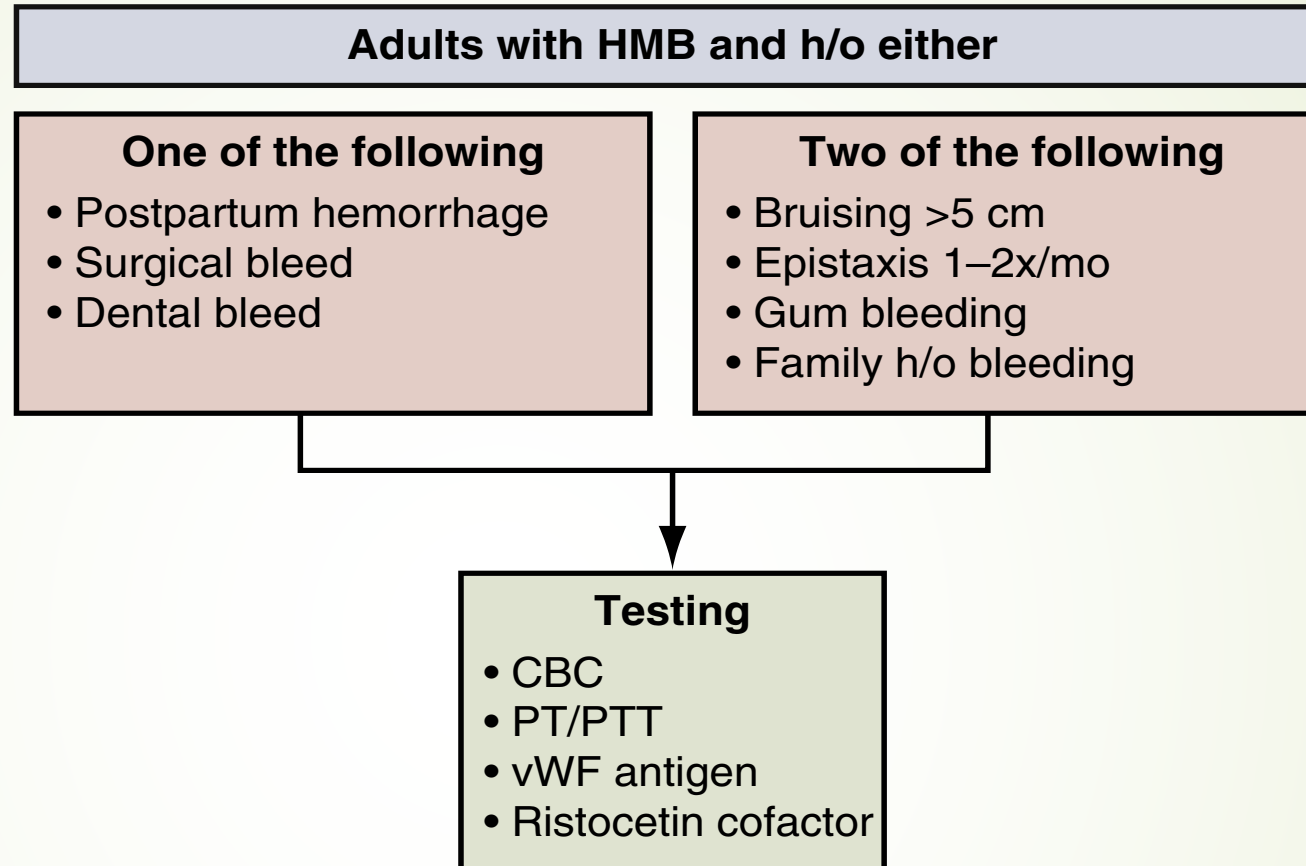
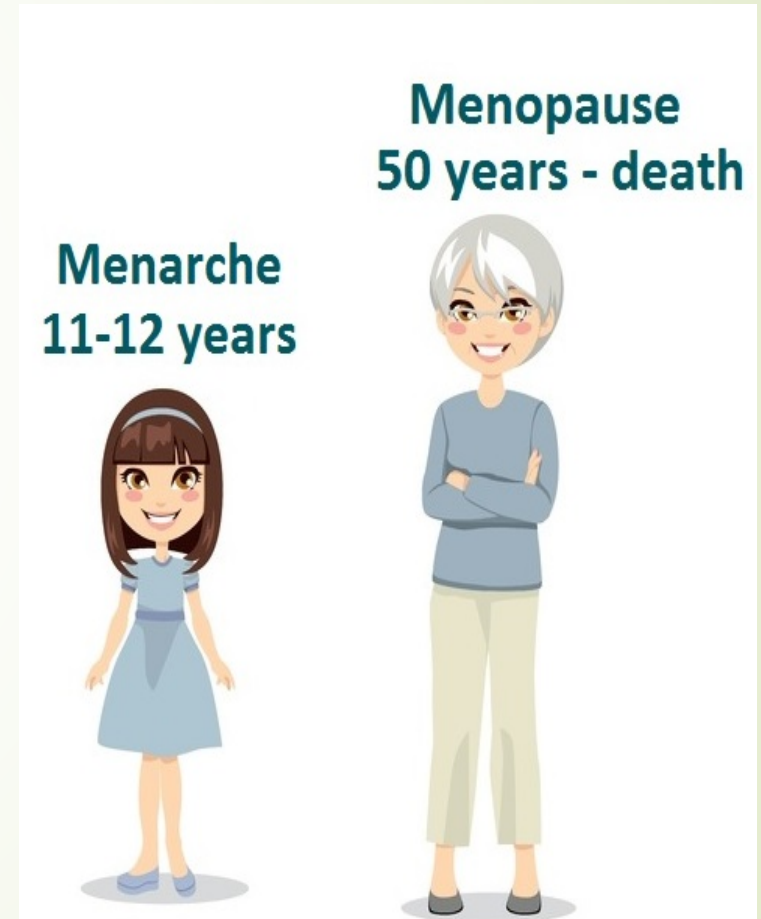


Figure 26.6 Diagnostic approach to adults with abnormal uterine bleeding due to coagulopathy. (Data from Kouides PA, Conard J, Peyvandi F, et al. Hemostasis and menstruation: appropriate investigation for underlying disorders of hemostasis in women with excessive menstrual bleeding. *Fertil Steril.* 2005;84[5]:1345-1351.)

OVULATORY DYSFUNCTION (AUB-O)

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- ▶ Anovulatory bleeding is most common during the *extremes of reproductive life*: in the first few years *after menarche* and during *perimenopause*.
 - ▶ In the adolescent: anovulation is due to an *immaturity of the hypothalamic-pituitary-ovarian (HPO) axis* and failure of positive feedback of estradiol to cause a luteinizing hormone (LH) surge.
 - ▶ In the perimenopausal woman: *lack of synchronization between the components of the HPO axis* occurs as the woman approaches ovarian decline at menopause.

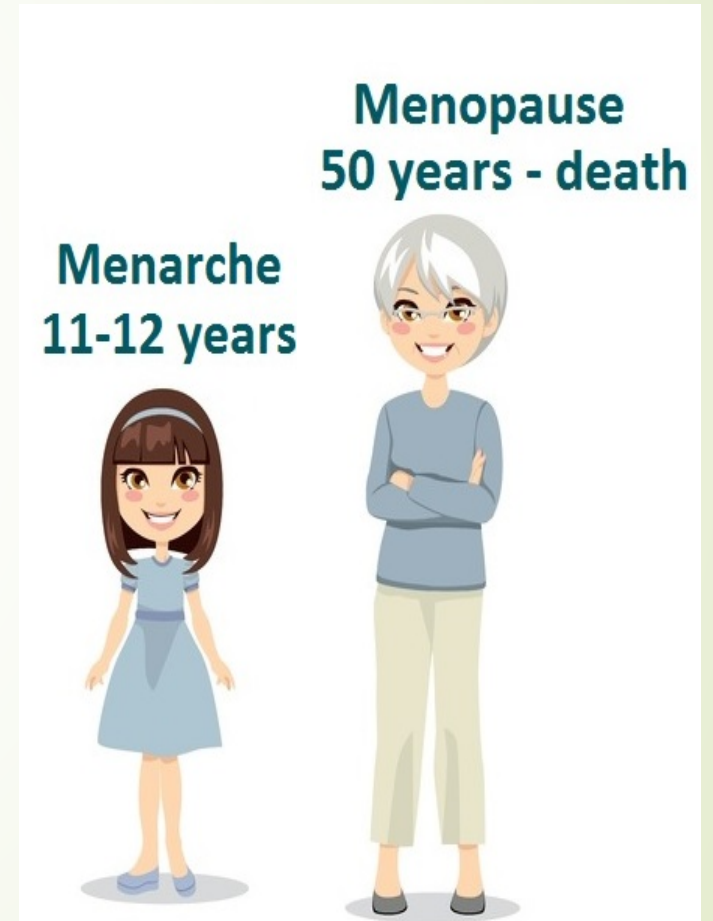


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OVULATORY DYSFUNCTION (AUB-O)

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- ▶ the predominant cause of ovulatory dysfunction postmenarchal and premenopausal women is secondary to **alterations in neuroendocrine function**.
- ▶ there is **continuous estradiol production** without corpus luteum formation and progesterone production → **continuously proliferating endometrium**, which may outgrow its blood supply → necrosis.
- ▶ **uniform slough to the basalis layer does not occur**, which produces excessive uterine bleeding.



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OVULATORY DYSFUNCTION (AUB-O)

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- ▶ the patterns of anovulatory bleeding may be oligomenorrhea, intermenstrual bleeding, or heavy menstrual bleeding.
- ▶ What are the causes of anovulation?
 1. *extremes of reproductive life*
 2. *polycystic ovary syndrome (PCOS)*
 3. *hypothalamic dysfunction (related to weight loss, severe exercise, stress, or drug use)*
 4. *abnormalities of other nonreproductive hormone (thyroid hormone, prolactin, and cortisol)*

IATROGENIC (AUB-I)

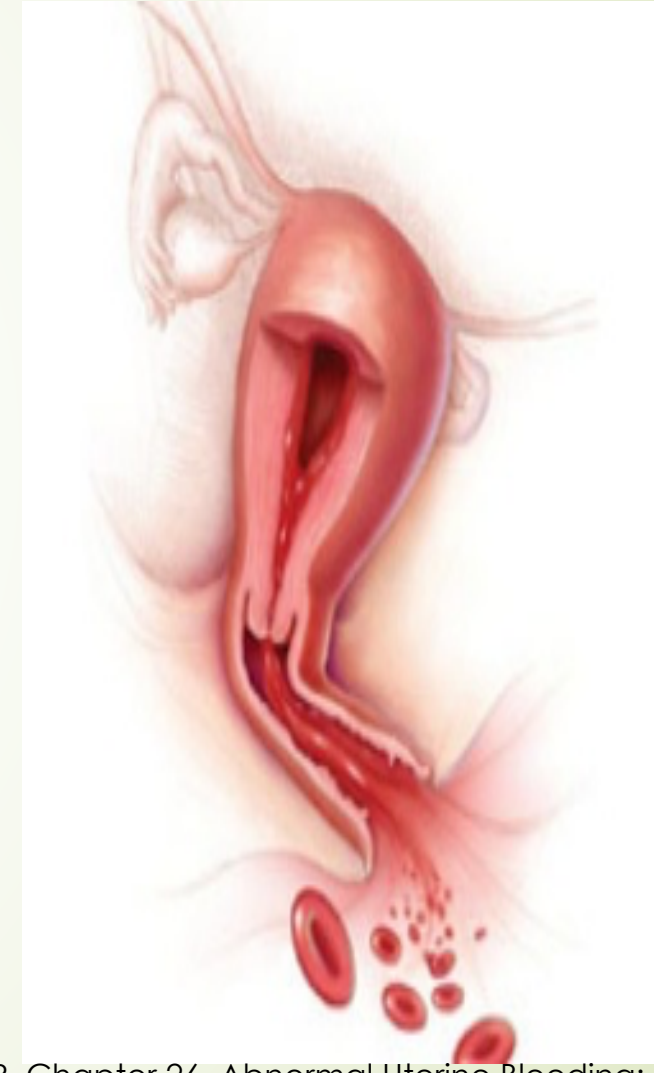
P
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- ▶ abnormal bleeding resulting from medications
- ▶ most common of these are **hormonal preparations**, including selective estrogen receptor modulators, and gonadotrophic releasing hormone agonists and antagonists.
- ▶ Hyperprolactinemia can result from central nervous system dopamine antagonism of certain antipsychotic drugs (eg risperidone)
- ▶ combined and progesterone-only oral contraceptives may result in breakthrough bleeding (BTB).
- ▶ interactions between oral contraceptives and other medications, such as **antibiotics and anticonvulsants** may alter circulating levels of steroids, allowing follicular recruitment and increased endogenous levels of estrogen.

ENDOMETRIAL (AUB-E)

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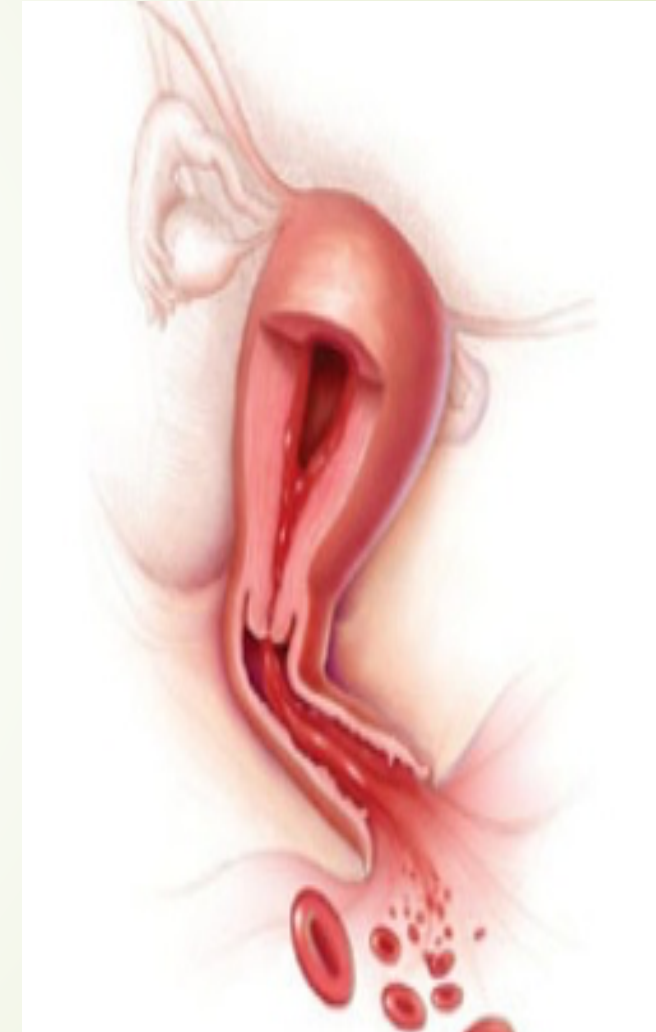
- ▶ heavy menstrual bleeding in the absence of other abnormalities are thought to have underlying disorders of the endometrium or are otherwise unclassified.
- ▶ In the past, this category has been called **“ovulatory dysfunctional uterine bleeding.”**
- ▶ the primary line of defense to excessive bleeding during normal menses is the formation of the platelet plug, followed by uterine contractility, largely mediated by **prostaglandin F2α (PGF2α)**.



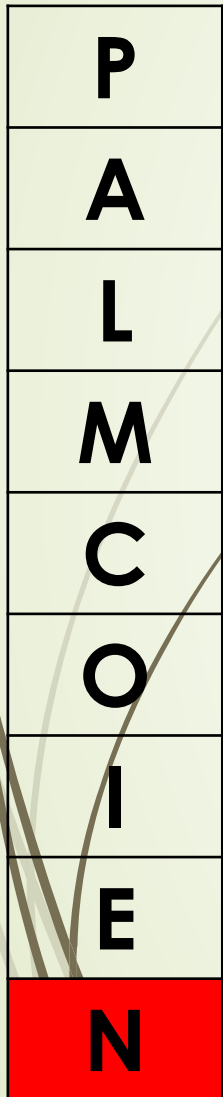
ENDOMETRIAL (AUB-E)

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- ▶ thus prolonged and heavy bleeding can occur with abnormalities of the platelet plug or inadequate uterine levels of PGF2a.
- ▶ In some women with heavy menstrual bleeding, there is excessive uterine production of **prostacyclin**, a **vasodilatory** prostaglandin that opposes platelet adhesion and may also interfere with uterine contractility.
- ▶ Deficiency of uterine PGF2a or excessive production of **PGE** (**vasodilatory** prostaglandin) may also explain ovulatory DUB
- ▶ **Low PGF2a/PGE → increase menstrual blood loss**



NOT OTHERWISE CLASSIFIED (AUB-N)



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C
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N

- Abnormal bleeding not classified in the previous categories is considered AUB-N.
- Examples of such conditions may include foreign bodies or trauma. Treatment is tailored to the specific cause.
- New example: niche or isthmocoele associated with previous CS

Summary of changes to FIGO AUB System 2 Causes or Contributors to AUB in the Reproductive Years (PALM-COEIN)

System 2 Category	Change
AUB-A	Refined sonographic diagnostic criteria
AUB-L	Inclusion of Type 3 as a submucous leiomyoma Type definitions and distinctions Distinction between Types 0 and 1; 6 and 7 Distinction between Types 2 and 3; 4 and 5
AUB-C	No longer includes AUB associated with pharmacologic agents that impair blood coagulation which are now included in AUB-I

Summary of changes to FIGO AUB System 2 Causes or Contributors to AUB in the Reproductive Years (PALM-COEIN)

System 2 Category	Change
AUB-I	Now includes AUB associated with all iatrogenic processes including the use of pharmacological agents used for anticoagulation and those thought to interfere with ovulation
AUB-O	No longer includes ovulatory disorders associated with drugs known or suspected to interfere with ovulation
AUB-N	The name of the category has been changed from “Not Yet Classified” to Not Otherwise Classified There is a brief discussion of a potential new cause of AUB the so-called uterine “niche” or isthmocoele following lower segment cesarean section

Examples of the use of a matrix to guide FIGO-based evaluation of patients with chronic AUB.

(A) System 1 (Symptoms)

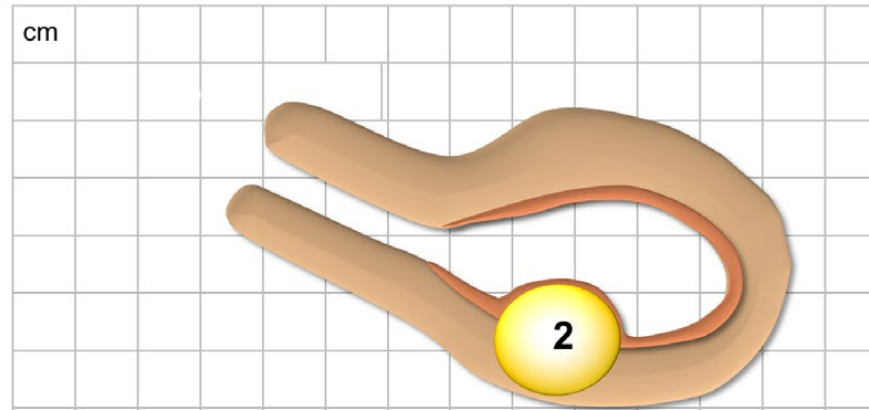
- Cycle Length: 30 days
- Regularity: ± 2 days
- Duration: 10 days
- Volume: Heavy
- Intermenstrual Bleeding: -

System 2 (PALM-COEIN)

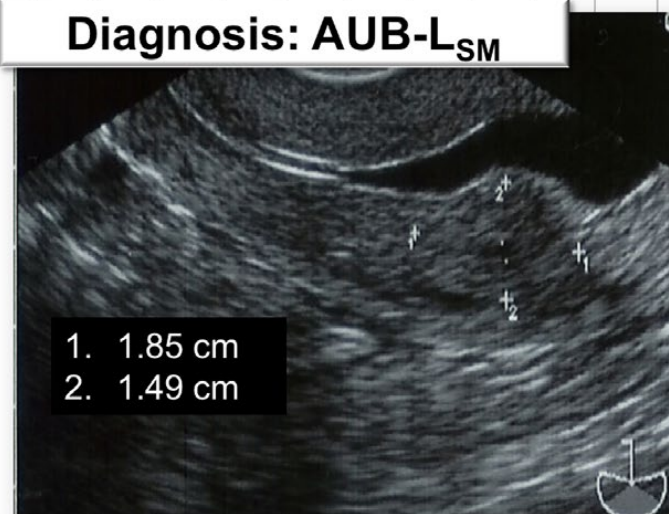
- Leiomyoma: Type 2

	Y	N	?
P		X	
A		X	
L _{sm}	X		
M		X	

C		X	
O		X	
E		X	
I		X	
N		X	



Diagnosis: AUB-L_{SM}



Examples of the use of a matrix to guide FIGO-based evaluation of patients with chronic AUB.

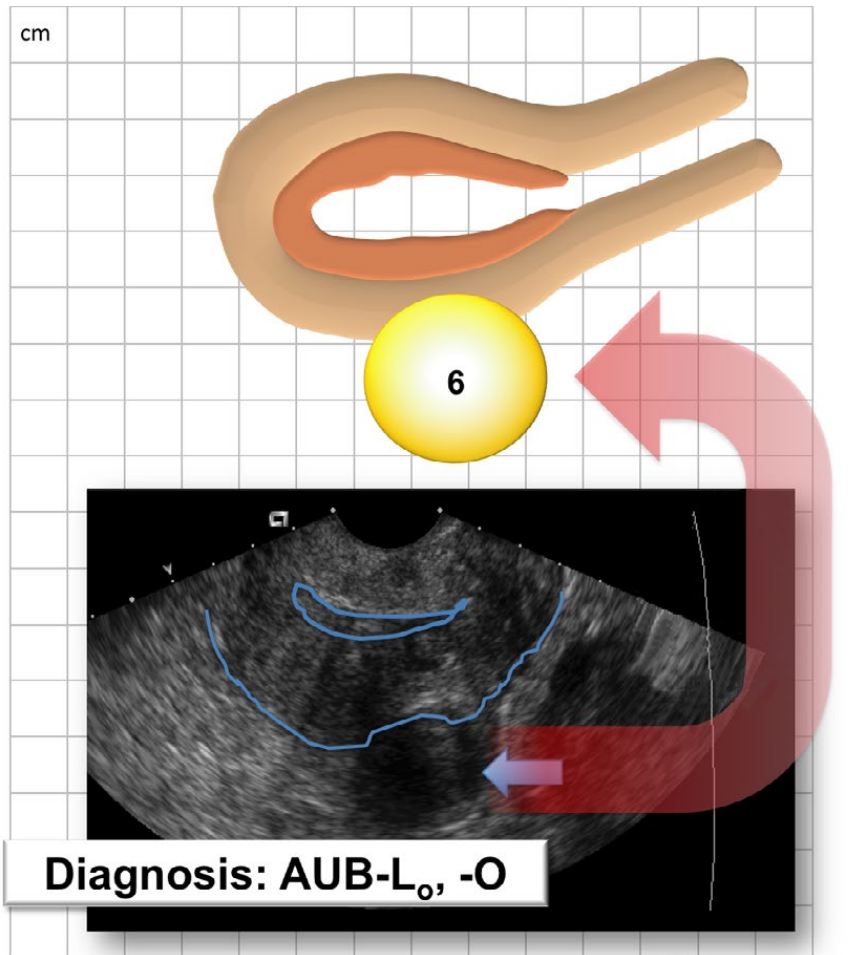
(B) System 1 (Symptoms)

- Cycle Length: 14-60 days
- Regularity: \pm 46 days
- Duration: 2-11 days
- Volume: Normal to Heavy
- Intermenstrual Bleeding

System 2 (PALM-COEIN)

- Leiomyoma: Type 6
- Ovulatory Disorder

	Y	N	?
P		X	
A		X	
L _o	X		
M		X	
C		X	
O	X		
E		X	
I		X	
N		X	



Examples of the use of a matrix to guide FIGO-based evaluation of patients with chronic AUB.

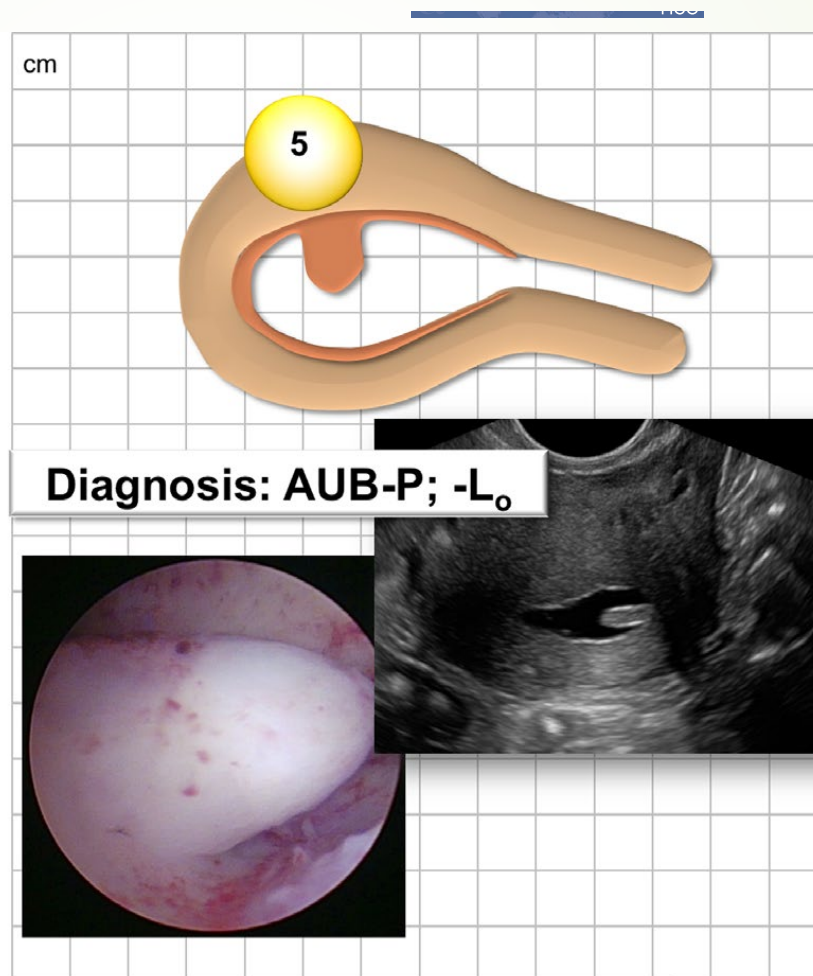
(C) System 1 (Symptoms)

- Cycle Length: 31 days
- Regularity: ± 3 days
- Duration: 4 days
- Volume: Normal
- Intermenstrual Bleeding: +

System 2 (PALM-COEIN)

- Polyp: Endometrial
- Leiomyoma: Type 5

	Y	N	?
P	X		
A		X	
L ₀	X		
M		X	
C		X	
O		X	
E		X	
I		X	
N		X	



Examples of the use of a matrix to guide FIGO-based evaluation of patients with chronic AUB.

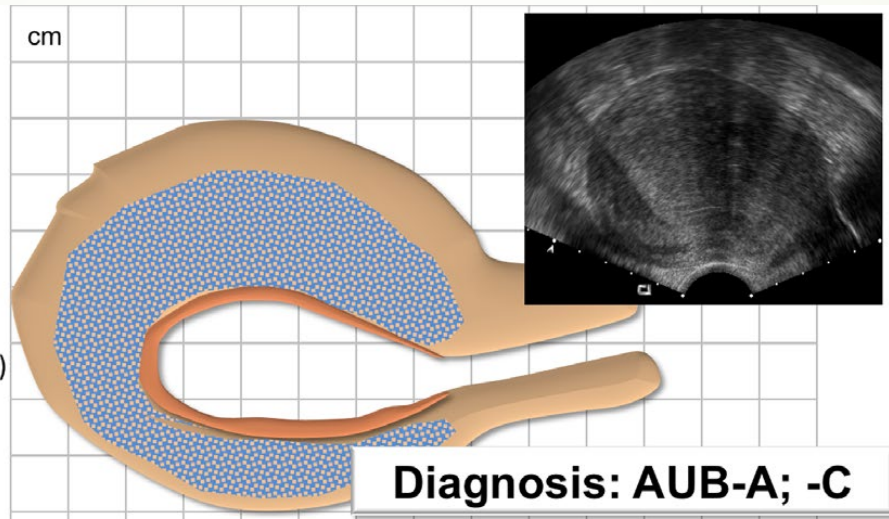
(D) System 1 (Symptoms)

- Cycle Length: 33 days
- Regularity: ± 3 days
- Duration: 9 days
- Volume: Heavy
- Intermenstrual Bleeding: -

System 2 (PALM-COIN)

- Adenomyosis
- Coagulopathy (vWD, Type 1)

	Y	N	?
P		X	
A	X		
L		X	
M		X	
C	X		X
O		X	
E		X	
I		X	
N		X	



Test	Result	Normal	Interpretation
vWF	45%	55-200%	+
Ristocetin CoF	17 IU/dL	50-200 IU/dL	+
aPTT	45 sec	28-38 sec	+
PT	17 sec	9.5 – 13.8 sec	+
Factor VIII	36	55-200%	+

Screen



Diagnostic approach

History, Physical examination, and Laboratory exams

1. Medical History

- Menstrual history: frequency, duration, and amount of bleeding
- inquire whether and when the menstrual pattern changed.
- Describe the menstrual abnormality as oligomenorrhea, polymenorrhea, heavy menstrual bleeding, or intermenstrual bleeding.
- Menstrual calendar to record her bleeding episodes → helpful way to characterize definitively the bleeding episodes.
- Symptoms present for the majority of the preceding 6 months are considered **chronic**

TABLE 3 Screening instrument for coagulopathies in women with the symptom of heavy menstrual bleeding.^{a,b}

Initial screening for an underlying disorder of hemostasis in patients with excessive menstrual bleeding should be by a structured history. A positive screening result comprises any of the following:^c

1. Heavy menstrual bleeding since menarche
2. One of the following:
 - a Postpartum hemorrhage
 - b Surgical related bleeding
 - c Bleeding associated with dental work
3. Two or more of the following symptoms:
 - a Bruising 1–2 times per month
 - b Epistaxis 1–2 times per month
 - c Frequent gum bleeding
 - d Family history of bleeding symptoms

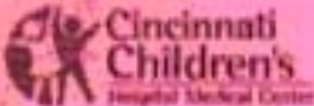
^aReproduced with permission.⁴⁵

The menstrual history

For all patients:

- Age at menarche
- Cycle length
- Duration of bleeding
- Perception of flow: heavy, medium or light
- Menstrual product use
- First day of LMP
- Dysmenorrhea

THE MENSTRUAL CALENDAR



 Cincinnati Children's
 Hospital Medical Center

MENSTRUAL FLOW CHART

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31
JAN																															
FEB	X	X	X	X																					X	X	X	X	X		
MAR																															
APR	X	X	X	X	X	X																									
MAY			X	X	X	X																				S	X	X	X		
JUN																					X	X	X								
JUL																	X	X	X	X											
AUG																															
SEP																															
OCT																															
NOV																															
DEC																															

Type of flow: Bleeding Spotting

Please have this chart with you when you call or visit your health care provider

The menstrual history

For patients reporting heavy menstrual bleeding:

- Lasts more than 7 days
- Soaking through pads/tampons in 1h for 2-3h in a row
- Require frequent pad or tampon changes (soaking more than one every 1-2 hour.
- Passing blood clots \geq 1 inch in diameter (“about the size of a quarter”)

Holland-Hall C. Heavy menstrual bleeding in adolescents: Normal variant or a bleeding disorder. <http://contemporaryobgyn.modernmedicine.com/>

Menstruation in girls and adolescents: using the menstrual cycle as a vital sign. Committee Opinion No. 651. American College of Obstetricians and Gynecologists. *Obstet Gynecol* 2015;126:e143–6

The menstrual history

For patients reporting heavy menstrual bleeding:

- Using “double protection” (pad plus tampon or 2 pads together)
- Flooding or gushing sensation
- Frequent “accidents” or leaking through protection
- Hemorrhage from a corpus luteum
- Diagnosed with anemia
- Associated with history of excessive bruising or bleeding or a family history of bleeding disorder

Holland-Hall C. Heavy menstrual bleeding in adolescents: Normal variant or a bleeding disorder. <http://contemporaryobgyn.modernmedicine.com/>

Menstruation in girls and adolescents: using the menstrual cycle as a vital sign. Committee Opinion No. 651. American College of Obstetricians and Gynecologists. *Obstet Gynecol* 2015;126:e143–6

MEDICAL history

For patients reporting personal history of ≥ 1 of the following symptoms:

- Epistaxis (>10min, or requiring medical attention), spontaneous bruising (>2cm), or minor wound bleeding (>5min)
- Bleeding from oral cavity or GI tract without an obvious anatomic lesion
- Prolonged or excessive bleeding after dental extraction or surgery
- Hemorrhage that required transfusion

Holland-Hall C. Heavy menstrual bleeding in adolescents: Normal variant or a bleeding disorder. <http://contemporaryobgyn.modernmedicine.com/>

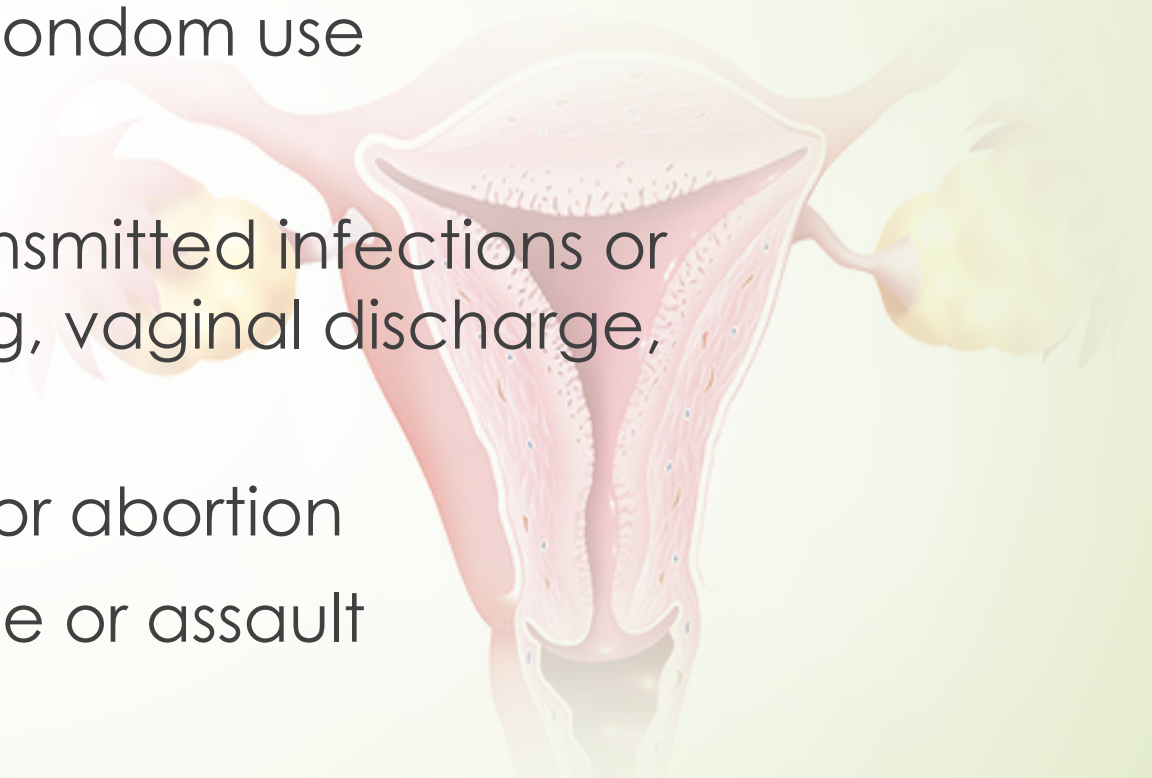
Menstruation in girls and adolescents: using the menstrual cycle as a vital sign. Committee Opinion No. 651. American College of Obstetricians and Gynecologists. *Obstet Gynecol* 2015;126:e143–6

MEDICAL history

- Social history –social stressors, substance use, and exercise patterns, and athletic competition.
- Family history –bleeding disorders, menstrual disorders, diabetes and thyroid
- Past medical history – systemic illness, including hematologic or renal disease, and current or recent medications

MEDICAL history

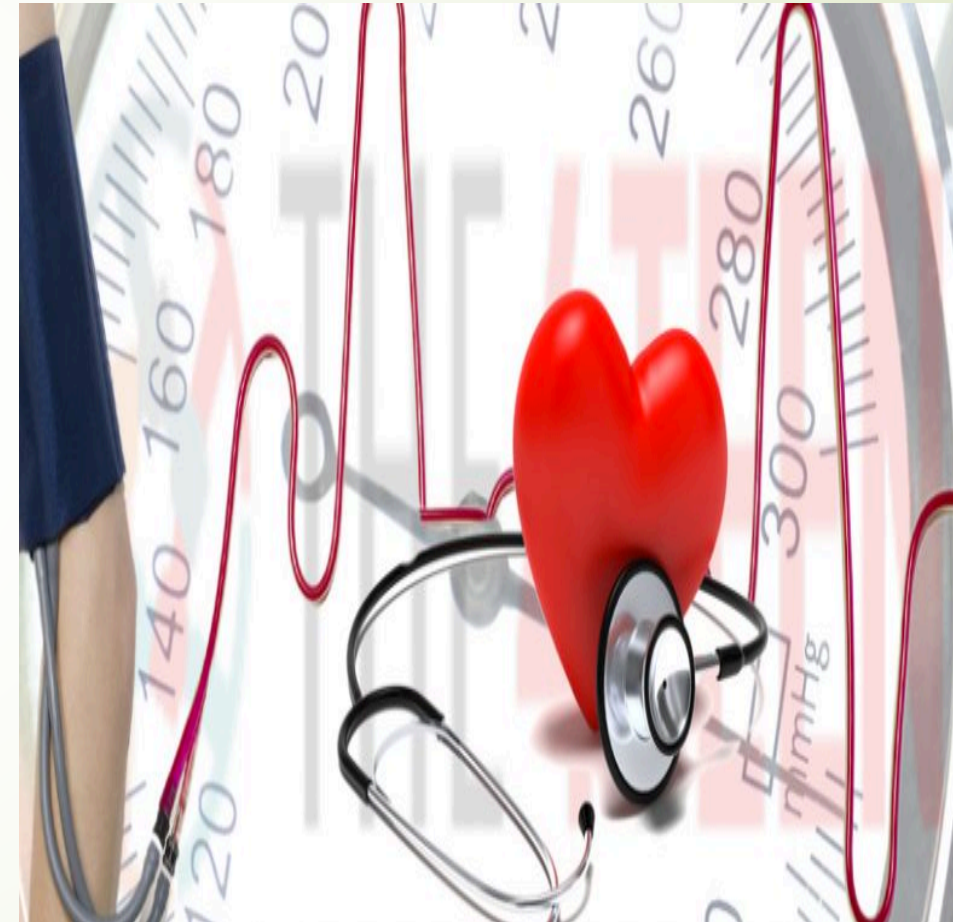
- Sexual history
 - contraception and condom use
 - number of partners
 - history of sexually transmitted infections or current symptoms (eg, vaginal discharge, pelvic pain);
 - previous pregnancy or abortion
 - history of sexual abuse or assault



Physical Exam

- Vital signs
 - tachycardia and hypotension may signal acute hemodynamic instability and the need for rapid intervention
 - The presence of tachycardia, pallor, or a heart murmur suggests anemia

Ryntz T, Lobo R. Chapter 26. Abnormal Uterine Bleeding; In Comprehensive Gynecology 7th edition, 2017;Lobo RA, Gershenson DM, Lentz GM, Valea FA editors; pp 621-633.



Physical Exam

- ▶ Petechiae or excessive bruising: may suggest a platelet defect or another bleeding disorder.
- ▶ Obesity, acne, hirsutism, and acanthosis nigricans : may be present in a patient with PCOS.

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Physical Exam

- Palpation of the thyroid gland for enlargement or other abnormalities.
- Examination of the optic fundi and visual field testing (pituitary tumor)
- Sexual maturity rating of the breasts and assessment for galactorrhea.
- Palpation of the abdomen (pregnancy, uterine/ovarian mass).

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Rydz N and Jamieson MA. Managing heavy menstrual bleeding in adolescents. 2013. <http://contemporaryobgyn.modernmedicine.com/>



Physical Exam

- External inspection of the genitalia is sufficient for diagnosis in most patients.
- A sexually active patient may warrant a complete pelvic examination (speculum and bimanual exams).

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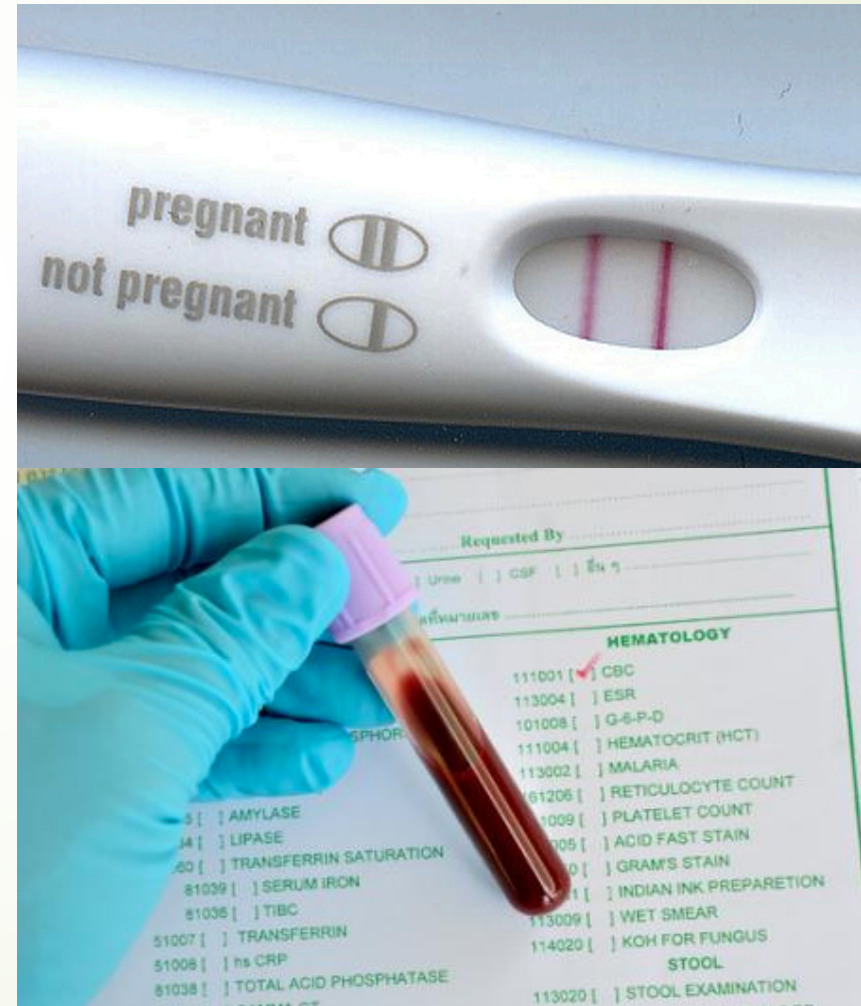
Rydz N and Jamieson MA. Managing heavy menstrual bleeding in adolescents. 2013. <http://contemporaryobgyn.modernmedicine.com/>



Laboratory evaluation

- Pregnancy test
- Complete blood count including differential and platelet count; blood typing
- Measure of iron stores
- prothrombin time and activated partial thromboplastin time

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Laboratory evaluation

- ▶ von Willebrand studies (factor VII von Willebrand factor antigen (VWF:Ag), and ristocetin cofactor (VWF:RCo) activities.)
- ▶ TSH
- ▶ Test for *Chlamydia trachomatis* and *Neisseria gonorrhoea*
- ▶ pelvic ultrasound

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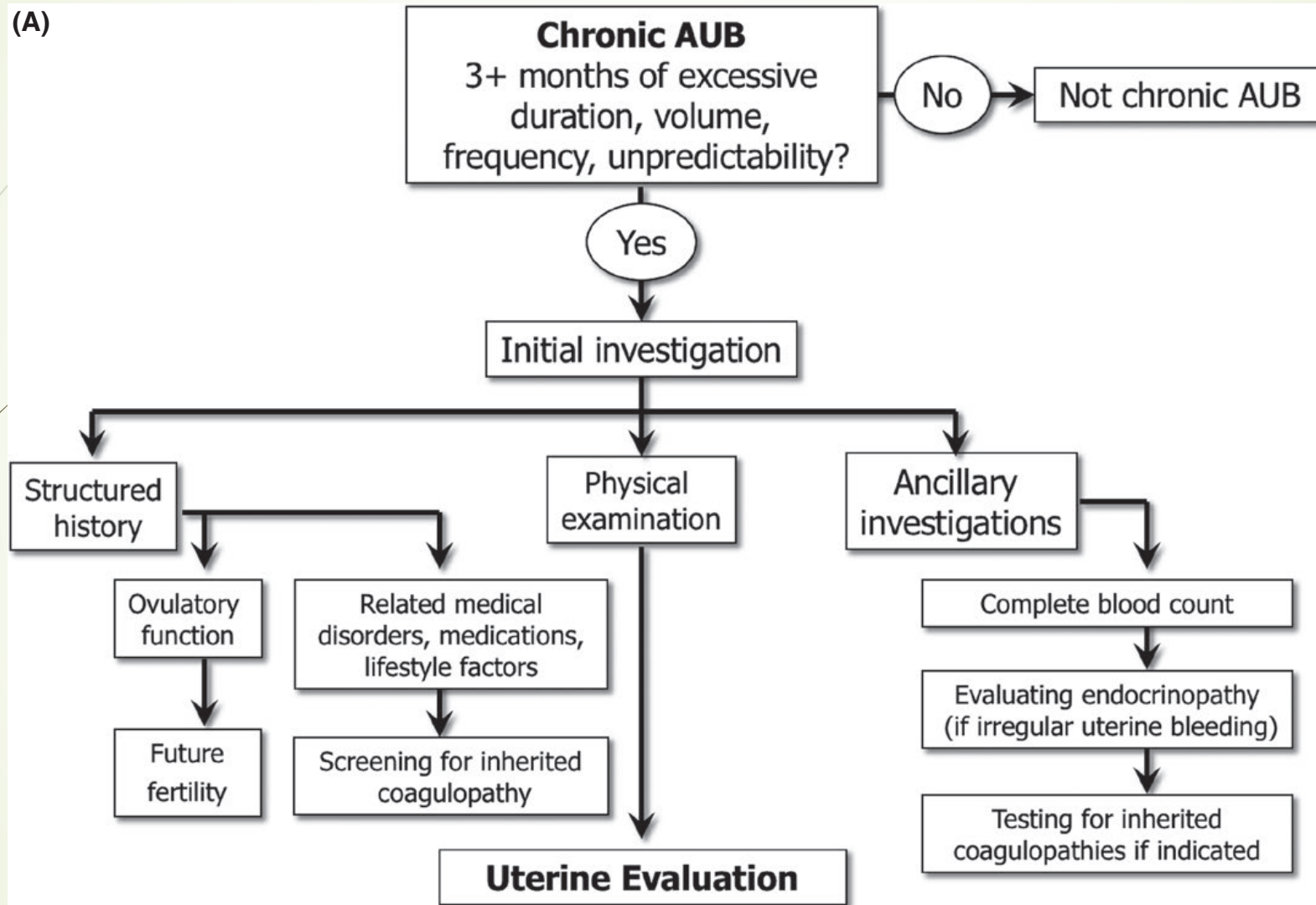
Laboratory evaluation

- ▶ Patients with a history of amenorrhea or irregular bleeding prior to the onset of heavy bleeding should have:
 - ▶ FSH and LH
 - ▶ total and free testosterone levels
 - ▶ Dehydroepiandrosterone
 - ▶ prolactin level

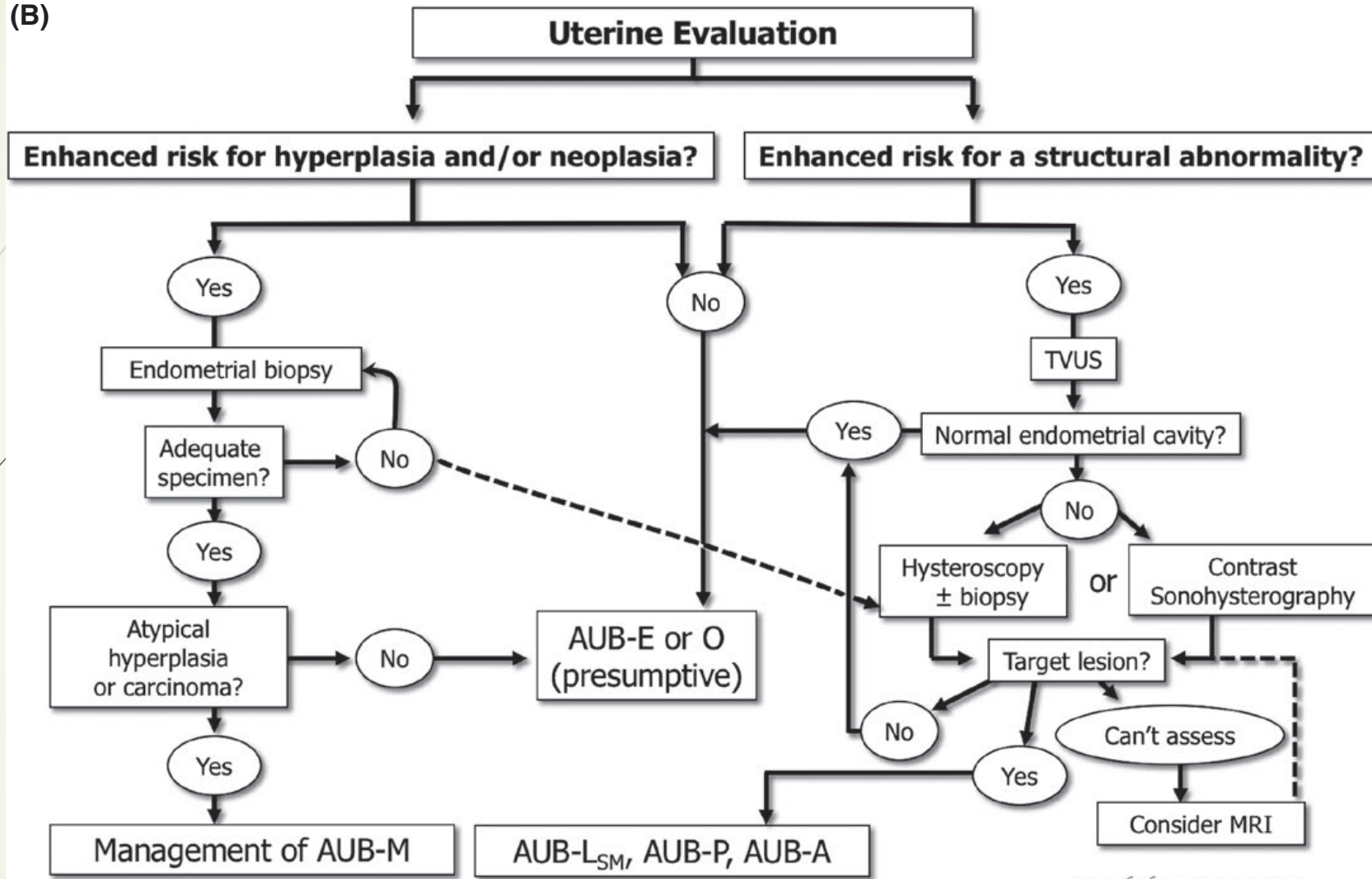
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(A)



(B)





TREATMENT

Management

- ▶ The management of AUB depends on:
 - ▶ assessment of whether or not the patient is hemodynamically stable
 - ▶ determination of the underlying cause
 - ▶ medical management based on etiology and the severity of anemia.

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The goals of treatment are to:

- Establish and/or maintain hemodynamic stability
- Correct acute or chronic anemia
- Return to a pattern of normal menstrual cycles
- Prevention of recurrence
- Prevent long-term consequences of anovulation (eg, anemia, infertility, endometrial cancer)



Medical treatment

- The goal of medical therapy is to **stabilize the endometrium with estrogen** that will provide initial hemostasis, followed by progestins for endometrial stability.
- Typically, this is achieved with **combined oral contraceptive pills (OCPs)** taken continuously for several months until hemodynamically stable, as withdrawal of either hormone will cause recurrent bleeding.



Medical treatment

- Episodes of moderate-to-severe bleeding can typically be treated effectively with frequent dosing of combined oral contraceptive pills.

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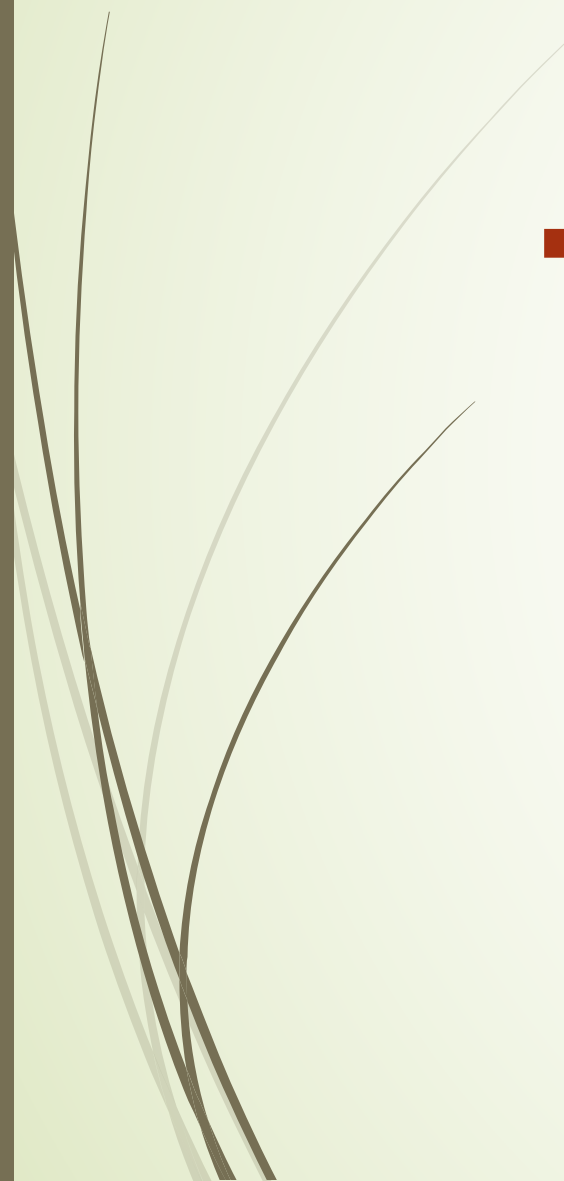
Bennet AR and Gray SH. What to do when she's bleeding through: the recognition, evaluation, and management of abnormal uterine bleeding in adolescents. *Curr Opin Pediatr* 2014, 26:413–419



Treatment

- In the absence of an organic cause for excessive uterine bleeding, it **is preferable to use medical instead of surgical treatment**, especially if the woman desires to retain her uterus for future childbearing or will be undergoing natural menopause within a short time.
- the **type of treatment** depends on whether it is used to **stop an acute heavy bleeding (acute AUB)** episode or is given to **reduce the amount of MBL in subsequent menstrual cycles (Chronic AUB)**



- 
- 
- ▶ A **definitive diagnosis** is required before instituting long-term treatment, and should be made on the basis of *hysteroscopy, sonohysterography, or directed endometrial biopsies*



ABNORMAL UTERINE BLEEDING: OVULATORY DYSFUNCTION

A. Adolescents:

- ▶ after ruling out coagulation disorders, the **main direction of therapy is to temporize** because once the **HPO axis matures**, the problem will be corrected.
- ▶ cyclic progestogen (medroxyprogesterone acetate, 10 mg for 10 days each month for a few months) to produce reliable and controlled menstrual cycles.
- ▶ oral contraceptive (OC) may be an option if the problem persists beyond 6 months.



ABNORMAL UTERINE BLEEDING: OVULATORY DYSFUNCTION

B. Perimenopausal woman:

- low-dose (20- μ g) combined oral contraceptives (in a nonsmoking woman).
- Cyclic Progestogens

C. Reproductive-aged women:

- chronic anovulatory bleeding is primarily caused by hypothalamic dysfunction or PCOS.
- Combined oral contraceptives
- cyclic progestogens



ABNORMAL UTERINE BLEEDING: ENDOMETRIAL

- ▶ For women with heavy menstrual bleeding, for whom there is no known cause and anatomic lesions have been ruled out, the **aim of therapy is to reduce the amount of excessive bleeding.**
- ▶ some women with AUB-E have abnormal prostaglandin production and some have alterations of endometrial blood flow.
- ▶ Options for treatment to reduce blood loss include:
 - ▶ prolonged regimen of progestogens (3 weeks each month);
 - ▶ Oral contraceptive pills will reduce the blood loss by at least 35% in women with AUB
 - ▶ levonorgestrel intrauterine system (LNG-IUS)

NONSTEROIDAL ANTI-INFLAMMATORY DRUGS

- ▶ prostaglandin synthetase inhibitors that inhibit the biosynthesis of the cyclic endoperoxides, which convert arachidonic acid to prostaglandins.
- ▶ block the action of prostaglandins by interfering directly at their receptor sites..
- ▶ All NSAIDs are cyclooxygenase inhibitors and thus block the formation of both thromboxane and the prostacyclin pathway. Nevertheless, NSAIDs have been shown to reduce MBL, primarily in women who ovulate.
- ▶ Examples:
 - ▶ mefenamic acid (500 mg, three times daily)
 - ▶ ibuprofen (400 mg, three times daily),
 - ▶ naproxen sodium (275 mg, every 6 hours after a loading dose of 550 mg)

Given in the first 3 days of menses or whole duration of bleeding



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Anti-fibrinolytic Agents

- ▶ ε-Aminocaproic acid (EACA), tranexamic acid (AMCA), and para-aminomethyl benzoic acid (PAMBA) are potent inhibitors of fibrinolysis
- ▶ their use is somewhat limited by side effects
 - ▶ mainly GI side effects and can be minimized by reducing the dose and limiting therapy to the first 3 to 5 days of bleeding.
 - ▶ Due to the increased risks of thrombosis and myocardial infarction, **antifibrinolytic agents should not be combined with oral contraceptives.** Combined treatment with tranexamic acid and the oral contraceptive pill has been implicated in coronary ulcerated plaque and acute myocardial infarction



Gonadotropin-Releasing Hormone Agonists

- GnRH agonists may be used to **inhibit ovarian steroid production**, as estrogen production is necessary for endometrial proliferation.
- Because of the expense and menopausal side effects of these agents, their use is limited to women with severe MBL who fail to respond to other methods of medical management and wish to retain their childbearing capacity.
- More commonly, GnRH agonists are an effective means of bridging patients to surgical treatment, allowing for correction of anemia.
- Use of an estrogen or progestogen (add-back therapy) together with the agonist will help prevent bone loss.

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MANAGEMENT OF ACUTE BLEEDING





Acute AUB

- In women who are bleeding heavily and are hemodynamically unstable, the **quickest way to stop acute bleeding is with curettage.**
- Curettage should also be the preferred approach for older women and those with medical risk factors for whom high-dose hormonal therapy may pose a great risk.
- May also be managed medically (pharmacologic agents)...





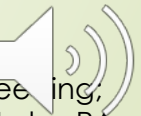
PHARMACOLOGIC AGENTS FOR ACUTE BLEEDING

- To stop acute bleeding that does not require curettage, the most effective regimen involves **high-dose estrogen**.
- High-dose estrogen is aimed at stopping acute bleeding, and is merely a temporary measure.



Estrogens

- estrogen in pharmacologic doses causes rapid growth of the endometrium.
- a rapid growth of endometrial tissue occurs over the denuded and raw epithelial surfaces
- large doses of estrogen may alter platelet activity, thus promoting platelet adhesiveness.
 1. oral conjugated equine estrogen (CEE) 10 mg/day, in four divided doses
 2. IV conjugated estrogen: 25 mg q4-6h until the bleeding stops. (No more than six doses should be administered)
 3. combination oral contraceptive (both estrogen and progestin). Four tablets of an oral contraceptive containing 30 to 35 µg of estrogen taken every 24 hours in divided doses.



Progestogens

- For patients with contraindication to estrogen (e.g., those with prior thrombosis, certain rheumatologic diseases, estrogen-responsive cancer).
- Progestogens not only stop endometrial growth but also support and organize the endometrium so that an organized slough occurs after their withdrawal.
- With progestogen treatment, an organized slough to the basalis layer allows a rapid cessation of bleeding.
- progestogens stimulate arachidonic acid formation in the endometrium, increasing the $\text{PGF2}\alpha/\text{PGE}$ ratio.
 - medroxyprogesterone acetate (MPA) at a dose of 60 mg daily (20 mg three times daily) for 7 days followed by 20 mg per day for 3 weeks
 - Depo-MPA 150 mg intramuscularly followed by oral MPA 60 mg (20 mg three times daily) for 3 days
 - norethindrone acetate (30 mg per day)

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ANDROGENS

- Danazol is a synthetic androgen used in doses of 200 mg daily for the treatment of heavy menstrual bleeding
- Limited use because of the side effects of weight gain and skin problems

Management of Acute bleeding

Tranexamic acid	10 mg/kg IV q 8h (max 600 mg/ dose) or 1.3 g PO q 8 for 5 days
COC	Monophasic 30-50ug estrogen-containing OCP TID
Oral Progestins	Medroxyprogesterone acetate 20 mg TID x 7 days
Conjugated EE	25 mg IV q 4-6H w/ IV antiemetic agents x 24 hours

Indications for hospitalization

- Hemodynamic instability (eg, tachycardia, hypotension)
- Hemoglobin concentration <7 g/dL or <10 g/dL with active heavy bleeding
- Symptomatic anemia (eg, fatigue, lethargy)
- Need for intravenous conjugated estrogen (eg, cannot take oral medications, continued heavy bleeding after 24 hours of estrogen-progestin combination therapy)
- Need for surgical intervention (rare)

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De Silva N. Abnormal uterine bleeding in adolescents: Management. March 2017. www.uptodate.com





Surgical management of Acute AUB



1. Dilatation and curettage (D&C)

- Both diagnostic and is therapeutic for the immediate management of severe bleeding.
- For women with *markedly excessive uterine bleeding* who may be hypovolemic, a D&C is the quickest way to stop acute bleeding → treatment of choice in hypovolemic women
- D&C may be preferred as an approach to stop an acute bleeding episode in women older than 35 when the incidence of pathologic findings increases.

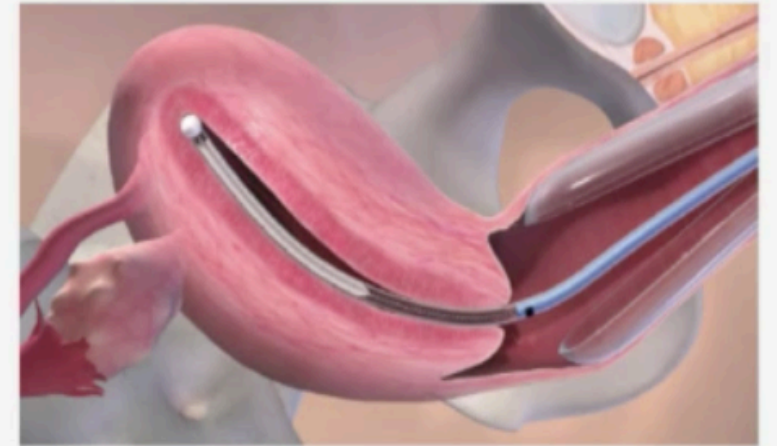


1. Dilatation and curettage (D&C)

- 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.
- All other women, after having an endometrial biopsy, sonohysterography, or diagnostic hysteroscopy to rule out organic disease, are best treated with medical therapy, without D&C.

Perform endometrial biopsy when indicated

- Age > 40
- Risk factors for endometrial cancer
 - obesity (BMI > 30 kg/m²), nulliparity, history of PCOS, diabetes, family history of hereditary non-polyposis colorectal cancer
- Failure of medical treatment
- Significant intermenstrual bleeding
- Infrequent menses suggestive of anovulatory cycles





2. Endometrial Ablation

- if medical therapy is not effective or is contraindicated.
- Exceptions are women who have very large uteri caused by fibroids or abnormal pathology, such as endometrial hyperplasia or cancer.
- Alternative to hysterectomy

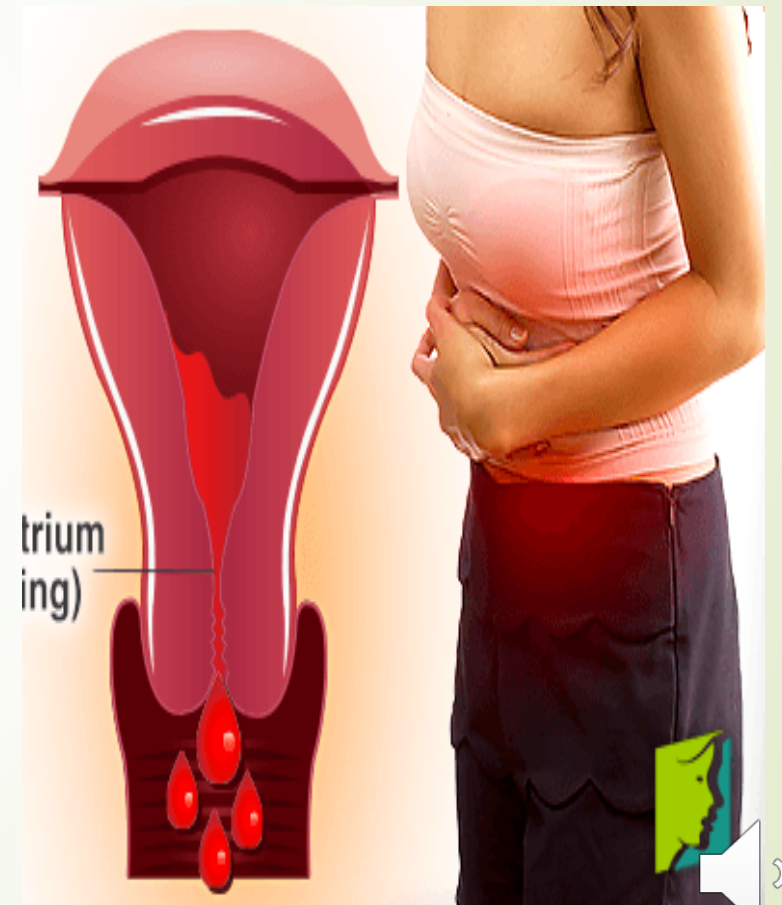


3. Hysterectomy

- Surgical removal of the uterus.
- reserved for the woman with other indications for hysterectomy, such as leiomyoma or uterine prolapse.
- Usually offered to women with completed family size (no longer desirous of pregnancy)
- used to treat persistent abnormal uterine bleeding after all medical therapy has failed, or medical therapy is contraindicated.

Chronic AUB

- Multiple treatment options are available for long-term treatment of chronic AUB:
 - levonorgestrel intrauterine system
 - OCs (monthly or extended cycles)
 - progestin therapy (oral or intramuscular)
 - tranexamic acid
 - NSAIDs
 - GnRHa



NEW!

- FDA approved for the management of HMB associated with uterine leiomyomas (fibroids) in premenopausal women
- AbbVie
- Oriahnn™ consists of 2 capsules:
 - Morning capsule:
 - elagolix, a GnRH receptor antagonist (300mg)
 - Estradiol 1mg
 - Norethindrone acetate 0.5mg
 - Evening capsule: elagolix 300mg



RX PRESCRIPTION

NAME _____

ADDRESS _____

DATE _____

AGE _____

Thank you!