

# Abnormal Uterine Bleeding

What is it and how do we treat it?

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# Normal Menstruation in Adolescents

- Median age of menarche is 12-13 years
- Cycles are 21-45 days in length
- Bleeding lasts 2-7 days
- 30 to 40 mL of blood loss per cycle



# What is Abnormal Uterine Bleeding (AUB)?

- Any aberration of menstrual volume, regulation, frequency, and duration
- Term created by FIGO
- Old terms:
  - Oligomenorrhea
  - Menorrhagia
  - Metrorrhagia
  - Menometrorrhagia
  - Polymenorrhea



# AUB - PALM COEIN

- Classification system of etiology of AUB
  - Structural vs non-structural causes of AUB
- 
- Polyp
  - Adenomyosis
  - Leiomyoma
  - Malignancy
  - Coagulopathy
  - Ovulatory dysfunction
  - Endometrial
  - Iatrogenic
  - Not yet classified



# What About Dysfunctional Uterine Bleeding?

- “Anovulatory uterine bleeding”
- AUB - O(vulatory dysfunction)



# Heavy Menstrual Bleeding (HMB)

- Bleeding for >7 days
- Blood loss >80mL
  
- Woman's perspective of increased menstrual volume
- Excessive menstrual blood loss that interferes with the woman's physical, emotional, social, and material quality of life



# Concerning History

Table. Menstrual and Bleeding History: Indications for Possible Bleeding Disorder

Menstrual History Elements	Bleeding Symptoms <sup>a</sup>
Heavy bleeding at menarche	Spontaneous episodes of epistaxis lasting >10 min (in absence of allergic rhinitis)
Prolonged menstrual bleeding lasting >8 d	Gingival/oral bleeding lasting >10 min (in absence of gingivitis)
Frequent menstrual bleeding, cycles <24 d	Prolonged cutaneous bleeding from superficial lacerations or abrasions lasting >10 min
Severe iron deficiency anemia, especially if resulting in pRBC transfusion	Excessive or unexpected bleeding from surgeries or dental extractions
Flooding, heavy leakage onto clothing, or gushing of blood	Muscle or joint bleeding
Passage of clots, especially if >2 cm in size	Postpartum hemorrhage
Increased menstrual hygiene product use, saturating/changing every 120 min or less	Any excessive bleeding requiring blood transfusion

Abbreviation: pRBC, packed red blood cells.

<sup>a</sup> Adapted from the ISTH BAT.<sup>44</sup>



# Work up to Consider

**Table 5**  
Tiered Approach to the Investigation of HMB<sup>40,42,55,63,64</sup>

Laboratory Test	Abnormality
<b>First tier</b>	
Pregnancy test	Disorders of pregnancy (ie, spontaneous miscarriage)
Complete blood count with differential	Anemia, microcytosis, thrombocytopenia
Ferritin	Iron deficiency
Prothrombin time	Factor VII deficiency if prolonged
Activated partial thromboplastin time	Factors VIII, IX, XI, XII deficiencies if prolonged
Thrombin time	Hypofibrinogenemia dysfibrinogenemia or heparin contamination if prolonged
Fibrinogen	Hypofibrinogenemia or dysfibrinogenemia
<b>Second tier</b>	
<i>Chlamydia trachomatis</i> , <i>Neisseria gonorrhoeae</i> vaginal, cervical, or urine testing	Sexually transmitted infection
Thyroid stimulating hormone	Thyroid abnormalities
von Willebrand profile (von Willebrand factor antigen, ristocetin cofactor assay, factor VIII, multimer analysis)	von Willebrand disease
Total and free testosterone, dehydroepiandrosterone sulfate, androstenedione	Polycystic ovary syndrome and other causes of hyperandrogenism
<b>Third tier</b>	
Platelet function and aggregation testing	Platelet aggregation and secretion abnormalities

HMB, heavy menstrual bleeding



# Treatment of AUB

- Acute vs Chronic?
- Treatment of underlying cause if applicable
- Hormonal treatment vs non hormonal treatment
- Iron replacement



# Hormonal Contraception

- Can usually provide menstrual management
- Many options, but they are not all created equal
- CDC Medical Eligibility Criteria (MEC)
- CDC Selected Practice Recommendations (SPR)
  - Initiation
  - Tests/exams
  - Follow up
  - Troubleshooting



# MEC

Condition	Sub-Condition	Cu-IUD		LNG-IUD		Implant		DMPA		POP		CHC	
		I	C	I	C	I	C	I	C	I	C	I	C
Age		Menarche to <20 yrs:2		Menarche to <20 yrs:2		Menarche to <18 yrs:1		Menarche to <18 yrs:2		Menarche to <18 yrs:1		Menarche to <40 yrs:1	
		≥20 yrs:1		≥20 yrs:1		18-45 yrs:1		18-45 yrs:1		18-45 yrs:1		≥40 yrs:2	
				>45 yrs:1		>45 yrs:2		>45 yrs:1					
Anatomical abnormalities	a) Distorted uterine cavity	4	4										
	b) Other abnormalities	2	2										
Anemias	a) Thalassemia	2	1	1	1	1	1	1	1	1	1	1	1
	b) Sickle cell disease <sup>†</sup>	2	1	1	1	1	1	1	1	1	1	2	2
	c) Iron-deficiency anemia	2	1	1	1	1	1	1	1	1	1	1	1
Benign ovarian tumors	(including cysts)	1	1	1	1	1	1	1	1	1	1	1	1
Breast disease	a) Undiagnosed mass	1	2	2*	2*	2*	2*	2*	2*	2*	2*	2*	2*
	b) Benign breast disease	1	1	1	1	1	1	1	1	1	1	1	1
	c) Family history of cancer	1	1	1	1	1	1	1	1	1	1	1	1
	d) Breast cancer <sup>†</sup>												
	i) Current	1	4	4	4	4	4	4	4	4	4	4	4
ii) Past and no evidence of current disease for 5 years	1	3	3	3	3	3	3	3	3	3	3	3	
Breastfeeding	a) <21 days postpartum					2*	2*	2*	2*	2*	2*	4*	4*
	b) 21 to <30 days postpartum												
	i) With other risk factors for VTE					2*	2*	2*	2*	2*	2*	3*	3*
	ii) Without other risk factors for VTE					2*	2*	2*	2*	2*	2*	3*	3*
	c) 30-42 days postpartum												
	i) With other risk factors for VTE					1*	1*	1*	1*	1*	1*	3*	3*
	ii) Without other risk factors for VTE					1*	1*	1*	1*	1*	1*	2*	2*
d) >42 days postpartum					1*	1*	1*	1*	1*	1*	2*	2*	
Cervical cancer	Awaiting treatment	4	2	4	2	2	2	2	2	1	1	2	2
Cervical ectropion		1	1	1	1	1	1	1	1	1	1	1	1
Cervical intraepithelial neoplasia		1	2	2	2	2	2	1	1	1	2	2	2
Cirrhosis	a) Mild (compensated)	1	1	1	1	1	1	1	1	1	1	1	1
	b) Severe <sup>†</sup> (decompensated)	1	3	3	3	3	3	3	3	3	4	4	4
Cystic fibrosis <sup>†</sup>		1*	1*	1*	1*	2*	2*	1*	1*	1*	1*	1*	1*
Deep venous thrombosis (DVT)/Pulmonary embolism (PE)	a) History of DVT/PE, not receiving anticoagulant therapy												
	i) Higher risk for recurrent DVT/PE	1	2	2	2	2	2	2	2	2	4	4	4
	ii) Lower risk for recurrent DVT/PE	1	2	2	2	2	2	2	2	2	3	3	3
	b) Acute DVT/PE	2	2	2	2	2	2	2	2	2	4	4	4
	c) DVT/PE and established anticoagulant therapy for at least 3 months												
	i) Higher risk for recurrent DVT/PE	2	2	2	2	2	2	2	2	2	4*	4*	4*
	ii) Lower risk for recurrent DVT/PE	2	2	2	2	2	2	2	2	2	3*	3*	3*
	d) Family history (first-degree relatives)	1	1	1	1	1	1	1	1	1	2	2	2
	e) Major surgery												
	i) With prolonged immobilization	1	2	2	2	2	2	2	2	2	4	4	4
ii) Without prolonged immobilization	1	1	1	1	1	1	1	1	1	2	2	2	
f) Minor surgery without immobilization	1	1	1	1	1	1	1	1	1	1	1	1	
Depressive disorders		1*	1*	1*	1*	1*	1*	1*	1*	1*	1*	1*	1*

# MEC

Condition	Sub-Condition	Cu-IUD		LNG-IUD		Implant		DMPA		POP		CHC	
		I	C	I	C	I	C	I	C	I	C	I	C
Diabetes	a) History of gestational disease	1		1		1		1		1		1	
	b) Nonvascular disease												
	i) Non-insulin dependent	1	2	2	2	2	2	2	2	2	2	2	2
	ii) Insulin dependent	1	2	2	2	2	2	2	2	2	2	2	2
	c) Nephropathy/retinopathy/neuropathy <sup>†</sup>	1	2	2	2	3	2	3/4*					
d) Other vascular disease or diabetes of >20 years' duration <sup>†</sup>	1	2	2	2	3	2	3/4*						
Dysmenorrhea	Severe	2		1		1		1		1		1	
Endometrial cancer <sup>†</sup>		4	2	4	2	1		1		1		1	
Endometrial hyperplasia		1		1		1		1		1		1	
Endometriosis		2		1		1		1		1		1	
Epilepsy <sup>†</sup>	(see also Drug Interactions)	1		1		1*		1*		1*		1*	
Gallbladder disease	a) Symptomatic												
	i) Treated by cholecystectomy	1		2		2		2		2		2	
	ii) Medically treated	1		2		2		2		2		3	
	iii) Current	1		2		2		2		2		3	
	b) Asymptomatic	1		2		2		2		2		2	
Gestational trophoblastic disease <sup>†</sup>	a) Suspected GTD (immediate postevacuation)												
	i) Uterine size first trimester	1*		1*		1*		1*		1*		1*	
	ii) Uterine size second trimester	2*		2*		1*		1*		1*		1*	
	b) Confirmed GTD												
	i) Undetectable/non-pregnant β-hCG levels	1*	1*	1*	1*	1*		1*		1*		1*	
	ii) Decreasing β-hCG levels	2*	1*	2*	1*	1*		1*		1*		1*	
	iii) Persistently elevated β-hCG levels or malignant disease, with no evidence or suspicion of intrauterine disease	2*	1*	2*	1*	1*		1*		1*		1*	
	iv) Persistently elevated β-hCG levels or malignant disease, with evidence or suspicion of intrauterine disease	4*	2*	4*	2*	1*		1*		1*		1*	
Headaches	a) Nonmigraine (mild or severe)	1		1		1		1		1		1*	
	b) Migraine												
	i) Without aura (includes menstrual migraine)	1		1		1		1		1		2*	
ii) With aura	1		1		1		1		1		4*		
History of bariatric surgery <sup>†</sup>	a) Restrictive procedures	1		1		1		1		1		1	
	b) Malabsorptive procedures	1		1		1		1		3		COCs: 3 P/R: 1	
History of cholestasis	a) Pregnancy related	1		1		1		1		1		2	
	b) Past COC related	1		2		2		2		2		3	
History of high blood pressure during pregnancy		1		1		1		1		1		2	
History of Pelvic surgery		1		1		1		1		1		1	
HIV	a) High risk for HIV	1*	1*	1*	1*	1		1		1		1	
	b) HIV infection					1*		1*		1*		1*	
	i) Clinically well receiving ARV therapy	1	1	1	1								If on treatment, see Drug Interactions
	ii) Not clinically well or not receiving ARV therapy <sup>†</sup>	2	1	2	1								If on treatment, see Drug Interactions



# MEC

Condition	Sub-Condition	Cu-IUD		LNG-IUD		Implant		DMPA		POP		CHC	
		I	C	I	C	I	C	I	C	I	C	I	C
Hypertension	a) Adequately controlled hypertension	1*		1*		1*		2*		1*		3*	
	b) Elevated blood pressure levels (properly taken measurements)												
	i) Systolic 140-159 or diastolic 90-99	1*		1*		1*		2*		1*		3*	
	ii) Systolic $\geq 160$ or diastolic $\geq 100$ <sup>1</sup>	1*		2*		2*		3*		2*		4*	
c) Vascular disease	1*		2*		2*		3*		2*		4*		
Inflammatory bowel disease	(Ulcerative colitis, Crohn's disease)	1		1		1		2		2		2/3*	
Ischemic heart disease <sup>1</sup>	Current and history of	1	2	3	2	3	3	3	2	3	4		
Known thrombogenic mutations <sup>1</sup>		1*		2*		2*		2*		2*		4*	
Liver tumors	a) Benign												
	i) Focal nodular hyperplasia	1		2		2		2		2		2	
	ii) Hepatocellular adenoma <sup>1</sup>	1		3		3		3		3		4	
	b) Malignant <sup>1</sup> (hepatoma)	1		3		3		3		3		4	
Malaria		1		1		1		1		1		1	
Multiple risk factors for atherosclerotic cardiovascular disease	(e.g., older age, smoking, diabetes, hypertension, low HDL, high LDL, or high triglyceride levels)	1		2		2*		3*		2*		3/4*	
Multiple sclerosis	a) With prolonged immobility	1		1		1		2		1		3	
	b) Without prolonged immobility	1		1		1		2		1		1	
Obesity	a) Body mass index (BMI) $\geq 30$ kg/m <sup>2</sup>	1		1		1		1		1		2	
	b) Menarche to <18 years and BMI $\geq 30$ kg/m <sup>2</sup>	1		1		1		2		1		2	
Ovarian cancer <sup>1</sup>		1		1		1		1		1		1	
Parity	a) Nulliparous	2		2		1		1		1		1	
	b) Parous	1		1		1		1		1		1	
Past ectopic pregnancy		1		1		1		1		2		1	
Pelvic inflammatory disease	a) Past												
	i) With subsequent pregnancy	1	1	1	1	1	1	1	1	1	1	1	1
	ii) Without subsequent pregnancy	2	2	2	2	1	1	1	1	1	1	1	1
	b) Current	4	2*	4	2*	1	1	1	1	1	1	1	1
Peripartum cardiomyopathy <sup>1</sup>	a) Normal or mildly impaired cardiac function												
	i) <6 months	2		2		1		1		1		4	
	ii) $\geq 6$ months	2		2		1		1		1		3	
	b) Moderately or severely impaired cardiac function	2		2		2		2		2		4	
Postabortion	a) First trimester	1*		1*		1*		1*		1*		1*	
	b) Second trimester	2*		2*		1*		1*		1*		1*	
	c) Immediate postseptic abortion	4		4		1*		1*		1*		1*	
Postpartum (nonbreastfeeding women)	a) <21 days					1		1		1		4	
	b) 21 days to 42 days												
	i) With other risk factors for VTE					1		1		1		3*	
	ii) Without other risk factors for VTE					1		1		1		2	
	c) >42 days					1		1		1		1	
Postpartum (in breastfeeding or non-breastfeeding women, including cesarean delivery)	a) <10 minutes after delivery of the placenta												
	i) Breastfeeding	1*		2*									
	ii) Nonbreastfeeding	1*		1*									
	b) 10 minutes after delivery of the placenta to <4 weeks	2*		2*									
	c) $\geq 4$ weeks	1*		1*									
	d) Postpartum sepsis	4		4									

# MEC

Condition	Sub-Condition	Cu-IUD		LNG-IUD		Implant		DMPA		POP		CHC	
		I	C	I	C	I	C	I	C	I	C	I	C
Pregnancy		4*		4*		NA*		NA*		NA*		NA*	
Rheumatoid arthritis	a) On immunosuppressive therapy	2	1	2	1	1		2/3*		1		2	
	b) Not on immunosuppressive therapy	1		1		1		2		1		2	
Schistosomiasis	a) Uncomplicated	1		1		1		1		1		1	
	b) Fibrosis of the liver <sup>†</sup>	1		1		1		1		1		1	
Sexually transmitted diseases (STDs)	a) Current purulent cervicitis or chlamydial infection or gonococcal infection	4	2*	4	2*	1		1		1		1	
	b) Vaginitis (including trichomonas vaginalis and bacterial vaginosis)	2	2	2	2	1		1		1		1	
	c) Other factors relating to STDs	2*	2	2*	2	1		1		1		1	
Smoking	a) Age <35	1		1		1		1		1		2	
	b) Age ≥35, <15 cigarettes/day	1		1		1		1		1		3	
	c) Age ≥35, ≥15 cigarettes/day	1		1		1		1		1		4	
Solid organ transplantation <sup>†</sup>	a) Complicated	3	2	3	2	2		2		2		4	
	b) Uncomplicated	2		2		2		2		2		2*	
Stroke <sup>†</sup>	History of cerebrovascular accident	1		2		2	3	3		2	3	4	
Superficial venous disorders	a) Varicose veins	1		1		1		1		1		1	
	b) Superficial venous thrombosis (acute or history)	1		1		1		1		1		3*	
Systemic lupus erythematosus <sup>†</sup>	a) Positive (or unknown) antiphospholipid antibodies	1*	1*	3*		3*		3*	3*	3*		4*	
	b) Severe thrombocytopenia	3*	2*	2*		2*		3*	2*	2*		2*	
	c) Immunosuppressive therapy	2*	1*	2*		2*		2*	2*	2*		2*	
	d) None of the above	1*	1*	2*		2*		2*	2*	2*		2*	
Thyroid disorders	Simple goiter/ hyperthyroid/hypothyroid	1		1		1		1		1		1	
Tuberculosis <sup>†</sup> (see also Drug Interactions)	a) Nonpelvic	1	1	1	1	1*		1*		1*		1*	
	b) Pelvic	4	3	4	3	1*		1*		1*		1*	
Unexplained vaginal bleeding	(suspicious for serious condition) before evaluation	4*	2*	4*	2*	3*		3*		2*		2*	
Uterine fibroids		2		2		1		1		1		1	
Valvular heart disease	a) Uncomplicated	1		1		1		1		1		2	
	b) Complicated <sup>†</sup>	1		1		1		1		1		4	
Vaginal bleeding patterns	a) Irregular pattern without heavy bleeding	1	1	1		2		2		2		1	
	b) Heavy or prolonged bleeding	2*	1*	2*		2*		2*		2*		1*	
Viral hepatitis	a) Acute or flare	1		1		1		1		1		3/4*	2
	b) Carrier/Chronic	1		1		1		1		1		1	1
<b>Drug Interactions</b>													
Antiretrovirals used for prevention (PrEP) or treatment of HIV	Fosamprenavir (FPV)	1/2*	1*	1/2*	1*	2*		2*		2*		3*	
	All other ARVs are 1 or 2 for all methods.												
Anticonvulsant therapy	a) Certain anticonvulsants (phenytoin, carbamazepine, barbiturates, primidone, topiramate, oxcarbazepine)	1		1		2*		1*		3*		3*	
	b) Lamotrigine	1		1		1		1		1		3*	
Antimicrobial therapy	a) Broad spectrum antibiotics	1		1		1		1		1		1	
	b) Antifungals	1		1		1		1		1		1	
	c) Antiparasitics	1		1		1		1		1		1	
	d) Rifampin or rifabutin therapy	1		1		2*		1*		3*		3*	
SSRIs		1		1		1		1		1		1	
St. John's wort		1		1		2		1		2		2	

# Contraceptives used for AUB treatment

- Combined oral contraceptive pill
- Patch
- Ring
- Progesterone only pills
- Depo medroxyprogesterone
- Levonorgestrel intrauterine device



# Combined Oral Contraceptive Pill

- Ethinyl Estradiol
  - Varies from 10-50 mcg
  - Generally recommend 30-35 mcg pill
- 4 generations of progesterone
  - Based on when they were released
  - Third and fourth generations are considered less androgenic





# Combined Oral Contraceptive Pill

- Side Effects
  - Nausea
  - Breast tenderness
  - Headaches
  - Bloating
  - Unscheduled bleeding or amenorrhea
  - Thromboembolism



# Combined Oral Contraceptive Pill

- Other benefits
  - Contraception
  - Hyperandrogenism
  - Pelvic pain
  - Ovarian cysts
  - PMS/PMDD



# Which pill to chose?

- 30-35 mcg of estrogen
- Tri phasic is not necessary
- 28 vs 91 pill pack



# The Patch

- Ethinyl estradiol and norelgestromin
- Ethinyl estradiol and levonorgestrel



# The Patch

- Use MEC for eligibility of use
- Side effects similar to OCPs
- Skin irritation
- Contraindicated in BMI >30
- Risk of thromboembolism
- Change weekly for 3 weeks, 1 patch free week
- May use in extended fashion



# The Ring

- Ethinyl Estradiol and etonogestrel
  - Insert for 3 weeks, followed by 1 week ring free
  - New ring inserted each cycle
  - Requires refrigeration prior to use
- Ethinyl estradiol and segesterone
  - Insert for 3 weeks, followed by 1 week ring free
  - Same ring used for 13 cycles
  - No refrigeration



# The Ring

- Use MEC for eligibility criteria
- Similar side effects
- Vaginitis, vaginal wetness, and leukorrhea
- May use in extended cycling



# Progesterone Only Pill

- Norethindrone acetate
  - 5-15 mg daily
  - Continuous
  - Not contraception
- Medroxyprogesterone acetate
  - 5-30 mg daily
  - Generally cyclic dosing
  - Not contraception
- Norethindrone
  - 35 mcg daily
  - Continuous
  - Not studied for AUB treatment





# Progesterone Only Pill

- No serious complications
- Bleeding pattern changes
- Mood changes



# Depot Medroxyprogesterone Acetate

- 150mg given IM or SubQ
- Dosed every 3 months (12-15 weeks)
- May be given as often as every 10 weeks



# Depot Medroxyprogesterone Acetate

- Off label for AUB treatment
- Decreased bone mineral density
- Weight gain?
- Headaches



# Levonorgestrel Intrauterine Device

- Varying levels of LNG
  - 52 mg
  - 19.5 mg
  - 13.5 mg
- 52 mg is approved for HMB



# Levonorgestrel Intrauterine Device

- Procedure for placement
- Irregular cramping and bleeding for 3-6 months
- Irregular bleeding patterns long term
- PID?
- Expulsion



# Non hormonal Options

- Nonsteroidal antiinflammatory drugs (NSAIDs)
- Tranexamic acid
- Aminocaproic acid



# Nonsteroidal Anti-inflammatory Drugs

- Decrease the prostaglandin production in the endometrium → vasoconstriction → decreased blood loss
- Ibuprofen
  - 600mg, once per day
- Naproxen
  - 500mg at onset and repeat dose in 3-5 hours
  - 250-500mg every 12 hours
- Mefanamic Acid
  - 500mg, three times a day



# Tranexamic Acid

- Antifibrinolytic agent
- Approved for the treatment of HMB
- Used only during menstruation
  - 1300mg, three times a day
  - Up to 5 days





# Aminocaproic Acid

- Antifibrinolytic agent
- Used only during menstruation
  - 50-100 mg/kg every 6 hours



# Acute Management of HMB

Drug	Suggested Dose	Dose Schedule
Conjugated equine estrogen <sup>†</sup>	25 mg IV	Every 4–6 hours for 24 hours
Combined oral contraceptives <sup>‡§</sup>	Monophasic combined oral contraceptive pills that contain 30–50 micrograms of ethinyl estradiol	Every 6–8 hours until cessation of bleeding
Medroxyprogesterone acetate <sup>  ¶</sup>	20 mg orally	Three times per day for 7 days
Tranexamic acid <sup>‡</sup>	1.3 g orally <sup>‡</sup> or 10 mg/kg IV (maximum 600 mg/dose)	Three times per day for 5 days (every 8 hours)

Abbreviations: FDA, U.S. Food and Drug Administration; IV, intravenously.



# Ferrous Sulfate

- Screen for iron deficiency
- Ferrous sulfate 325mg QD-BID
- Side effects include nausea and constipation



# References

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