ABNORMAL UTERINE BLEEDING

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OBJECTIVES

- To understand the terminology of abnormal uterine bleeding.
- To review the etiology of abnormal uterine bleeding.
- To understand the basic investigation of abnormal uterine bleeding.
- To review the potential medical and surgical approaches in the treatment of abnormal uterine bleeding.

CHARACTERISTICS OF THE NORMAL MENSTRUAL CYCLE

- Flow lasts 2-7 days.
- Cycle 21-35 days.
- Total menstrual blood loss < 80 ml.

ABNORMAL UTERINE BLEEDING (AUB)

- An alteration in the volume, pattern, and or duration of menstrual blood flow.
- Most common reason for gynecologic referral
- More than 10 million women in USA currently suffer from AUB.
- 6 million seek medical help each year.
- AUB accounts for 15% of office visits and almost 25 % of gynecologic operations.

DYSFUNCTIONAL UTERINE BLEEDING (DUB)

- ABNORMAL uterine bleeding with no demonstrable organic, genital, or extragenital cause.
- Diagnosis of EXCLUSION
- Patient presents with “abnormal uterine bleeding”
- Occurs most often shortly after menarche and at the end of the reproductive years (20% adolescents, 50% 40-50 yo)
- Most frequently due to anovulation

QUESTION #1:

- Which statement is TRUE?

(A) The normal menstrual cycle is 24 days with flow for 8 days with 90 ml of blood loss.

(B) Dysfunction uterine bleeding is most frequently due to ovulation.

(C) Abnormal uterine bleeding is the most common gynecololgic referral.

(D) Dysfunction uterine bleeding most often occurs for women ages 25-35.

DEFINITIONS

- Menorrhagia (hypermenorrhea)→ prolonged (>7days) and or excessive (>80ml) uterine bleeding occurring at REGULAR intervals
- Metrorrhagia → uterine bleeding occurring at completely irregular but frequent intervals, the amount being variable.
- Menometrorrhagia → uterine bleeding that is prolonged AND occurs at completely irregular intervals.

DEFINITIONS

- Polymenorrhea → uterine bleeding at regular intervals of < 21 days.
- Intermenstrual Bleeding → bleeding of variable amounts occurring between regular menstrual periods.
- Oligomenorrhea → uterine bleeding at regular intervals from 35 days to 6 months.
- Amenorrhea → ABSENCE of uterine bleeding for > 6 months.
- Postmenopausal Bleeding → uterine bleeding that occurs more than 1 year after last menses in a woman with ovarian failure.

DIFFERENTIAL DIAGNOSIS OF AUB

- Organic (reproductive tract disease, systemic disease and iatrogenic causes)
- Non-organic (DUB)

"YOU MUST EXCLUDE ALL ORGANIC CAUSES FIRST!"

- Pregnancy related causes
- Medications
- Anatomic
- Infectious disease
- Endocrine abnormalities
- Bleeding disorders
- Endometrial hyperplasia
- Neoplasm

AUB—Prior to Menarche

- Rule –malignancy, trauma, sexual abuse
- Workup starts with Pelvic Exam (consider anesthesia)
- Most common = FOREIGN BODY

AUB RELATED TO AGE

- Prior to Menarche
- Reproductive Age
- Postmenopausal

AUB—Reproductive Age

- Pregnancy and pregnancy related complications
- Medications and other iatrogenic causes
- Systemic conditions
- Genital tract pathology

Pregnancy Related AUB

- Spontaneous abortion
- Ectopic pregnancy
- Placenta previa
- Placental abruption
- Gestational Trophoblastic Disease
- Puerperal complications

Iatrogenic Causes

- Medications (Anticoagulants, SSRI, Antipsychotics, Corticosteroids, Hormonal medications, IUD, Tamoxifen)
- Herbal substances (ginseng, ginkgo, soy--estrogenic properties) (Motherworth—coumarin containing herb)

Medications

- Warfarin—bleeding complications usually occur when INR exceeds therapeutic range
- NSAIDS
- Fish oil—concentrated omega 3 impairs platelet activitation

Medications—Contraceptive Bleeding

- OCPs (lower dose, skipped pills, altered absorption/metabolism) (39% starting OCPs will have irregular bleeding—midcycle within first 3 months)
- Depo Provera (50% irregular bleeding after 1st dose, 25 % after 1 year← biggest reason for discontinuation)

Medications—Hormone Replacement Therapy

- Greatly decreased use secondary to WHI study findings
- Lower dose formulations promoted for shorter term use to relieve menopausal vasomotor symptoms
- Continuous therapy—40% will bleed in the first 4-6 months
- Sequential therapy—bleeding near progesterone therapy, monthly, can experience abnormal bleeding pattern 2-4 months

Systemic Causes

- Thyroid disease
- Polycystic ovary disease
- Coagulopathies
- Hepatic disease
- Adrenal hyperplasia and Cushings
- Pituitary adenoma or hyperprolactinemia
- Hypothalamic suppression (from stress, weight loss, excessive exercise

Endocrine Abnormalities

- Hypothyroidism
- PCOS
- Cushing’s syndrome
- CAH

Bleeding Disorders

- Formation of a platelet plug is the first step of homeostasis during menstruation
- 2 most common disorders → von Willebrand's disease and Thrombocytopenia
- May be particularily severe at menarche due to the dominant estrogen stimulation causing increased vascularity
- Hospitalized patient, 1/3 have coagulopathy (vWD, Factor XI deficiency)

Bleeding Disorders

- If heavy with first menses, 45% have a coagulopathy
- If heavy with subsequent menses, 20% have a coagulopathy
- 65% report heavy menstrual bleed from menarche.
- Within 3 years postmenarche ¾ of cycles are ovulatory.

Bleeding Disorders—Von Willebrand's Disease

- Most common inherited bleeding disorder
- Up to 78% report AUB
- 3 major types (Type 1 most common [80%])
- Screening tests—PT, aPTT
- Diagnosis vWD Panel – FVIII activity, vWF antigen, Ristocetin cofactor
- Hematology consult

Question #2:

- Which statement is FALSE?

(A) When a patient presents with abnormal uterine bleeding one must always rule out organic causes first.

(B) Bleeding disorders, Systemic Diseases, Medications can all cause abnormal uterine bleeding.

(C) Pregnancy is not part of the evaluation for AUB since pregnant women can experience bleeding during their pregnancy.

(D) Prior to menarche the most common cause for AUB is a foreign body.

Bleeding Disorders—ACOG Recommendations for Testing

- Adolescents—severe menorrhagia
- Women with significant menorrhagia without identifiable cause
- Prior to hysterectomy for menorrhagia

Genital Tract Pathology

- Infections—cervicitis, endometritis, salpingitis
- Trauma—foreign body, abrasions, lacerations

Genital Tract Pathology—Infectious Causes

- PID (fever, pelvic discomfort, cervical motion tenderness, adnexal tenderness).
- Can cause menorrhagia or metrorrhagia
- More common during menstruation and with BV
- Trichomonas
- Endocervicitis

Genital Tract Pathology--Neoplastic

- Benign—adenomyosis, leiomyoma, polyps of cervix or endometrium
- Premalignant—cervical dysplasia, endometrial hyperplasia
- Malignant—cervical, endometrial, ovarian, leiomyosarcoma

Genital Tract Pathology—Benign--Fibroids

- Often asymptomatic
- Risk factors→nulliparity, obesity, family history, hypertension, African-American
- Usually causes heavier or prolonged menses
- Treatment options—expectant, medical, embolization, ablation, surgery

Genital Tract Pathology—Benign--Adenomyosis

- Endometrial glands within the myometrium.
- Usually asymptomatic.
- Can present with heavy or prolonged bleeding.
- Often accompanied by painful menses (dysmenorrhea) up to 1 week before menses.
- Symptoms usually occur after age 40
- Diagnosis by pathology

Genital Tract Pathology--Polyps

- Endometrial (intermenstrual bleeding, irregular bleeding, menorrhagia)
- Cervical (intermenstrual bleeding, postcoital spotting)

Genital Tract Pathology—Postcoital Bleeding

- Women age 20-40
- 2/3 with no underlying pathology
- 25% cervical eversion
- Endocervical polyps, cervicitis (Chlamydia)
- Dysplasia/cancer
- Vaginal atrophy
- Unexplained = Colposcopy

Genital Tract Pathology—Premalignant—Endometrial Hyperplasia

- Overgrowth of glandular epithelium of the endometrial lining.
- Usually occurs when a patient is exposed to unopposed estrogen (either estrogenically or because of anovulation)
- Rate of neoplasm (simple to complex, 1 to 30%)

Genital Tract Pathology—Premalignant—Endometrial Hyperplasia

- Simple—often regresses spontaneously, progestin treatment used for treating bleeding may help in treating hyperplasia as well
- Complex with atypia—1 study found incidence of concomitant endometrial cancer in 40% of cases

Genital Tract Pathology—Malignant—Uterine Cancer

- 4th most common cancer in women
- Risk factors (nulliparity, late menopause [after age 52], obesity, diabetes, unopposed estrogen therapy, tamoxifen, history of atypical endometrial hyperplasia)
- Most often presents as postmenopausal bleeding in the sixth and seventh decade (only 10% of patients with PMB will have endometrial cancer)
- Perimenopausally can present as menometrorrhagia

AUB Evaluation: Historical Details

- Possibility of a hemostatic problem (bleeding with dental work, mucosal bleeding [epistaxis], postpartum bleeding, postop bleeding, excessive bleeding since menarche, history of easy bruising

AUB Evaluation: Assessment of Severity

- Assessment of volume
- History of anemia or iron supplementation
- Patient perception of cycle [pad count, clots, frequency, duration]

AUB Evaluation: Physical Examination

- BMI, Hirsutism, Acne
- Acanthosis nigrans
- Thyroid nodule
- Eccyhmoses
- Pelvic Examination (establish that this is uterine bleeding)

General Principles in Differential Diagnosis of AUB

- ALWAYS exclude pregnancy
- Adolescents (most likely anovulation (immature H-P-O axis) but exclude STDs and vWD
- Reproductive Age (anovulatory, exclude precancer/cancer if >35 yo but most likely PCOS
- Reproductive Age (ovulatory, exclude uterine causes such as fibroids or polyps but most likely idiopathic)

General Principles in Differential Diagnosis of AUB

- Perimenopausal/postmenopausal (ALWAYS exclude cancer, usually isn't, if bleeding persists exclude it again, most likely benign cause)

Anovulatory Cycles

- Unpredictable cycle length
- Unpredictable bleeding pattern
- Frequent spotting
- Infrequent heavy bleeding
- 90-95% reproductive age
- Cause = Systemic hormonal imbalance
- Always a relative progestin-deficient state
- Assess for secondary hypothalamic disorder (stress, eating disorder, excessive exericise, weight loss, chronic illness

Anovulatory Cycles

- Check TSH
- Test for PCOS if indicated
- Treatment = Addressing underling disorder

Anovulatory Cycles--Adolescents

- Most likely due to immature Hypothalamic Pituitary axis
- Rule out pregnancy
- Consider bleeding disorder
- Treatment→ observation or cyclic progesterone or OCPs

Anovulatory Cycles--Adults

- Identify secondary cause of Hypothalamic Pituitary dysfunction
- Address underlying cause
- Manage with cyclic progesterone or monthly OCPs (*regulates cycles, protects against endometrial cancer).

Ovulatory Bleeding

- Usually underlying prostaglandin imbalance ("DUB")→ defect in local endometrial hormonal hemostasis
- Structural lesions (fibroids, adenomyosis, polyps)
- Systemic disease (Liver, Renal, Bleeding disorder)
- Not common (5-10%)
- Consider empiric treatment without further workup if exam normal (NSAIDS, OCPs, Progesterone--IUD)
- If treatment fails, proceed with workup (labs, EMB, imaging)

General Principles of Evaluation for AUB

- Pregnancy test
- Pap, cultures for STDs
- Screen for vWD when appropriate
- CBC (anemia workup)
- Endocrine testing (when anovulatory)
- Imaging (Is it a focal lesion?)
- Endometrial Biopsy (Unsatisfactory if it is a focal lesion)

Question #3:

- A 38 yo female, G0, non-smoker, has a history of regular but heavy, painful menses. Menses last 8 days and the first 3 days she changes pads every 4 hours. She does not desire future fertility. BMI is 38. What step(s) should be done to evaluate her AUB.

(A) CBC

(B) US

(C) EMB

(D) Screen for PCOS, Thyroid, and vWD

(E) A, B and C

Evaluation of AUB--Endometrial Biopsy

- Generalized endometrial thickening—office biopsy is adequate
- Focal endometrial thickening—hysteroscopic directed biopsy
- Failed biopsy requires further evaluation
- Rates of obtaining an adequate sample depends on age of patient
- Not effective as the sole treatment for heavy menses
- Cancer detection failure rate 0.9%

Evaluation of AUB: Imaging—Transvaginal Ultrasound

- Endometrial thickness in postmenopausal women 5 mm cut off--
- Atrophic 3.4 ± 1.2 mm
- Hyperplasia 9.7 ± 2.5 mm
- Endometrial cancer 18.2 ± 6.2 mm
- 4-5 mm cut off 95-97 % sensitivity

Evaluation of AUB: Imaging—Transvaginal Ultrasound

- Endometrial thickness in premenopausal women--
- Guidelines for evaluation NOT established.
- Accept age related recommendation for biopsy (35 or older).
- If at risk for cancer in female < 35 → chronic anovulation, diabetes, obesity, hypertension, tamoxifen use.

Evaluation of AUB: Imaging—Transvaginal Ultrasound

- For the reproductive age patient, less accurate in the diagnosis of focal endometrial pathology
- Sensitivity for detecting all intracavity lesions ranges from 48-96%
- Specificity ranges from 68-95%

Evaluation of AUB: Imaging—Transvaginal Ultrasound

- Abnormal endometrial echoes require further evaluation (intermingled hypo-hyperechoic area, fluid collection).
- Focal intrauterine pathology requires further evaluation.

Evaluation of AUB: Imaging-1 MRI

- Equivocal results by ultrasound
- Suspicion for adenomyosis
- Assess location for surgical or radiologic treatment

Diagnostic Algorithm—Premenopausal Women

- If anovulatory→ start with endocrine work up and endometrial biopsy if patient has risks
- If ovulatory → start with transvaginal US

Diagnostic Algorithm—Postmenopausal Women

- Start with an ULTRASOUND

AUB TREATMENT GOALS

- Alleviation of any acute bleeding
- Prevention of future noncyclic bleeding
- Decrease in the patient's future risk of long-term health problems secondary to anovulation
- Improvement in the patient's quality of life

AUB TREATMENT: Medical Management before Surgical

- Effective Methods include:

  estrogen, progesterone, or both

  NSAIDS

  Antifibrinolytic Agents

  Danazol

  GnRH agonists

AUB TREATMENT: Acute Bleeding—Estrogen Therapy Outpatient

- Oral conjugated equine estrogen (2.5 mg PO Q6 hours PRN for 24 hours)
- Antiemetic for nausea during high dose estrogen therapy
- NSAIDS during active bleeding

AUB TREATMENT: Acute Bleeding—Estrogen Therapy Outpatient

- Response after 24 hours then begin OCPs
- OCP of choice QID x 4 days, then
- OCP of choice TID x 3 days, then
- OCP of choice BID x 2 days, then
- OCP as directed for 3 months
- Or 4 tablets per day for 1 week after bleeding stops
- (35 mcg or less ethinyllestradiol)
- Medication for nausea

AUB TREATMENT: Acute Bleeding—Estrogen Therapy Outpatient

- If No response in 24 hours requires further evaluation (Ultrasound and possible surgical intervention)

AUB TREATMENT: Acute Bleeding—Estrogen Therapy Inpatient

- 25 mg IV every 4 to 12 hours for 24 hours then switch to oral treatment
- Bleeding usually diminishes in 24 hours
- IV fluids and blood work
- Antiemetic
- Foley catheter with a 30 ml balloon

AUB TREATMENT: Other Medical Therapy Options– Prostaglandin Synthetase inhibitors

- Mefanamic acid, Ibuprofen, Naproxen
- Blood loss can be cut in half
- Taken only during menses
- Does not address issues of future noncyclic bleeding and decreasing health risks due to ovulation

AUB TREATMENT: Other Medical Therapy Options-- Progestins

- Induce withdrawal bleeding
- Decrease the risk of future hyperplasia and or endometrial cancer
- Continued for 7-12 days each cycle
- Medroxyprogesterone 10 mg x 10 days monthly (common regimen)
- Norethindrone (Aygestin), Norethindrone (Micronor), Micronized Progesterone (Prometrium)
- IUD (Levonorgestrel [Mirena])
- Depot preparation

AUB TREATMENT: Other Medical Therapy Options—Oral Contraceptives

- Option for treatment of both acute episode of bleeding and future episodes, as well as prevention of long term health problems from anovulation.
- Variety of options

AUB TREATMENT: Surgical Options

- *D/C
- Endometrial Ablation
- Operative Hysteroscopy
- Myomectomy (Hysteroscopic, Laparoscopic, Open)
- Uterine Fibroid Embolization (UFE)
- **Hysterectomy

Question #4:

- A 42 yo female with a +tobacco use history reports regular 10 days of bleeding with the first 3 days requiring changing pads every 3 hours. US and EMB are normal. She does not desires future fertility. What option(s) does she have for management?

(A) Medical therapy is not an options because of her tobacco use.

(B) Refer to gynecology for hysterectomy since childbearing is completed.

(C) Discuss R/B/I/SE for progestin only medical management.

(D) Discuss referral to gynecology for counseling regarding ablation procedure.

(E) C or B is a reasonable approach.

AUB Update

- 2/2005 35 physicians/scientific experts in menstrual disorders
- Recommendations for discarded terminology (eg. Menorrhagia, menometrorrhagia, DUB) (Woolcock)
- Recommendations for accepted abbreviations (AUB, HMB, HPMB, IMB, PMB) (Frasier)

AUB Update

- Descriptive terms should be use→
- Frequency of menses (frequent, normal, infrequent)
- Regularity of menses (absent, regular, irregular)
- Duration of flow (prolonged, normal, shortened) (Frasier)

AUB Update—Classification for Causes of AUB

- **P**olyps (AUB-P)
- **A**denomyosis (AUB-A)
- **L**eiomyoma (AUB-L)
- **M**alignancy (AUB-M)

- **C**oagulopathy (AUB-C)
- **O**vulatory disorders (AUB-O)
- **E**ndometrial (AUB-E)
- **I**atrogenic (AUB-I)
- **N**ot classified (AUB-N)

(Munro)

Summary: Key Points

- Differential diagnosis depends on patient's age
- ALWAYS exclude pregnancy
- Adolescent females (most likely anovulatory but exclude STDs and vWD)
- Reproductive Age females (if anovulatory exclude cancer/precancer if >35 but most likely PCOS)
- Reproductive Age females (if ovulatory exclude organic causes such as fibroid or polyps but most likely idiopathic)

Summary: Key Points

- Perimenopausal/Postmenopausal (always exclude cancer but usually is not cancer)
- Consider risks for endometrial cancer (nulliparity, late menopause [after age 52], obesity, diabetes, unopposed estrogen therapy, tamoxifen, and history of atypical endometrial hyperplasia)
- Whether reality or perception, heavy bleeding disrupts a women's quality of life.

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THANK YOU