PALM-COEIN Classification System for Abnormal Uterine Bleeding: Implications on Clinical Practice

LTC Elizabeth Nutter, CNM

1115 -1215 (ET)

23 January 2020
LTC Elizabeth Nutter, DNP, CNM, OB-RNC
Women's Health Nursing Consultant to the Army Surgeon General
Chief of OBGYN Ambulatory Services & Midwifery Services
Madigan Army Medical Center
Joint Base Lewis-McChord, WA
Dr. Nutter is an active duty Lieutenant Colonel serving in the Army. She is currently serving as the Chief of OBGYN Ambulatory Services & Midwifery Services at Madigan Army Medical Center.

She is also the Women’s Health Nursing Consultant to the Army Surgeon General. She received her commission in 2001 from the University of Portland, Oregon.

She graduated with a Master in Nursing from Radford University, Virginia with a certificate of midwifery from Shenandoah University, Virginia in 2009.

She completed a Doctor of Nursing Practice from Frontier Nursing University, Kentucky in 2013. The focus of her doctoral work is waterbirth.

She has peer-reviewed articles and multiple book chapters on waterbirth published. She is the co-author of the American College of Nurse Midwives Model Practice Template for Hydrotherapy in Labor and Birth.
Disclosures

- LTC Nutter has no relevant financial or non-financial relationships to disclose relating to the content of this activity; or presenter(s) must disclose the type of affiliation/financial interest (e.g. employee, speaker, consultant, principal investigator, grant recipient) with company name(s) included.

- The views expressed in this presentation are those of the author and do not necessarily reflect the official policy or position of the Department of Defense, nor the U.S. Government.

- This continuing education activity is managed and accredited by the Defense Health Agency J-7 Continuing Education Program Office (DHA J-7 CEPO). DHA J-7 CEPO and all accrediting organizations do not support or endorse any product or service mentioned in this activity.

- DHA J-7 CEPO staff, as well as activity planners and reviewers have no relevant financial or non-financial interest to disclose.

- Commercial support was not received for this activity.
Learning Objectives

At the conclusion of this activity, participants will be able to:

1. Define abnormal uterine bleeding
2. Describe the Polyp, Adenomyosis, Leiomyoma, Malignancy, Coagulopathy, Ovulatory dysfunction, Endometrial, Iatrogenic, and Not otherwise classified (PALM-COEIN) classification system
3. Distinguish structural etiologies of abnormal uterine bleeding from non-structural etiologies
4. Discuss guidelines for evaluation and management of abnormal uterine bleeding in the nongravid women of reproductive age utilizing the PALM-COEIN classification system

“Medically Ready Force...Ready Medical Force”
Abnormal Uterine Bleeding

- Abnormal uterine bleeding (AUB)
  - Replaces *dysfunctional uterine bleeding*
  - Alteration in the volume, pattern, or duration of menstrual blood flow

- 30% of women experience abnormal uterine bleeding during their lifetime
  - Most common reason for gynecologic referral
  - Most common in the years prior to menopause
Abnormal Uterine Bleeding

- Impacts
  - Quality of life
  - Productivity
  - Health care use
  - Health care costs

“Medically Ready Force...Ready Medical Force”
Normal Menstruation

- Look at the previous six months cycles
- Evaluate four components
  - Frequency
  - Duration
  - Volume
  - Intermenstrual bleeding
Normal Frequency

- Regular and reasonably predictable intervals
- Cycle length
  - Days from start (day 1) of menses until the start (day 1) of the next menses
- Expect an episode of menstrual bleeding every 24 to 38 days
  - 14 to 21 days in the *follicular phase*
  - 14 days in the *luteal phase*
Normal Frequency

- Adolescence menstrual cycles are often irregular
  - 60-80% of cycles are 21-24 days long by the third year after menarche
  - Little cycle variability among women between 20-40 years
  - Significantly more cycle variability
    - 5-7 years after menarche
    - 10 years before menopause
Normal Duration

- Number of bleeding days in a single menstrual period
  - Normal duration up to eight days
  - Average cycle duration 4-8 days
Normal Volume

**How Heavy Is Your Period?**

<table>
<thead>
<tr>
<th>Pads/Tampons Used Per Day</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Spotting</strong></td>
</tr>
<tr>
<td><strong>Very Light Flow</strong></td>
</tr>
<tr>
<td><strong>Light Flow</strong></td>
</tr>
<tr>
<td><strong>Medium Flow</strong></td>
</tr>
<tr>
<td><strong>Heavy Flow</strong></td>
</tr>
<tr>
<td><strong>Super Heavy Flow</strong></td>
</tr>
</tbody>
</table>
Abnormal Uterine Bleeding (AUB)

- Acute AUB
- Chronic AUB
  - Irregular menstrual bleeding
  - Disturbances
    - frequency
    - duration
    - volume

“Medically Ready Force...Ready Medical Force”
Acute AUB Defined

- A single episode of heavy bleeding
  - In a woman of reproductive age
  - Who is not pregnant
  - With a sufficient quantity of blood loss to require immediate intervention to prevent further blood loss
Chronic AUB Defined

- Bleeding from the uterine corpus
  - Abnormal in volume, regularity, and/or timing
  - Has been present for 4-6 months

- **Chronic AUB** replaces
  - Menometrorrhagia
  - Menorrhagia

- Further classified into disturbances of
  - Frequency
  - Duration
  - Volume
Disturbances of Frequency

- Due to changes in the follicular phase

- **Frequent uterine bleeding**
  - Cycle starts more frequently than every 24 days in a 90 day time frame

- **Infrequent uterine bleeding**
  - Cycle starts less often than every 38 days in 90 day time frame
  - *Infrequent uterine bleeding* replaces *oligomenorrhea*
Disturbances of Frequency

- **Amenorrhea**
  - No uterine bleeding for 180 days
    - *Primary amenorrhea*
      - No menarche by age 16
    - *Secondary amenorrhea*
      - Previously menstruating woman with no menstrual cycle for 90 days of longer
  - Duration of the period of amenorrhea should be specified
  - 2-5% women of childbearing age in the United States
Disturbances in Duration

- **Prolonged menstrual bleeding**
  - Duration consistently more than 8 days
  - No consensus on the lower limit of normal
Disturbances in Volume

- MOST common AUB presentation
- **Heavy menstrual bleeding**
  - Subjectively defined
    - Excessive blood loss that interferes with physical, emotional, social, and material quality of life
  - Objectively defined
    - Drop in hemoglobin or in the number of menstrual products used (tampons and or pads) per day
Irregular Menstrual Bleeding

- **Intermenstrual bleeding (IMB)**
  - Uterine bleeding that occurs between regular menstrual cycles
  - May be
    - Light flow
    - Short duration
    - Occurring between menstrual periods
    - Occur during or following sexual intercourse
    - Cyclical, with predictable bleeding
    - Acyclical, occurring at random times between menses

   - **Intermenstrual bleeding** replaces *metrorrhagia*
Cyclic Midcycle IMB

- Cyclic midcycle intermenstrual bleeding
  - Often light and short
  - Consistently occurring between regular menstrual periods
  - Usually periovulatory bleeding
  - Considered physiologic normal
  - Associated with the physiologic nadir in circulating estradiol levels at midcycle
  - Occurs in 1-2% of women
Cyclic Premenstrual or Postmenstrual IMB

- *Cyclic premenstrual or postmenstrual intermenstrual bleeding*
  - Occurs during the follicular phase or luteal phase
  - Typically presents as very light bleeding
  - Bleeding for one or more days
  - Indicative of
    - Luteal phase defect (late cycle bleeding)
    - Endometriosis
    - Endometrial polyps
    - Other structural lesions of the genital tract
Acyclic IMB

- **Acyclic intermenstrual bleeding**
  - Not cyclical or predictable
  - Associated with benign lesions
    - Chronic cervicitis
    - Polyps
    - Cervical cancer
    - Endometrial cancer
Poll Question

Are you using the PALM-COEIN classification system currently in your clinical practice to help you evaluate abnormal uterine bleeding?

- Yes
- No
PALM-COEIN Classification System

Nomenclature and classification of uterine bleeding

Abnormal Uterine Bleeding (AUB)
- Acute
- Intermittent
- Chronic

Frequency
- Regularity
- Duration
- Volume

Polyp
Adenomyosis
Leiomyoma
Malignancy

Coagulopathy
Ovulatory dysfunction
Endometrial
Iatrogenic
Not otherwise classified

“Medically Ready Force...Ready Medical Force”
Polyps (AUB-P)

https://www.fertilitysa.com/

“Medically Ready Force...Ready Medical Force”
Clinical Presentation Polyps

- AUB is the most common presenting symptom
- Occurs in 64-88% of women with polyps
- *Intermenstrual bleeding* is the most frequent symptom in premenopausal women with polyps
- Volume of bleeding is usually small (spotting)
- Some women experience heavier bleeding between menstrual cycles
Polyps

- **Risk factors**
  - Increased levels endogenous or exogenous estrogen
  - Tamoxifen
    - Develop 2-36 % of postmenopausal
    - Polyps may be large (>2 cm) and multiple
  - Obesity
    - BMI ≥30
Polyps

- **Pathogenesis**
  - Endometrial hyperplasia
  - Overexpression of endometrial aromatase
  - Gene mutations

- **Epidemiology**
  - Rare among adolescents
  - Prevalence appears to rise with increasing age
  - Highest in premenopausal
Adenomyosis (AUB-A)
Clinical Presentation Adenomyosis

- Dysmenorrhea
- *Heavy menstrual bleeding*
  - Approximately 60% of women with adenomyosis
- Chronic pelvic pain may also occur
- Symptoms develop between 40 and 50 years
- Approximately 1/3 of women are asymptomatic
Adenomyosis

- Epidemiology
  - Affects 20 percent of women
  - Epidemiology of the disease is limited
  - More common in parous women
  - Prior uterine surgery may also be a risk

- Pathogenesis
  - Unknown
  - Theory
    - Develops from endomyometrial invasion of the endometrium
Leiomyoma (AUB-L)

Types of uterine fibroids

- Pedunculated subserosal
- Pedunculated submucosal
- Subserosal
- Intramural
- Subserosal
- Cervical canal
- Vagina
- Ovary
- Broad ligament

https://fertility.womenandinfants.org/
Clinical Presentation Leiomyoma

- Heavy or prolonged menstrual bleeding
  - Most common fibroid symptom

- Bulk-related symptoms
  - Enlarged and irregularly shaped uterus
  - Causes symptoms due to pressure from at particular locations
    - Pelvic pressure or pain
    - Back pain
    - Urinary tract or bowel issues

- Painful menses
  - Heavy menstrual flow and/or passage of clots
Clinical Presentation Leiomyoma

- Majority are small and asymptomatic
- Symptoms are related to the number, size, and location
  - Heavy menstrual bleeding
  - Increasing abdominal girth
  - Sense of abdominal fullness similar to pregnancy
  - AUB and menstrual cramps are the most common symptoms occurring in about 26 to 29% of women

- Symptoms are classified into categories
  - Heavy or prolonged menstrual bleeding
  - Bulk-related symptoms, such as pelvic pressure and pain
  - Painful menses
Leiomyoma

Prevalence

- Increases with age during the reproductive years
- Occasionally noted in adolescents
- Most women have shrinkage of leiomyoma's after menopause
Leiomyoma Risk Factors

- **Race**
  - 2-3 greater risk in black women

- **Parity**
  - Nullipara increases risk

- **Early menarche**
  - <10 years old

- **Obesity**
  - Increasing BMI

- **Diet**
  - Red meat (1.7-fold)
  - Ham (1.3-fold)

- **Genetics**
  - Specific susceptibility genes

- **Other factors**
  - Hypertension
Endometrial Hyperplasia (AUB-M)

https://medlineplus.gov/ency/imagepages/17087.htm

“Medically Ready Force...Ready Medical Force”
Clinical Presentation
Endometrial Hyperplasia

- AUB
- Abnormal findings on cervical cytology
WHO Hyperplasia Classification

Endometrial Hyperplasia

Endometrial hyperplasia refers to an unusually thickened endometrial lining. Typically, it is caused by high, unopposed levels of estrogen. Often this occurs at or after menopause or as the result of medications such as exogenous hormone replacement therapy or the breast cancer treatment Tamoxifen.

With increased estrogenic stimulation, the range of pathologic features changes from mild cellular proliferation to complex architectural abnormalities. Clinically, endometrial hyperplasia manifests as anovulatory or excessive bleeding.

Risk of endometrial cancer

Endometrial hyperplasia is a precursor to endometrial cancer. Hyperplasia without atypia (A-1 or B-1) is a benign pathology which may be reversed through the management of risk factors. Hyperplasia with atypia, however, has a much greater risk of progressing to endometrial cancer.

Normal proliferative stage:
The endometrium is a thick layer consisting of:
A. Simple columnar epithelium
B. Simple tubular uterine glands
C. Stroma

Simple Hyperplasia:
A. Proliferation and pseudocyst formation of epithelial cells often leads to multilayered columnar/cuboidal epithelial cells with prominent cilia
B. Glands dilate forming different sized cysts

Complex Hyperplasia:
A. Muscular surface becomes irregular with polypoid projections
B. Endometrial glands proliferate at different rates and become crowded, creating nodules and outgrowths into adjacent stroma

Hyperplasia with atypia:
A. Increased gland-to-stroma ratio with back-to-back crowding of glands
B. Architectural features: Cells and nuclei are enlarged with prominent nucleoli and loss of polarity

“Medically Ready Force...Ready Medical Force”
Endometrial Cancer

- Indicator of risk of endometrial carcinoma
  - Presence of nuclear atypia

- Cancer risk based on histologic category
  - Simple hyperplasia without atypia 1%
  - Complex hyperplasia without atypia 3%
  - Simple atypical hyperplasia 8%
  - Complex atypical hyperplasia 29%
Endometrial Hyperplasia

■ Epidemiology
  - Incidence 133 per 100,000 women
  - Rare <30 years
  - Simple and complex hyperplasia without atypia
    ▪ Women age 50 to 54
  - Atypical hyperplasia
    ▪ Women age 60 to 64

■ Risk factors
  - Exposure to continuous estrogen unopposed by a progestin
  - Lynch syndrome (hereditary nonpolyposis colorectal cancer)
PALM-COEIN Classification System
Coagulopathy (AUB-C)
Clinical Presentation Coagulopathy

■ History of bruising, epistaxis, anemia
■ Thrombocytopenia or myelosuppression caused by chemotherapy
■ *Heavy menstrual bleeding*
  - Common consequence of the use of anticoagulant drugs
13% of women with heavy menstrual bleeding have biochemistry detectable systemic disorders of hemostasis

Most common bleeding disorder in women
- Von Willebrand disease affects up to 1% of the U.S. population
- An autosomal dominant disorder
- Caused by a defect in or deficiency of von Willebrand factor

Women may also have mild hemophilia (“symptomatic carriers”)
- Carrying the gene and also exhibit symptoms
- Hemophilia A or factor VIII deficiency
- Hemophilia B or factor IX deficiency
- Rare factor disorders factor I, II, VI, VII, XI and XIII deficiency
Ovulatory Dysfunction (AUB-O)


“Medically Ready Force...Ready Medical Force”
Epidemiology Ovulatory Dysfunction

- Conditions associated with ovulatory dysfunction
  - Polycystic ovary syndrome
  - Hypothyroidism
  - Hyperprolactinemia
  - Mental stress
  - Obesity
  - Anorexia
  - Weight loss
  - Extreme exercise such as elite athletes
Endometrial (AUB-E)

“Medically Ready Force...Ready Medical Force”
Epidemiology AUB-E

- Heavy menstrual bleeding
  - Issue with mechanisms regulating the endometrial stability
- Intermenstrual bleeding or prolonged bleeding
  - Endometrial inflammation
  - Infection (particularly Chlamydia)
  - Abnormalities in endometrial vasculogenesis
Iatrogenic (AUB-I)

Paragard® IUD
Intrauterine device
Copper-based
Hormone free
Up to 10 years

https://www.gblawyers.com/paragard-iud-lawsuit/
Epidemiology AUB-I

- Systemically administered single-agent or combination gonadal steroids
  - Impact the control of ovarian steroidogenesis via effects on the Hypothalamic-Pituitary-Ovarian axis (HPO axis)
  - Exert a direct effect on the endometrium

- Continuous cycling or progestin-only agents
  - Any bleeding is considered to be unscheduled and classified as AUB-I
Compliance issues gonadal steroids
- Missed, delayed, or erratic use of pills, transdermal patches, or vaginal rings

Anticonvulsants and antibiotics
- Rifampin (Rifadin) and Griseofulvin (Gris-PEG)

Cigarette smoking

Levonorgestrel-releasing intrauterine system (LNG-IUS)

Tricyclic antidepressants
- Amitriptyline (Elavil)
- Nortriptyline (Aventyl)
- Phenothiazines
Not Yet Classified (AUB-N)

- Unexplained reason or poorly understood reason for endometrial instability
  - Arteriovenous malformations
  - Chronic endometriosis
  - Myometrial hypertrophy
  - Other disorders defined by only biochemical markers
  - Any future entities not yet classified
General Evaluation AUB

- General assessment
  - Rule out undiagnosed pregnancy
  - Ensure blood is emanating from the cervical canal, rather than another location
  - Women with both acute and chronic AUB should be evaluated for anemia
    - Complete Blood Count (CBC)
  - Once the bleeding has been confirmed
    - Proceed in a systematic fashion addressing each of the components of the PALM-COEIN classification system
Diagnosis of Chronic AUB

- Requires experience of 1 or a combination of unpredictability, excessive duration, abnormal volume, or abnormal frequency of menses for at least the previous 3 months
- Structured history to determine
  - Ovulatory function
  - Potential related medical disorders
  - Medications
  - Lifestyle factors that might contribute to AUB
- Understanding the future fertility desires of the woman
- Ancillary investigations include
  - Hemoglobin and/or a hematocrit assessment
  - Appropriate tests for features that could contribute to an ovulatory disorder (thyroid function, prolactin, and serum androgens)
General Evaluation AUB

- Initial positive screen screening AUB-C comprises
  - Heavy menstrual bleeding since menarche
  - One of the following:
    - Postpartum hemorrhage
    - Surgical-related bleeding
    - Bleeding associated with dental work
    - Two or more of the following symptoms:
      - Bruising 1–2 times per month
      - Epistaxis 1–2 times per month
      - Frequent gum bleeding
      - Family history of bleeding symptoms
Screening for AUB-C

- A positive screen further testing is necessary
- Often following consultation under the direction of a hematologist
- Such tests may include:
  - Assays for von Willebrand factor
Screening for AUB-O

- **Ovulation**
  - Predictable cyclic menses every 22–35 days

- **Anovulation**
  - Bleeding irregular in timing and flow, and often interspersed with episodes of amenorrhea

- Diagnostic tests
  - Timed to the best estimate of mid-luteal phase
  - Measurement of serum progesterone
  - Endometrial biopsy
Uterine Evaluation

- Guided by history and other elements of the clinical situation
  - Patient age
  - Presence of an apparent chronic ovulatory disorder
  - Presence of other risk factors for endometrial hyperplasia or malignancy
- For those at increased risk
  - Endometrial biopsy is probably warranted
  - If there is a risk of structural anomaly
    - “Screening” transvaginal ultrasound (TVUS) examination
Endometrial Evaluation

- Endometrial biopsy is not required for AUB
- Endometrial biopsy is based on risk of atypical hyperplasia or carcinoma
  - Age >45 years
  - Personal and genetic risk factors
    - Family history nonpolyposis colorectal cancer syndrome
  - Consider Sexually Transmitted Infection (STI) evaluation in symptomatic patients
  - Persistent AUB that is unexplained or not adequately treated
    - In association with hysteroscopic evaluation of the uterine cavity
For those at increased risk

- Endometrial biopsy
- If there is a risk of structural anomaly
  - Transvaginal ultrasound (TVUS) examination
    - Abnormal TVUS examination or endometrial sampling has not provided an adequate specimen
      - Hysteroscopy and saline infusion sonography (SIS)
- MRI may be of value, if available
Evaluation of Endometrial Cavity Structures

- **Transvaginal ultrasound**
  - performed first or early in the course of the investigation

- **Negative ultrasound**
  - Endometrial cavity may presumptively be considered normal

- **Positive ultrasound consult with specialist**
  - Sonohysteroscopy and hysterosonography or hysteroscopy
Evaluation of Endometrial Cavity Structures

With the PALM-COEIN classification

- P (for endometrial and endocervical polyps) is confirmed only with documentation of 1 or more clearly defined polyps, generally with either SIS or hysteroscopy.

- Usually, a patient may be categorized with 1 or more submucosal leiomyomas (AUB-LSM) with either SIS or hysteroscopy.
Myometrial Assessment

- Leiomyoma assessed
  - TVUS and transabdominal ultrasound
  - Negative ultrasound plus either hysteroscopy or SIS fail to identify leiomyomas patient would be classified as L0
  - Positive ultrasound lesion leads to an L1 assignment
    - Place consult for specialist for the secondary and tertiary subclassification
    - Perform some combination of TVUS, SIS, hysteroscopy, and MRI
Treatment AUB-P

Hysteroscopic Polypectomy

https://www.angelsfertility.com/services/hysteroscopic-polypectomy/
Treatment AUB-A

- Nonsteroidal Anti-inflammatory Drugs (NSAIDs)
- Levonorgestrel-releasing intrauterine device (LNG-IUD)
  - Mirena, Skyla, Liletta
- Conservative excision if focal
- Uterine artery embolization or endometrial ablation if the adenomyosis depth is less than 2.5 mm
- Extensive disease
  - Hysterectomy is recommended
Treatment AUB-L

- Asymptomatic
  - No treatment is required

- Symptomatic
  - GnRH agonists Leuprolide (Lupron)
  - Mifepristone (Mifeprex/RU486)
  - Ulipristal acetate (Ella)
  - Aromatase inhibitors
  - Uterine artery embolization
  - Hysterectomy
  - Myomectomy
Treatment AUB-M

- Preserve fertility
  - High-dose progesterone treatment can be utilized with close follow-up
- Hysterectomy is recommended due to the high incidence of progression to endometrial cancer
Treatment AUB-O

- Treatment Goals = Prevention
  - Anemia
  - Endometrial intraepithelial neoplasia
  - Endometrial cancer
- Progestins
- Combined hormonal contraception
- Medroxyprogesterone (Provera)
- Injectable medroxyprogesterone acetate (Depo-Provera)
- Micronized progesterone (Prometrium)
- Levonorgestrel-releasing intrauterine device (LNG-IUD)
Treatment AUB-E

- NSAIDs
- Tranexamic acid
- Combined hormonal contraception
- Levonorgestrel-releasing intrauterine device
- Menstrual ablation
Treatment AUB-I & AUB-N

- *Iatrogenic: AUB-I*
  - Bleeding usually resolves when the causative medication has been discontinued

- *Not Classified: AUB-N*
  - The treatment goal for women with AUB-N is to control AUB with previously mentioned therapies
Key Takeaways

- Treatment is based on
  - Specific etiology of AUB
  - A woman’s reproductive wishes
  - Prevention of morbidity from AUB

- Use of the PALM-COEIN system helps
  - Eliminate confusion about the etiology of AUB
  - Provide effective communication of that diagnosis to other providers
  - Result in better coordination of care
  - Facilitate research on the etiology and treatment of this condition and the prediction of endometrial cancer
References


References


Questions?
How to Obtain Continuing Education Credits

To receive CE/CME credit, you must register by 0800 ET on 24 January 2020 to qualify for the receipt of CE/CME credit or certificate of attendance. You must complete the program posttest and evaluation before collecting your certificate. The posttest and evaluation will be available through 6 February 2020 at 2359 ET. Please complete the following steps to obtain CE/CME credit:

2. Click on the REGISTER/TAKE COURSE tab
   a. If you have previously used the CEPO CMS, click login.
   b. If you have not previously used the CEPO CMS, click register to create a new account.
3. Click “ENROLL.”
4. Follow the onscreen prompts to complete the following for each session you wish to claim CE/CME Credit:
   a. Read the Accreditation Statement
   b. Select the CE/CME credit type(s) you are seeking
   c. Complete the Evaluation
   d. Take the Posttest
   e. Download your Certificate(s)
   f. Complete the Commitment to Change survey (optional)
5. After completing the posttest at 80% or above, your certificate will be available for print or download.
6. You can return to the site at any time in the future to print your certificate and transcripts at https://www.dhaj7-cepo.com/
7. If you require further support, please contact us at dha.ncr.j7.mbx.cepo-cms-support@mail.mil

“Medically Ready Force...Ready Medical Force”