AUB & Office Tricks to Manage It

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Normal:
Mean interval is 28 days
+/- 7 days.
Mean duration is 4 days.
More than 7 days is normal.
Average blood loss with Menstruation is 35-50cc.

95% of women lose <60cc.
40% of women with blood loss >80cc considered their flow to be small or moderate.

14% of women with <20cc loss thought their flow was heavy.

Hallberg, et al., 1966
AUB Definitions

- **Menorrhagia** – heavy or prolonged uterine bleeding that occurs at the regular intervals. Usually >7 days or >80ml blood loss.
- **Metrorrhagia** – irregular menstrual bleeding or bleeding between periods. Usually normal or reduced flow.
- **Menometrorrhagia** – irregular menstrual bleeding with excessive volume and duration of flow.
- **Oligomenorrhea** – cycle length >35 days.
- **Polymenorrhea** – cycle length <21 days.
- **Amenorrhea** – absence of menstruation for at least 6 months.
Differential Diagnosis

- **Hormonal**
  - Anovulatory bleeding
    (lack of ovulation-decreased progesterone)
  - Hypogonadotrophic hypogonadism
  - Hormonal contraception (BCPs, Depo-Provera)
- **Pregnancy**
- **Malignancy/ Uterine Anatomical Issues**
  - Uterine or Cervical cancer
  - Endometrial hyperplasia (potentially pre-malignant)
  - Chemotherapy or radiation
- **Fibroids, Polyps, Adenomyosis, Endometriosis**
- **Bleeding Disorders**
  - von Willebrand’s Disease, Hemophilia,
    ITP, Factor deficiencies, platelet disorders
Systemic Etiologies

- Coagulation defects
- Leukemia
- ITP
- Thyroid dysfunction
- Advanced liver disease
- Medications (Coumadin, Steroids)
- Pituitary or Hypothalamic Disorders or tumors
Evaluation and Work-up: Early Reproductive Years/Adolescent

- Thorough history - be mindful of eating disorders - oligo/amenorrhea
- Pelvic U/S
- Labs:
  - CBC, PT, PTT, hCG, Fe, Bleeding Time
In a 9 year review of 59 cases of Acute menorrhagia in adolescents it was discovered that 20% had a primary coagulation disorder.

Claessens, et al., 1981
Von Willebrand's Disease is the most common inherited bleeding disorder with a frequency of 1/800 - 1000.

Harrison's Principles of Internal Medicine, 14th edition
Reproductive Tract Causes

- Gestational events
- Malignancies
- Benign
  - Atrophy
  - Leiomyoma
  - Polyps - cervical or endometrial
  - Cervical ectropion (post-coital bleeding)
- Foreign body
- Infections
- Ovarian cysts
- Adenomyosis, Endometriosis
Reproductive Tract Causes

- Gestational events
  - Abortions
  - Ectopic pregnancies
  - Trophoblastic disease
  - IUP
Reproductive Tract Causes

- Malignancies
  - Endometrial
  - Cervical
  - Ovarian
Endometrial Cancer

- Most common genital tract malignancy. Incidence 1 in 50.
- 4th most common malignancy after breast, bowel, and lung.
- 34,000 new cases annually
- >6,000 deaths annually
Cervical Cancer

- Worldwide, cervical cancer is the second leading cause of cancer mortality in women.
- Among the ~500,000 new cases each year, ~75% occur in developing countries.
- Cervical cytologic testing has reduced the incidence of cervical cancer by 70% in countries where it is easily available.
- Human papillomavirus (HPV) is central to cervical carcinogenesis.
- Worldwide, the prevalence of HPV in cervical tumors is 99.7%.
Abnormal Uterine Bleeding Workup

- **History**
  - Timing of bleeding, quantity of bleeding, menstrual history, associated symptoms.
  - Family history of bleeding disorders. Excessive psychological stress, exercise, weight loss
  - Medications (Plavix, Aspirin, Coumadin, Lovenox, Xarelto, Pradaxa, Eliquis

- **Physical Exam**
  - pap smear (rule out cervical cancer)
  - endometrial biopsy (rule out uterine cancer)
  - excessive facial hair growth, obesity (BMI>25) (polycystic ovarian disease 6-10% of women)
  - abnormal breast discharge (prolactin disorders)
  - anorexia signs (hypothalamic dysfunction)
  - goiter, weight loss or gain (thyroid disease)
  - other disease states (advanced liver disease, leukemia, hypersplenism, chemo, radiation)

- **Labs**
  - Pregnancy test, CBC, Iron
  - FSH, LH, Estradiol, TSH, Prolactin
  - DHEA-S, Testosterone, PT, PTT, Bleeding Time

- **Imaging**
  - Pelvic ultrasound (transvaginal)
  - Saline Sono (Sonohysterogram -saline infusion ultrasound)

- **Surgical**
  - Hysteroscopy
  - D&C
Post-menopausal bleeding

Bleeding after the lapse of one year after the last menstruation.
Endometrial Cancer is diagnosed in approximately 10% of women with PMB. An equal number will have hyperplasia.\textsuperscript{1}

PMB incurs a 64-fold increased risk for developing endometrial CA.\textsuperscript{2}

\textsuperscript{1}Karlsson, \textit{et al.}, 1995
\textsuperscript{2}Gull, \textit{et al.}, 2003
Endometrial Cancer
Risk Factors

• Nulliparity: 2 – 3 times
• Diabetes: 2.8 times
• Unopposed estrogen: 4 – 8 times
• Weight gain
  - 20 to 50 pounds: 3 times
  - Greater than 50 pounds: 10 times
Evaluation and Work-up: Post-menopausal Women

- History & Exam with Pap Smear
- Transvaginal U/S
- EMB or
- Hysteroscopy with endometrial sampling
Transvaginal Ultrasonography (TVS)

- Inexpensive, noninvasive, and convenient
- Indirect visualization of the endometrial cavity, myometrium, and adnexa
- Measurement of endometrial thickness (<5 mm vs. >5 mm). Remember 5mm is for PMB!
- May be used to increase index of suspicion for endometrial atrophy, hyperplasia, cancer, leiomyomas, and polyps
- May not always distinguish among submucosal fibroid, polyp, or adenomyosis
Not a single case of endometrial CA was missed when a <4mm cut-off for the endometrial stripe was used on their 10 yr follow-up study.

Specificity 60%, PPV 25%, NPV 100%

Gull, et al., 2003
However, 3 women with stripe width of 5-6mm developed recurrent PMB and were diagnosed with endometrial cancer within 3-5 years.

Gull, et al., 2003
Nevertheless, there is a 7.1% risk of endometrial atypia in those women with a stripe width less than or equal to 4mm and recurrent bleeding.

Gull, et al., 2003
The stripe thickness measures between 4-8mm in women on cyclic HRT and about 5mm if they are receiving combined HRT.

Good, 1997

PMB is often iatrogenic secondary to HRT/BHRT, but MUST be worked up to exclude occult malignancy.
Saline Infusion Sonography (SIS)

- Relatively new technique
- Very useful for evaluation of AUB in pre-, peri-, and postmenopausal women
- May be superior to TVS alone (94.1% vs. 23.5% for detection of focal intrauterine pathology)
- SIS + biopsy: 96.2% sensitivity and 98% specificity
- Disadvantage: small irregularities may be misinterpreted as polyps
- Able to determine penetration depth of uterine fibroids
Uterine Imaging

Routine Ultrasound

Saline Sonogram

Submucous myoma

Endometrial polyp
Endometrial Biopsy

- Safe, relatively simple procedure useful in perimenopausal or high risk women
- Not sensitive for detecting structural abnormalities (eg. Polyps or fibroids)
- Office-based techniques (gold standard replacing D& C)
  - Disposable devices (eg. Pipelle, Tis-u-Trap, Accurette, Z-sampler)
  - Reusable instruments (eg. Novak curette, Randall curette, Vabra Aspierator)
Possible Path Reports with EMB:

- Simple or complex hyperplasia WITHOUT atypia
- Simple or complex hyperplasia WITH atypia
- Endometrial cancer
Hysteroscopy
Uterine Imaging
Hysteroscopy

Polyps
Myoma
Atrophy
Hyperplasia
Adenocarcinoma
Tenaculum retracts cervix

Dilation of cervix with Pratt dilator
Evaluation and Work-up: Women of Reproductive Age

- hCG, CBC, Fe (FSH/LH/E/P)
- Exam, Assess pap, Cervical cultures
- Pelvic U/S
- EMB
- Hysteroscopy
Anovulation (PCO, Ovarian cysts)
  - Fibroids
  - Polyps
  - Cervical lesions
  - Foreign body
  - Infections
  - Atrophy
The majority of dysfunctional AUB in the premenopausal woman is a result of anovulation.
With anovulation a corpus luteum is NOT produced and the ovary thereby fails to secrete progesterone.
However, estrogen production continues, resulting in endometrial proliferation and subsequent AUB.
Uterine Polyps
Incidence of Endometrial Cancer in Perimenopausal Women

2.3/100,000 in 30-34 yr old
6.1/100,000 in 35-39 yr old
36/100,000 in 40-49 yr old

ACOG Practice Bulletin #14, 2000
Therefore, based upon age alone, an EMB to exclude malignancy is indicated in any woman >35 years of age with AUB.

ACOG Practice Bulletin #14, March 2000
Management

Prior to initiation of therapy: pregnancy and malignancy must be ruled out
Management Options

- Progestins - easy, versatile
- Estrogen - acute hemorrhage IV
- Ocs (‘4-3-2-1’) 
- NSAIDs - 20% decrease (?)
- Antifibrinolytics - Lysteda - 40%
- Mirena IUD - 75%
- Surgical - D&C, Ablation, Myomectomy, Hysterectomy
Progestins are the preferred treatment for those women with anovulatory AUB.

(Provera, Norethindrone, Megace)

Cyclic progesterone is not recommended for ovulatory AUB.
Progestins: Mechanisms of Action

- Inhibit endometrial growth
  - Inhibit synthesis of estrogen receptors
  - Promote conversion of estradiol > estrone
  - Inhibit LH
- Organized slough to basalis layer
- Stimulate arachidonic acid formation
Progestational Agents

- Cyclic Medroxyprogesterone 5-10mg daily for 10-14 days.
- Continuous Medroxyprogesterone 2.5-20mg or Norethindrone 2.5-10 daily or 25 days monthly
- Progesterone in oil, 100mg every 4 weeks
- DepoProvera 150mg IM every 3 months
- Levonorgestrel IUD-Mirena (5 years)
Antifibrinolytics:
Tranexamic Acid - Cyklokapron

- Used extensively in Europe
- Mainstay of treatment of ovulatory AUB in most of the world
- Reduces blood loss by 30-40%
- Non-FDA labeled indication
- Lysteda 650mg 2 po TID for 1-5 days
Cervical Polyp Office Kit

- Monsel’s Solution (Ferric Subsulfate)
- Long Allis Clamp
- Sponge Stick
- Lolly’s (Rectal Swabs)
- Silver Nitrate
Treatment
Small Submucous Myomas, Polyps

Hysteroscopic Resection/Myosure
Endometrial Ablation

• Endometrial ablations are effective treatment for abnormal uterine bleeding
• Office or Outpatient procedure- 70% office in my practice.
• >90% patient satisfaction rate
• 30% amenorrhea rate
• Longterm studies are finding~ 75% of ablation patients do not proceed to need hysterectomy.
• An ablation will hamper any later workup for peri- or PMB.
Endometrial Hyperplasia

It is reasonable for you to initiate a progestational agent if an EMB path report indicates simple hypersplasia WITHOUT atypia. Provera 10 mg or Megace 40-80mg daily with a f/u EMB in 6 months.

Referral is prudent if bleeding persists or worsens.
Adolescent anovulatory patients are ideally suited for progestins as the development of the immature hypothalamic-pituitary axis is not impeded. If sexually active, suppression of ovulation with menstrual control will be better.
Conclusions

• Abnormal menstruation is extremely common

• Most common cause of a sudden change in bleeding patterns is a complication of pregnancy!

• PMB is Endometrial CA until proven otherwise.

• Decrease volume & duration of menses; restore a pattern to anovulatory bleeders.

• BARE BONES WORKUP: Pelvic Exam, CBC & Preg test, Pelvic US, & Endometrial Sampling!
Thank You for Coming

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