Abnormal Uterine Bleeding
A Practical Guide to Evaluation and Treatment

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Objectives
• Define normal menses
• Describe the differential diagnosis of abnormal uterine bleeding (AUB)
• Review strategies for evaluation
• Discuss how to manage AUB using both medical and surgical therapies
• Work through some cases to utilize these evaluation and treatment options

Primer: The Basics
• Normal Menstrual Bleeding
  • Cycle every 21-35 days
  • Duration 2-8 days
  • Average blood loss 40 cc (3 Tbsp) per cycle
  • Heavy blood loss is >80 cc per cycle

Definitions
• Polymenorrhea: bleeding occurs < 21 days apart
• Menorrhagia: blood loss > 80 mls/cycle
• Oligomenorrhea: <9 menses per year
• Menometrorrhagia: frequent and heavy menses
• Amenorrhea: no periods for 6 months
• Intermenstrual bleeding: bleeding or spotting between otherwise normal menses
Evaluating Menstrual Blood Loss

Where is the bleeding coming from? Or...confirm that the bleeding is uterine...

How old is the patient?
- Premenarchal
- Reproductive age
- Perimenopausal
- Postmenopausal

Is she sexually active? Or...could she be pregnant?
- An adolescent?
- Woman using hormonal contraceptives?
- An IUD user?
- Status post tubal ligation?
- Partner with vasectomy?
- A perimenopausal patient with infrequent menses?

- Pregnancy should ALWAYS be ruled out ....in most patients...

A practical approach to abnormal uterine bleeding...
Is the bleeding ovulatory or anovulatory?

Or...What makes bleeding a “period” or a menstrual bleed?

The Menstrual Cycle!

- Estrogen causes endometrium to thicken
- Ovulation occurs
- Corpus luteum cyst produces progesterone
- (If no pregnancy occurs)
- Corpus luteum cyst resolves
- Progesterone level decreases
- Thickened endometrium sheds \( \rightarrow \) MENSES!

Ovulatory Bleeding

Anovulatory Bleeding
Anovulatory Bleeding Patterns

When does the bleeding occur...Or, is it intermenstrual?

- Pelvic infection
- Cervical or endometrial polyps
- Cancer
- Ectropion
- Ovulatory
- "Breakthrough bleeding"

Anovulatory Cycles

When does the bleeding occur? Or is it postmenopausal?

- No ovulation secondary to ovarian failure
- Rule out malignancy

Summary

- Ovulatory bleeding:
  - Regular/cyclic
  - Predictable
  - Associated with moliminal sx
  - Can be heavy/prolonged
  - Normal sex steroid levels
  - Often structural or a hemostasis issue

- Anovulatory bleeding:
  - Irregular
  - Unpredictable
  - Variable in flow and duration
  - Often associated with oligomenorrhea
  - Common at menarche and perimenopause
  - PCOS, endocrine disorders, stress

Evaluation

- Step 1...History
- Step 2...Examination
- Step 3...Basic laboratory evaluation
- Step 4...Additional evaluation
Step 3...Basic laboratory evaluation
a thinking practitioner’s guide

- CBC
- Pregnancy test
- TSH
- Prolactin
- FSH, estradiol

- GC/CT
- Coagulation tests
- Androgen levels
- Cervical cytology
- Endometrial biopsy...who?

When to Biopsy?

<table>
<thead>
<tr>
<th>Age</th>
<th>Endometrial cancer risk per 100,000</th>
<th>Consider if chronic anovulation or if unresponsive to medication</th>
</tr>
</thead>
<tbody>
<tr>
<td>19-40 years</td>
<td>2.3 - 6.1</td>
<td>Biopsy unless pregnant or other reason to avoid sampling endometrium</td>
</tr>
<tr>
<td>40-49 years</td>
<td>36.0</td>
<td></td>
</tr>
</tbody>
</table>

ACOG. Int J Gynaecol Obstet. 2001

Additional Evaluation

- Ultrasound examination
- Saline infusion sonography
- CT scan or MRI
- Hysterosalpingogram
- Hysteroscopy

Endometrial evaluation

Risk Factors for Endometrial Cancer

- Age greater than 40
- Family history of uterine, breast, ovarian, or colon cancer
- Obesity
- Diabetes
- Bleeding longer than 10 days or more frequently than every 21 days
- History of unopposed estrogen and anovulation

Utility of endometrial biopsy to detect pathology

- Office endometrial biopsy equivalent to D and C
- Detection of cancer
  - 99.6% in postmenopausal patients
  - 91% in premenopausal patients
- Greatest pickup in cases where pathology involves at least 50% of endometrium
Transvaginal Ultrasound

- Endometrial stripe thickness
  - <4 mm
    - false negative = 0.25-0.5%
  - <5mm
    - false negative = 1-4%
- TVUS not useful
- Premenopausal women
- Women on unopposed estrogen or cyclic progesterone
- On Tamoxifen therapy
- With heterogeneous stripes

NSAIDS

- NSAIDS effectively reduce volume of menstrual bleeding by 20-50%
- Reduces prostaglandin synthesis in endometrium which leads to vasoconstruction of spiral arteries
- Start full dose day before the onset of menses or at the first sign of menstrual bleeding

Therapeutic Options: Goals

- Treat underlying medical conditions
- Consider hormonal/medical management
- Surgical management
  - Minimally invasive
  - Major and definitive
- Think about associated risk factors and address

Tranexamic Acid: antifibrinolytic

- Plasminogen Activator
- Clot
- Tranexamic acid
- Plasmin

Heavy menstrual bleeding

How do you use it?

- Tranexamic acid
  - Tradename: Lysteda® 650mg tablets
  - Start with menses
  - Take 2 tablets three times daily
  - Up to a maximum of 5 days
  - Contraindications: current/history/increased risk of VTE
Medical Management

Combination OCPs

- All combination OCPs are progesterone dominant → reduce endometrial proliferation
- Cyclic use
  - 28 day cycles, 7 day placebo allows regular withdrawal
- Continuous use
  - Suppression of endometrial growth, no withdrawal
- End result
  - Regular, predictable, light bleeding
  - Cessation of menses (+/- breakthrough bleeding)

Medical Management: reduction in menstrual blood loss

Contraindications to estrogen?

- Cyclic Progesterone
  - 10-14 days → withdrawal bleed
  - Restores orderly bleeding, lighter?
  - Protects endometrium from unopposed estrogen
  - No contraceptive benefit!
- Continuous Progesterone
  - Depo Provera
  - POPs
  - Implanon/Nexplanon
  - Mirena IUD

Levonorgestrel IUS...Mirena
LNG IUS: Treatment Heavy Bleeding

Endometrial Ablation

LNG IUS vs. 35mcg NET

Endometrial ablation

Reasonable to consider when
- no hyperplasia or malignancy
- no significant cavity distortion
- no desire for pregnancy
- pre-menopausal

Amenorrhea 37-50%

Patient satisfaction - 70-90% at 5 years
- Risk of subsequent surgery is double in women under age 45
- 68% satisfaction vs 76% satisfaction with hysterectomy

Pick up your scalpel... or balloon or loop or stent...

Uterine Artery Embolization
Uterine Artery Embolization for fibroid-related AUB

• Improvement of bleeding in 85 to 94%
• 29% developed post-procedure amenorrhea
• 14-20% underwent an additional invasive procedure within 5 years
• Risk of ovarian impairment more likely in older women: 8% of women age > 45
• Pregnancy contraindicated

Polycystic Ovary Syndrome: PCOS

Let’s Practice...

Diagnostic Criteria for PCOS

• Rotterdam Criteria (2003): 2 of 3...
  • Clinical and/or biochemical evidence of hyperandrogenism
  • Oligo-ovulation and/or anovulation (<6 periods per year)
  • Presence of polycystic ovaries on pelvic ultrasound
• NIH Criteria (1990):
  • Chronic anovulation
  • Chemical and/or biochemical signs of hyperandrogenism

NOTE: Neither includes obesity or laboratory testing!

“I’m on my period all the time”

• 36 yo G3P2012 with intermittent heavy bleeding and spotting for most of the month, “no pattern”
• Obese, facial hair, acne. Normal pelvic exam.
• Normal TSH, prolactin. Slightly elevated free testosterone. Hct 32%.

“Heavy periods, passing tomato sized clots”

• 32 yo G2P2002 with increasingly heavy, regular menses over the past two years. No intermenstrual bleeding.
• Uterus normal size, contour. No masses. No thyromegaly.
• Hct 30%. Normal plts. Elevated TSH. Ultrasound with submucosal fibroid.
"What’s the problem? I only bleed every 4-5 months and I like it this way"

- 43 yo G0 with 4 year history of infrequent menses. Bleeding when she does have it is heavy and prolonged. Intermittent “hot flashes”.
- Obese. No thyromegaly, galactorrhea. Normal uterus/pelvic exam. Pelvic ultrasound with “thickened endometrium”.
- Normal CBC, TSH, prolactin, FSH. Endometrial biopsy: what are the possibilities?
“I bleed every time I have sex”

- 28 yo G0 with postcoital bleeding for the past 2 mos. On OCPs. Two new sexual partners in the past year. History of ASCUS pap. Has regular, monthly menses. Intermittent pelvic "cramping".
- Pap normal. GC/CT negative. Pelvic ultrasound and sonohysterogram with endometrial polyp.
"I don’t understand why I started having periods again at age 62"

- 62 yo G4P4004 with cessation of bleeding in "early 50's", has had intermittent light vaginal bleeding for the past 5 mos.
- Normal CBC, coags, pap. Transvaginal ultrasound reveals endometrial stripe of 9 mms.

Step 1...the History

- Age
- Are you sexually active?
- What are menstrual cycles like? Sxs of ovulation
- Nature of bleeding: frequency, duration, volume, relationship to activities?
- Associated sxs?
- Systemic illness or medications?
- Change in weight, excessive exercise,eating d/o or stress?
- Personal or family history of bleeding disorder?

Summary

- AUB is common
- Goals of evaluation
  - Rule out pregnancy
  - Rule out malignancy
  - Determine if bleeding is ovulatory or anovulatory
- Choose a treatment modality
  - Many options for medical management exist and can be used to successfully avoid surgery, provide additional health benefits
  - Minor surgical procedures
  - Major and definitive surgery

Step 2...the Examination

- Rule out bleeding site other than uterus
- Evaluate for mass, laceration, ulceration, vaginal discharge, foreign body
- Assess size, contour, tenderness of the uterus
- Examine the adnexae
- Evaluate for pain, sxs of infection
- General exam to look for systemic illness: infection, liver disease, thyroid, signs of hyperandrogenism, insulin resistance, hyperprolactinemia

Thank you!

Questions?
Summary: Ovulatory Bleeding Management

- Treat underlying conditions
  - Infection
  - Malignancy
  - Coagulopathies
- Hormonal/medical management
  - Goal to decrease bleeding frequency/volume
  - Cause cessation of menstrual bleeding
- Surgical management
  - Address fibroids/polyps if not responsive to medical tx
  - Endometrial ablation
  - Hysterectomy

Summary: Anovulatory Bleeding Management

- Treat underlying conditions
  - Thyroid disorder
  - Pituitary dysfunction/hyperprolactinemia
- Hormonal management
  - Goal to protect endometrium
  - Lead to regular cyclic withdrawal bleeding or cessation of bleeding
  - Think about associated risk factors and address
    - Hyperplasia, malignancy
    - Dyslipidemia, diabetes, metabolic syndrome