“Why am I bleeding?”
Diagnosis and Treatment

Jody Steinauer, MD, MAS
Dept. Ob/Gyn & Reproductive Sciences

Disclosures
July, 2016
I have no disclosures.

The Questions
• Too much (& too early or too late)
  – Differential and approach to work-up
  – Does she need an endometrial biopsy (EMB) or u/s?
• Too fast: She’s hemorrhaging—what do I do?
• Side effect: due to hormonal contraception
• Too little: A quick review of amenorrhea

Case 1
A 46 yo G3P2T1 reports her periods have become increasingly irregular and heavy over the last 6-8 months. Sometimes they come 2 times per month and sometimes there are 2 months between. LMP 2 months ago. She bleeds 10 days with clots and frequently bleeds through pads to her clothes. She occasionally has hot flashes. She also has diabetes and is obese.

1. What term describes her symptoms?
2. Physiologically, what causes this type of bleeding pattern?
3. What is the differential?
Q1: In addition to a urine pregnancy test and TSH, which of the following is the most appropriate test to obtain at this time?

1. FSH
2. Testosterone & DHEAS
3. Serum beta-HCG
4. Transvaginal Ultrasound (TVUS)
5. Endometrial Biopsy (EMB)

Terminology: What is abnormal?

- **Normal:** Cycle = 28 days ± 7 d (21-35); Length = 2-7 days; Heavyness = self-defined
- Too little bleeding: amenorrhea or oligomenorrhea
- Too much bleeding: Menorrhagia (regular timing but heavy (according to patient) OR long flow (>7 days)
- Irregular bleeding: Metrorrhagia, intermenstrual or post-coital bleeding
- Irregular and Excessive: Menometrorrhagia
- Preferred term for non-pregnant bleeding issues = Abnormal Uterine Bleeding (AUB)
  - Avoid “DUB” - dysfunctional uterine bleeding.

Pathophysiology: Anovulatory Bleeding

**Bricks & Mortar**

**Estrogen** = Bricks, build endometrium

**Progesterone** (P) = Mortar, stabilizes, only have P if ovulate

**Normal menses:** Withdrawal of P causes wall to fall down, all at once (orderly bleed)

**Anovulation:** No P so when wall grows too tall, it falls. It is heavy when wall is tall. Bricks can also fall intermittently & incompletely – irregularly, irregular

Differential: AUB

Step 1: Pregnant?

**Pregnant**

- Ectopic
- Spontaneous Abortion
- Threatened Abortion
- Molar Pregnancy
- Trauma
- Some non-pregnant causes

**Not Pregnant**

- Anovulation ***
- Anatomic/structural **
- Neoplastic *
- Infectious
- Iatrogenic
- Non-gynecologic

* = Most likely for this patient
Causes of Anovulation

<table>
<thead>
<tr>
<th>Physiologic</th>
<th>Hyperandrogenic</th>
<th>CNS</th>
<th>Iatrogenic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peri-menarche/Peri-menopause</td>
<td>PCOS</td>
<td>Hypo/Hyper Thyroid</td>
<td><strong>Anorexia</strong>/<strong>Over-exercise</strong></td>
</tr>
<tr>
<td>Obesity (via insulin effect in ovary)*</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Referenced: Causes of Anovulation

<table>
<thead>
<tr>
<th>Physiologic</th>
<th>Hyperandrogenic</th>
<th>CNS</th>
<th>Iatrogenic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pregnancy*</td>
<td>PCOS+</td>
<td>Pituitary adenoma (prolactin-secreting)*</td>
<td>Levonorgestrel IUD#</td>
</tr>
<tr>
<td>Peri-menarche+</td>
<td>Adult-onset congenital adrenal hyperplasia+</td>
<td>Neuroleptic agents (via increased prolactin)*</td>
<td>Progestin injection*#</td>
</tr>
<tr>
<td>Peri-menopause+</td>
<td>Breast-feeding*</td>
<td>Hypo or hyper thyroid (* or +)</td>
<td>Progestin implant#</td>
</tr>
<tr>
<td>Obesity (via insulin effect in ovary)+</td>
<td></td>
<td>Hypothalamic (stress, anorexia)*</td>
<td>Combined hormonal contraception#</td>
</tr>
</tbody>
</table>

Reference: AUB Differential

<table>
<thead>
<tr>
<th>Not Pregnant</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Anovulation</td>
<td>Anatomic</td>
<td>Neoplastic</td>
<td>Infectious</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

PALM-COEIN

Initial Work-up: Menometrorrhagia

- **Always:** Urine pregnancy
- **Usually:** TSH
- **Maybe:** Hct, r/o coagulopathy
- **Maybe:** EMB (Endometrial Biopsy)
- **Maybe but later:** Transvaginal Ultrasound
- **Usually not necessary:** FSH, LH, Testosterone, Estradiol
Does she need an EMB?

Endometrial Cancer Facts

• 4th most common cancer in women; average age 61 but 25% occur in premenopause.
• 10% of post-menopausal women with bleeding have cancer.
• Presents at early stage with bleeding; rare in the absence of bleeding. Vast majority are effectively treated with simple hysterectomy.
• Risk factor = Increased estrogen (long h/o anovulation e.g. PCOS, obesity). Protective = smoking, OCP's.

The Problem

• Irregular bleeding is common
• Endometrial cancer is relatively common
• Risk prediction models are not useful
• Little evidence to guide us about when to do EMB
• ACOG guidelines (expert opinion) recommend biopsy in MANY women

ACOG, July 2012

- When is endometrial tissue sampling indicated in patients with abnormal uterine bleeding and how should it be performed?

The primary role of endometrial sampling in patients with AUB is to determine whether carcinoma or premalignant lesions are present, although other pathology related to bleeding may be found. Endometrial tissue sampling should be performed in patients with AUB who are older than 45 years as a first-line test (see Fig. 2). Endometrial sampling also should be performed in patients younger than 45 years with a history of unopposed estrogen exposure (such as seen in obesity or PCOS), failed medical management, and persistent AUB ON.

ACOG Practice Bulletin 128, Diagnosis of AUB in Reproductive-Aged Women

Perimenopause

• Averages 4 years
• 12% suddenly stop menstruating
• 18% have longer, heavier menses
• 70% have short, irregular menses

Should we therefore perform EMB on all but 12% of women?
The Evidence...

• One prospective cohort study of 1000 women to test less aggressive EMB Clinical Pathway
• All eligible for biopsy using ACOG guidelines. Only biopsied those that were post-menopausal or had at least 1 risk factor (n=570)
• No cancers/hyperplasia in 2 yrs f/u in those that weren’t biopsied. (under-powered to answer this question)

A Rational Approach to EMB

• Natural history: Endometrial cancer takes many years to develop. We have time to detect it.
• Bleeding pattern cues: Cancer & hyperplasia present most commonly with menometrorrhagia, sometimes with intermenstrual bleeding. Rarely with regularly-timed menses.
• Progestins (IUD, progestin-only pill) have been shown to treat hyperplasia and cancer.

A Rational Approach to EMB

Post-Menopause: ALL women WITH ANY BLEEDING (except 4-6 months after starting HRT)
Recent onset irregular bleeding: Consider treating first and if bleeding normalizes, no need EMB
>50: All women with recurrent, irregular bleeding (consider not doing if periods light and spacing out)
45-50: Recurrent irregular bleeding plus ≥1 risk factor OR > 6 mos menometrorrhagia
<45: Long history (>2 yr? >5yrs?) of untreated anovulatory bleeding (eg PCOS)

A Rational Approach to EMB (cont’d)

Other reasons: Pap with atypical glandular cells or endometrial cells (ie if pap not done at time of menses).
EMB is not perfectly sensitive so further evaluation mandatory if:
1. Persistent AUB after negative EMB
2. Persistent AUB after 3-6 months of medical therapy
**Do all women with AUB need an ultrasound?**

Although TVUS is the best imaging choice for pelvic pathology (i.e., better than MRI, CT)...
- 80% with heavy menstrual bleeding have no anatomic pathology
- Incidental findings such as functional ovarian cysts and small fibroids (~50%) are often found leading to anxiety and unnecessary treatments
- SO....treat first, TVUS if treatment fails

---

**What about U/S instead of EMB for post-menopausal bleeding?**

**Transvaginal Ultrasound**
- Measure endometrial stripe
- Abnormal= >4 mm (or 5)
- Non-specific: myomas, polyps also cause thick EM
- Operator skill mandatory
- NOT USEFUL PRE-MENOPAUSE

---

**TVUS vs EMB to Detect Cancer** *(in post-menopausal women)*

<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>TVUS</td>
<td>96%</td>
<td>61%</td>
<td>99%</td>
</tr>
<tr>
<td>EMB</td>
<td>94%</td>
<td>99%</td>
<td></td>
</tr>
</tbody>
</table>

Further w/u necessary? <5%

Can offer patient choice as long as either is quickly available and patient understands she may need EMB after U/S

---

**Q1:** In addition to a urine pregnancy test and TSH, which of the following is the most appropriate test to order at this time?

1. FSH
2. Testosterone & DHEAS
3. Serum beta-HCG
4. Transvaginal Ultrasound
5. Endometrial Biopsy

A 46 yr G3P2T1 reports her periods have become increasingly irregular and heavy over the last 6-8 months. Sometimes they come 2 times per month and sometimes there are 2 months between LMP. 2 months ago, she bleeds 10 days with clots and frequently bleeds through pads to her clothes. She occasionally has hot flashes. She also has diabetes and is obese.
EMB=“Disordered Proliferative”. How do I stop the bleeding?

**Medical**
- NSAID’s
- Tranexamic Acid
- Oral E+P
- E+P patch, ring
- HRT (lower dose E+P)
- HRT patch
- Oral Progestin
- Progestin IUD
- IM Progestin
- GnRHa agonist

**Surgical**
- Endometrial ablation
- (D&C/Hysteroscopy)
- Hysterectomy (failed medical management)

---

**Non-hormonal Treatment: NSAID’s**
- 5 days around the clock (eg 600 mg tid)
- Many dosages and types proven effective in multiple RCT’s to decrease bleeding by ~40%
- Use alone or with other therapies
  DON’T FORGET NSAIDs!

---

**First Line Hormonal Treatments**
- First choice: Levonorgestrel IUD
  - >80% reduction in blood loss, decreased cramping, prevents/treats hyperplasia, highly effective birth control
  - Very few contraindications to using
  - Blood loss and satisfaction comparable to ablation, satisfaction comparable to hyst.
- 2nd choice: combined contraceptives (pill, patch, ring) or progestin injection
  - Proven to decrease irregular peri-menopausal bleeding
  - Any type ok, 20 mcg dose preferred for women >40
  - Estrogen contraindications: smokers>35, HTN, complicated DM, multiple RF for CAD, h/o DVT, migraines >35 or with aura

---

**Second Line Hormonal Options**
- Cyclic Progestins:
  - Less effective than NSAID’s and Levo IUD
  - 21-day therapy more effective than 10-day - poorly tolerated
- HT (post-menopausal dosing):
  - More difficult to gain cycle control compared with OCP
  - Same contraindications as Combined Hormonal Contraception
Tranexamic Acid

- Anti-fibrinolytic; available in Europe for many years—available in US 2011
- In RCT's, more effective than NSAID, cyclic provera.
  - Less effective than Mirena. Improves QOL by 80% by 3rd cycle
- Dose: 2 tabs tid for 5 days (1300 mg q 8 h = 3900 mg/day)
- Risks: Theoretic risk of VTE. No increase in large studies. Contraindicated in those with history of or risk factors for VTE. Unknown if safe in conjunction with CHC.
- Side effects: Minimal

Surgical Treatments

- D&C, Hysteroscopy:
  - Not really a treatment. Temporary reduction in bleeding. Diagnostic, not curative (except if polyp removed).
- Endometrial Ablation
  - Reduces but doesn’t eliminate menses
  - ~25% repeat ablation or hyst in 5 years
  - Must rule out cancer first
  - Can’t be done in >12 week uteri or for women who want fertility

Perimenopausal/Anovulatory Bleeding: Summary

R/o pregnancy, thyroid dz
↓
EMB if meets criteria
↓
Treat first as if anovulatory bleeding:
  - NSAID’s *
  - Hormones (Levo IUD, CHC, DMPA)
↓
If persists:
  - U/S to check for anatomic causes (and EMB if not already done)
  - Discuss surgical options for bleeding refractory to medical management.

Case 2: Is it the fibroids?

Same history as Case 1 except she has fibroids....

A 46 yo G2P2 woman presents stating that her fibroids are causing irregular bleeding.

She has a known fibroid uterus and complains of increasingly irregular and heavy periods. Sometimes they come 2 times per month and sometimes there are 2 months between. LMP 2 months ago. She bleeds 10 days with clots and frequently bleeds through pads to her clothes. She occasionally has hot flashes. She also has diabetes and is obese.

On exam, her uterus is 16 weeks size and irregular.
Fibroids......

- Very common → 80% of hysterectomy specimens (done for any reason) and ~75% have on U/S at age 50.
- 2-3 fold higher incidence in black women
- About 50% are asymptomatic
- Grow slowly until menopause and then decrease by ~50% (can still cause bleeding post-menopause)

Fibroid Symptoms

- Bleeding
  - Usually normal or menorrhagia (heavy but regular). Fibroids stretch endometrium = more bleeding
  - Occasionally menometrorrhagia if submucous or intracavitary (Fibroids distort endometrium so it can’t be stable)
- Pressure (not pain)
- Dysmenorrhea

Is the bleeding due to the fibroids?

- Fibroids are common in later 40s
- Anovulation is common in later 40s
- The increased bleeding seen with fibroids is typically due to increased volume or distortion of the endometrium
- Therefore: Decrease the amount of endometrium by treating as anovulatory bleeding. This often works.

AUB with Known Fibroids: Work-up and Treatment

- R/o cancer (using “rational emb algorithm”) and pregnancy (don’t blame fibroids for the bleeding)
  ↓
- NSAID’s and hormones
  ↓
- If no better, blame the fibroids!
  ↓
- +/- Lupron— as a bridge to menopause or pre-op to shrink to obtain less invasive route of hysterectomy
  ↓
- Surgical therapies (hysteroscopic resection if <3 cm, myomectomy, hysterectomy, UAE)
Hysterectomy

- Very high patient satisfaction (90%) (higher than ablation)
- Improved quality of life, sexual satisfaction and decreased pain
- Increased long-term risks of prolapse, incontinence

Uterine Artery Embolization

- Benefits: 40% decrease size, 75-90% improved bleeding
- Re-grow? In 5yr f/u of RCT, 25% had hysterectomy
- Not for: women who want fertility
- A "major" non-surgical procedure:
  - Often requires hospitalization for pain control
  - ~2 weeks to return to full activities (due to pain and fever)
  - Risks: emergent hyst (1-2%), 5% expel myoma through cervix, 40% have fever

Case 3... Too Fast

41 year old woman presents with dizziness and heavy vaginal bleeding for 2 weeks straight.

Prior to this, occasional irregular periods but nothing like this!

Hemoglobin=9

Acute Menorrhagia Treatment

ABC's and Stop the bleeding!

- Consider ED for transfusion
- Estrogen—2-4 OCPs (30-35 mcg E2)
  - Oral as effective as IV (so use oral)
- Give with anti-emetic
- Small RCT suggests high-dose provera may be effective as well, 20mg tid
- If not effective, options: D&C, Foley bulb tamponade, emergency hysterectomy
OCP Taper

- Don't want to give 2-4 OCP's per day and then stop suddenly b/c will have large withdrawal bleed
- Taper: 4 x 4 days, 3 x 4 days, 2 x 4 days then 1 per day for 1-2 months (66-96 pills required).
- Instruct not to take placebos and give at least 3 packs of pills at once.
- Give with anti-emetic, split bid (i.e. 2 bid rather than 4 all at once)

Case 4: Because of her contraceptive...

- A 32 year-old woman has recently initiated the birth control pill.
- She has had spotting for 30 straight days! She is annoyed.

Case 4: Because of the injection...

- A 32 year-old woman has recently initiated the contraceptive injection.
- She has had spotting for 30 straight days! She is annoyed.

Case 4: Because of the implant...

- A 32 year-old woman has recently initiated the contraceptive implant.
- She has had spotting for 30 straight days! She is annoyed.
**Case 4: Because of the IUD...**

- A 32 year-old woman has recently initiated the levonorgestrel IUD.
- She has had spotting for 30 straight days! She is annoyed.

---

**Reasons for dissatisfaction leading to pill, condom, implant or injection discontinuation**

<table>
<thead>
<tr>
<th>Reason</th>
<th>Contraceptive</th>
<th>Pill</th>
<th>Injection</th>
<th>OCP Implant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Too expensive</td>
<td>2.3</td>
<td>3.2</td>
<td>1.1</td>
<td>5.1</td>
</tr>
<tr>
<td>Too difficult or messy to use</td>
<td>15.4</td>
<td>15.8</td>
<td>14.3</td>
<td>12.6</td>
</tr>
<tr>
<td>Hormonal side effects</td>
<td>10.6</td>
<td>12.7</td>
<td>10.3</td>
<td>14.2</td>
</tr>
<tr>
<td>Unplanned pregnancy</td>
<td>21.9</td>
<td>23.5</td>
<td>26.2</td>
<td>26.4</td>
</tr>
<tr>
<td>Did not like the changes in menstrual periods</td>
<td>2.5</td>
<td>17.7</td>
<td>6.7</td>
<td>19.3</td>
</tr>
<tr>
<td>Experienced contraceptive failure</td>
<td>4.7</td>
<td>9.4</td>
<td>4.7</td>
<td>9.3</td>
</tr>
<tr>
<td>Experienced side effects</td>
<td>2.2</td>
<td>3</td>
<td>2.2</td>
<td>3</td>
</tr>
<tr>
<td>Worried about effectiveness</td>
<td>13.2</td>
<td>3</td>
<td>2.2</td>
<td>0</td>
</tr>
<tr>
<td>Did not like the changes in menstrual periods</td>
<td>13.2</td>
<td>3</td>
<td>2.2</td>
<td>0</td>
</tr>
<tr>
<td>Other reasons</td>
<td>15.4</td>
<td>10.6</td>
<td>10.2</td>
<td>10.2</td>
</tr>
</tbody>
</table>

---

**Mechanism for Abnormal Bleeding with Hormonal Contraceptives**

- Fragile and superficial blood vessels in endometrium
- Unstable endometrial stroma and glands
- Transition from thick to thin endometrium
- Altered endometrial remodeling
- Irregular bleeding

---

**COCs: Setting Expectations**

- Rates of unscheduled bleeding
  - 10-30% in the first month
  - Less than 10% by the third month
- Rates of amenorrhea
  - Less than 2% in the first year
  - Up to 5% after 1 year
COCs: General Counseling

- Take pill at the same time each day
  - Inconsistent pill use associated with increased risk of unscheduled bleeding\(^1\)
- Stop smoking!
  - Smokers more likely to experience unscheduled bleeding/spotting\(^1\)
  - Among smokers, bleeding more likely to persist through subsequent cycles


COCs: Regimens

Cyclic Use

Extended Cycle

Treating Bleeding on Cyclic COCs

- **Supplemental estrogen**\(^1\)
  - Oral CEE 1.25mg x 7 days
  - Oral estradiol 2mg x 7 days

**Double or triple birth control**

- Switch to vaginal ring


Treating Bleeding on Extended COCs

- **Discontinue the COCs for 3-4 consecutive days**\(^3\)
  - A 3-day hormone free interval was associated with greater resolution in breakthrough bleeding/spotting in comparison to continuing active pills\(^2\)
  - After the first 21 days of the hormone

2. Sulak PJ et al. AJOG, 2006
**DMPA: Setting Expectations**

- Abnormal bleeding is common in the first year
- Rates of unscheduled bleeding¹
  - Up to 70% in the first year
  - Approximately 10% after the first year
- Amenorrhea is more likely over time¹

<table>
<thead>
<tr>
<th>Rate of amenorrhea</th>
<th>Within 3 months</th>
<th>After 1 year</th>
<th>At 5 years</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>12%</td>
<td>46%</td>
<td>80%</td>
</tr>
</tbody>
</table>

¹ Speroff L, Darney PD. Clinical Guide for Contraception. 4th Ed. 2011

**Estrogens and Contraceptive Injection**

- RCT of DMPA users with unscheduled bleeding¹
  - Ethinyl estradiol 50 mcg
  - Estrone sulfate 2.5 mg
  - Placebo

**Conclusions**
- Ethinyl estradiol effective in stopping bleeding during treatment
- Bleeding tended to recur after discontinuation of estrogen


**NSAIDs and Contraceptive Injection**

- **Valdecoxib¹**
  - Dose: 40mg daily x 5d
  - More women in the treatment group had cessation of bleeding (77% vs. 33%)
  - Treatment group had a higher mean number of bleeding-free days in the following month (17.8 vs. 11.5 days)²

| *statistically significant* |

- **Mefenamic acid²**
  - Dose: 500mg bid x 5 d
  - More women in treatment group had cessation of bleeding in the week following treatment (69% vs. 40%)
  - No significant difference in bleeding-free days in the following month (16.1 in treatment grp vs. 12.4 in placebo grp)


**Tranexamic Acid and Injection**

- **Tranexamic acid**
  - 250mg qid x 5 days

| % stopped bleeding in 1st wk | 88% | 8.20% |
| % stopped bleeding in 4 wk | 68% | 0% |
| Mean number of days of bleeding/spotting | 5.7 | 17.5 |

Summary: Injection Bleeding

Enhanced Counseling
- Bleeding patterns
- Reassurance

Continued DMPA
- More injections, less bleeding

TREAT
- NSAIDs x 5-7 days
- Estrogen (COCs or supplemental estrogen x 10-20 days)
- Tranexamic acid

Etonogestrel Implant: Setting Expectations

- Most women experience a reduction of menstrual bleeding
  - Bothersome bleeding reported in 25% of patients
    - 6.7% reported frequent bleeding
    - 17.7% prolonged bleeding
- Rates of amenorrhea
  - Approximately 20% in first year
  - 30-40% after 1 year

Contraceptive Implant: Bleeding Patterns

- Number of unscheduled bleeding days:
  - Is HIGHEST in the first 3 months
  - DECREASES over the first year
  - PLATEAUS in the second and third year

Contraceptive Implant: Bleeding Patterns

- More unpredictable bleeding pattern
  - Amenorrhea may not be sustained if achieved
  - "Favorable" pattern in the first 3 months predicts a continued favorable pattern
  - For those with an "unfavorable" bleeding pattern, 50% report improvement over time

**NSAIDs and Etonogestrel Implant**

- Limited data
- Variable efficacy of NSAIDs in LNG implant\(^1,2\)
  - Various regimens
  - Small number of studies and participants
- One RCT evaluated NSAIDs in women with ETG implants\(^3\)
  - Randomized to placebo or mefenamic acid (500mg tid)
  - 65% stopped bleeding within 1 week in NSAID group vs. 21% in the placebo
  - Less bleeding in the subsequent 4 weeks in the women who had received NSAIDs


**Estrogen and LNG Implant**

- Recommendations based on studies of LNG implant
- Systematic review of estrogen vs. placebo treatment for irregular bleeding with LNG implant\(^1\)
  - Decreased the days of ongoing bleeding
  - Effect lasted for several months after treatment
  - More side effects in treatment group (nausea, GI upset)


**Implant Bleeding Management**

- US Selected Practice Recommendation for Contraceptive Use, 2013
- **EXPECTANT MANAGEMENT** for 6–12 months
- Supplemental estrogen
- NSAIDs x 5–7 days
- CDCs -10–20 days
- Oral estrogen - 1.25mg CEE -2mg estradiol
- Transdermal estrogen -0.1mg/day

**LNG-IUS: Setting Expectations**

- Unscheduled spotting or light bleeding is common, especially during the first 3–6 months
- For LNG 52/5, spotting was present in 25% of the users at 6 months and decreased over time.\(^1\)
**LNG IUS: Setting Expectations**

- 79-97% reduction in bleeding
- 33% developed oligo/amenorrhea in first 3 months, 70% at 2 yrs
- Amenorrhea at 1 yr: 20%
- Amenorrhea at 2 yrs: 30-40%

- Amenorrhea at 1 yr: 6%
- Amenorrhea at 2 yrs: 12%

**LNG-IUS: Interventions for Bothersome Bleeding**

- Estrogen
  - Estradiol patch weekly x 12 weeks
  - Greater number of bleeding/spotting days compared to placebo (non-significant)
  - More dissatisfaction with treatment

- NSAIDs
  - Naproxen 500mg bid x 5 days every 4 weeks for 12 weeks
  - Fewer number of bleeding/spotting days compared to placebo (non-significant)
  - More dissatisfaction with treatment

“**No direct evidence was found regarding therapeutic treatments for bleeding irregularities during LNG-IUD use.**”

-US SPR, 2013


**LNG IUD Bleeding**

- Provide excellent counseling pre-insertion
  - Discuss bleeding/spotting in first 3-6 months
  - Discuss amenorrhea
- Provide reassurance as bleeding likely to improve
- Confirm appropriate location of IUD

**Irregular Bleeding by Contraceptive**

<table>
<thead>
<tr>
<th>Contraceptive</th>
<th>Rates of irregular bleeding</th>
</tr>
</thead>
<tbody>
<tr>
<td>COCs</td>
<td>10-30% in first month of use</td>
</tr>
<tr>
<td></td>
<td>&lt;10% by the third month of use</td>
</tr>
<tr>
<td>Vaginal Ring</td>
<td>Less common in comparison to COCs</td>
</tr>
<tr>
<td></td>
<td>Up to 6% in first year</td>
</tr>
<tr>
<td>Patch</td>
<td>Similar to COCs except slightly higher rate of spotting in first 2 cycles</td>
</tr>
<tr>
<td>Injectable</td>
<td>70% in first year</td>
</tr>
<tr>
<td></td>
<td>10% after the first year</td>
</tr>
<tr>
<td>Implant</td>
<td>Up to 25% in first 2 years</td>
</tr>
<tr>
<td>Cu-IUD</td>
<td>Less irregular bleeding compared to LNG-IUS</td>
</tr>
<tr>
<td>LNG-IUS</td>
<td>Up to 25% at 6 months</td>
</tr>
<tr>
<td></td>
<td>8-11% at 18-24 months</td>
</tr>
</tbody>
</table>
Amenorrhea by Contraceptive

**RATES OF AMENORRHEA**

<table>
<thead>
<tr>
<th>Within 1st year</th>
<th>At 1 year</th>
<th>Beyond</th>
</tr>
</thead>
<tbody>
<tr>
<td>COCs</td>
<td>&lt;2%</td>
<td>Up to 5%</td>
</tr>
<tr>
<td>Vaginal Ring</td>
<td>Similar to COCs</td>
<td></td>
</tr>
<tr>
<td>Patch</td>
<td>Similar to COCs</td>
<td></td>
</tr>
<tr>
<td>Injectable</td>
<td>12%</td>
<td>46%</td>
</tr>
<tr>
<td>Implant</td>
<td>21%</td>
<td>30-40%</td>
</tr>
<tr>
<td>Cu-IUD</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>LNG-20</td>
<td>20%</td>
<td>30-40% at 2 yrs</td>
</tr>
<tr>
<td>LNG-14</td>
<td>6%</td>
<td>12% at 2 years</td>
</tr>
</tbody>
</table>

**What about too little bleeding?**

**Seven questions in evaluation of 2° amenorrhea**

1. Pregnant?
2. Excessive hair growth or acne? → PCOS
3. Overweight? → Obesity-induced anovulation
4. Breast secretions? → Hyperprolactinemia
5. Very thin, over-exercise, stress? → Functional hypothalamic amenorrhea
6. Hot flashes? → Premature ovarian failure
7. Pregnant recently complicated with infection or uterine surgery (D&C)? → Asherman’s syndrome

**WORK-UP: Amenorrhea**

• **Always:**
  - Urine pregnancy test
  - If Neg: TSH & Prolactin

• **If hot flashes:**
  - FSH

• **If hirsute/obese:**
  - Usually no further testing needed. (If deep voice or clitoromegaly: testosterone. If family history hirsutism or onset at puberty: 17 OH-P)
**Reference: Progestin Challenge Test**

- **Progestin challenge test**: (10 mg Provera x 10 days)
  - Bleeding after confirms endogenous estrogen is present
  - Distinguishes hypothalamic amenorrhea (no bleeding or just spots) from PCOS/anovulation (full withdrawal bleed)
- **Estrogen challenge test**: (Premarin 2.5 mg qd x 3 wks then Provera x 10 days) distinguishes hypothalamic amenorrhea (full withdrawal bleed) from Asherman’s (no bleeding or just spots)

**Amenorrhea Treatment**

1. **PCOS** → Protect the endometrium! (from hyperplasia due to unopposed E2) → combined contraceptives, DMPA, LNG IUD
2. **Obesity induced anovulation** → same
3. **Hyperprolactinemia due to microadenoma** → OCPs or nothing, Bromocriptine if desires pregnancy or to treat sx
4. **Functional hypothalamic amenorrhea** → protect the bones! (from lack of E2) → estrogen-containing contraceptives
5. **Premature ovarian failure** → same
6. **Asherman’s syndrome** → Hysteroscopy

**Conclusions**

- **Diagnosis**: think of anovulation
- **Treatment**: all bleeding treated similarly
  - NSAID’s plus hormones. Persistent abnormal bleeding requires continued work-up even if EMB and/or ultrasound are negative.
  - Hormonal or copper birth control: set expectations