Dysfunctional Uterine Bleeding

John G. Pierce, Jr., MD
Department of Obstetrics and Gynecology
Virginia Commonwealth University
School of Medicine
Medical College of Virginia Campus

Definition:
• Excessive uterine bleeding for which no specific cause has been found
• Often implies a mechanism of anovulation
• A diagnosis of exclusion

3 Patients with DUB

Patient # 1
15 yo with menarche at age 13 presents with heavy vaginal bleeding, - UPT, and HGB = 9gm

Patient # 2
33 G0 yo with heavy, irregular periods lasting 10 days, microcytic anemia, and tobacco use

Patient #3
42 yo G0 with heavy vaginal bleeding for 4 weeks, Hgb = 9, obesity, Type II DM

Menstruation

Definition:
• The physiologic discharge of blood, mucus, and cellular debris from the endometrium which occurs in a cyclic and recurring pattern from puberty to menopause except during pregnancy and lactation

Average Interval:
• 28 ± 7 days
Range:
• 21- 35 days
Usual duration:
• 4- 6 days
Normal volume:
• 30 ml
Abnormal volume:
• > 80 ml

Menstruation

• Menarche is followed by 5-7 years of increasing regularity
• In 40s, cycles begin to lengthen
• As women approach menopause, cycle length becomes more irregular - ie. anovulation
Traditional Definitions

- **Oligomenorrhea** - intervals greater than 35 days
- **Polymenorrhea** - intervals less than 21 days
- **Menorrhagia** - regular, normal intervals with excessive flow and duration
- **Metrorrhagia** - irregular intervals, usually normal amounts but longer duration

Menstrual Cycle

4 Phases
1. Menstrual
2. Proliferative (Follicular)
3. Secretory (Luteal)
4. Premenstrual (Late Secretory)

Menstrual Endometrium

Proliferative Endometrium

Secretory Endometrium
Phase of Endometrial Breakdown

- Breakdown occurs in absence of fertilization, implantation, and consequent lack of sustaining quantities of HCG
- Fixed lifespan of the corpus luteum is complete and E and P levels wane
- Withdrawal of E and P initiates 3 endometrial events:
  - Vasomotor reactions
  - Tissue loss
  - Menstruation

Phase of Endometrial Breakdown

- The most prominent immediate effect of this hormonal withdrawal is a modest shrinking of the tissue height and remarkable spiral arteriole vasomotor responses.
- Vasoconstriction and myometrial contractions associated with menstrual events are believed to be significantly mediated by prostaglandins

Uterine Vasculature

The Vascular Mechanism

Premenstrual Phase
- Arteriolar coiling ↑s markedly and appears knotted
- Stasis/slowing of the circulation and vasodilatation
- Vasoconstriction mediated by decrease in steroid hormones (4–24 hrs before blood escapes). Leads to cell lysosomal leakage of PG synthetase enzymes, proteases, and collagenases.

The Vascular Mechanism

Menses
- Ischemia to the outer 1/2 to 2/3 of endometrium results
- Arterioles relax and hemorrhage occurs
- Upper 2/3 of endometrium is sloughed
- Bleeding continues until coiled arterioles return to vasoconstriction

The Vascular Mechanism

- Active proliferation of remaining basal stroma, glandular elements, and vasculature is stimulated by increasing estrogen
- Clotting assists in controlling bleeding
Characteristics of a Normal E - P Withdrawal Bleeding

- Universal, simultaneous change in all segments of the endometrium
- An orderly progression of events involving a rigid, compact structure
- Vasomotor rhythmicity with vasoconstriction, structural collapse, and clotting

Differential Diagnosis of Abnormal Bleeding

A. Organic Causes: Reproductive Tract Disease
   - Accidents of pregnancy
   - Malignancy
     - Endometrial
     - Cervical
     - Ovarian, vulvar, vaginal, oviductal cancers
   - Upper genital tract disease
     - Endometritis, fibroids, endometrial polyps
     - Cervical diseases - Erosions, polyps, cervicitis
   - Trauma, foreign bodies

B. Dysfunctional (DUB) or Endocrine Causes
   - Ovulatory
     - 10%
     - Hormones same as normal menstrual cycle
     - ? prostaglandin related
     - Usually after adolescent yrs and before perimenopause
   - Anovulatory
     - 90%
     - Continuous estradiol production w/o corpus luteum formation and progesterone production

Major Categories of DUB

- Estrogen Breakthrough
  - Low dose → intermittent spotting
  - High levels → amenorrhea then heavy bleed

- Estrogen Withdrawal
  - After BSO or D/C estrog., XRT of mature follicle
  - Midcycle bleeding with ↓ estrogen before ovulation

- Progesterin Breakthrough
  - Only in the presence of high P:E ratio → long-acting progesterin only contraceptives

- Progesterin Withdrawal
  - Removal of corpus luteum
  - Withdrawal of non-estrogenic progesterin

Theory for Why Anovulatory Bleeding is Excessive

- Most instances of anovulatory bleeding are examples of estrogen withdrawal and estrogen breakthrough bleeding. (PCOS, obesity, immaturity of the hypothalamic-pituitary axis, and late ovulation)
- In the absence of growth limiting progesterone and periodic desquamation, the endometrium attains an abnormal height without concomitant structural support. Tissue increasingly displays intense vascularity, back to back glandularity, but without an intervening stromal support matrix.
- Hence, tissue is fragile and will suffer spontaneous superficial breakdown and bleeding.
  - Larger quantity of endometrium
  - Disorderly, abrupt, and random breakdown of tissue with consequent opening of multiple vascular channels
  - No vasoconstrictive rhythmicity, no tight coiling of spiral vessels, and no orderly collapse to induce stasis.
  - Local bleeding is stopped by the "healing" effects of estrogen
Work-up of DUB

• History
• Physical
• * For women 20-35, normal weight, no risk factors for STDs, no signs of androgen excess, no use of hormones, and a normal exam, management can be based on a clinical diagnosis.

Labs
• CBC
• PT / PTT and / or bleeding time
• ± von Willebrand factor activity
• Luteal phase serum progesterone measurement, daily BBT, premenstrual sampling of the endometrium

Imaging studies
• Pelvic ultrasound / sonohysterography, HSC

Endometrial Sampling
• D & C
• Endometrial biopsy

Transvaginal Ultrasound (TVS)

Can assess
• Size of uterus
• Endometrial thickness or “stripe”
• Myometrial consistency
• Ovaries

Sonographic Detection of Intrauterine Lesions with TVS

<table>
<thead>
<tr>
<th>Lesion</th>
<th>Detection Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Endometrial Polyps</td>
<td>Unreliable to 58% - 90%</td>
</tr>
<tr>
<td></td>
<td>(depending on use and timing of SIS)</td>
</tr>
<tr>
<td>Submucous Fibroids</td>
<td>Up to 99%</td>
</tr>
</tbody>
</table>
Sonoinfusion Sonography (SIS) Detection of Intrauterine Lesions with TVS

Sonoinfusion Sonography (SIS) Correlation with Resection at Hysteroscopy

Indications for Ultrasound
• Unable to assess uterus by physical exam
• Unable to sample endometrium and surgery not desired

Work-up of DUB
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How accurate is an endometrial biopsy to rule out malignancy?
Comprehensive Gynecology 2001

Endometrial Biopsy
• > 95% accurate in diagnosing a malignancy when compared with subsequent findings at hysterectomy
• If perimenopausal bleeding persists, consider additional diagnostic procedures
Management of DUB

**General Concepts:**
- Medical Rx is preferable over surgical
- Treatment should depend on whether it is given to stop an acute heavy bleeding episode or to reduce the amount of MBL in subsequent menstrual cycles
- Definitive treatment is determined by diagnosis

Medical Management of DUB

**Estrogens:**
- Causes rapid growth of the endometrium
- Repairs denuded and raw epithelial surfaces
- Used to stop an acute bleed

**Medical Management of DUB**

**Estrogen Rx Option # 1**
- Oral conjugated estrogens 1.25 - 2.5 mg q 6 hrs x 24 hrs or IV at 25 mg q 3-6 hrs x 24 hrs.
- After bleeding stops, cont. estrogen at same dose and add a progestin (usually MPA 10mg/d) for 7-10 d.
- Withdrawal of both causes bleed

**Estrogen Rx Option # 2**
- One 50mcg oral contraceptive pill q 6 hours x ~24 hours or until bleeding stops
- Then continue for one ~ week and stop

**Medical Management of DUB**

**Progestins**
- Stops endometrial growth
- Supports and organizes the endometrium to allow for a uniform slough
- Stimulates arachadonic acid formation in endometrium (PGF2α)
- Usually not for an acute bleed

**Other Medical Options:**
- Progestin Releasing IUD
- NSAIDS - ↓ MBL by 30 - 50%
- Antifibrinolytic agents
- Androgenic steroids (Danazol)
- GnRH agonists
Surgical Management of DUB

• D & C
  – Questionable therapeutic tool except for excessive bleeding and hypovolemia
  – Not curative
• Hysteroscopy
• Endometrial Ablation
• Myomectomy
• Hysterectomy

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