Abnormal Uterine Bleeding

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Physiology of Menstrual Cycle

CNS-Hypothalamus-Pituitary Ovary-uterus Interaction

Neural control
Chemical control

Dopamine
Norepinephrine
Endorphines

Hypothalamus
Gn-RH
Ant. pituitary
FSH, LH
Estrogen
Ovaries
Progesterone
Uterus
Menses
Control of The Menstrual Cycle

I- Achieving Regularity of the menses
• The cyclicity of the menstrual cycle is dependent on the intact/tight coordination along the hypothalamic-pituitary-ovarian axis through a NEGATIVE feedback mechanisms.

II- Achieving endometrial haemostasis:
• Is dependent on the local mechanisms: platelet adhesion, vasoconstrictors (endothelin, PGF2α & TAX-A2), vaso-dilators (PGI2, PGE2 & NO) and coagulant/fibrinolytic activities.

• Equal in importance is the onset of endometrial regeneration.

Disorders of the Menstrual Cycle

• Amenorrhea
• Dysmenorrhea
• Premenstrual Syndrome
• Abnormal Uterine Bleeding
Abnormal Uterine Bleeding (AUB) by age Group

- **In newborn female:** Physiologic bleeding, due to Estrogen withdrawal obtained from mother.
- **Childhood bleeding:** AUB during childhood period (organic lesion or precocious puberty)
- **Adolescent bleeding:** AUB after puberty (< 20 years)
- **In women of childbearing age:** AUB includes any change in menstrual-period frequency or duration, or amount of flow, as well as bleeding between cycles.
- **In postmenopausal women:** AUB includes vaginal bleeding 12 months or more after the cessation of menses
- **In perimenopausal women:** AUB during perimenopausal years (> 40 y up to 1 y after menopause)

Clinical Types of AUB

- **Menorrhagia:** Heavy or prolonged uterine bleeding that occurs at regular intervals. The loss of $\geq 80 \text{ mL } / \text{ cycle or bleeding } > 7 \text{ days.}$
- **Hypomenorrhea:** Periods with unusually light flow or short duration < 2 days.
- **Menorrhagia:** Irregular menstrual bleeding or bleeding between periods
- **Meno-menorrhagia:** Menorrhagia associated with $> 80 \text{ mL}$
- **Polymenorrhea:** Frequent menstrual bleeding. Strictly, menses occur q 21 d or less
- **Oligomenorrhea:** Infrequent menses > 35 d apart.
### Differential Diagnosis of AUB

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### Etiology of Abnormal Uterine Bleeding

#### A- Organic causes of AUB

- Organic AUB may be associated with conditions that are not dysfunctional in nature or pregnancy related.
- Organic conditions, such as polyps, uterine fibroids, endometritis, endometrial hyperplasia, ……etc, blood dyscrasias or systemic diseases.
- Fibroids, polyps, adenomyosis, and blood dyscrasias usually present with *menorrhagia/polymenorrhea* (i.e., Regular excessive cyclic bleeding) since these lesions do not affect ovulatory function.
- Endometritis, cervicitis, endometrial polyps often present with Irregular spotting or Irregular bleeding usually (i.e. *Menorrhagia, Meno-Menorrhagia*).
B-Dysfunctional AUB (DUB)

- It is an abnormal bleeding from the uterus in the absence of organic disease of the genital tract, pregnancy problems or systemic diseases.

- It is characterized by dysfunction of the uterus, ovary, pituitary and hypothalamus.

- The pattern of bleeding is mainly heavy & regular (menorrhagia) but it could be irregular uterine bleeding or intermenstrual bleeding.

- In 90% of DUB due to anovulation (Anovulatory bleeding). NO premenstrual symptoms

- In 10% of DUB due to corpus luteum dysfunction (Ovulatory bleeding)

Pathophysiology of Anovulatory DUB

- Corpus luteum is not produced
  - Ovary fails to secrete progesterone (P), although estrogen (E) production continues
  - Result is continuous, unopposed E stimulation of endometrium: Endometrial proliferation without P-induced differentiation / stabilization
  - Endometrium becomes excessively vascular without stromal support → fragility and irregular endometrial bleeding → Endometrial Hyperplasia, on longterm
  - Occurs after menarche and before menopause
Etiology of Anovulatory DUB

1. Polycystic ovary syndrome (PCOS).
2. Immaturity of the hypothalamic-pituitary-ovarian axis
3. Dysfunction of the hypothalamic-pituitary-ovarian axis (Hyperprolactinemia, Stress and anxiety, Rapid weight loss. Borderline anorexia nervosa, Hypothyroidism and Perimenopause)
4. Abnormalities of normal feedback signals (hepatic disease or thyroid abnormalities, Adipose tissue and E producing tumors)

Evaluation and Diagnosis of AUB

AIMS:
1. Nature & severity of bleeding
2. Exclusion of organic, systemic or pregnancy causes
3. Ovulatory or anovulatory dysfunctional bleeding is a diagnosis after exclusion of all previous causes

STEPS:
I. Full History:
II. Careful General and Local Examination.
III. Investigation:
III- Investigation of AUB

1. CBC, serum ferritin
2. B-hCG
3. TSH
4. Consider according to presentation:
   - Coagulation profile (esp. adolescent)
   - Prolactin if amenorrheic
   - FSH, LH
   - Serum androgens (esp. free testosterone)
   - Day 21 (luteal phase) progesterone to confirm ovulation
   - Pap smear
   - Pelvic USS - detect polyps, fibroids; measure endometrial thickness (useful in postmenopausal women)
   - Saline sonohysterography - very sensitive for intrauterine pathology (polyps, submucous fibroids)
   - HYSTEROSCOPY
   - Endometrial sampling - in women >40 y or risky for endometrial CA.

**Transvaginal Ultrasound**
- Evaluate ovaries for PCOS.
- Evaluate ut. for fibroids
- Evaluate endometrial stripe.

**Sonohysterography**:
- most useful for differentiating focal from diffuse endometrial abnormalities
- can guide the decision of doing a hysteroscopy or dilatation and curettage.
Ultrasound is the first-line diagnostic tool for identifying structural abnormalities.

- **Endometrial polyp**
- **Submucous myoma**
- **Endometrial Hyperplasia**

**Diagnostic Hysteroscopy**

- Direct exploration of the uterine abnormalities like fibroids and endometrial polyps.
- Hysteroscopic specific biopsy of lesions.
- H&C better than D&C or endometrial biopsy.
A- Treatment of Organic causes of AUB

- The cause of the abnormal bleeding should determine the treatment options available to the patient.
- Systemic Hormonal or medical conditions causing the bleeding should be addressed.
- Structural causes (Organic) are often addressed surgically (as in the case of fibroids, polyps, or cancers), but conservative therapies may also be appropriate.

B- Treatment of Dysfunctional (DUB)

- *DUB* is diagnosed by excluding pregnancy, iatrogenic causes, systemic conditions, and genital tract pathology.
- Before treatment, take in consideration:
  1. Patient age group
  2. Desire for conception
  3. Need for contraception
  4. Pattern of DUB (*regular* or *irregular*)
  5. Severity of bleeding.
  6. Need for preservation of uterus
  7. Risk of endometrial carcinoma
I- Medical Treatment of DUB:

Mild DUB
• NSAIDs
• anti-fibrinolytic (e.g. Cyklokapron®) at time of menses
• Combined OCP
• Progestins (Provera®) on first 10-14 days of each month
• Mirena® IUD
• Danazol

Acute, severe DUB
• Replace fluid losses/consider admission
• Medical treatment
  a) estrogen (Premarin®) 25 mg N q4h x 24h with Gravol® 50 mg N/pO q4hor
  b) Ovral® 1 tab PO q4h x 24h with Gravol® 50 mg N/pO q4h.
  Taper Ovral®: 1 tab tid x 2d ---- bid x 2d -, OD
• after (a) or (b), maintain patient on monophasic OCP for next
  several months or consider alternative medical treatment

Clomiphene citrate
• patients who are anovulatory and who wish to get pregnant

Levonorgestrel releasing IUS (Mirena®)

• Levonorgestrel 20 mcg/24 hours,
• Mirena first registered in Finland for contraception in 1990.
• Failure rate similar to sterilisation
• Main effect noted to be marked
  reduction in menstrual blood loss.
• Used for DUB since 1995 (UK) and since 2000 (USA)

Effects:
1. Comparable to endometrial resection in DUB
2. Superior to medical treatment
3. May be an alternative to hysterectomy.

Side effects:
1. BTB in the first cycles
2. 20% develop amenorrhea within 1 yr
3. Functional ovarian cysts
II- Surgical Treatment

1. Dilatation and curettage is not effective for treatment of heavy dysfunctional menstrual bleeding.

2. Endometrial ablation is satisfactory than oral therapy, but 40% reoperation rate after 5 y.

3. Similar satisfaction rate and efficacy for endometrial ablation and the LNG-IUS system.

4. Vaginal hysterectomy is better when compared with laparoscopically assisted vaginal hysterectomy.

5. Endometrial ablation and vaginal hysterectomy are preferable to abdominal hysterectomy.

Endometrial ablation

- All result in destruction of the endometrium.
- Most women will not experience long term amenorrhea after treatment.
- Risk of endometrial cancer is not eliminated.

Indications:
1. Failure of medical treatment
2. Family is completed
3. Normal Uterine cavity <10 cm
4. Submucos fibroid <5 cm
5. Endometrium is normal or low risk hyperplasia.
I. Hysteroscopic Endometrial Ablation Techniques (First Generation)

Techniques
1. Laser photocoagulation
2. Electrosurgical:
   a. Roller ball
   b. Resection

Advantages:
• 80-85% satisfaction rate
• Complication rate 2-6.4%
• Long-term amenorrhoea 60%
• Subsequent procedure >30%
• Failure may occur up to 3 years
• Less morbidity
• Less expensive

II- Non hysteroscopic endometrial Ablation Techniques (Second Generation)

Advantages:
1- Minimal operator skill
2- Satisfactory outcome
3- Out-patient/office procedure

Commonest Techniques:
A- Thermal Balloon Systems
B- Bipolar Electrosurgery
C- Microwave ablation
Thermal Balloon Endometrial Ablation

- **Thermachoice®**
  - A balloon placed in the uterine cavity and Hot water is circulated inside the balloon to destroy the endometrium.
  - Central element heats liquid circulated in balloon $87 \, ^\circ \text{C}$ for 8 minutes.
- **Limitations:**
  - Uterine cavity size 6-10 cm;
  - Contraindication:
    - Suspicious of malignancy
    - Distorted uterus (multiple fibroids, anomalies)

Bipolar Electrosurgery

- **NovaSure system®**
  - Wire mesh on a triangular frame
  - Suction to ensure mesh contact with endometrium
  - Switches off when tissue impedance confirms tissue desiccation
  - 90 second treatment time
Microwave Endometrial Ablation

- Microwave probe inserted (GA or sedation), endometrium heated to 80°C
- day case procedure
- 70-80% satisfaction rates
- 95% return to normal activities within 3 wk.

Post-menopausal bleeding

- **Definition**: bleeding is a term given for any vaginal bleeding whatever its amount occurring after one year of menopause
- **Etiology**
  1. Malignant neoplasm of the genital organs: cancer body, cancer cervix, tubes, ovaries, vulva and vagina (any case of postmenopausal should be diagnosed as malignant lesion until prove otherwise)
  2. Oestrogen withdrawal bleeding (oestrogen therapy used for senile vaginitis or osteoporosis when stopped can cause vaginal bleeding)
  3. Endometrial hyperplasia and polyps: oestrogen from supra renal gland or exogenous oestrogen therapy or SERM
Etiology

4. Benign neoplasm: as fibroid polyp with sloughing and necrosis
5. Traumatic lesions as trophic ulcers or genital proplapse, accidental trauma or neglected pessary
6. Rectal and urethral conditions
7. General causes as blood coagulation defects, leukaemia, hypertension or CHF (rare causes)
8. No definite causes in 15%

Diagnosis:

I- History:
• Onset, amount and duration of bleeding, duration of menopause, administration of hormones, bleeding from other orifices, associated conditions as vaginal discharges
• Loss of body weight, abdominal masses, abdominal pain, urinary and rectal symptoms, bluish skin discoloration after minimal trauma (leukemia and purpura)
II- EXAMINATION:
- General Examination (for hypertension, CHF, cachexia or peticheal hemorrhage)
- Abdominal for palpable spleen, liver, ovarian and uterine swelling.
- Pelvic examination urethral, vulval and rectal lesions.
- PVE for carcinoma or polyps or ulcers of vagina and cervix
- Bimanual examination for size of the uterus and ovaries.
- Speculum for inspection of the vagina and cervix.
- PR for cancer of the rectum.

Investigation:
- Pelvic Transvaginal USS - detect polyps, fibroids; measure endometrial thickness (useful in postmenopausal women)
- Saline sonohysterography - very sensitive for intrauterine pathology (polyps, submucous fibroids)
- Hysteroscopy and directed biopsy
- Complete fractional curettage must be taken for any suspicious lesion.
Management:

1. Malignancy should be ruled out in every patient with postmenopausal bleeding
2. Cases with detectable causes: the treatment is directed to the cause.
3. Cases without detectable causes: discharge and observe for bleeding and if recur, for appropriate medical or surgical treatment

AUB at a Glance

I. Organic lesions
   Systemic Diseases
   Pregnancy problems
   Dysfunctional bleeding
THANK YOU