CLINICAL ASPECTS OF THE MENSTRUAL CYCLE
M2 Reproduction Sequence
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Learning Objectives:

1. Understand the clinical aspects of normal menstruation.
2. Describe the clinical aspects of dysmenorrhea and possible management.
3. Understand the pathogenesis of abnormal uterine bleeding.
4. Identify the physiologic basis for the evaluation and management of abnormal bleeding.
5. Explain the approach to the patient with abnormal bleeding and the variations due to age.
6. Understand the pathogenesis of primary and secondary amenorrhea.
7. Explain the evaluation and treatment of amenorrhea.

Study Questions:

What is normal menstruation? What factors are key to the regulation of menstruation? Why do women develop dysmenorrhea?
What are the sources of abnormal uterine bleeding? How would you evaluate the patient for each? Will your evaluation vary depending on the patient’s age or menopausal status?
Why do women stop menstruating? Why might someone never begin to menstruate? What is the most likely cause of each? What would you expect on examination and/or evaluation? What tests would help discern the etiology of ‘no bleeding’?

Key Terms and Definitions:

Menarche: Age at onset of menstruation
Primary amenorrhea: Absence of menstruation despite signs of puberty
Secondary amenorrhea: Absence of menstruation for 3-6 months in a woman who previously menstruated
Dysfunctional uterine bleeding: Irregular bleeding, unrelated to anatomic lesions of the uterus, therefore due to anovulation or anovulatory cycle
Polymenorrhea: Menstrual interval less than 21 days
Oligomenorrhea: Menstrual interval greater than 35 days
Hypomenorrhea: Scant amount of menstrual flow
Hypermenorrhea: Large amount of menstrual flow
Menorrhagia: Regular menstrual intervals, excessive flow and duration
Metrorrhagia: Irregular menstrual intervals, excessive flow and duration
Anovulation/anovulatory: Menstrual cycle without ovulation
Mittleschmertz: Pain with ovulation
Molimina: Symptoms preceding menses
Menorrhoea: Menstrual cramping/pain
Threatened abortion: Vaginal bleeding within first 12 weeks of pregnancy
Inevitable abortion: Dilation of cervix, vaginal bleeding, products visible
Incomplete abortion: Some products of conception expelled but not all, bleeding, dilation
Complete abortion: Products of conception expelled, os closed, minimal bleeding
Missed abortion: Embryonic demise, no products of conception passed

Normal Menstruation
Endometrium with cyclic growth and regression in response to estrogen and progesterone
   Proliferative phase
   Secretory phase

Menarche average age 12, normal range 9-16

Rate and quality of follicular growth and development determines cycle length.
   - highest incidence of anovulatory cycles <20 yo age and >40 yo age

Normal menstrual interval 21-35 days
   - counting from 1st day to 1st day of flow
   - only 15% of reproductive age cycles are 28 days

Usual flow 4-6 days, with normal range 2-8 days
   - what could affect length of flow?

Normal flow 30-40 mL, excessive flow >80mL
   - difficult to quantify
   - anemia as evidence of heavy bleeding

Cyclic events
   - changes in vaginal discharge
   - mittleschmertz
   - molimina
   - dysmenorrhea
   - symptoms with menses
   - Premenstrual syndrome
     - prevalence
     - symptoms
     - cultural conditioning
     - treatment
   - psychological dependence on “cycle”

**Dysmenorrhea**

-- Primary dysmenorrhea
   - pathophysiology
   - symptoms
   - treatment

-- Secondary dysmenorrhea
   - pathophysiology
symptoms
etologies: endometriosis, pelvic inflammation, leiomyomas, adenomyosis, ovarian cysts, pelvic congestion

--Chronic pelvic pain (> 6 months duration)
viscerosomatic convergence
multiple potential sources of pain
h/o physical/sexual assault

**Abnormal Uterine Bleeding (AUB)**

Must exclude pregnancy as source of abnormal bleeding. In a reproductive age female, pregnancy is the most common cause of secondary amenorrhea.

**AUB due to pregnancy:**
- Implantation bleeding
- Threatened abortion
- Inevitable abortion
- Incomplete abortion
- Complete abortion
- Missed abortion
- Ectopic pregnancy
- Molar pregnancy

**Dysfunctional Uterine Bleeding:**

Irregular bleeding unrelated to anatomical lesions of the reproductive tract, usually due to anovulatory cycles

DUB is a common cause of AUB in post-pubertal and peri-menopausal patients

Hormonal causes of anovulation:
Hypothalamic-Pituitary-Ovarian axis dysfunction
- polycystic ovarian syndrome
- thyroid dysfunction
- hyperprolactinemia
- stress
- obesity
- exercise changes

[AUB due to anatomic lesions:]

[UTERINE]
Uterine leiomyomas
Endometrial polyps
Endometritis
Endometrial Carcinoma

[CERVIX]
Carcinoma of cervix
Cervical dysplasia
Endocervical polyps
Cervicitis

[VULVA/VAGINA]
Carcinoma of vulva or vagina
Vaginitis
Trauma/lacerations
Foreign bodies
Pessaries

**AUB due to systemic causes:**

Bleeding disorders
  - intrinsic
  - iatrogenic

**Evaluation of AUB**

Dependent on age and reproductive considerations of the patient
In a reproductive age woman, exclude pregnancy

**History/Physical Testing**

- Papanicolaou smear
- Wet prep
- CBC
- Thyroid function tests
- Prolactin
- Evaluation of endometrium
- Biopsy of suspicious lesions
- Role of FSH/Estradiol

**Imaging**

- Pelvic ultrasound
- Hysterosonogram/Sonohysterogram

**Age specific issues in evaluation:**

**Adolescent**
- Anovulation due to immaturity of H-P-O axis
- Unopposed estrogen stimulation of endometrium
- Rule out pregnancy
- Blood dyscrasias common as etiology of menorrhagia
- Strategies for respectful pelvic exam
- Consider ultrasound

**Childbearing/Reproductive age woman**
- Pregnancy complications
- Organic lesions more common
- Pap smear
- Consider hypothyroidism and hyperprolactinemia
- Possible evaluation of endometrium with endometrial biopsy

**Perimenopausal woman**
- MUST rule out malignant and pre-malignant conditions of uterus and cervix
- Anovulatory cycles prevalent
- Consider endometrial sampling
- Consider hypothyroidism and hyperprolactinemia

**Postmenopausal woman**
- Endometrial cancer until proven otherwise
- MUST sample endometrium

**Treatment options for AUB:**

**Non-hormonal options:**
- NSAIDs for menorrhagia
- Iron supplementation

**Hormonal options:** (if NO malignancy)
- OCPs
- HRT
- Cyclic progesterone
- Thyroid replacement
- Bromocriptine

**Surgical options:**
- Dilation and curettage
- Hysteroscopy
- Hysterectomy
- Myomectomy
- Endometrial ablation

**Amenorrhea**

Primary amenorrhea: lack of menses by age 16
- More likely due to congenital abnormality, genetic disorder, or defective gonad

Secondary amenorrhea: Cessation of menses for > 3 months
Most common cause of secondary amenorrhea is pregnancy

H-P-O axis dysfunction:
- Alteration in pulsatile GnRH secretion
- Diagnosis of exclusion

Functional causes: weight loss, excessive exercise, obesity, head trauma
Neoplastic causes: pituitary adenoma, craniopharyngioma
Psychiatric causes: anxiety, eating disorders
Pharmacologic causes: tranquilizers, marijuana

Ovarian Failure:
- Menopause
  - Hypoestrogenic symptoms
  - Elevated FSH, decreased estradiol

- Premature
  - Autoimmune
  - Alkylating chemotherapeutic agents

Gonadal dysgenesis (Turner’s syndrome)
- 45 XO or mosaic
- congenital webbed neck, low set ears
- cubitus valgus, short stature
- shield chest, high-arched palate, increased pigmented nevi
- association with congenital cardiac disease

Androgen insensitivity
- Genotypic male, phenotypic female
- Normal breast development
- Sparse axillary and pubic hair
- Presence of vaginal dimple
- Absence of female genital organs
- Testicles in inguinal canal or intraabdominal
- Orchiectomy

Polycystic ovarian syndrome:
- Amenorrhea, obesity, hirsutism, acne
- Hyperandrogenism
- Hyperinsulinemia

Outflow obstruction:
Imperforate hymen: bulging at introitus
Molimina without bleeding

Absent uterus/vagina: secondary sex characteristics present
Mayer-Rokitansky-Kuster-Hauser syndrome
Associated renal and skeletal anomalies

Asherman’s syndrome: scarring of uterine cavity after D&C
Increased risk with infection, retained POCs

**Evaluation of Amenorrhea:**

**History**
- Sexual activity and contraception use/need
- Menopausal symptoms
- Medication use
- Prior surgeries

**History (cont.)**
- Eating habits
- Exercise habits
- Weight changes
- Hirsuitism
- Galactorrhea

**Physical Exam**
- Evaluate for breast budding, axillary and pubic hair
- Pelvic exam

**Laboratory evaluation**
- Pregnancy test
- TSH, Prolactin levels
- Androgen levels
- FSH, estradiol
- Karyotyping

**Diagnostic studies**
- Pelvic Ultrasound
- Pelvic MRI
- MRI of sella turcica

**Progesterone challenge**

**Treatment of Amenorrhea:**
Diagnosis dependent
Hormonal
Behavioral
Modification of nutrition/exercise
Surgical reconstruction
Non-surgical reconstruction

For an enhanced understanding peruse this supplemental reading:
Chapter 4: Female Reproductive Physiology
Chapter 32: Puberty and Disorders of Pubertal Development
Chapter 33: Amenorrhea, Oligomenorrhea, and Hyperandrogenic Disorders