CLINICAL ASPECTS OF THE MENSTRUAL CYCLE

M2 Reproduction Sequence

Caren M. Stalburg, M.D., M.A.
Clinical Assistant Professor
Department of Obstetrics and Gynecology
Department of Medical Education

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
Dysmenorrhea: 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
etiologies: 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:	Dilitation 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:
Hacker, Moore, Gambone, Essentials of Obstetrics and Gynecology 4th edition
Chapter 4: Female Reproductive Physiology
Chapter 32: Puberty and Disorders of Pubertal Development
Chapter 33: Amenorrhea, Oligomenorrhea, and Hyperandrogenic Disorders