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Clinical Aspects of the Menstrual Cycle

M2 - Reproduction Sequence

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Winter, 2009



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 variations due to age
6. Understand the pathogenesis of primary and secondary amenorrhea
7. Explain the evaluation and treatment of amenorrhea

Resources in Syllabus

- Study questions
- Vander' s Human Physiology
- Outline
- Powerpoint

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 due to anovulation or anovulatory cycle
- **Oligomenorrhea:** Menstrual interval greater than 35 days

Key terms and definitions

- **Menorrhagia:** Regular menstrual intervals, excessive flow and duration
- **Metrorrhagia:** Irregular menstrual intervals, excessive flow and duration
- **Anovulation/anovulatory:** Menstrual cycle without ovulation
- **Mittelschmerz:** Pain with ovulation
- **Molimina:** Symptoms preceding menses
- **Dysmenorrhea:** Menstrual cramping/pain

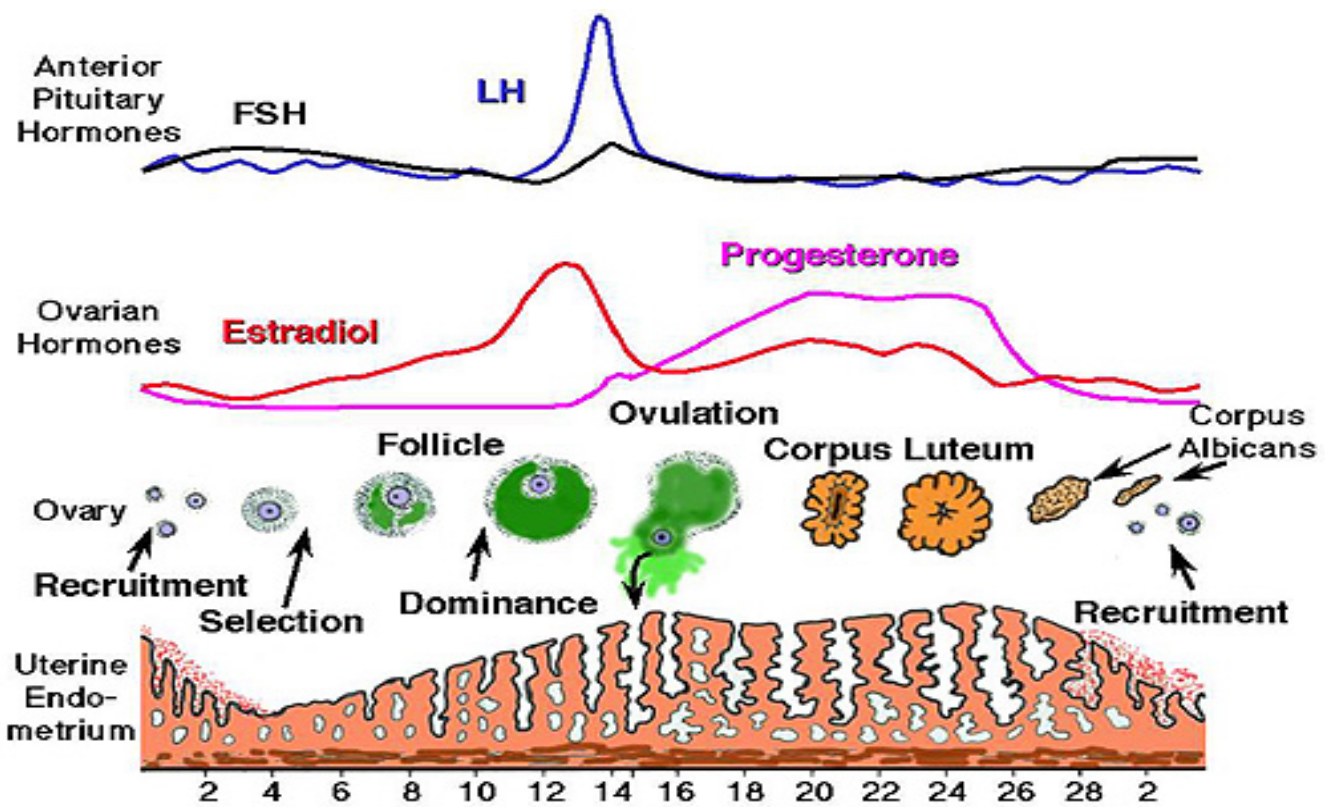
Key terms and definitions

- **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, cervical dilation
- **Complete abortion:** Products of conception expelled, cervical os closed, minimal bleeding
- **Missed abortion:** Embryonic demise, no products of conception passed

Overview

- Normal Menstruation
- Dysmenorrhea
- Abnormal Bleeding
 - Pregnancy related
 - Anovulation
 - Anatomic causes
 - Age-specific evaluation
- Amenorrhea

Chaos Theory ??



Ovarian Two Cell System

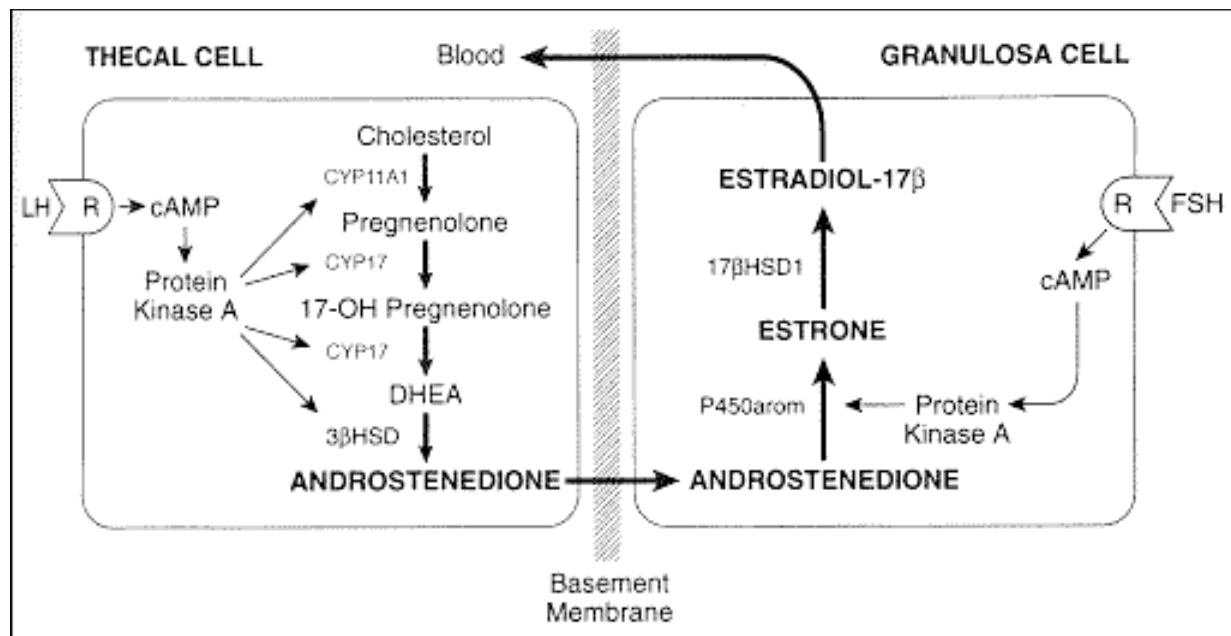


Figure 3. Two-cell, two-gonadotropin hypothesis of regulation of estrogen synthesis in the human ovary. Adapted by Carr, BR. Diseases of the ovary and Reproductive Tract.

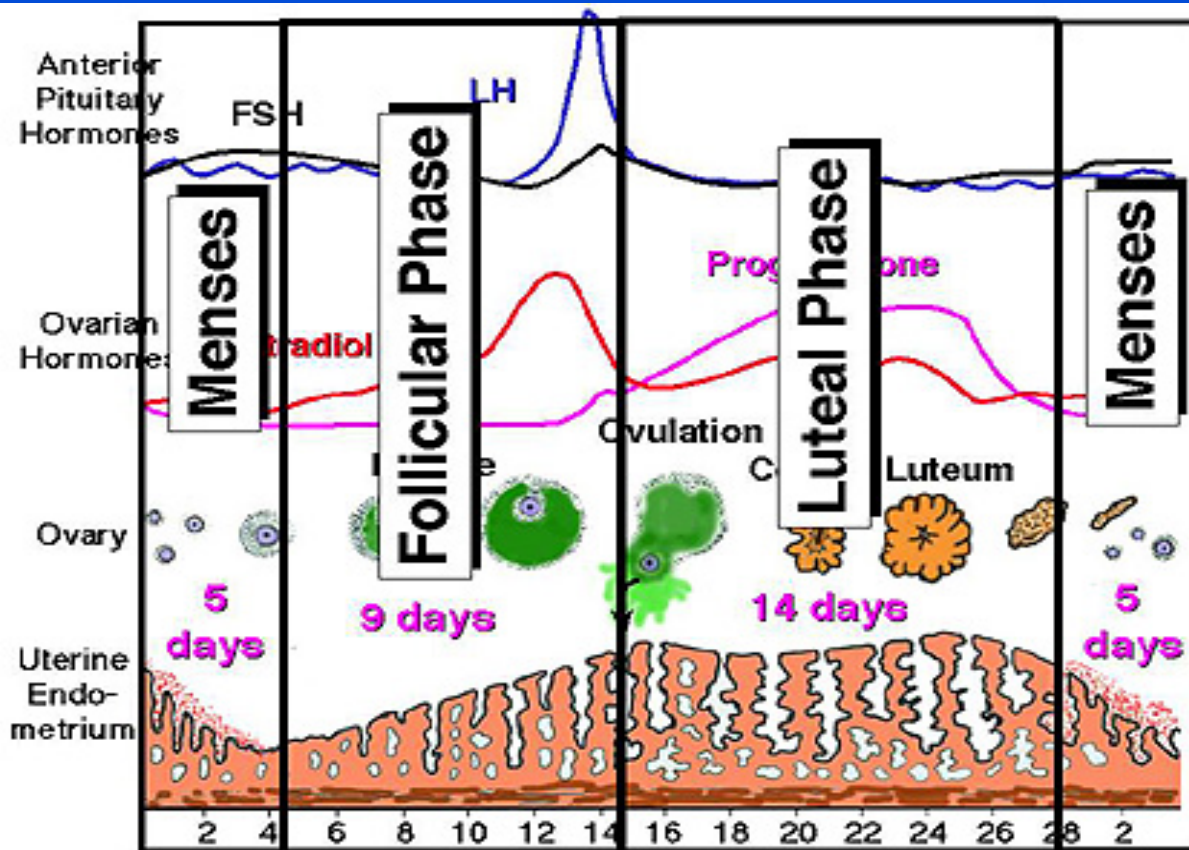
Normal Menstruation



- Highest rate of anovulatory cycles <20 or >40 yo age
- Duration of flow 2-8 days
- Amount of flow dependent on how rapid endometrium sheds
- Incomplete shedding = heavier flow, blood loss anemia

Normal Menstruation

- Count from 1st day of flow
- Normal 21-35 days
- 14 day luteal phase
- Cyclic events
 - Vaginal discharge
 - Mittelschmerz
 - Mollimina
 - PMS???



Premenstrual Syndrome

- Prevalence?
 - Variable symptoms, retrospective association
 - Cultural conditioning: negative view of menstruation
- Myriad of luteal phase symptoms in varying degrees
- Premenstrual Dysphoric Disorder
- Treatment options:
 - Inhibition of prostaglandin release
 - SSRIs
 - OCPs

Dysmenorrhea

- Primary
- Secondary
- Chronic pelvic pain

“Doctor, I’ m bleeding funny”

- What is your first question?
- How do you help her define “bleeding funny”?
- How do you quantify her bleeding?

Differential diagnosis of Abnormal Uterine Bleeding

- AUB due to pregnancy
- Dysfunctional uterine bleeding/anovulation
- Anatomical causes
- Systemic causes

AUB due to pregnancy

- First trimester bleeding
- Large differential diagnosis
 - Implantation bleeding at time of missed menses
 - Abortion/Miscarriage
 - Ectopic pregnancy
 - Molar pregnancy/gestational trophoblastic disease
 - Normal early pregnancy
- PE, beta hCG, pelvic USN, Rh determination

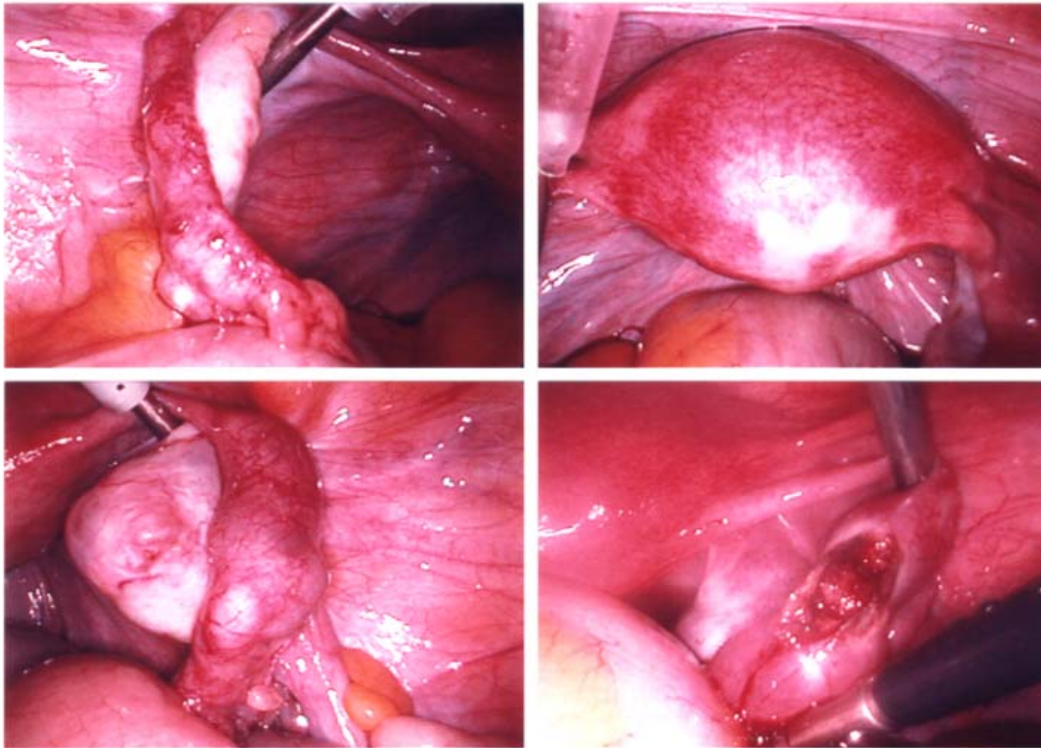
Abortion/Miscarriage

- Threatened
- Incomplete
- Complete
- Bleeding in first trimester
- Bleeding, cx dilatation, some products expelled
- Min. bleeding, cx closed, products expelled

Ectopic Pregnancy

- Implantation of pregnancy outside of uterus
- Risk factors
 - STDs, PID, cervical dysplasia, ART
- Abdominal pain, amenorrhea, vaginal bleeding
- Physical exam findings: ruptured/unruptured
- Quantitative hCG, USN
- Medical vs. surgical management

Unruptured ectopic pregnancy



Molar Pregnancy

Gestational trophoblastic neoplasia

Hydatidiform mole

- **COMPLETE**

- Diploid
- 46 XX
- Paternal only
- “Empty egg”
- Rarely a fetus

- **PARTIAL/INCOMPLETE**

- Triploid
- 69XXY (80%)
- Dispermy
- Fetus often present

Differential diagnosis of Abnormal Uterine Bleeding

- AUB due to pregnancy
- Dysfunctional uterine bleeding/anovulation
- Anatomical causes
- Systemic causes

Dysfunctional Uterine Bleeding

- Irregular bleeding unrelated to anatomical causes
- Intermittent anovulation = occasional ovulation
- Constant, non-cyclic exposure to estrogen
- Sloughing of proliferative phase endometrium

Dysfunctional Uterine Bleeding

- H-P-O axis dysfunction
 - Thyroid dysfunction
 - Decrease T4, increase TRH
 - TRH causes PRL release
 - Increased PRL causes increased DA release
 - Both PRL and DA inhibit pulsatile GnRH
 - Hyperprolactinemia
 - Stress
 - Exercise changes

Polycystic Ovarian Syndrome

A special case of DUB

- Persistent anovulation
- Polycystic ovaries
- Obesity
- Hirsutism
- Insulin resistance
- Hyperinsulinemia
- Hyperandrogenism

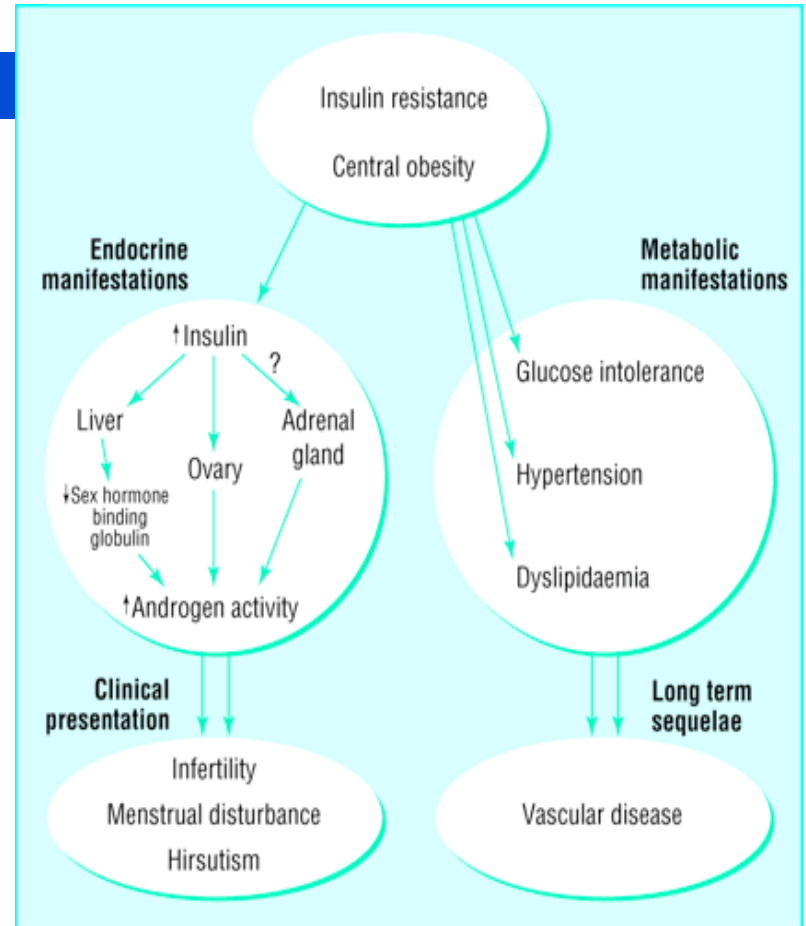
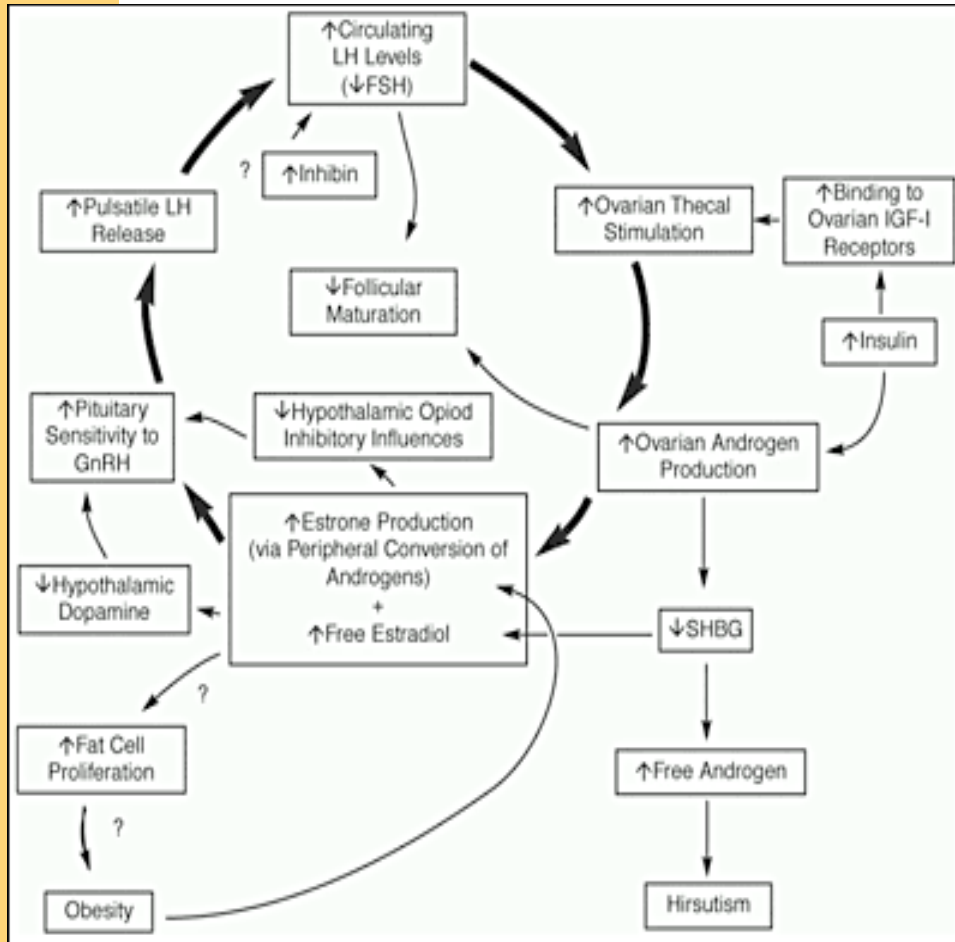
Polycystic Ovarian Syndrome

A special case of DUB

- Steady state of high LH and low FSH
- Increased androgens
 - Follicular atresia, hirsutism
 - Unopposed estrogen
- Insulin resistance and obesity
- Metabolic syndrome (3 or more of the following)
 - HTN, low HDL, elevated triglycerides, abdominal obesity, elevated fasting glucose $>110\text{mg/dL}$

Hyperinsulinemia probably induces hyperandrogenism

What's in a name???



Differential diagnosis of Abnormal Uterine Bleeding

- AUB due to pregnancy
- Dysfunctional uterine bleeding/anovulation
- Anatomical causes
- Systemic causes

AUB due to uterine lesions

- Uterine leiomyomas
- Endometrial polyps
- Endometritis
- Endometrial carcinoma

AUB due to cervical lesions

- Cervical carcinoma
- Cervical dysplasia
- Endocervical polyps
- Cervicitis

AUB due to vulvar/vaginal lesions

- Carcinoma
- Trauma/lacerations
- Foreign bodies
- Pessaries

Differential diagnosis of Abnormal Uterine Bleeding

- AUB due to pregnancy
- Dysfunctional uterine bleeding/anovulation
- Anatomical causes
- **Systemic causes**

AUB due to systemic causes

- Intrinsic bleeding disorders
 - Blood dyscrasias
- Iatrogenic bleeding abnormality
 - Treatment with anti-coagulants
- Hepatic or renal failure
 - Alterations in estrogen metabolism

“Doctor, I’ m bleeding funny”

- What is your first question?
- How do you help her define “bleeding funny”?
- How do you quantify her bleeding?

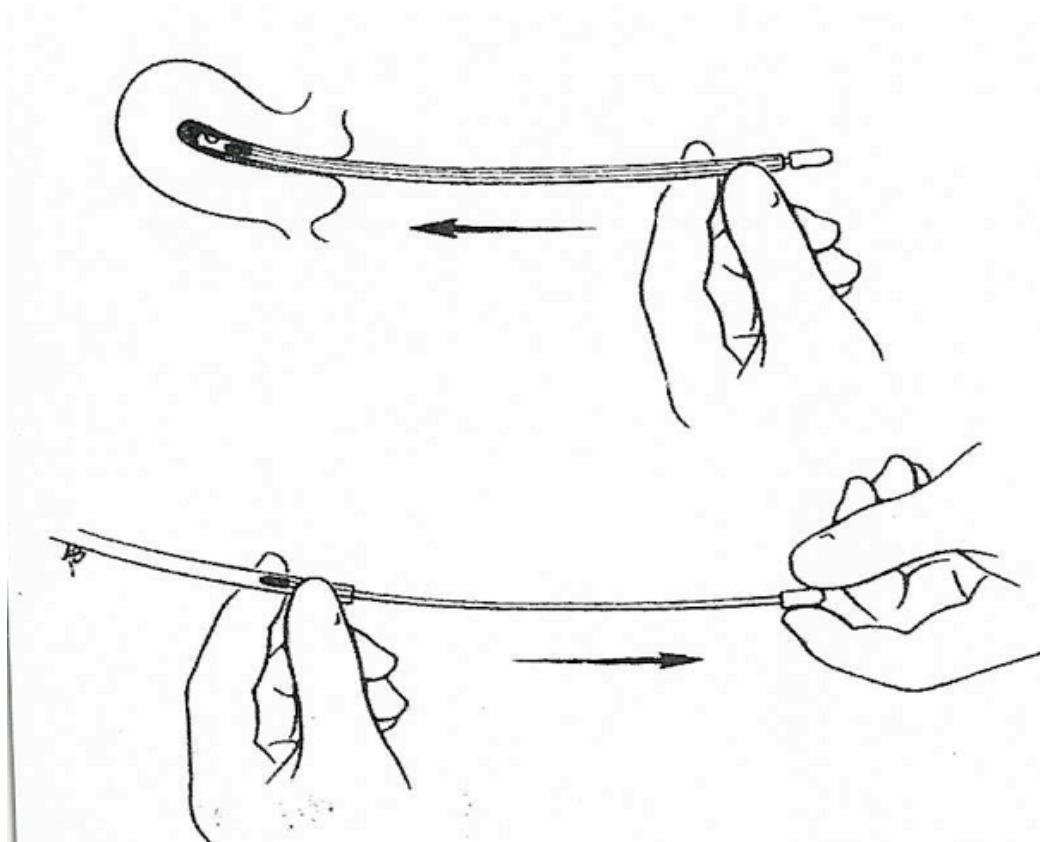
- How do you diagnose the cause of her bleeding?

Evaluation of AUB

Exclude pregnancy

- History/Physical
 - Bleeding pattern
 - Medications
 - Physical findings
- Laboratory testing
- Imaging
 - USN techniques

Endometrial biopsy



Ultrasounds....



Age specific issues in evaluation: Adolescents

15 yo noted menarche at the age of 14 but has only had 3 or 4 periods since. She has missed school because of “bad cramps” and “massive bleeding”

Age specific issues in evaluation: Reproductive Age

24 yo woman who can't predict when her period will come and when it does it is very heavy and painful. Some months it's ok though.

Age specific issues in evaluation: Perimenopausal

49 yo woman now with heavy irregular menses
but they used to be “like clockwork”

Age specific issues in evaluation: Post-Menopausal

69 yo woman, no vaginal bleeding for last 10 years noted two days of spotting like light period

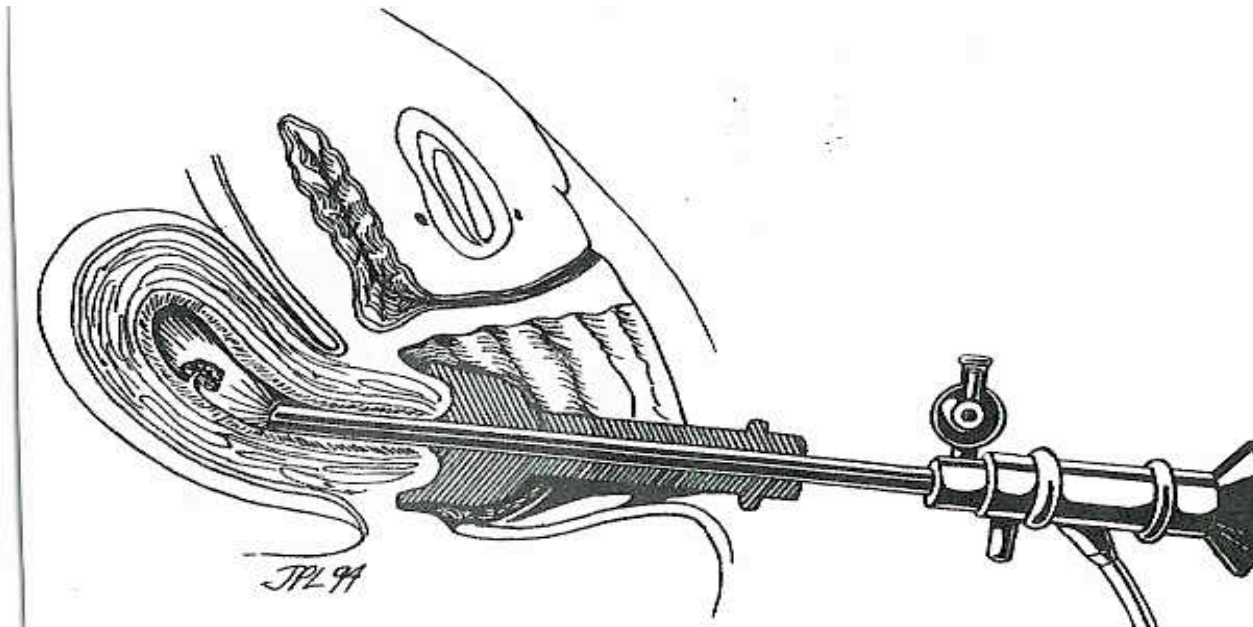
Treatment options for AUB: Medical

- Non-hormonal
 - NSAIDs
 - Iron supplementation
- Hormonal (if NO malignancy)
 - OCPs
 - HRT
 - Cyclic progesterone
 - Thyroid replacement
 - Bromocriptine

Treatment options for AUB: Surgical

- Dilatation and curettage
- Hysteroscopy
- Hysterectomy
- Myomectomy
- Endometrial ablation

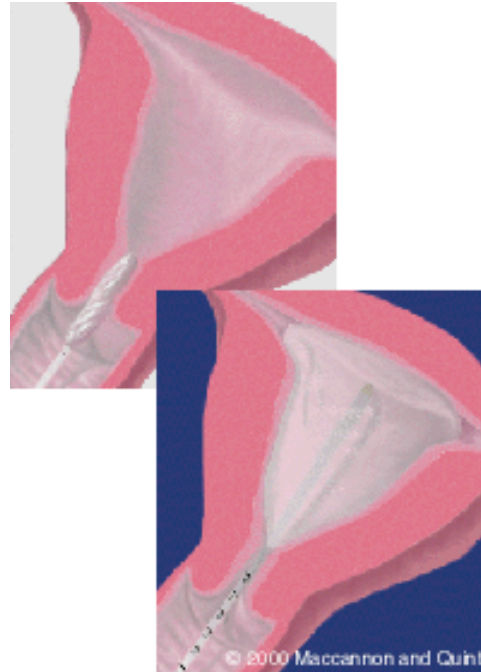
Hysteroscopy



Hysterectomy

Image of
hysterectomy
procedure
removed

Endometrial Ablation



“Doctor, I’ m not getting my period”

(blank, like no period.....)

Amenorrhea

- Primary--lack of menses by age 16
 - Why?
- Secondary--cessation of menses for > 3 mos.
- Most common cause of secondary amenorrhea is..... PREGNANCY

Secondary Amenorrhea

- Absence of ovulation
- Relative progesterone deficiency
- Inadequate growth of endometrium due to decreased estrogen levels

H-P-O axis dysfunction

Alteration in pulsatile GnRH secretion

Diagnosis of exclusion

Multiple causes

exercise, weight, stress, medications, tumor

Ovarian Failure

- Menopause
 - Hypoestrogenic state
- Premature ovarian failure
 - Autoimmune, chemotherapy
- Gonadal dysgenesis (Turner's syndrome)
 - 45XO, physical findings
- Androgen insensitivity
 - Genotypic male, phenotypic female
 - Absent mullerian system
 - 46XY with testicles, at risk for testicular cancer

Outflow Obstruction Leading to Amenorrhea

- Imperforate hymen
 - Bulging at hymen
 - Membrane or partial membrane
- Absent uterus/vagina
 - Mayer-Rokitansky-Kuster-Hauser Syndrome
- Asherman's syndrome
 - Scarring of uterine cavity after D&C with interruption of basalis layer

Evaluation of Amenorrhea

- History
- PE
- Labs
 - Rule out pregnancy
- Diagnostic studies
 - USN, MRI, MRI of sella turcica
- Progesterone challenge
 - What does withdrawal bleed confirm?

Treatment of Amenorrhea

- Diagnosis dependent
- Hormonal
- Behavioral
- Surgical reconstruction
 - Neovagina
- Non-surgical reconstruction
 - Vaginal dilators

Summary

- What constitutes normal uterine bleeding?
- Rule out pregnancy related causes of AUB
- Is it anovulatory bleeding?
- Is there a specific lesion causing bleeding?
- What is the most likely etiology based on patient's age?
- Why is there no bleeding?

Additional Source Information

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Slide 11: Williams Textbook of Endocrinology 9th edition. WB Saunders, Philadelphia, p.751-817.

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Slide 38: Source Undetermined

Slide 39: Source Undetermined (All Images)

Slide 46: JPL, 94

Slide 48: Maccannon and Quint, 2000