
بسم الله الرحمن الرحيم

Abnormal Uterine Bleeding

Department of Obstetrics and Gynecology

Objectives

- Physiology
- Definitions
- Etiologies
- Evaluation
- Management
  - Medical
  - Surgical

Phases of Reproductive Cycle

- Follicular phase
- Ovulation
- Luteal phase
- Menses

Phases of Reproductive Cycle

- Follicular phase
  - Onset of menses to LH surge
  - 14 days (varies)
  - Dominant follicle
    - greatest number of granulosa cells and FSH receptors
- Ovulation
- Luteal phase

Phases of Reproductive Cycle

- Follicular phase
- Ovulation
  - 30-36 hours after LH surge
- Luteal phase
  - LH surge to menses
  - 14 days (constant)

Menses

- Involution of corpus luteum
- Decrease progesterone and estrogen
- 20-60 cc of dark blood and endometrial tissue

How does Ovulation happen?

- Positive feedback to pituitary from estradiol
- LH surge
- Ovulation triggered
- Granulosa and theca cells now produce progesterone
- Oocyte expelled from follicle
- Follicle converts to corpus luteum

Luteal Phase

- Predominance of progesterone
- Abdominal bloating
- Fluid retention
- Mood and appetite changes

Phases of Reproductive Cycle

- Endometrium
  - Proliferative phase
  - Secretory phase

Abnormal uterine bleeding

- Change in frequency, duration and amount of menstrual bleeding

Definitions

- Normal menses
- Every 28 days +/- 7 days
- Mean duration is 4 days.
- More than 7 days is abnormal.

Normal Menses

Average blood loss with menstruation is 35-50cc.

95% of women lose <60cc.

Definitions

Menorrhagia:

Prolonged bleeding

> 7 days or > 80 cc

occurring at regular intervals.

Frequency of AUB

- Menorrhagia occurs in 9-14% of healthy women.
- Most common Gyn disorder of reproductive age women

Definitions

Metrorrhagia:

Uterine bleeding occurring at irregular but frequent intervals.

Definitions

Menometrorrhagia:

Prolonged uterine bleeding occurring at irregular intervals.

Definitions

Oligomenorrhea:

- Reduction in frequency of menses
- Between 35 days and 6 months.

Definitions

Amenorrhea:

- Primary amenorrhea
- Secondary amenorrhea
  - No menses for 3-6 months

Primary amenorrhea

- No menses by age 13
  - No secondary sexual development
- No menses by age 15
  - Secondary sexual development present

Definitions

- Menarche
  - average age 12.43 years
- Menopause
  - average age 51.4 years
- Ovulatory cycles for over 30 years

Menstrual bleeding stops IF:

- Prostaglandins cause contractions and expulsion
- Endometrial healing and cessation of bleeding with increasing estrogen

Systemic Etiologies

- Coagulation defects
  - ITP
  - VonWillebrand's

Routine screening for coagulation defects should be reserved for the young patient who has heavy flow with the onset of menstruation.

Comprehensive Gynecology, 4th edition

von Willebrand's Disease is the most common inherited bleeding disorder with a frequency of 1/800-1000.

Harrison's Principles of Internal Medicine, 14th edition

Hypothyroidism can be associated with menorrhagia or metrorrhagia.

The incidence has been reported to be 0.3-2.5%.

Wilansky, *et al.*, 1989

Most Common Causes of Reproductive Tract AUB

- Pre-menarchal
  - Foreign body
- Reproductive age
  - Gestational event
- Post-menopausal
  - Atrophy

Reproductive Tract Causes

- Gestational events
- Malignancies
- Benign
  - Atrophy
  - Leiomyoma
  - Polyps
  - Cervical lesions
  - Foreign body
  - Infections

Reproductive Tract Causes

- Gestational events
  - Abortions
  - Ectopic pregnancies
  - Trophoblastic disease
  - IUP

Reproductive Tract Causes

- Malignancies
  - Endometrial
  - Ovarian
  - Cervical

10% of women with postmenopausal bleeding will be diagnosed with endometrial cancer

Karlsson, *et al.*, 1995

FIGO System

- PALM-COEIN
  - Polyp
  - Adenomyosis
  - Leiomyoma
  - Malignancy and hyperplasia
  - Coagulopathy
  - Ovulatory disorders
  - Endometrium
  - Iatrogenic
  - Not classified

Reproductive Tract Causes of Benign Origin

- Uterine
- Vaginal or labial lesions
- Cervical lesions
- Urethral lesions
- GI

Reproductive Tract Causes of Benign Origin

- Uterine
  - Pregnancy
  - Leiomyomas
  - Polyps
  - Hyperplasia
  - Carcinoma

Proposed Etiologies of Menorrhagia with Leiomyoma

- Increased vessel number
- Increased endometrial surface area
- Impeded uterine contraction with menstruation
- Clotting less efficient locally

Wegienka, *et al.*, 2003

Leiomyoma in any location is associated with increased risks of gushing or high pad/tampon use.

Wegienka, *et al.*, 2003

Reproductive Tract Causes of Benign Origin

- Uterine
- Vaginal or labial lesions
  - Carcinoma
  - Sarcoma
  - Adenosis
  - Lacerations
  - Foreign body

Reproductive Tract Causes of Benign Origin

- Uterine
- Vaginal or labial lesions
- Cervical lesions
  - Polyps
  - Condyloma
  - Cervicitis
  - Neoplasia

Causes of Benign Origin

- Uterine
- Vaginal or labial lesions
- Cervical lesions
- Urethral
  - Caruncle
  - Diverticulum
- GI
  - Hemorrhoids

Iatrogenic Causes of AUB

- Intra-uterine device
- Oral and injectable steroids
- Psychotropic drugs
  - MAOI's

- Physiology of Abnormal Uterine Bleeding

With anovulation a corpus luteum is NOT produced and the ovary thereby fails to secrete progesterone.

However, estrogen production continues, resulting in endometrial proliferation and subsequent AUB.

PGE_2 → vasodilation

$PGF_{2\alpha}$ → vasoconstriction

Progesterone is necessary to increase arachidonic acid, the precursor to $PGF_{2\alpha}$.

With decreased progesterone there is a decreased $PGF_{2\alpha}/PGE_2$ ratio.

Evaluation and Work-up:
Early Reproductive Years/Adolescent

- Thorough history
- Screen for eating disorder
- Labs:
  - CBC, PT, PTT,FSH, TSH, hCG

Evaluation and Work-up:
Women of Reproductive Age

- hCG, LH/FSH, CBC, TSH
- Cervical cultures
- U/S
- Hysteroscopy
- EMB

Evaluation and Work-up: Post-menopausal Women

- Transvaginal U/S
- EMB

Causes of Postmenopausal Bleeding

60% atrophy

- Karlsson, et al., 1995

An endometrial cancer is diagnosed in approximately 10% of women with PMB.[1]

PMB incurs a 64-fold increased risk for developing endometrial CA.[2]

[1]Karlsson, *et al.*, 1995

[2]Gull, *et al.*, 2003

Not a single case of endometrial CA was missed when a <4mm cut-off for the endometrial stripe was used in their 10 yr follow-up study.

Specificity 60%, PPV 25%, NPV 100%

Gull, *et al.*, 2003

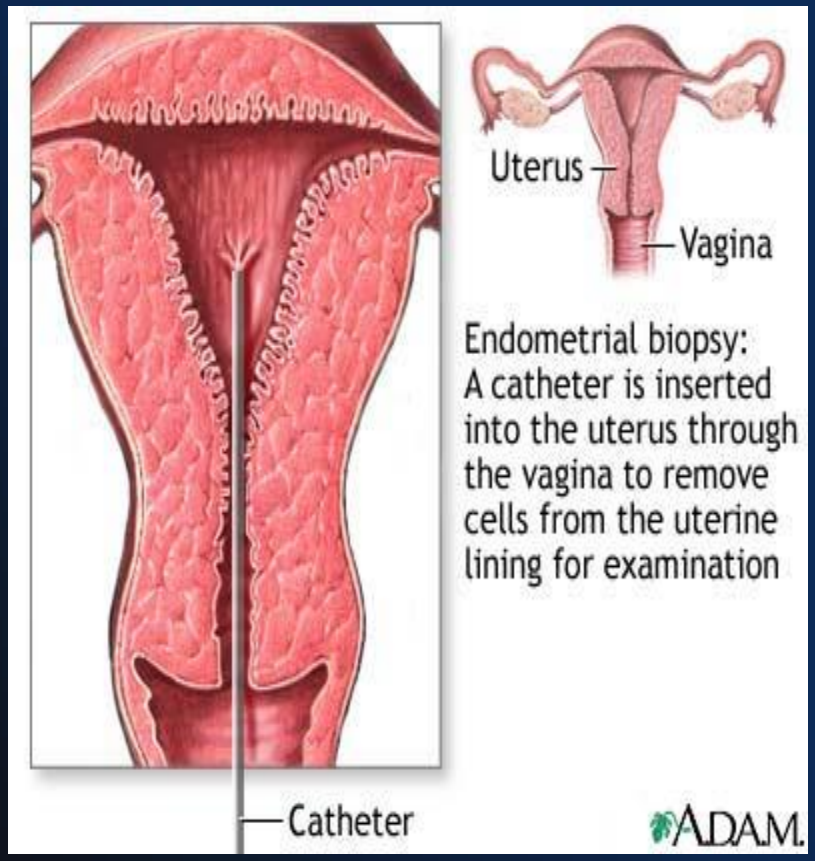
EMB

Complications rare. Rate of perforation 1-2/1,000. Infection and bleeding rarer.

Comprehensive Gynecology, 4th ed.

EMB

- Sensitivity 90-95%
- Easy to perform
- Numerous sampling devices available



Incidence of Endometrial Cancer in Premenopausal Women

2.3/100,000 in 30-34 yr old

6.1/100,000 in 35-39 yr old

36/100,000 in 40-49 yr old

ACOG Practice Bulletin #14, 2000

Therefore, based upon age alone, an EMB to exclude malignancy is indicated in any woman > 35 years of age with AUB.

ACOG Practice Bulletin #14, March 2000

Endometrial Cancer

- Most common genital tract malignancy. Incidence 1 in 50!
- 4th most common malignancy after breast, bowel, and lung.
- 34,000 new cases annually
- > 6,000 deaths annually

Endometrial Cancer Risk Factors

- Nulliparity: 2-3 times
- Diabetes: 2.8 times
- Unopposed estrogen: 4-8 times
- Weight gain
  - 20 to 50 pounds: 3 times
  - Greater than 50 lbs: 10 times!

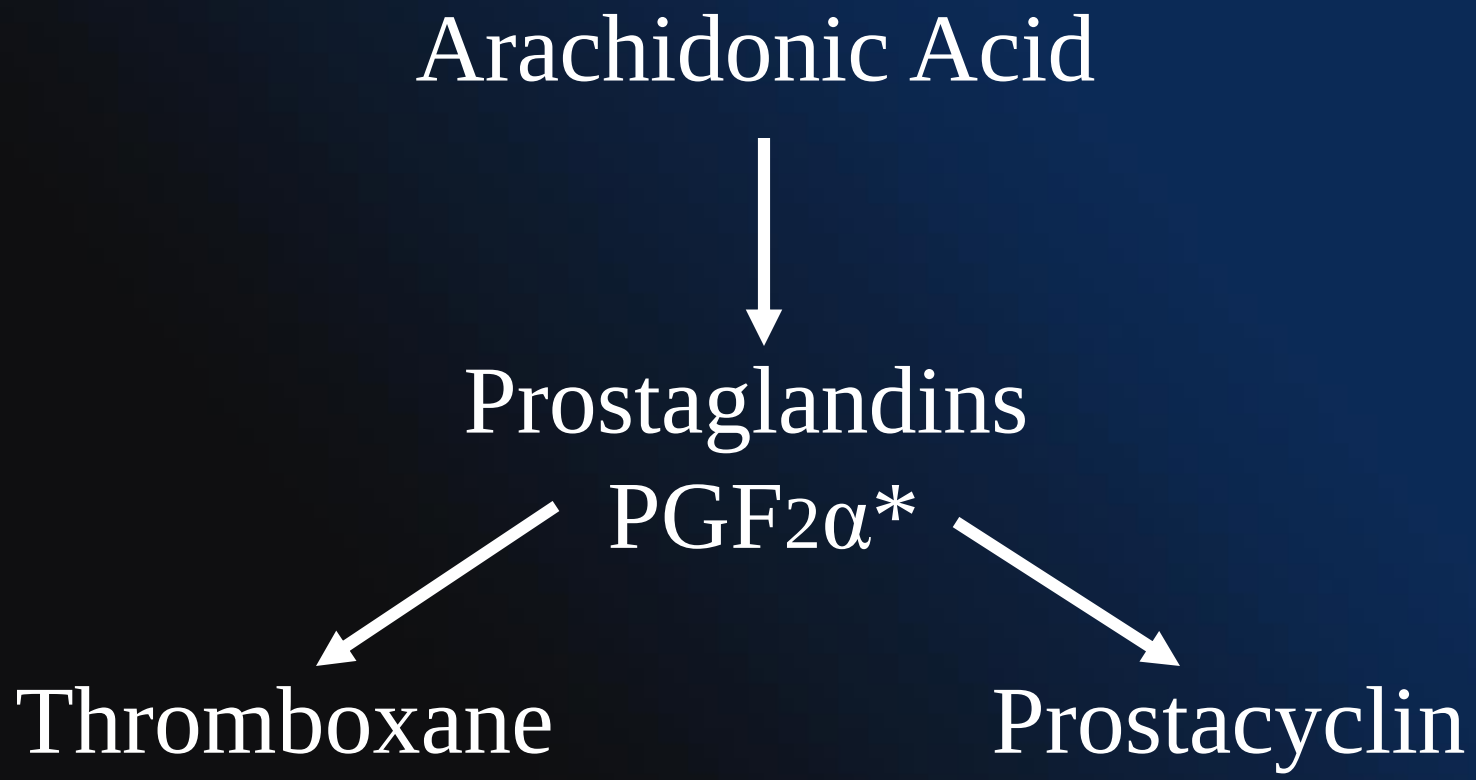
AUB Management Options:

- Progesterone
- Estrogen
- OCP’s
- NSAIDs
- Surgical

Progestins: Mechanisms of Action

- Inhibit endometrial growth
  - Inhibit synthesis of estrogen receptors
  - Promote conversion of estradiol → estrone
  - Inhibit LH
- Organized slough to basalis layer
- Stimulate arachidonic acid formation

Management: Progesterone Cyclooxygenase Pathway



*Net result is increased PGF2α/PGE ratio

Progestational Agents

- Cyclic Provera 2.5-10mg daily for 10-14 days
- Continuous Provera 2.5-5mg daily
- DepoProvera® 150mg IM every 3 months
- Levonorgestrel IUD (5 years)

Endometrial Hyperplasia

*EMB path report

simple hypersplasia WITHOUT atypia.

*Progesterone therapy

Provera® 5-10 mg daily

Mirena IUD

*Repeat EMB in 3-6 months

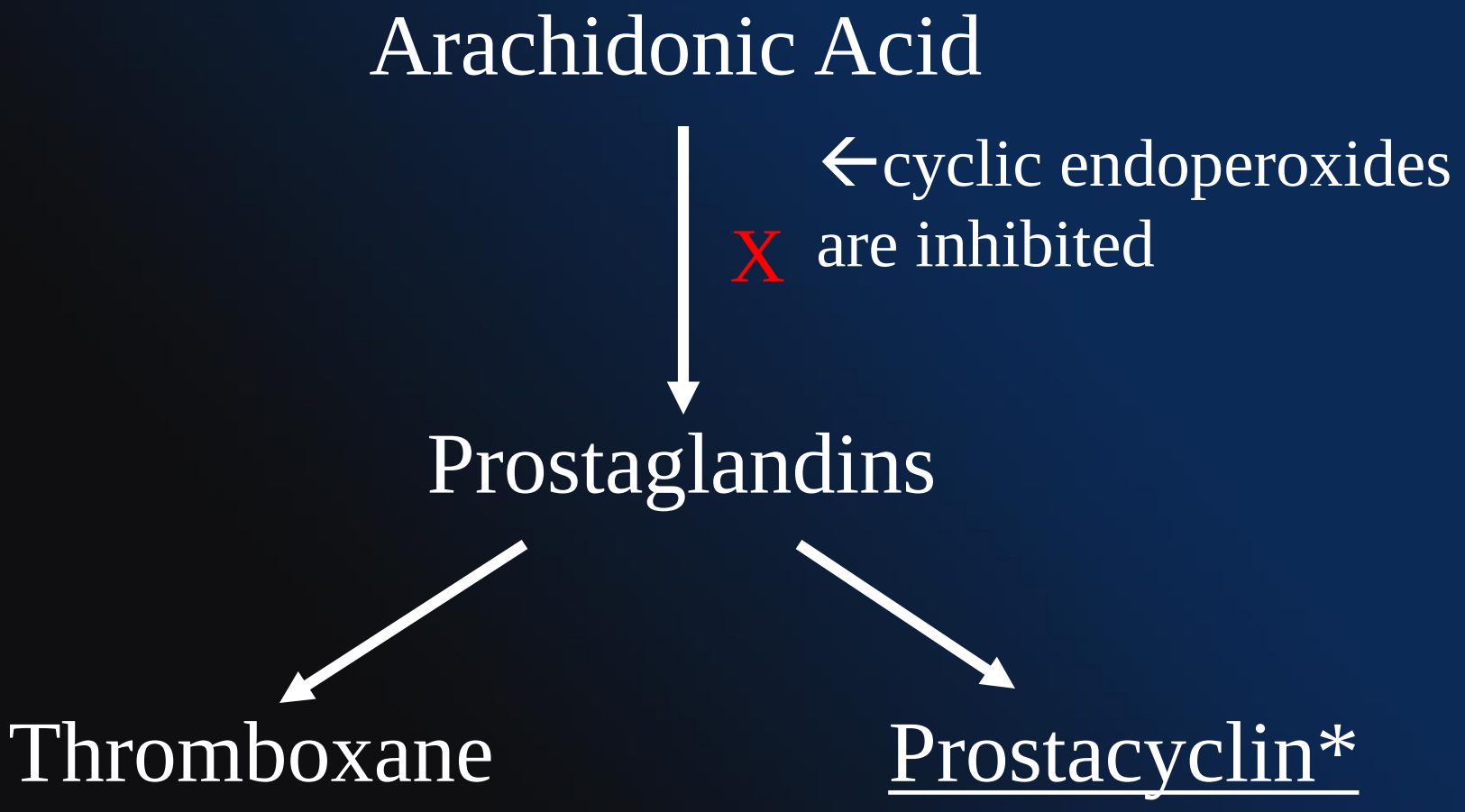
Management acute Bleeding: Estrogen

IV Estrogen 25mg q6 hours

OR

Premarin® 1.25mg, 2 tabs QID

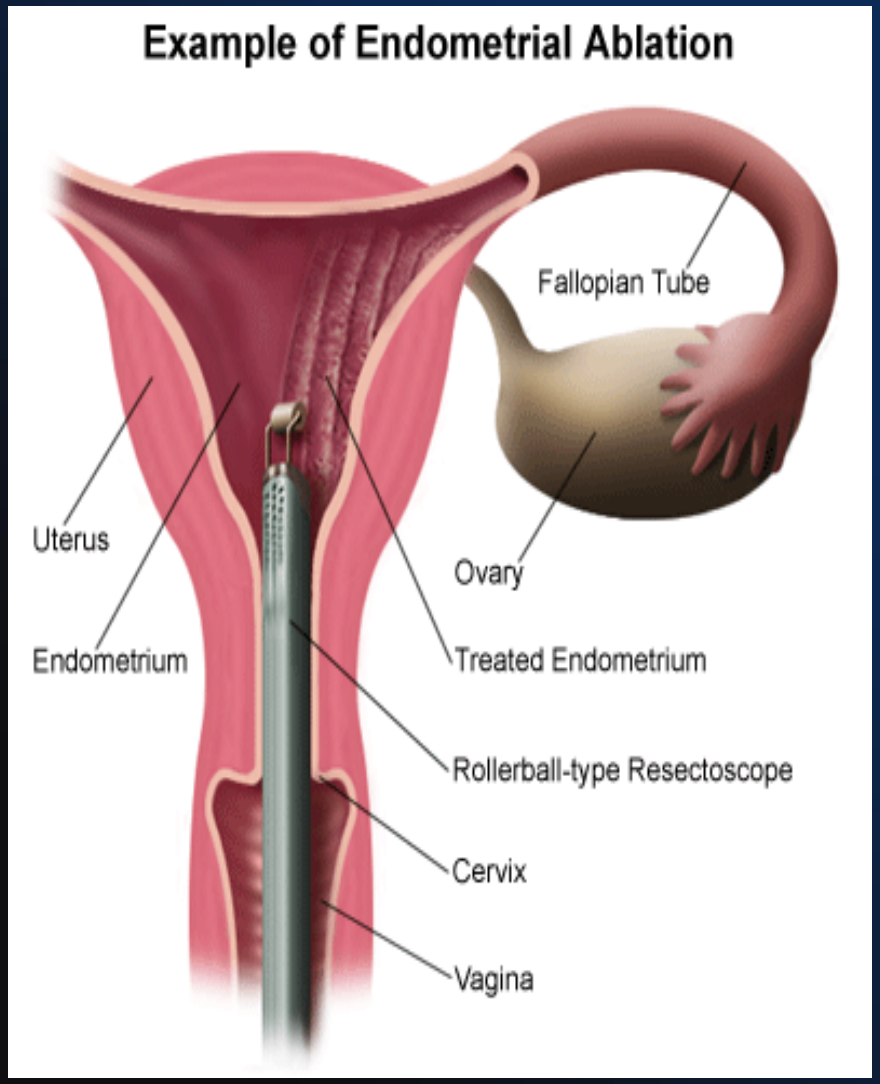
AUB Management: NSAIDs

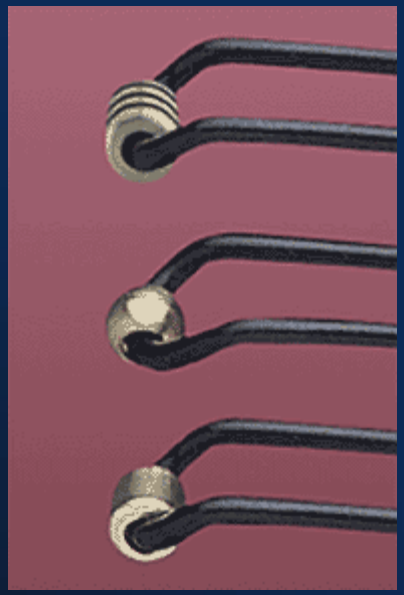


*Causes vasodilation and inhibits platelet aggregation

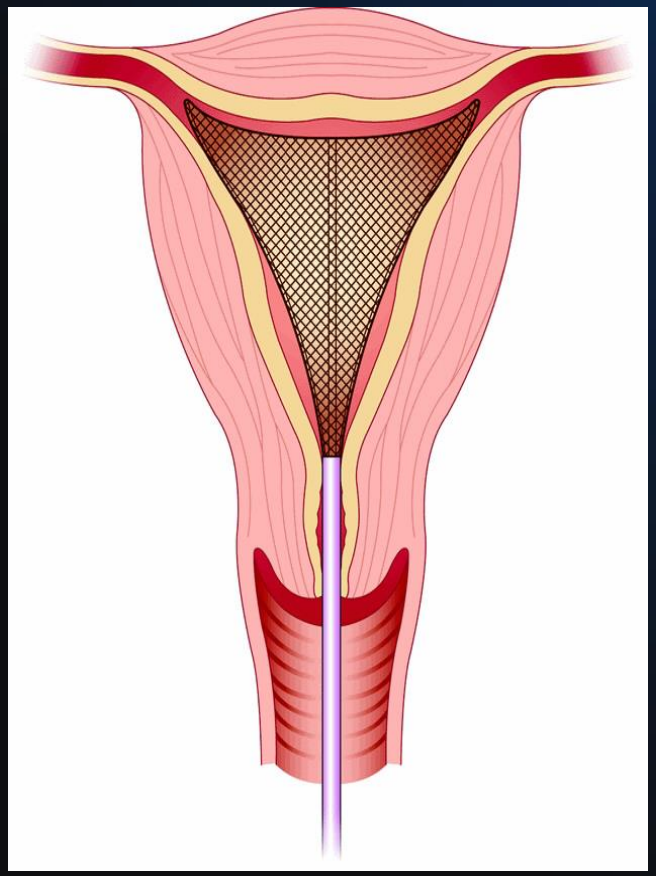
Surgical Options:

- Endometrial Ablation
- Hysterectomy

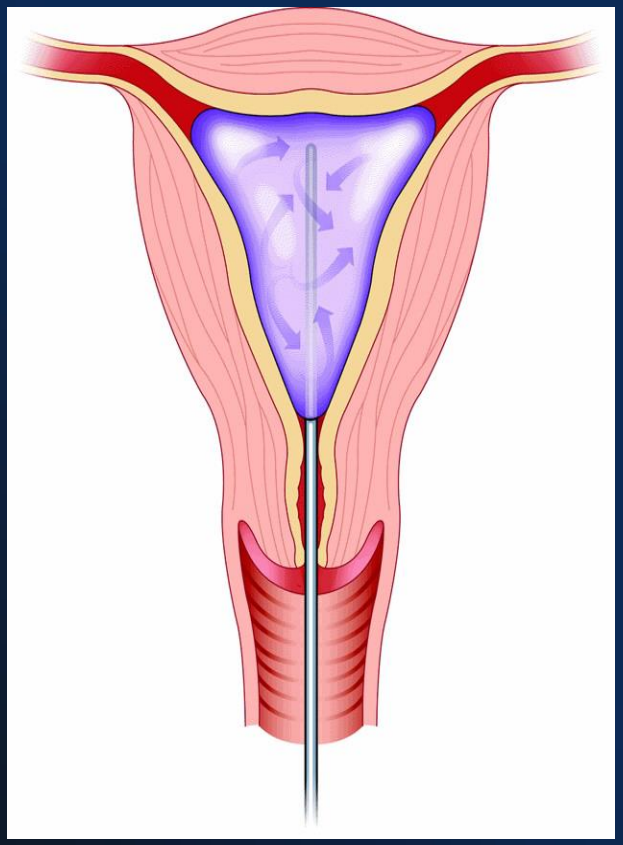

Example of Endometrial Ablation
Fallopian Tube
Uterus
Ovary
Endometrium
Treated Endometrium
Rollerball-type Resectoscope
Cervix
Vagina



NovaSure



ThermaChoice



Summary

- Think coagulation defect in the menarchal adolescent patient with severe menorrhagia
- Gestational events are the single most likely cause of AUB in reproductive age women
- 35 yrs and older with AUB → EMB
- If Rx estrogen be sure to screen for contraindications
- Levonorgestrel IUD is excellent means to control AUB

Summary

- Most common cause of AUB in post-menopausal women is atrophy
- TVS is an excellent screening tool for the evaluation of PMB
- Women with recurrent PMB require definitive F/U
- Endometrial CA risk factors: age, obesity, unopposed estrogen, DM, and ↑BP