

•
•
•
•
•
•
•
•
•
•

Menopause and Hormone Replacement Therapy



Daniel Breitkopf, MD

Department of Obstetrics and
Gynecology

University of Texas Medical Branch

Galveston, Texas USA

• • • • • • • • •

-
-
-

Objectives

- Define the indications and contraindications for HRT
- Describe the HRT regimens in use today and their clinical usage
- Describe the management of bleeding irregularities on HRT
 - When to do an endometrial biopsy
 - When to order an ultrasound/sonohysterogram

-
-
-

Menopause

- At birth, the female has 1-2 million oocytes
- By puberty, only 440,000 oocytes remain
- By age 30-35 the number has dropped to 100,000
- Follicular maturation is induced by the pituitary release of Follicle Stimulating Hormone (FSH)

-
-
-

Menopause

- With advancing age, the remaining oocytes become increasingly resistant to FSH
- FSH gradually rises until menopause when it is usually greater than 30 mIU/ml

-
-
-

Menopause

- Menopause is defined as the absence of menstrual periods for at least 6 months in a woman over 40
- In the USA, the average age of a woman at menopause is 51
- 1% of women will undergo menopause before age 40\
- Women who smoke cigarettes and who are malnourished will have earlier menopause

-
-
-

Menopause-Symptoms

- First symptoms are often menstrual irregularities
 - Menstrual cycles shorten or lengthen
- Hot flushes and vasomotor instability
 - sudden sensation of warmth, skin of face and chest will become flushed
 - then patient will experience a chill
 - this is the result of lower estrogen levels
 - more bothersome at night

-
-
-

Menopause-Symptoms

- Sleep disturbance
 - The time it takes to fall asleep is longer than when the woman was younger
 - Total length of time asleep is shorter
- Vaginal dryness/genital tract atrophy
 - vaginal mucosa and endometrium become thin and dry
 - irritation, difficulty with sexual intercourse may develop

-
-
-

Menopause-Symptoms

- Mood changes
 - Depression, crying spells may develop
- Skin and nails
 - skin and nails become thinner
- Osteoporosis
 - Bone density is lost at a rate of 1-2% per year after menopause
 - Risk of hip and vertebral fracture increases as soon as 5 years after menopause

-
-
-

Menopause-Symptoms

- Cardiovascular Lipid changes
 - Total cholesterol increases, high density lipoprotein (HDL) cholesterol decreases, and low density lipoprotein increases
 - Risk of heart attack and stroke increases in women after menopause

-
-
-

Menopause Diagnosis

- Use symptoms and signs
- Do not depend upon FSH
- FSH will often not rise until late in the perimenopausal period and may fluctuate
- Normal FSH does not exclude the perimenopause
- Consider thyroid disease if FSH is normal
- No need for biopsy prior to starting HRT

-
-
-

Menopause-Therapy

- For asymptomatic women, no therapy or treatment is necessary
 - Calcium intake should be at least 1500 milligrams a day
 - Weight bearing exercise will help in preventing osteoporosis
- For symptomatic women or for prevention of osteoporosis and heart disease, hormonal therapy is useful

•
•Hormone Replacement Therapy (HRT)
Indications/Contraindications

- Indications

- Relief of menopausal symptoms

- Hot flashes, mood irritability, vaginal dryness, loss of libido

- Osteoporosis prevention

- Modify risk of heart attack, stroke

- Contraindications

- Undiagnosed abnormal genital bleeding

- Estrogen dependent neoplasia (Breast, Uterus)

- History of thromboembolism, stroke

- Liver dysfunction/disease

-
-
-

HRT Regimens

- Unopposed estrogen is associated with endometrial hyperplasia and carcinoma
- Progesterone withdrawal required at a minimum of every three months
- In last five years continuous suppression of the endometrium with combined therapy has become popular

-
-
-

HRT Regimens-cyclic

- Cyclic regimens
 - Conjugated estrogens(Premarin) 0.625 mg + MPA (Provera) 10 mg, 10 days every month
 - May substitute esterified estrogen
 - May use other progestins
 - Norethindrone (Aygestin) 5 mg
 - Norethindrone 0.7 mg (0.35 mg in minipill)
 - Megesterol (Megace) 20 mg
 - Micronized progesterone (Prometrium) 100 mg

-
-
-

HRT Regimens-cyclic

- Oral contraceptives
 - use of newer 20 microgram pills
 - 0.625 mg conjugated estrogens =5 micrograms of ethinyl estradiol
 - May have hot flashes during hormone free interval
 - Better control of bleeding in younger patients

-
-
-

HRT Regimens-cyclic

- Advantage to cyclic regimen is that bleeding is predictable and controlled
- Will usually have withdrawal periods (80-90%), while bleeding is less with continuous regimens
- Better for younger patients (<50) because of better cycle control

-
-
-

HRT Regimens-continuous

- Premarin(conjugated estrogens) 0.625 mg/Provera (medroxyprogesterone) 2.5 mg
- Premarin 0.625 mg/Provera 5 mg
- Advantages: compliance, induction of amenorrhea
- Disadvantages: irregular bleeding/spotting
 - 40-60% will have breakthrough bleeding in first 6 months
 - 20% will have breakthrough bleeding after one year

-
-
-

Selection of regimen

- If bleeding is heavy and irregular, try cyclic regimen first for cycle control
 - May try switch to continuous after one year
- Younger women tend to have less irregular bleeding with cyclic regimens
- Continuous better for women who are amenorrheic or older than 50
- Younger women, surgically menopausal tend to need more estrogen at first-may need to titrate dose/schedule

-
-
-

Addition of Androgen

- Use of testosterone supplements
- Postmenopausal ovary does produce testosterone
- Supplementation may improve libido and hot flashes
- Adverse effect on lipid profile

-
-
-

Side effect management

- Progestin problems: bloating, breast tenderness, mood alteration
 - try another formulation first
 - combination patch
- GI upset-nausea
 - decrease estrogen dose (can go as low as Premarin 0.3 mg)
 - use estrogen patches

-
-
-

Management of bleeding

- Expect some irregular spotting for the first three months, especially with continuous progestins
 - if persists can try increasing progestin dose or switching to cyclic regimen
 - Investigate irregular bleeding if it occurs after the first 6 months
- Always need to evaluate unscheduled bleeding on cyclic regimens
 - Withdrawal bleed should occur at the end or after the progestin is administered

•
•
•

Bleeding on HRT-evaluation

- What test should be performed on the patient with persistent irregular bleeding on HRT?
- What you are trying to rule in or out?

•
•
•

Postmenopausal Bleeding

- Etiologies:
 - Atrophic Endometritis: 30%
 - Endometrial Polyps: 10%
 - Submucosal Fibroids: 10%
 - Endometrial Hyperplasia: 10%
 - Uterine Malignancy: 10%
 - Miscellaneous: 30%

-
-
-

Postmenopausal Bleeding

- Workup
 - Endometrial biopsy
 - If Endometrial biopsy negative, observation
 - If persistent, then Dilation & Curettage
 - Hysteroscopy as adjunct to Dilation & Curettage

-
-
-

Evaluation of irregular bleeding on HRT

- Etiology
 - Hormonal-breakthrough bleeding, inadequate progesterone
 - Structural-Polyps, myomas
 - Neoplasia-hyperplasia, carcinoma
- Endometrial biopsy is the standard test for any abnormal bleeding
 - very sensitive for neoplasia
 - not sensitive for polyps, fibroids

-
-
-

Evaluation of irregular bleeding on HRT

- **Ultrasound**

- Transvaginal ultrasound allows for high resolution imaging of the endometrium
- Normal is less than 5 millimeters by most studies
- Stripe of greater than 5 millimeters requires further evaluation
- If EMB is negative, can use sonohysterography or hysteroscopy for further evaluation
- Many patients with negative EMB and thickened EMS will have polyps

-
-
-

Sonohysterography

- Saline infusion via trans-cervical catheter while performing ultrasound
- Helps to evaluate abnormally thickened endometrial stripe
- Polyps and fibroids visualized easily
- Focal thickening of stripe can be seen indicative of hyperplasia/carcinoma

⋮

Triage of Postmenopausal Bleeding

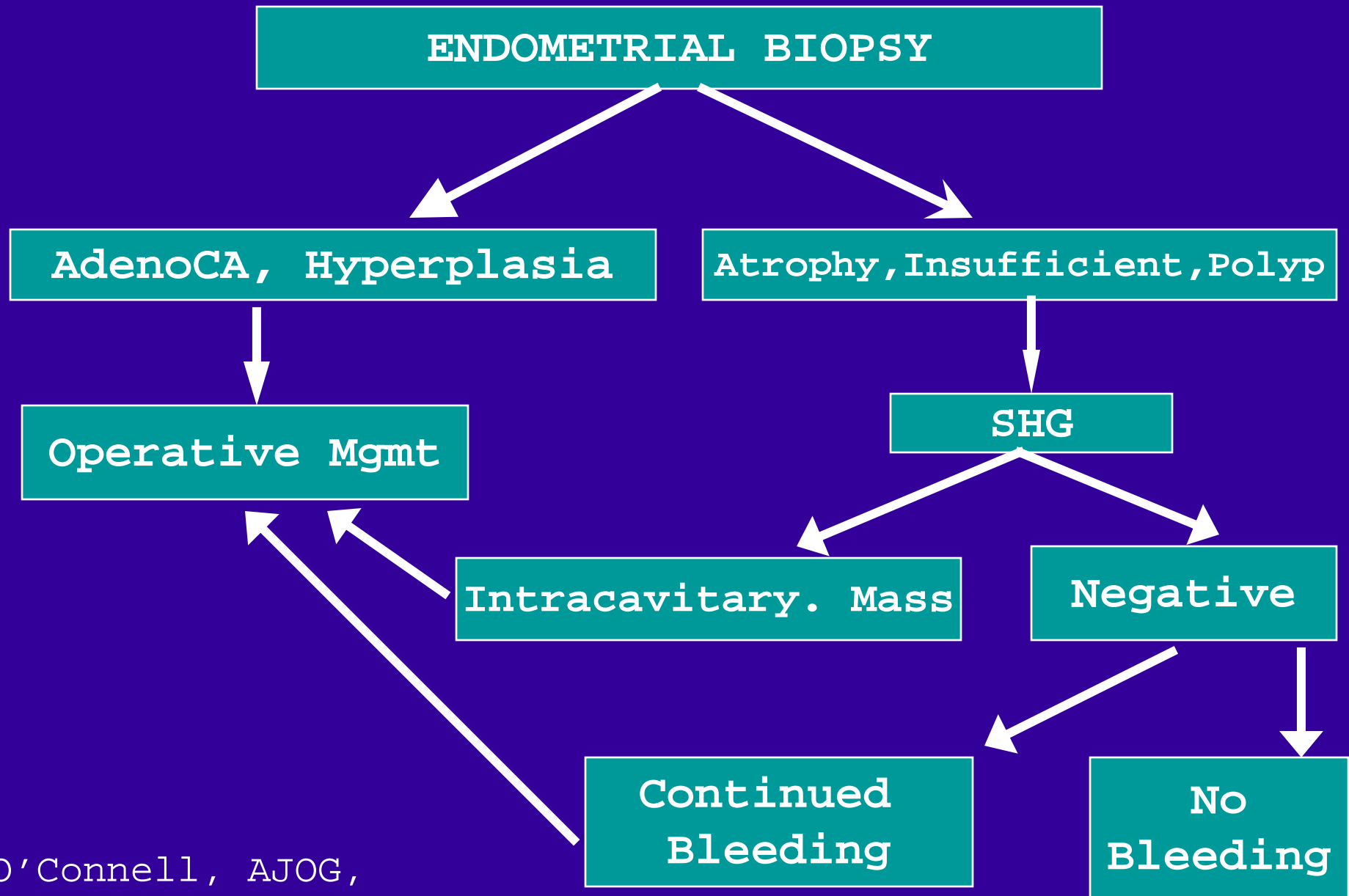
TEST	Sensitivity	Specificity	PPV	NPV
EMB+SHG	95	98	98	96
EMB	23	100	100	60
EMS>5mm	79	57	59	74
SHG	88	96	95	90

N=92

O'Connell, AJOG, 1998

⋮

TRIAGE OF POSTMENOPAUSAL BLEEDING



O'Connell, AJOG,
1988