VIRGINIA ACP CLINICAL UPDATE

Clinical Pearls:

Menopause

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Disclosure

No conflicts of interest or financial disclosures to report
Our patient
48 yo woman c/o changes in menses & frequent bothersome hot flashes. Wants BCP.

- Periods have changed during the past 9 months, less regular, mostly with shorter cycles & one skipped period.
- She is a nonsmoker, has normal BMI, BP & lipids & is on no meds.
- PMH & FH are unremarkable.
- Breast & pelvic exam with Pap are normal.
- Mammogram UTD.
- Urine pregnancy test negative.

You did check a pregnancy test, right?
Which is the most appropriate next step?

A. Reassure her that this bleeding pattern is consistent with perimenopause & advise against taking a hormonal contraceptive

B. Reassure her that this bleeding pattern is consistent with perimenopause & prescribe a hormonal contraceptive

C. Recommend menopausal hormone therapy because she is in perimenopause

D. Recommend a levonorgestrel releasing IUD

E. Refer for endometrial biopsy
Best answer

A. Reassure her that this bleeding pattern is consistent with perimenopause & advise against taking a hormonal contraceptive

B. Reassure her that this bleeding pattern is consistent with perimenopause & prescribe a hormonal contraceptive

C. Recommend menopausal hormone therapy because she is in perimenopause

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Perimenopause

- Perimenopause is the interval from the onset of menstrual changes & associated symptoms through menopause (occurs after 12 months of amenorrhea)

- The hallmark of perimenopause is shortened & irregular menstrual cycles, sometimes associated with vasomotor symptoms

- The perimenopausal transition varies in length & may begin as early as 6-7 years before the final menstrual period

- Menstrual cycles & flow may increase or decrease in length as anovulation becomes more frequent – changes in flow, duration & frequency are common
Who needs endometrial sampling?

- Bleeding that is excessive or persistent
- Bleeding between periods
- Post-coital bleeding
- Abnormal TVUS – endometrial stripe $\geq 4$ mm or irregular
Who needs endometrial sampling?

- Those at increased risk for endometrial cancer:
  - obesity, diabetes, breast, ovarian or colorectal cancer, endometrial polyps or hyperplasia, tamoxifen, & FH of endometrial cancer
Contraception in the Perimenopause

There is no contraceptive method that is contraindicated solely on the basis of age.

Although risk associated with hormonal methods may increase based on underlying medical issues, this should be weighed against the significantly increased risks of a late age, high risk pregnancy.

Contraindications to Combined Hormonal Contraception

- Smokers age ≥ 35
- Migraine
- Uncontrolled hypertension
- CV or thrombotic risk, including h/o VTE, CVA or heart disease
- Breast cancer

CDC. U.S. Medical Eligibility Criteria for contraceptive use. MMWR. 2010;59 (RR-4):1-86
DOWNLOAD THE FREE CDC MEC SUMMARY CHART
This pt needs relief of her severe vasomotor symptoms in addition to contraception. Thus, in the absence of contraindications, a hormonal method is appropriate.

Depending on pt preference, she can be offered pill, patch, or ring.
Can she have a levonorgestrel IUD?

- Yes – it provides effective contraception & will likely help diminish bleeding

- However, it will leave the pt with her troubling vasomotor symptoms & she would still need an additional prescription
# CDC MEC
## Medical Eligibility Criteria

<table>
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<tr>
<th>Condition</th>
<th>Sub-Condition</th>
<th>CDC</th>
<th>POP</th>
<th>Injection</th>
<th>Implant</th>
<th>LNG-IUD</th>
<th>Cu-IUD</th>
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<td>Anatomic abnormalities</td>
<td>a) Distorted uterine cavity</td>
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<td>a) Unilateral mass</td>
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<td>Cervical cancer</td>
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<tr>
<td>Cervix</td>
<td>a) Mild (compensated)</td>
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<td>Deep venous thrombosis (DVT)/Pulmonary embolism (PE)</td>
<td>i) Higher risk for recurrent DVT/PE</td>
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<tr>
<td>Human immunodeficiency virus (HIV)</td>
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<tr>
<td>Inflammatory bowel disease (IBD)</td>
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</tbody>
</table>
| Depressive disorders | a) History of gestational DM 
| Diabetes mellitus (DM) |  |     |     |           |         |         |        |
Clinical Pearls

- Irregular bleeding is the hallmark of perimenopause.

- Typical perimenopausal bleeding is related to changes in menstrual flow, frequency & duration.

- Evaluation must factor in medical risk comorbidities.

- There is no contraceptive method that is contraindicated solely on the basis of age.
Back to our patient:
You give her a low dose BCP & she does well, with relief of symptoms. She is seen intermittently for routine care & remains without significant health issues. At age 51, she comes in for an annual visit & asks whether it is safe to stop using contraception. You recommend:

A. Check FSH during the placebo pill week
B. Stop BCP & see if menses returns
C. Stop BCP & check FSH 14 days after last active pill
D. Obtain TVUS for an antral follicle count
E. Check FSH & estradiol during the placebo week
Best answer

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B. Stop BCP & see if menses returns
C. Stop BCP & check FSH 14 days after last active pill
D. Obtain TVUS for an antral follicle count
E. Check FSH & estradiol during the placebo week
Confirming menopause in a woman on hormonal contraception

- If over age 50, check FSH 14 days after the last active pill or patch or vaginal ring
- A single FSH in perimenopause is not definitive – repeat after 6-8 weeks
- FSH ≥ 30 IU/L
- USE ALTERNATIVE BIRTH CONTROL


When can sterility can be assumed by amenorrhea criteria without serum testing?

- Under age 50, after 2 years of amenorrhea
- From age 50, after 1 year of amenorrhea
  (12 months from LMP)
Natural Menopause

- Generally, medical & menstrual history & symptoms are sufficient to confirm menopause.
- No tests are routinely recommended for confirming menopause if amenorrheic ≥ 12 months.
• Women often ask for baseline or intermittent hormone testing --- there is no scientific basis for this practice

• There is no indication for salivary or urinary hormone testing in clinical practice – in spite of what compounding pharmacies may tell patients
Clinical Pearls

- To determine whether menopause has been reached *in a woman on hormonal contraception*, hold method, use back up, & check serum FSH 14 days after last use

- **Repeat in 6-8 weeks**

- If FSH is not $\geq 30$ IU/L x 2, contraception is needed
Back to our patient:
FSH ≥30 IU/l is obtained x 2. The pt stops OCPs. 7 months later, she is back in your office weeping, c/o drenching hot flashes that are disrupting her work & her sleep. She has tried yoga, layered clothing, & paced breathing. She wants something that will help. You recommend:

A. Oral estradiol and oral progesterone
B. Transdermal estradiol and oral progesterone
C. Low dose paroxetine
D. Bazodoxifene/conjugated estrogen
E. Any one of these is reasonable
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“Treatment for hot flashes should be considered if symptoms are bothersome, disrupt sleep, or adversely affect quality of life.

Therapy should be tailored to the individual woman’s medical history, treatment goals, personal attitudes toward menopause and medication use.”

Hot off the press: Duration of Hot Flashes
SWAN, JAMA, Feb 2015

✓ 2/3 of women start in perimenopause
✓ The earlier HF start, the longer they continue
✓ Hot flash median duration 7.4 years
✓ 1/3 of women still with moderate-severe HFs
  > 9yrs after menopause
✓ Confirmed racial/ethnic influences: Black & Hispanic >> White & Asian

Avis et al. Duration of Menopausal Vasomotor Symptoms Over the Menopause Transition. JAMA. Feb 2015. Epub ahead of print
Clinical Evaluation in Treating Menopause

- Risk stratification with attention to CVD risk & cancer screening guidelines

- Age & years since menopause
  \[ \leq 60 \text{ yo and } \leq 10 \text{ years from menopause} \]
Contraindications to HT

- Possibility of pregnancy
- Undiagnosed vaginal bleeding
- History of breast cancer
- Estrogen sensitive cancers
- History of stroke or MI
- History of DVT or PE
- Liver dysfunction or disease
Prescribing HT

✓ Standard prescription hormones such as estradiol & micronized progesterone are bioidentical. Compounding is not necessary.

✓ Use the lowest dose that relieves symptoms.

✓ Unless hysterectomized, women using estradiol must also have progesterone.
Which dosing regimen?

- Continuous combined E + P avoids cyclic bleeding, preferred by most

- Breakthrough bleeding (BTB) occurs in 40% during first 6 months of HT

- BTB likelihood is greater if within 2 years of menopause

- Can begin with cyclic & then switch to continuous combined to reduce BTB
Transdermal vs Oral

**Transdermal**
- Avoids hepatic metabolism
- Perhaps less risk of VTE
- Comes in ultralow doses
- More expensive

**Oral**
- Beneficial effect on lipids
- Easy to use
- Risk of VTE
- Increases triglycerides

‘Lowest possible dose… shortest possible time’

- Works for most women
- May need to start higher when symptoms are severe and down titrate once relief is achieved
- The ‘shortest possible time’ may be longer than you think
Nonhormonal Options

For women who are not HT candidates:

- Low dose paroxetine (7.5 mg) – FDA approved for this indication
- Low dose escitalopram
- Low dose venlafaxine
- Low dose desvenlafaxine
- Low dose fluoxetine
- Low dose gabapentina
Bazodoxifene/CEE

- Combination novel SERM & conjugated estrogen
- FDA approved in 2013 for treatment of vasomotor symptoms & for osteoporosis prevention
- Favorable safety profile but studies included only generally healthy subjects
- Possible breast protection
Clinical Pearls

- HT is an acceptable option for treating troubling menopausal symptoms in healthy women less than 60 or within 10 years of menopause.
- Use the lowest dose that relieves symptoms.
- Continuous combined E+P safely achieves amenorrhea over time in a woman with a uterus.
Back to our patient: She does well on continuous combined oral estradiol & micronized progesterone. A year later, you are informed that she is in an MVA necessitating hip ORIF. You recommend:

A. Hold HT while VTE risk is increased
B. Change to transdermal estradiol
C. Continue HT if routine VTE prophylaxis is being provided
D. Lower the dose of estradiol
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B. Change to transdermal estradiol
C. Continue HT if routine VTE prophylaxis is being provided
D. Lower the dose of estradiol
Back to our patient:
Over time, you decrease the HT & then stop. Three years later, the patient comes in with a c/o vaginal dryness & dyspareunia. Lubricants are not helping. Hot flashes still occur but are tolerable. You recommend:

A. Vaginal estradiol cream & oral progesterone
B. Low dose vaginal estradiol tablets & oral progesterone
C. Low dose vaginal estradiol tablets
D. Ospemifene & progesterone
Best answer

A. Vaginal estradiol cream & oral progesterone
B. Low dose vaginal estradiol tablets & oral progesterone
C. Low dose vaginal estradiol tablets
D. Ospemifene & progesterone
Genitourinary Syndrome of Menopause (GSM)

- New terminology for vulvovaginal atrophy from the International Society for the Study of Women's Sexual Health and the North American Menopause Society

- Medically more accurate

- More acceptable

Menopause. 2014 Oct;21(10):1063
Genitourinary Symptoms of Menopause (GSM)

- S/sxs associated with ↓ estrogen & involving changes to the labia majora/minora, clitoris, introitus, vagina, urethra and/or bladder
- May include genital dryness, burning, & irritation, lack of lubrication, dyspareunia, impaired sexual function, urinary urgency, dysuria & recurrent UTI

Menopause. 2014 Oct;21(10):1063
GSM treatment

✓ First line: non-hormonal lubricants
✓ Use vaginal estrogen when GSM is the only menopausal symptom
✓ Progesterone not indicated with low dose vaginal estrogen
✓ Serum absorption is negligible
✓ Safe to continue
✓ Ospemifene – novel SERM approved for dyspareunia

Clinical Pearls

- Use vaginal estrogen when GSM is the only menopausal symptom
- No progesterone is needed when treating with low dose vaginal estradiol
- Safe to continue since serum estrogen levels reported with use are within postmenopausal range
The MenoPro app from The North American Menopause Society (NAMS) has 2 modes: one for clinicians and one for women/patients, to support shared decision making.

Are you a Health Care Provider or Woman/Patient?

- Estrogen Therapy options and dosages
- Duration of treatment
- Handout on risks/benefits of HT
- Email summary and handout to patient and/or yourself