Vaginal Health after Menopause
Vaginal Atrophy: Pathophysiology

Vaginal environment before menopause:
- Ovaries produce estrogen
- The vaginal lining is thick and moist
- There is good blood flow to vaginal tissues
- Vaginal fluid is secreted during sexual activity
- Vaginal walls are elastic

Vaginal environment after estrogen loss:
- Ovaries produce less estrogen (or none at all)
- The vaginal lining becomes thin and dry
- There is decreased blood flow to vaginal tissues
- Vaginal elasticity decreases
- There is less secretion of fluids during sexual activity
- The vagina narrows and shortens

Vaginal Atrophy: Pathophysiology

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  - Vaginal walls are elastic
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  - There is decreased blood flow to vaginal tissues

Vaginal Epithelium

Layers
- superficial
- intermediate
- parabasal
- basal

Estrogenized

Atrophic

Three Types (Or Stages) of Vaginal Epithelial Cells

All scored to quantify estrogenization in the **Vaginal Maturation Index**

The Vaginal Maturation Index quantifies the relative proportion of the vaginal parabasal (P), intermediate (I), and superficial (S) cells presented as % P / % I / % S.

*Sources: Mills, Histology for Pathologists. 3rd Edition; LWW, 2006. Wheater, Functional Histology. 2nd Edition; Bibbo, 1997*
Vaginal histology

Vaginal lining with estrogen

Vaginal lining in low-estrogen state
Vaginal symptoms

• May lag behind vasomotor symptoms by several years
• Most common complaints are dryness and pain with penetration
• Reduced thickness of vaginal epithelium increases susceptibility to infection
• Dyspareunia frequently leads to diminished libido
<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Signs</th>
</tr>
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<tbody>
<tr>
<td>Genital dryness</td>
<td>Decreased moisture</td>
</tr>
<tr>
<td>Decreased lubrication with sexual activity</td>
<td>Decreased elasticity</td>
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<tr>
<td>Discomfort or pain with sexual activity</td>
<td>Labia minora resorption</td>
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<tr>
<td>Post-coital bleeding</td>
<td>Pallor/Erythema</td>
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<tr>
<td>Decreased arousal, orgasm, desire</td>
<td>Loss of vaginal rugae</td>
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<tr>
<td>Irritation/Burning/Itching of vulva or vagina</td>
<td>Tissue fragility/fissures/petechiae</td>
</tr>
<tr>
<td>Dysuria</td>
<td>Urethral eversion or prolapse</td>
</tr>
<tr>
<td>Urinary frequency/urgency</td>
<td>Loss of hymenal remnants</td>
</tr>
<tr>
<td></td>
<td>Prominence of urethral meatus</td>
</tr>
<tr>
<td></td>
<td>Introital retraction</td>
</tr>
<tr>
<td></td>
<td>Recurrent urinary tract infections</td>
</tr>
</tbody>
</table>

Supportive findings: pH > 5, increased parabasal cells on maturation index, and decreased superficial cells on wet mount or maturation index.
Scope of the problem

- 40-60% of postmenopausal women have GSM but only 6-7% treated
- Many unaware that symptoms worsen over time
- When sex is good it adds ~15-20% value to relationship but when it is bad, it diminishes the relationship by 50-75%
Nonpharmacologic treatment strategies: Initial and mainstay treatments

• Lubricants
  • Used as needed for sexual activity to increase comfort/pleasure
  • Can be used with other therapies
  • Water/Silicone/Oil-based
  • Avoid potential irritants

• Moisturizers
  • Used daily or every few days to maintain moisture
  • Can be used with other therapies
  • Mimics normal vaginal secretions
  • Does not reverse cellular/pH changes or GSM
Non-Rx therapies for vaginal sx

- Vaginal moisturizers effective; also produce low pH to guard against infection
- Vaginal lubricants ease penetration
- Avoid use of petroleum-based products
- Douches may worsen condition; antihistamines may have drying effect
- Continued sexual activity and/or stimulation may benefit vaginal health
Vaginal Symptoms

- ET is most effective treatment of moderate to severe symptoms of vulvar and vaginal atrophy.
- Many systemic HT and local vaginal ET products are available for treating one or both of these symptoms.

Vaginal ET: Effectiveness

- Typically provides greater benefit than nonhormonal interventions
- Preferred mode of delivery when vaginal symptoms are the only complaint
- Shown in clinical trials to be more effective than systemic oral ET
- May also reduce risk of urinary urgency and recurrent urinary tract infections

US FDA-approved vaginal ET products

- Estradiol vaginal cream (Estrace)
- Conjugated estrogen vaginal cream (Premarin)
- Estradiol vaginal ring (Estring)
- Estradiol acetate vaginal ring (Femring)\(^a\)
- Estradiol hemihydrate vaginal tablet 4 mcg (Imvexxy), 10 mcg (Vagifem, Yuvalfem)

- All are effective at recommended doses
- Choice depends on clinical experience and patient preference (including cost)

\(^a\)This product delivers systemic levels of estradiol.
• In this large prospective cohort study, compared to nonusers of vaginal estrogen, users had similar risks of:
  • invasive breast cancer
  • stroke
  • colorectal cancer
  • endometrial cancer, and
  • venous thromboembolism

• Did not find evidence for elevated risk of CHD or death in vaginal estrogen users compared with non-users
Vaginal estrogen products

• Estradiol tablets 10 mcg vaginally daily for two weeks, then twice weekly
• Estradiol vaginal ring (Estring) 2mg vaginally every 3 months
• Estradiol or conjugated estrogen cream (Estrace or Premarin)
• Estradiol inserts (Imvexxy) 10 mcg, 4 mcg
Estring vs Vagifem

Randomized controlled trial comparing Estring and Vagifem for 12mos
No difference in efficacy or endometrial thickness
Fewer patients with bleeding in Estring group (0 vs 6%)

Weisberg, Ayton, et.al. Climacteric 2005
Breast cancer, endometrial cancer, and cardiovascular events in participants who used vaginal estrogen in the Women’s Health Initiative Observational Study

Carolyn J. Crandall, MD, MS, Kathleen M. Hovey, MS, Christopher A. Andrews, PhD, Rowan T. Chlebowski, MD, PhD, Marcia L. Stefanick, PhD, Dorothy S. Lane, MD, MPH, Jan Shifren, MD, Chu Chen, PhD, Andrew M. Kaunitz, MD, Jane A. Cauley, DrPH, and JoAnn E. Manson, MD, DrPH
WHI observational study

Figure 1. Algorithm of Study Participants

- Exclusions:
  - current HT users (oral, transdermal estrogen and/or progestogen) at baseline or during follow-up (N= 41,630)
  - history of breast, ovarian, endometrial cancer (N= 7,079)
  - missing HT use data (N= 85)
  - missing info hysterectomy status (N= 454)
  - no follow-up data (N= 473)

N = 93,676 WHI-Observational Study

N = 45,663

N = 32,433 Intact uterus*

N = 1,207 Vaginal estrogen users

N = 3,003 Vaginal estrogen users

N = 14,133 Hysterectomy*

*numbers don’t add up to 45,663 due to time-varying nature of hysterectomy status: 903 change from no hysterectomy to hysterectomy and are counted in both cells (Crandall et al, Menopause 2017)
Presumed lower risk than commonly used doses of systemic ET

Serum estrogen levels reported with use are within postmenopausal range
Vaginal ET: Adverse effects

- Vulvovaginal candidiasis, uterine bleeding, mastalgia, and nausea have been reported; may be dose-related

- Data for women at high risk for venous thromboembolism are lacking

- Endometrial carcinoma can be a concern with use of ET in women who have a uterus
Improvement in symptoms typically occurs within a few weeks of starting treatment.

Vaginal ET may be continued as long as distressing symptoms remain.
Insufficient data to recommend annual endometrial surveillance in asymptomatic women

Closer surveillance may be required if a woman is

- Using a higher dose of vaginal ET
- At high risk for endometrial cancer
- Having symptoms such as spotting, breakthrough bleeding
• Tablet vs. crm – 6 months
  • Estradiol tablet 25 mcg once/wk or CEE cream 1.25 mg/d X 21 days f/b 1 wk off for 6-month intervention
    • Tablet: 1/49 proliferative endometrium;
    • Cream: 7/49 proliferative endometrium, 2/49 endometrial hyperplasia (Rioux et al Menopause 2000)

• Tablet without comparison group – 12 months
  • Estradiol vaginal tablet 10mcg, 2 studies
    • No hyperplasia or endometrial ca (Ulrich Climactieric 2010)
    • 2 events of hyperplasia and carcinoma in 386 evaluable biopsy samples (incidence rate 0.52% per year) (vs. background incidence of 0% - 1%) (Simon Obstet Gynecol 2010)
Bothersome GSM symptoms—consideration of low-dose vaginal ET

- Low-dose vaginal ET used for the GSM has minimal systemic absorption (blood levels in the post-menopause range) and, on the basis of limited observational data, appears to hold minimal to no demonstrated risk for recurrence of endometrial or breast cancer. (Level II)

- For women with early endometrial cancer who have completed successful treatment, including hysterectomy, consideration may be given for low-dose vaginal ET for relief of GSM if non-hormone options are not successful, based on limited short-term safety trials. (Level II)

- For women who are survivors of breast cancer, decisions about low-dose vaginal ET should involve the woman’s oncologist, particularly for women using AIs who have lowered overall estradiol levels. (Level III)

*North American Menopause Society position statement, Menopause, 2017*
• 30 RCTs comparing vaginal estrogen formulations to each other or placebo
• Poor quality studies
• All approved vaginal therapy products more effective than placebo
• No formulation superior to others
• Low-dose vaginal estrogen preparations approved by the U.S. Food and Drug Administration carry the same boxed warning about health risks as the systemic formulations of estrogen alone and combination estrogen plus progestogen carry.

• This labeling is based on extrapolations of data from clinical trials of systemic hormone therapy, which:
  • involved substantially higher levels of systemic exposure, and
  • were not based on evidence from clinical trials of vaginal estrogen.

FDA response

• On May 29, 2018, the FDA rejected a proposal to modify package labelling of low-dose vaginal estrogen products to accurately reflect evidence-based information for low-dose vaginal estrogen products approved for treating symptoms of vulvovaginal atrophy.

(Docket No. FDA-2016-P-1246)
The North American Menopause Society (NAMS) joins The International Society for the Study of Women’s Sexual Health, the American College of Obstetricians and Gynecologists, and other major organizations in recognizing the Centers for Medicare and Medicaid Services (CMS) for acting on a major health concern for postmenopausal women by no longer excluding from Medicare Part D coverage drugs for the treatment of moderate to severe dyspareunia due to menopause when used consistent with this labeling under their “Prescription Drug Benefits” section 1860D-2(e)(2)(A) of the Social Security Act. Postmenopausal women can now receive access to newer, tested, and effective FDA-approved therapies to relieve symptoms and signs of vulvovaginal atrophy (VVA), a component of the genitourinary syndrome of menopause (GSM). Dyspareunia in postmenopausal women should not be considered sexual dysfunction but rather the most common presenting symptom of GSM, a chronic, progressive medical condition that is the result of lowered estrogen levels in vaginal and urogenital tissue after menopause, resulting in thinning of the vaginal tissues.
Alternative prescription therapies

- Ospemifene (Osphena) which is indicated for dyspareunia
- Prasterone (Intrarosa)
Ospemifene

- Nonhormonal selective estrogen-receptor modulator (SERM)
- Only SERM approved in the United States to treat moderate to severe dyspareunia
Two 12-week studies showed improvements with daily use (60 mg) in
- Vaginal maturation index
- Vaginal pH
- Most bothersome symptom (vaginal dryness)

52-week extension study showed sustained improvements with no cases of VTE, endometrial hyperplasia or carcinoma
Ospemifene: Adverse effects

- Vasomotor symptoms most common
- Prescribing information contains precautions similar to those for estrogens and other SERMs
- Data in women with breast cancer or at high risk of developing breast cancer are lacking so use is not recommended

Prasterone (Intrarosa)

• 6.5 mg insert, vaginal, once daily
• DHEA is converted by aromatase activity into testosterone and estradiol
• Approved for treatment of dyspareunia due to GSM
Clinical trials (12 weeks):

- More effective than placebo in improving vaginal dryness and dyspareunia
- No significant impact on serum levels of DHEA, DHEA-S, E₂ or T
- Negligible endometrial effect
- Labeling lists breast cancer as warning, not contraindication
The techno vagina: The laser and radiofrequency device boom in gynecology

OBG Management, September 2018
Is applying energy to the vagina the answer?

- Women seek non-hormonal treatment, especially breast cancer survivors
- Cost of ongoing therapy may be a factor
- Short-term treatment may be appealing
Use of a Novel Fractional CO$_2$ Laser for the Treatment of Genitourinary Syndrome of Menopause: 1-Year Outcomes

Eric R. Sokol MD$^1$, Mickey M. Karram MD$^2$

$^1$ Urogynecology and Pelvic Reconstructive Surgery, Stanford University, Stanford, California
$^2$ Advanced Urogynecology and Pelvic Surgery, The Christ Hospital, Cincinnati, Ohio

*Menopause.* July 2017
All GSM symptoms significantly improved at 12 months
Before and after vaginal laser
Vaginal laser therapy

- FDA cleared for general gynecologic indications
- Not approved specifically for treatment of GSM or dyspareunia
- FDA July 2018: “warns against use of energy based devices to perform vaginal ‘rejuvenation’ or vaginal cosmetic procedures”
- FDA encouraged randomized trials before wide acceptance
Radiofrequency-based devices

- Variable mechanisms of action but generally deliver energy to deeper connective tissue of vaginal wall
- May be monopolar, bipolar, multipolar
- FDA cleared for nonspecific electrocoagulation and hemostasis, not cleared for treatment of any vaginal conditions or symptoms
Radiofrequency-based devices

- Based on small, short term studies, most without placebo arm
- Preliminary data reassuring regarding benefits and risks
- Not compared to standard therapy (local estrogen treatment)
- Experts advise long-term randomized sham-controlled trials
Breast Cancer Survivors
GSM and Breast Cancer

• 3.1 million survivors of breast cancer
• >250,000 women diagnosed with breast cancer each year
  • 11% under 44 years of age
• Add women at high risk for breast cancer
• Most will suffer from GSM and will go undiagnosed and untreated!
Key Points

• High risk women
  • Observational data suggest that local or systemic hormone therapy do not further increase risk for breast cancer in women already at high risk

• Estrogen receptor-positive disease
  • Nonhormonal therapy first line
  • Consider local hormone therapy after discussion with oncologist (women receiving AIs might first consider switching to tamoxifen)
Key Points

• Triple-negative breast cancers
  • Theoretically no increased risk associated with local or systemic hormone therapy, but data are lacking

• Metastatic disease
  • Quality of life, comfort, and sexual intimacy most important
  • Optimal choices will vary with probability of long-term survival
## Factors affecting decision-making regarding local hormone therapy

<table>
<thead>
<tr>
<th>Factors</th>
<th>More desirable candidates</th>
<th>Less desirable candidates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage of disease</td>
<td>Stage 0, 1, and 2 or metastatic with limited life expectancy</td>
<td>Stage 3 or metastatic with extended life expectancy</td>
</tr>
<tr>
<td>Grade of disease</td>
<td>Low or intermediate grade</td>
<td>High grade</td>
</tr>
<tr>
<td>Lymph node involvement</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Hormone-receptor status</td>
<td>Negative</td>
<td>Positive</td>
</tr>
<tr>
<td>Endocrine Therapy</td>
<td>Tamoxifen</td>
<td>Als</td>
</tr>
<tr>
<td>Risk of recurrence</td>
<td>Low</td>
<td>High</td>
</tr>
<tr>
<td>Time since diagnosis</td>
<td>Remote</td>
<td>Recent</td>
</tr>
<tr>
<td>Symptom severity</td>
<td>Severe</td>
<td>Mild</td>
</tr>
<tr>
<td>Nonhormone therapies</td>
<td>Failed</td>
<td>Effective</td>
</tr>
<tr>
<td>Effect on QOL</td>
<td>Severe</td>
<td>Mild</td>
</tr>
</tbody>
</table>

Als: aromatase inhibitor; QOL: quality of life
• FDA-approved DHEA not studied in breast cancer survivors; label warns against its use
• No studies directly comparing estrogen to DHEA in levels or efficacy
• One cannot be recommended over the other in this population

SERMS and risk

• Ospemifene
  • Systemically administered SERM FDA-approved for treatment of moderate to severe dyspareunia
  • Anti-estrogenic breast effects in pre-clinical trials
  • Not studied in breast cancer survivors
  • Not approved by FDA for US women with or at high risk for breast cancer
  • Not contraindicated in Europe in breast cancer survivors who have completed treatment

# Pharmacologic treatment strategies

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Product Name</th>
<th>Initial Diagnosis</th>
<th>Maintenance Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Vaginal creams</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>17β-estradiol</td>
<td>Estrace; generic</td>
<td>0.5 – 1 gm/d x 2 wks</td>
<td>0.5 – 1 gm 1–3 x wk</td>
</tr>
<tr>
<td>Conjugated estrogens</td>
<td>Premarin</td>
<td>0.5 – 1 gm/d x 2 wks</td>
<td>0.5 – 1 gm 1–3 x wk</td>
</tr>
<tr>
<td><strong>Vaginal inserts</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Estradiol hemihydrate</td>
<td>Vagifem; Yuvalfem; generic</td>
<td>10 µg insert 1/d x 2 wk</td>
<td>1 twice wk</td>
</tr>
<tr>
<td>DHEA (prasterone)</td>
<td>Intrarosa</td>
<td>6.5 mg 1/d</td>
<td>6.5 mg 1/d</td>
</tr>
<tr>
<td><strong>Vaginal ring</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>17β-estradiol</td>
<td>Estring</td>
<td>2 mg releases about 7.5 µg/d x 90 d</td>
<td>Changed q 90 d</td>
</tr>
<tr>
<td><strong>SERM</strong></td>
<td></td>
<td></td>
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<tr>
<td>Ospemifene</td>
<td>Osphanena</td>
<td>60 mg orally/d</td>
<td>60 mg orally/d</td>
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<tr>
<td><strong>Other</strong></td>
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<tr>
<td>Lidocaine</td>
<td>4% aqueous lidocaine</td>
<td>Applied to vestibule before sexual activity</td>
<td></td>
</tr>
</tbody>
</table>
Oral Contraceptives in Special Populations
U.S. Contraceptive Use

- OC: 28%
- Female sterilization: 27%
- Male condom: 16%
- IUD: 4-4$
- Withdrawal: 4-1$
- Other hormonal method: 2-4$
- DMPA: 2-1$
- Other non-hormonal method: 0-4$

% of women ages 15-44 by method type

Unintended Pregnancy Rate (no. per 1000)

- 1981
- 1987
- 2001
- 2008
- 2011

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U.S. Medical Eligibility Criteria for Contraceptive Use, 2016
Contraceptive Methods in US MEC

- Combined hormonal contraceptives
- Progestin-only contraceptives
- Emergency contraceptive pills
- Intrauterine devices
- Barrier contraceptive methods
- Fertility Awareness-Based Methods
- Lactational Amenorrhea Method
- Coitus Interruptus
- Female and Male Sterilization
<table>
<thead>
<tr>
<th>Category</th>
<th>Restriction</th>
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<tbody>
<tr>
<td>1</td>
<td>No restriction</td>
</tr>
<tr>
<td>2</td>
<td>Advantages generally outweigh theoretical or proven risks</td>
</tr>
<tr>
<td>3</td>
<td>Theoretical or proven risks usually outweigh advantages</td>
</tr>
<tr>
<td>4</td>
<td>Unacceptable health risk</td>
</tr>
</tbody>
</table>
# US Medical Eligibility Criteria

## Summary Chart of U.S. Medical Eligibility Criteria for Contraceptive Use

<table>
<thead>
<tr>
<th>Condition</th>
<th>Sub-Condition</th>
<th>Cu-IUD</th>
<th>LNG-IUD</th>
<th>Implant</th>
<th>DMPA</th>
<th>POP</th>
<th>CHC</th>
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<tbody>
<tr>
<td>Age</td>
<td>Menarche &lt; 20 yrs</td>
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<td>Menarche ≥ 20 yrs</td>
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<td>Menarche &lt; 18 yrs</td>
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<td>Menarche ≥ 18 yrs</td>
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<td>Menarche &lt; 60 yrs</td>
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<td>Anatomical abnormalities</td>
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<td>Sickle cell disease</td>
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<td>With other risk factors for VTE</td>
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<td>Without other risk factors for VTE</td>
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<td>&gt; 42 days postpartum</td>
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<td>Awaiting treatment</td>
<td>4</td>
<td>2</td>
<td>4</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Cervical erosion</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cervical intraepithelial neoplasia</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cystic fibrosis</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Deep venous thrombosis (DVT)/Pulmonary embolism (PE)</td>
<td>History of DVT/PE, not receiving anticoagulant therapy</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Higher risk for recurrent DVT/PE</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Lower risk for recurrent DVT/PE</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Acute DVT/PE</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>DVT/PE and established anticoagulant therapy for at least 3 months</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Higher risk for recurrent DVT/PE</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Lower risk for recurrent DVT/PE</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Family history (first-degree relatives)</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Major surgery</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>With prolonged immobilization</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Without prolonged immobilization</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Depressive disorders</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Key: 1. No restriction (method can be used) 2. Advantages generally outweigh theoretical or proven risks 3. Theoretical or proven risks usually outweigh the advantages 4. Interpersonal health risk makes use of method not feasible</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Condition**

- Diabetes
- Dysmenorrhea
- Endometrial cancer
- Endometrial hyperplasia
- Epilepsy
- Gallbladder disease
- Gestational trophoblastic disease
- Headaches
- History of bariatric surgery
- History of cholecystectomy
- History of high blood pressure during pregnancy
- History of Polycystic Ovary Syndrome
- HIV

**Abbriviations:** Cu-IUD = Copper intraretroplacental device; LNG-IUD = levonorgestrel intraretroplacental device; Implant = subdermal implant containing etonogestrel; DMPA = depot medroxyprogesterone acetate; POP = oral contraceptive; CHC = combination oral contraceptive; OC = oral contraceptive; EM = estrogen minus; OC = oral contraceptive; MPR = ethinyl estradiol-containing contraceptive monophasic pill; MNPP = ethinyl estradiol-containing monophasic pill, see also Drug Interactions (Condition imposes a woman to increased risk as a result of pregnancy); *Please see the complete guidance for a certification to this classification: www.cdc.gov/reproductivehealth/medicationguidanceforuse/USMEC.htm.*
US MEC Recommendations

• Recommendations for use of contraceptive methods, based on specific conditions

• Conditions defined as:
  – Individual’s characteristics
  – Known preexisting medical/pathologic condition

• Refer to methods being used for contraception, not treatment of a medical condition
<table>
<thead>
<tr>
<th>Conditions Associated with Increased Risk for Adverse Health Events as a Result of Unintended Pregnancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast cancer</td>
</tr>
<tr>
<td>Complicated valvular heart disease</td>
</tr>
<tr>
<td>Diabetes: insulin dependent; with nephropathy/retinopathy/neuropathy or other vascular disease; or of &gt;20 years’ duration</td>
</tr>
<tr>
<td>Endometrial or ovarian cancer</td>
</tr>
<tr>
<td>Epilepsy</td>
</tr>
<tr>
<td>Hypertension (systolic &gt; 160 mm Hg or diastolic &gt; 100 mm Hg)</td>
</tr>
<tr>
<td>History of bariatric surgery within past 2 years</td>
</tr>
<tr>
<td>HIV/AIDS</td>
</tr>
<tr>
<td>Ischemic heart disease</td>
</tr>
<tr>
<td>Malignant gestational trophoblastic disease</td>
</tr>
</tbody>
</table>
### Example: Smoking and Contraceptive Use

<table>
<thead>
<tr>
<th>Condition</th>
<th>COC/P/R</th>
<th>POP</th>
<th>DMPA</th>
<th>Implants</th>
<th>Cu-IUD</th>
<th>LNG-IUD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smoking</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>a. Age &lt;35</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>b. Age ≥35</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>i. &lt;15 cigarettes/day</td>
<td>3</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>ii. ≥15 cigarettes/day</td>
<td>4</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

Separate columns if recommendations differ for:

- Initiation criteria (preexisting conditions)
- Continuation criteria (condition develops or worsens)

<table>
<thead>
<tr>
<th>Headache</th>
<th>Initiative</th>
<th>Continuation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-migrainous (mild or severe)</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td><strong>Migraine</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Without aura</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age &lt; 35 years</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Age &gt;= 35 years</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>With aura, at any age</td>
<td>4</td>
<td>4</td>
</tr>
</tbody>
</table>
How to use the US MEC
Provider Tools and Learning Aids

- Summary tables in English, Spanish
- US MEC Wheel
- iPhone and iPad app
- Continuing Education Activities
- Speaker-ready slides
- Contraceptive Effectiveness Chart
Take Home Messages

- US MEC provides evidence-based recommendations for safe use of contraceptive methods by women and men with various conditions
- Most women can safely use most contraceptive methods
- Certain conditions are associated with increased risk for adverse health events as a result of unintended pregnancy
- Women at risk of unintended pregnancy need access to highly effective contraceptive methods
- Women, men and couples should be informed of full range of methods to decide what will be best for them
U.S. Selected Practice Recommendations for Contraceptive Use, 2013
Adapted from the World Health Organization Selected Practice Recommendations for Contraceptive Use, 2nd Edition
U.S. Selected Practice Recommendations for Contraceptive Use, 2016
COMMITTEE OPINION

Number 577 • November 2013

Committee on Gynecologic Practice
This document reflects emerging clinical and scientific advances as of the date issued and is subject to change. The information should not be construed as dictating an exclusive course of treatment or procedure to be followed.

Understanding and Using the U.S. Selected Practice Recommendations for Contraceptive Use, 2013

ABSTRACT: The U.S. Selected Practice Recommendations for Contraceptive Use, 2013 (U.S. SPR), issued by the Centers for Disease Control and Prevention is a companion piece to the Centers for Disease Control and Prevention’s U.S. Medical Eligibility Criteria for Contraceptive Use, 2010. The U.S. Medical Eligibility Criteria for Contraceptive Use, 2010, provides guidance for which contraceptive methods are safe for women with selected characteristics and medical conditions, whereas the U.S. SPR offers guidance on how to use these methods most effectively. The American College of Obstetricians and Gynecologists endorses the U.S. SPR and encourages its use by Fellows; providers should always consider the specific clinical situation when applying these guidelines to individual clinical care.
Follow-up to US Medical Eligibility Criteria for Contraceptive Use, 2010 (US MEC):
- Recommendations for who can safely use contraception

Adapted from World Health Organization (WHO) SPR

Intent: Evidence-based guidance for common, yet controversial, contraceptive management questions
- When to start
- Missed pills
- Bleeding problems
- Exams and tests
- Follow-up
- How to be reasonably certain that a woman is not pregnant
Target audience: health-care providers

Purpose: to assist health care providers when they counsel patients about contraceptive use

Selected Recommendations

- NOT comprehensive textbook
- NOT the US MEC
- NOT rigid guidelines
- NOT well-woman care
Take Home Messages

• Most women can start most methods anytime
• Few, if any, exams or tests are needed
• Recommendations for anticipatory counseling for potential bleeding problems and proper management provided
• Routine follow-up generally not required
• Many circumstances call for consideration of emergency contraception use
• Regular contraception should be started after EC
Scenario 2

38 year old G2P2 female with diabetes has been using condoms for contraception and is looking for a more effective method. What methods are safe for her to use?

A. IUD (copper or levonorgestrel)
B. Progestin-only methods (pill, injectable, implant)
C. Combined hormonal methods (pill, patch, ring)
Evidence

Use of COCs among women with history of gestational diabetes does not increase risk of developing noninsulin-dependent diabetes.

Use of COCs among women with insulin- or noninsulin-dependent diabetes:

- **Limited effect on daily insulin requirements**
- **No effect on long-term diabetes control**
- **No effect on progression to retinopathy**

*CDC, MMWR 2010, 59, No RR-4*
# Diabetes

<table>
<thead>
<tr>
<th>Condition</th>
<th>COC/P/R</th>
<th>POP</th>
<th>DMPA</th>
<th>Implants</th>
<th>LNG-IUD</th>
<th>Cu-IUD</th>
</tr>
</thead>
<tbody>
<tr>
<td>History of gestational disease</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Nonvascular disease</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Noninsulin-dependent</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Insulin-dependent§</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Nephropathy/retinopathy/neuropathy§</td>
<td>3/4†</td>
<td>2</td>
<td>3</td>
<td>2</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Other vascular disease or diabetes of &gt;20 yrs' duration§</td>
<td>3/4†</td>
<td>2</td>
<td>3</td>
<td>2</td>
<td>2</td>
<td>1</td>
</tr>
</tbody>
</table>

§ Condition that exposes a woman to increased risk as a result of unintended pregnancy
† This category should be assessed according to the severity of the condition
Scenario 2

38 year old G2P2 female with diabetes has been using condoms for contraception and is looking for a more effective method. You now know that she is non-insulin dependent and has no vascular disease. What methods are safe for her to use?

A. IUD (copper or levonorgestrel)
B. Progestin-only methods (pill, injectable, implant)
C. Combined hormonal methods (pill, patch, ring)
ALL OF THE ABOVE
Scenario 3

24 y.o. female comes to office desiring contraception and wants to start pills

– Q: When can she start?
When to start a contraceptive method

Barriers to starting
- Filling a prescription
- Starting during menses
- Coming back for a second (or more) visit

Starting when woman requests contraception ("Quick start")
- May reduce time woman is at risk for pregnancy
- May reduce barriers to starting
Evidence for Risk of Pregnancy

Two types of risk:

Risk of already being pregnant
  – Risk that woman already pregnant with “Quick start” of CHCs low

Risk of becoming pregnant
  – Risk of pregnancy with “Quick start” of CHCs low

• Brahmi, Contraception, 2013.
Other findings

Starting CHCs on different days of the cycle does not affect bleeding changes or other side effects.

“Quick start” may increase continuation of combined oral contraceptives (COCs) and patch in the short term; this difference disappears over time.

- Brahmi, Contraception, 2013.
No increased risk for adverse outcomes (congenital anomalies, neonatal death, infant death) among infants exposed in utero to COCs

Need for back-up contraception

Later start days are associated with greater follicular activity, but not ovulation, through day 5 (implications for back up)

- Brahmi, Contraception, 2013.
<table>
<thead>
<tr>
<th>Contraceptive Method</th>
<th>When to start, if provider is reasonably certain woman is not pregnant</th>
<th>Back-up needed</th>
</tr>
</thead>
<tbody>
<tr>
<td>LNG IUD</td>
<td>Any time</td>
<td>If &gt; 7 days of cycle, use back-up method or abstain for 7 days</td>
</tr>
<tr>
<td>Copper IUD</td>
<td>Any time</td>
<td>Not needed</td>
</tr>
<tr>
<td>Implant (etongestrel)</td>
<td>Any time</td>
<td>If &gt; 5 days of cycle, use back-up method or abstain for 7 days</td>
</tr>
<tr>
<td>Injectable</td>
<td>Any time</td>
<td>If &gt; 7 days of cycle, use back-up method or abstain for 7 days</td>
</tr>
<tr>
<td>CHC</td>
<td>Any time</td>
<td>If &gt; 5 days of cycle, use back-up method or abstain for 7 days</td>
</tr>
<tr>
<td>Progestin-Only Pills (POPs)</td>
<td>Any time</td>
<td>If &gt; 5 days of cycle, use back-up method or abstain for 2 days</td>
</tr>
</tbody>
</table>
Guidance for Special Considerations

Amenorrheic

Postpartum
  – Breastfeeding
  – Not breastfeeding

Postabortion

Switching from another contraceptive method
24 y.o. female comes to office desiring contraception and wants to start pills

- **Q:** When can she start?
- **A:**
  - Anytime, if reasonably certain she is not pregnant.
  - If it has been more than 5 days since menstrual bleeding started, she will need to abstain from sex or use additional contraceptive protection for the next 7 days.
Scenario 4: How to be reasonably certain that a woman is not pregnant

24 y.o. female comes to office desiring contraception and wants to start pills

– Q: How can you be reasonably certain she is not pregnant?
Evidence: Pregnancy test limitations

Pregnancy detection rates can vary based on sensitivity of test and timing with respect to missed menses

Pregnancy test not able to detect pregnancy resulting from recent intercourse

Pregnancy test may remain positive several weeks after pregnancy ends

BOX 1. How To Be Reasonably Certain that a Woman Is Not Pregnant

A health-care provider can be reasonably certain that a woman is not pregnant if she has no symptoms or signs of pregnancy and meets any one of the following criteria:

- is ≤7 days after the start of normal menses
- has not had sexual intercourse since the start of last normal menses
- has been correctly and consistently using a reliable method of contraception
- is ≤7 days after spontaneous or induced abortion
- is within 4 weeks postpartum
- is fully or nearly fully breastfeeding (exclusively breastfeeding or the vast majority [≥85%] of feeds are breastfeeds),* amenorrheic, and <6 months postpartum

Scenario 4

24 y.o. female comes to office desiring contraception and wants to start pills

- **Q**: How can you be reasonably certain she is not pregnant?

- **A**: If she has no signs or symptoms of pregnancy and fulfills one of criteria, a provider can be reasonably certain that the woman is not pregnant.
Clinical scenario 5: Exams and tests

24 y.o. female comes to office desiring contraception and wants to start pills

- **Q:** Do you need to do any exams or tests before she starts?
Unnecessary tests may be barrier to starting

- Women (adolescents) may not be comfortable with pelvic exam
- Coming back for a second (or more) visit to receive test results

Recommendations address exams and tests needed prior to initiation

- **Class A** = essential and mandatory
- **Class B** = contributes substantially to safe and effective use, but implementation may be considered within the public health and/or service context
- **Class C** = does not contribute substantially to safe and effective use of the contraceptive method
### When to Start Using Specific Contraceptive Methods

<table>
<thead>
<tr>
<th>Contraceptive method</th>
<th>When to start (if the provider is reasonably certain that the woman is not pregnant)</th>
<th>Additional contraception (i.e., back up) needed</th>
<th>Examinations or tests needed before initiation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Copper-containing IUD</td>
<td>Anytime</td>
<td>Not needed</td>
<td>Bimanual examination and cervical inspection ¹</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Implant</td>
<td>Anytime</td>
<td>If &gt;5 days after menses started, use back-up method or abtain for 7 days.</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Combined hormonal contraceptive</td>
<td>Anytime</td>
<td>If &gt;5 days after menses started, use back-up method or abtain for 7 days.</td>
<td>Blood pressure measurement</td>
</tr>
</tbody>
</table>

**Abbreviations:** BMI = body mass index; IUD = intrauterine device; STD = sexually transmitted disease; U.S. MEC = U.S. Medical Eligibility Criteria for Contraceptive Use

¹ Weight (BMI) measurement is not needed to determine medical eligibility for any methods of contraception because all methods can be used (U.S. MEC 1) or generally can be used (U.S. MEC 2) among obese women. However, measuring weight and calculating BMI (weight [kg]/height [m²]) at baseline might be helpful for monitoring any changes and counseling women who might be concerned about weight change perceived to be associated with their contraceptive method.

² Most women do not require additional STD screening at the time of IUD insertion. If a woman with risk factors for STDs has not been screened for gonorrhea and chlamydia according to CDC’s STD Treatment Guidelines (http://www.cdc.gov/std/treatment), screening can be performed at the time of IUD insertion, and insertion should not be delayed. Women with current purulent cervicitis or chlamydial infection or gonococcal infection should not undergo IUD insertion (U.S. MEC 4).
# US SPR

## Exams and tests prior to initiation

<table>
<thead>
<tr>
<th>Examination or test</th>
<th>LNG and Cu-IUD</th>
<th>Implant</th>
<th>Injectable</th>
<th>CHC</th>
<th>POP</th>
<th>Condom</th>
<th>Diaphragm or cervical cap</th>
<th>Spermicide</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood pressure</td>
<td>C</td>
<td>C</td>
<td>C</td>
<td>A*</td>
<td>C</td>
<td>C</td>
<td>C</td>
<td>C</td>
</tr>
<tr>
<td>Weight (BMI)</td>
<td>— †</td>
<td>—†</td>
<td>—†</td>
<td>—†</td>
<td>—†</td>
<td>C</td>
<td>C</td>
<td>C</td>
</tr>
<tr>
<td>Clinical breast examination</td>
<td>C</td>
<td>C</td>
<td>C</td>
<td>C</td>
<td>C</td>
<td>C</td>
<td>C</td>
<td>C</td>
</tr>
<tr>
<td>Bimanual examination and cervical inspection</td>
<td>A</td>
<td>C</td>
<td>C</td>
<td>C</td>
<td>C</td>
<td>C</td>
<td>A</td>
<td>C</td>
</tr>
</tbody>
</table>

## Laboratory test

<table>
<thead>
<tr>
<th>Examination or test</th>
<th>LNG and Cu-IUD</th>
<th>Implant</th>
<th>Injectable</th>
<th>CHC</th>
<th>POP</th>
<th>Condom</th>
<th>Diaphragm or cervical cap</th>
<th>Spermicide</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose</td>
<td>C</td>
<td>C</td>
<td>C</td>
<td>C</td>
<td>C</td>
<td>C</td>
<td>C</td>
<td>C</td>
</tr>
<tr>
<td>Lipids</td>
<td>C</td>
<td>C</td>
<td>C</td>
<td>C</td>
<td>C</td>
<td>C</td>
<td>C</td>
<td>C</td>
</tr>
<tr>
<td>Liver enzymes</td>
<td>C</td>
<td>C</td>
<td>C</td>
<td>C</td>
<td>C</td>
<td>C</td>
<td>C</td>
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<tr>
<td>Hemoglobin</td>
<td>C</td>
<td>C</td>
<td>C</td>
<td>C</td>
<td>C</td>
<td>C</td>
<td>C</td>
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</tr>
<tr>
<td>Thrombogenic mutations</td>
<td>C</td>
<td>C</td>
<td>C</td>
<td>C</td>
<td>C</td>
<td>C</td>
<td>C</td>
<td>C</td>
</tr>
<tr>
<td>Cervical cytology (Papanicolaou smear)</td>
<td>C</td>
<td>C</td>
<td>C</td>
<td>C</td>
<td>C</td>
<td>C</td>
<td>C</td>
<td>C</td>
</tr>
<tr>
<td>STD screening with laboratory tests</td>
<td>—§</td>
<td>C</td>
<td>C</td>
<td>C</td>
<td>C</td>
<td>C</td>
<td>C</td>
<td>C</td>
</tr>
<tr>
<td>HIV screening with laboratory tests</td>
<td>C</td>
<td>C</td>
<td>C</td>
<td>C</td>
<td>C</td>
<td>C</td>
<td>C</td>
<td>C</td>
</tr>
</tbody>
</table>
### US SPR Exams and tests prior to initiation

<table>
<thead>
<tr>
<th>Examination or test</th>
<th>Contraceptive method and class</th>
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<tbody>
<tr>
<td></td>
<td>LNG and Cu-IUD</td>
</tr>
<tr>
<td>Blood pressure</td>
<td>C</td>
</tr>
<tr>
<td>Weight (BMI)</td>
<td>—†</td>
</tr>
<tr>
<td>Clinical breast examination</td>
<td>C</td>
</tr>
<tr>
<td>Bimanual examination and cervical inspection</td>
<td>A</td>
</tr>
</tbody>
</table>

| Laboratory test                                          |                        | C       | C          | C  | C  | C       | C                       | C          | C          |
| Glucose                                                 | C              | C       | C          | C  | C  | C       | C                       | C          |
| Lipids                                                  | C              | C       | C          | C  | C  | C       | C                       | C          |
| Liver enzymes                                           | C              | C       | C          | C  | C  | C       | C                       | C          |
| Hemoglobin                                              | C              | C       | C          | C  | C  | C       | C                       | C          |
| Thrombogenic mutations                                  | C              | C       | C          | C  | C  | C       | C                       | C          |
| Cervical cytology (Papanicolaou smear)                  | C              | C       | C          | C  | C  | C       | C                       | C          |
| STD screening with laboratory tests                     | —§             | C       | C          | C  | C  | C       | C                       | C          |
| HIV screening with laboratory tests                     | C              | C       | C          | C  | C  | C       | C                       | C          |
Evidence: BP measurement

6 case-control studies

– Women who did not have blood pressure check prior to COC initiation had higher odds of acute myocardial infarction and ischemic stroke than women who had blood pressure check

– No increased risk for hemorrhagic stroke based on whether or not blood pressure measured

No evidence identified on other hormonal methods

• Tepper, Contraception, 2012.
### US SPR

**Exams and tests prior to initiation**

<table>
<thead>
<tr>
<th>Examination or test</th>
<th>LNG and Cu-IUD</th>
<th>Implant</th>
<th>Injectable</th>
<th>CHC</th>
<th>POP</th>
<th>Condom</th>
<th>Diaphragm or cervical cap</th>
<th>Spermicide</th>
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<tbody>
<tr>
<td>Blood pressure</td>
<td>C</td>
<td>C</td>
<td>C</td>
<td>A*</td>
<td>C</td>
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<td>C</td>
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<tr>
<td>Bimanual examination and cervical inspection</td>
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<td>C</td>
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<td>C</td>
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<td>Lipids</td>
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<td>C</td>
<td>C</td>
<td>C</td>
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<tr>
<td>Liver enzymes</td>
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<tr>
<td>Thrombogenic mutations</td>
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<td>C</td>
<td>C</td>
<td>C</td>
<td>C</td>
<td>C</td>
<td>C</td>
</tr>
<tr>
<td>Cervical cytology (Papanicolaou smear)</td>
<td>C</td>
<td>C</td>
<td>C</td>
<td>C</td>
<td>C</td>
<td>C</td>
<td>C</td>
<td>C</td>
</tr>
<tr>
<td>STD screening with laboratory tests</td>
<td>___§</td>
<td>C</td>
<td>C</td>
<td>C</td>
<td>C</td>
<td>C</td>
<td>C</td>
<td>C</td>
</tr>
<tr>
<td>HIV screening with laboratory tests</td>
<td>C</td>
<td>C</td>
<td>C</td>
<td>C</td>
<td>C</td>
<td>C</td>
<td>C</td>
<td>C</td>
</tr>
</tbody>
</table>
Clinical scenario 3: Exams and tests

24 y.o. female comes to office desiring contraception and wants to start pills

- **Q**: Do you need to do any exams or tests before she starts?
- **A**: Blood pressure measurement essential
Pelvic Exam before Initiating CHCs

Is not necessary before starting CHCs

No concerning conditions will be detected by pelvic exam

Evidence:
- Two case-control studies
- Delayed versus immediate pelvic exam before contraception

• Tepper Contraception 2013
Clinical scenario 6: When to stop contracepting

46 y.o. female with a history of hypertension has been using progestin-only pills and wants to know when she can stop her contraception.

– Q: When can a woman stop contracepting?
Evidence

There are no reliable tests to confirm a woman’s definitive loss of fertility.

FSH levels may not be accurate.

The median age of menopause is approximately 51 years in North America with a range of 40-60 years.

Clinical scenario 6: When to stop contracepting

46 y.o. female with a history of hypertension has been using progestin-only pills and wants to know when she can stop her contraception.

- **Q**: When can a woman stop contracepting?
- **A**: Contraceptive protection is still needed in women older than 44 years of age, if the woman wishes to avoid pregnancy.
Scenario 7: What if a woman has menstrual abnormalities using CHCs

28 y.o. female has been using continuous combined OCPs for the last 6 months but has had persistent spotting for the last month.

- Q: What can she do if she wants treatment?
Management of Women with Bleeding Irregularities While Using Contraception*

If bleeding persists, or if woman requests it, medical treatment can be considered.

Cu-IUD users
- For unscheduled spotting or light bleeding or for heavy or prolonged bleeding:
  - NSAIDs (5-7 days of treatment)

LNG-IUD users
- For unscheduled spotting or light bleeding or heavy/prolonged bleeding:
  - NSAIDs (5-7 days of treatment)
  - Hormonal treatment (if medically eligible) with COCs or estrogen (10-20 days of treatment)

Implant users
- For unscheduled spotting or light bleeding or heavy/prolonged bleeding:
  - NSAIDs (5-7 days of treatment)
  - Hormonal treatment (if medically eligible) with COCs or estrogen (10-20 days of treatment)

Injectable (DMPA) users
- For unscheduled spotting or light bleeding:
  - NSAIDs (5-7 days of treatment)
- For heavy or prolonged bleeding:
  - NSAIDs (5-7 days of treatment)
  - Hormonal treatment (if medically eligible) with COCs or estrogen (10-20 days of treatment)

CHC users (extended or continuous regimen)
- Hormone-free interval for 3-4 consecutive days
- Not recommended during the first 21 days of extended or continuous CHC use
- Not recommended more than once per month because contraceptive effectiveness might be reduced

If bleeding disorder persists or woman finds it unacceptable

Counsel on alternative methods, offer another method, if desired

*If clinically warranted, evaluate for underlying condition. Treat the condition or refer for care. Heavy or prolonged bleeding, either unscheduled or menstrual, is uncommon among LNG-IUD users and implant users.

Abbreviations: CHC = combined hormonal contraceptive; COC = combined oral contraceptive; Cu-IUD = copper-containing intrauterine device; DMPA = depot medroxyprogesterone acetate; LNG-IUD = levonorgestrel-releasing intrauterine device; NSAIDs = nonsteroidal anti-inflammatory drugs.

Source: For full recommendations and updates, see the U.S. Selected Practice Recommendations for Contraceptive Use webpage at http://www.cdc.gov/reproductivehealth/unistendedpregnancy/usspr.htm.
28 y.o. female has been using continuous oral contraceptive pills (OCPs) but has had persistent spotting for the last month.

- **Q:** What can she do if she wants treatment?
- **A:**
  - Emphasize importance of correct use and timing
  - Discuss HFI (hormone free interval) for 3-4 days if taking OCPs >21 days
Evidence

Anticipatory counseling decreases method discontinuation from bleeding irregularities with DMPA

Hormone-free Interval (HFI) of 3-4 days improves bleeding after 2 weeks

Doxycycline has not been shown to improve bleeding
Clinical scenario 8: Emergency Contraception

38 y.o. obese female had unprotected intercourse 4 days ago and is worried about pregnancy.

– Q: What are her emergency contraception options?
Four options for EC available in the US

Intrauterine device
- copper intrauterine device (Cu-IUD)

Emergency contraceptive pills (ECPs)
- ulipristal acetate (UPA) available in a single dose (30 mg)
- levonorgestrel (LNG) in a single dose combined
- estrogen/progestin in 2 doses
Large systematic review of 42 studies showed that the pregnancy rate among emergency IUD users is 0.09%.

UPA and LNG ECPs have similar effectiveness when taken within 3 days after unprotected intercourse.

- UPA has been shown to be more effective than the LNG formulation between 3 and 5 days after unprotected intercourse.

UPA may be more effective than LNG for women who are obese.

The combined estrogen/progestin regimen is less effective than UPA or LNG and is associated with more frequent side effects.
% of women experiencing an unintended pregnancy within the first year of use

- Implant: / -/ 4$
- LNG IUS: / -1$
- Copper IUD: / -7$
- Female Sterilization: / -4$

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Salpingectomy for Ovarian Cancer Prevention

ABSTRACT: Ovarian cancer has the highest mortality rate out of all types of gynecologic cancer and is the fifth leading cause of cancer deaths among women. Current attempts at screening for ovarian cancer have been unsuccessful and are associated with false-positive test results that lead to unnecessary surgery and surgical complications. Prophylactic salpingectomy may offer clinicians the opportunity to prevent ovarian cancer in their patients. Randomized controlled trials are needed to support the validity of this approach to reduce the incidence of ovarian cancer. The approach to hysterectomy or sterilization should not be influenced by the theoretical benefit of salpingectomy. Surgeons should continue to observe and practice minimally invasive techniques.

Based on the current understanding of ovarian carcinogenesis and the safety of salpingectomy, the American College of Obstetricians and Gynecologists supports the following recommendations and conclusions:

- The surgeon and patient should discuss the potential benefits of the removal of the fallopian tubes during a hysterectomy in women at population risk of ovarian cancer who are not having an oophorectomy.
- When counseling women about laparoscopic sterilization methods, clinicians can communicate that bilateral salpingectomy can be considered a method that provides effective contraception.
- Prophylactic salpingectomy may offer clinicians the opportunity to prevent ovarian cancer in their patients.
- Randomized controlled trials are needed to support the validity of this approach to reduce the incidence of ovarian cancer.

Ovarian cancer has the highest mortality rate out and are associated with false-positive test results that lead to unnecessary surgery and surgical complications (1–4). Prophylactic salpingectomy may offer clinicians the opportunity to prevent ovarian cancer in their patients.

The most compelling theory of epithelial ovarian carcinogenesis suggests that serous, endometrioid, and clear cell carcinomas are derived from the fallopian tube and the endometrium and not directly from the ovary (5–9). This is in contrast to the traditional view of ovarian carcinogenesis in which ovarian surface epithelium (mesothelium) undergoes metaplastic changes leading to the different histologic types of epithelial ovarian cancer. In women with a genetic predisposition for ovarian cancer, lesions have been found in the fallopian tubes that closely resemble ovarian high-grade serous carcinomas or serous tubal intraepithelial carcinomas. These lesions are thought to be the primary source of ovarian carcinoma that secondarily involves the ovary. Genetics studies show that these tubal lesions express a common TP53 mutation, as do high-grade serous, high-grade endometrioid, and undifferentiated carcinomas. In addi-
CAYA contoured diaphragm

**Product Benefits:**
- Easy insertion and removal
- Easy fit (one size fits most)
- Comfortable for both partners
- Eliminates latex-related odors
- Hormone-Free Contraceptive

**Product Specifications:**
- Elastic body: 50 shore-A durometer medical-grade silicone
- Core: Contoured, one-piece polymer spring
- Overall length: 75 mm
- Overall width: 67 mm
- Membrane: 0.0010” nominal thickness

**Product Features:**

**Dynamic contours**
- Folds in optimal insertion shape
- Embeds gently in supportive tissue

**Gentle folding dynamics**
- Soft, easy folding during insertion and removal
- Slides gently out of the vagina

**Firm insertion edge**
- Folds compactly for easy insertion
- Stable shape when pushing into vagina
- Supports cervical cup in posterior fornix

**Grip dimples (nubs)**
- Enhanced grip when slippery
- Cue for bending locations

**Cervical cup membrane**
- Sized to fit a range of cervical positions
- Surrounds the cervix

**Relief arch**
- Provides finger rest during insertion
- Extra clearance for partner

**Fingertip removal dome**
- Enables easy hooking for removal (from top or bottom)
- Cue for insertion orientation
Future New Method: PATH Women’s Condom

• PATH
• Polyurethane condom pouch
• Adherence to vaginal walls improved by foam dots
• Soft outer ring
• Dissolving capsule
Future New Method: EE + LNG Transdermal Patch

• Agile Therapeutics
• Twirla
• Low-dose, once-weekly patch
• Minimizes seepage of adhesive at edge of patch ("cold flow")
• ↓ chance of residue on skin
• NDA submitted
Future New Method: Monthly Injectable (Cyclofem®)

- Concept Foundation & Sun Pharmaceutical Industries
- 25 mg MPA + 5 mg estradiol cypionante
- Same formulation as injectable previously marketed in the US (Lunelle®)
- Seeking FDA approval for US

www.conceptfoundation.org/hormonal-contraception.php
Future New Method: Nestorone/Ethinyl Estradiol 1-Yr Ring

• Population Council
• Releases 150 mcg nestorone + 15 mcg ethinyl estradiol/day
• Used like existing ring (3 weeks in, 1 week out)
• Lasts 13 cycles
• Awaiting FDA approval
• Also studying topical gel

NES Core

NES / EE Core

8.4 mm (3/8”) in cross-section
58 mm (2 1/14”) in diameter
**Future New Method:**
Many Pills are in Development

<table>
<thead>
<tr>
<th>Company</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Teva</strong></td>
<td>OC continuous regimen of LNG 0.15 mg / EE 20 mcg x42d, 25 mcg x21d, 30 mcg x21d, EE mcg x 7d</td>
</tr>
<tr>
<td><strong>Bayer</strong></td>
<td>Combined OC extended regimens w/ drospirenone 3 mg / EE 20 mcg</td>
</tr>
<tr>
<td><strong>Merck</strong></td>
<td>OC containing nomegestrol acetate 2.5 mg, 17β-estradiol 1.5 mg</td>
</tr>
<tr>
<td><strong>BioSante and Pantarhei Bioscience</strong></td>
<td>OC with estrogen, progestin, and androgen</td>
</tr>
</tbody>
</table>
Resources

- Download US MEC/SPR to your computer, phone
- ACOG LARC program
- Association of Reproductive Health Professionals
- Contraceptive Technology
- Bedsider.org
Resources

Method Match
www.arhp.org/methodmatch

US Clinical Trials Database
ClinicalTrials.gov

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Abnormal Uterine Bleeding
Normal menstrual cycle

### Sonographic appearance of endometrium

<table>
<thead>
<tr>
<th>Phase</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early proliferative</td>
<td>Thin, Linear, Echogenic</td>
</tr>
<tr>
<td>phase endometrium</td>
<td></td>
</tr>
<tr>
<td>Late proliferative</td>
<td>Thick, Trilaminar appearance:</td>
</tr>
<tr>
<td>phase endometrium</td>
<td>1. Central thin, echogenic line</td>
</tr>
<tr>
<td></td>
<td>2. Darker echolucent rim in the middle</td>
</tr>
<tr>
<td></td>
<td>3. Surrounding echogenic basilar layer</td>
</tr>
<tr>
<td>Secretory phase</td>
<td>Thick, Hyperechoic</td>
</tr>
<tr>
<td>endometrium</td>
<td>Homogeneous</td>
</tr>
</tbody>
</table>
Definition of Normal Cycle

• Cycle length of 21 to 35 days
• Duration of flow of 3 to 7 days
• Blood loss of less than 75 ml per cycle, average 36ml
• Spotting mixed with mucus for 1 to 2 days at midcycle consistent with ovulation can be considered normal
• Luteal phase most consistent at 12-14 days
### STRAW (Stages of Reproductive Aging Workshop) 2011

#### Table 1: Stages of Reproductive Aging

<table>
<thead>
<tr>
<th>Stage</th>
<th>Terminology</th>
<th>PRINCIPAL CRITERIA</th>
<th>SUPPORTIVE CRITERIA</th>
<th>DESCRIPTIVE CHARACTERISTICS</th>
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</thead>
<tbody>
<tr>
<td></td>
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<tr>
<td>-5</td>
<td>REPRODUCTIVE</td>
<td></td>
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<tr>
<td>-4</td>
<td>MENOPAUSAL TRANSITION</td>
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<tr>
<td>-3b</td>
<td>Early</td>
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<tr>
<td>-3a</td>
<td>Peak</td>
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<tr>
<td>-2</td>
<td>Late</td>
<td></td>
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<td>-1</td>
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<td>+1 a</td>
<td>Late</td>
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<td></td>
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</tr>
<tr>
<td>+1 b</td>
<td>Early</td>
<td></td>
<td></td>
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<tr>
<td>+1 c</td>
<td>Late</td>
<td></td>
<td></td>
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<tr>
<td>+2</td>
<td>Remaining lifespan</td>
<td></td>
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</tr>
</tbody>
</table>

#### Menarche

**Menstrual Cycle**
- Variable to regular

**Subtle changes in Flow/Length**
- Variable Length
- Persistent ≥7- day difference in length of consecutive cycles

**Interval of amenorrhea of ≥60 days**

**Endocrine**
- FSH
- AMH
- Inhibin B

**Variable**
- Low
- Low

**Variable**
- Low
- Low

**Variable**
- Low
- Low

**Variable**
- Low
- Low

**Variable**
- Low
- Low

**Variable**
- Low
- Low

**Stabilizes**
- Very Low
- Very Low

**Antral Follicle Count**
- Low
- Low
- Low
- Very Low
- Very Low

**Vasomotor symptoms**
- Likely
- Most Likely

**Increasing symptoms of urogenital atrophy**

* Blood draw on cycle days 2-5 ↑ = elevated

**Approximate expected level based on assays using current international pituitary standard**

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Abnormal Bleeding Patterns

• Polymenorrhea—frequent menses regularly occurring at intervals less than 21 days
• Hypermenorrhea—excessive bleeding in amount during normal duration of regular menses
• Hypomenorrhea—decreased bleeding in amount during regular menstrual cycles
Abnormal Uterine Bleeding (AUB)

- *Dysfunctional uterine bleeding, menorrhagia, metrorrhagia* terms considered obsolete
- Chronic AUB: Abnormal in volume, regularity and/or timing for most of the past 6 mos
- Acute AUB: episode of heavy bleeding of sufficient quantity to require immediate intervention to prevent further blood loss

*Munro, et.al. IJGO, 2011*
Bleeding Disorders; AUB-C

- Von Willebrand’s Disease—the most common
- Immune thrombocytopenic purpura
- Leukemia
- Other inherited or acquired blood dyscrasias
- 19% of adolescents hospitalized for AUB have coagulopathy
Hepatic Disease

- Impaired synthesis of coagulation factors
- Impaired synthesis of sex steroids (e.g. estrogen)
- Impaired synthesis of sex hormone binding globulin
AUB-O: Physiologic Causes

- Adolescence
- Perimenopause
- Pregnancy
- Lactation
AUB-O: Pathologic Causes

- hyperandrogenic anovulation (PCOS)
- hypothalamic dysfunction
- hyperprolactinemia
- thyroid disease
- primary pituitary disease
- premature ovarian insufficiency
- medications
Iatrogenic Causes: AUB-I

- Anticoagulants
- Aspirin
- Oral contraceptives
- Progestins
- Corticosteroids
Endometrial causes: AUB-E

Primary disorder of mechanisms regulating local endometrial hemostasis:

- deficiencies in local vasoconstrictors
- accelerated lysis of clot due to elevated plasminogen activator
- increased local production of vasodilators
- inflammation poorly understood
Chronic AUB

3+ months of excessive duration, volume, frequency, unpredictability?

Yes

No

Initial investigation

Structured history

Physical examination

Ancillary investigations

Ovulatory function

Related medical disorders, medications, lifestyle factors

Screening for inherited coagulopathy

Complete blood count

Evaluating endocrinopathy (if oligoanovulation)

Testing for inherited coagulopathies if indicated

Future fertility

Uterine evaluation

Evaluation of Abnormal Bleeding--

History

• Detailed history of bleeding pattern
• Medication and supplement history
• Sexual and contraceptive history
• Obstetrics and past gynecologic history
• Associated symptoms
• Systemic diseases
Evaluation of Abnormal Bleeding—Physical Exam

• Complete pelvic exam: Determine the source of the bleeding (uterine, cervical, vaginal, vulvar, urethral or rectal). Look for visible or palpable lesions

• General exam: Thyroid, breasts, abdomen, skin, vital signs. Especially note obesity, hirsutism, ecchymosis
Evaluation of AUB: Labs

- Pap smear if not done in last year or if cervix is grossly abnormal or bleeding is post-coital
- CBC with platelet count
- Beta HCG
- TSH
- Others depending on history (Prolactin, Ferritin, FSH, LH, Androgens, Progesterone, Coagulation studies, Chlamydia)
Screening for bleeding disorder

Clinical screening for an underlying disorder of hemostasis in the patient with excessive menstrual bleeding.\textsuperscript{a}

Initial screening for an underlying disorder of hemostasis in patients with excessive menstrual bleeding should be by a structured history (positive screen comprises any of the following): \textsuperscript{b}

\begin{itemize}
  \item Heavy menstrual bleeding since menarche
  \item One of the following:
    \begin{itemize}
      \item Postpartum hemorrhage
      \item Surgical-related bleeding
      \item Bleeding associated with dental work
    \end{itemize}
  \item Two or more of the following symptoms:
    \begin{itemize}
      \item Bruising 1–2 times per month
      \item Epistaxis 1–2 times per month
      \item Frequent gum bleeding
    \end{itemize}
  \item Family history of bleeding symptoms
\end{itemize}

\textsuperscript{a} Table reproduced, with permission, from Ref. [51].

\textsuperscript{b} Patients with a positive screen should be considered for further evaluation, including consultation with a hematologist and/or testing of von Willebrand factor and Ristocetin cofactor.

PALM-COIEN classification system

<table>
<thead>
<tr>
<th>Polyp</th>
<th>Coagulopathy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adenomyosis</td>
<td>Ovulatory dysfunction</td>
</tr>
<tr>
<td>Leiomyoma</td>
<td>Endometrial</td>
</tr>
<tr>
<td>Malignancy &amp; hyperplasia</td>
<td>Iatrogenic</td>
</tr>
<tr>
<td>Submucosal</td>
<td>Not yet classified</td>
</tr>
<tr>
<td>Other</td>
<td></td>
</tr>
</tbody>
</table>

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Evaluation of Abnormal Bleeding—Ultrasound and Sonohysterogram

- If EMB is not possible
- If EMB is normal but abnormal bleeding persists, especially if ovulatory or exam abnormal or if not responsive to hormonal treatments
- SHG +EMB has similar sensitivity to hysteroscopy but lower specificity
- 4% false negative rate with ET<5mm
- Schedule day 5 to 8 of menstrual cycle
# AUB-L (Leiomyoma)

## Leiomyoma Subclassification System

<table>
<thead>
<tr>
<th>SM - Submucosal</th>
<th>O - Other</th>
<th>Hybrid leiomyomas (impact both endometrium and serosa)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 Pedunculated intracavitary</td>
<td>3 Contacts endometrium; 100% intramural</td>
<td>2-5 Submucosal and subserosal, each with less than half the diameter in the endometrial and peritoneal cavities, respectively.</td>
</tr>
<tr>
<td>1 &lt;50% intramural</td>
<td>4 Intramural</td>
<td></td>
</tr>
<tr>
<td>2 ≥50% intramural</td>
<td>5 Subserosal ≥50% intramural</td>
<td></td>
</tr>
<tr>
<td>6 Subserosal &lt;50% intramural</td>
<td>7 Subserosal pedunculated</td>
<td></td>
</tr>
<tr>
<td>8 Other (specify e.g., cervical, parasitic)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Evaluation of Abnormal Bleeding—Endometrial Biopsy

- Indicated in women >45 yrs
- Also consider in younger women when high risk for hyperplasia or cancer (chronic anovulation, obesity (BMI over 30), family history, diabetes, hypertension) or if not responsive to treatment
- Misoprostol 200-400 mcg vaginally 4 to 8 hours prior to EMB facilitates if cervix is stenotic
Evaluation of Abnormal Bleeding---Hysteroscopy

• Gold standard for diagnosis of intrauterine lesions
• Office hysteroscopy with local anesthesia can be done for diagnosis and directed biopsy
• Operative hysteroscopy requires OR and anesthesia. D&C, myomectomy or polypectomy can be done at same time
Evaluation of Abnormal Bleeding—Other Studies

• MRI to assess fibroids and look for adenomyosis in some circumstances
• Laparoscopy occasionally required to look for endometriosis or pelvic inflammatory disease
PALM-COIEN classification system

- Polyp
- Adenomyosis
- Leiomyoma
- Malignancy & hyperplasia

- Coagulopathy
- Ovulatory dysfunction
- Endometrial
- Iatrogenic
- Not yet classified

Submucosal
Other
Treatment of Acute Heavy Menstrual Bleeding

- Exam including orthostatic vital signs
- Add coag studies (CBC, plts, PT, PTT) and type and cross to labs
- Start IV fluids if profuse or unstable vital signs
Treatment of Acute Bleeding

- Conjugated estrogen 2.5 mg p.o. q 6 h or 25 mg IV q 4-6h works within 3 hours in 72% (38% in placebo)
- Tranexamic acid 10mg/kg IV (max 600mg/dose) or 1300mg po tid x 5 days
- Intrauterine tamponade with Foley catheter
- If patient is unstable or unresponsive to hormonal treatments, D&C in OR may be needed
Treatment of Acute Bleeding

- If bleeding is heavy but can wait 24 to 48 hours for significant decrease, can use combo OCP (35 mcg estrogen) bid-tid for 7 days, then daily for 2 more weeks
- MPA 20mg tid x 7 days
- Norethindrone 5 mg tid until bleeding stops, then qd-bid for 21 days total also usually effective with less nausea and risk
- Once hormonal therapies are stopped, withdrawal bleeding will occur
Treatment of AUB-O

• Levonorgestrel-releasing IUD
• COCs if no contraindications-reduced HMB by up to 77% but less than IUD
• Cyclic progestin:
  • Norethindrone 5mg day 16-25 of each cycle
  • Medroxyprogesterone acetate 10mg day 16-25
  • Micronized progesterone may require 200-400mg to achieve similar effect
Treatment of Chronic AUB-O

- Levonorgestrel-releasing IUD (Mirena)
- Oral contraceptives if no contraindication
- Cyclic progestogen (norethindrone or medroxyprogesterone) for 10-14 days per month
- Ovulation induction if pregnancy desired
Progestin treatment

- Encourage patient to chart cycles on paper or an app such as Clue Period, Menstrual Tracker
- If amenorrheic, can use progestin day 1-10 of each calendar month for convenience
- May take several mos to get regulated. Menses often lighten after several months of use
- in perimenopausal women, continue until 3 consecutive cycles without withdrawal bleeding
Treatment of AUB: Surgery

- **Hysteroscopy, D&C, polypectomy.** Blind D&C indicated only for profuse bleeding or pregnancy related complications. Polypectomy can be therapeutic.
- **Hysteroscopic myomectomy** for submucous fibroids <4 cm and >50% intracavitary. May be combined with ablation.
Treatment of AUB—Surgical Options

• **Endometrial ablation:** multiple techniques (we use Minerva radiofrequency ablation)
  - Most done in OR with anesthesia, but some can be done in office with local
  - Pregnancy contraindicated after procedure
  - Indicated for hypermenorrhea or menorrhagia when hormonal treatments fail, contraindicated or not tolerated
  - Amenorrhea or eumenorrhea rate 84-90% but 27% had further surgery by 5 years
Treatment of AUB-L: Surgery

- **Myomectomy** by laparoscopy or laparotomy
- **Uterine Artery Embolization**
  - Indicated for leiomyomata causing bleeding or pressure symptoms
  - Average shrinkage about 40%
  - About 76% patient satisfaction
  - Not recommended for women desiring fertility except for life-threatening hemorrhage.
Hysterectomy

- Definitive treatment when other treatments are ineffective or not tolerated, or for malignant or premalignant conditions.

  - High rate of patient satisfaction compared to medical management or ablation, but higher cost and morbidity.

  -50% of women choose hysterectomy after a trial of medical management for chronic menorrhagia, but rate varies by cause of bleeding.
The Sonata System was designed to transcervically ablate types 1, 2, 3, 4 and 2-5 (transmural) fibroids and is also capable of partially ablating type 5 and type 6 myomata.

Extramural (eg, cervical, broad ligament) and pedunculated fibroids (types 0, 7) are not intended for treatment with Sonata.

<table>
<thead>
<tr>
<th>Submucosal</th>
<th>0</th>
<th>Pedunculated intracavity</th>
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<tr>
<td></td>
<td>1</td>
<td>&lt;50% Intramural</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>≥50% Intramural</td>
</tr>
<tr>
<td>Intramural</td>
<td>3</td>
<td>Contacts endometrium; 100% Intramural</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>Intramural</td>
</tr>
<tr>
<td>Subserosal</td>
<td>5</td>
<td>Subserosal, ≥50% Intramural</td>
</tr>
<tr>
<td></td>
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Transmural: 2-5 Submucosal and subserosal, each with less than half the diameter in the endometrial and peritoneal cavities respectively.

## Choosing a treatment option

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Hysterectomy

• Vaginal is favored route when possible. Ovaries can be removed also
• Laparoscopic/Robotic
• Abdominal may be necessary with larger fibroids, prior surgery, or additional pathology
• Supracervical?