Obstetrics and Gynecology

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Learning Objectives:

1. Recommend contraceptive products, infertility, menstrual disorders, endometriosis, and postmenopausal therapy based on patient-specific information.
2. Recommend treatment of common acute and chronic conditions in pregnancy.
3. Educate patients regarding medication use during pregnancy and lactation, contraception, infertility, menstrual disorders, endometriosis, and postmenopausal therapy.
4. Identify resources for additional information for health care providers and patients for contraception, infertility, pregnancy and lactation, menstrual disorders, endometriosis, postmenopausal therapy, and patient assistance programs.

Self-Assessment Questions:

Answers and explanations to these questions may be found at the end of the chapter.

The following case pertains to questions 1 and 2.

A 36-year-old woman is at the clinic for her checkup. At 2 weeks postpartum checkup, she wants to know what she should use for contraception. She is upset because she had to stop breastfeeding after her stroke when she was 5 days postpartum. Her medical history is significant for morbid obesity, tilted and bicornate uterus, allergic rhinitis, and cerebral vascular accident (5 days postpartum). She is allergic to latex. Current medications are lisinopril 5 mg/day, hydrochlorothiazide 12.5 mg/day, simvastatin 20 mg every night, and aspirin 81 mg/day (all medications started 1.5 weeks ago).

1. Which one of the following is the best contraceptive recommendation for this woman?
   A. Depot medroxyprogesterone acetate.
   B. Levonorgestrel intrauterine device (IUD).
   C. Contraceptive sponge.
   D. Polyurethane condom.

2. The patient calls to ask for another contraceptive choice because she cannot afford the item you recommended. She states that the free clinic does not carry the item either. Which one of the alternative contraceptives that can be provided for free from either your clinic or the free clinic is the best recommendation?
   A. Female condom.
   B. Male latex condom.
   C. Yaz (ethinyl estradiol and drospirenone).
   D. Ella One (ulipristal).

3. A double-blind, randomized trial is planning to evaluate the effects of depot medroxyprogesterone, leuprolide, and placebo on the bone mineral density of 600 patients with endometriosis. Which one of the following statistical tests is most appropriate?
   A. Student t-test.
   B. Fisher exact test.
   C. Kruskal-Wallis test.
   D. Analysis of variance.

4. A 40-year-old woman asks to see the pharmacist after her physician appointment. She states that she was prescribed a new drug during her pregnancy. She is uncomfortable taking medications during her pregnancy because her family said that they all cause risk. Which one of the following is the best information to include when educating the patient on the risks and benefits of the drug?
   A. Rate of birth defects in animal data.
   B. Gestational timing of risks and pregnancy.
   C. Molecular weight of the drug.
   D. Degree of ionization.

5. A 32-year-old woman who is 2 weeks postpartum calls your office asking whether it is okay for her to start terbinafine for 6 months for toe onychomycosis that began during the pregnancy. She states she saw a podiatrist yesterday and was given this prescription. She denies pain, redness, or difficulty walking but states she does not like how her toes look when wearing sandals. She is currently breastfeeding every 2 hours. You will find the following information regarding use in breastfeeding in Hale TW. *Medications and Mothers' Milk,* 2008: Milk/plasma ratio, unknown; relative infant dose, unknown; half-life ($t_{1/2}$), 26 hours; 99% protein bound; molecular weight, 291. Which one of the following is the best recommendation?
   A. Delay treatment until finished breastfeeding.
   B. Change to itraconazole.
   C. Use topical terbinafine.
   D. Schedule doses right after feedings.

6. A 21-year-old woman is at the office for a follow-up of her dysmenorrhea. She states that ibuprofen has only slightly improved her pain and would like something else. She is currently in a monogamous relationship and would like contraceptive protection as well. Today: 5′5″ 220 lb, blood pressure 118/68 mm Hg, and heart rate 72 beats/minute. Which one of the following is the best recommendation?
   A. Ethinyl estradiol and norelgestromin (Ortho-Evra) 1 patch once weekly for 3 weeks.
   B. Ethinyl estradiol and norelgestromin (Ortho-Evra) 1 patch every week for 11 weeks.
   C. Ethinyl estradiol 35 mcg and ethynodiol diacetate 1 mg (Demulen 1/35) 1 tablet every day for 3 weeks.
   D. Ethinyl estradiol 35 mcg and ethynodiol diacetate 1 mg (Demulen 1/35) 1 tablet every day for 11 weeks.

7. A 49-year-old woman is starting estradiol valerate and dienogest (Natazia) for perimenopausal symptoms and contraceptive needs. You are asked to educate the patient about this product. Which one of the following is the minimal length of time that a backup method of contraception should be used after initiation?
   A. 48 hours.
   B. 7 days.
   C. 9 days.
   D. 28 days.

8. A 38-year-old woman is calling because of intolerable vasomotor symptoms that interfere with her daily activities. She states her hot flashes occur at least 12 times/day and cause her to change clothes often. She would like additional therapy. Her medical history includes breast cancer (diagnosed 1 month ago). She takes trastuzumab. Blood pressure is 104/64 mm Hg, and heart rate is 66 beats/minute. Which one of the following is the best recommendation?
   A. Conjugated equine estrogens.
   B. Venlafaxine.
   C. Clonidine.
   D. Black cohosh.

9. A 25-year-old woman was recently given a diagnosis of endometriosis. She is having trouble coping with the diagnosis and wants to find a support group. Which one of the following is the best resource for finding local support groups?
   A. Association of Reproductive Healthcare Providers.
   B. American College of Obstetricians and Gynecologists.
   C. Endometriosis Association.
   D. National Women's Health Network.

I. CONTRACEPTION

Patient Case

A 39-year-old woman is requesting hormonal contraception. She plans to start attempting conception in about 12 months. She is currently 6 weeks postpartum and is formula feeding the infant. Her medical history is significant for gestational diabetes, hypertension, and hyperthyroidism. Current medications are propylthiouracil 100 mg 3 times/day, lisinopril 10 mg/day, hydrochlorothiazide 25 mg/day, and a prenatal vitamin 1 tablet/day. Social history: Patient denies tobacco use, uses ethanol socially, and denies illegal drugs. Her height is 5′5″; her weight today is 250 lb (pre-pregnancy weight of 230 lb). Blood pressure is 178/96 mm Hg today (188/102 mm Hg 2 weeks ago).

1. Which one of the following is the most appropriate hormonal contraceptive recommendation?
   A. Depo-Provera (medroxyprogesterone acetate).
   B. Ortho-Evra (ethinyl estradiol and norelgestromin).
   C. Yaz (ethinyl estradiol and drospirenone).
   D. Micronor (norethindrone).

A. Product Overview

Table 1. Hormonal Contraceptive Comparison

Product	Hormones	Route	Administration (Standard)	Return of Ovulation	Notes
Monophasics	Estrogen-progestin	Oral	Daily for 21 days or see below	3 months	
	• Mircette: 21 active tablets, 2 placebo tablets, and 5 tablets of 10 mcg of estrogen: Decrease estrogen withdrawal symptoms during menses • Yaz and Lo-Estrin 24: 24 active tablets; lighter, shorter menses • Seasonale: 84 active tablets to have menses every 3 months • Seasonique: 84 active; then 10 mcg of estrogen for 7 days for menses every 3 months and less estrogen withdrawal symptoms during menses • Lybrel: 30 active tablets for no menses but high rates of breakthrough bleeding				
Multiphasics	Estrogen-progestin	Oral	Daily for 21 days	3 months	• Biphasic, triphasic, and quadriphasic
NuvaRing	Estrogen-progestin	Vaginal	3 weeks	3 months	• Only one strength available • Can safely be removed for up to 3 hours during intercourse • Rinse product and then reinsert
Ortho-Evra	Estrogen-progestin	Topical	Weekly for 3 weeks	3 months	• Only one strength available • Higher cumulative estrogen exposure than most oral contraceptives • Reduced efficacy for body weight > 90 kg
Progestin-only pills	Progestin	Oral	Daily for 28 days	1 month	• Must be taken within 3 hours of usual time or backup method of contraception needed for 48 hours
Depo-Provera, Depo-SQ-Provera	Progestin	Intramuscular Subcutaneous	Every 12 ± 2 weeks	9 months	• Risk of bone loss after 2 years of continued use, although reversible on discontinuation • Weight gain
Implanon	Progestin	Intradermal	Every 3 years	1 month	
Mirena	Progestin	Intrauterine	Every 5 years	1 month	

B. Extended-Interval Dosing (i.e., stacking packs):
   1. Monophasics
      a. Take 3 weeks of active pills from pack 1.
      b. Throw out placebo tablets from pack 1. Start active pills from pack 2 immediately.
      c. Extends cycle by an additional 3 weeks
      d. Can use multiple packs in a row to extend cycle
   2. Multiphasics
      a. Option 1 (to extend cycle by 5–11 days depending on brand of contraceptive)
         i. Take 3 weeks of active pills from pack 1.

ii. Throw out the placebo tablets from pack 1. Start highest-progestin-level active pills in pack (usually 7 [range 5–11] tablets depending on brand).
iii. Use of each additional pack extends the cycle by 1 week.

b. Option 2 (to extend cycle by several weeks)

Table 2. Using Multiple Packs of Multiphasic Contraceptives (example of two packs)

Steps	Directions
1	Take level 1 tablet (ex. Week 1—Low-estrogen, low-progestin tablets) of pack 1
2	Take level 1 tablets of pack 2. Repeat with number of packs using to extend cycle
3	Take level 2 tablets (ex. Week 2—high-estrogen, low-progestin tablets) of pack 2
4	Take level 2 tablets of pack 2. Repeat with number of packs using to extend cycle
5	Take level 3 tablets (ex. Week 3—high-estrogen, high-progestin tablets) of pack 1
6	Take level 3 tablets of pack 2. Repeat with number of packs using to extend cycle

3. NuvaRing
   a. Insert vaginal ring for 3 weeks and remove.
   b. Immediately insert a new ring for 3 weeks (may use several rings in a row to extend cycle).
4. Ortho-Evra
   a. Place one patch on for 1 week and remove.
   b. Immediately place a new patch on for 1 week.
   c. May use several patches in a row to extend cycle

C. Advantages/Disadvantages of Products
1. Estrogen-progestin products
   a. Advantages
      i. High efficacy if taken as instructed
      ii. Improve menstrual symptoms; decrease amount and length of menses
      iii. Decrease risk of ectopic pregnancies
      iv. Safe throughout reproduction years
      v. Readily reversible
      vi. Cycle manipulation
      vii. Decrease incidence and severity of pelvic inflammatory disease (PID); decrease menstrual blood loss, which may act as a medium for bacterial growth
      viii. Decrease risk of ovarian and endometrial cancer
      ix. Decrease risk of functional ovarian cysts
      x. Decrease risk of fibrocystic breast disease
      xi. Helpful for patients with PCOS
         (a) Decrease stimulation of androgen production in the ovaries
         (b) Decrease free testosterone by increasing sex hormone–binding globulin
      xii. Decrease acne
   b. Disadvantages
      i. No protection against sexually transmitted infections
      ii. Pills require timely daily administration.
      iii. Increase blood pressure
         (a) Increase angiotensinogen

(b) Sodium and water retention
iv. Increase risk of stroke and myocardial infarction
(a) Mainly with 50 mcg of ethinyl estradiol products and concomitant risk factors
(b) Smokers older than 35 years
v. Increase risk of thromboembolic disorders
vi. Increase risk of glucose intolerance
vii. Increase risk of chlamydia infections
(a) Associated with cervical ectopy (cervical surface becomes covered with mucus-secreting cells that normally line the cervical canal), increasing the risk of chlamydial infections
(b) Pelvic inflammatory disease infection rate is not increased.
viii. Increase risk of gallbladder disease

2. Progestin-only products
a. Advantages of progestin-only pills
i. Used for patients with contraindications to estrogen products (e.g., older than 35 years and smoke 15 or more cigarettes per day, thromboembolism)
ii. Good for patients with intolerable adverse events to estrogen products
iii. Less risk of myocardial infarction in stroke patients older than 35 years
iv. Safe for breastfeeding patients; progestins have no effect on milk production, whereas estrogens decrease milk production
b. Disadvantages of progestin-only pills
i. Timely daily administration
ii. Irregular menses and increased risk of breakthrough bleeding and spotting
iii. Increased risk of ectopic pregnancy
iv. Increased need for adherence and consistent administration time (use backup method of contraception for 48 hours if dose is taken 3 or more hours late)
v. Increased risk of ovulation because of lower progestin dose
c. Advantages of depot medroxyprogesterone acetate
i. Progestin-only pill advantages
ii. Less user variance/error with less frequent administration
iii. Scant-to-light menstrual bleeding with continued use
iv. Decreased risk of anemia secondary to decreased menstrual bleeding
v. Decreased menstrual cramps and mittelschmerz pain
vi. Decreased risk of endometrial and ovarian cancer
vii. Decreased risk of PID
viii. Useful in treatment of endometriosis secondary to light menstrual bleeding or amenorrhea with continued use
ix. No drug interactions
d. Disadvantages of depot medroxyprogesterone acetate
i. Delayed onset of returned fertility
ii. Menstrual irregularities with first several injections
iii. Increased risk of bone loss
iv. Decreases high-density lipoproteins
e. Advantages of progestin-only IUD
i Progestin-only pill advantages
ii. Can be left in place for up to 5 years
iii. Provide two mechanisms of action
iv. Twenty percent have amenorrhea for 1 year.

f. Disadvantages of progestin-only IUD
   i. Need to check daily for strings
   ii. Should avoid if patient has a history or increased risk of PID
   iii. Heavy menstrual bleeding and cramping after placement

D. Adverse Events

Table 3. Signs/Symptoms of Hormone Excesses and Deficiencies

Estrogen Excess	Progestin Excess	Androgen Excess	Estrogen Deficiency	Progestin Deficiency
Nausea	Moodiness	Increased appetite	Irritability	Weight loss
Dizziness	Noncyclic weight gain	Noncyclic weight gain	Nervousness	Heavy menstrual bleeding
Edema	Fatigue	Increased libido	Vasomotor symptoms	Late-cycle breakthrough bleeding/ spotting
Bloating	Depression	Oily skin	Early-midcycle breakthrough bleeding/spotting	Delayed onset of menstrual bleeding
Cyclic weight gain	Increased libido	Hirsutism	Decreased libido	
Chloasma	Alopecia	Acne	Headaches	
Uterine cramps	Decreased menstrual bleeding length	Pruritus	Depression	
Irritability	Insulin resistance		Dry vaginal mucosa	
Depression	Headaches between pill packs		Atrophic vaginitis	
Fat deposition	Vaginal candidiasis		Dyspareunia	
Poor contact lens fit	Hypertension		Uterine prolapse	
Headaches during active pills	Breast tenderness			
Hypertension	Leg vein dilation			
Breast tenderness	Decreased breast size			
Increased breast size				
Thrombophlebitis				
Stroke				
Myocardial infarction				
Suppress lactation				

Patient Case
A 21-year-old woman has been taking contraceptive X for the past 8 months. She calls today because she has been experiencing breakthrough bleeding for 2 days, and then her menses begin 4–5 days later. She states it is bothersome to have so much bleeding in the past two cycles. Her medical history includes dysmenorrhea.

Product	Estrogen Activity	Progestin Activity	Androgenic Activity
X	++	++	++
A	++	+++	++
B	+++	++	++
C	+	++	++
D	++	+	++

2. Which one of the following is the best recommendation?
   A. A.
   B. B.
   C. C.
   D. D.

1. Adjusting products
   a. Identify whether adverse event is related to hormone deficiency/excess; need to rule out that adverse event is related to incorrect use or administration timing (i.e., nausea with morning dose)
   b. Select a product with more or less activity than the hormone abnormality.
   c. If you choose a product with higher endometrial activity, you can switch products at any time in the pack. If the new product has less endometrial activity, wait until the next cycle before changing.
   d. Use the Dickey Managing Contraceptive Pill Patients reference tables.

E. Contraindications

Table 4. Contraindications to Hormonal Contraceptives (*U.S. Medical Eligibility Criteria and World Health Organization*)

	Estrogen-Progestin		Progestin Only		IUD	
	Relative	Absolute	Relative	Absolute	Relative	Absolute
Breast cancer						
-Disease free for > 5 years	✓				✓ LNG	
-Current breast cancer		✓		✓		✓ LNG
Cerebrovascular						
-Stroke		✓	✓			
Diabetes mellitus						
-Diagnosed more than 20 years ago	✓					
-Diabetes with end-organ damage		✓				
Gallbladder						
-Symptomatic gallstones without cholecystectomy	✓					
-Hormone-related gallstones	✓					
Heart Disease						
-Ischemic heart disease		✓	✓		✓ LNG	
-Complicated valvular heart disease		✓				
Hypertension						
-Well-controlled blood pressure	✓					
-SBP 140–160 or DBP 90–100	✓					
-SBP > 160 or DBP > 100		✓				
-Hypertension + vascular disease		✓				
IBD[a]						
Moderate disease or increased risk of VTE	✓					
Liver						
-Mild cirrhosis	✓					
-Severe cirrhosis		✓	✓		✓ LNG	
-Tumors (benign or malignant)		✓	✓		✓ LNG	
-Active viral hepatitis		✓			✓ LNG	
Migraines						
-Without aura and > 35 years old	✓					
-With aura (all ages)		✓				
Peripartum cardiomyopathy						
-Class I or II						
< 6 months		✓				
≥ 6 months	✓					
-Class III or IV		✓				
Postpartum						
-Breastfeeding < 1 month	✓					
-Not breastfeeding and < 21 days	✓					
-Puerperal sepsis						✓
-Immediate post-septic abortion						✓

Table 4. Contraindications to Hormonal Contraceptives (*U.S. Medical Eligibility Criteria and World Health Organization*) *(Contintued)*

	Estrogen-Progestin		Progestin Only		IUD	
	Relative	Absolute	Relative	Absolute	Relative	Absolute
Surgery						
-Major with prolonged immobility		✓				
-Had gastric bypass surgery	✓ (oral)		✓ (oral)			
Thromboembolism						
-History of DVT/PE with ≥ 1 risk factor		✓				
-History of DVT/PE without risk factor	✓					
-DVT/PE on anticoagulation		✓				
-Known thrombogenic mutations		✓				
Transplant						
Complicated[b]		✓			✓[c]	
Sexually Transmitted Infections						
-Current pelvic inflammatory disease						✓
-Purulent cervicitis, chlamydia, gonorrhea						✓
-Pelvic tuberculosis					✓	✓[c]
Systemic Lupus Erythematous						
-Positive antiphospholipid antibodies		✓				
-Severe thrombocytopenia			✓[c]			
Tobacco Use						
-< 15 cigarettes/day and ≥ 35 years old	✓					
-≥ 15 cigarettes/day and ≥ 35 years old		✓				
Urogenital						
-Unexplained vaginal bleeding						✓[c]
-Gestational trophoblastic disease						
+No hCG or decreasing hCG					✓	
+hCG persistently elevated						✓
-Endometrials/cervical cancer awaiting treatment						✓[c]

[a]Increased risk of IBD: active or extensive disease, surgery, immobilization, corticosteroid use, vitamin deficiencies, fluid depletion.
[b]Complicated transplant: Graft failure, rejection, cardiac allograft vasculopathy.
[c]Initiation of product.
DBP = diastolic blood pressure; DVT = deep venous thrombosis; hCG = human chorionic gonadotropin; IBD = inflammatory bowel disease; IUD = intrauterine device; LNG = levonorgestrel IUD; PE = pulmonary embolism; SBP = systolic blood pressure; VTE = venous thromboembolism.