Hormonal Contraception: A Case-Based Approach

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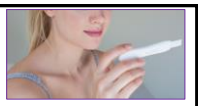
1

Objectives

- The pharmacist participant will be able to:
  - Identify and describe hormonal contraceptive options that pharmacists can prescribe in New Mexico: oral contraceptives; vaginal ring; patch; depo medroxyprogesterone injection.
  - Describe differences in efficacy and safety of hormonal contraceptive options.
  - Given a patient case, describe how to engage in shared decision-making with a patient in order to prescribe hormonal contraception.
  - Given a patient case, identify adverse effects of hormonal contraception and describe how to manage them.
- The pharmacy technician participant will be able to:
  - Identify and describe hormonal contraceptive options that pharmacists can prescribe in New Mexico: oral contraceptives; vaginal ring; patch; depo medroxyprogesterone injection.
  - Describe differences in efficacy and safety of hormonal contraceptive options.
  - Refer patients for pharmacist counseling on contraceptive choices and management.

2

Approach to Contraception



- Undesired fertility: a "chronic condition"?
  - "Childbearing age" defined by CDC as 15-44 years old
  - Average age at menarche in U.S. is ~12.5 years old
  - Average of menopause in U.S. ~51 years old
  - U.S. birth rate is <2 per woman
- Patient's reproductive life plan; contraceptive preferences; safety of methods – all may change
- Should be re-evaluated and managed appropriately throughout patient's entire reproductive lifetime

3

Approach to Contraception

The best contraceptive method is the one the patient will **consistently use** **AND** is **effective, safe,** and **fits her lifestyle and preferences**

4

Women trust pharmacists to help them make decisions about contraception

- **Direct Access Study**
  - 195 women in Seattle
  - 97.7% "satisfied" or "very satisfied"
  - 97.1% would recommend the pharmacist to a friend
  - 96.6% felt they could ask the pharmacist any questions

Source: Gardner, et al. https://www.ncbi.nlm.nih.gov/pubmed/18359734

5

Pharmacists can help prevent unintended pregnancy

- **Oregon Medicaid**
  - January 2016—December 2017
  - 1,313 RXs for women in Oregon Medicaid program
  - Estimated to prevent 51 unintended pregnancies
  - Estimated $1.6 million dollars saved
  - Authors projected New Mexico could save $2.3 million

Source: Rodríguez, et al. https://www.ncbi.nlm.nih.gov/pubmed/31083125

6

Pharmacists may not be referring patients for LARC

- **California & Oregon**
  - August 2016—February 2017
  - 381 pharmacists; 2,117 visits
  - Did not identify any referrals for long-acting reversible contraception (LARC)
  - Reasons unknown
    - Women may self-select for pharmacy services
    - Pharmacist counseling may guide women

Source: Lu, et al. https://www.ncbi.nlm.nih.gov/pubmed/30562478

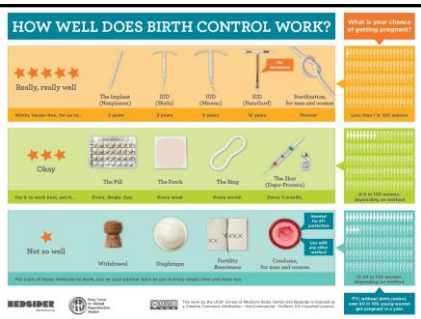
7

Women may prefer LARC when cost & access are not factors

- The pill and female sterilization are the most popular forms of contraception in the U.S.
- Contraceptive CHOICE Project: participants offered a method of their choice at no cost for 2-3 years
- 75% of participants chose LARC (IUD or implant)
  - Rates in U.S. <1% to 6%
- LARC methods were 20 times more effective than non-LARC methods
- LARC methods had higher continuation rates at 12 & 24 months

Sources: The Contraceptive CHOICE Project in Review. https://www.ncbi.nlm.nih.gov/pubmed/25825986
Guttmacher Institute. https://www.guttmacher.org/fact-sheet/contraceptive-use-united-states

8



Source: https://www.bedsider.org/

9

US Medical Eligibility Criteria for Contraceptive Use

- https://www.cdc.gov/reproductivehealth/contraception/mmwr/mec/summary.html
- Downloadable print version available
- App for iOS and Android: search "Contraception"

10

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

Condition	Sub-Condition	Cu-IUD		LNG-IUD		Implant		DMPA		POP		CHC	
		I	C	I	C	I	C	I	C	I	C	I	C
Diabetes	a) History of gestational disease	1		1		1		1		1		1	
	b) Nonvascular disease												
	i) Non-insulin dependent	1		2		2		2		2		2	
	ii) Insulin dependent	1		2		2		2		2		2	
	c) Nephropathy/retinopathy/neuropathy[3]	1		2		2		3		2		3/4*	
	d) Other vascular disease or diabetes of >20 years' duration[3]	1		2		2		3		2		3/4*	
Dysmenorrhea	Severe	2		1		1		1		1		1	
Endometrial cancer[2]		4	2	4	2	1		1		1		1	
Endometrial hyperplasia		1		1		1		1		1		1	
Endometriosis		2		1		1		1		1		1	
Epilepsy[3]	(see also Drug Interactions)	1		1		1*		1*		1*		1*	
Gallbladder disease	a) Symptomatic												
	i) Treated by cholecystectomy	1		2		2		2		2		2	
	ii) Medically treated	1		2		2		2		2		3	
	iii) Current	1		2		2		2		2		3	
	b) Asymptomatic	1		2		2		2		2		2	

Example of MEC – many more disease states are included in full document

11

Many factors influence contraceptive choices

- Worked in the past
- Heard about from a friend or family member
- In the news
- Adherence
- Convenience
- Cost
- Effect on menstrual cycle
- Need to keep method hidden
- Return to fertility/desire for future pregnancies
- Timing and spacing of pregnancies
- …and more

12

Pharmacists with hormonal contraception prescriptive authority can prescribe:

- Hormonal contraceptive vaginal ring
- Hormonal contraceptive patch
- Depot medroxyprogesterone acetate (DMPA) injection
- Combined oral contraceptives
- Progestin-only oral contraceptives
- Emergency contraception, excluding IUDs
  - Plan B
  - Ella
- Other FDA-approved hormonal or non-hormonal methods, excluding implants/IUDs (e.g., condoms)

13

Nuvaring ® etonogestrel/ethinyl estradiol 120/15 mcg/day
Annovera™ segesterone acetate/ethinyl estradiol 150/13 mcg/day
Approved August 2018

>99% effective (perfect use)
91% effective (typical use)

Mechanism of Action	How to Use	Notes
Progesterone and estrogen combination Prevention of ovulation; thickening of cervical mucus, inhibiting sperm Estrogen component also helps to stabilize endometrium, decreasing breakthrough bleeding	Nuvaring 1 ring inserted into the vagina for 3 weeks, then removed for 1 week *(off-label: use continuously for 4 weeks, then replace with new ring)* Annovera 1 ring inserted into vagina for 3 weeks, then removed for 1 week; clean, dry, and store ring during off week; repeat	Adherence may be higher vs. pill Easier to hide than patch or pill Continuous, steady release of hormones & lowest serum levels of hormones vs. other combined hormonal methods

14

Xulane ® norelgestromin and ethinyl estradiol 150/35 mcg/day

>99% effective with perfect use
91% effective typical use

Mechanism of Action	How to Use	Notes
Progesterone and estrogen combination Prevention of ovulation; thickening of cervical mucus, inhibiting sperm Estrogen component also helps to stabilize endometrium, decreasing breakthrough bleeding	1 patch applied each week for 3 weeks, then 1 week off *(off-label: wear for 3 weeks, remove and replace with new patch immediately)*	Adherence may be higher vs. pill Higher estrogen exposure than pills or ring → may increase VTE risk Less effective in women >90kg (198 lbs)

15

Depomedroxyprogesterone (DMPA)
150 mg (IM); 104 mg (SQ)

99.8% effective perfect use
94% effective typical use

Mechanism of Action	How to Use	Notes
Progestin-only method Prevention of ovulation Thinning of endometrium	IM or SQ injection every 3 months *(11-15 weeks)*	Easier to keep hidden vs. other methods High discontinuation rate compared to other methods (~44-77% in various studies) Slow baseline return to fertility (~10 months avg; up to 18+ months)

16

Pill (combined: estrogen and progestin)
Contain ethinyl estradiol (EE) and a progestin
a few contain mestranol, which is metabolized to EE

99.7% effective perfect use
91% effective typical use

Mechanism of Action	How to Use	Notes
Progesterone and estrogen combination Prevention of ovulation; thickening of cervical mucus, inhibiting sperm Estrogen component also helps to stabilize endometrium, decreasing breakthrough bleeding	1 tablet by mouth every day (at about the same time) May skip placebos or use extended-cycle formulation to avoid withdrawal bleeding	There is no clear evidence to indicate a significant difference in efficacy, side effects, or tolerability between formulations

17

Pill (progestin-only)
Norethindrone 0.35mg – "mini pill"; POP

99.7% effective (perfect use)
91% effective (typical use)

Mechanism of Action	How to Use	Notes
Primarily works by thickening cervical mucus; ovulation suppressed in only ~60% of users Thickening of cervical mucus occurs ~2-4 hours after taking the pill & lasts about 22 hours	1 tablet by mouth every day at the SAME TIME (>3 hours late = "missed dose") No placebo tablets; take continuously	As effective as combined oral contraceptives with correct use Take mid-day for increased efficacy?

18

Emergency Contraception

Method	Mechanism of Action	How to Use	Notes
Levonorgestrel (Plan B One Step; Next Choice; My Way, etc.)	Prevention of ovulation	1 tablet taken within 72 hours of unprotected intercourse (more effective the earlier it is taken; may use up to 120 hrs but less effective)	- Should be offered to all women using short-acting hormonal contraception to have on hand in the event of missed doses ~98-99% effective; less effective in overweight/obese women
Ulipristal acetate 30 mg (Ella)	Progesterone receptor modulator; inhibits or delays ovulation; may prevent implantation	1 tablet taken within 120 hours (5 days) of unprotected intercourse	~98-99% effective; less effective in obese women
Copper IUD ***not included in prescriptive authority**	May interfere with implantation	Place within 5 days of unprotected intercourse	Most effective emergency contraceptive method (1/1000 failure rate)

19

Cases

- New Start
- Problem with the Pill
- Emergency Contraception
- Shared Decision-Making

20

Case 1: New Start

- 19-year-old female, a student at UNM
- 5'8", 135 pounds, normal BMI
- Blood pressure **114/76 mmHg**
- **Last menstrual period was 6 days ago**; no unprotected intercourse since then
- **History of mild headaches** "when I'm stressed at school"; no other PMH; non-smoker
- Has **never taken hormonal contraceptives before**; uses condoms; has a "friend with benefits"
- Interested in starting the pill
- **Does not want anything implanted in her body**
- Confident she can remember to take a pill every day: "I'll set an alarm on my phone."
- "This is the birth control my roommate takes, and she really likes it."

21

Case 1: New Start

- **Effective?**
  91-99.7% effective (highly dependent on patient adherence)
- **Safe?**
  Patient has PMH of headaches (non-migraine) > combined oral contraceptives are category 1

22

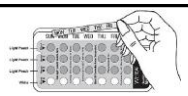
Case 1: New Start

- In general, start with 30-35mcg EE
  - Higher EE (50mcg EE) = increased VTE risk
  - Very low EE content (<20mcg EE) = increased breakthrough bleeding
- No clear evidence to recommend any progestin over another
- In general, start with a monophasic regimen
  - Multiphasic regimens designed to mimic "natural" menstrual cycle & reduce side effects
  - No clear evidence
  - Can be confusing to patients

Sources: Pharmacist's Letter. Document: 23(12):231207; Comparison of oral contraceptives and non-oral alternatives. Allen, et al. Managing Contraception.

23

Case 1: New Start



When should the patient start taking her pill?

Quick start – start the day of visit; use back-up method for 7 days

Sunday start – use back-up method for 7 days

First day of next period – no back-up method needed

24

Women who start their pill the day of clinic visit are more likely to start & to continue using oral contraceptives

- **QuickStart Trial**
  - 88% of women who took their first dose in clinic continued to 2nd pack
  - 74% of women who planned to start later continued to 2nd pack
  - 4.5% of women who planned to start later never started taking the 1st pack
- Up to 25% of women who receive an Rx for birth control never fill it

Sources: Westhoff, et al. https://www.ncbi.nlm.nih.gov/pubmed/12384200
Oakley, et al. https://www.ncbi.nlm.nih.gov/pubmed/1936216

25

Case 1: New Start

"I saw a commercial that said you can use the pill to skip your period; could I try that?"

26

Extended use of oral contraceptives appears to be safe & may be more effective

- Placebo pills increase "acceptability" of oral contraceptives
- No clear medical reason to have a withdrawal bleed
- May experience breakthrough bleeding initially
- May improve dysmenorrhea, anemia, endometriosis, ovarian cysts
- Decreased probability of "breakthrough ovulation"
- No difference in lipid profiles or coagulation activity (small studies)
- Lack of long-term data
- Many women choose this option if offered information (FLEXO study)
- Use a monophasic pill/extended-cycle formulation

Sources: Page Wright & Johnson. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2621397/
Lete, et al. https://www.ncbi.nlm.nih.gov/pubmed/30203678
Hee, et al. https://www.ncbi.nlm.nih.gov/pubmed/23083413

27

Case 2: Problem with the Pill

- The patient from case #1 returns to the pharmacy 3 months later to pick up a refill
- She tells you she has been **having some breakthrough bleeding**, but nothing too bothersome & she expects it to improve based on your initial counseling
- But – **"My face is all broken out! And I never had acne before I was on the pill."**

28

Case 2: Problem with the Pill

- Breakthrough bleeding (BTB) usually resolves in 3-6 cycles
- Assess adherence – take pill at same time daily
- More common with low-dose EE
- Smoking may increase BTB

29

Case 2: Problem with the Pill

Progestins are often grouped by "generation"

This terminology may refer to year marketed; structure; activity – **not standardized!**

No clear data from RCTs on differences; no clear algorithm for switching

1st generation: norethindrone – may have higher risk of irregular bleeding

2nd generation: levonorgestrel – more androgenic activity (acne, hirsutism, dyslipidemia)

3rd generation: norgestimate; desogestrel – lower androgenic activity; increased risk of VTE???

4th generation: drosperinone – anti-mineralcorticoid & anti-androgenic effects; increased risk of VTE???

Source: Pharmacist's Letter. Document: 23(12):231207; Comparison of oral contraceptives and non-oral alternative

30

Case 3: Emergency Contraception

- A young woman presents to the pharmacy and asks if she can purchase Plan B
- "Sorry, I'm a little out of breath. I jogged over here from my apartment. I've been working out a lot and today I am finally under 200 pounds!"

31

Case 3: Emergency Contraception

- Norlevo brand labeling changes (2013)
  - French manufacturer
  - "Less effective in women weighing 75kg or more and not effective in women weighing 80 kg or more"
  - Warning deleted in 2014
  - US FDA decided to review available data

32

Case 3: Emergency Contraception

- Meta-analysis of two RCTs (2011)
  - Studies compared ulipristal acetate (UPA) to levonorgestrel (LNG)
  - Sought to identify factors associated with EC failure
  - Overall rate of pregnancy was low
  - Relative risk of pregnancy more than doubled in overweight women using LNG as compared to normal or underweight women
  - Risk was up to 4x greater for obese LNG users
  - LNG ineffective at BMI ≥ 26 or weight ≥ 80kg
  - Risk was up to 2x greater for obese UPA users or weight ≥85 kg
  - **Conclusion:** Women with BMI >25 should be offered IUDs or UPA

Source: Glasier, et al. https://www.ncbi.nlm.nih.gov/pubmed/21920190

33

Case 3: Emergency Contraception

- Systematic review (2016)
  - Decreased efficacy with weight ≥ 80 kg or BMI ≥30
  - Pregnancy rates 2-4 times higher
- Review of 4 WHO-HRP randomized trials (2017)
  - 6873 women
  - Pregnancy rates in all groups of women were low
  - Reduced efficacy in women with BMI ≥ 30
  - Small number of women ≥80 kg
- Studies not designed for purpose of evaluating effects of weight on efficacy
- Conducted in Nigeria & Hong Kong

Sources: Jatlaoui & Curtis. https://www.ncbi.nlm.nih.gov/pubmed/27234874
Festin, et al. https://www.ncbi.nlm.nih.gov/pubmed/27527670

34

Case 3: Emergency Contraception

- Some experts recommend a 3mg dose (off label, not well studied)
- Pharmacokinetics study (2016)
  - 10 women, 90% non-Hispanic Caucasian
  - 5 normal BMI, 5 obese
  - 3 mg dose resulted in similar serum concentrations in obese users as compared to normal BMI users with single dose
  - Well tolerated
  - No data on pregnancy outcomes

Source: Edelman, et al. https://www.ncbi.nlm.nih.gov/pubmed/27000896

35

Case 3: Emergency Contraception

- The FDA concluded that data was conflicting and too limited to make any change in labeling for LNG EC (May 2016)
- Copper IUD is most effective option for obese women
- No safety concerns for LNG or UPA – no reason to deny
  - Patient should be made aware of possible reduction in efficacy

Sources: Festin, et al. https://www.ncbi.nlm.nih.gov/pubmed/27527670
Plan B Information. https://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm109775.htm

36

Case 4: Shared Decision-Making

- 23-year-old female, just graduated UNM; planning to pursue a Master's & PhD in psychology; works as a waitress at Cracker Barrel
- Blood pressure **118/70 mmHg**
- **Last menstrual period was about two weeks ago**; no intercourse since then
- No PMH; **smokes cigarettes (~1 pack per day)**
- Not in a monogamous relationship; sexually active with occasional "Tinder hook-ups"; uses condoms "most of the time"
- Used to take Sprintec "but I'm really busy with work and school, and I kept forgetting to take it."

37

Case 4: Shared Decision-Making

"I need to get back on birth control. I don't think I ever want to have kids, but I know **having a baby right now would ruin my life."**

38

39

Case 4: Shared Decision-Making

- Patient desires **highly effective** method that is compatible with her busy schedule
- Possible options could include DMPA, IUD, or implant
- LARC methods (IUDs & implants) are >99% effective
- LARC is appropriate for adolescents; women who have not had children; women not in monogamous relationships
- Encourage regular condom use if not in monogamous relationship

Sources: Mirena; Skyla; Kyleena; and Liletta prescribing information; Managing Contraception; Paragard prescribing information

40

IUD (>99% effective)

- **Non-hormonal:** Copper IUD (Paragard®)
  - **Mechanism of action:** Copper ions inhibit sperm; inflammatory reaction in endometrium
  - FDA approved for 10 years; effective 12+ years
  - May increase menstrual bleeding/cramping
- **Hormonal:** all contain levonorgestrel (a progestin; LNG)
  - **Mechanism of action:** Thickening of cervical mucus; alteration of endometrium; some anovulatory effects
  - Serum levels of LNG are lower than with implant or pill
  - May cause irregular spotting/bleeding when starting
  - About half of women using Mirena® experience amenorrhea within 1 year
- Rare but serious side effects include infection, expulsion, perforation, pregnancy complications

Sources: Mirena; Skyla; Kyleena; and Liletta prescribing information; Managing Contraception; Paragard prescribing information

41

Name	Levonorgestrel content	Replace after _ years FDA/ *off-label*
Mirena ®	52 mg (20 mcg/day)	5 years / *7 years*
Liletta ®	52 mg (18.6 mcg/day)	5 years / *7 years*
Kyleena ®	19.5 mg (17.5 mcg/day)	5 years
Skyla ®	13.5 mg (14 mcg/day)	3 years

42

Implant (>99% effective)

- Nexplanon ®
  - Contains 68mg etonogestrel (a progestin)
  - Implanted under the skin in the upper arm
  - Releases ~40-70 mcg daily
  - FDA approved for 3 years
  - *Off-label* remains effective for 4-5 years
  - Irregular bleeding is common (~33%) & frequent cause of discontinuation
  - Other side effects include headache, acne, depression, and weight gain (1-2%)
  - Infection after placement may occur but is very rare
  - Some implants may be difficult to remove and may require imaging and/or minor surgery to remove

Sources: Managing Contraception; Nexplanon prescribing information

43

Case 4: Shared Decision-Making

- IUDs and implants are not included in pharmacist prescriptive authority
- LARC use remains low in the U.S. but is increasing
- Half of women surveyed expressed concern about side effects & safety of LARC
- Pharmacists should be prepared to discuss risks and benefits

Sources: Teal & Romer. https://www.ncbi.nlm.nih.gov/pubmed/23535055
Burns, et al. https://www.ncbi.nlm.nih.gov/pubmed/23535055

44

Thank you!

Questions?

45