Hormonal Contraceptives: where do we begin?

Stephanie Schauner, PharmD
Clinical Associate Professor
UMKC School of Pharmacy
schauners@umkc.edu

Clinical Pharmacist
Goppert-Trinity Family Care Clinic
Kansas City, MO
Learning Objectives

Objective 1
Describe the mechanism of action, formulations, doses, and uses of hormonal contraceptives.

Objective 2
Compare the benefits vs. risks of oral contraceptives.

Objective 3
Develop appropriate counseling points to share with patients regarding oral contraceptives.

Objective 4
Identify useful resources available for hormonal use of contraceptives.
• Stephanie Schauner does not have any potential conflicts of interest in relation to this presentation.
Unintended Pregnancy in the US

1 YEAR: 6.7 MILLION PREGNANCIES

- Intended: 51%
- Unintended births: 23%
- Elective abortions: 21%
- Fetal losses: 5%

State Unintended Pregnancy Rates

Unintended pregnancy rates varied widely in 2010.

No of unintended pregnancies per 1,000 women aged 15–44.

- 32–40
- 41–47
- 48–54
- 55–62


Unintended Pregnancy in the U.S.

Guttmacher Institute
Figure 1. Percent distribution of women aged 15–44 years, by whether they are using contraception and by reasons for nonuse and methods used: United States, 2006–2010
Among U.S. women at risk of unintended pregnancy...

- The 68% who use contraception consistently and correctly account for only 5% of unintended pregnancies.

Modern Contraception Works

The two-thirds of U.S. women at risk of unintended pregnancy who practice contraception consistently and correctly account for only 5% of unintended pregnancies.

Women at Risk (43 Million in 2008)

- 14% Nonuse or long gaps in use
- 18% Inconsistent use
- 68% Consistent use

By consistency of method use all year

Unintended Pregnancies (3.1 Million)

- 5% Consistent use
- 54% Nonuse
- 41% Inconsistent use

By consistency of method use during month of conception

Source: Guttmacher Institute
Healthy People 2020  Family Planning\textsuperscript{FP-1-16}

- Increase the number of intended pregnancies\textsubscript{FP-1}
  - 51% \rightarrow 56%

- Increase the percentage of women aged 15 to 44 years that adopt or continue use of the most effective or moderately effective methods of contraception\textsubscript{FP-16}
  - 63.1% \rightarrow 69.3%
Pharmacists as Prescribers

• Several states with legislation pending
  – Missouri

Do I know enough about contraceptives to safely prescribe?

How do I stay up to date with my knowledge on this topic?

What are the processes and procedure required for implementing these services?
Self-Assessment

• Understanding of the menstrual cycle
  1 2 3 4 5

• Knowledge of available contraceptive products
  1 2 3 4 5

• Comfort with ability to safely and effectively prescribe oral contraceptives
  1 2 3 4 5

1=Least  5=Most
Menstrual Cycle
Classifications of Contraception

• Intercourse-related methods
  – Physical barriers: condoms, diaphragm, cervical cap, periodic abstinence

• Hormonal methods
  – Combined contraceptives (estrogen + progestin)
    • Oral
    • Patch
    • Ring
  – Progestin only
    • Oral
    • Injection
    • Intrauterine device

• Non-hormonal
  • Copper intrauterine device

• Permanent methods
  – Female tubal ligation
  – Male vasectomy
Effectiveness of Family Planning Methods

Most Effective

- Implant: 0.05%
- Reversible Intrauterine Device (IUD): LNG - 0.2%, Copper T - 0.8%
- Male Sterilization (Vasectomy): 0.15%
- Permanent Female Sterilization (Abdominal, Laparoscopic, Hysteroscopic): 0.5%

How to make your method most effective

- After procedure, little or nothing to do or remember.
- Vasectomy and hysteroscopic sterilization: Use another method for first 3 months.

- Injectable: Get repeat injections on time.
- Pills: Take a pill each day.
- Patch, Ring: Keep in place, change on time.
- Diaphragm: Use correctly every time you have sex.

- Male Condom: 18%
- Female Condom: 21%
- Withdrawal: 22%
- Sponge: 24% parous women, 12% nulliparous women
- Fertility-Awareness Based Methods
  - Spermicide: JANUARY

* The percentages indicate the number out of every 100 women who experienced an unintended pregnancy within the first year of typical use of each contraceptive method.

CONDOMS SHOULD ALWAYS BE USED TO REDUCE THE RISK OF SEXUALLY TRANSMITTED INFECTIONS.

Source: US Department of Health and Human Services Centers for Disease Control and Prevention
## Contraceptive Method Choice

Most effective method used in the past month by U.S. women, 2012

<table>
<thead>
<tr>
<th>Method</th>
<th>No. of users</th>
<th>% of women aged 15–44</th>
<th>% of women at risk of unintended pregnancy</th>
<th>% of contraceptive users</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pill</td>
<td>9,720,000</td>
<td>16.0</td>
<td>23.3</td>
<td>25.9</td>
</tr>
<tr>
<td>Tubal (female) sterilization</td>
<td>9,443,000</td>
<td>15.5</td>
<td>22.6</td>
<td>25.1</td>
</tr>
<tr>
<td>Male condom</td>
<td>5,739,000</td>
<td>9.4</td>
<td>13.7</td>
<td>15.3</td>
</tr>
<tr>
<td>IUD</td>
<td>3,884,000</td>
<td>6.4</td>
<td>9.3</td>
<td>10.3</td>
</tr>
<tr>
<td>Vasectomy (male sterilization)</td>
<td>3,084,000</td>
<td>5.1</td>
<td>7.4</td>
<td>8.2</td>
</tr>
<tr>
<td>Withdrawal</td>
<td>1,817,000</td>
<td>3.0</td>
<td>4.4</td>
<td>4.8</td>
</tr>
<tr>
<td>Injectable</td>
<td>1,697,000</td>
<td>2.8</td>
<td>4.1</td>
<td>4.5</td>
</tr>
<tr>
<td>Vaginal ring</td>
<td>759,000</td>
<td>1.2</td>
<td>1.8</td>
<td>2.0</td>
</tr>
<tr>
<td>Fertility awareness-based methods</td>
<td>509,000</td>
<td>0.8</td>
<td>1.2</td>
<td>1.4</td>
</tr>
<tr>
<td>Implant</td>
<td>492,000</td>
<td>0.8</td>
<td>1.2</td>
<td>1.3</td>
</tr>
<tr>
<td>Patch</td>
<td>217,000</td>
<td>0.4</td>
<td>0.5</td>
<td>0.6</td>
</tr>
<tr>
<td>Emergency contraception</td>
<td>91,000</td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
</tr>
<tr>
<td>Other methods*</td>
<td>133,000</td>
<td>0.2</td>
<td>0.3</td>
<td>0.4</td>
</tr>
<tr>
<td>No method, at risk of unintended pregnancy</td>
<td>4,175,000</td>
<td>6.9</td>
<td>10.0</td>
<td>na</td>
</tr>
<tr>
<td>No method, not at risk</td>
<td>19,126,000</td>
<td>31.4</td>
<td>na</td>
<td>na</td>
</tr>
<tr>
<td>Total</td>
<td>60,887,000</td>
<td>100.0</td>
<td>100.0</td>
<td>100.0</td>
</tr>
</tbody>
</table>

*Note: “At risk” refers to women who are sexually active; not pregnant, seeking to become pregnant, or postpartum; and not noncontraceptively sterile. na=not applicable. *Includes diaphragm, female condom, foam, cervical cap, sponge, suppository, jelly/cream and other methods.

Source: Guttmacher Institute
COMBINED HORMONAL CONTRACEPTIVES (CHC)

Objective 1

Describe the mechanism of action, formulations, doses, and uses of hormonal contraceptives
Mechanism of Action

• Prevent the development of the dominant follicle by suppressing FSH secretion
• Prevent ovulation by suppressing LH secretion
• Thicken cervical mucus
• Cause alterations in the endometrial lining
Estrogen Component

• Ethinyl estradiol (EE)
  – Most common form

• Mestranol
  – Biologically inactive prodrug of EE
  – Bioequivalent to 35µg of ethinylestradiol

• Estradiol valerate
  – Converted to the naturally occurring estrogen, estradiol
## Progestin Component

<table>
<thead>
<tr>
<th>Generation</th>
<th>Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>First (Estrane Family)</td>
<td>Norethindrone</td>
</tr>
<tr>
<td></td>
<td>Norethindrone acetate</td>
</tr>
<tr>
<td></td>
<td>Ethynodiol diacetate</td>
</tr>
<tr>
<td>Second (Gonane Family)</td>
<td>Levonorgestrel</td>
</tr>
<tr>
<td></td>
<td>Norgestrel</td>
</tr>
<tr>
<td>Third (Gonane Family)</td>
<td>Desogestrel</td>
</tr>
<tr>
<td></td>
<td>Norgestimate</td>
</tr>
<tr>
<td>Fourth (Other)</td>
<td>Drospirenone</td>
</tr>
<tr>
<td></td>
<td>Dienogest</td>
</tr>
<tr>
<td>Progestin Class</td>
<td>Estrogen Activity</td>
</tr>
<tr>
<td>------------------</td>
<td>-------------------</td>
</tr>
<tr>
<td>First Generation</td>
<td>++</td>
</tr>
<tr>
<td></td>
<td>++</td>
</tr>
<tr>
<td></td>
<td>++</td>
</tr>
<tr>
<td>Second Generation</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>-</td>
</tr>
<tr>
<td>Third Generation</td>
<td>+/-</td>
</tr>
<tr>
<td></td>
<td>+/-</td>
</tr>
<tr>
<td>Fourth/Other Generation</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>-</td>
</tr>
</tbody>
</table>
Formulations

• Monophasic
  – ratio of estrogen:progestin is fixed throughout the cycle
• Multiphasic
  – Biphasic
  – Triphasic
  – Four-phasic
• Extended cycle
  – Delays menstruation
• Continuous cycle
  – Eliminates menstruation
Dosing of CHCs

• Estrogen
  – 20mcg is a good starting dose
  – 30mcg if taking CYP450 inducers

• Progestins with low androgenic activity*
  < 1 mg norethindrone (1st generation)
  ≤ 0.1mg of levonorgestrel (2nd generation)
  ≤ 0.25 mg of norgestimate (3rd generation)

*general rule of thumb
## CHC Adverse Effects

<table>
<thead>
<tr>
<th>Condition</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Too much estrogen</td>
<td>Nausea, breast tenderness, increased blood pressure, melasma, headache.</td>
</tr>
<tr>
<td>Too little estrogen</td>
<td>Early or mid-cycle breakthrough bleeding, increased spotting, hypomenorrhea.</td>
</tr>
<tr>
<td>Too much progestin</td>
<td>Breast tenderness, headache, fatigue, changes in mood.</td>
</tr>
<tr>
<td>Too little progestin</td>
<td>Late breakthrough bleeding.</td>
</tr>
<tr>
<td>Too much androgen</td>
<td>Increased appetite, weight gain, acne, oily skin, hirsutism, increased LDL cholesterol, decreased HDL cholesterol.</td>
</tr>
</tbody>
</table>
Oral

PROGESTIN-ONLY CONTRACEPTIVES
Progestin ONLY

• Advantages
  – May be used in lactating women
  – May be used in women with estrogen contraindications

• Disadvantages
  – Increased amenorrhea or frequent spotting
  – Must be taken at same time everyday

• Patient Education
  – Missed dose (see “Missed Doses” slides)
  – Irregular menses
How do the different estrogen components available in combined hormonal contraceptives compare?

A. Estradiol valerate is the most common form occurring in commercially available oral contraceptives
B. Estradiol valerate is the most effective form
C. Ethinyl estradiol is converted to a naturally occurring estrogen
D. Mestranol is the biologically inactive prodrug of ethinyl estradiol
Which of the following is true when comparing monophasic hormonal contraceptives to multiphasic hormonal contraceptives?

A. Monophasic are harder to use
B. Monophasic are a fixed ratio of estrogen to progestin throughout the cycle
C. Multiphasic have more studies to support their use
D. Multiphasic are associated with less side effects
Objective 2

Compare the benefits vs. risks of oral contraceptives.
Choosing the “Right” Contraceptive

• Must consider the patient’s:
  – Medical history
    • Does the patient have a contraindication to estrogen?
  – Medication use
    • What other medications does the patient take?
    • Are there any significant drug interactions may impact the contraceptive of choice?
  – Preferences
    • Does the patient “know” what they prefer to use? Why?
    • Is the patient preference: safe, realistic, affordable, etc
  – Adherence
    • Can the patient maintain the regimen?
### Categories of medical eligibility criteria for contraceptive use

<table>
<thead>
<tr>
<th></th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>A condition for which there is no restriction for the use of the contraceptive method</td>
</tr>
<tr>
<td>2</td>
<td>A condition for which the advantages of using the method generally outweigh the theoretical or proven risks</td>
</tr>
<tr>
<td>3</td>
<td>A condition for which the theoretical or proven risks usually outweigh the advantages of using the method</td>
</tr>
<tr>
<td>4</td>
<td>A condition that represents an unacceptable health risk if the contraceptive method is used</td>
</tr>
</tbody>
</table>
Unacceptable health risk  MEC cat 4

- Breastfeeding or Non-breastfeeding < 21 days postpartum
- History/risk of or current deep vein thrombosis/pulmonary embolism (not on anticoagulant therapy); thrombogenic mutations
- Cerebrovascular or coronary artery disease
- Migraines with aura, any age
- Major surgery with prolonged immobilization
- Current and history of ischemic heart disease
- History of cerebrovascular accident
- Complicated valvular heart disease
- Moderately or significantly impaired cardiac function; normal or mildly impaired cardiac function < 6 months
- Systolic blood pressure ≥ 160mmHg or diastolic ≥ 100mmHg
- Complicated solid organ transplantation
- Current breast cancer
- Severe (decompensated) cirrhosis
- Benign hepatocellular adenoma or malignant liver tumor
- Smoking ≥ 15 cigarettes/day & ≥ 35 years of age
- SLE; positive or unknown antiphospholipid antibodies
Example from CDC MEC

<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>
</tr>
</thead>
<tbody>
<tr>
<td>Deep venous thrombosis (DVT)/Pulmonary embolism (PE)</td>
<td>a) History of DVT/PE, not receiving anticoagulant therapy</td>
<td>I</td>
<td>C</td>
<td>I</td>
<td>C</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td></td>
<td>i) Higher risk for recurrent DVT/PE</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>ii) Lower risk for recurrent DVT/PE</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>b) Acute DVT/PE</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>c) DVT/PE and established anticoagulant therapy for at least 3 months</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>i) Higher risk for recurrent DVT/PE</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>4*</td>
</tr>
<tr>
<td></td>
<td>ii) Lower risk for recurrent DVT/PE</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>3*</td>
</tr>
<tr>
<td></td>
<td>d) Family history (first-degree relatives)</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>e) Major surgery</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>i) With prolonged immobilization</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>ii) Without prolonged immobilization</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>f) Minor surgery without immobilization</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>
Thrombosis Risk

* Pregnancy data based on actual duration of pregnancy in the reference studies. Based on a model assumption that pregnancy duration is nine months, the rate is 7 to 27 per 10,000 WY.
VTE Risk and Contraceptive

Greater Risk

Patch
3rd & 4th generation CHCs
Vaginal ring

Lower Risk

Progestin-only (IUD, oral, implant)
First generation CHCs
Second generation CHCs
Drug Interactions

- Interference of absorption
- Liver enzyme induction – anti-epileptic drugs (AEDs)
- Use alternative contraception
- Reported antibiotic cases:
  - Tetracycline
  - Minocycline
  - Erthromycin
  - Penicillins
  - Cephalosporins
# Drug Interactions

<table>
<thead>
<tr>
<th>Drugs interfering with OC Efficacy</th>
<th>OC interfering with Efficacy of Other Drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ascorbic acid</td>
<td>Alprazolam</td>
</tr>
<tr>
<td>APAP-scheduled</td>
<td>Chlordiazepoxide</td>
</tr>
<tr>
<td>Atorvastatin</td>
<td>Diazepam</td>
</tr>
<tr>
<td>Rosuvastatin</td>
<td>Theophylline</td>
</tr>
<tr>
<td>NNRTIs</td>
<td>Cyclosporine</td>
</tr>
<tr>
<td>PIs</td>
<td>Corticosteroids</td>
</tr>
<tr>
<td></td>
<td>Alcohol</td>
</tr>
<tr>
<td>Anticonvulsants</td>
<td>B-Blockers</td>
</tr>
<tr>
<td>Antibiotics</td>
<td>TCAs</td>
</tr>
<tr>
<td>Rifampin</td>
<td>Ropinirole</td>
</tr>
<tr>
<td>Theophylline</td>
<td>Zolmitriptan</td>
</tr>
<tr>
<td>St. John’s Wort</td>
<td></td>
</tr>
<tr>
<td>NNRTI-nevirapine PIs</td>
<td></td>
</tr>
<tr>
<td>Sulfonamides</td>
<td></td>
</tr>
<tr>
<td>Griseofulvin</td>
<td></td>
</tr>
<tr>
<td>Bosentan</td>
<td></td>
</tr>
<tr>
<td>Tacrolimus</td>
<td></td>
</tr>
<tr>
<td>Modafinil</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Temazepam</td>
</tr>
<tr>
<td></td>
<td>Warfarin</td>
</tr>
<tr>
<td></td>
<td>Thyroid agents</td>
</tr>
<tr>
<td></td>
<td>Hypoglycemics</td>
</tr>
<tr>
<td></td>
<td>Methyldopa</td>
</tr>
<tr>
<td></td>
<td>Metformin</td>
</tr>
<tr>
<td></td>
<td>Amprenavir</td>
</tr>
</tbody>
</table>
Additional Benefits of CHCs

• Regulate menstrual cycle
• Decrease risk of anemia
• Decrease incidence of ovarian cysts
• Decrease risk of ovarian and uterine cancers
• Decrease acne
• Decrease pelvic inflammatory risk
Patient Education for Oral CHC Use

• Compliance

• Missed doses (see “Missed Doses slides)

• No protection against STIs/HIV
  – Condom use

• Signs/symptoms of VTE
  – ACHES
    • Abdominal pain, chest pain, headache, eye problems, severe leg pain

• Drug interactions
COMBINED HORMONAL CONTRACEPTIVES (CHC)

Objective 3

Develop appropriate counseling points to share with patients regarding oral contraceptives.
Initiating Oral Contraceptives

• Quick Start
  – Contraceptive method started immediately
  – Back up method x 7 days

• Day 1 Start
  – Contraceptive method started on the first day of menses

• Sunday Start
  – First Sunday after next menses begins
  – Back up method x 7 days
### Missed or Late Combined Oral Contraceptives (28-day packs*)

**Information does NOT apply to Natazia, see product labeling**

<table>
<thead>
<tr>
<th>Late pill: &lt;24 hrs since a pill should have been taken</th>
<th>Two or more consecutive active pills missed (&gt;48 hrs since a pill should have been taken)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Missed pill: 24 or more hrs since a pill should have been taken</td>
<td></td>
</tr>
</tbody>
</table>

- Take the late or missed pill as soon as possible.
- Take the remaining pills at the usual time, even if that means taking two pills on the same day.
- Consider emergency contraception if other active pills were missed earlier in the cycle or in the last week of the previous cycle.

- Take the most recent missed pill.
- Discard other missed pills.
- Take the remaining pills in the pack at the usual time, even if that means taking two pills on the same day.
- Use back-up contraception (e.g., condoms) or avoid intercourse until active pills have been taken for seven consecutive days.
- If pills were missed in the last week of active pills (e.g., days 15 to 21 for 28-day mono-, bi-, and triphasic packs):
  - Omit the hormone-free pills (and estrogen-only pills, if applicable); finish the active pills in the current pack, and start a new pack the next day.
  - If a new pack cannot be started immediately, use back-up contraception (e.g., condoms) or avoid intercourse until active pills from a new pack have been taken for seven consecutive days.
- Consider emergency contraception, especially if active pills were missed during the first week and unprotected intercourse occurred in the previous five days.

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*Pharmacists Letter. June 2014*
Missed Doses – Progestin Only (Oral)

Late/Missed pill > 3 hours since it should have been taken

- Take one pill as soon as possible.
- Take the remaining pills at the usual time, even if it means taking two pills in the same day.
- Use back-up contraception (condoms) or avoid intercourse until pills have been taken on time for two consecutive days.
- Consider emergency contraception if unprotected intercourse has occurred.
Monitoring

• 3-6 months after initiation
• Follow up with a primary care provider
  • Well woman exam
  • Papanicolaou and pelvic exam
  • Breast exams – self and clinical
  • Appropriate lab work
According to the CDC MEC document, a condition that represents an unacceptable health risk if the contraceptive method is used, would be noted with a number 4.

A. True
B. False
LY is a 22 y.o. female who recently started an oral CHC containing 30mcg of EE and 0.15 mg levonorgestrel. She is on her third pack of pills and states she feels really tired, is cranky all the time, and she has gained 3 lbs. She wants to keep taking a pill, but is going to stop this one due to the problems she is having. What course of action would you recommend?

A. Stay on the same pill. These adverse effects will go away.
B. Switch to a CHC with 3mg of drospirenone.
C. Switch to a CHC with 20mcg of EE.
D. Switch to a CHC with 0.35mg of norgestimate.
OBJECTIVE 4
Identify useful resources available for hormonal contraceptives.
Useful Resources

• CDC Medical Eligibility Criteria for Contraceptive Use
  • http://www.cdc.gov/mmwr/volumes/65/rr/pdfs/rr6503.pdf

• World Health Organization
  – http://www.who.int/topics/family_planning/en/
  – Medical Eligibility Criteria for Contraceptive Use
    • http://www.who.int/reproductivehealth/publications/family_planning/9789241563888/en

• Pharmacists Letter

• Planned Parenthood
  – http://www.plannedparenthood.com

• Association of Reproductive Health Professionals (ARHP)
  – http://www.arhp.org

• http://www.womenshealth.gov
References

5. Lexi-Comp Online. [http://www.lexi.com](http://www.lexi.com)