CLINICAL PEARLS IN CONTRACEPTION

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**Speaker Disclosure:** Dr. Borgelt has no actual or potential conflicts of interest in relation to this program.

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CLINICAL PEARLS IN CONTRACEPTION

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Target Audience: Pharmacists, Technicians, & Nurses

Program Overview: Throughout history, little was known about women’s reproductive systems. Even more, what people actually believed bordered on the bizarre. Even though it is now the 21st century, it’s amazing what type of information is circling about regarding birth control and getting pregnant. Unfortunately, women (and men) still get a lot of misinformation from well-meaning friends, sisters, and others and when it comes to contraception, and this misinformation can cause big problems. The more health care providers know about contraceptives and the correct way to use them, the better guidance and/or counseling they can offer their patients.

Objectives:

• Compare and contrast the advantages and disadvantages of combination oral contraceptives to other contraceptive methods
• Design a therapeutic plan to manage the most common side effects associated with combined contraceptives
• Describe how emergency contraception works and how to counsel patients regarding its proper use

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Learning Objectives

- Compare and contrast the advantages and disadvantages of combination oral contraceptives to other contraceptive methods.

- Design a therapeutic plan to manage the most common side effects associated with combined contraceptives.

- Describe how emergency contraception works and how to counsel patients regarding its proper use.
Outline

- Introduction
- Prescription contraceptives
- Clinical Pearls in Contraception
  * Contraindications
  * Extended cycling
  * Missed doses
  * Generic vs. brand
- Conclusions

* Initiation of method
* Drug interactions
* Emergency Contraception
* Side effects
Contraceptive Options

COMBINED PILLS - 20 mcg PILLS

ALESSE - 28 TABLETS
(0.1 mg levonorgestrel/20 mcg ethinyl estradiol)
Wyeth-Ayerst

LEV[LIT]E™ - 28 TABLETS
(0.1 mg levonorgestrel/20 mcg ethinyl estradiol)
Berlex

LOESTRIN® FE 1/20
(1 mg norethindrone acetate/20 mcg ethinyl estradiol/75 mcg progesterone)

MIRCETTE - 28 TABLETS
(0.15 mg desogestrel/20 mcg ethinyl estradiol/75 mcg progesterone)

Depo-Provera
## Perfect and Typical Use

### Percent of Women Experiencing Unintended Pregnancy in First Year of Use

<table>
<thead>
<tr>
<th>Method</th>
<th>% with Typical Use</th>
<th>% with Perfect Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>No method</td>
<td>85%</td>
<td>85%</td>
</tr>
<tr>
<td>Spermicide</td>
<td>29%</td>
<td>18%</td>
</tr>
<tr>
<td>Withdrawal</td>
<td>18%</td>
<td>4%</td>
</tr>
<tr>
<td>Periodic abstinence</td>
<td>25%</td>
<td>---</td>
</tr>
<tr>
<td>Diaphragm</td>
<td>16%</td>
<td>6%</td>
</tr>
<tr>
<td>Male condom</td>
<td>17%</td>
<td>2%</td>
</tr>
<tr>
<td>Female condom</td>
<td>27%</td>
<td>5%</td>
</tr>
<tr>
<td>Pill (COCs)</td>
<td>9%</td>
<td>0.3%</td>
</tr>
<tr>
<td>Combined patch</td>
<td>8%</td>
<td>0.3%</td>
</tr>
<tr>
<td>Depo-Provera</td>
<td>7%</td>
<td>0.3%</td>
</tr>
<tr>
<td>Combined vaginal ring</td>
<td>8%</td>
<td>0.3%</td>
</tr>
<tr>
<td>Copper T 380A IUD</td>
<td>1%</td>
<td>0.6%</td>
</tr>
<tr>
<td>LNG 20 IUD</td>
<td>0.1%</td>
<td>0.1%</td>
</tr>
</tbody>
</table>

[Link to source](http://www.guttmacher.org/pubs/fb_contr_use.html)
Optimizing Patient Choices

- Effectiveness
- Importance of not being pregnant
- Likelihood and ability to comply
- Frequency of intercourse
- Age
- Cost and ability to pay
- Side effects
- Risk/benefit, perceptions, misperceptions
- Other drugs used
- Health status and habits
- Noncontraceptive benefits
Prescription Contraceptives

- Combined contraceptives
  - Oral
  - Patch
  - Vaginal ring

- Progestin-only contraceptives
  - Oral
  - Injectable
  - Implant

- Intrauterine contraception
  - Copper intrauterine device
  - Levonorgestrel intrauterine system

- Barrier methods
  - Cervical cap
  - Diaphragm
Combined Contraceptives

- **Estrogen**
  - Ethinyl estradiol
  - Mestranol

- **Progestin**
  - Norethindrone
  - Norethindrone acetate
  - Ethynodiol diacetate
  - Norgestrel
  - Levonorgestrel
  - Desogestrel, etonogestrel
  - Norgestimate, norelgestromin
  - Drospirenone
Combined Contraceptives

Mechanism of Action

- Suppress ovulation
- Reduce sperm transport in upper genital tract (fallopian tubes)
- Change endometrium making implantation less likely
- Thicken cervical mucus (preventing sperm penetration)
Clinical Pearl: Contraindications

What women should not take combined contraceptives?
Contraindications for Combined Contraceptives

- World Health Organization (WHO) medical eligibility criteria
- Separated into four categories
  1. A condition for which there is no restriction for the use of the contraceptive method.
  2. A condition where the advantages of using the method generally outweigh the theoretical or proven risks.
  3. A condition where the theoretical or proven risks usually outweigh the advantages of using the method.
  4. A condition which represents an unacceptable health risk if the contraceptive method is used.
Contraindications for Combined Contraceptives (Category 4)

- Breastfeeding <6 wks postpartum
- Smoker ≥ 35 yrs, ≥15 cigs/d
- Multiple risk factors for CVD
- BP ≥160/100
- Vascular disease
- Current, history of, or on treatment for DVT/PE
- Complicated diabetes
- Presence of liver tumors, severe cirrhosis, or active viral hepatitis
- Major surgery with prolonged mobilization
- Known thrombogenic mutations
- + antiphospholipid antibodies
- Current and history of ischemic heart disease
- Stroke (history of CVA)
- Complicated valvular heart disease
- Migraine headache with aura
- Current breast cancer

http://apps.who.int/rhl/fertility/contraception/mec.pdf
Clinical Pearl: Initiating Combined Oral Contraceptives (COCs)

How and when should a woman start her birth control pill?
Oral: Starting Pills

- Choose backup method
- Take 1 pill daily at the same time
  - Daily use: take 21 days, stop taking pills or take inactive pills for 7 days and then start new pack
  - Extended use: take 21 days, begin new pack immediately (discard last 7 inactive days)
- Start according to appropriate schedule (next slide)
### Oral: Administration

<table>
<thead>
<tr>
<th>When to start</th>
<th>Back up contraception</th>
</tr>
</thead>
<tbody>
<tr>
<td>First day of menses (preferred)</td>
<td>None needed</td>
</tr>
<tr>
<td>Immediately, if pregnancy excluded</td>
<td>Backup x 7days</td>
</tr>
<tr>
<td>First Sunday after next menses begins</td>
<td>Backup x 7days (if more than 5 days since menstrual bleeding started)</td>
</tr>
<tr>
<td>Within 5 days after start of menstrual bleeding</td>
<td>None needed</td>
</tr>
</tbody>
</table>

*Backup contraception for the first cycle is useful with all contraceptives and is necessary for progestin-only oral contraceptives*
### Oral Contraceptives: Administration

<table>
<thead>
<tr>
<th>Scenario</th>
<th>Information</th>
</tr>
</thead>
<tbody>
<tr>
<td>Switching from another hormonal method*</td>
<td>Start COC immediately if method has been used correctly. No backup needed.</td>
</tr>
<tr>
<td>Switching from a non-hormonal method</td>
<td>Start COC within 5 days of menstrual bleeding - no backup needed. Also can start any time if not pregnant – backup x 7 days</td>
</tr>
<tr>
<td>Switching from IUD</td>
<td>Start COC within 5 days of menstrual bleeding - no backup needed. Also can start any time if not pregnant – backup x 7 days</td>
</tr>
<tr>
<td>After emergency contraception pills (ECP)</td>
<td>Day after ECP – backup x 7 days. Sunday start and first day start also possible.</td>
</tr>
</tbody>
</table>

*If hormonal method was injection, start COCs when repeat injection would have been given*
Clinical Pearl: Extended Use

Is it okay to have menstrual periods infrequently? Never?
Types of Oral Contraception

- **Monophasic**: same amount throughout
- **Biphasic**: same estrogen, but differing amounts of progestin that change half-way through active pills
- **Triphasic**: varying amounts of estrogen or progestin every week of active pills
Continuous or Extended Use

- Monophasic estrogen and progestin pills
- Extended-cycle birth control
- May have more spotting initially; no periods
- Seasonale®, Seasonique®
  - 84 days of active pill, 7 days inactive or low dose estrogen pill
- Lybrel™
  - Pill taken every day
- Yaz®, Loestrin-24 FE®
  - 24/4 day cycle
Clinical Pearl: Missed Doses and Emergency Contraception

What do I tell a patient to do if she misses one or more doses? Should emergency contraception always be offered?
Oral: Missed Doses

- Missed one pill
  - Take missed pill ASAP. Take next pill as usual. Back up x 7 days. May offer ECPs.

- Missed two pills
  - Take one of forgotten pills every 12 hours until caught up, then continue pack. Backup x 7 days. May offer ECPs.

- Missed more than two pills
  - Offer ECPs. If taken, restart OCPs next day and use backup x 7 days.
  - If ECPs not taken, skip missed pills and complete rest of pills in pack, but use barrier method until next menses. Pills may not provide protection, but will help control cycle.

Emergency Contraception (EC)

“The use of hormonal medications within 72 to 120 hours after unprotected or underprotected coitus for the prevention of unintended pregnancy.”

- Progestin-only (levonorgestrel)
  - Plan B OneStep®, Next Choice®, Plan B®

- Combined estrogen-progestin (Yuzpe - two doses of 100 mcg EE plus ≥ 0.5 mg levonorgestrel)

<table>
<thead>
<tr>
<th>Brand</th>
<th>Color and Number of Pills</th>
<th>Estrogen</th>
<th>Progestin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alesse</td>
<td>5 pink pills</td>
<td>100 mcg EE</td>
<td>0.50 mg LNG</td>
</tr>
<tr>
<td>Nordette</td>
<td>4 light-orange pills</td>
<td>120 mcg EE</td>
<td>0.60 mg LNG</td>
</tr>
</tbody>
</table>

EC: Dosing

- Levonorgestrel (0.75 mg) regimen
  - 2 doses: 1 tablet ASAP (within 72-120 hours), 1 tablet 12 hours later
  - 2 doses: 1 tablet ASAP (within 72-120 hours), 1 tablet up to 24 hours later
  - 1 dose: 2 tablets at the same time

- Yuzpe regimen
  - 2 doses: #x tablets ASAP (within 72-120 hours), #x tablets 12 hours later

Lancet 2002;360:1803-1810
Contraception 2002;66:269-273
Hum Reprod 2004;20:307-311
Hormonal EC: Mechanism of Action

- Preventing or postponing ovulation by suppressing, blunting, or delaying LH surge

- Interference with sperm transport by thickening cervical mucus and alkalinizing the uterine cavity to immobilize sperm

## EC: Effectiveness

<table>
<thead>
<tr>
<th>Method</th>
<th>Effectiveness</th>
<th># Expected Pregnancies</th>
</tr>
</thead>
<tbody>
<tr>
<td>No treatment</td>
<td>N/A</td>
<td>80/1000</td>
</tr>
<tr>
<td>Copper IUD</td>
<td>99% (99-100%)</td>
<td>1/1000</td>
</tr>
<tr>
<td>Levonorgestrel</td>
<td>89% (59-94%)</td>
<td>10/1000</td>
</tr>
<tr>
<td>Yuzpe regimen</td>
<td>74% (47-89%)</td>
<td>20/1000</td>
</tr>
</tbody>
</table>

EC: Effectiveness
EC: Patient Counseling

- Make certain that the patient does not want pregnancy
- Explain that EC does not protect from STIs
- Explain how to take EC regimen
- Describe side effects: nausea and vomiting, headaches, breast tenderness, and dizziness
- Recommend an at home pregnancy test and medical follow up if the patient does not have a normal period within 3 weeks
- Recommend not having unprotected intercourse in the days or weeks following treatment
- If patient takes COCs, start again the following day
After EC taken, menses usually occurs within 1 week before or after the expected time.
EC: Patient Counseling

- As a pharmacist, if a woman comes in for EC, take the opportunity to counsel on the following:
  - Proper contraception techniques and methods available
  - Risk of sexually transmitted infections and regular examinations by a physician or health care provider
Clinical Pearl:
Managing Common Side Effects

Should a woman change her oral contraceptive if unexpected bleeding occurs? Nausea and/or vomiting?
Side Effects

- Discontinuation of contraceptives most often due to bleeding irregularities, nausea, weight gain and mood swings.
- Side effects occur when hormone activity of contraceptive is greater or less than the hormone effect of a woman’s own ovarian steroids.

## Side Effects of Combined Contraceptives

<table>
<thead>
<tr>
<th>Estrogen</th>
<th>Estrogen and progestin</th>
<th>Progestin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea</td>
<td>Breast tenderness</td>
<td>↑ appetite and wt gain</td>
</tr>
<tr>
<td>↑ breast size</td>
<td>Headaches</td>
<td>Depression</td>
</tr>
<tr>
<td>HTN</td>
<td>HTN</td>
<td>Fatigue</td>
</tr>
<tr>
<td>↓ libido</td>
<td>Cyclic wt gain</td>
<td>Acne, oily skin</td>
</tr>
<tr>
<td></td>
<td>Bleeding</td>
<td>Bloating</td>
</tr>
</tbody>
</table>
Management of Side Effects

- Determine if symptom indicates presence or potential for serious illness. If yes, discontinue immediately.
- Identify probable cause
- Make decision about probable clinical course of side effect if contraceptive continued
- Most side effects will diminish or disappear by 2nd or 3rd cycle…encourage use for 3 months!
- Consider contraceptive switch
Management of Side Effects: Breakthrough Bleeding and Spotting

- If unexpected bleeding occurs, use additional contraception until bleeding completely ceases
- Rule out potential causes (i.e., PID)
- Encourage continuation if first few cycles
- When switch is indicated:
  - Increase estrogen dose:
    - If bleeding begins during first 14 days
    - If absence of withdrawal menses
    - If menses continues into active pill cycle
Management of Side Effects: Breakthrough Bleeding and Spotting

- When switch is indicated:
  - Change progestin (more progestin activity or increase dose of same progestin):
    - If bleeding begins after 14 days (of active med)
    - Dysmenorrhea or heavy bleeding that occurs anytime in cycle
    - May consider triphasic oral contraceptive (higher progestin doses at end of cycle)
    - Progestin should have higher progestational (desogestrel) and/or androgenic activity (levonorgestrel)
  - Increase both estrogen and progestin:
    - If bleeding occurs midcycle
Management of Side Effects: Nausea and Vomiting

- Most severe during first cycles and usually disappear with time
- Related to estrogen dose
- Take with food or at bedtime
- If persists after third cycle, switch to contraceptive with lower estrogen dose
Management of Side Effects: Acne

- Non-pharmacologic measures
- Choose contraceptive with low androgenic activity
  - Desogestrel
  - Norgestimate
  - Drospirenone
- Choose contraceptive with higher estrogen doses (30-35 mcg)
- FDA indications for acne: Ortho Tri-Cyclen, Estrostep, Yaz
A 28 year-old female makes you aware that she is having unpredictable bleeding in between regular periods. She is taking Loestrin FE 1/20 (20 mcg EE, 1.0 mg norethindrone acetate).

What information should you obtain before giving advice to this patient?

The PCP inquires as to what COC would be good to use. What do you advise?
A 25 year-old female calls your pharmacy complaining of nausea. Upon review of her patient profile, you find that she started Demulen 1/35 (35 mcg EE, 1.0 mg ethynodiol diacetate) taking two weeks ago.

How would you handle this?
Clinical Pearl: Drug Interactions

Does a backup method need to be used when antibiotics are taken while on combined oral contraceptives?
Combined Contraceptives: Drug Interactions

- Similar drug interactions reported for all forms of combined contraceptives
- The lower the dose of estrogen or progestin in a contraceptive, the greater the risk that another medication could decrease its effectiveness
- Back-up contraception should be used if a drug interaction is possible
Combined Contraceptives: Drug Interactions

- Hepatic enzyme inducers
  - Agents most likely to cause breakdown of estrogen or progestin: phenobarbital, phenytoin, topirimate, carbamazepine, primidone
  - Sodium valproate, ethosuximide, lamotrigine and vigabatrin do not effect contraceptive hormone levels
  - Management
    - Use another method
    - Use different anticonvulsant
    - Increase dose of contraceptive
Combined Contraceptives: Drug Interactions - Antibiotics

- **Rifampin** - significant risk of failure; counsel about the use of additional nonhormonal contraceptive methods during the course of rifampin therapy

- **Other antibiotics** - small risk of interactions; lack of pharmacokinetic and clinical evidence; not possible to identify women who may be at risk of OC failure. Counsel about the additional use of nonhormonal contraception or alternate methods for:
  - Those not comfortable with small risk of interaction
  - Those with previous failures or who develop breakthrough bleeding during use of antibiotics

Obstet Gynecol 2001;98:53-60
Combined Contraceptives: Drug Interactions

- Protease inhibitors
  - Can cause changes in mean AUC of estrogen
  - Consider different contraceptive options

- St. John’s Wort
  - Induces cytochrome P450 and could decrease effectiveness of oral contraceptives
  - Concurrent condom use is excellent safety measure
A physician would like to start erythromycin in a 18-year old female who has been taking Nordette (30 mcg EE, 0.15 mg levonorgestrel) for six months. He asks you about potential drug interactions.

How might an astute pharmacist handle this situation?
Clinical Pearl: Generic vs. Brand

Are generic birth control pills really the same and as effective as brand name?
Generic Oral Contraceptives

- Not required to have clinical testing
- Must prove blood level equivalency to be considered equivalent (80-125% of parent compound’s blood levels)
- Theoretically could have an impact for very low dose COCs (20 mcg ethinyl estradiol)
- No evidence that generics are less effective than brand name products
Combined Contraceptives: Advantages

- Effective
- Safe
- Easy to use
- Reversible
- Menstrual cycle
- Reduction of several cancers
- Decreased risk of benign breast tumors
- Prevention of ectopic pregnancy
- Improves androgen-excess conditions
- Suppression of endometriosis
- Sexual enjoyment
- Emergency contraception
- Transition therapy for perimenopause
Combined Contraceptives: Disadvantages

- No HIV/STI protection
- Patient adherence
- Expensive
- Side effects
- Circulatory complications
- Menstrual cycle changes
- Sexual/psychological effects
- Hepatocellular adenoma
- Gallbladder disease
- Drug interactions
Clinical Pearl: Contraceptive Alternatives

If combined contraceptives are not ideal for an individual patient, what other options could be considered?
# Contraceptive Alternatives

<table>
<thead>
<tr>
<th>Method</th>
<th>Duration of effectiveness</th>
<th>Hormone content</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>DMPA</td>
<td>3 months</td>
<td>Progestin</td>
<td>BMD warning</td>
</tr>
<tr>
<td>Mirena® IUS</td>
<td>5 years</td>
<td>Progestin</td>
<td>Approved for heavy bleeding</td>
</tr>
<tr>
<td>Copper IUD</td>
<td>10 years</td>
<td>None</td>
<td>May increase bleeding</td>
</tr>
<tr>
<td>Barrier</td>
<td>Immediate</td>
<td>None</td>
<td>Adherence</td>
</tr>
</tbody>
</table>
Conclusions

- Important to consider perfect and typical use rates to determine contraceptive effectiveness.
- Combined hormonal contraceptives work primarily by suppressing ovulation.
- Side effects of combined contraceptives can be due to excess or deficiency of estrogen or progestin components, but a 3-month trial often needed.
- Drug interactions with combined contraceptives may be significant enough to consider other forms of contraception.
- Missed doses of combined contraceptives should be managed appropriately and emergency contraception should be offered if needed.
- Monophasic combined contraceptives can be used in an extended manner to eliminate monthly menstrual cycles.
- Advantages and disadvantages of various contraceptives must be considered for individual use.
Questions?

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