Hormonal Contraception
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Contraceptive Effectiveness
- Most Effective
  - Oral Contraceptives*
  - Depo-Provera
  - Norplant
  - IUD
  - Sterilization
- Less Effective
  - Condoms
  - Diaphragm
  - Cervical Cap
  - Withdrawal
  - Periodic abstinence
  - Spermicides

Non-hormonal
- Advantages
  - Easily accessible
  - Generally inexpensive
- Disadvantages
  - Less effective

Components of Oral Contraceptives (OCs)
- Estrogen
  - ethinyl estradiol, mestranol
- Progestins
  - norethindrone, norethindrone acetate, ethyodiol, levonorgestrel, norgestrel, norgestimate, desogestrel, drospirenone

Activity of COCs
- Type of progestin and ratio of components
- Estrogens
- Progestins
- Androgen Activity

Norgestimate versus Levonorgestrel
- Less progestational activity
- No estrogenic effects
- Less androgenic activity
Components of OCs
- Drosperinone
  - Analog of spironolactone
  - Progestogenic
  - Anitandrogenic
  - Antimineralocorticoid

Estrogens: MOA
- Inhibits ovulation
- Inhibits implantation
- Accelerated ovum transport
- Induces luteolysis

Progestins: MOA
- Production of thick cervical mucus
- Inhibits ovulation
- Inhibits implantation
- Slows ovum transport
- Inability for sperm to capacitate

COC Mechanism of Action
- Inhibits ovulation
  - prevents FSH and LH surge
- Inhibits sperm penetration
  - thickens cervical mucus
  - ↓ sperm penetration into the ovum
- Inhibits implantation
  - “hostile” endometrial environment

DMPA Mechanism of Action
- Inhibits ovulation
- Thickens cervical mucus
- Suppresses endometrial growth

COC General Information
- Estrogen and Progestin daily
- Preferred agent EE ≤ 35 mcg
- One pill qd x 21 days then placebo x 7 days
### Monophasic OCPs
- Constant dose of estrogen and progestin
- Less complicated
- More flexible
- Easy to identify and rectify ADRs
- Chewable available
- Preferred OCP

### Seasonale
- 3 month supply- 84 active, 7 inactive
- Advantages
  - Fewer menses (one q3 months)
  - Less blood loss
  - May help with estrogen withdrawal migraines
- Disadvantages
  - More BTB/spotting during early cycles

### Multi-Phasic OCPs
- Biphasic associated with increased BTB and spotting
- More confusing
- Less flexible
- More difficult to rectify ADRs

### PROGESTIN-ONLY OC (MINIPILL)
- Same dose of progestin every day
- Lower progestin dose than in COC
- No hormonal-free interval
- Mechanism of action
  - MUST take at the same time every day

### Progestin-Only Pills
- Advantages
  - SLE patients
  - Breastfeeding
  - Smokers > 35 years old
  - Intolerable ADRs from estrogen
- Disadvantages
  - Irregular menses
  - ↑ BTB and spotting
  - ↑ Ectopic pregnancy risk
  - Generally less effective
  - Compliance
    - Backup method x 48h if pill is ≥ 3 hours late

### Question
- Which of the following is:
  - Monophasic
  - Biphasic
  - Triphasic
  - Mini-Pill
**Question**

- Which has the:
  - Most estrogenic activity
  - Least estrogenic activity
  - Most progestational activity
  - Least progestational activity

**Injectables**

- Depo-Provera
  - Q3 months
- Lunelle
  - Monthly injectable
  - No longer available

**DMPA Advantages**

- Long acting
- 99% effective
- No drug interactions
- May decrease sickle cell
- May decrease seizures
- Decrease iron-deficiency anemia
- Improved compliance

**DMPA Disadvantages**

- Menstrual irregularities common
- Weight gain
- Delayed return to fertility

**Lunelle**

- Advantages
  - Return to fertility quicker than DMPA
  - Efficacy similar to OCPs
  - Improved compliance (vs OCPs)
- Disadvantages
  - Monthly injections
  - One dose

**Ortho Evra**

- Advantages
  - Efficacy similar to OCPs
  - Improved compliance
  - Similar ADRs to OCPs
- Disadvantages
  - Skin irritation
  - Patch detachment
  - One dose
  - Loss of privacy
  - Pts > 90 kg
  - Breast tenderness
  - Drug Interactions
NuvaRing

- Advantages
  - Efficacy similar to OCPs
  - Improved compliance
  - Patient and partner acceptance
  - Similar ADRs to OCPs

- Disadvantages
  - Late withdrawal bleeding
  - Vaginal discomfort
  - One dose
  - Drug Interactions
  - Partner acceptance

Case

- MJ is a 21 year old female who comes to your pharmacy wanting to know advantages and disadvantages between Alesse and Ortho-Evra?

How to Choose Hormonal Contraception for a Patient

- Step 1
  - Identify patient specific contraindications, risk/benefits, and drug interactions that may limit or indicate the use of hormonal contraception

Case

- MJ is a 21 year old female who comes to your pharmacy wanting to know advantages and disadvantages between Alesse and Ortho-Evra?

Case

- A. Alesse is much more effective than Ortho-Evra
- B. Compliance is usually better with Ortho-Evra leading to improved effectiveness
- C. If ADRs occur with Alesse, another pill can be chosen, whereas there is only one strength of the patch
- D. Adverse effects are similar for the two
- E. Skin irritation can occur with the patch, but rarely leads to discontinuation

Case

- CJ is a 30 year old female who presents to your clinic requesting birth control. She used OCPs in the past, but has not used them for the past 3 years. She currently smokes 1 ppd of cigarettes

How to Choose Hormonal Contraception for a Patient

- Step 1
  - Identify patient specific contraindications, risk/benefits, and drug interactions that may limit or indicate the use of hormonal contraception

Case

- Which of the following is/are contraindicated in CJ?
  - A. Ortho-Tri Cyclen
  - B. DMPA
  - C. NuvaRing
  - D. Micronor
Contraindications to COCs
- Thromboembolism
- CVA, CAD/IHD
- Structural Heart Disease
- Diabetes with complications
- Breast cancer
- Pregnancy
- Lactation (<6 weeks postpartum)
- Impaired liver function

Contraindications to COCs
- Migraines
- Major surgery
- Smoker >35 years
- Uncontrolled HTN

Case
- CJ is a 30 year old female who presents to your clinic requesting birth control. She used OCPs in the past, but has not used them for the past 3 years. She currently smokes 1 ppd of cigarettes

Case
- Which of the following is/are contraindicated in CJ?
  - A. Ortho-Tri Cyclen
  - B. DMPA
  - C. NuvaRing
  - D. Micronor

Benefits
- Menstrual Symptoms
  - Less iron deficient anemia
  - Lighter and decreased length of menstrual bleeding
  - Less dysmenorrhea and midcycle pain from ovulation
  - Less PMS
  - Less ectopic pregnancies (EXCEPT minipills)

Benefits
- Endometrial Cancer
- Ovarian Cancer
- Ovarian Cysts
- Benign Breast Disease
- Endometriosis
- Acne
- Polycystic Ovarian Syndrome
- Colorectal Cancer
- PID
RISKS
- Hypertension
- Thromboembolic disease
- MI
- Stroke
- Insulin Resistance
- Lipids effects
- Gallbladder disease

Risks/Uncertainties
- Breast Cancer
- Cervical Cancer
- Hepatic Adenoma and Cancer

Depo-Provera®
- Benefits
  - Decreases anemia
  - May reduce seizures by ~30%
  - Decrease endometrial and ovarian cancer
  - Amenorrhea
  - Compliance
  - Efficacy not reduced by increased weight or drug interactions
  - Decreases risk of PID and ectopic pregnancies

Depo-Provera®
- Risks
  - Increased risk of osteoporosis
  - Decreases HDL, increase LDL

Case
- CJ is a 30 year old female who presents to your clinic requesting birth control. She used OCPs in the past, but has not used them for the past 3 years. She currently smokes 1 ppd of cigarettes

Which of the following is/are contraindicated in CJ?
- A. Ortho-Tri Cyclen
- B. DMPA
- C. Lunelle
- D. Micronor
Drug Interactions

“Certain drugs may interact with birth control pills to make them less effective in preventing pregnancy or cause an increase in breakthrough bleeding. Such drugs include rifampin, drugs used for epilepsy such as barbiturates (for example, phenobarbital), anticonvulsants such as carbamazepine (Tegretol is one brand of this drug), phenytoin (Dilantin is one brand of this drug), phenylbutazone (Butazolidin is one brand) and possible certain antibiotics. You may need to use additional contraception when you take drugs which can make oral contraceptives less effective.”
- FDA Detailed Patient Labeling

Drug Interaction Case 1

CT is a 19 year old female who has just been diagnosed with epilepsy. She is started on carbamazepine. She is going to be getting married in 3 months. Which of the following hormonal contraception methods is an option for CT? (CT does not have any other PMH or SH.)

a. Progestin only pill
b. Ortho-Tricyclen
c. Ovral
d. DMPA

Drug Interaction Case 2

MC is a 47 year old woman who was diagnosed with diabetes about a year ago. She is on glipizide 10 mg and pioglitazone 15 mg qd. Ten months after being diagnosed she comes to the clinic wanting to see if she is going through “the change” in life. For the past year her periods have been sporadic, but has not had a period in 3 months. She c/o of N/V for the past 3 months as well. She does not use any form of birth control and does not smoke.

Which of the following drugs can cause ovulation in some premenopausal anovulatory women
A. glipizide
B. metformin
C. pioglitazone

Drug Interaction Case 3

MP is on desogen and comes to your pharmacy with a prescription for penicillin.
Drug Interaction Case 3

- What is your management of the two medications?
  a. No backup birth control needed
  b. Use backup method for 10 days
  c. Use backup method for 7 days after stopping PCN
  d. Use backup method during PCN then for 7 days afterward and preferably until the next cycle

Drug Interactions

- Ortho-Evra
  - Tetracycline- no effect
- NuvaRing
  - Spermicide and miconazole- not clinically significant
- Lunelle
  - No studies done
- DMPA
  - None

Step 2

- Select and Recommend a hormonal contraceptive agent based on patient specific concurrent disease states, risk/benefit, contraindications, drug interactions, and compliance with past contraceptives

Criteria to consider

- Smoker > 35
- Uncontrolled HTN
- Diabetes with complications or > 20 years
- DVT/PE
- IHD
- Migraines with neurological symptoms
- TIA/Stroke

Criteria to consider

- Personal history of breast cancer
- Active liver disease
- Breast feeding
- Major surgery with immobilization

- If Yes
  - Consider progestin only method
  - Exception (breast cancer)
- If No
  - Can use low dose COC
Choosing an Initial Oral Contraceptive

- LOW DOSE FORMULATIONS ARE THE STANDARD
  - <50mcg ethinyl estradiol (EE)
  - <1mg NE, <0.15mg desogestrel or levonorgestrel, or <0.25mg norgestimate

- Appropriate for most patients, including adolescents, postpartum mothers, perimenopausal women


Compelling Indications

- Teenagers
  - Low dose OCP
  - Injectable or patch for improved compliance

- Perimenopausal women
  - OCP with EE 30-35 ug
  - DMPA

- Breastfeeding women
  - Non-estrogen containing form

- Seizures Disorders
  - 50 ug EE if using enzyme inducing agent
  - DMPA

- Diabetes
  - No vascular dz present-OCP
  - Vascular dz present- DMPA, POP

Compelling Indications

- HTN
  - Controlled- combination OCP
  - Uncontrolled- progestin only method

- Cardiovascular/Thromboembolism
  - Progestin only method

- Systemic lupus erythematosus
  - pregnancy may exacerbate
  - SLE is relative or absolute contraindication
    - COC can exacerbate symptoms
    - increase thromboembolic risk
    - vascular complications - absolute contraindication
  - IUD, POP, DMPA

- Smokers
  - <35- OCP with EE 20-35 ug
  - >35 progestin only method

- Breast Cancer
  - Non hormonal
Compelling Indications

- Tension Headache
  - OCP
- Estrogen withdrawal headache
  - Seasonale, Micrette
- Migraine headache
  - No focal symptoms - low dose OCP
  - D/C if neurological symptoms develop

Case

Rachel Green is a 30 year old female requesting contraception 1 year after her pregnancy. She is not breastfeeding and doesn’t smoke. She used Ortho-Cyclen before she was pregnant with no problems

- PMH: none
- Recommendation?

Case

Breastfeeding?
- DMPA or POP

Noncompliant?
- Ortho-Evra, NuvaRing, DMPA

Step 3

- Provide counseling, including monitoring for toxicities and potential ADRs, to patients starting hormonal contraceptives

Case

What counseling should you provide to Rachel?

Counseling-New Starts

- Take by mouth at the same time every day
  - establish a routine!!!
- No protection against STDs
- When to start
  - First day of menses
  - First Sunday after menses start
- Hormone-free period
- When period will occur
- What to do if still bleeding when time to start next pack
COUNSELING

- Onset of effectiveness
- Rescheduling the menstrual cycle

COUNSELING

- Consider using second means of contraception
  - first cycle
  - missed doses
  - severe diarrhea or vomiting
  - during BTB
  - during and at least 7 days after antibiotic therapy
  - condoms for STD prevention

Counseling

- Possible adverse effects
  - Common during the first few cycles
  - ACHES
- Drug interactions
- Address misconceptions
- Discuss benefits
- Demonstrate how to use pill pack

Case

- Rachel calls one month later stating she missed 2 pills during the second week.
- What should she do?
  - Take 2 tablets for 2 days
  - Use back-up contraception for 7 days, preferably the entire cycle

COUNSELING, MISSED PILLS

- What to do if pill/s are missed
  - 1: take ASAP or with next dose
  - 2 in the first 2 weeks
    - take 2 tablets for 2 days; use backup contraception for 7 days
  - 2 in the 3rd week or ≥ 3 anytime
    - Sunday starts: Take 1 pill/day until Sunday then start a new pack
    - Day 1 starts: start a new pack immediately
    - Use backup contraception for 7 days

Danger Signs- ACHES

- Abdominal pain: gallbladder dz, hepatic adenoma, thrombus, pancreatitis
- Chest pain: MI, PE
- Headaches: stroke, HTN, migraine
- Eye problems: stroke, HTN, migraine
- Severe leg pain: DVT

ADVERSE EFFECTS
- First 3 months
  - BTB
  - Dizziness
  - Cyclic weight gain
  - Breast fullness/tender
  - N/V
  - Contact lenses
  - Cramping
- Constant
  - HA during active pills
  - Anxiety
  - Fatigue
  - Depression
  - Decreased libido
  - Acne
  - Thyroid abnormalities

ADVERSE EFFECTS
- Worse over time
  - HA during inactive pills
  - Weight gain
  - Melasma
  - Hypertension
  - Hirsuitism
  - Vaginal candidiasis

Case
- After starting her OCP, Rachel calls your office complaining of BTB after one month of starting her OCP.
- What is your response?
  - This is common in first 2-3 months. Wait until end of 3rd month before we adjust.

Transdermal Contraception
- Ortho-Evra
- One patch worn for 7 days, 3 weeks, then off for 1 week
- < 90 kg
- Same DI, CI, ADRs as COCs

Ortho-Evra
- Patient Instructions
  - Sunday Start
  - First Day Start
  - Apply patch on same day every week for 3 weeks
  - One week patch free
  - Apply to clean, dry, intact skin on buttock, abdomen, upper outer arm, or torso

Ortho Evra
- Patient Instructions
  - Wear only for 1 week
  - Do NOT remove while swimming, bathing, etc
  - Do NOT use creams or lotions around patch
  - If patch is partially or completely detached
    - If < 24 hours, reapply to same place or replace with new patch immediately. No back-up needed
    - If > 24 hours or not sure, start a new cycle immediately by applying a new patch. Use back up for first week of new cycle
**NuvaRing**
- Worn for 3 weeks, then removed for 1 week
- May be removed for up to 3 hours
- If removed > 3 hours - use back-up contraception for 7 days
- Insert ring after 7 days even if still bleeding
- One week extended use

**Counseling- Minipills**
- Take one daily
- No hormone free period
- Missed pills
- Irregular menses

**DMPA Case**
- Since Donna can’t remember to take the pill, she is going to start DMPA
- How often is it administered?
  - Every 3 months
- What ADRs should Donna be counseled about?
  - Weight gain
  - Menstrual irregularities

**Depo-Provera®**
- 150mg IM every 13 weeks
- Must be given within 5 days after the beginning of menses
  - Effective immediately
- If menses is irregular give after a negative pregnancy test
  - Effective in 2 weeks

**DMPA- ADRs**
- Weight gain
- Delay to fertility
- Menstrual irregularities

**Step 4**
- Adjust or change therapies depending on ADRs experienced, compliance, compliance, new contraindications/risk factors
Principles for adjusting OCPs based on ADRs

- Determine the cause of the ADR
- Look at relative composition of current OCP
- Try to keep the non-offending component of the OCP the same
- Adjust the offending component by 2 pluses, if possible
- Wait 3 months after starting OCP to change

Adverse Effects: Estrogen

- Excess
  - Nausea
  - Dizziness
  - Bloating
  - HA during active pills
  - Breast tenderness
- Deficiency
  - Nervousness
  - Vomotor symptoms
  - Absence of withdrawal bleeding
  - BTB/spotting: Days 1-9
  - Atrophic vaginitis

Adverse Effects: Progestin

- Excess
  - Increased appetite
  - Noncyclic weight gain
  - Hirsutism
  - Acne
  - Oily skin
  - Increased libido
  - Pruritis
- Deficiency
  - Heavy menstrual flow
  - BTB/spotting: Days 10-21
  - Delayed onset of menses

Adverse Effects: Androgens

- Excess
  - Increased appetite
  - Noncyclic weight gain
  - Hirsutism
  - Acne
  - Oily skin
  - Increased libido
  - Pruritis

RELATIONSHIP OF ADVERSE EFFECTS TO HORMONE CONTENT

<table>
<thead>
<tr>
<th>ESTROGEN EXCESS</th>
<th>ESTROGEN DEFICIENCY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast cyclic change, ↑ Breast size</td>
<td>Absence of withdrawal bleeding, amenorrhea</td>
</tr>
<tr>
<td>Dysmenorrhea, leukorrhea, menorrhagia, clotting abnormalities</td>
<td>Continuous bleeding and spotting</td>
</tr>
<tr>
<td>Uterine enlargement at time of delivery</td>
<td>Amenorrhea, leukorrhea, dysmenorrhea, anovulation, polycystic ovaries</td>
</tr>
</tbody>
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<tr>
<th>PROGESTIN EXCESS</th>
<th>PROGESTIN DEFICIENCY</th>
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</thead>
<tbody>
<tr>
<td>HA during pill pack</td>
<td>Light bleeding</td>
</tr>
<tr>
<td>Flow length decrease</td>
<td>Menorrhagia</td>
</tr>
<tr>
<td>Progestin increase</td>
<td>Depression</td>
</tr>
<tr>
<td>Fatigue</td>
<td>Weight loss</td>
</tr>
<tr>
<td>Hair loss</td>
<td>Amenorrhea</td>
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Dickey RP. Managing Contraceptive Pill Patients, 9th Ed. EMIS, Inc., 1998

Case

After being on her OCP for 4 months, Rachel is still experiencing BTB/spotting during the last week of her pill pack.

- What is the reason?
  - Progestin deficiency
- Of the following, which should correct the problem?
  - Desogen
Case

- Elaine Benis has decided to give up the sponge and start an OCP. She is started on Alesse. After four months, she is complaining of vaginal dryness.
  - What is the reason
    - Estrogen deficiency
  - Which should correct the problem?
    - Ortho Novum, Ortho-Cyclen

Case

- Abby just turned 36 and has come in for her yearly check-up. She is currently using the Ortho-Evra patch with no complaints.
  - SH: smoked 1ppd x 20 years (doesn’t want to quit)
  - What are her options?
    - DMPA, POP, non-hormonal

Emergency contraception

- “Morning After Pill”
- High dose hormonal agents
- First dose within 72 hours of unprotected intercourse and second dose 12 hours later
- MOA:
  - Before ovulation: inhibits/delays ovulation, thickens cervical mucous
  - After ovulation: prevents implantation
  - WILL NOT disrupt implantation once implantation has occurred

Preven vs. Plan B

- 4 tab EE 50mcg + LN 0.25mg and pregnancy test
  - Nausea / vomiting: 50% / 20%
  - Pregnancy rates: 24hr: 2.0%, 25-48hr: 4.1%, 49-72hr: 4.7%

- 2 tab LN 0.75mg
  - Nausea / vomiting: 20% / 5.6%
  - Pregnancy rates: 24hr: 0.4%, 25-48hr: 1.2%, 49-72hr: 2.7%


LN levonorgestrel, EE ethinyl estradiol

Counseling

- ACHES
- Nausea and vomiting
- When to restart OCPs? DMPA?
- If no period for 3-4 weeks, repeat pregnancy test

Questions???

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