Combination Oral Contraceptives

Sabrina Wyatt, MD
Assistant Professor
Department of OB/GYN
Objectives

- Review history of “The Pill”
- Discuss COC components
- Understand pill selection
- Learn counseling points for pill start and missed pills
History

- 1839
- Charles Goodyear
- 1873
- Comstock Act
History

- 1916
  - Margaret Sanger

- 1953
  - Katherine McCormick
  - Gregory Pincus
  - John Rock

“No woman can call herself free who does not control her own body” — Margaret Sanger
1960
- FDA approves Enovid
- 150 mcg mestranol
- 9.85mg norethynodrel
History

- 1965
  - Griswold vs. Connecticut
  - Comstock Act overturned
• Confer the majority of contraceptive action
• Thickens cervical mucus to block sperm
• Blocks LH surge to prevent ovulation
Progestins

- **Bioavailability**
  - % absorbed into bloodstream

- **Dose required for ovulation inhibition**
  - Increased bioavailability, decrease dose needed

- **Half-Life**
  - Longer = reduced breakthrough bleeding
  - Longer = reduced chance of failure if pills missed
First Generation Progestins

- Norethynodrel
- Norethindrone
- Ethynodiol

- Lowest potency
- Short half-lives
- Low progestational effect
First Generation Progestins

- Worked great at higher doses
- Unscheduled bleeding occurred as doses went down
First Generation Progestins

Progestin

- Norethindrone
- Ethynodiol

Brand OCP

- Necon 1/35, 0.5/35
- Ovcon-35
- Loestrin 1.5/30, 1/20
- Loestrin 24 Fe
- Necon 7/7/7
- Zovia 1/35
- Demulen 1/35
Second Generation Progestins

Levonorgestrel

- Extremely potent
- Mirena
- Norplant

Norgestrel

- Racemic mixture
  - Levonorgestrel
  - Dextronorgestrel

- To adjust – dose x 2
## Second Generation Progestins

<table>
<thead>
<tr>
<th>Progestin</th>
<th>Brand OCP</th>
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<tbody>
<tr>
<td>Norgestrel</td>
<td>Cryselle</td>
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<tr>
<td>Levonorgestrel</td>
<td>Lo - Ovral</td>
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<td>Seasonique</td>
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<td>Alesse</td>
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<td>Lutera</td>
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<td>Triphasil</td>
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Third Generation Progestins

- Desogestrel
- Norgestimate

- Introduced to maintain potency but reduce androgenic side effects
- Increased estrogen expression
### Third Generation Progestins

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<td>Mircette</td>
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Fourth Generation Progestins

- Drosperinone
- Yasmin, YAZ
  - Spironolactone analog
  - Antimineralocorticoid
  - Antiandrogenic
Cases – Progestin Choice

- 32yo obese female with PCOS and hirsutism
- 28yo with h/o gestational diabetes and strong family hx of DM
- 30yo with low libido on OCPs
- 18yo with acne
- 26yo desiring less periods per year
Estrogen

- Mestranol – prodrug to ethinyl estradiol
- Dose initially 150mcg
- Steadily decreased (150 -100-80-50)
- All sub-50mcg pills have bioactive EE
- Current doses
  - 10
  - 20
  - 30
  - 35
Cases – Estrogen Choice

• 17yo starting OCs for the first time
• 26yo with breakthrough bleeding on 20mcg OC
• 26yo desiring less periods per year
• 27yo smoker who desires OCs for contraception
Formulations

- **Monophasic**
  - Same combination EE/progestin
  - in every active pill
  - 21 day
  - 24 day
  - 84 day
  - Continuous

- **Multiphasic**
  - EE and/or progestin doses
  - vary during cycle
  - Biphasic
  - Triphasic
Formulations

• Monophasic
  • Extended cycle
  • Less inactive days increases effectiveness
  • Decreased menstrual episodes
  • Increased patient satisfaction/compliance

• Multiphasic
  • Intended to mimic natural cycle more closely
Pill Selection

• **Contraception**
  - Perfect use failure rate <1%
  - Typical use failure rate 8%

**Escape Ovulation Rates**
- Higher dose COCs – 2%
- Lower dose (current) COCs – 8.3%

Pill Selection

• Post Ovulation Ovarian Cyst Prevention

  • Use a longer half life progestin
  • Decrease pill free interval

• Seasonique, Loestrin 24

Pill Selection

• **Menstrual Migraines**
  • Caused by estrogen withdrawal
  • Increased severity on COCs
  • Treat with continuous or extended cycle OCs

Pill Selection

• **Acne**
  - Suppress ovarian production of testosterone
  - Induce hepatic production of SHBG
  - Drospirenone also blocks testosterone receptors and decreases conversion to dihydrotestosterone
  
• FDA Approved: YAZ, Estrostep, Ortho Tricyclen

• Decrease acne by 2/3, max effect at 6 months

• **Hirsutism**
  - Progestin with low androgenic effect and higher EE dose
  - Desogen, Apri, Yasmin
  - 1-2 years for max effect

Pill Selection

- **Endometriosis**
  - Induce pseudo decidualization of implants with continuous use COCs

Pill Selection

- **Emergency Contraception**
  - Yuzpe regimen
  - 100-120 mcg EE
  - 0.5-0.6 mg levonorgestrel
  - Ex. Alesse 5 active pills, 12 hours apart
  - Within 72 hours of unprotected intercourse
  - Give Phenergan
Prescribing COCs

Quick Start (Same Day Start) - Preferred

Start pack on day of visit
If in 1st 6 days of cycle, no backup method needed
If not in 1st 6 days of cycle, backup method x 7 days

25% of women prescribed COCs and NOT instructed to use Quick Start method failed to start COCs

Other Start Methods

- First Day Start
  - Start pack on first day of next menses
  - No backup method needed
  - Introduced to gain early control of ovarian follicles

- Sunday Start
  - Start pack on first Sunday after menses
  - If menses 5 or more days before pill start, backup method needed x 7 days
  - Refills harder to get on weekends
Missed Pill Counseling

One pill:

Take missed pill as soon as you remember

If at time of next dose, take both pills

Continue pack

No backup method needed
Prescribing COCs

Missed Pill Counseling

Two or more pills:

- Take last pill missed and current dose

Use backup method x 7 days

If unprotected intercourse in 7 days prior – need emergency contraception
Other Concerns

• **Metabolism**
  - EE – Activates cytochrome p450 enzymes
  - Increased rates of drug clearance if metabolized by liver
    - Phenobarbital
  - Other drugs that affect p450 pathway alter COC effect
    - Rifampin
Other Concerns

• **Anticonvulsants**
  • Effect depends on the drug
  • Ex. Lamictal levels drop by 50% when COC started
  • Ex. Depakote – no effect
Other Concerns

• **Chronic NSAIDs/ACE Inhibitors**
  • Check potassium in first cycle if using drospirenone

• **St John’s Wort**
  • Increases liver metabolism
  • Decreases COC effectiveness
Summary

- **Progestin Choice**
  - 1\textsuperscript{st} Gen: Low progestational effect, increased BTB
  - 2\textsuperscript{nd} Gen: Decreased BTB, increased androgen activity
  - 3\textsuperscript{rd} Gen: Reduced androgenic effect, increased EE effect
  - 4\textsuperscript{th} Gen: Anti-androgen effect, diuretic

- **EE Choice**
  - Start low, increase if BTB occurs
  - Decrease dose if nausea an issue
Summary

• **Start Method**
  • Quick Start method preferred

• **Missed Pills**
  • Backup method needed if miss ≥ 2 pills
Questions