XII. Birth Control

A. Pharmacological approaches

1. Contraception — prevention of conception by interference with fertilization. Inhibition of:
   - sperm production
   - sperm motility,
   - ovulation
   - encounter between sperm and ovum

2. Interception (postcoital) — interference with implantation of fertilized ovum

3. Abortion — interception of a fertilized ovum, dislodging of blastocyst, embryo, or fetus

4. Apparent safety and efficacy
XII. Birth Control

Contraception versus interception!
So who cares?
XII. Birth Control

• Rep. Coburn (Oklahoma), that’s who.

• Richmond Times Dispatch reported that Rep. Coburn attempted to hold up 1998/1999 federal budget of $500 billion in House/Senate budget conference.

• Disallow medroxyprogesterone acetate reimbursement in public health clinics.

• Pregnancy rates decreasing in teenagers due to either public health messages or contraception.
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A. Pharmacological approaches

5. Methods used worldwide

Female sterilization — 17%
IUD — 12%
IUD (U.S.) — 2%
The Pill (E + P) — 8%
Other methods
  Depo-Provera
  Norplant
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B. Combination Pill

1. Chemistry
   a) Fixed concentration of estrogen and progestin — 20-21 days
   b) Combination allows lower doses to be effective.

2. Mechanism of action
   a) Contraception
      1) Estrogen inhibits FSH secretion and progesterone inhibits LH release
      2) Progestins delay ovum transport through fallopian tube
      3) Progestins produce thick mucus secretion, retards sperm travel
   
   b) Interception
      1) Progestin-induced thick mucus delays passage of the fertilized ovum
      2) Estrogenic agents accelerate transport of fertilized ovum
Estrogen contraception

Regulation of FSH

FSH

Menses

Follicular

Luteal

FSH

LH

Estradiol

Progesterone

2 4 6 8 10 12 14 16 18 20 22 24 26 28

Egg

Corpus luteum
XII. Birth Control

B. Combination Pill

3. Factors altering effectiveness
   a). Non-compliance

   b) Doubling the dose could trigger release of LH and ovulation

   c) Diarrhea and concurrent administration of mineral oil decreases the absorption of estrogen and progestin

   d) Agents that increase metabolism (rifampicin, barbiturates, and phenytoin).

   e) Agents that reduce enterohepatic recirculation. Tetracyclines and ampicillin reduce gut flora, reduce deconjugation, and thereby increase excretion. Issue with lose-dose pills.
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B. Combination Pill

4. Untoward effects (dose-related)

a) Cancer

Breast - not increased for most women who use O.C.’s during most of reproductive years (20-45)

Small subset of women who took high dose O.C. before age 20 or 5 years of use before giving birth reported 1.5 fold increase in breast cancer before age 45. Not all reports support this conclusion. This risk is decreased with doses > 50 µg of estrogen.

Suggestion that O.C. use at time of menopause may increase breast cancer.

Endometrial cancer - Combination O.C. DECREASE the incidence by 50%. Protection lasts up to 1.5 years after taking O.C.’s. Effect due to progestin which opposes estrogen proliferation.

Ovarian cancer - Decreased by O.C.’s

Cervical cancer - no evidence. Increased incidence may be due to higher incidence of viral infection in O.C. users because of no barrier protection.
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B. Combination Pill

4. Untoward effects (cont.)

b) Thromboembolic complications: Estrogens produce dose related increased incidence of cardiovascular and thromboembolic complications.

c) Cardiovascular effects. Myocardial infarction is not a risk in nonsmokers without other risk factors. Smokers over 35 have increased risk even with low-dose pills.

High-dose oral combinations caused hypertension in 4-5% normotensive women and increased blood pressure in 10-15% women with preexisting hypertension. Lower incidence with low-dose preparations. (Estrogens increase HDL and decrease LDL. Progesterone has opposite effect).

d) Vaginal cancer in offspring
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B. Combination Pill

4. Untoward effects (cont.)

e) Gall bladder disease -- O.C.'s increase incidence of gallstones 2-3 fold because of alteration of cholesterol to bile acid ratio in bile.

f) Diabetagenic -- oral contraceptives aggravate diabetes mellitus and can disturb CHO metabolism. Less consequence in non-diabetic individuals.

g) Post-pill amenorrhea - 1-10% of users fail to menstruate following cessation of "pill" use
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C. Sequential Pills

1. Sequential pills
   (Tri-Norinly and Ortho-Novum 7/7/7).

2. Both products contain 25 µg estradiol for 21 days and varying amounts of progestin.

3. Effectiveness questioned.

4. Advantages?
XII. Birth Control

D. Low Dose Progesterone

1. “Mini-pills” (Micronor, Nor-Q.D. and Ovrette)

2. Rationale -- Estrogens side-effects

3. Mechanism of action -- alter cervical and uterine

4. Side effects -- irregular menses, bleeding, amenorrhea

5. Major uses -- patients with high risk to estrogens
XII. Birth Control

E. Postcoital or “Morning-After” Preparations

1. Mechanism of action: Interceptive
   1) Render the endometrium non-conducive to implantation
   2) Cause rapid expulsion of the fertilized ovum

2. Regimens:
   Ethinyl estradiol (100 µg) and norgestrel (1mg) taken twice 12 hr apart
   Ethinyl estradiol alone (2.5 mg twice daily for 5 days)
   Conjugated estrogens (30 mg daily for 5 days)
   Estrone (5 mg three times daily for 5 days)
   Diethylstilbestrol (25 mg twice daily for 5 days).

3. 90-98% effectiveness if initiated within 72 hours of coitus.

4. Adverse effects of high doses: headache, dizziness, breast tenderness
   leg cramps, abdominal cramps, nausea/vomiting (antiemetics).
Emergency Contraception

• Copper-T IUD
  – Can be inserted up to 5 days after unprotected intercourse or 5 days after expected ovulation to prevent pregnancy
  – 99% effective
  – Can be left in place for up to 10 years
  – Higher risk of sexually transmitted infections
Postcoital Preparations

- Schering PC4 (top) and Gedeon Richter Postinor (bottom)
- 1 PC4 = 1 Orval
- 1 Postinor = 20 Orvette
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F. Long-Acting Preparations

1. Depro-Provera
   a) Use -- FDA approved for contraception
   b) Mechanism of action -- inhibits LH and changes in cervical mucus
   c) Administration -- dosage of DMPA is 150 mg every 90 days IM
   d) Serious side effects
      a) depression and headache
      b) amenorrhea
      c) prolonged, unpredictable menstrual bleeding
      d) weight gain (15 lbs)
   e) Indications:
      a) contraception
      b) hormonal castration
XII. Birth Control

F. Long-Acting Preparations

2. Quinestrol and Quingestanol

QUINESTROL (17alpha-ethinylestradiol 3-cyclopentyl ether)

QUINGESTRONE (progesterone cyclopentyl-3-enol ether)
XII. Birth Control

F. Long-Acting Preparations

3. Norplant

a) Subdermal implant system — six Silastic capsules contain levonorgestrel

b) Year 1 Release — 60-80 µg/day
   Year 2-5 Release — 30 µg/day

c) Pregnancy rate = 0.5-1/100 women years of use

d) Mechanism thought to be effects on cervical mucus and endometrium

e) Side effects: irregular bleeding, other effects minor, difficulty in removal
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G. New generation of progestins

Desogestrel, norgestimate and gestodene
Active orally
Minimal androgenic and anti-estrogenic activity
Cause fewer adverse effects such as acne and hirsutism
Should not switch to newer progestins unless problems with current OC
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H. New contraceptives

Oral combinations with 20 µg ethinyl estradiol plus new progestins
IUD that delivers levonorgestrel directly into uterus
Vaginal rings that deliver progestins (easily removed)
Norplant II (only two rods)
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I. Future contraceptives

- Non-latex condoms to avoid allergic reactions
- Spermicidal/microbicidal creams, gels, films, and foams.
- Immunocontraception — immunize against progesterone or cytokines necessary for implantation or embryo growth
“People think that just because there are roughly 100 million people a day having intercourse, this is a huge market. It is not. Why should a pharmaceutical company take these risks?”

—Djerassi*

*Developer of norethindrone, the first progestational oral contraceptive in 1951.
XIII. Pharmacotherapy for Sexual Offenders

A. Pathology

1. Paraphilias
   Includes exhibitionism, fetishism, frotteurism, pedophilias, sexual masochism or sadism, travestic fetishism and voyeurism

2. Characteristics of paraphilias
   Intense recurrent sexual urges selectively focused on non-human objects, children, non-consenting adults or oneself

3. Rape — sexual expression of aggression
Treatment options!
XIII. Pharmacotherapy for Sexual Offenders

B. Cyproterone acetate

1. Antiandrogenic and antigonadotrophic
   Inhibits cellular uptake of testosterone
   Blocks receptor binding
2. Decreases sexual drive and interest and sexual deviant fantasies.
   Does not alter erectile response to erotica
3. Doses of 50-200 mg/day
4. Administer for few months for antilibidinal effects
   Effects reverse in three to six weeks after treatment
XIII. Pharmacotherapy for Sexual Offenders

C. Medroxyprogesterone acetate

1. As effective as CPA
2. Duration of treatment similar to CPA
3. Libido and sexual arousal depressed
4. Adverse effects include weight gain, mild lethargy, cold sweats, nightmares, dyspnea, hyperglycemia and leg cramps
XIII. Pharmacotherapy for Sexual Offenders

D. LHRH antagonist

1. Nafarelin continued administration suppresses response to GnRH
2. Decreases testosterone to castration levels
3. Eliminated exhibitionist behavior
4. Patient could maintain erectile capacity
5. Exhibitionistic behavior returned 9 weeks after cessation of therapy