Contraception

Hormonal Methods
Hormonal Contraceptives: Mechanism of Action

- Synthetic estrogen and/or synthetic progesterone
- Combination hormone contraceptives halt ovulation (release of egg)
- No egg = no pregnancy
- [HybridMedical video: Ovulation](https://www.youtube.com) (YouTube)
Hormone-Based Contraception

• **Estrogen**
  – Usually ethinyl estradiol

• **Progestin**
  – Many types
  – Types vary in terms of side effects
    • Blood lipids
    • Break-through bleeding
    • Weight gain/metabolism
    • Acne

Source: Dawn Stacey, About.com
Estrogen

- Estrogen suppresses development of follicle within ovary
- Estrogen changes the endometrial lining, making the uterine environment less accommodating to a fertilized ovum
Estrogen

• Estrogen makes progestin activity stronger
  • Progestin manipulates one of the hormones responsible for ovulation
  • So, even if estrogen does not completely prevent follicle development, it works with progestin to prevent ovulation
Progestin

• Progestin thickens cervical mucus
  – Thicker mucus hampers sperm movement
• Progestin also changes the endometrial lining in uterus
  – Reduces likelihood for egg implantation
• Progestin-only methods may not inhibit ovulation
  – Varies from one cycle to another
  – Method dependent (Depo-Provera inhibits ovulation, minipills may not)
  – Effectiveness due to cervical mucus, endometrial changes
Bottom Line: Estrogen & Progestin Roles in Hormonal Contraception

- Hormonal contraceptive methods work to prevent ovulation
- Hormonal methods thicken cervical mucus to make sperm transport difficult
- Hormonal contraceptive methods change the lining in uterus to make fertilized egg implantation difficult
Hormonal Contraceptives Side Effects

- Estrogen effects
- Progestin effects
- Androgen effects
- Chart (Dawn Stacey, about.com)
Ortho Evra

- “The patch”
- Beige plastic patch applied to the skin
  - Once a week for three weeks
  - Stomach, upper arm, upper torso
  - First day of menses or first Sunday after period starts
- Releases estrogen and progestin
Ortho Evra: Patch Failure

- According to OrthoEvra website, if patch partially detaches or detaches for a day or less, then reapply or use a new patch
- If patch detaches for more than a day or for unknown timeframe, apply a new patch and start a new four-week cycle
Ortho Evra

• **Cost**: Included with insurance; average wholesale price is ~$0-80/month (Planned Parenthood)

• **Patch should be applied on same week day**

• **Effectiveness**: 99%
Ortho Evra: Side Effects

- Breast tenderness (~20%)
- Headache
- Sensitivity to adhesive
- Nausea
- Menstrual cramping
- Increase in HDL, LDL, triglycerides
- **Upper respiratory infections**
- Increased blood clot risk vs contraceptive pills

*Source: OrthoEvra.com*
Ortho Evra: Contraindications

- Patch should not be used among those with history of venous clots, coronary artery disease, stroke, diabetes with blood vessel damage, high blood pressure, breast cancer, abnormal bleeding, liver problems
- Antibiotic use reduces effectiveness
- Patch not as effective among women weighing more than 90kg (80kg) (reference: Cochrane Collaboration, 2013)
NuvaRing

- Insertion of ring into vagina
- Remains in place for three weeks
- Combination method: estrogen and progestin released
- Cost: $0-80/month (Planned Parenthood)
- **Insertion** (YouTube, 0:45-1:20)
NuvaRing: Side Effects

• Vaginal irritation
• Nausea
• Weight gain
• Irregular bleeding/spotting
• Rash
• Serious, rare: blood clots, gallbladder disease, cancer, liver growths, pancreatic inflammation (triglycerides), cardiovascular incidents
NuvaRing: Contraindications

- Those with history of blood clots, heart attack, stroke, chest pain, very high blood pressure, diabetes with complications, headaches, liver issues, known pregnancy, sensitivity/allergy to NuvaRing, history of TSS
- Smoking
- Obesity: NuvaRing appears a better choice than OrthoEvra, oral contraceptives

Nexplanon/Implanon

- Implanon approved by FDA in 2006
- An implant
  - One rod (Norplant-six)
  - Inserted under skin, inner arm
  - Can feel implant
- Low-dose progestin release
- Good for three years
Nexplanon/Implanon

- 1.5 inches in length
- Effectiveness: 99%
- Cost: Included with insurance; $0-800 (Source: Planned Parenthood)
- Upon removal, fertility returns to normal within several weeks
- Sensitive Implanon insertion video (YouTube, 2:08)
- Nexplanon insertion (YouTube, 0:42)
Nexplanon/Implanon: Side Effects

- Irregular bleeding
- Headache
- Depression
- Breast tenderness
- Acne
- Weight gain
Nexplanon/Implanon: Contraindications

- Liver problems
- Blood clots
- Abnormal bleeding
- Breast cancer
- Obesity and effectiveness: being investigated; original trials = normal weight individuals
Depo-Provera

- Approved by the FDA in 1992
- Progestin-only contraceptive for females
- Hormone is injected every three months
  - Arm
  - Buttocks
- Depo-Provera works by preventing ovulation, thickening cervical mucus, altering endometrium
Depo-Provera

- **Effectiveness**
  - Protection immediate if first shot occurs during first five days of period; otherwise, use other contraceptive method for two weeks
  - Greater than 99% effectiveness (MayoClinic.com=97%)

- **Cost:** quarterly doctor visit + $0-100 quarterly injection (Planned Parenthood)
Depo-Provera: Side Effects

- Headaches
- Dizziness
- Nausea
- Breast tenderness
- Fatigue
- Weight gain
  - 5 pounds or more after one year
- Appetite change
Depo-Provera: Side Effects

• Abdominal pain
• Acne
• Mood changes
• Bloating
• Menstrual irregularities (lighter, heavier, cessation)
• Bone density loss
  – Unclear whether condition will improve when injections stop
    • Calcium supplements
    • Weight bearing exercise advocated
  – FDA’s “black box” warning in 2004
    • Avoid long-term use (> 2 years)
  – Association of Reproductive Health Professionals report concern might be less than originally thought
Depo-Provera

- Reduced sexual appetite
- Hot flashes
- Hair loss
- May reduce risk for ovarian, endometrial cancers

- Other, rare side effects: chest pain, pulmonary embolus, tachycardia, fever, breast lumps, anemia, fainting, vaginal cysts, asthma ([rxlist.com](https://www.rxlist.com))
Depo-Provera: Side Effects

- Side effects may continue until Depo-Provera is out of system, up to six months
- Some women experience no reversibility problems; others take 6-18 months to return to normal
Depo-Provera: Contraindications

- Liver problems
- Blood clots
- Stroke
- Abnormal bleeding
- Breast, reproductive organ cancer
- Allergy
Depo-subQ Provera 104

• Subcutaneous, rather than deep muscle, injection
  – Thigh or abdomen
• 31% lower dose of progestin (Dawn Stacey, about.com)
• Similar side effects
• Since newer product, less information known
Beyaz, Yaz and Yasmin

- Yasmin = “Yaz” on higher dose
- Approved 2001
- Marketed as closer to natural progesterone than other synthetic progestins
- The progestin used may have advantages
  - Reduced water retention
  - Less likely to trigger acne
  - Less likely to trigger facial hair growth
Beyaz, Yaz and Yasmin

• Made with drospirenone and ethinyl estradiol (progestin and estrogen)
• Beyaz – most recent; folate added; higher price
• Prevents ovulation, changes cervical mucus and endometrium
• 28-day pill pack
  – 21 active pills, 7 inactive tablets
  – Missing one day ok; beyond one day, back-up contraception is required, and package may need to be discarded
• Effectiveness: 99%
Beyaz, Yaz and Yasmin: Side Effects

- Headache
- Nausea
- Abdominal pain
- Breast pain, tenderness
- Hair growth changes
- Weight change; swelling of hands, feet
- Changes in menstrual periods
Beyaz, Yaz and Yasmin: Side Effects

• More serious side effects:
  – Depression
  – Dark urine/jaundice
  – Blood clots
  – Chest pain/heaviness
  – Sudden headache, confusion
  – Sudden numbness/weakness
  – Gall bladder problems

• 2009: Bayer in trouble for commercials
  – Yaz not evaluated for premenstrual syndrome (PMS vs PMDD)
  – Labels OK, but commercials were misleading
Beyaz, Yaz and Yasmin: Contraindications

- High blood pressure
- Liver problems
- Migraines
- Unusual bleeding
- Cancer
- History of stroke, blood clot, diabetes
- Adrenal gland disorders
- Smoking
- Obesity?
Yaz and Yasmin: Ups and Downs

• Bonuses of being new
  – Newer “must” be better
  – Popularity
  – Money

• Drawbacks of being new
  – Lack of collected data over long time period
  – Litigation: Bayer settled over 8000 lawsuits, ~$1.7b
    (lawyersandsettlements.com)
  – Latest: increased risk for blood clots (FDA, 2011, YouTube; 3:02)
Chewable Contraceptive Pills

- Femcon Fe approved in 2006
  - First chewable contraceptive pill
  - Spearmint
  - Norethindrone, ethinyl estradiol
  - Generics: Zeosa, Zenchent, Wymzya

- Others:
  - Generess – generic approved 1/2016
  - Minastrin

Source: Rocky Mountain Health Plans
Chewable Contraceptive Pills

• Pill can be swallowed or chewed
  – Not dissolved in mouth
  – Followed by eight ounces of water
  – Toothbrushing ok afterward

• Similar to other combination oral contraceptives regarding side effects, complications

• Effectiveness: 99%
Continuous Cycle Contraceptive Pills

- Like other hormone-based methods, they prevent ovulation
- Combination pill
- One pill every day for three months (Seasonique, Seasonale, generic equivalents)
- One pill every day for a year (Amethyst)

Source: Rocky Mountain Health Plan
Continuous cycle

• Consumers may be **skeptical** of longer-term/continuous contraceptives

• Similar side effects, complications to other combination (estrogen and progestin) oral contraceptives
  – Irregular/break-through bleeding
  – Breast tenderness
  – Headache
  – Heart attack, stroke in serious, rare circumstances
Oral Contraceptive: Natazia

• Like other hormone methods, Natazia prevents ovulation
• FDA approval in 2010
• No generic available until 2016
• Difference is a new estrogen
  – Estradiol valerate
  – Other pills have ethinyl estradiol
• Natazia is four-phase pill

Source: Sharecare.com
Natazia Side Effects

• According to Natazia press release, most commonly reported:
  – Headache and migraine headache (13.2%)
  – Irregular bleeding (8%)
  – Breast discomfort (6.6%)
  – Nausea, vomiting (6.5%)
  – Acne (3.9%)
  – Weight gain (2.8%)

Source: Natazia.com

• Bleeding may be reduced with Natazia
Emergency Contraception

- Available over the counter
- A variety of pills
- Copper IUD
- No age restrictions
- Washington state: [Pharmacy Owners Cannot Cite Religion to Deny Medicine](msn.com)

Source: Emergency Contraception, Princeton University
Long-Term Contraception & Sterilization: Project Prevention

• Societal aid or eugenics?
  – FOX News program (1:30 minutes)
  – ABC News program (2:19 minutes)
Contraception in the Future: Nestorone

- Estrogen and progestin
- Gel
- Spray
- Population Council Announcement, 2010
- Phase III trials (Antares Pharma)
Contraception: The Future

• Male hormonal contraceptive: monthly testosterone injection
• 5/ 2009: China clinical trials
  – 1 in 100 fathered a child
  – Reversible six months after stopping injections
  – 1/3 of 1000 participants did not complete; no reason provided
  – Few side effects reported (acne, weight gain), but more research needed
  – Photo from BBC
Contraception: The Future

• Male *contraceptive pill research* at UW (KOMO report, 2009, 2:10, YouTube)
Contraception: The Future

• RISUG
  – Reversible Inhibition of Sperm Under Guidance
  – Contraceptive method for men
  – Clinical trials in India
  – Injection into vas deferens of male (video, wired.com, :34)
  – RISUG disrupts membranes of sperm so they cannot fertilize
  – One injection to last 10 years
  – Reversibility not well tested, though reports on primates appear positive (requires another injection)
  – Marketing challenges
Contraception: The Past

- Male Contraceptive: Heat
  - Prolonged heat exposure can impair sperm production in testes
  - Ancient method
  - Effectiveness?
    - 116 degree bath
    - 45 minutes
    - Every day
    - Three weeks
Contraception: Impact of Heat on Sperm

Figure: Semen microphotograph from an OAT case. A very high percentage of sperms with morphological abnormalities of head, midpiece and tail are seen: coiled tail (CT), amorphous head (AH), pinpoint head (PP), dilated midpiece (DM), thick tail (TT) (x400).
Contraception: Impact of Heat on Sperm

Contraception: Impact of Heat on Sperm

- Upper left: coiled tail
- Upper right: bent tail
- Lower left: double head
- Lower right: triple head

United Nations: Contraceptive Prevalence Across the World, 2005