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 (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 manipulates hormones to suppress development of follicle within ovary
- Estrogen changes the endometrial lining, making the uterine environment less accommodating to a fertilized ovum
- Estrogen supplements progestin activity
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

- Varying levels of estrogen and progestin can influence effects
- **Chart** (Dawn Stacey, about.com)
- Estrogen – cardiovascular effects, headache, weight gain; interfere with milk production; smokers at much higher CV effect risk
- Progestin – fewer CV effects, more irregular and break-through bleeding (spotting); influence on mucus and endometrium = consistency is important
Ortho Evra

• “The patch”
  – Applied 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

• If detaches for less than a day, apply a new patch; if more than a day, apply new patch and begin new cycle
Ortho Evra

- Cost: Included with insurance; average wholesale price is ~$0-150/month plus exam (Planned Parenthood)
- Available via physician, Planned Parenthood
- Available online some states, including WA
  - Nurx.com
  - Pjkt Ruby (also donates to one month of pills to developing country)
  - More (bedside.org, 10/26/17)
- Patch should be applied on same week day
- Effectiveness: 99%
Ortho Evra: Side Effects, Contraindications

- 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
- Contraindications: cardiovascular conditions, some cancers, liver issues; some medications; overweight/obesity (less effective in women >90kg)

Source: OrthoEvra.com
NuvaRing

- Insertion of ring into vagina
- Remains in place for three weeks
- Combination method: estrogen & progestin
- Effectiveness: 90-99%
- Cost: $0-200/month *(Planned Parenthood)*
- Physician, Planned Parenthood, online
- [Insertion](https://www.youtube.com/watch?v=example) (YouTube, 0:45-1:20)
NuvaRing: Side Effects, Contraindications

- Vaginal irritation
- Nausea
- Weight gain
- Irregular bleeding/spotting
- Rash
- Serious, rare: blood clots, gallbladder disease, cancer, liver growths, pancreatic inflammation (triglycerides), cardiovascular incidents
- Contraindications: same as OrthoEvra, but also toxic shock syndrome
- Obesity/overweight: NuvaRing works better than patch

Nexplanon/Implanon

- An implant
  - One rod inserted under skin, inner arm
  - Can feel implant
- Low-dose progestin-only
- Effectiveness: 99%
- Lasts up to three years
- Cost: $0-1300 (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

• Progestin-only, so cardiovascular effects may be less pronounced than combination methods
• Irregular bleeding
• Headache
• Depression
• Breast tenderness
• Acne
• Weight gain
• Contraindications: liver issues, blood clots, abnormal bleeding, breast cancer; obesity/overweight – need more research
Depo-Provera

- Progestin-only contraceptive
- Cost: $0-100 (Planned Parenthood)
- Effectiveness: 94-99%
- Hormone is injected every three months
  - Arm
  - Buttocks
- Depo-Provera works by preventing ovulation, thickening cervical mucus, altering endometrium
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
- In high-risk populations, may increase risk of acquiring HIV
  - Possibly thins epithelial cells that keep toxic agents out of body
- Other, rare side effects: chest pain, pulmonary embolus, tachycardia, fever, breast lumps, anemia, fainting, vaginal cysts, asthma (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.
- Contraindications: liver issues, cardiovascular conditions, abnormal bleeding, some cancers.
Contraceptive Pills
Contraceptive Pills

• Combination
  – Two synthetic hormones: estrogen (usually ethinyl estradiol) plus progestin
  – Many types of pills
    • Varies by hormone release
    • Varies by type of progestin
    • Varies by amount of hormone
      – Low estrogen (20 mcg)
      – Higher estrogen (30-35mcg)

• Minipill
  – One synthetic hormone: progestin
  – Norethindrone
  – 28-pill pack (no placebo)
    • Not all minipill users ovulate consistently, so bleeding may be unpredictable
  – Fewer serious side effects
  – Less effective (91-97%)

Dawn Stacey, PhD & LMHC & Meredith Shur, MD, verywell.com
Oral Contraceptive Technology

- Traditional 21-day hormone pill packs
- 24-day hormone packs
- Chewable packs
  - Femcon
- Extended pill cycles
  - Seasonique,
  - Loseasonique,
  - Seasonale, Lybrel
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%
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)
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