Sex Hormones
Pharmacology

University of Hawai‘i Hilo Pre-Nursing Program
NURS 203 - General Pharmacology
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Learning Objectives:

- Understand the regulation of sex hormone release
- Know the general information about estrogen, progesterone, and testosterone
- Know the indications for all medications discussed
- Compare drugs within same drug classes
- Recognize unusual pharmacokinetic characteristics between drug classes and the drugs within one class
Releasing Hormones

Hypothalamus

Gonadotropin releasing Hormone (GnRH)

Anterior Pituitary

Follicle Stimulating Hormone (FSH) & Luteinizing Hormone (LH)

Sexual organs of males and females

Sex Steroids

Androgens, progesterone, & estrogen

- LH
  - Androgens - men
  - Androgens & progesterone - women
- FSH
  - Estrogens - women
Releasing Hormones

Hypothalamus

Gonadotropin releasing Hormone (GnRH)

Anterior Pituitary

Follicle Stimulating Hormone (FSH) & Luteinizing Hormone (LH)

Sexual organs of males and females

Sex Steroids

Androgens, progesterone, & estrogen

Negative Feedback Loop
Sex Hormones

- **Androgens - Testosterone**
  - Growth
    - Male sex characteristics
    - Increased muscle growth
    - Increased bone growth
  - CNS
    - Mental & physical energy
    - Increased libido
    - Aggression
  - Cancers
    - Androgen cancers (prostate)

5-10 X less than males
Sex Hormones

- **Estrogen**
  - Growth
    - Decreases
      - Muscle, bone, & breakdown of bone
    - Increases
      - Breast, endometrial, & uterine
  - Vasculature
    - Decrease
      - Blood pressure & atherosclerosis (women)
    - Increases
      - Risk of DVT
      - Anti-inflammatory
  - Cancers
    - Estrogen dependent (breast cancer - some)
Sex Hormones

- Progesterone
  - Reproductive
    - Decreases
      - Breast, endometrial, & uterine growth
      - Maternal immune response
      - Lactation
      - Uterine contraction
    - Increases
      - Body temperature

Fig. 2. Increase in estrogen output during pregnancy.
Hormone Replacement Therapy (HRT)

- Estrogen uses:
  - Vasomotor symptoms - Hot flashes, night sweats, vaginal dryness, pain during intercourse, and mood swings
  - Prevent osteoporosis
  - Others
Hormone Replacement Therapy (HRT)

- Estrogen - Dosage forms
  - Topical preparations
  - Tablets
  - Injections
  - Transdermal
  - Compounded
    - Sublingual
    - Topical - cream, gel, emulsion, spray, silicone ring
    - Capsules
    - Drops
    - Pellets
    - Troches
Hormone Replacement Therapy (HRT)

- **Adverse effects**
  - **Common**
    - Dizziness & headache
    - Abdominal cramps & bloating
  - **Serious**
    - Breast cancer
    - Endometrial cancer
    - DVT, PE, stroke, MI
    - Dementia

- **Intact uterus**
  - Use in combination with progesterone
- **Hysterectomy**
  - May use estrogen as monotherapy
Hormone Replacement Therapy (HRT)

- **Estrogen**
  - Increases Growth & mutation of endometrium
  - Intact uterus
  - Use in combination with progesterone
  - Hysterectomy
  - May use estrogen as monotherapy

- **Progesterone**
  - Decreases Growth and mutation of endometrium

**WHY??**
Hormone Replacement Therapy (HRT)

- Estrogen - contraindications
  - Vaginal bleeding
  - History of clots - DVT, PE, stroke, MI
  - Estrogen dependent cancer
  - Liver disease
  - Porphyria
  - Pregnancy
Hormone Related Cancers

- Breast cancer and SERMS (selective estrogen receptor modulators)
  - Tamoxifen (MOA)
    - Bone - Acts as an estrogen agonist to save bone (inhibit resorption)
    - Endometrium - Acts as a partial estrogen agonist & promotes growth
    - Breast - Acts as an estrogen antagonist & inhibits growth of cancer cells
  - Kinetics
    - Oral administration
    - Taking with food doubles the absorption
    - 90% protein bound
    - Metabolized by CYP 2D6 & 3A4
    - Half life 10 hours
    - Excreted 69% in feces, 24% in urine
Hormone Related Cancers

- Breast cancer and SERMS (selective estrogen receptor modulators)
  - Tamoxifen - drug interactions
    - Enzyme inhibitors or inducers
    - Warfarin levels increased
    - Certain chemotherapeutic agents
  - ADRs
    - Common - Hot flashes or amenorrhea
    - Avoid in endometrial cancer - can increase risk, also DVT/PE
Oral Contraceptive Pills (OCPs)

- The main component
  - Ethinylestradiol (EE)
    - MOA - sustained levels of estrogen decreases surges of LH and FSH
- Uses:
  - Birth control
  - Acne
  - Premenstrual dysphoric disorder
    - *Mood disorders*: despair, irritability, anxiety, mood swings
    - CNS: headaches, fatigue, hunger, sleep disorders
    - Other: bloating, palpitations, breast tenderness
Oral Contraceptive Pills (OCPs)

- Kinetics (EE)
  - Bioavailability - 40%
  - 98% protein bound
  - Metabolized by CYP3A4
  - Half life 24 hours
  - Excretion in urine and feces
Oral Contraceptive Pills (OCPs)

**Increased Risk**
- DVT/PE
- Stroke
- MI
- Liver tumor
- Gallbladder disease
- Visual disturbances
- Fetal abnormalities
- Hypertension

**Common ADRs**
- Nausea
- Skin darkening/spots
- Breast tenderness
- Breakthrough bleeding

*Boxed Warning: NO smoking!*
Oral Contraceptive Pills (OCPs)

- **Progestin only**
  - **Pills - “mini pill or POP”**
    - **MOA - Increased viscosity of cervical mucous (no egg implantation)**
      - Decreased: Ovulation, implantation, fertilization
    - Continuous active pills
    - No menses - trick body into believing pregnant
  - **Injections - Depo-Provera**
    - Same as above
  - Alternate uses
    - Amenorrhea
    - Abnormal uterine bleeding
    - Endometriosis
    - HRT
Prostate & Male Sexual Dysfunction

- Testosterone - lipophilic
- Converted into DHT
  - More active
- Enzyme involved - 5 alpha reductase
- 5 alpha reductase - two types
  - Type 1
    - Liver & Skin
  - Type 2
    - Prostate, testicles, & hair follicles
Prostate & Male Sexual Dysfunction

- Dutasteride
  - Non-selective
  - Uses: BPH & prostate cancer prevention
- Kinetics
  - Oral
  - Bioavailability 60%
  - Lipophilic
  - CYP3A4 - active metabolites
  - Half life 5 weeks
  - Excreted in urine and feces

Cell:
- Liver
- Skin
- Prostate
- Testicles
- Hair follicles

5 alpha reductase
- Type 1
- Type 2

DHT
Prostate & Male Sexual Dysfunction

- Dutasteride
  - Non-selective
  - Uses: BPH & prostate cancer prevention
  - ADRs
    - Sexual dysfunction
Prostate & Male Sexual Dysfunction

- **Finasteride**
  - **Selective**
  - **Uses:** BPH, prostate cancer prevention, & male patterned baldness
  - **Kinetics**
    - Oral
    - Bioavailability 60%
    - Hydrophilic
    - CYP3A4 - metabolites not very active
    - Half life 6 hours
    - Excreted in urine and feces

Cell:
- Liver
- Skin
- Prostate
- Testicles
- Hair follicles

5 alpha reductase 2
- Type 1
- Type 2

DHT
Prostate & Male Sexual Dysfunction

- Finasteride
  - Selective
  - Uses: BPH, prostate cancer prevention, & male patterned baldness
- ADRs
  - Sexual dysfunction

Cell:
- Liver
- Skin
- Prostate
- Testicles
- Hair follicles

5 alpha reductase:
- Type 1
- Type 2

DHT
Prostate & Male Sexual Dysfunction

- Drug interactions
  - CYP enzyme inhibitors/inducers

- Contraindications
  - Not to be used in children or women of child bearing ages

- Special handling
  - Women of child bearing ages should not handle these medications. Active ingredient could be absorbed through hands and negatively impact the development of the fetus
Questions