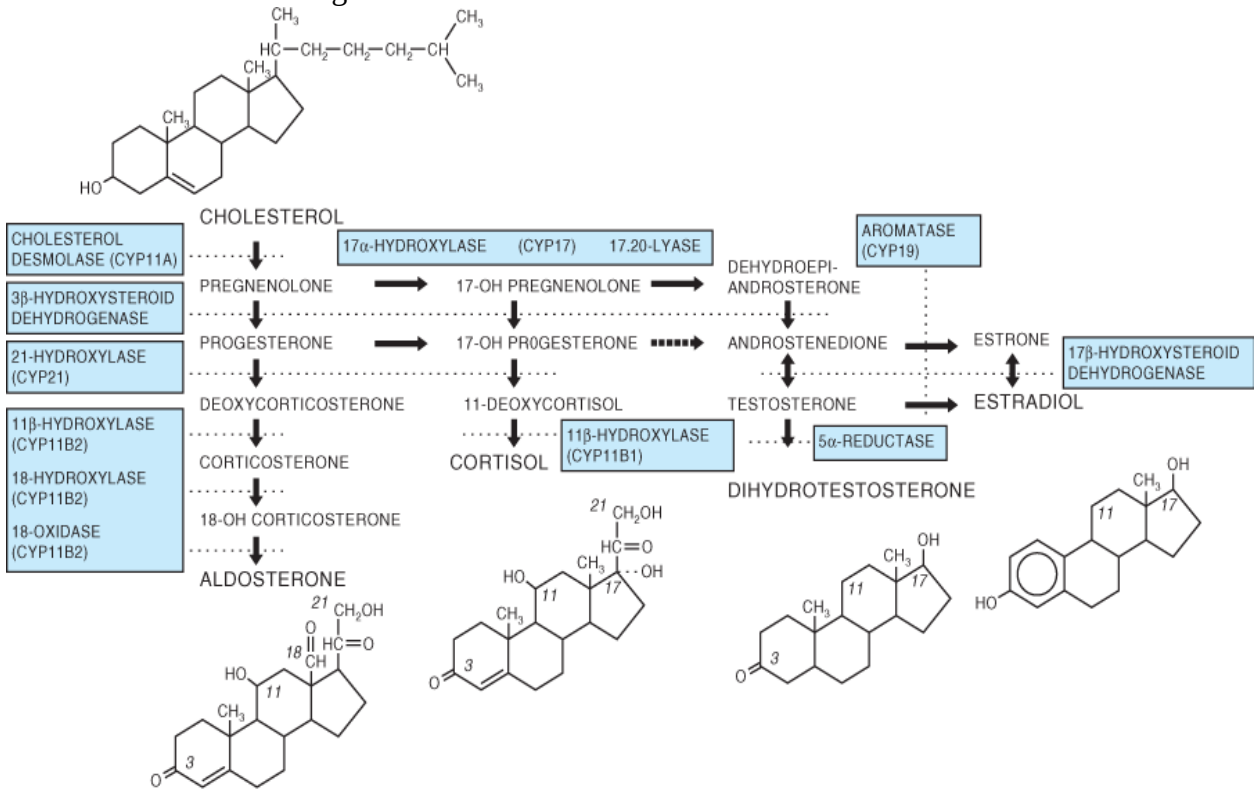
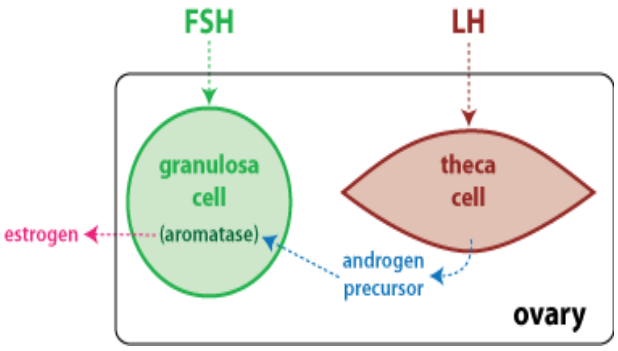
Unit IV – Problem 7 – Biochemistry: Biosynthesis of Female Sex Hormones

- **Precursor is: cholesterol which is containing 27 carbons.**
  - **Cholesterol** is converted to **pregnenolone** via the enzyme cholesterol desmolase.
  - **Pregnenolone** can be converted to **progesterone** via the enzyme 3β-hydroxysteroid dehydrogenase.
  - **Pregnenolone** can also be converted to **17-hydroxypregnenolone** through 17α-hydroxylase.
  - **17-hydroxypregnenolone** is converted to **dehydroepiandrosterone** and then to **androsteindione** through 3β-hydroxysteroid dehydrogenase.
  - **Androstendione** is converted to **testosterone** which –in turn- can be converted to estradiol through aromatase.



- **Hormonal stimulation:**
  - **Luteinizing Hormone (LH):** binding to its receptors which are found on theca cells to stimulate the production of androgens.
  - **Follicle Stimulating Hormone (FSH):** binding to its receptors which are found on the surface of granulose cells to stimulate the conversion of androgens to estradiol via the action of aromatase.
- **Circulating sex hormones:**
  - They are also known as gonadal steroid because they are produced by the gonads (ovaries or testes), adrenal cortex (in zona reticularis) or by conversion of androstendione to estrogen in adipose tissue (which has the enzyme aromatase).
- **Estrogens and progesterone:**
  - They are mainly produced by the ovaries. Other sources include: adrenal gland, pituitary gland and the placenta (especially during pregnancy).
  - They stimulate secondary sexual characteristics, development of mammary glands and regulate the function of the menstrual cycle.
- **Types of estrogen:**
  - **17β-estradiol**: it is the predominant form in non-pregnant females and produced from testosterone via the action of the aromatase enzyme.
  - **Estrone**: produced by the action of the aromatase enzyme in adipose tissue.
  - **Estriol**: it is the primary estrogen of pregnancy which is produced by the placenta.

- **Synthesis of estrogen:**
  - LH will bind to LH-receptors which are present on the surface of theca cells to enhance the conversion of cholesterol to androgens.
  - FSH will bind to FSH-receptors present on the surface of granulose cells to enhance the conversion of androgens to estrogen via the action of the enzyme aromatase.
  - Notice that progesterone is produced and secreted by corpus luteum.



- **Role of corpus luteum:**
  - LH and hCG (human Chorionic Gonadotropin) are produced by fetal trophoblasts at the 10^{th} day of ovulation → therefore, enhancing theca cells to produce androgens.
  - Aromatase activity increases in granulose cells by LH to aromatize androgens to estrogen.
  - LH induces cells to produce progesterone.
  - The secretion of progesterone and estradiol is episodic and correlates with the LH-pulses (pulsatile).
  - FSH has minimal influence on progesterone production but stimulates estrogen production during luteal phase.
- **Transport and storage:**
  - **Estrogens bind to**: Sex Hormones Binding Globulin (SHBG).
  - **Progestins bind to**: Corticosteroid Binding Globulin (CBG).
    Notice that free hormones are the ones which are biologically active. There is not storage of these hormones → they are secreted when needed.
- **Estrogens and progestins metabolism:**
  - Estrogens are conjugated with glucuronide or sulfate in the liver (to make them more water soluble which will then be excreted in: bile, feces or urine).
  - Estrogens can be given orally but not progesterone (why?) → conjugation of progestins to metabolites in the liver (predominantly sodium pregnanediol-20-glucuronide) is very active.
- **Steroid hormone receptors were explained in previous problems.**