- 11β-hydroxylase: mitochondrial enzyme

C. Androgen Synthesis

- **Dehydroepiandrosterone (DHEA):** major androgen/androgen precursor produced by the adrenal cortex
  - Prehormone converted into androstenedione via **3β-OHSD and $\Delta^{5,4}$-isomerase**
- **Androstenedione:** also formed in the adrenal via conversion of 17-hydroxypregnenolone via **17,20-lyase**
  - Reduced at C_{17} position to form testosterone
- **Testosterone**: most potent androgen
  - Small amounts produced in the adrenal
  - Mainly produced in the testes
- Most of the 17-hydroxypregnenolone follows the glucocorticoid pathway
  - Some subjected to oxidative fission and removal of the 2-carbon side chain by **17,20-lyase**
    - Dual-function protein
    - Important in both adrenals and gonads
    - Acts exclusively on 17α-hydroxy-containg molecules
- ↑Adrenal androgen production: if glucocorticoid biosynthesis is impaired by the lack of one hydroxylase
  - **Adrenogenital syndrome**

D. Testicular Steroidogenesis

- **Interstitial cells of Leydig:** synthesize testicular androgens
- **Cholesterol:** immediate precursor of gonadal cells
- **Rate limiting step:** delivery of cholesterol to the inner mitochondrial membrane by the transport protein StAR
- This conversion is similar in the adrenal, ovary, and testis. However, in the latter two tissues the process is promoted by LH rather than ACTH.
- Conversion of pregnenolone to testosterone requires **five enzyme activities**:
  - (1) 3β-OSHD and (2) $\Delta^{5,4}$-isomerase
  - (3) 17α-hydroxylase and (4) 17,20-lyase
  - (5) 17β-OSHD
- Pregnenolone can also be converted to testosterone by the **dehydroepiandrosterone (or Δ^5) pathway**
  - mostly used in the human testes
- Metabolism of Testosterone
  1. **Oxidation at the 17 position**
     - Occurs in many tissues, including the liver
     - Produces generally inactive or less active 17-ketosteroids
  2. Reduction of the A ring double bond and the 3-ketone
     - Less efficient pathway
     - Occurs in target tissues
     - Produces potent DHT
- **DHT**: most significant metabolic product of testosterone
  - active in prostate, external genitalia, and some areas of the skin
  - plasma content in adult male: DHT (~400 µg) <<< Testosterone (5 mg)
    - about 50 to 100 µg of DHT: secreted by **testes**
    - others: produced peripherally from testosterone in NADPH-dependent **5α-reductase**

E. Ovarian Steroidogenesis

- **17β-estradiol**: primary estrogen of ovarian origin
- Estrogens are formed by the aromatization of androgens in three hydroxylation processes, each requires O_2 and NADPH
  - Aromatase enzyme complex: include P450 monooxygenase
- Forms of estrogen
  - **Estrone**
    - Synthesized in numerous tissues
    - More abundant
    - Formed from the aromatization of androstenedione
    - Major source of estrogens in postmenopausal women
  - **Estriol**
    - Produced more during pregnancy
  - **Estradiol**
    - Formed if the substrate of the enzyme complex is testosterone
- Theca cells produce androstenedione and testosterone
  - These products are acted upon by aromatase enzyme in granulosa cells to form estrone and estradiol
- **Progesterone**
  - Precursor for all steroid hormones
  - Produced and secreted by the corpus luteum as an end-product