

- 11 β -hydroxylase: mitochondrial enzyme

C. Androgen Synthesis

- **Dehydroepiandrosterone (DHEA):** major androgen/androgen precursor produced by the adrenal cortex
 - Prehormone converted into androstenedione via **3 β -OHSD and $\Delta^{5,4}$ -isomerase**
- **Androstenedione:** also formed in the adrenal via conversion of 17-hydroxypregnenolone via **17,20-lyase**
 - Reduced at C₁₇ 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 17 α -hydroxy-containing molecules
- $\uparrow$ Adrenal androgen production: if glucocorticoid biosynthesis is impaired by the lack of 11 β -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) 3 β -OHSD and (2) $\Delta^{5,4}$ -isomerase
 - (3) 17 α -hydroxylase and (4) 17,20-lyase
 - (5) 17 β -OHSD
- 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 μ g) <<< Testosterone (5 mg)
 - about 50 to 100 μ g of DHT: secreted by **testes**
 - others: produced peripherally from testosterone in NADPH-dependent **5 α -reductase**

E. Ovarian Steroidogenesis

- **17 β -Estradiol:** primary estrogen of ovarian origin
- Estrogens are formed by the aromatization of androgens in three hydroxylation processes, each requires O₂ 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