• 11β-hydroxylase: mitochondrial enzyme

C. Androgen Synthesis
• Dehydroepiandrosterone (DHEA): major androgen/androgen precursor produced by the adrenal cortex
  ○ Prehormone converted into androstenedione via 3β-OSHD and Δ5,4-isomerase
• Androstenedione: also formed in the adrenal via conversion of 17-hydroxyprogrenolone 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-hydroxyprogrenolone 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-containing molecules
• 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) Δ5,4-isomerase
  ○ (3) 17α-hydroxylase and (4) 17,20-lyase
  ○ (5) 17β-OSHD
• Pregnenolone can also be converted to testosterone by the dehydroepiandrosterone (or Δ5) 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
• 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
  ▪ Estradiol
    ▪ 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