Steroid Hormones

A) 21 or fewer carbon atoms

B) Precursor is 27 carbon cholesterol

C) major classes of steroid hormones

1) Progestagens
   a) progesterone - prepares lining of the uterus for implantation of an ovum
   b) site of synthesis: corpus luteum
      - maintenance of pregnancy

2) Glucocorticoids
   a) cortisol - promote gluconegenesis / formation of glycogen
      - degradation of fat & protein
   b) site of synthesis: adrenal cortex

3) mineralocorticoids
   a) aldosterone - increase kidney reabsorption of Na⁺, Cl⁻ & HCO₃⁻
      - increase blood volume & blood pressure
   b) site of synthesis: adrenal cortex

4) Androgens
   a) testosterone - development of male secondary sex characteristics
   b) site of synthesis: testes

5) Estrogens
   a) estradiol - development of female secondary sex characteristics
   b) site of synthesis: ovary
STEROIDOGENESIS

Hydroxylation (OH) reactions require: NADPH and O₂
O for the OH group comes from O₂ and not from H₂O

\[ RH + O₂ + NADPH + H⁺ \rightarrow ROH + H₂O + NADP⁺ \]

Cytochrome P₄₅₀ terminal; component of an electron-transport chain
NADPH transfers its high-potential e- to a flavoprotein

adrenodoxin (nonheme iron protein) \( \rightarrow \) e- oxidized form of cytochrome P₄₅₀
reduced form of P₄₅₀ activates O₂

1) Adrenocorticotrophic hormone (ACTH)
   polypeptide from anterior pituitary gland stimulates
   conversion of cholesterol \( \rightarrow \) pregnenolone (precursor to all
   steroid hormones)

2) cholesterol 6-carbon side chain broken off at C₂₀

3) inner membrane of mitochondrial cristae \( \rightarrow \)
   mixed-function oxygenases enzymes (cytochrome P₄₅₀s)

4) Side-chain cleavage (scc) of cholesterol by P₄₅₀scc
   requires reducing factor (NADPH) \( \rightarrow \) pregnenolone (C₂₁)

5) Pregnenolone transported out of mitochondria \( \rightarrow \)
   endoplasmic reticulum
Progesterone ($C_{21}H_{30}O_2$) from pregnenolone synthesized two steps:
1) 3-hydroxyl group oxidized to 3-keto group
2) 5-double bond is isomerized to 4 double bond

Cortisol ($C_{21}H_{28}O_5$) from progesterone
1) hydroxylations at C$_{17}$ before C$_{21}$, whereas C$_{11}$ at any step
2) hydroxylating enzymes: high specific → inherited disorders of steroid metabolism

Aldosterone ($C_{21}H_{28}O_5$) from progesterone
1) hydroxylation at C$_{21}$
2) hydroxylation at C$_{11}$
3) C$_{18}$ angular methyl group oxidized to aldehyde

Testosterone ($C_{19}H_{28}O_2$ androgen) from progesterone
1) hydroxylation at C$_{17}$
2) C$_{10}$ & C$_{21}$ cleaved to yield androstenedione
3) 19 carbons

Estradiol ($C_{18}H_{24}O_2$ estrogen) from androgens
1) loss of C$_{19}$ angular methyl group
2) formation of an aromatic A ring require NADPH & O$_2$
3) 18 carbons
Figure 15.5  Model for cholesterol homeostasis in the adrenal. (From Brown, Kovanen, and Goldstein [4]. with permission.)