



Figure 2-19. Steroidogenesis. Gonadal steroid hormones originate from cholesterol. Cholesterol is composed of 27 atoms of carbon arranged into a basic structure of four rings (A-D); representative carbons are numbered within the structure. The mitochondrial cytochrome P450 (named for its absorption maximum at 450 nm) binds cholesterol and catalyzes a series of reactions resulting in the cleavage of the cholesterol side-chain - thereby forming a molecule of pregnenolone (1). Pregnenolone ( $P_5$ ) can be shunted into one of two pathways depending upon the relative concentrations of enzymes competing for this substrate (2 vs. 3). Only modified sites are illustrated. The delta-4 pathway proceeds to progesterone ( $P_4$ ; note the shift in double bond from carbon position 5-6 to 4-5). The delta-5 pathway terminates at dehydroepiandrosterone (DHEA). Three  $\beta$ -hydroxysteroid dehydrogenase (HSD) removes a molecule of hydrogen at the designated position; an isomerase transfers the C=C bond from the B to A ring (2). Seventeen  $\alpha$ -hydroxylase transforms pregnenolone into 17 $\alpha$ -hydroxypregnenolone and progesterone into 17 $\alpha$ -hydroxyprogesterone (3). Progestogens are made up of 21 carbons. Cleavage by a desmolase of the carbon bond between position 17 and 20 of 17 $\alpha$ -progestogens (4) produces the 19-carbon androgens - DHEA and androstenedione (steps 3 and 4 are actually achieved by a single enzyme complex - cytochrome P450 C-21 side-chain cleavage). Androstenedione (A) is transformed into testosterone (T) via reduction at carbon-17 (5) (dehydrogenases can accept or transfer an atom of hydrogen). Aromatization of the A ring (6) of androstenedione or testosterone results in the formation of 18-carbon estrogens - estrone ( $E_1$ ) or estradiol ( $E_2$ ). Progesterone can also be converted into corticoids. Mineralocorticoids and glucocorticoids (eg., cortisol) are produced within the cortex of the adrenal gland. Genes that regulate expression of steroidogenic enzymes are controlled by specific transcription factors (eg., steroidogenic factor [SF]-1).

- 1 = cytochrome P450 C-27 side-chain cleavage  
 2 = 3β-HSD; isomerase  
 3 = 17α-hydroxylase  
 4 = 17, 20 desmolase  
 5 = 17β-HSD  
 6 = aromatase