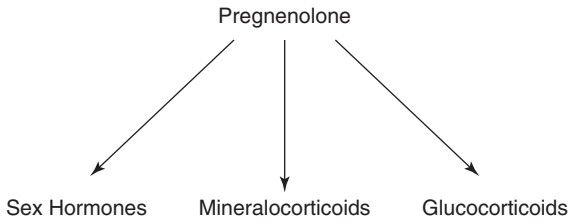

Figure 13-36 Pregnenolone is the precursor to the sex hormones, glucocorticoids, and mineralocorticoids.

Progesterone is then derived from pregnenolone by oxidizing the 3-hydroxyl group to a ketone and shifting the double bond's position. **Figure 13-36** shows the general derivation from pregnenolone of the sex hormones (e.g., testosterone, estradiol), glucocorticoids (e.g., cortisol, the principal glucocorticoid), and mineralocorticoids (e.g., aldosterone, the principal mineralocorticoid).

QUESTIONS FOR DISCUSSION

1. Why might spinach be banned from the diet of a patient who has Refsum disease?
2. Suppose that you lived in the far north and had to spend the winter living on a diet of whale blubber. Explain why the concentration of ketone bodies in your blood would increase. Then explain why supplementing your diet with soda crackers might be a good idea.
3. Patients with methylmalonic aciduria have a high level of methymalonic acid in their blood and urine. Explain why a vegan diet, with little or no intake of vitamin B_{12}, might lead to this condition.
4. Studies on cultured fibroblasts from certain patients' skin, emphasizing the cells' ability to metabolize phytanic acid, demonstrated the incompetence of the cells to metabolize this lipid. When the same cell cultures were given pristanic acid, however, the pristanic acid was metabolized at a normal rate (see Figure 13-12 for the chemical structures of phytanic and pristanic acids). What is the enzymatic defect responsible for the inability of these cells to metabolize phytanic acid?
5. In Figure 13-12, explain the presence of propionyl-CoA and 2-methylpropionyl-CoA, in addition to acetyl-CoA, as end products of the oxidation of phytanic acid.
6. Humans are unable to synthesize biotin, so they depend on dietary sources to secure enough of the cofactor for maintaining activity of biotin-dependent enzymes. Most dietary biotin is bound to protein and must be released through the action of the pancreatic enzyme biotinidase, which hydrolyzes the amide linkage of biotin to the protein. The free biotin is then absorbed from the gut via a sodium-dependent transport system. However, certain proteins are known to sequester biotin—for example, the egg-white protein avidin, which binds biotin with a binding constant on the order of 10^{12} M^{-1}. What would be the biochemical consequences of a defect in either the activity of the biotinidase enzyme or the activity of the intestinal transporter protein for biotin?
7. Valproic acid (2-*n*-propylpentanoic acid) is used for control of epilepsy and seizures. It is a substrate for the β-oxidation pathway in mitochondria, which may account for 40% or more of the overall metabolism of the drug (30–50% of the drug is excreted in the urine

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