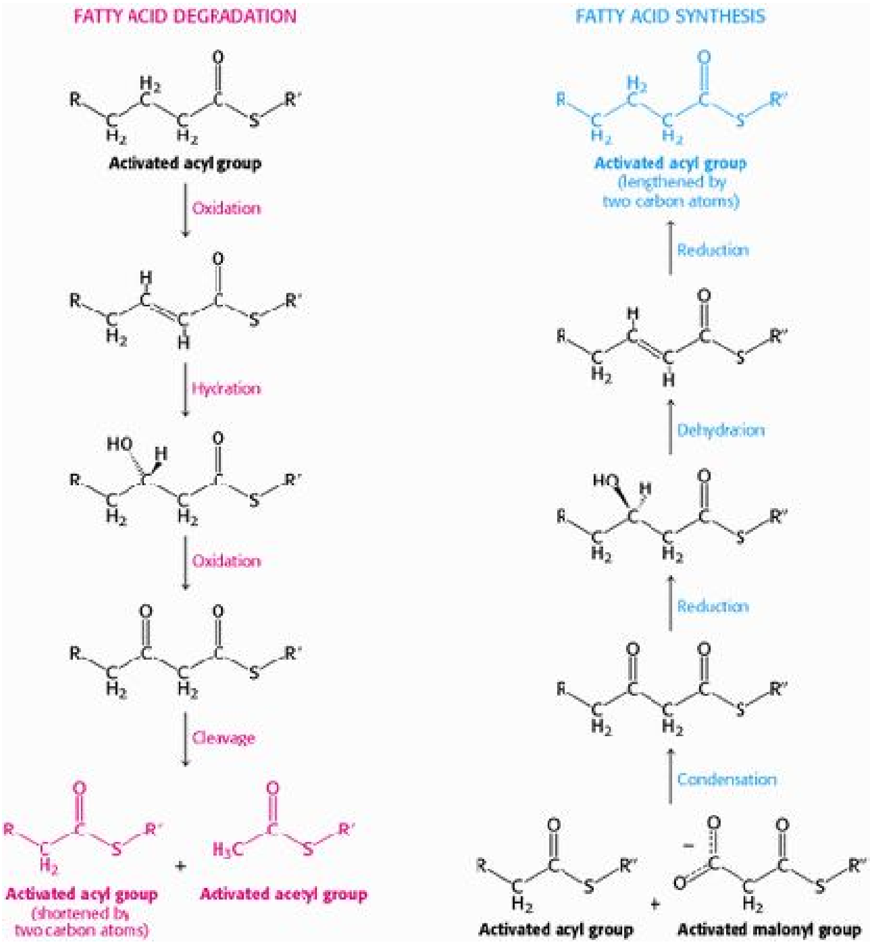
Fatty Acid Metabolism

We turn now from the metabolism of carbohydrates to that of fatty acids. A fatty acid contains a long hydrocarbon chain and a terminal carboxylate group. Fatty acids have four major physiological roles. First, *fatty acids are building blocks of phospholipids and glycolipids*. These amphipathic molecules are important components of biological membranes, as we discussed in Chapter 12. Second, many proteins are modified by the *covalent attachment of fatty acids, which targets them to membrane locations* (Section 12.5.3). Third, *fatty acids are fuel molecules*. They are stored as *triacylglycerols* (also called *neutral fats* or *triglycerides*), which are uncharged esters of fatty acids with glycerol (Figure 22.1). Fatty acids mobilized from triacylglycerols are oxidized to meet the energy needs of a cell or organism. Fourth, *fatty acid derivatives serve as hormones and intracellular messengers*. In this chapter, we will focus on the oxidation and synthesis of fatty acids, processes that are reciprocally regulated in response to hormones.

22.0.1. An Overview of Fatty Acid Metabolism

Fatty acid degradation and synthesis are relatively simple processes that are essentially the reverse of each other. The process of degradation converts an aliphatic compound into a set of activated acetyl units (acetyl CoA) that can be processed by the citric acid cycle (Figure 22.2). An activated fatty acid is oxidized to introduce a double bond; the double bond is hydrated to introduce an oxygen; the alcohol is oxidized to a ketone; and, finally, the four carbon fragment is cleaved by coenzyme A to yield acetyl CoA and a fatty acid chain two carbons shorter. If the fatty acid has an even number of carbon atoms and is saturated, the process is simply repeated until the fatty acid is completely converted into acetyl CoA units.

Fatty acid synthesis is essentially the reverse of this process. Because the result is a polymer, the process starts with monomers in this case with activated acyl group (most simply, an acetyl unit) and malonyl units (see Figure 22.2). The malonyl unit is condensed with the acetyl unit to form a four-carbon fragment. To produce the required hydrocarbon chain, the carbonyl must be reduced. The fragment is reduced, dehydrated, and reduced again, exactly the opposite of degradation, to bring the carbonyl group to the level of a methylene group with the formation of butyryl CoA. Another activated malonyl group condenses with the butyryl unit and the process is repeated until a C_{16} fatty acid is synthesized



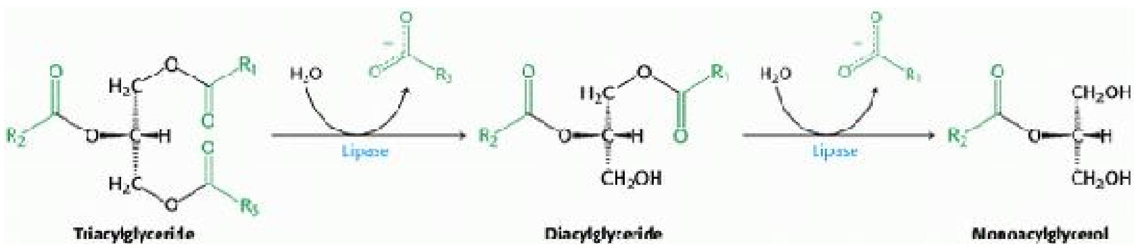
Dietary Lipids Are Digested by Pancreatic Lipases

Most lipids are ingested in the form of triacylglycerols but must be degraded to fatty acids for absorption across
the intestinal epithelium. Recall that lipids are not easily solubilized, yet they must be in order to be degraded.
Triacylglycerols in the intestinal lumen are incorporated into micelles formed with the aid of *bile salts* (Figure 22.3),
amphipathic molecules synthesized from cholesterol in the liver and secreted from the gall bladder. Incorporation of
lipids into micelles orients the ester bonds of the lipid toward the surface of the micelle, rendering the bonds more
susceptible to digestion by pancreatic lipases that are in aqueous solution. If the production of bile salts is inadequate
owing to liver disease, large amounts of fats (as much as 30 g day^{-1}) are excreted in the feces. This condition is referred
to as steatorrhea, from the Greek *steato*, "fat."
The lipases digest the triacylglycerols into free fatty acids and monoacylglycerol (Figure 22.4). These digestion products
are carried in micelles to the intestinal epithelium where they are absorbed across the plasma membrane.

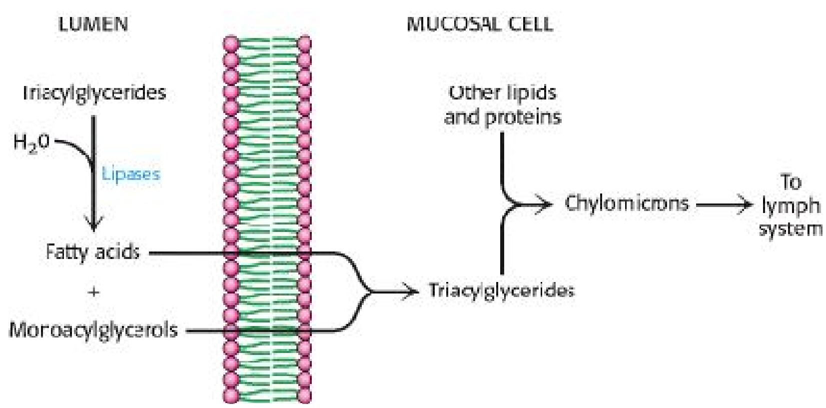
Dietary Lipids Are Transported in Chylomicrons

In the intestinal mucosal cells, the triacylglycerols are resynthesized from fatty acids and monoacylglycerols and then

packaged into lipoprotein transport particles called *chylomicrons*, stable particles ranging from approximately 180 to 500
nm in diameter (Figure 22.5). These particles are composed mainly of triacylglycerols, with apoprotein B-48 as the main
protein component. Protein constituents of lipoprotein particles are called *apolipoproteins*. Chylomicrons also function
in the transport of fat-soluble vitamins and cholesterol.
The chylomicrons are released into the lymph system and then into the blood. These particles bind to membrane-bound
lipoprotein lipases, primarily at adipose tissue and muscle, where the triacylglycerols are once again degraded into free fatty acids and monoacylglycerol for transport into the tissue. The triacylglycerols are then resynthesized inside the cell
and stored.



Action of Pancreatic Lipases. Lipases secreted by the pancreas convert triacylglycerols into fatty acids and monoacylglycerol for absorption into the intestine.



Free fatty acids and monoacylglycerols are absorbed by intestinal epithelialcells. Triacylglycerols are resynthesized and packaged with other lipids and apoprotein B-48 to form chylomicrons, which are then released into the lymph system.