Fig. 16.1. Basic physiologic processes in lipoprotein metabolism. The three major processes that affect [lipoprotein] and thus [TG] and [cholesterol] are (1) synthesis of chylomicrons in enterocytes and VLDL in hepatocytes, (2) LPL-catalyzed lipolysis on endothelial cell membranes, and (3) hepatocyte clearance of lipoprotein remnants. There are two major metabolic pathways for lipids, one for endogenous and one for exogenous lipids.

- Exogenous or dietary lipids: Ingested TG in the presence of bile acids and LPS undergoes lipolysis to form MG and FA. After absorption by enterocytes, MG and FA are reassembled into TG. Enterocytes also produce CE, phospholipids, and apolipoproteins A and B and then assemble the molecules into TG-rich lipoproteins called *chylomicrons*. The chylomicrons are secreted into lymphatic vessels and then enter blood via the thoracic duct. In blood, chylomicrons obtain C and E apolipoproteins from circulating HDL. In the presence of insulin, apolipoprotein C-II activates LPL (on endothelial cell membranes) that catalyzes the lipolysis of TG to generate FA. The FA enters adipocytes to be stored in TG or enters muscle fibers (or other cells) to undergo oxidation to generate energy. After removal of most TG molecules, the chylomicron remnants are cleared from plasma by hepatocytes in a process involving B apolipoproteins.

Fig. 16.1. *continued*

- Endogenous lipids produced by hepatocytes: Hepatocytes produce TG, phospholipids, apolipoproteins, and CE that may form from dietary cholesterol or de novo synthesis.
  - TG-rich VLDL is assembled in hepatocytes and secreted into sinusoidal blood. In the presence of insulin, apolipoproteins C-II on the VLDL activate LPL on endothelial cells to initiate lipolysis and liberation of FA from TG. As VLDL loses TG, it becomes denser to form IDL, which may also undergo additional lipolysis to form LDL. LDL delivers cholesterol to many cells for maintenance of cell membranes or steroid hormone synthesis. Hepatocyte clearance of LDL involves the action of hepatic lipase and the binding of a cholesterol-rich remnant to a B-apolipoprotein receptor on hepatocytes. LDL is also removed by macrophages in either receptor or non–receptor-mediated processes.
  - Discoid HDL particles consisting primarily of apolipoproteins and phospholipid are produced by hepatocytes and have two major functions: (1) they serve as a source of C and E apolipoproteins for other lipoproteins, and (2) they accept cholesterol from plasma membranes or lipoproteins and transport it for reutilization (in hepatocytes) or degradation (in hepatocytes or macrophages). Cholesterol is captured by the LCAT-catalyzed formation of cholesterol ester and lysolecithin from lecithin and cholesterol. This is supported by apolipoprotein A. As HDL accumulates cholesterol in circulation, they become larger and acquire their spherical form.
- The outer surfaces of lipoproteins contain phospholipids, nonesterified cholesterol, and apolipoproteins.

Shaded letters A, B, C, and E are A, B, C, and E apolipoproteins; AcCoA, acetyl-coenzyme A; ATP, adenosine 5′-triphosphate; CE, cholesterol ester; Chol, cholesterol; FA, fatty acid; LPL, lipoprotein lipase; LPS, pancreatic lipase; MG, monoglyceride; PL, phospholipid; and TG, triglyceride.