BLOOD LIPIDS

Blood lipids, which include cholesterol, phospholipids, and triglycerides, are derived from the diet or synthesized by the liver and intestine. Most cholesterol is found in body cells, where it is a component of cell membranes and performs other essential functions. In cells of the adrenal glands, ovaries, and testes, cholesterol is required for the synthesis of steroid hormones (eg, cortisol, estrogen, progesterone, and testosterone). In liver cells, cholesterol is used to form cholic acid. The cholic acid is then conjugated with other substances to form bile salts, which promote absorption and digestion of fats. In addition, a small amount is found in blood serum. Serum cholesterol is the portion of total body cholesterol involved in formation of atherosclerotic plaques. Unless a person has a genetic disorder of lipid metabolism, the amount of cholesterol in the blood is strongly related to dietary intake of saturated fat. Phospholipids are essential components of cell membranes, and triglycerides provide energy for cellular metabolism.

Blood lipids are transported in plasma by specific proteins called *lipoproteins*. Each lipoprotein contains cholesterol, phospholipid, and triglyceride bound to protein. The lipoproteins vary in density and amounts of lipid and protein. Density is determined mainly by the amount of protein, which is more dense than fat. Thus, density increases as the proportion of protein increases. The lipoproteins are differentiated according to these properties, which can be measured in the laboratory. For example, high-density lipoprotein (HDL) cholesterol contains larger amounts of protein and smaller amounts of lipid; low-density lipoprotein (LDL) cholesterol contains less protein and larger amounts of lipid. Other plasma lipoproteins are chylomicrons and very–low-density lipoproteins (VLDL). Additional characteristics of lipoproteins are described in Box 58–1.

The Third Report of The National Cholesterol Education Program Expert Panel on Detection, Evaluation and Treatment of High Blood Cholesterol in Adults classifies blood lipid levels as follows:

BOX 58–1 TYPES OF LIPOPROTEINS

Chylomicrons, the largest lipoprotein molecules, are synthesized in the wall of the small intestine. They carry recently ingested dietary cholesterol and triglycerides that have been absorbed from the gastrointestinal tract. Hyperchylomicronemia normally occurs after a fatty meal, reaches peak levels in 3 to 4 hours, and subsides within 12 to 14 hours. Chylomicrons carry triglycerides to fat and muscle cells, where the enzyme lipoprotein lipase breaks down the molecule and releases fatty acids to be used for energy or stored as fat. This process leaves a remnant containing cholesterol, which is then transported to the liver. Thus, chylomicrons transport triglycerides to peripheral tissues and cholesterol to the liver.

Low-density lipoprotein (LDL) cholesterol, sometimes called "bad cholesterol," transports approximately 75% of serum cholesterol and carries it to peripheral tissues and the liver. LDL cholesterol is removed from the circulation by receptor and nonreceptor mechanisms. The receptor mechanism involves the binding of LDL cholesterol to receptors on cell surface membranes. The bound LDL molecule is then engulfed into the cell, where it is broken down by enzymes and releases free cholesterol into the cytoplasm.

Most LDL cholesterol receptors are located in the liver. However, nonhepatic tissues (eg, adrenal glands, smooth muscle cells, endothelial cells, and lymphoid cells) also have receptors by which they obtain the cholesterol needed for building cell membranes and synthesizing hormones. These cells can regulate their cholesterol intake by adding or removing LDL receptors.

Approximately two thirds of the LDL cholesterol is removed from the bloodstream by the receptor-dependent mechanism. The number of LDL receptors on cell membranes determines the amount of LDL degradation (ie, the more receptors on cells, the more LDL is broken down). Conditions that decrease the number or function of receptors (eg, high dietary intake of cholesterol, saturated fat, or calories), increase blood levels of LDL.

The remaining one third is removed by mechanisms that do not involve receptors. Nonreceptor uptake occurs in various cells, especially when levels of circulating LDL cholesterol are high. For example, macrophage cells in arterial walls can attach LDL, thereby promoting accumulation of cholesterol and the development of atherosclerosis. The amount of LDL cholesterol removed by nonreceptor mechanisms is increased with inadequate numbers of receptors or excessive amounts of LDL cholesterol.

A high serum level of LDL cholesterol is atherogenic and a strong risk factor for coronary heart disease. The body normally attempts to compensate for high serum levels by inhibiting hepatic synthesis of cholesterol and cellular synthesis of new LDL receptors.

Very–low-density lipoprotein (VLDL) contains approximately 75% triglycerides and 25% cholesterol. It transports endogenous triglycerides (those synthesized in the liver and intestine, not those derived exogenously, from food) to fat and muscle cells. There, as with chylomicrons, lipoprotein lipase breaks down the molecule and releases fatty acids to be used for energy or stored as fat. The removal of triglycerides from VLDL leaves a cholesterol-rich remnant, which returns to the liver. Then the cholesterol is secreted into the intestine, mostly as bile acids, or it is used to form more VLDL and recirculated.

High-density lipoprotein (HDL) cholesterol, often referred to as "good cholesterol," is a small but very important lipoprotein. It is synthesized in the liver and intestine and some is derived from the enzymatic breakdown of chylomicrons and VLDL. It contains moderate amounts of cholesterol. However, this cholesterol is transported from blood vessel walls to the liver for catabolism and excretion. This reverse transport of cholesterol has protective effects against coronary heart disease.

The mechanisms by which HDL cholesterol exerts protective effects are unknown. Possible mechanisms include clearing cholesterol from atheromatous plaque; increasing excretion of cholesterol so less is available for reuse in the formation of LDL cholesterol; and inhibiting cellular uptake of LDL cholesterol. Regular exercise and moderate alcohol consumption are associated with increased levels of HDL cholesterol; obesity, diabetes mellitus, genetic factors, smoking, and some medications (eg, steroids and beta blockers) are associated with decreased levels. HDL cholesterol levels are not directly affected by diet.