FUNCTION OF APOLIPOPROTEIN E

Apolipoprotein E from human plasma is a glycoprotein composed of 299 amino acids of known sequence that is synthesized in the liver and in several peripheral tissues of the body. In plasma apo E is present on different lipoprotein particles. It is a constituent of plasma chylomicrons that carry exogenous lipids and of their catabolic products called remnants that are generated from chylomicrons by hydrolysis of core triglycerides through the action of lipoprotein lipase (LPL). Such remnants are not present in the plasma of healthy fasting humans since they are rapidly taken up by the liver through receptor mediated endocytosis (Fig. 1). The ligand on the surface of chylomicrons that is recognized by the remnant-receptor on liver cells is apo E.

A second class of lipoproteins that contains apo E are the very low density lipoproteins (VLDL) that are the transport vehicles for endogenous cholesterol and triglycerides and that are assembled in the liver. VLDL initially have the same fate in plasma as chylomicrons. Their core triglycerides are hydrolyzed by LPL resulting in intermediate density lipoproteins (IDL=VLDL-remnants; see Fig. 1). The further processing of VLDL-remnants is different from that of chylomicron-remnants. A fraction of IDL may be taken up directly by the liver. However at least in healthy humans most IDL-particles are converted to LDL. Both pathways seem to depend on the presence of functional apo E molecules on LDL but the precise role of apo E in these steps has not yet been defined with certainty. The factors that regulate the metabolic channeling of IDL are presently unknown but may include the activities of lipases as well as those of specific liver cell surface receptors. Liver cell plasma membranes exhibit two specific receptors that are able to bind IDL in vitro, the classical LDL-receptor that recognizes apo B-100 and apo E—both of which are constituents of IDL—and the apo E or remnant receptor. The relative contribution in vivo of both types of receptors for IDL uptake has yet to be defined.

Third apo E is present on a subpopulation of high density lipoproteins called HDL-I or HDL when induced by cholesterol feeding. This HDL fraction is believed to deliver cholesterol from extrahepatic tissues to the liver where it is taken up through the specific hepatic receptors. In summary apo E is involved in three important pathways of cholesterol e.g. 1. the uptake of dietary cholesterol by the liver, 2. the transport of endogenous cholesterol back to the liver and 3. in the transport of cholesterol from peripheral cells to the liver, a pathway called re-
Fig. 1. Receptor mediated transport of cholesterol in human plasma. For simplicity only those apoproteins that play a known role in the pathways indicated are shown.