LIPOPROTEINS AND LIPID TRANSPORT

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Abbreviations used in this paper:

VLDL, LDL and HDL are very low density, low density and high density lipoproteins; LCAT is lecithin-cholesterol acyl transferase; A-apoproteins refer to the two major apoproteins of HDL, B-apoprotein to the major apoprotein of LDL and C-apoproteins to the three proteins of low molecular weight that are shared between VLDL and HDL in humans and rats.

Lipids are transported in blood plasma in association with proteins. Some polar lipids are transported by albumin (free fatty acids, bile acids) or by specific binding proteins (retinol-binding protein). Nonpolar lipids are transported in large complexes containing polar lipids and specific apoproteins (which serve functions beyond that of "packaged"). These complexes comprise the macromolecular particles that we generally think of when we apply the term "lipoproteins" to blood plasma and other extra-cellular fluids. These lipoproteins and their role in transport of nonpolar lipids are the subject of this short and eclectic review.

A striking feature of the plasma lipoproteins is the lability of their concentration in a given species under differing physiological and pathological states and also among different animal species. Among mammals, these differences cannot be explained solely on
the basis of differences in the rate at which the nonpolar lipids are transported in the blood. Even within species, rates of transport vary among particles that differ from each other in rather subtle ways and evidence for species differences in the pathways of metabolism of a given lipoprotein class is also emerging.

This subject was reviewed very briefly at the last of these Symposia (1). Here I will develop the subject somewhat more extensively and will emphasize new developments during the past three years. Finally, aspects of human hyperlipoproteinemias that have been illuminated by these developments will be discussed.

LIPOPROTEIN STRUCTURE

Increasing evidence supports the "pseudomicellar" model for the structure of the major lipoprotein classes in normal human blood plasma. It envisions lipoproteins as spherical particles composed of a liquid core of nonpolar lipids (chiefly triglycerides and cholesteryl esters) covered by a monomolecular film of polar lipids (chiefly phospholipids and cholesterol) and apoproteins that differ among lipoprotein classes. Variation in size is related to the volume of the apolar core, whereas the surface has essentially a constant mean thickness on the order of 22 Å (i.e., that of a monolayer of a phospholipid-cholesterol mixture). Regions of the various apoproteins may penetrate the monolayer or interact with the polar groups of the lipids in the manner described elsewhere in this volume by Dr. Gotto. A spherical shape is indicated from electron microscopy, using both negative and positive staining methods (2, 3) and from viscometry (4). Evidence for the location of core and surface components includes the precise relationship between the chemical composition and the size of very low density lipoprotein particles having a narrow range of diameters (5). This relationship also predicts the diameter of human LDL to the 220 Å and that of HDL to be 120 Å. The value for LDL corresponds closely with the observed diameter by electron microscopy of 216 Å (2, 4), whereas the value for HDL (d 1.063-1.21) exceeds those obtained from electron microscopy of 100 Å for HDL₂ and 75 Å for HDL₃ (6). Low angle x-ray diffraction patterns of HDL (7-9) also support this model but the pattern of LDL is more complex and difficult to interpret (10, 11). The observation of temperature-dependent changes in the structure of LDL (12) may