PSU Researchers Probe Cholesterol

New knowledge about the way cholesterol gets its first foothold in the body—the root process of atherosclerosis—has, been developed by scientists at The Pennsylvania State University.

It demonstrates that a modest accumulation of cholesterol and other fatty substances is normal—and necessary.

"Our studies provide further evidence," says Dr. Stuart Patton, Evan Pugh Research Professor of Agriculture, "that lipids (fats) are essential to the cell's structure and functioning."

Excessive buildup of such substances, however, can lead to pathologies such as atherosclerosis. Accumulating in the blood vessel walls as "plaque", fatty materials can constrict those vessels, impede blood circulation and bring on heart attacks and strokes.

Patton's research pinpoints the primary site, the place where the lipids first take hold.

"It is the outer membrane of the cell, the so-called plasma membrane Our evidence indicates that two fatty substances, cholesterol and sphingomyelin, show particular persistence in this layer

"They lodge there and they

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stay there, becoming, in fact, a ' relatively permanent part of the structure of that layer and defining some of its properties."

One rather famous plasma membrane—protecting the fibrous portion of a nerve cell—is a case in point. It is called myelin and it forms

what is known as the myelin sheath. in this case the membrane's special function—to protect the "main line" of the nerve, along which signals are conveyed—is carried out only because lipid has accumulated to the point where it makes up 80 percent of the material in the membrane.

A b n o t m a lities in "myelination" are associated with multiple sclerosis and other diseases of the nervous system.

Retention of sphingomyelin in plasma membrane has been observed in research on the liver cell at the Oak Ridge Laboratory. The Patton group studied

mammary cells, which make milk

Studies of other cells have shown that a high level of the two lipids occurs in plasma membrane at any given time; the Patton study shows that they are retained. The phenomenon," says Dr.

Patton, "is apparently widespread, not confined to a single cell system."

Patton, who is the principal author of a paper presenting the results in NATURE NEW BIOLOGY, used freshly drawn milk because it is a unique and continuing source of mammary cell plasma membrane. In the milk secretion process small amounts of the mebrane continuously pass from the lactating cell into the milk.

By labelling (making radioactive) the phosphorous components of certain lipids in a live, lactating goat the researchers were able to trace the behavior of those lipids in the outer membrance.

While other lipids tend to 'turn over' and are reduced in quantity, sphingomyelin and cholesterol show a distinct tendency to stay in the membrane: they are incorporated as part of its sructure."

Patton, a specialist on scientific study of milk, has previously shown that there is a positive correlation between the concentration of sphingomyelin and cholesterol in membranes.

"Indeed, the formation of plasma membrane with its elevated levels of these lipids appears to result from membrane aging within the cell.

"These substances, especially cholesterol, are always building up in artery walls of adult humans; why this buildup accelerates in some people remains to be determined."

Studies on live monkeys at the University of Oregon Medical School provided the observation that plasma membrane accumulation appears to be a precursor of atherosclerosis.

"Combining these clinical findings with what we have found from the study of cell membranes," says Patton, "leads us to postulate that plasma membrane formation, accumulation, and infiltration with additional cholesterol are early steps in the progression that leads to atherosclerosis."

Aside from throwing new light on the origin of the most widespread of vascular diseases, Dr. Patton's findings might prove to have additional significance. It is becoming increasingly evident to the biological community that membranes, far from being merely passive films or layers of material, play a most active part in the production and selective flow of materials, information etc. in and between cells.

"Any new facts about their nature and behavior could have a significant influence on attempts to conquer various pathological conditions in which whole cells participate."

Co-authors of the paper with Dr. Patton are Dr.'s R.D. Mc-Carthy, P. E. Plantz, and R. F. Lee. The research was supported, in part, by the National Heart and Lung Institute, USPHS.

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