How food gets into cells

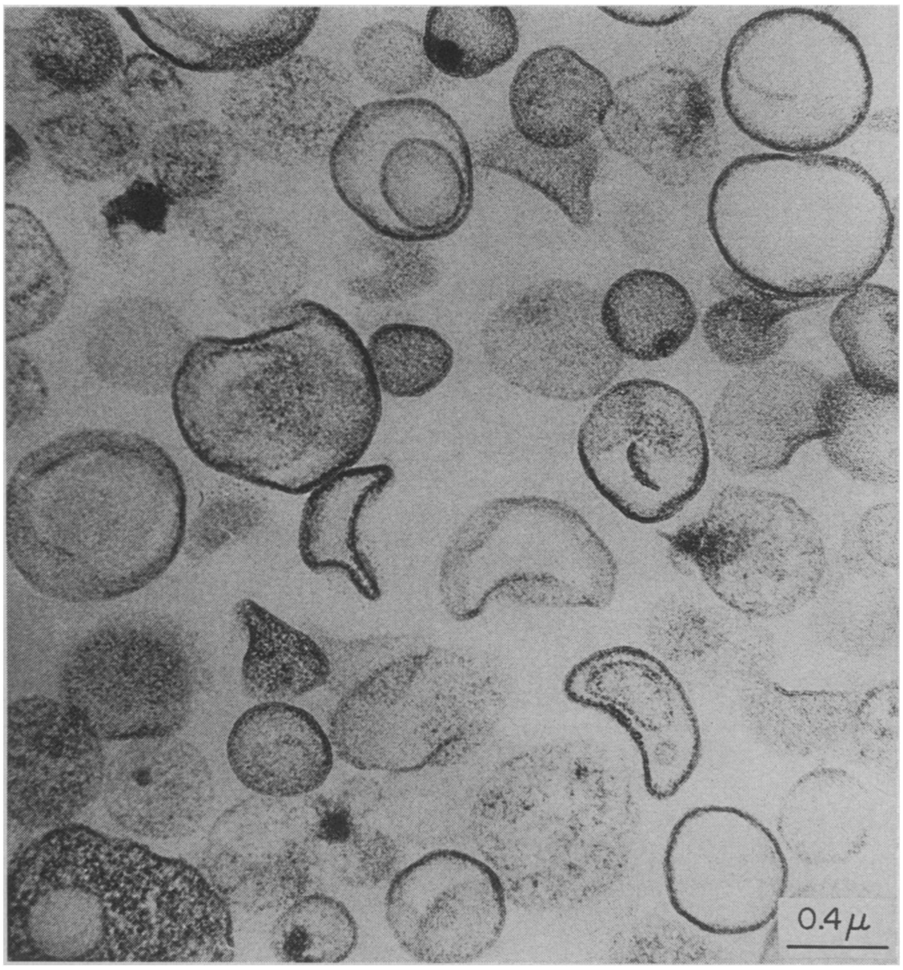
Biochemists have abundant evidence but still little understanding of how nutrients and trace elements get through the cell membrane

by Joan Arehart-Treichel

There are 180 billion cells in the human body. Each of these little factories is carrying out hundreds of chemical processes at a speed that astounds the mind. It is little wonder that as microscopic and biochemical techniques have become more refined in recent years, biologists have turned their attention to life's activities at the cellular level. A number of investigators are now trying to find out how different kinds of nutrients and trace elements get into a cell through its thin, pliable membrane. But even with the latest instruments, they are finding the membrane does not give up its secrets easily.

Ronald Kayback of the Roche Institute of Molecular Biology and a pioneer in the biochemistry of nutrient transport puts it this way: "Although evidence is accumulating, much of our work is still incomplete." Declares Frank Harold of the National Jewish Hospital in Denver and a researcher in trace element transport through the membrane: "The experimental evidence is plentiful, but we have little real understanding. It is my guess that we are where molecular geneticists were in 1950, before the breakthrough that gives you a basic principle. None of us is sure we are on the right track."

Regardless, some of the evidence and theories are worth examining. For, out of an expanding arsenal of facts and theories, a principle of cell transport of nutrients may emerge.



Ronald Kayback

Membrane vesicles 160,000 times larger than life under electron microscope.

Over the past 12 years Kayback and his team have devised a model system for studying nutrient transport through the membrane. The system is now being used by many researchers. They isolate membranes from thousands of bacterial cells, and these membranes appear as tiny closed bags, or vesicles. The membranes are then put in a vial and are exposed to nutrients and other chemicals to see how they behave. Kayback concedes that such "fun and games" need not correspond to what really happen when the vesicles in an intact membrane enclose a cell and pump nutrients into the cell. Yet these preparations will carry out many of the transport phenomena exhibited by a whole cell.

Using this system Kayback has shown that the energy required for the transport of different nutrients is highly specific, depending upon the particular type of nutrient accumulated. These results, and more, strongly indicate that Kayback's model is a valid representation of what takes place in the living cell.

One of their more interesting findings is that a chemical naturally found in the cytoplasm of one type of bacteria cell, D-lactate, causes the membrane vesicles to concentrate amino acids. It appears that D-lactate contributes electrons, which carry energy, along a chain of enzymes located in each membrane vesicle. As energy is passed from D-lactate to one enzyme, then another and another—like a football—it is finally dissipated until it is reduced to oxygen and water. Also a step in the energy-transfer sequence that lets the amino acids through the membrane has been pinned down. It appears then, at least in this particular kind of bacteria cell, that the D-lactate enzyme transfer of energy is an integral operation in a membrane vesicle. It is required to get nutrients through the vesicles into the cell.

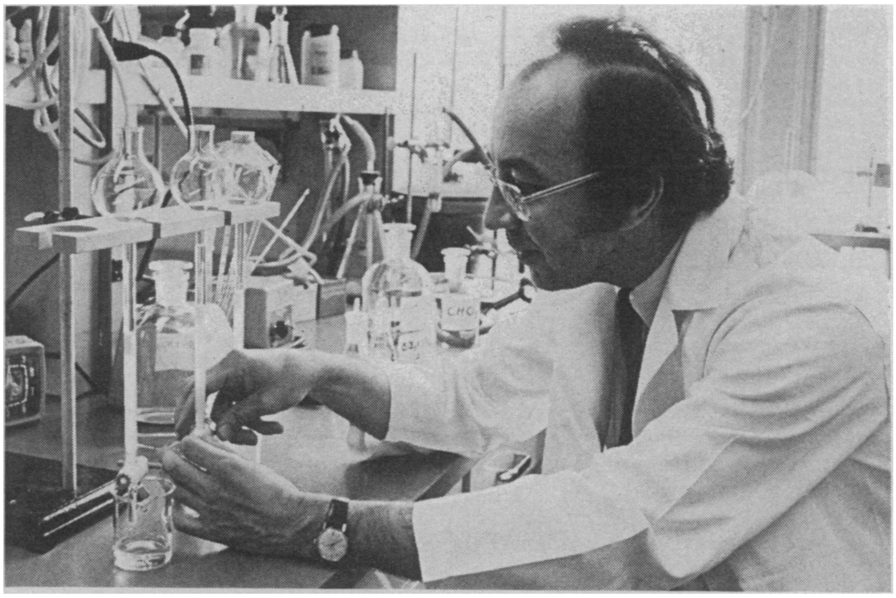
The Nutley, N.J., biochemist and his group have also isolated several proteins (probably enzymes) that bind selectively to certain amino acids that would normally enter a cell. So they speculate that the proteins may play some role in transporting amino acids through the membrane. Perhaps these proteins provide the crucial transport step noted in the D-lactate energy transfer system. It is possible, Kayback asserts, that the proteins are situated along the energy transport chain in a membrane vesicle and help pass energy. Thus, as a protein helps transfer an electron, it changes its own molecular configuration a bit, and this configurational change may allow a protein to carry an amino acid into the cell.

To prove his protein-carrier idea in the bacteria cell, Kayback must document electron transfer from enzyme to protein to enzyme. "You might call it solid-state biochemistry instead of solid-state physics," he says. "Little is known about biochemistry on this level."

Biochemist Joseph Holden of the City of Hope Medical Center in Duarte, Calif., another pioneer in nutrient transport, supports Kayback's idea that protein carriers in the cell membrane bring amino acids into a cell. But Holden believes that lipids in the cell membrane may also exert subtle effects on the carriers and on amino acid transport.

Holden and his colleagues made cells that were deficient in lipids. These cells transported the same kind of amino acids as the normal cell, but in lesser amounts. In other words, the lipid-deficient cells were leaky. The protein carriers, or pumps, were working, the amino acids were being pushed into the cell, but after they got to a certain level they began to leak out again. The investigators determined that some of the pumps were working at a normal rate, but others were working faster or slower than normal. "So in addition to affecting the whole business of leakage," Holden concludes, "lipids seem to influence how the protein carriers work."

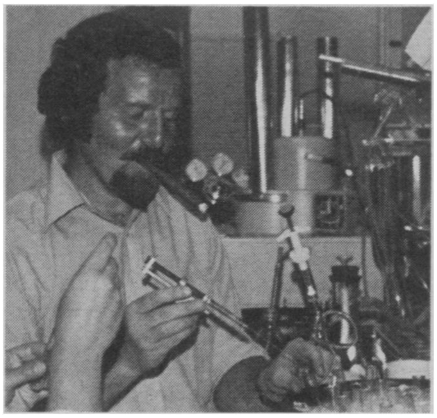
During the past seven years Saul Roseman, Werner Kundig and Robert Simoni of Johns Hopkins University have figured out and documented how certain sugars get into the bacteria cell. What happens, Roseman says, is that a molecule in the cell cytoplasm, phosphoenolpyruvate (PEP), gives up phosphate to a protein in the cytoplasm. This protein passes the phosphate to another protein in the cytoplasm. The phosphate is then tossed to a third protein located in either the cytoplasm or in the membrane. Finally the phosphate is received by a fourth protein definitely known to be located in the membrane. This membrane protein gives up the phosphate to a sugar situated on the outside of the membrane and waiting to enter the cell. The sugar is phosphorylated at the same time as it is moved by the membrane protein from the outside of the cell into the cell. This entry is believed to be due to the energy given off during the phosphate transfer to the sugar.


City of Hope Medical Center

Holden: Lipids in cell membrane may exert subtle effects on protein carriers.

The Baltimore biochemists have isolated all four of the proteins involved in this phosphate transfer system. The final two in the transfer chain are specific for different sugars—two proteins help usher a glucose molecule into the cell, two other proteins are needed to bring in fructose, and so forth. "One of the intriguing aspects of this sugar transport system," Roseman says, "is that the high-energy compound that triggers the reaction, PEP, has twice as much energy as the well-known high-energy compound adenosinetriphosphate (ATP), which performs many functions within the cell."

The passage of amino acids and sugars through the cell membrane is frontier research, but even less is known about the transfer of fats into the cell. "Lipids are particularly hard to study," Kayback says, "because they tend to stick to the lipids in the membrane." Evidence for the passage of trace elements through the membrane is perhaps even fuzzier than for lipids. But at a recent microbiology meeting in Philadelphia, C. E. Lankford, Kenneth Todar and J. H. Truez of the University of Texas reported that iron appears to enter the bacteria cell in two forms. It can be bound to another chemical or it can exist as ions (charged molecules with unpaired electrons). The Austin biologists have reason to think that either way, proteins in the membrane may help bring the iron into the cell.


Joan Arehart-Treichel

Kayback: A model system for study.

Scientists have scarcely tapped vitamin entry into a cell. But Holden foresees a strong interest in vitamin deficiencies at the cellular and cell membrane levels.

Nutrient passage through the cell membrane and its possible relationship to cancer is commanding some attention. Max Burger of Princeton University has shown that when a normal cell is treated for several seconds with a protein-degrading enzyme, the cell starts growing and acting like a tumor cell. Also the quantity and quality of the uptake of amino acids and sugar by the cell is changed. Burger has not yet tested the tumor-like cells for changes in trace element uptakes. It is too early to say what these findings mean to theories on nutrient passage through the membrane.

Most nutrient transport research has been conducted on bacteria cells, which have but one outer (plasma) membrane. Mammalian cells have membranes in their cytoplasm too, and they probably interact with the plasma membrane. The lipids that comprise the plasma membrane, for example, are known to be made through a complex series of steps in the mitochondrial membrane. Given such intricacies, bacterial and mammalian membranes will probably challenge biologists for some years to come. □