tin, a protein that contains a large quantity of iron and can thus be seen in electron micrographs, binds to the membrane of normal cells at certain areas that are indented and have fuzzy coats. Other investigators have suggested that these areas are the sites where formation of the internal vesicles is initiated. Although cells from patients with familial hypercholesteremia have the indented areas, they do not bind the ferritin-labeled LDL the way normal cells do.

The next step is the merger of the vesicles with the lysosomes (membranous sacs containing enzymes that break down a variety of biological molecules). The enzymes digest the protein components of LDL and split the cholesterol esters with the release of free cholesterol, which is the form used by cells to synthesize membranes. In addition, the liberated cholesterol has three important regulatory roles. It reduces cholesterol synthesis by suppressing the key regulatory enzyme; it activates another enzyme (cholesterol acyltransferase), which catalyzes the formation of new cholesterol esters for storage; and it suppresses the synthesis of the LDL receptor and thus prevents accumulation of too much cholesterol by the cell.

Support for the role of the lysosome in this scheme comes from experiments in which Brown and Goldstein showed that cells deficient in a lysosomal enzyme that splits cholesterol esters can accumulate LDL in the lysosomes but that the esters are hydrolyzed at a reduced rate. Thus, the release of free cholesterol is delayed, as are the regulatory events.

However, if these cells or the cells lacking the receptors are supplied with free cholesterol in a form that can penetrate the membrane, they will respond to the sterol in the normal manner. That is, the enzyme regulating cholesterol synthesis will be suppressed and the one reesterifying the sterol will be activated. According to Andrew Kandutsch of the Jackson Laboratory, certain oxygenated derivatives of cholesterol are even more effective than the parent compound in producing these responses in both normal cells and those from individuals with familial hypercholesteremia. This could point the way to more effective methods for lowering elevated blood cholesterol concentrations than are now available.

Brown and Goldstein think that the effects of LDL, acting through the receptor, could explain the low rate of cholesterol synthesis normally seen in many cell types in vivo. On the other hand, lack of functional receptors could contribute to elevated LDL concentrations in the blood in two ways. Peripheral cells would be unable to take up and metabolize LDL adequately. In addition, the enzyme regulating cholesterol synthesis would not be suppressed and the cells would continue to produce the sterol in spite of the high plasma concentrations.

Recent epidemiological studies also support the concept that high concentrations of LDL may contribute to the development of atherosclerosis and coronary artery disease. William Kannel, director of the Framingham study, a large prospective epidemiological study designed to identify the risk factors associated with heart disease, says that their data indicate that as the concentration of plasma LDL increases, the risk of having a heart attack also increases. On the other hand, persons with high concentrations of HDL have fewer heart attacks than persons with low concentrations, according to Kannel and William Castelli, also of Framingham. The effects of the two lipoproteins on the risk of coronary heart disease appear to be independent of one another. This result, and those from other investigations, imply that HDL may somehow protect against the development of atherosclerotic lesions.

These findings are consistent with the physiological roles postulated for LDL and HDL in cholesterol transport. Investigators* think that lipoproteins do not just function to solubilize lipids, but that the proteins on the surfaces of the particles carry information that specifies the

Coal Liquefaction Plant Goes Ahead

The Energy Research and Development Administration (ERDA) finally announced last month that it had signed contracts for construction of an experimental coal liquefaction plant at Catlettsburg, Kentucky. Negotiations over the contract had been protracted, and had nearly foundered over the issue of cost-sharing between ERDA and industry. The pilot plant is designed to treat 600 tons of high-sulfur eastern coal per day, converting it to a low-sulfur fuel oil by a catalytic hydrogenation technique known as the H-coal process (*Science*, 3 Sept., p. 873). The plant will be the largest coal conversion facility yet built in the United States.

The plant will be potentially large enough to permit scaling up directly to commercial size, about 10,000 tons per day, without an intermediate step. Construction is to begin 1 December, with operation scheduled to get under way in the autumn of 1978. Three major oil companies—Mobil, Conoco, and Standard of Indiana—are expected to participate in the industrial consortium that will fund a portion of the $180 million plant, in addition to the prime contractors, Hydrocarbon Research, Inc., which initially developed the H-coal process, and a subsidiary of Ashland Oil, which will manage the plant's construction and operation.

The contract is notable as evidence of a significant shift in government policy on risk-sharing for such experimental plants. ERDA will put up $142 million and industry $36 million for this major step toward development of the proprietary liquefaction process. In assuming such a large share of the cost, ERDA is departing from the two-thirds to one-third cost-sharing formula that has prevailed for several years. Apparently, ERDA convinced the Office of Management and Budget of what industry has been saying for some time, that the old formula was too rigid and that government should assume a greater portion of the risk. Observers familiar with the internal discussions say that the arguments for a more flexible approach prevailed some time ago, but this contract is the first tangible evidence of the new policy.

Martin Neuworth, of the ERDA synthetic fuel staff, points out that the H-coal contract is the first real test of industry-government cofunding of a coal conversion project on this scale, since the total industrial contribution to several previous synthetic fuel projects was $40 million spread over 4 years.

Equally encouraging to observers in industry are indications that ERDA will leave day-to-day management of the project largely up to Ashland, indicating, perhaps, that the agency has learned from earlier and largely unsuccessful attempts to manage the nuclear breeder program from Washington. A technical advisory committee representing ERDA and the other consortium partners will oversee major decisions.—ALLEN L. HAMMOND