to 78 μg/l.

That finding prompted a more extensive study of other foodstuffs and the discovery that some California wines contained far more arsenic than other foodstuffs did. For example, two bottles of a California pink Chablis, purchased in Milwaukee, contained 240 μg/l and 287 μg/l of arsenic respectively, while some California Burgundies, rosés, ports and vermouths contained lesser, but still high concentrations of arsenic.

According to the authors of the still unreleased report, present U.S. Public Health Service directives assert that the maximum allowed level for arsenic in drinking water is 50 μg/l and that a safe level is 10 μg/l.

Spokesmen for the California wine growers argued that arsenic levels in a few bottles of wine do not constitute enough evidence to damn the entire output of an industry. Nevertheless, based on the unreleased ACS meeting paper, the public health department of the state of California will begin immediately to measure arsenic levels in wine produced in the state. As for where all that arsenic may be coming from, agricultural chemists speculate that it is probably the residue of the arsenical pesticides that were used extensively in California grape fields until about two years ago.

Following the premature newspaper story of the data that was never presented formally, public information personnel at the ACS were bombarded with statements which gave a few clues as to why the paper was withdrawn. A dispatch from the lawyer of Vitek, Bors and Houser stated that "the sensationalism created from portions of the data being printed in the newspapers in advance of the agreed upon release date has detracted from the purely scientific nature of the paper."

From the West Allis Memorial Hospital public relations director, Bob Betts, came the explanation that "this material was being utilized without the knowledge or consent of the director of the hospital's laboratory, Dr. Harold J. Conlon."

To counter that statement, Vitek, Houser and Bors said they had a perfect right to use information from their own laboratory records and that they had followed normal procedure for obtaining authorization to use such data.

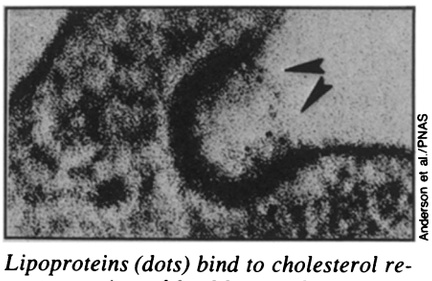
"However, due to a misunderstanding, some hospital officials were unaware this data was to be published and have sought to retract the permission previously granted," the authors' lawyer said, adding: "In withdrawing their paper from the ACS program, the authors voluntarily accede to this request, even though substantial portions of the paper are the result of the authors' independent research not involving the facilities of the hospital's laboratories." In the lawyer's statement, it was stressed that the authors' method for analyzing arsenic levels in foodstuffs and other substances (the chief reason the paper was scheduled) "is valid and that the data generated by their study are confirmed and substantiated and can be readily duplicated."

Further, he noted that their paper calls for further research into arsenic and foodstuffs "and is not intended to imply that all wines or fruit juices pose a substantial hazard or that scientific investigation was complete."

Controversy over the paper and its findings will undoubtedly continue, but it is distinctly possible that if the results had not appeared prematurely in the Wisconsin newspaper, where they provoked the flurry of statements, the paper would have appeared quietly on the ACS program with only a fraction of the attention it ultimately received.

At the same time, the ruckus it caused was primarily responsible for getting the California public health officials to start checking arsenic levels in the state's wine output. □

Localizing missing cholesterol receptors



Anderson et al./PNAS

Lipoproteins (dots) bind to cholesterol receptor region of healthy membranes.

There are several kinds of inherited diseases whereby persons make too much cholesterol and suffer heart attacks. One is familial hypercholesterolemia. One out of every million Americans is a homozygote (carries a gene from both parents) for the disease and usually suffers a heart attack by age 20. One out of every 500 Americans is a heterozygote (carries a gene from one parent) for the disease and usually suffers a heart attack around age 40. First genetic and biochemical evidence, and now electron microscopic evidence, are unmasking the genetic defect underlying the disease. It is a paucity of cell membrane receptors for cholesterol.

During the early 1970s, Joseph L. Goldstein and Michael S. Brown of the University of Texas Health Sciences Center in Dallas learned that cells called fibroblasts have receptors on them that bind with cholesterol-lipoprotein complexes in the blood. When the complexes bind to the receptors, an enzyme that regulates the rate of cholesterol synthesis reads that as a signal that no further cholesterol is needed. The cholesterol production is arrested until the complexes have dwindled enough in the blood to turn cholesterol synthesis back on.

Goldstein and Brown had reason to believe that there is nothing wrong with this enzyme in persons with familial hypercholesterolemia. Instead it seemed that the enzyme does not receive the proper cues for turning off cholesterol synthesis because cholesterol-lipoprotein complexes do not bind to fibroblasts. They tested their hypothesis by radioactively tagging lipoproteins and putting them in the presence of cells from healthy subjects, from heterozygotes and from homozygotes for familial hypercholesterolemia. The lipoproteins bound efficiently to the cells from the healthy subjects, but with only 40 percent efficiency to the cells from the heterozygotes and with only 3.6 percent efficiency to the cells of the homozygotes. Clearly then, the genetic defect underlying the disease consists of missing cholesterol receptors. Because heterozygotes have one faulty gene, they make some receptors, but an insufficient number. Because homozygotes have two faulty genes, they make virtually no receptors (SN: 7/13/74, p. 22).

Now Goldstein and Brown, with help of Richard G. W. Anderson, also at the University of Texas Health Sciences Center, have pinpointed those areas of the cell membrane where the cholesterol receptors are normally present but lacking in persons with familial cholesterolemia. They radioactively tagged lipoproteins and put them in the presence of healthy fibroblasts and of fibroblasts from a patient homozygous for familial hypercholesterolemia, then examined the materials under an electron microscope. The lipoproteins could be seen to bind preferentially to specific receptor sites on the cell surface membrane of healthy fibroblasts—specifically, at indented regions. Although the defective fibroblasts had the same number of indented membrane regions per millimeter of cell surface as did the normal cells, no lipoproteins could be seen bound to these regions.

"The present ultrastructural data," the investigators conclude in the July PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES, "are consistent with previous biochemical and genetic evidence indicating that the lipoprotein exerts its regulatory action on cellular cholesterol metabolism in fibroblasts through an interaction with a specific cell surface receptor and that this receptor is defective in homozygous familial hypercholesterolemia fibroblasts." Although they did not examine the cell membranes of heterozygotes, presumably they would show some lipoprotein binding, but not nearly as much as healthy cells.

This basic research has therapeutic implications, the researchers believe. As Goldstein told SCIENCE NEWS, "The most important, I think, is that as we get more molecular information, we will be able to apply rational therapy at that level rather than just lower serum cholesterol with drugs or diet." □