Biomedicine

Rick Weiss reports from New Orleans at the annual meeting of the Society for Neuroscience

Alzheimer's: A cancer-like mechanism?

For several years, Alzheimer's disease has been a much-discussed and somewhat controversial topic among neuroscientists. The progressively debilitating disease is now the fourth — and may soon be the third — leading cause of death in the United States, yet its underlying biology remains largely a mystery.

Because many of the symptoms of Alzheimer's disease resemble those of normal aging, much of the current research effort is aimed at finding biochemical "markers" that are unique to Alzheimer patients. Peter Davies, of the Albert Einstein College of Medicine in New York City, reported last year the first (and still the only) such marker — a protein found in the brain tissue of Alzheimer patients but absent in the normal elderly (SN: 11/22/86, p.327). Researchers still don't know what role the protein plays in the course of the disease, but more information should be forthcoming once its amino acid sequence is determined. That process may be completed in a matter of months, Davies says.

Meanwhile, Davies last week presented some surprising new evidence that the protein in question, called A68, is *not* entirely unique to Alzheimer patients, but is found in the normal developing fetus and infant. "It appears around 32 weeks of fetal life and disappears by age 2," Davies says. "This suggests that the protein normally has a function to assist in brain development."

One intriguing possibility, he says, is that the protein may be involved in the "programmed killing" of brain cells that is characteristic of early brain development. Scientists have long known that during the first years of life the brain makes more neurons than it needs, and that many of these neurons are systematically killed. Davies says A68 distribution in the immature brain is similar to the distribution of cells that are known to die during periods of programmed killing. However, he says, "We don't know if [A68 is] just a marker for cell death — showing us the cells that are about to die — or if it is something that actually contributes to cell death."

In any case, he says, the protein's reappearance in adults with Alzheimer's may represent an error in gene regulation similar to that seen in certain cancers. Cancer involves the repeated replication of adult cells as if they were still in their early developmental stages.

"Thinking of Alzheimer's disease as sharing some of the characteristics of cancer is truly a novel idea," Davies says. However, he adds, such a model is compatible with current scientific knowledge about Alzheimer's disease, including the apparent combination of both genetic influences and unidentified environmental factors that seem to play a role in triggering the disease.

Other explanations for Alzheimer's abound. The "autoimmune school," for example, has maintained a dedicated following, but the proposition that Alzheimer's is essentially an autoimmune disease continues to stir controversy. Although there is evidence that immune system cells and proteins may be present in the brains of some Alzheimer's patients, such evidence is difficult to interpret: Is the immune reaction the cause or the effect of Alzheimer's disease?

Whatever the answer, the research is stimulating some scientists to question the traditional assumption that the brain is immunologically "privileged," or anatomically isolated from the body's immune system. Alzheimer researchers are finding increasing evidence of immune components in the brain, including T cells, natural killer cells and human leukocyte antigens. They say this suggests that the blood-brain barrier may not be as impermeable as scientists have assumed, or that the central nervous system may even have its own independent immune arsenal.

Diane D. Edwards reports from Anaheim, Calif., at the 60th annual Scientific Sessions of the American Heart Association

Up and down on the lipoprotein seesaw

Too much fat pumping through your bloodstream is not a pretty thought. But the story of unhealthy lipids and their carriers in the blood isn't as straightforward as once believed. Although both lipoproteins carry cholesterol, many studies suggest that high-density lipoprotein (HDL) reduces the cholesterol buildup in blood vessel walls that leads to atherosclerosis, whereas low-density lipoprotein (LDL) contributes to fatty accumulation (SN: 11/30/85, p.343).

There are a number of factors that evidently can influence a person's HDL/LDL ratio. Researchers at the meeting discussed new findings on some of these factors, including alcohol consumption and prescription drugs.

Several studies in recent years had exposed a curious aspect of alcohol's relationship to heart disease: Having one or two alcoholic drinks a day appears to reduce the risk of coronary heart disease (SN: 6/1/85, p.345). In an attempt to explain this, a group of researchers at Harvard Medical School and Brigham and Women's Hospital in Boston looked at the interactions among heart attacks, alcohol and specific subgroups of HDL in 789 subjects. Of those, 366 had suffered their first heart attack; the remainder were matched controls who had not had an attack.

Heavy drinking — defined in this study as five or more drinks per day — is "unequivocally" bad in terms of heart disease, says Harvard's Charles H. Hennekens. However, light to moderate drinking — defined here as two beers or glasses of wine, or one liquor-based drink daily — was associated with a 46 percent lower risk of having a heart attack when compared to that of nondrinkers. The only explanation of the finding at this point, says Hennekens, is that alcohol apparently changes the levels of HDL. The group found that both major HDL components, HDL_2 and HDL_3, are elevated in those who drink conservatively.

Another study supports the observation that small amounts of alcohol help protect against heart disease by altering HDL concentrations. Using squirrel monkeys fed diets in which alcohol ranged from 0 to 36 percent of the total calories, researchers of the University of Lowell (Mass.) and the Zablocki Veterans Administration Center in Wood, Wis., found that a little goes a long way. The lowest LDL levels and highest proportion of HDL_2 occurred in animals fed diets of 12 percent alcohol, a dose consistent with that seen in nutritional surveys of nondrinkers, say the scientists. But a small increase to 18 percent, although it further raised HDL, also caused a significant elevation in the levels of LDL constituents linked to atherosclerosis.

Despite these findings, the scientists do not recommend that nondrinkers begin consuming alcohol, which can lead to its own set of health problems. A more logical approach, says Hennekens, would be to design drugs that duplicate alcohol's boosting effect on HDL components.

Researchers have been searching for ways to increase HDL levels in an effort to undermine lipid profiles that might lead to heart disease. For example, one of the latest in cholesterol-lowering drugs, called gemfibrozil, appears to reduce by 34 percent the incidence of coronary heart disease, according to a report in the Nov. 12 NEW ENGLAND JOURNAL OF MEDICINE. The Swedish study concludes that gemfibrozil increases HDL and decreases LDL levels.

Tinkering with HDL levels, however, may prove unwise; new results from a joint Soviet/U.S. study may reverse the general opinion that HDL is advantageous. Scientists at Columbia University in New York City and the Academy of Medical Sciences in Leningrad found that in nearly 8,000 Soviet men, higher levels of one type of HDL are associated with higher mortality from coronary heart disease.