# Plaque hemorrhage linked to stroke

Stroke, the third most frequent cause of death in the United States, can result from the buildup of fatty plaque, which narrows the arteries and induces blood to form clots that block blood flow to the brain.

In recent years, some physicians have also come to suspect that small hemorrhages in the plaque's own capillary networks may further increase the risk of stroke or prestroke symptoms. The results of a new study support this link and, at the same time, demonstrate the usefulness of computer tomography (CT) scanning for pinpointing the cause of blood flow blockage.

At the 12th International Joint Conference on Stroke and Cerebral Circulation held recently in Tampa, Fla., Antonio Culebras of the State University of New York at Syracuse described his use of CT scanning in identifying plaque features in the neck's carotid arteries, which may lead to stroke. CT scanning is used for imaging the brain, but Culebras and his co-workers were the first to develop the technique for arterial studies in the neck. They have found that a plaque hemorrhage shows up on a CT scan as a small dot called a "lucent defect."

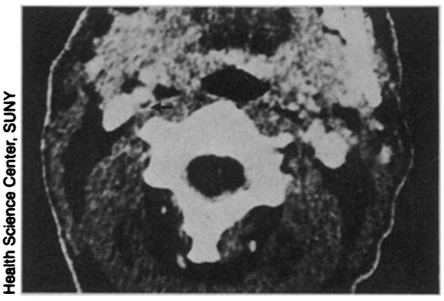
The researchers looked for lucent defects in the CT neck scans of 95 patients who, in the previous three months, had suffered a stroke or a transient ischemic attack (TIA), a temporary blockage of blood vessels that is often followed by a major stroke within days to months. For those patients who had plaque hemorrhages, Culebras's group found a high correlation between the side of the neck in which the plaque hemorrhage was discovered and the side of the body that experienced stroke or TIA. He says his group is now conducting a larger prospective study to further test the link between stroke and plaque hemorrhages.

Lucent defects were not correlated with every stroke or TIA case, but Culebras says that plaque hemorrhages make "a convincing contribution to the development of symptoms." He and others think that the hemorrhage causes the plaque to grow, which further narrows the artery and may cause the plaque to burst open into the vessel, producing stroke- or TIA-triggering clots.

Louis R. Caplan at Tufts University School of Medicine in Boston cautions that there have been other studies indicating that plaque hemorrhages do not play much of a part in strokes. He thinks that the importance of both CT neck scanning and an ultrasound technique being developed in Germany is that, unlike conventional methods, they show detailed cross sections of arteries: "They have real potential for letting people know what's happening with the arterial wall . . . and the more you know about [that], the more intelligently you can pick appropriate treatment," such as what kind of anticoagulant to administer.

He also notes the importance of imaging carotid arteries in particular, because his research has shown that strokes in some groups, particularly white males, are initiated predominantly in the neck.

Culebras says that CT scanning reveals all the stroke-related features of plaque seen by conventional imaging techniques, but it is the only "tool that can show us the microhemorrhage of the plaque." Moreover, he says that CT scanning is safer than the commonly used arteriography, in which X-rays are taken of vessels that have been injected with an X-ray opaque dye. "This allows us to follow up on those patients at short intervals — such as every four to six months — with very little risk to the patient," he notes. "By knowing how the plaque is behaving over time, it permits us to plan more reasonable treatment strategies." In particular, he hopes the identification of lucent defects will lead to better-informed decisions about whether or not to resort to carotid endarterectomy surgery—which he says currently is overused — to clean out carotid arteries (SN: 2/8/86, p.89). — *S. Weisburd*



Health Science Center, SUNY

*CT scanning of a carotid artery produces a cross section that shows much more detail — such as the plaque hemorrhage marked by the arrow — than do other imaging techniques.*

# Gene defect located for Gaucher's disease

Using recently developed methods for genetic analysis, scientists have located a rare gene defect that often leads to a potentially fatal enzyme deficiency in infants. Shoji Tsuji of the National Institute of Mental Health (NIMH) and his colleagues tracked the mutation to a site on chromosome 1.

The finding will improve genetic counseling for victims of the the most serious forms of Gaucher's disease, which is caused by the enzyme deficiency, report the researchers in the March 5 NEW ENGLAND JOURNAL OF MEDICINE.

The enzyme in question, glucocerebrosidase, breaks down a critical fat in certain body tissues. When the undegraded fat builds up, it can cause several types of Gaucher's disease. Type 1, the most common form, is characterized by an enlarged spleen and liver, and bone deterioration. The genetic mutation for type 1 is carried by one in 600 Jews of Eastern European ancestry. Type 2 kills infants by about 2½ years of age, often because motor and respiratory control is severely hindered. In type 3, nonfatal neurological symptoms, including epilepsy, dementia and difficulty in controlling eye movements, begin during adolescence. Most of the estimated 10,000 to 20,000 people in the United States with Gaucher's disease have relatively mild cases of type 1. About 2 percent have types 2 or 3.

All three types are known to result from mutations in the gene that codes for glucocerebrosidase. The investigators cloned the sequence of chemical subunits that determine protein production for a normal glucocerebrosidase gene and compared it with a sequence cloned from a patient with type 2 Gaucher's disease. An alteration at just one location was identified in the latter sequence. This chemical substitution leads to the synthesis of an abnormal enzyme that fails to break down the key fat in body tissues.

The genetic-code change was then checked in a larger sample using an enzyme that slices DNA at points signaling either the presence of a normal glucocerebrosidase gene sequence or the Gaucher's disease mutation. Four of 5 patients with type 2 disease and all 11 patients with type 3 disease had the mutation on at least one of two chromosome strands, or alleles, that were isolated from blood samples. One strand is inherited from the mother, the other from the father. Two of 5 patients with type 2 disease and 7 of 11 with type 3 had the mutation on both alleles. The mutation showed up on a single allele for 4 of 20 patients with type 1 disease. None of 29 healthy controls had the mutant allele.

"Clearly, this mutation is not responsible for all cases of type 2 and 3," says project director Edward I. Ginns of NIMH. "But we can now predict whether neurological problems are likely to occur later in life for children with symptoms of Gaucher's disease." There may be another mutation, he contends, that will distinguish between type 2 and type 3.

Work is under way on the development of gene therapy to treat Gaucher's disease. NIMH investigators, working with scientists at the Whitehead Institute in Boston, have transferred the normal gene into Gaucher's cells with a type 2 mutation and corrected the enzyme deficiency in tissue culture. The next step, says Ginns, is to transfer the normal human