Biomedicine

Joanne Silberner reports from Sarasota, Fla., at the American Heart Association's Science Writers Forum

To cut or not to cut

Contrary to the primary dictum of the Hippocratic oath, surgeons performing a particular type of surgery to prevent strokes may be doing more harm than good, according to Mark L. Dyken, a neurologist at Indiana University School of Medicine in Indianapolis.

Carotid endarterectomy, in which a clogged artery leading to the brain is surgically cleaned out, is "a clinical application looking for some good science," Dyken says. While it may prove worthwhile in the hands of experienced surgeons operating on carefully selected people experiencing strokelike symptoms, that has yet to be shown, he says.

Studies have found that 3 to 9 percent of people with signs of an impending stroke who are treated with drug therapy alone die of a stroke within a year. Using the National Hospital Discharge Survey, Dyken and Robert Pokras of the National Center for Health Statistics in Hyattsville, Md., found that nearly as many—2.8 percent—of the people who get carotid endarterectomies die *before* being discharged from the hospital. And other studies have reported that anywhere from one to five times as many more surgery patients suffer surgery-related stroke or death after discharge. Based on these and other data, Dyken and Pokras calculate there were 3,808 to 11,560 strokes or deaths resulting from the 103,000 procedures done in 1984.

For this, the hospital bill was $309 million; with doctors' fees the total is more like $500 million to $1 billion.

Recently extracranial-intracranial (EC/IC) bypass surgery, another procedure purported to protect against stroke, was shown in a carefully controlled prospective study to be of no value in reducing illness or death (SN: 11/16/85, p. 309).

Neurosurgeon James T. Robertson of the University of Tennessee in Memphis agrees with Dyken's figures, but says there has already been a heightened awareness among surgeons about the questionable value of the operation. Recently instituted training programs and more careful selection of patients have already resulted in fewer such operations being done and a lower complication rate, he says.

Both Dyken and Robertson agreed that a large multicenter evaluation similar to the EC/IC trial is needed to determine who may benefit from the operation.

And then there were many

Angiogenesis—the growth of new blood vessels—is a necessary part of fetal development, but in the adult it causes problems. New vessels interfere with the functioning of arthritic joints, allow the growth of tumors and interfere with retinal function in the eyes of many diabetics.

Clifford A. Barger of Harvard University has found that angiogenesis also occurs within the walls of thickened atherosclerotic arteries, and has proposed that leakage from these new vessels may spark heart attacks (SN: 3/16/85, p. 170).

Scientists have long sought the biological trigger of angiogenesis. Recently, two competing Harvard University laboratories found apparently different angiogenic proteins (SN: 10/5/85, p. 213), and now another Harvard group, led by Bruce R. Zetter, has found yet another molecule that initiates angiogenesis in fat deposits on the surface of the heart.

If the discovery is confirmed, Zetter says, it will provide another correlation between fat and heart disease, and explain how some currently used drugs fight heart disease.

Zetter and his colleagues failed to find an angiogenic factor in the vessel walls of atherosclerotic arteries. But they did find it in the fat in which the coronary arteries are embedded. The activity of the as-yet-uncharacterized factor is blocked by a prostaglandin inhibitor, suggesting that prostaglandin inhibitors may work by preventing new blood vessel formation in coronary artery walls.

Biotechnology

Julie Ann Miller reports from Baltimore at the Annual Congress for Recombinant DNA Research

Interferon helps cells help themselves

The natural chemical interferon has engendered high expectations for therapeutic applications, including protection against the common cold (SN: 1/11/86, p. 20), but little is known about how it acts. Charles Weissmann at the University of Zurich in Switzerland and his colleagues are examining the means by which interferon, naturally produced in response to a viral infection, makes cells resistant to further attack.

Interferon triggers production of at least 10 cellular proteins, only some of which have been identified so far, Weissmann reports. But when interferon protects mouse cells against the influenza virus, only one protein is required. "This is the first identification of a single protein [that confers] resistance to a specific virus," Weissmann says.

Some mouse strains are sensitive to influenza virus, while others are naturally resistant. But even the resistant mice are killed by influenza virus after they are treated with antibody against interferon. The scientists have identified the gene that is turned on by interferon and that differs in the influenza-resistant and -susceptible mice. In the susceptible animals the gene, called Mx, makes a truncated version of its normal product. With recombinant DNA techniques, the scientists have transferred many copies of a normal Mx gene into cells of susceptible animals. These cells then resist influenza, but not other viral infections. In fact, the cells do not even need interferon to induce the resistance. Weissmann suggests Mx function may reflect a peculiarity of influenza virus infection, its stealing of a piece of host messenger RNA. "My guess is that this [single protein resistance] is not often the case," he says.

Attack on cancer cells

Interferon is being tested as an agent to fight cancers (SN: 7/27/85, p. 58) as well as viruses. Results reported by Gilbert Jay and his colleagues at the National Cancer Institute in Bethesda, Md., indicate how this natural chemical may help fight malignancies and suggest new means of bolstering the immune system's attack.

Jay has been investigating the cancer-related role of the "classical transplantation antigens," those cell-surface proteins responsible for rejection of transplanted organs. He suggests cancer cells may evade the host immune system by omitting one group of these proteins, called class I antigens, from cell surfaces. Interferon's role, then, in fighting cancer may be to stimulate cancer cells to reveal their class I antigens, thereby making them better targets for immune attack.

Jay used recombinant DNA techniques to insert extra copies of the gene for a class I antigen into malignant (transformed) cells that do not normally show high levels of the surface proteins. The cells were no longer able to cause tumors. Treatment with interferon can also make malignant cells produce class I antigens. In animal experiments, the scientists injected malignant cells that normally cause tumors, then injected interferon. Jay says, "There was complete protection against this tumor."

Another approach to the problem is to enhance the immune system's sensitivity to the scarce class I antigens that may be present on malignant cells. "The low level may be sufficient if the animal's immune system is angry enough," Jay says. He immunized animals with a dose of malignant cells treated with interferon (or given extra genes of a class I antigen). He also injected the animals with malignant cells of the same type but which had not undergone antigen-producing treatment. Instead of developing fast-growing tumors, the animals remained healthy. The immunization was successfully given a week before, on the same day or two days after injection of the malignant cells. Jay speculates that it may be possible to immunize patients against their own tumor cells.