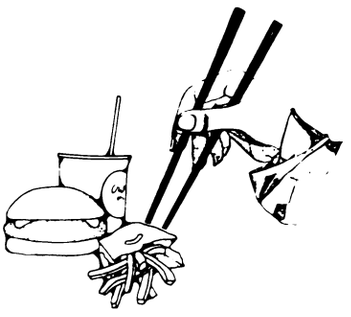
# Japanese Stroke Clues

## Are there risks to low cholesterol?



By KATHY A. FACKELMANN

In Tokyo, you may find an American hamburger more easily than the traditional Japanese repast of fish and rice. Even in rural areas, the Japanese have replaced low-fat foods with red meat, dairy products and eggs. Their fatty diet has led to higher blood levels of cholesterol, a key risk factor for heart attacks and for strokes caused by blood clots.

New research, however, suggests an ironic twist on that trend. A long-term Japanese study, corroborated by U.S. reports, now indicates that people with extremely *low* blood cholesterol levels may be at increased risk of an even more lethal type of stroke — cerebral hemorrhage, caused when a brain artery bursts.

The Japanese study, described in the March CIRCULATION, supports a long-standing contention by Japanese researchers that a Western-type diet protects against cerebral hemorrhage. For years, U.S. scientists have disputed Japanese claims about this cholesterol benefit. But the recent studies have spurred U.S. scientists to take a closer look at the link between low cholesterol and hemorrhagic stroke, which strikes an estimated 50,000 Americans each year, killing about half its victims.

Takashi Shimamoto of the University of Tsukuba and colleagues conducted a 20-year disease-surveillance and population survey of Ikawa Town, a farming community 250 miles north of Tokyo. During the study period, from 1963 to 1983, the vestiges of a traditional rural lifestyle were replaced by a more urban existence. Rice farmers mechanized their operations, home refrigerators became more common, and cholesterol levels rose as the spartan Japanese diet gave way to meals laden with animal fat.

The two-decade span witnessed a dramatic decline in all types of stroke, including cerebral hemorrhage. For Ikawa Town men aged 40 to 69, the incidence of all stroke declined 61 percent. For women in the same age range, the incidence dropped 60 percent. Cerebral hemorrhage cases fell 65 percent for males and 94 percent for females, the researchers report.

Lowered blood pressure among Ikawa Town residents accounts for much of the decline in stroke incidence, the researchers say. They attribute the blood pressure decline to intensified treatment programs for hypertension and to dietary changes such as lower salt intake, a trend made possible when families began preserving their food through refrigeration rather than salting. Hypertension adds to the risk of stroke by straining blood vessels, increasing the likelihood of clot formation or cerebral hemorrhage.

But hypertension may not act alone in boosting a person's risk of cerebral hemorrhage, the study suggests. The Japanese team looked at 2,257 Ikawa Town residents from 1963 to 1973 and discovered an inverse relationship between cholesterol levels and risk of cerebral hemorrhage. They found more cerebral hemorrhage cases among the men and women who had the lowest cholesterol levels — those with cholesterol levels below the mean of 178 milligrams per deciliter (mg/dl) for men and 190 mg/dl for women. A second study of 2,711 residents followed from 1972 to 1983 showed no relationship between low cholesterol and stroke, a finding the researchers ascribe to the low incidence of stroke during that time.

Shimamoto's group suggests a mechanism to explain how low blood cholesterol increases the risk of cerebral hemorrhage. Because cholesterol plays a vital role in maintaining cell membranes, they say, a lack of cholesterol could lead to weak artery walls prone to rupture, especially when under high pressure.

Supportive evidence in the Western world comes from a six-year U.S. study of 350,977 black and white middle-aged men enrolled in the Multiple Risk Factor Intervention Trial (MRFIT).

Researchers reported the first MRFIT findings in 1982. In a new analysis of MRFIT data reported in the April 6 NEW ENGLAND JOURNAL OF MEDICINE, scientists found a sixfold greater threat of death from cerebral hemorrhage in middle-aged American men with total serum cholesterol levels lower than 160 mg/dl and elevated blood pressure above 90 mm mercury diastolic. The inverse relationship between cholesterol and hemorrhage disappeared for people with normal blood pressure and for those with cholesterol levels above 160 mg/dl. The study was led by Hiroyasu Iso of The Center for Adult Disease in Osaka, Japan, working at the University of Minnesota in Minneapolis with David R. Jacobs Jr. and colleagues. Iso was also a coauthor of the Ikawa Town study.

Data from the Honolulu Heart Program fortify the link between low cholesterol and cerebral hemorrhage, says program director Dwayne M. Reed of the National Heart, Lung, and Blood Institute. Starting in 1965, Reed and his colleagues studied 7,850 American men of Japanese descent for 19 years. The yet-unpublished results, he says, show that men with cholesterol levels below 190 mg/dl had more than twice the risk of cerebral hemorrhage compared with men with cholesterol levels above 190 mg/dl. Men with cholesterol levels below 150 mg/dl had four times the risk of this type of stroke compared with men with cholesterol levels above 190 mg/dl, Reed reports.

In an editorial accompanying the Ikawa Town report, Jacobs and Minnesota colleague Henry Blackburn say the adage about moderation may well apply to cholesterol: Too much can clog arteries and lead to heart attacks and strokes caused by blood clots, but too little seems associated with an increased risk of strokes caused by hemorrhage.

Blackburn told SCIENCE NEWS he thinks the Japanese will see an "epidemic" of heart disease if their cholesterol levels keep rising. Shimamoto's group found no jump in heart disease cases during the 20-year study, but the average Japanese man currently has cholesterol values of about 180 mg/dl. In comparison, more than 60 percent of adults in the United States have cholesterol levels exceeding that figure, Blackburn notes.

Scientists have a long way to go to unravel the complicated relationship between cholesterol and hemorrhagic stroke. "We have a couple of studies where an association has been demonstrated," says Jeremiah Stamler of the Northwestern University Medical School in Chicago. "The problem is: What does it mean?" He notes that very sick patients, including cancer patients, often have low cholesterol levels; the fact that cerebral hemorrhage patients have lower-than-average cholesterol values may not be

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*takes as it drains. The local conditions and forces acting on the draining water swamp the extremely small influence from the Coriolis effect. The consequences of the Coriolis effect are far more obvious in larger systems such as cyclones, which rotate counterclockwise in the Northern Hemisphere and clockwise in the Southern Hemisphere. The smallness of the Coriolis effect's influence on draining water, however, does not logically preclude its involvement there or in processes like crystallization. Since no explanation is yet available for the curling crystal phenomenon observed by Fuchs and his colleagues, no one can rule out a possible role for the Coriolis effect.* —I. Amato

### Out of sight and mind

"Environmental costs of keeping baby dry" (SN: 3/4/89, p.141) clearly illustrates the critical problem of solid waste disposal. However, one of the researcher's suggested alternatives — "flushable disposables" — would only relocate the problem.

The general misconception that sewage collection systems provide a simple disposal solution for anything flushable has been allowed to continue for too long. As any municipality operating a sewage treatment facility knows all too well, the introduction of such materials ultimately leads to expensive cleaning and repair of equipment as well as significantly increasing the sewage sludge that must be disposed — often in a landfill.

Flushable disposables would be even less desirable where conventional septic systems are in use.

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significant. Other researchers suggest low cholesterol is a marker for a protein or some element in the diet that may cause cerebral hemorrhage.

Because scientists have yet to demonstrate that low cholesterol actually *causes* hemorrhagic stroke, public health messages to Americans are unlikely to change. Adults in the United States have an average blood cholesterol level of 210 mg/dl, and it seems a reasonable goal to reduce that by 20 mg/dl, Blackburn says.

A National Research Council committee agrees. Its March report on diet and health urges Americans to reduce their dietary fat and cholesterol. Having reviewed the data on hemorrhagic stroke, the committee concludes that any risk seems confined to people with a combination of very low cholesterol levels and high blood pressure.

If researchers were indeed to establish a causative link between low cholesterol and cerebral hemorrhage, the next step would be to identify and treat these high-risk individuals, the panel says. For the rest of the U.S. population, it would still be a good idea to work toward reducing cholesterol levels. The result would be a reduction in heart-disease deaths — a benefit that far outweighs any possible risk of low cholesterol, the committee adds. □