

## Is rheumatic fever making a comeback?

A stealthy form of strep throat that doesn't cause symptoms may underlie a recent increase in the number of rheumatic fever cases seen at a Utah hospital. Primary Children's Hospital in Salt Lake City recorded 62 cases so far in 1998, a larger number than in any of the previous 38 full years. This tally kindles fears that a disease once on the decline may be reawakening.

Rheumatic fever, which can cause serious heart damage, evolves from an untreated *Streptococcus A* infection—strep throat. The sore throat is contagious but curable with penicillin. With antibiotic treatment of strep throats, deaths from rheumatic fever heart complications have fallen from about 15,000 in 1950 to 5,147 in 1995 nationwide. Many recent fatalities among the elderly stem from childhood rheumatic fever.

When scientists reviewed 478 cases of rheumatic fever treated between 1985 and 1998 at the Salt Lake City hospital, they found that only 20 percent of the patients had sought medical attention for throat problems before coming down with rheumatic fever symptoms. Nevertheless, more than 90 percent of these patients had manufactured antibodies against strep, says Lloyd Y. Tani, a pediatric cardiologist at the hospital, who presented the findings.

The deadliest complication of rheumatic fever is heart inflammation and is probably an autoimmune response. Doctors treat mild cases of heart inflammation with an anti-inflammatory drug, such as aspirin, and bed rest. In severe cases, they prescribe steroids. In this study, of the 297 patients whose rheumatic fever led to inflammation of the heart, 12 required surgery to repair damaged valves.

The best weapon against rheumatic fever is prevention, Tani says. If doctors see any signs of rheumatic fever in the community, they should start monitoring sore throats more carefully.

From a historical perspective, the new cases of rheumatic fever present a mystery, he says. Early in this century, health officials believed that crowded living conditions and poverty led to the spread of the strep bacteria. Most of the patients in the recent study, however, weren't considered poor. —N.S.

## Gene therapy advances go to the heart

By changing the genetic instructions issued within the cells that make up blood vessels in and around the heart, researchers are finding ways to replenish blood flow to damaged heart muscle. Such gene therapy also shows promise in vein grafts around a blocked vessel in the leg, an operation similar to heart bypass surgery.

These studies, though small, offer intriguing signs that such genetic manipulation may someday be an alternative to some heart surgery, researchers say.

Investigators have found it difficult to get new blood vessels to grow in areas of the heart damaged by clots that stop blood flow. Doctors usually use balloon angioplasty to open up a heart artery and a device called a stent to prop it open. Or surgeons take a vein from another part of the body and graft it onto the heart to bypass a blockage. Many patients' hearts, however, fail again when these new or repaired vessels accumulate plaque—the same kind of clogging that caused the original damage.

Using gene therapy, Jeffrey M. Isner and his colleagues at St. Elizabeth's Medical Center in Boston have treated 16 heart-disease patients who averaged two bypass operations apiece; 11 had also had one to three angioplasties. "These are patients that even cardiovascular surgeons don't like to see . . . patients that come in for a second or third bypass operation—where the operation carries a higher risk," Isner says.

All the patients received DNA injections into heart muscle receiving inadequate blood supply. The DNA is a fragment of *VEGF* (*vascular endothelial growth factor*), a gene that directs blood vessel growth. Among 11 patients who have been followed for more than 90 days, Isner reports, 6 patients are entirely free of

angina, a tightness in the chest that indicates restricted blood flow. Among these 11 patients, use of nitroglycerin to relieve angina has fallen from an average of 60 pills a week to 2.5.

Gene therapy is also showing some ability to limit plaque formation in grafted blood vessels in the leg. About half of all bypass grafts clog up again. At Brigham and Women's Hospital in Boston, Michael J. Mann and his colleagues bathed replacement vessels in a solution of DNA segments that suppress the growth of new cells along the inner lining of blood vessels. This gene therapy, done before surgery, improved success rates and added only 10 minutes to the procedure.

Mann reports that of 17 bypass patients treated with gene therapy, only 5 had an obstruction in the new leg vessel 7 months later. Of 16 others whose grafts weren't so treated, 10 had obstructions.

The treatment genes persist only a week or 2, but they seem to spur continuing damage control in the vessel. "A genetic switch is turned on right after surgery that [often] leads to disease," he says. "We are changing that switch." —N.S.

## Estrogen helps some more than others

The so-called bad cholesterol, LDL, can come in two sizes—big, buoyant particles and small, dense ones. The latter lodge in blood vessel walls more easily.

Researchers now find that women who have the smaller form of LDL are at higher risk of heart disease but are also more likely to see cholesterol reduction from hormone-replacement therapy. Genetics determines which type of LDL predominates, says H. Robert Superko, a cardiologist at Berkeley HeartLab in San Mateo, Calif., and the Lawrence Berkeley (Calif.) National Laboratory.

In a study of 44 postmenopausal women, average age 58, Superko and his colleagues gave half of the women estrogen and half an inactive substance; after 4 months, each received the other substance for 4 months more. Estrogen cut LDL cholesterol by 15 percent among the women with the smaller form, compared with 4.6 percent for women with the larger form.

While only 8 to 10 percent of premenopausal women in the general population have the smaller form, known as pattern B LDL cholesterol, that percentage jumps to 30 to 40 percent after menopause. "Something happens during menopause where this inherited trait starts expressing itself," he says.

Estrogen is often prescribed to reduce osteoporosis risk, hot flashes, and other menopausal symptoms. Researchers have established that it also can protect against heart disease, although the mechanism by which it does so is not clearly known. The hormone may suppress the gene that influences LDL patterns and place some women at risk, Superko speculates.

This study calls into question the use of estrogen replacement strictly as a cardiovascular aid to lower LDL cholesterol in women with the larger form of LDL, or pattern A, he says.

A commercially available test to determine whether a person's LDL is pattern A or B costs about \$160. Roughly 7,000 doctors routinely send blood samples to Berkeley HeartLab for this analysis, Superko says. —N.S.

## Most smokers light up after heart surgery

Most cigarette smokers who undergo heart surgery return to the habit that may have helped land them in the operating room, new research shows.

Of 463 smokers tracked after balloon angioplasty to open a clogged coronary artery or following a bypass operation to restore blood flow to heart muscle, 58 percent admitted to having resumed smoking in the first 5 years. During this period, researchers telephoned the patients once a year, says Bonnie H. Weiner of the University of Massachusetts Medical School in Worcester. Patients who are black or less than 60 years old are more likely than the others to resume smoking, she says. —N.S.