

heart problems. To Fishman's delight, however, the zebra fish have shown that mutations in a single gene can provoke quite specific heart problems. One mutation, for example, causes a heart to form without any valves. Another makes blood vessels loop the wrong way. Yet another makes the heart beat slowly. With that information in hand, "it's conceivable that one could make parts of hearts again" and regenerate damaged tissue, he says.

Important genetic clues are also coming from such unexpected places as the quaint Italian village of Limone sul Garda. Many villagers, descendants of an 18th century resident named Giovanni Pomaroli, have eternally young hearts. Although they smoke and drink, have high cholesterol levels, and gobble fats and salt with abandon, Pomaroli's descendants have virtually no heart disease and often live well into their 90s.

The reason seems to be a genetic mutation researchers have dubbed "Apo-A-1 Milano." It produces some kind of protective protein akin to high-density lipoproteins (HDLs), the so-called good cholesterol associated with a reduced risk of heart disease. Elide Fava, 36, has the Milano gene, and so do her two children. She lets them eat all the

rhythm called tachycardia. By combing Mormon genealogical records, Keating has uncovered three mutant genes related to proper functioning of the heart's electrical circuitry. Simple measures, such as prescribing potassium supplements and the heart drugs called beta blockers, are believed to disarm these genetic time bombs. The treatment is already being given to people with the mutations.

## GENE THERAPY

About 300,000 patients each year undergo bypass surgery to try to restore good blood flow to their hearts. Now comes a revolutionary development: At New York Hospital/Cornell Medical Center, gene-therapy pioneer Ronald G. Crystal, surgeon Todd K. Rosengart, and others are working with genes and human proteins that spark "angiogenesis"—the growth of new blood vessels. The idea is to prompt the growth of new arteries when existing coronary arteries are failing. Crystal calls it "biobypass."

In studies with pigs, Crystal has used genetically engineered viruses to transfer a gene called VEG-F to the heart. It made new vessels grow and restored blood flow in pigs whose coronary arteries were clamped shut. He

hopes to begin human trials within a year.

Biotech pioneer Genentech is experimenting with a gene-spliced form of VEG-F that could be given as a drug.

A related phenomenon has emerged unexpectedly from a surgical technique doctors began performing several years ago to route more blood into oxygen-starved areas of the heart. Using lasers,

doctors drilled about two dozen tiny holes in the heart to create physical channels to bring more blood in. The researchers have since learned that the physical disruption of the heart tissue by the lasers stimulated angiogenesis. Cardiogenesis Corp., a maker of cardiac lasers, is joining biotech company Chiron Corp. to explore how the laser technique could

## HEART-CARE MARKETS

BILLIONS

CARDIOVASCULAR DRUGS	\$14.0
IMPLANTABLE DEVICES AND SURGICAL SUPPLIES	9.0
GENERIC HEART DRUGS	1.2
CARDIAC IMAGING AND DIAGNOSTIC EQUIPMENT	.75
HEART VALVES AND IMPLANTS	.3

SOURCE: FROST & SULLIVAN, AMERICAN HEART ASSOCIATION

be paired with biobypass, with the hope of obviating some surgical bypass.

## ARTIFICIAL HEARTS

Early efforts to create artificial hearts, going as far back as 1969, were resounding failures—patients felt miserable, they suffered repeated strokes, and many had trouble even getting out of bed. But the picture has changed. "This technology has made a lot of strides and will make even more in the next decade," says pioneer surgeon Frazier of the Texas Heart Institute in Houston. By 2000, Frazier hopes to implant a total replacement heart made by ABIOMED Inc. in Danvers, Mass. It's a long way from the primitive Jarvik-7 heart that dentist Barney Clark received at the University of Utah in 1982. ABIOMED's device is one of several designs that will be fully implantable, with no wires or tubes protruding from the skin. The Jarvik-7, in contrast, was tethered to a device the size of a washing machine.

Another innovative design is a smaller assist pump called the Streamliner under development by Bartley Griffith, a cardiologist at the University of Pittsburgh. The Streamliner, about the size of a D-cell battery, whirls like a tiny turbine, pumping blood not in heartbeats but in a continuous flow: patients who get it will have no pulse.

"The perception is that the artificial heart failed and is dead," says David M. Lederman,

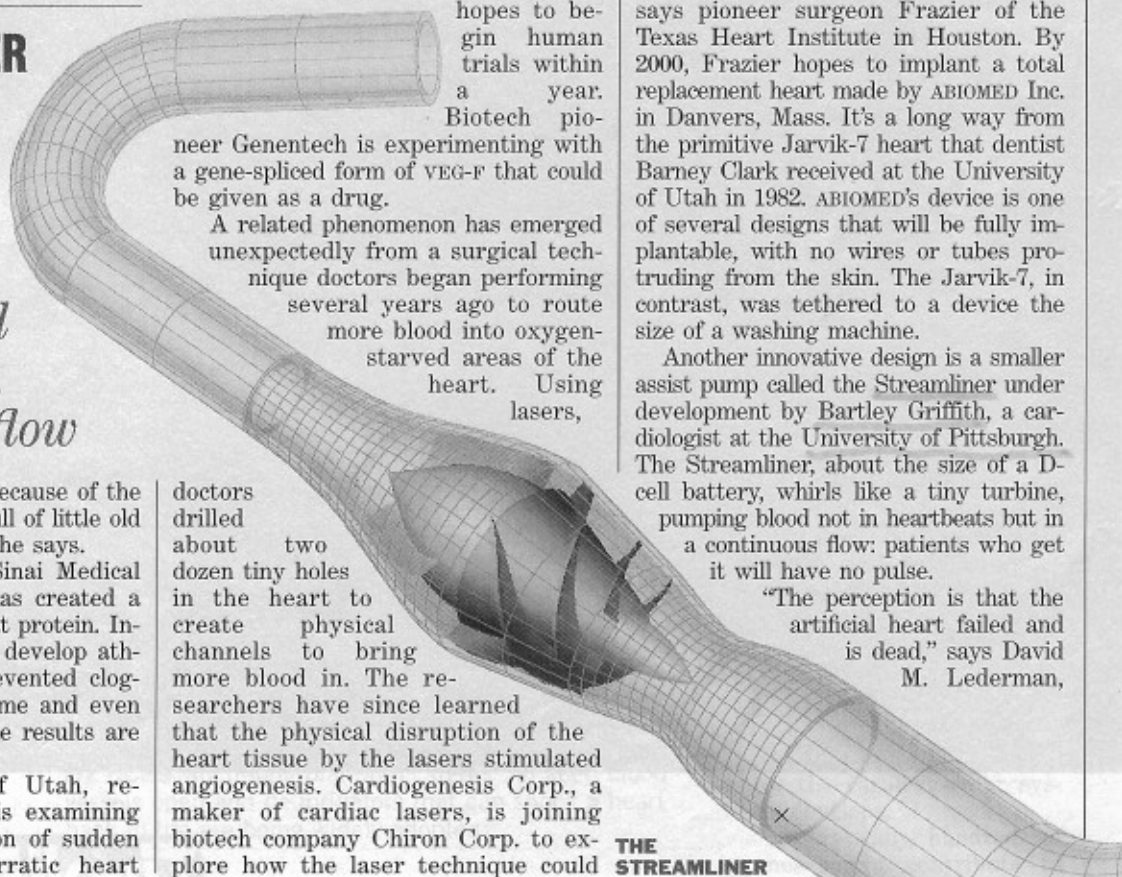
## TURBO TICKER

*The size of a D-cell battery, this device pumps blood in a smooth, continuous flow*

potato chips they want. Because of the Milano gene, "Limone is full of little old people who look young," she says.

P. K. Shah of Cedars-Sinai Medical Center in Los Angeles has created a gene-spliced version of that protein. Injected into mice prone to develop atherosclerosis, the drug prevented clogging of the arteries in some and even reversed it in others. "The results are very exciting," he says.

At the University of Utah, researcher Mark Keating is examining the terrifying phenomenon of sudden death caused by an erratic heart



THE STREAMLINER