Helping heart attack survivors escape later cardiac death

People who are lucky enough to survive a first heart attack (death of heart muscle) aren't home free. They are at risk of a subsequent cardiac-related death, especially during the first year after their attacks. Yet medical science coupled with clinical experience is increasing their chances of survival, scientists and clinicians concurred last week at a symposium on survivors of heart attacks at the American Heart Association's 55th scientific sessions in Dallas.

A number of clinical trials have been conducted to see which treatments might help heart attack survivors escape subsequent cardiac-related death, reported Curt D. Furberg of the National Heart, Lung and Blood Institute in Bethesda, Md. Ten trials, he said, have attempted to determine whether beta-blocking drugs (drugs that interfere with nervous stimulation of beta-adrenoreceptors in the heart) can increase heart attack patients' chances of subsequent survival. Nine out of 10 of the trials found that the drugs could. And of seven trials testing the effects of exercise on heart attack patients' subsequent survival, six showed a favorable trend. "These results are intriguing," he said, "but I do not think they are fully conclusive." Although lipid-lowering drugs, anticoagulants and platelet inhibitors have had no demonstrable effect on patients' subsequent survival, they may still prove of benefit to select patients, he pointed out.

Some 60 percent of patients who survive heart attacks do so without complications — that is, four to five days after an attack have no more ischemia (reduced blood flow to the heart), no failure of the left ventricle of the heart and no heart arrhythmias. How the results of the above trials might benefit this particular subset of heart attack survivors was discussed by Roman W. DeSanctis of Harvard Medical School in Boston, both on the basis of the latest clinical trials and his own clinical experience. Such patients should receive beta-blocking drugs, he said, plus the antiangina drug nitroglycerin and possibly platelet inhibitors. In addition, they should give up smoking because studies have shown that giving it up after a heart attack reduces the risk of death; exercise because of exercise's apparently favorable influence on subsequent survival; reduce caloric intake to achieve desirable weight; and reduce their saturated fat intake.

Patients who experience complications after a heart attack are at a higher risk of subsequent cardiac-related death than are patients who don't. This high-risk group may benefit not just from the above treatments and behavior modifications but from other treatments as well. For instance, if such patients are diagnosed for heart disease in two or more arteries supplying their hearts with blood, they may profit from coronary bypass surgery, pointed out Melvin D. Cheitlin of the University of California at San Francisco. While some patients who have arrhythmias after attacks benefit from antiarrhythmia drugs, others seem to profit more from antiischemia drugs, reported J. Thomas Bigger of Columbia University College of Physicians and Surgeons in New York City. A study is now in progress to determine which type of drug is more advantageous for such patients, he said.

Regardless of the treatment that heart attack survivors receive, what they are most endangered by in subsequent months, it appears, isn't another heart attack but a particularly deadly arrhythmia of the ventricles of the heart called ventricular fibrillation, which can result in sudden death. For instance, 50 to 60 percent of heart attack patients who die from a heart-related death in the year after their heart attacks do so because of ventricular fibrillation, Bigger and his colleagues have found. The ventricular fibrillation in turn, they suspect, is probably due to deprivation of blood flow to the heart. In fact, Leonard A. Cobb of the University of Washington School of Medicine in Seattle and colleagues have found that this is the case. They studied 450 patients who had had heart attacks and who subsequently went on to have near-fatal ventricular fibrillation. They found that two-thirds of the patients had experienced ventricular fibrillation because of deprivation of blood flow to the heart; the other one-third had fibrillation as a result of a new heart attack.

The patient who survives near-death due to ventricular fibrillation is at high risk for it again. While beta-blocking drugs do not appear to mitigate this risk, bypass surgery appears to do so, Cobb and his team have found. Antiarrhythmia drugs can help reduce the risk too, reported Richard O. Russell of the University of Alabama at Birmingham. —*J.A. Treichel*

RNA that acts like an enzyme

A molecule of ribonucleic acid, RNA, can perform complex biochemical reactions without the aid of any protein, report scientists from the University of Colorado. This surprising finding comes out of work on a single-celled pond animal called *Tetrahymena thermophila*. The results add support to the idea that RNA rather than DNA was the primordial genetic material.

Thomas R. Cech and colleagues were studying a piece of RNA that goes into ribosomes, the structures that snythesize protein in a cell. This piece of RNA (called pre-rRNA) is processed to remove and make a circle of an intervening sequence and to join the remaining pieces. In other instances where RNA molecules are spliced, typical enzymes are responsible.

As the scientists purified pre-rRNA, it unexpectedly continued to break and ligate at the specific points, as long as certain salts and nucleic acids were present. At first the scientists thought proteins must be very tightly bound and acting as enzymes, but that did not prove to be the case. Cech and colleagues report in the November CELL that even when the original piece was synthesized in a test tube containing no protein that might catalyze the splicing, the RNA molecule still cleaved itself and joined the fragments in the appropriate pattern. In fact the intervening sequence by itself was able to form a covalent bond to make a circle, so at least part of the activity resides in the intervening sequence region of the molecule.

The biochemical reactions of pre-rRNA require no ATP or GTP, the carriers of free energy in biological systems. Each chemical bond that forms requiring energy is balanced with a bond cleavage that releases energy. But still, activation energy must be provided to break the bonds, and the site of breakage must be specified (to only two sites out of a possible 1,300).

Cech and colleagues propose the secondary and tertiary structures of RNA are responsible: "We envision the RNA molecule folded in such a way that one of its own bonds is weakened either by physical stretching or withdrawal of electrons." They also propose it has a specific binding site for a cofactor and forms an active site for transfer of a chemical group.

There is one property of an enzyme that the RNA lacks. It does not seem to promote reaction of other pre-rRNA molecules. So Cech and colleagues have coined the word ribozyme to mean an RNA molecule with enzyme characteristics, "the intrinsic ability to break and form covalent bonds."

This new-found ability of RNA has led to speculation. The excision of the intervening sequence may be reversible; under certain conditions a piece of RNA might insert itself into an RNA molecule different from its original host. (Such movable pieces of genetic material are observed in DNA.) Cech suggests this mechanism may underlie DNA rearrangements during cellular differentiation.

In primordial organisms with a limited variety of molecules, self-rearranging RNA might have increased the diversity of RNA sequences. The possibility that RNA can catalyze reactions as well as store genetic information supports the theory that RNA was the earliest genetic material. "What we now see in the *Tetrahymena* pre-rRNA could be a vestige of this ancient process, evolved to the point where splicing is very rapid and absolutely precise," Cech concludes. —*J.A. Miller*