

Grafted muscle cells aid damaged hearts

Some survivors of heart attacks suffer years of failing health as their hearts strain to pump adequate quantities of blood. Now researchers report that damaged heart muscle in rabbits can get a boost from muscle cells transplanted from their legs, a finding that may lead to new therapies for patients.

Scientists at Duke University Medical Center in Durham, N.C., froze portions of the hearts of 12 rabbits, killing about the same number of heart cells as die in the kind of heart attacks that lead to the prolonged decline in heart function known as heart failure. The researchers then transplanted 10 million muscle cells from a leg of each animal into its heart.

After receiving the transplants, pumping efficiency rose significantly in five of the seven hearts in which the transplants became established, the team reports in the August *NATURE MEDICINE*. The most successful transplant gave a four-fold boost. The researchers don't know why the transplants were unsuccessful in five of the rabbits, says Doris A. Taylor, one of the Duke researchers.

The study is the first to show that muscle cells contract after being transplanted into a working heart, says Ray C.J. Chiu, a cardiac surgeon at McGill University and Montreal General Hospital, both in Quebec. The Duke team "has made an important contribution," he says.

Among the seven rabbits in which the transplants survived, the pumping capacity increased twofold on average. However, it reached only 50 percent that of healthy animals, Taylor says. Still, similar grafts in patients may keep them alive until they can receive new hearts through transplantation, she adds.

The researchers have applied to the Food and Drug Administration for permission to test muscle cell transplantation in people. Clinical studies are needed to determine whether it will yield any benefit in patients, and if so, for how long, Taylor says.

The researchers monitored the rabbits for only 2 to 6 weeks after transplantation because implanted sensors that measure pumping efficiency become less effective after a few weeks, producing less reliable data, Taylor says. However, the grafted cells persisted in some of the animals for

a longer time, she notes.

Last month, Piero Anversa at New York Medical College in Valhalla and his colleagues observed cell division among surviving muscle cells in damaged hearts (SN: 07/25/98, p. 54), which might replenish the heart muscle without the aid of transplants. However, those results remain controversial.

In previous studies, researchers have transplanted into animal hearts muscle

cells taken from the animal's limbs. They have also transplanted cells from embryos and fetuses. However, none of those reports established that the transplanted cells began contracting in a working heart, Chiu says.

Unlike foreign fetal or embryonic cells, grafts taken from an animal's own body do not trigger an immunological reaction, Chiu notes. Ethical issues surrounding use of human embryonic and fetal tissues make them less likely to be available than a patient's own muscle, he adds. —J. Brainard

Antidepressant helps smokers to kick ash

As a treatment for depression, drugs such as Prozac, which boost activity of the neurotransmitter serotonin, have in the past few years largely replaced tricyclic antidepressants, which increase the action of the neurotransmitter dopamine. But at least one tricyclic medication now shows signs of life as an aid to cigarette smokers who want to kick their habit, according to a new study.

More cigarette smokers given nortriptyline for 3 months remained abstinent over the following year than smokers provided with pills having no active ingredient, report psychologist Sharon M. Hall of the University of California, San Francisco and her colleagues. Nortriptyline treatment increased abstinence among smokers who had not experienced prior bouts of severe depression, the researchers note.

This finding comes on the heels of evidence that bupropion, a dopamine-enhancing drug but not a tricyclic, also increases abstinence in those trying to quit cigarettes (SN: 11/15/97, p. 319). Bupropion, which is more expensive than nortriptyline, has been approved by the Food and Drug Administration for use in programs to help people stop smoking.

"The outcome data suggest that nortriptyline is a useful adjunct to smoking cessation efforts," Hall and her coworkers conclude in the August *ARCHIVES OF GENERAL PSYCHIATRY*.

Through public service and newspaper ads, the scientists recruited 199 men and women, all of whom smoked 10 or more cigarettes daily. None exhibited symptoms of major depression, but 65 had been diagnosed with it previously.

Volunteers were randomly assigned to nortriptyline or placebo treatment. All attended eight weekly group sessions that focused either on monitoring abstinence efforts or promoting positive thoughts and activities linked to a non-smoking way of life. These group sessions took place during the last 2 months of treatment, allowing nortriptyline the several weeks required to begin exerting its effects.

Abstinence was confirmed by urine analyses at the end of treatment and at

three points during the following year.

Among participants with no history of depression, slightly more than 40 percent of those who received nortriptyline remained abstinent after 1 year. Around one-quarter of those who received placebos ended up cigarette-free. In neither case was there a difference attributable to which group sessions participants had attended.

Among previously depressed volunteers, the type of group sessions made a difference. About one-third of those who attended sessions that emphasized mood-boosting strategies were abstinent after 1 year in both the nortriptyline and placebo groups. Those who attended the other type of sessions achieved much lower abstinence rates, regardless of which type of pill they had received.

Self-reported mood in the first 3 days after quitting cigarettes was brighter for those who took the antidepressant, which may have increased their likelihood of achieving short-term abstinence.

However, it's tough to give up cigarettes for good. A majority of participants, including those given nortriptyline, resumed smoking after 1 year.

Scientists need to look for specific dopamine-enhancing actions of nortriptyline and bupropion that influence smoking abstinence, holds psychiatrist Alexander H. Glassman of Columbia University in a commentary accompanying Hall's findings. Indirect evidence for a dopamine role comes from three unpublished clinical trials, conducted several years ago, which found that Prozac and related serotonin boosters offer no help to those trying to quit cigarettes, Glassman says.

Drugs such as nortriptyline may help cigarette smokers negotiate the long process of dumping their habit, which typically includes seven or eight unsuccessful attempts, comments psychiatrist John R. Hughes of the University of Vermont in Burlington.

"Nortriptyline and bupropion treatment may prompt more quitting attempts by smokers," Hughes says. "Every time someone quits and fails, they learn something about their cigarette cravings that makes them more likely to quit for good on the next try." —B. Bower

Left: Light area (arrow) shows scarred heart muscle. Right: Transplanted leg muscle cells (arrow) function inside the scar.

