

Future promising for cartilage repair

As Americans remain active and live longer, damage to the body's cartilage is becoming increasingly recognized as a potentially disabling problem. Now, there is promising new research on ways to deal with cartilage damage.

Research findings reported by Duke University Medical Center and the university's Department of Biomedical Engineering, Durham, N.C., suggest that human fat cells may, in the future, be transformed into cartilage for joint repair.

Using immature fat cells harvested from people who underwent cosmetic surgery, scientists at Duke created cartilage by feeding the cells nutrients for the formation of collagen, a tough, fibrous protein contained in cartilage.

The finding is important, says Dr. Farshid Guilak, Director of Orthopedic Research at Duke, because it promises a "limitless source" of cells that can readily be transformed into cartilage for repair. He notes, however, that although the fat cells have been successfully transplanted in the laboratory, such transplants have not yet been attempted in clinical trials with human subjects.

"Using an approach similar to that for creating cartilage cells from bone marrow samples, we are able to grow and transplant a three-dimensional mold of cartilage cells," says Geoffrey Erickson, research team member.

"These are stem cells, which can go down different pathways depending on the cues they receive from their environment – in this case we're giving them cues to turn into cartilage cells," he explains.

"This holds the possibility of taking fat cells from someone with a cartilage injury and growing new cartilage within a mold to replace the damaged tissue."

Cartilage is the smooth protective covering lining the ends of the bones at the joints. Normally, cartilage acts as an effective shock absorber, tough enough to survive both the wear and tear of daily activities and high-level sports. It has an extremely low-friction surface that enables joints to bend and move easily and painlessly.

The most frequent damage to cartilage occurs in the knee, leading to a host of problems, from localized cartilage loss to widespread cartilage wear involving all the joint's surfaces.

According to Dr. Brian J. Cole, Medical Director of the Rush Cartilage Restoration Center in Chicago, wear and tear over time as well as trauma to the knee can injure cartilage. The difference between traumatic injury and normal wear and tear is that trauma typically causes a more localized form of cartilage injury.

Damage due to wear and tear, otherwise known as "degenerative arthritis" or "osteoarthritis," may start as a localized area of damage, but progress to involve larger areas of cartilage damage. There is loss of the normal lubricating and shock-absorbing function of the cartilage, says Dr. Cole.

Osteoarthritis, says Dr. Cole, probably begins with an abnormality of the

cells that produce the components of cartilage – collagen and proteoglycans (substances that provide resilience). The cartilage thins and wears away to expose underlying bone.

With more severe and long-standing arthritis, the bone beneath the cartilage may form spurs, areas of bone overgrowth that become painful. Ultimately the smooth, slippery surface of the cartilage becomes rough and pitted, and the joint can no longer move smoothly, says Dr. Cole.

Rheumatoid arthritis and many other autoimmune-type diseases also damage the joint's cartilage.

"The older a patient is, however, the more likely that the problem is related to wear and tear, including the extensive cartilage damage seen in osteoarthritis," says Dr. Cole. "And, some people seem genetically predisposed to accelerated cartilage loss."

Up until now, options have been limited for repairing joint damage since cartilage has little ability to heal itself once injured. For mild symptoms, patients may respond to exercise, physical therapy, cortisone shots and anti-inflammatory medications.

However, when cartilage loss is confined to a small area, a defect measuring less than 10 centimeters by 10 centimeters, new techniques have been developed to implant healthy cartilage cells.

Unlike organ transplantation, pa-

tient rejection of cartilage tissue is clinically insignificant and does not require patients to take special medications to prevent an immune response.

"Most cartilage transplantation has been performed on the distal femur bone in the knee," says Dr. Cole.

"The procedure is not indicated when damage is due to more widespread arthritis or infection."

The procedure is called "chondrocyte (cartilage cell) transplantation," and involves harvesting a small portion of cartilage from the outside edge of the patient's cartilage cushion, an area where no weight-bearing occurs and the loss of cartilage would not be missed.

The harvested cartilage is sent to Genzyme Biosurgery, a Boston laboratory that has patented a process for culturing cartilage cells. The healthy cartilage taken from the patient is placed in a nutrient broth that nourishes the cells and allows them to multiply many times over – a process known as "culturing" cartilage.

Finally, the laboratory-grown cells are transplanted back into the injured site. At the time of re-implantation in the patient's knee, there are over 12 million cells. These cartilage cells are placed into the area where the cartilage has worn away and covered with a membrane or patch obtained from an adjacent bone lining.

"Cartilage grows under the patch,"

says Dr. Cole. "It continues to improve and harden and eventually become part of the cartilage pad in your knee."

Patients who have undergone this form of knee surgery are allowed to place body weight on the knee within four to six weeks, but full recovery takes a minimum of eight to 12 months.

There is no way, says Dr. Cole, to know how long the cartilage implant will last. The results obtained with this treatment option have been carefully compiled from patients around the world, and demonstrate success rates of 80 to 85 percent.

"Effective implants for large patches of cartilage loss may be available within five years," says Dr. Cole. "The ultimate goal is to resurface an arthritic knee. It is something that may be applicable to other joints."

Another future repair option, synthetic cartilage, is being developed by researchers at the Georgia Institute of Technology in Atlanta who have produced a tissue named Salubria. Salubria is mainly a liquid gel, which has an elastic noodle-like texture similar to that of other human tissues. A private company, Salumedia, pioneered the development of this man-made cartilage, which has been tested in various animal trials.

Clinical trials designed to lead to Food and Drug Administration approval will begin in 2002 or 2003, says Dr. David N. Ku, Regents' professor at Georgia Tech and professor of surgery at Emory University in Atlanta.

Cartilage, says Dr. Ku, is 70 percent water and functions like a water bag, cushioning and distributing pressure when a person performs a task.

Dr. Ku says that a good cartilage replacement material "should have the same mechanical properties, wear the same and have the same stress distribution properties as normal cartilage."

"Salubria is the first hydrogel strong enough to do that," says Dr. Ku. "It has approximately the same water content as normal cartilage. If you feel cartilage and if you feel Salubria, it's hard to distinguish any differences."

Elbows, shoulders, fingers, hips, knees and ankles are all areas where artificial replacement cartilage such as Salubria might be used, says Dr. Ku.

"But the knee seems to be the area where the most patients seem to need help right away."

Other possible treatments for osteoarthritis are being sold as off-the-shelf products such as "glucosamine chondroitin" whose manufacturers suggest relief of joint pain for both people and their pets.

"It's unclear if nutritional supplements such as glucosamine truly rebuild cartilage," says Dr. Cole in Chicago. "Evidence seems to be emerging, however, that these products have a positive effect on the joint. The main effect may be to reduce pain and swelling."

When large amounts of cartilage have been lost or damaged in a joint such as the knee, hip or shoulder, an artificial joint may be the best option.

Dr. Cole suggests that joint-pain sufferers go over treatment options with a medical specialist.

—M.A.S.

Geoffrey Erickson (right), graduate student, and Dr. Farshid Guilak studying new cartilage cells in the laboratory at Duke