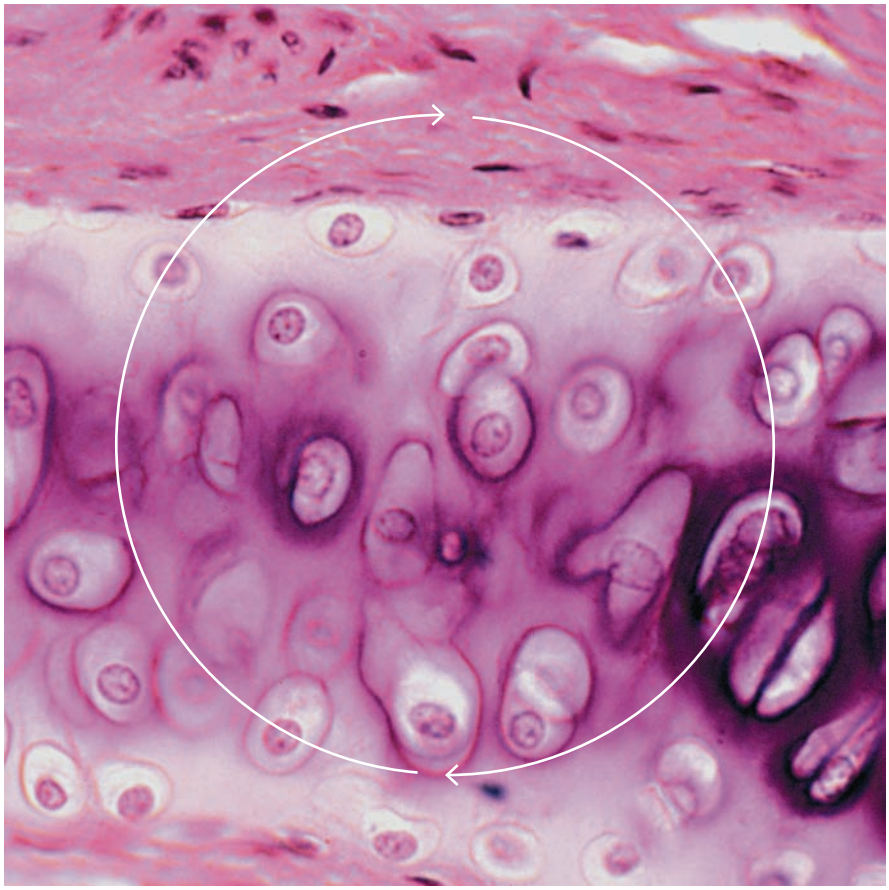

Cultivating Second Chances

Have an achy knee? Maybe you need to grow some new cartilage for it. By Charlotte Huff

DEREK JOHNSON didn't give much thought to the protective cartilage that cushioned his bones until a small area in his left knee wore down to the point that it was raw and painful. Following an evening on the basketball court, the 44-year-old woke up in the morning and knew he was in trouble: "I could barely walk," he says.

After babying the joint and consulting with an orthopedic surgeon, Johnson dialed back his physical activity for several years — no competitive basketball and more "timid" tennis and football sessions, as he describes it. But the pain flared up again last summer. Johnson returned to his surgeon at New York City's Hospital for Special Surgery (HSS) and learned that his once tiny area of cartilage loss was expanding. Soon thereafter, the 49-year-old father of two opted to try an experimental procedure — one that would use his own harvested cartilage cells to grow a new protective layer of tissue.

With limited cartilage-regeneration options available, Johnson believed this technique represented his best hope of one day resuming his sports passions. "I wasn't prepared — or willing — to become victim to a constrained way of life," he says.

The procedure, in which harvested cells grow along a three-dimensional scaffoldlike collagen device called a NeoCart, is one of several cartilage-regeneration approaches being explored by researchers in the United States and elsewhere who are striving to find a simple and cost-effective solution for a common problem: limited but painful cartilage loss in the knee. The NeoCart approach is focused on growing new articular cartilage, the layer of tissue that covers the ends of long bones in the joints.

For active people who, like Johnson, are decades from retirement, the loss of even a small area of articular cartilage can be emotionally and physically debilitating. "I call it musculoskeletal depression," says Riley J. Williams III, MD, Johnson's surgeon.

AS IT TURNS OUT, articular cartilage is a remarkably complex tissue, one that's difficult to repair or replicate. It's designed to provide a hard and resilient shield that prevents the ends of bones from rubbing against each other. Thus, cartilage lacks the nerves and blood vessels found in many other parts of the body. That's good in some respects, says Dr. Williams, director of the HSS Institute for Cartilage Repair, because "otherwise, every time you jumped, fell, or twisted, you would be in excruciating pain."

But the tissue's restorative abilities suffer. "It's not like bone. It's not like skin. It's not like the liver," he says. "Cartilage has such a poor capacity for repair that injuries are devastating unless you can go in and do something to fix it."

And the damage can be silent — sometimes for years. Johnson's cartilage loss measured half an inch at the time of his painful wake-up call. In that sense, he has some high-profile company. For a study published last year in the *Journal of Knee Surgery*, researchers performed magnetic resonance imaging on 14 National Basketball Association players who had no symptoms of cartilage damage; the scans revealed that half the players did have signs of cartilage damage in their knees.

At this stage of research, the cartilage-regeneration techniques being forged aren't designed for adults with widespread cartilage loss but rather for those with small gaps in no more than a few areas. (Typically, cartilage loss is more widespread once

people reach their mid-50s, according to several orthopedic surgeons interviewed for this story.) The goal is to prevent a small gap from expanding, thus averting, or at least delaying, knee-replacement surgery.

Knee replacement continues to be a highly effective and common procedure. By 2030, nearly 3.5 million will be performed annually — more than six times the number in 2005 — as a result of an aging population, increasing obesity, and other factors, according to projections presented at last year's meeting of the American Academy of Orthopedic Surgeons.

The drawback of knee replacements is that artificial knees can eventually wear out, and the second surgeries aren't necessarily as successful, says Hubert Kim, MD, director of the Cartilage Repair and Regeneration Center at the University of California, San Francisco. Other procedures, such as removing damaged cartilage, can be performed orthoscopically through small incisions by using specialized tools. But none of those procedures can replace the missing cartilage with normal tissue, Dr. Kim says.

"You see these [cartilage-damage] injuries all the time, and you are limited," Dr. Kim says. "I'd rather give them something that's living tissue rather than cobalt chrome if I could, especially for the young patient."

Growing healthy cartilage has proven to be more complex than just growing new cartilage cells, called chondrocytes, which make up less than five percent of the tissue's total volume, according to the International Cartilage Repair Society. Water is the primary element of cartilage, and in much smaller amounts, there are collagens, proteins, and other components. The cells also require some type of structure, frequently called a scaffold or a matrix, to adhere to as they grow. "They have to know where to go," Dr. Kim says.

One cartilage-regeneration approach that's traditionally been used is a procedure called microfracture, in which the surgeon drills tiny holes into the bone beneath the area where the cartilage loss occurs in an effort to encourage primitive stem cells to form new cartilage. "It's a good first-line option for many patients," says Brian Cole, MD, section head of the Cartilage Restoration Center, Division of Sports Medicine at Rush University Medical Center in Chicago.

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But drawbacks persist, including uncertainties from patient to patient regarding exactly how much cartilage will form.

And, Dr. Cole says, the tissue that results is fibrocartilage, a repair-type cartilage that's second best to nature's own. "It's not as stiff, and it's probably not as durable," he says.

LAST FALL, Johnson had two surgeries. The first was to remove a tablet-size piece of cartilage from a non-weight-bearing area of his left knee. Those cells were then grown for more than a month in a laboratory at Histogenics, which developed the NeoCart scaffolding device and is based in Waltham, Massachusetts. Once the three-dimensional implant was shipped back, with the cells layered throughout, it was cut to fit the area of cartilage loss — about an inch in Johnson's case.

Six weeks after his second surgery, during which the engineered tissue was implanted, Johnson was walking fine — with the exception of descending stairs. And according to Johnson, Dr. Williams "is rather bullish that come spring, I will have my full range of motion and mobility back." Johnson, eager to tear up the basketball court again, hopes that the procedure will provide more durable and longer-lasting cartilage than the traditional microfracture technique. "I'd love to ride this knee out with just this one procedure," he says.

Meanwhile, some researchers are pursuing other techniques in an effort to avoid patients having to endure the pain and expense of two surgeries. One approach, used by Dr. Cole, among other surgeons, involves the removal and mincing of a piece of cartilage right in the operating room. The cartilage is then immediately layered across a scaffolding device, which is then reinserted into the cartilage gap in an effort to stimulate cartilage-producing cells. The scaffold itself can be reabsorbed by the body. A randomized multicenter study has been approved for testing the technique.

One advantage of this approach, if it proves effective, is that the patient avoids a second surgery, Dr. Cole asserts. Plus, the cost of growing the cartilage should be reduced because an outside laboratory isn't involved.

Another method being studied is a way to coax mesenchymal cells — a type of adult stem cell that can develop into bone, cartilage, or fat cells, among other cell types — into becoming cartilage-producing cells.

According to Dr. Kim, if stem cells could be cultivated in this way, then they could also be used to fill cartilage gaps with the assistance of matrices and other scaffoldlike innovations. This particular breakthrough might be only a decade away and holds the promise of not only helping cartilage-challenged adults with limited tissue loss but also providing solutions for the much broader cartilage erosion that afflicts — and frustrates — many more Americans.

"The fact that there is so much research activity tackling the problem from so many different angles shows that we don't think any of these are perfect," Dr. Kim says. No doubt, replacing nature's own is a tough anatomical puzzle to crack. "We are doing pretty well today," Dr. Cole says. "But when will we be revolutionary rather than evolutionary? I would say we're five or 10 years away." AW

CHARLOTTE HUFF, a writer based in Fort Worth, Texas, is a regular *American Way* contributor. Her work has appeared in more than two dozen national publications, including *Arthritis Today*, *CURE*, and *Current Health*.

Slowing Cartilage Loss

Cartilage doesn't provide any wiggle room. Once it's gone, it's gone. While advancing age certainly can be blamed, that's not the whole story, says Robert Reeve, MD, director of the Division of Sports Medicine at Scott & White in Temple, Texas. "Some people who are up in their years don't have any significant [cartilage] wear," he says. "And I've seen teenagers who are starting to wear."

Genetics clearly plays a role, leaving some people more vulnerable, Dr. Reeve says. And an injury, such as a twisted knee or a torn anterior cruciate ligament, can also place nearby cartilage at risk.

But likely the biggest factor people can control is their weight. As someone's waist thickens, those extra pounds can place increasing force on those vulnerable weight-bearing knees.

In this respect, women in particular should pay attention. The smaller surface area of female joints means more pressure is exerted per square inch on that vital cartilage, Dr. Reeve says. That is yet one more reason to back off on dessert now — so you can catch up with your grandchildren in future years.