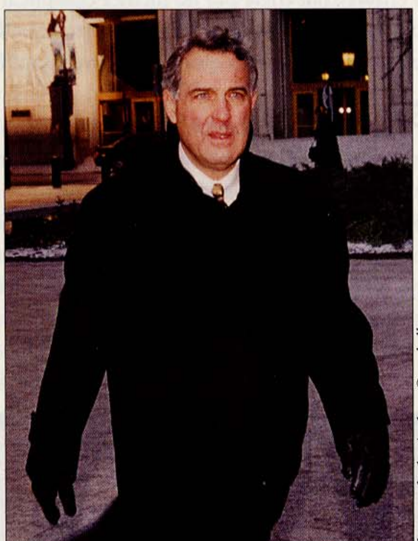
Whether you have given much thought to your knees recently is likely to depend on whether you are among the estimated 6 million people who — in the past year alone — have seen a physician because of knee pain. If you are one of those people, chances are there have been times when you could think of little else.

by Marie Mahoney



Photography by Andrew Campbell

Don Brown is among the 25 percent or so of patients who have undergone joint replacement surgery between the ages of 18 and 64.

The largest and strongest joint in the body, the knee can bear loads up to five times a person's weight — for a 180-pound man on his morning run, that's a whopping 900 pounds. The knee combines this brute strength with the capacity for a subtle range of motion — the freedom to twist, flex and rotate.

Yet, because the knee joins two bones — the thighbone and shinbone — that do not directly mate, it is also notoriously unstable and highly susceptible to injury.

For one athlete, an awkward landing after a jump can mark the beginning of years of trouble with the knee's ligaments, the sinewy tissue that connects the bones of the joint. For another, being on the receiving end of a particularly forceful tackle starts a spiral of damage to meniscal cartilage, crescent-shaped pillows of tissue that form a stabilizing platform between the bones of the knee. Sometimes the proverbial "bad knee" is the result of a lifetime of hard knocks. The knees are also vulnerable to the ravages of osteoarthritis, a degenerative disease that causes the gradual breakdown of the protective cartilage that covers the ends of bones.

Whatever the cause, disabling knee pain forces as many as 266,000 orthopedic patients each year to opt for knee replacement surgery, in which damaged portions of the knee are replaced with metal and plastic implants that mimic the structure and function of the normal joint.

Since its introduction in the 1960s, knee replacement surgery has logged an impressive track record for restoring mobility in people with advanced joint damage. Rush physicians and scientists are playing a lead role in efforts to extend the lifetime of knee replacements — through detailed studies of implant failure, through gene therapy to promote bone growth after surgery, and through laboratory research into the biology of bone and cartilage. In fact, Rush surgeons were among the first in Chicago to use new cartilage regeneration and transplantation techniques to repair early cartilage damage — potentially staving off advanced degeneration and eliminating the need for some joint replacements.

"What we're seeing with cartilage is the application of biologic techniques to the management of orthopedic problems," says Jorge O. Galante, MD, Grainger Director of the Rush Arthritis and

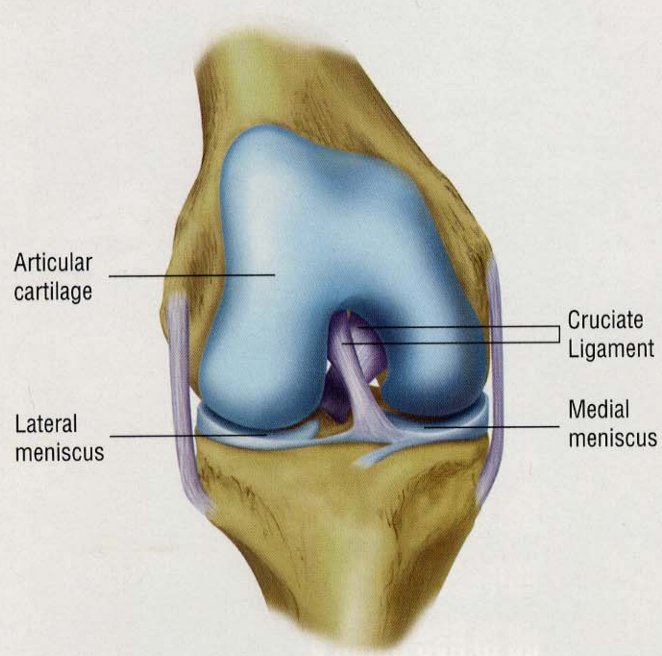
"These new techniques make it possible for us to regenerate and transplant cartilage before more advanced degeneration occurs."

Orthopedics Institute. "Thirty years ago, our goal was to create the perfect artificial joint, fashioned out of metal and plastic. Our research goal now is that we will one day be able to implant a joint made entirely from biologically engineered human tissues."

Setting the stage

The extent to which orthopedic researchers are within sight of that goal is due, in no small part, to developments in joint replacement surgery that Galante himself pioneered over a career spanning almost 40 years.

In the late 1960s, while on staff at the University of Illinois, Galante and his colleagues developed a cementless method of affixing knee implants that continues to provide an alternative to fixation with methyl methacrylate — a sort of super glue for joint replacements. Using a fibrous titanium mat attached to the implant to fit the shape of the joint's missing bone, Galante's method harnessed the power of the body to repair itself. The porous mat allows new bone and blood vessels to grow into the implant. This forms a biological bond between the bone and artificial replacement parts that, in some cases, is superior to bonds created by cement. Prostheses designed using this principle are industry standard today, used worldwide by surgeons who perform knee and hip replacements.



The knee joint is formed by two bones — the femur, the large bone of the thigh, and the tibia, or shinbone. A third bone, the patella (not shown), is not attached to either bone, but is suspended in place by ligaments that connect the femur and tibia. Crucial to the structure and function of the knee are two forms of cartilage. Meniscal cartilage, two crescent-shaped pillows of cartilage that sit between the femur and tibia, creates a stabilizing platform for the knee. The ends of bones are covered with another form of cartilage, articular cartilage. White and shiny, with a rubbery consistency, articular cartilage absorbs shock and provides a smooth bearing surface to ensure ease of motion.

Extending the lifetime of implants

Thanks to dramatic improvements in cementless and cemented implants alike, joint replacement failure is becoming increasingly uncommon. Nevertheless, joint replacements still have a limited lifetime, says Joshua Jacobs, MD, the Crown Family Professor of Orthopedic Surgery at Rush.

"Today," Jacobs says, "about 90 percent of implants are fine after 10 or 15 years." To find out what goes wrong in the other 10 percent of cases, Jacobs is involved in several research studies investigating osteolysis — an insidious process that causes implants to loosen and can lead to massive bone loss.

"Most of the time, when joint replacements fail, it is because of a biological reaction to microscopic particles released as a result of implant wear," Jacobs says. This microscopic debris throws a wrench into the complex process of bone remodeling, in which bone formation and breakdown occur at essentially the same pace. For instance, the presence of wear particles is a call to arms for macrophages, immune system cells that remove damaged tissue or foreign invaders. Once mobilized, the macrophages secrete substances that stimulate the breakdown of bone. At the same time, wear particles also make it difficult for osteoblasts, bone cells that play a crucial role in repair, to do their job.

Jacobs and his colleagues hope that deepened understanding of osteolysis will provide data that can be used to design better implants, to refine surgical techniques and to develop pharmacological agents to modify the body's response to wear particles.

An option for younger patients

An important goal of this research is to extend the lifetime of joint replacements for people like Chicago attorney Don Brown, who is among the 25 percent or so of patients who undergo joint replacement surgery between the ages of 18 and 64.

The 53-year-old Brown underwent a total knee replacement 18 months ago. He traces his knee damage to a high school football injury. His football career — along with further skirmishes with knee pain — continued through college. After college, he maintained a full calendar of sports activities, including softball, volleyball and regular running.

About eight years ago constant pain forced him to give up running. It was then that he consulted Rush orthopedic surgeon Charles Bush-Joseph, MD.

Bush-Joseph told Brown he would eventually need a knee replacement.

"He said I'd know when the time was," Brown recalls. The time came one night a couple of summers ago, when Brown woke up to excruciating pain. Taken by ambulance to a local hospital, Brown was then transferred to Rush, where arthroscopic examination revealed the source of his pain: bleeding from the bone marrow, where bone had been entirely worn away.

Ultimately, Busch-Joseph referred Brown to a colleague, Rush surgeon Aaron Rosenberg, MD, who specializes in complex knee

Photography by Andrew Campbell

As avid joggers, orthopedic surgeons Mitchell Sheinkop, MD (left), and Brian Cole, MD (right), appreciate the importance of strong and healthy knees.

surgeries. Today, Brown can enjoy an active life — within limits. He rides a bike, speed walks every day and keeps up a brisk pace on his frequent jaunts from his downtown office to the courtroom.

Repairing and regenerating cartilage

Yet, had Brown suffered his original injury today, it is possible surgeons would have been able to repair his cartilage — delaying or perhaps preventing the degeneration that ultimately made surgery his only option.

Today's orthopedic surgeons have at their disposal new techniques for transplanting and repairing cartilage that were not available as recently as five years ago. One technique, called autologous chondrocyte implantation, has shown initial success in treating small defects in the articular cartilage that protects the ends of bones.

In this procedure, surgeons harvest cartilage tissue from the patient's own knee. The tissue is sent to a cell-culturing facility, where it serves as a "starter" to grow millions of new cartilage cells. The surgeon then implants the new cells in the damaged part of the knee, where the cells continue to multiply and integrate with surrounding cartilage.

"These patients have cartilage defects that, if unchecked, would lead to advanced arthritis and, in many cases, knee replacement," says Brian Cole, MD, director of the Rush Cartilage Restoration Center, a program of the Arthritis and Orthopedics Institute. "In the past, we would have had to tell them to wait, watch and deal with their pain symptomatically. These new techniques make it possible for us to regenerate and transplant cartilage before more advanced degeneration occurs."

Stem cells hold promise for a new source of cartilage

So far, it appears that autologous chondrocyte implantation is useful only for the repair of relatively small cartilage defects. For this reason, researchers have begun to explore the possibility of using certain stem cells to create a more plentiful supply of cartilage cells that may one day allow surgeons to repair deeper, more widespread cartilage defects.

At Rush, basic research on these stem cells — called stromal cells — is under way in the laboratory of Amarjit S. Virdi, PhD, assistant professor of anatomy at Rush. Virdi, who recently set up shop in the new Robert H. and Terri Cohn Research Building, is conducting research to understand the process by which stromal cells differentiate into bone, cartilage and other cells.

The bionic ... knee?

Ironically, the ultimate stumbling block in creating a bioengineered knee implant may lie in the limits of our understanding of gross anatomical processes, rather than cellular and molecular processes, says Dale R. Sumner, PhD, chairman of the department of anatomy and director of the section of bone biology in the department of orthopedic surgery.

"We know a lot about stimulating bone formation at the molecular level," says Sumner, who is currently investigating the use of growth factors to enhance implant fixation and bone regeneration in total knee replacement.

We know less, he says, about the intricate process through which heredity and environment interact to create a functioning joint.

"Science, for various reasons, has been focusing lately on smaller and smaller biological structures. But there's still a tremendous need to understand how tissues function at the gross level," he cautions. "It doesn't do much good to get a cell to do handstands in a culture if you can't reproduce that at the level of gross anatomy." ■

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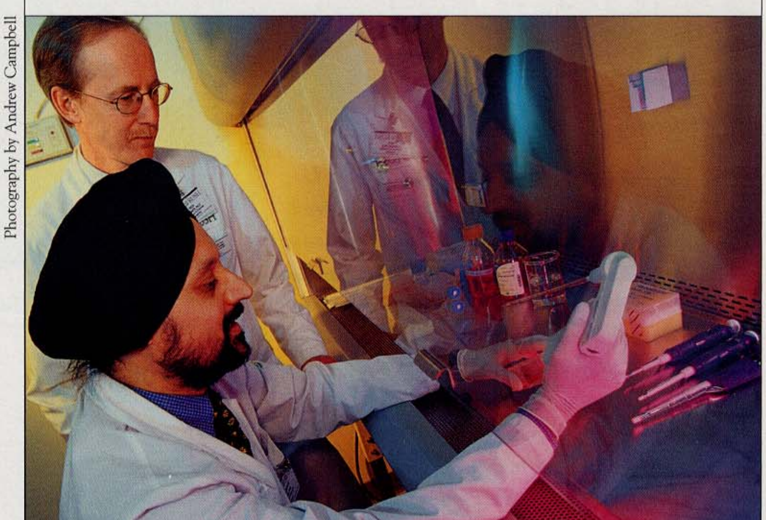

Amarjit S. Virdi, PhD (front), talks with anatomy chairman Dale R. Sumner, PhD (back). Virdi is conducting research to understand the process by which stromal cells differentiate into bone, cartilage and other cells.