

## **The Age of Arthritis**

### **We're headed for an epidemic of joint disease.**

#### ***What you can do to protect yourself***

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The first sign is often a twinge in your knee or your back or some stiffness at the base of your thumb. Or maybe you're getting out of the car and a sharp pain shoots down your leg from your hip to your calf. "Nothing serious," you think. "I must have just strained something. I'm too young to have arthritis."

Think again. If you are within even shouting distance of middle age, chances are you have osteoarthritis, a degenerative disorder in which the cartilage the natural shock absorber that cushions the insides of your joints begins to break down. Doctors used to think of it as a disease of old age, but they now believe that this form of arthritis, the most common of about 100 types, begins its relentless, initially painless course when you're still in your 30s, 20s or even younger. Most of the time you won't suspect anything is wrong until you're in your 40s or 50s and begin to feel those telltale twinges, signs that the disorder may be starting to affect your bones. By then the damage has been done, and even the best treatments can't do much more than ease the pain and try to maintain the status quo in what are already degenerating joints. The situation with arthritis is about to get worse a lot worse and very soon. At present, doctors believe that osteoarthritis affects more than 20 million Americans. By 2020, that number is expected to reach 40 million. (More on why in just a bit.) Some experts are starting to think that even the current situation is more dire than anyone had realized. In October, researchers from the Centers for Disease Control and Prevention published the results of the first nationwide survey measuring the total burden of arthritis and chronic joint symptoms. Their sobering conclusion: one-third of all American adults suffer from some type of joint disease.

It's almost as if we were watching the formation of an epidemiological perfect storm. First you have the demographic bulge of the baby-boom generation heading into its 50s prime time for arthritis. Add five decades of jogging (in less than perfect form), high-impact aerobics and fast-breaking sports like football, soccer, tennis and basketball, whose quick stops and sharp pivots do maximum damage to the knees and hips. (Gen Xers can look forward to the effects of video games on the thumbs, another body part that's particularly prone to osteoarthritis.) Finally, top it all off with a generation of Americans who are heavier than ever and whose weight is literally squeezing the life out of their joints.

There may be, however, some relief amid all the aches and pains. Researchers are starting to pay a lot more attention to osteoarthritis. They have discovered that what they thought was a fairly straightforward mechanical breakdown of the joints is a much more complicated process with lots of component parts. Although this means that any patients who expect a quick fix are likely to be disappointed, scientists are starting to gain the kind of insights that

can lead to more effective treatments, not to mention better strategies for heading off trouble before it begins.

How complex a process are we talking about? Doctors used to think that cartilage was the beginning, middle and end of the osteoarthritis story. Now they know that cartilage is important, but so is everything that surrounds it—muscles, bones, tendons and ligaments. The damage caused by wearing ill-fitting shoes or suffering a football injury can certainly give rise to arthritic joints. But the worst problems often stem from basic differences in the body's biochemical makeup. For example, some people's cartilage seems to resist damage better than others. (Scientists are tracking several genetic variations.) In addition, researchers have discovered an array of biochemical messages that are traded between bones, muscles and other parts of the body and play a key role in keeping joints healthy. "Ultimately, we think it's the biochemical approach that's going to solve the riddle of arthritis," says Dr. Mitchell Sheinkop, an orthopedic surgeon at the RushPresbyterianSt. Luke's Medical Center in Chicago. "Someday you may pop a pill and your cartilage will continue to grow, but that's 10 years away at least."

Until then, what doctors would like to have is some kind of test that will identify people in the earliest stages of osteoarthritis, before too much damage has occurred. That way their treatments might stand a better chance of arresting the degenerative process before disability sets in. Unfortunately, conventional X rays, which give very detailed pictures of bone, don't provide very good images of cartilage. And researchers haven't yet discovered any biological markers in the blood that reliably tell them, "Hey, this person's cartilage is starting to fall apart. Do something!"

To understand the latest insights and where they might be leading, it helps to know a little bit about how a joint is put together, and there's no better place to start than with the cartilage. Like so many tissues in the body, cartilage is composed mostly of water. Indeed, you can think of it as a damp sponge. The spongy part contains several important components, including the chondrocyte cells that generate new bits of cartilage and various molecules that give the "sponge" its structure and help hold it together.

With every step we take, our moving body puts pressure roughly equal to three times our weight on the knees and hips. As that pressure is distributed across those joints, cartilage is compressed, absorbing most of the load. And, as you might expect with something that resembles a damp sponge, water is squeezed out of the cartilage into the space between the bones. Once the pressure is released, the water flows back into the cartilage, carrying with it nutrients that were picked up from the synovial fluid, which fills the joint. This constant fluid exchange is critical to maintaining healthy, pliable cartilage and explains why joint-moving exercises, like walking, help delay the progress of osteoarthritis.

Sometime between ages 40 and 55, the activity of the chondrocytes starts slowing down and the cartilage takes longer and longer to replenish itself. As the cushion of cartilage grows progressively thinner, the bones begin to grind against one another. This is a normal consequence of aging, but aging isn't the only culprit. Something as simple as falling on an icy sidewalk or putting on some extra pounds can increase your risk of osteoarthritis. Anything that puts extra stress on the joints will wear out the cartilage that much faster.

That's simple enough. Now for the first wrinkle. "It appears that not all cartilage is created equal," says Dr. Roland Moskowitz, president of the Osteoarthritis Research Society International. Ankles, for example, bear the same heavy loads as knees and hips. Yet most people, unless they're ballet dancers, don't get osteoarthritis of the ankle. Similar discrepancies show up in non-weight-bearing joints as well. The wrist, for example, is much less prone to osteoarthritis than the joint at the base of the thumb. It could be that ankles and wrists have some mechanical advantage that protects them from osteoarthritis. But preliminary evidence suggests that the real advantage, at least for ankles, is biochemical; that there's something in their composition that allows them to bear greater loads and respond to changes in the joint without breaking down.

Some of the evidence for this comes from related research on bones. Most people think of bones as inert objects whose only job is to keep our bodies from collapsing into a puddle of flesh. But bones are actually quite active tissues, constantly building and rebuilding themselves from the inside out. Anytime you break a bone, the body produces repair proteins that direct cellular activities as the bone knits itself together. When investigators take these so-called osteogenic proteins and sprinkle them on laboratory samples of damaged cartilage, the cartilage begins to repair itself.

"Now here comes the interesting part," says Dr. Klaus Kuettner, professor of biochemistry at RushPresbyterianSt. Luke's. "The ankle joint responds better than the knee joint to osteogenic proteins." Is that why the ankle rarely gets osteoarthritis? "We don't know," says Kuettner, "but it's a hint in that direction."

Another hint comes from the observation that women with strong, healthy bones the kind that are least susceptible to the brittleness of osteoporosis are at greater risk of developing osteoarthritis. (Nature is often just not fair.) Once again, doctors suspect that a complex interplay of mechanical and biochemical factors is at work. Strong, healthy bones can support a heavier load. They also tend to replace old bone cells with new bone cells at a pretty fast clip. But somehow the biochemical signals that are responsible for the bone's increasing turnover rate trigger even greater damage to the cartilage.

Or is it the other way around? Is it the damaged cartilage that gets the degenerative process started by sending aberrant signals to the bone? "At this point, it would be a mistake to fight bitterly over whether osteoarthritis starts in the bones or cartilage, because in the end there may be different forms of the disease," says Dr. Bjorn Olsen, a cell biologist at Harvard University. "In some cases, it may start in the bone. In others, it might start in the cartilage." More clues about what could be going on come from Olsen's research into the genetics of cartilage. For the past 10 years, he and his colleagues have been studying a group of families that develop advanced cases of osteoarthritis unusually early, in their 40s and 50s. So far, Olsen's group has identified at least three genetic variations that make the cartilage of these patients more susceptible to overloading. Other scientists have found at least a dozen cartilage-disrupting enzymes that appear to be overactive in osteoarthritis. Yet even the interaction between bones and cartilage doesn't tell the whole story. You also need to take into account the ligaments, those tough bands of tissue that connect bones to bones, and the muscles that surround and stabilize the joints. Ligaments can get stretched or torn, and muscles can atrophy from underuse, disrupting a joint's finely tuned mechanism.

Take, for example, the quadriceps, the large muscles on the front of the thighs that help raise and lower the legs. "It's common knowledge that patients with osteoarthritis of the knee will have weakness in the quadriceps," says Dr. Kenneth Brandt, a rheumatologist at Indiana University in Indianapolis. For a long time, physicians assumed this was because their patients' pain prevented them from exercising. But five years ago, Brandt and his colleagues began studying a group of 400 elderly people living in central Indiana and discovered, much to their surprise, that weakness in the quadriceps in some cases preceded the advent of osteoarthritis.

It makes sense. The stronger the muscles, the greater the load they take off the joint, thus limiting damage to the cartilage. Brandt's group is trying to determine whether healthy seniors who strengthen their quads by doing exercises with elastic-bands can delay, or possibly prevent, the disabling consequences of osteoarthritis in their knees.

However the arthritic process gets started, the damage to the joint eventually begins to grow. That's when the body's immune system gets into the act. White blood cells rush into the joint and release destructive proteins that chew up the bits and pieces of damaged tissue. This so-called inflammatory process, which is often but not necessarily accompanied by swelling, works well when the body needs to fend off an acute attack, say, from invading viruses or bacteria. But when the problem is chronic, as in osteoarthritis, the white blood cells may overreact, repeatedly releasing so many of their "mopping up" proteins that even healthy tissue is laid waste. In rheumatoid arthritis (see box), the immune-system response is particularly aggressive.

None of these processes occur in isolation. "Everything is failing together," says Dr. David Felson, a rheumatologist at Boston University. "That includes bone damage, the responses to that, muscle weakness, inflammation of the lining of the joint and ligament disruption." It follows that to be successful, any treatment will have to deal with all these factors.

So what can you do? The first step for most patients is to try to get some immediate relief. About 15% don't seem to experience inflammation; for them, over-the-counter pain killers like acetaminophen (Tylenol) are often all that's necessary to control their symptoms. Things become more complicated when inflammation is involved. Old standbys like aspirin or ibuprofen are pretty good anti-inflammatories, but long-term use can trigger dangerous side effects like internal bleeding. Newer drugs, such as COX-2 inhibitors Vioxx and Celebrex, are safer but no substitute for some of the long-term changes you may need to make.

Indeed, some researchers believe there's too much emphasis on drug treatments for osteoarthritis. "It's clear that there are other things that can improve symptoms as much as pills," says Indiana University's Brandt. Losing as little as 10 lbs. can make a difference, for example, as can strengthening the muscles that surround a joint. Certain exercises, such as tracing circles in the air with the arms, have also proved helpful at keeping the joints from stiffening and losing mobility. That's not to say that Brandt discounts the benefits of drugs altogether. But they're more effective, he argues, when combined with lifestyle changes.

One person who is sold on a more holistic approach is Larry Nun, 56, a computer analyst who lives in Franklin, Ind. Nun first noticed the soreness around his kneecaps when he was

still in his 30s. A couple of accidents, one of which required surgery to repair torn cartilage, didn't help matters. Ten years ago, Nun, who stands 6 ft. 4 in. and weighs 345 lbs., adopted some of Brandt's exercise routines and resolved to lose weight. (One of the most effective ways to cope with sitting for long stretches, he found, was to warm up his legs with a series of leg raises before standing.) Now Nun's knees act up only when he's not moving. "I'd say I've been able to control it," he says. "And I know it's not getting worse."

Meanwhile, a lot of effort has gone into figuring out how to replace damaged cartilage. Many arthritis sufferers swear by the dietary supplements glucosamine and chondroitin. Preliminary studies suggest that they may relieve pain, but the jury's still out on whether they actually promote the growth of new cartilage. The first approved biotech cartilage implants have hit the inevitable stalemate: once the new cartilage is in place, it's subject to the same destructive forces that chewed up the original cartilage. In addition, transplanted cartilage does not seem to adhere very well to existing tissue, though researchers are trying new approaches to get around that problem.

Sometimes surgery is unavoidable. Each year doctors in the U.S. perform 270,000 knee replacements and 170,000 hip replacements. So many patients have benefited that a lot of people, like Mike Ditka, 63, the Chicago Bears' Hall of Fame tight end, have had both hips replaced. To keep his new joints in good condition, Ditka works out daily. "As you get older," he says, "whatever the complications are, they're going to become magnified a hundred times if you don't exercise."

No single approach works best for everyone. As researchers learn more about what triggers osteoarthritis, they're bound to come up with more effective treatments. As with any chronic condition, there are always some things you can't control. But there's still a lot you can do for yourself. So pay attention to those twinges. Someday, you'll be glad you did.

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