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## Tender Joints

*Shots of lubricant are becoming one of the most popular — yet frustrating — treatments for arthritic knees*

BY DALE BUSS

By 1998, the pain in David Miller's right knee was almost unbearable. A retired history professor and former competitive runner, he had torn the cartilage in the joint and had developed osteoarthritis. Pain relievers and nutritional supplements no longer provided any relief.

Finally, his doctor recommended a new therapy: "viscosupplementation," or injecting the knee with a synthesized lubricant. Happily, the 67-year-old Chicago resident found the results "so extremely satisfying" that he has undergone three rounds of injections over the past two years, and X-rays have shown no significant progression of the disease.

Since his set of shots in February, however, Mr. Miller has been worrying that the treatment might be wearing thin. "There's a slight puffiness to the knee, and it's been more tender this time, so I have had to up the use of [the anti-inflammatory drug] Celebrex, which I hadn't had to use every day before," he says. "I'm not sure what I'm going to do next."

Mr. Miller's experience is typical of the growing number of patients embracing viscosupplementation — at once one of the most exciting and puzzling therapies to emerge in recent years for arthritic knees. On the one hand, the treatment instantly delivers significant relief to a majority of patients. Equally attractive, Medicare and most private-insurance plans now are covering its price of about \$500 to \$900 per injection.

At the same time, though, no one is quite sure which patients the therapy will help or for how long. Even more perplexing, the treatment seems to play an unexpected, restorative role with cartilage that researchers don't yet understand.

One thing is clear: Demand for

viscosupplementation is soaring as the population ages and the number of sports injuries grows. Both trends are leaving more Americans with osteoarthritis, a wearing away of the cartilage covering the ends of the bone that is especially troublesome in weight-bearing joints like the knee. The condition afflicts more than 80% of people over age 65 in this country, and more than half of those are beset to a significant degree.

Administered usually only after a range of other therapies — exercise, pain relievers and steroids — have failed to halt the disease, viscosupplementation has emerged as a welcome course of last resort before knee-joint replacement is required. By the end of this year, nearly 800,000 Americans will have undergone the injection procedure in the three years since Food and Drug Administration approval, joining millions in Canada and overseas.

"It's sort of a no-brainer of trying injections for symptomatic relief vs. considering a knee replacement: One's surgery and the other is not," says Russell Windsor, an orthopedic surgeon affiliated with Cornell University, in Ithaca, N.Y. "A needle stick for most people isn't a big deal, but a lot of people are fearful of having surgery."

Thomas Vangsness, chief of sports medicine at the University of Southern California's Keck School of Medicine, admits that "we don't know exactly how" viscosupplementation works. "At the same time, anecdotally, we're getting great results. I have some patients who fare well and some who don't fare so well. It's quixotic in a sense, but what other alternative do I have to offer these patients?"

Knee problems motivate more people to visit doctors than any other joint difficulties — about six million

each year, according to Johns Hopkins University — and knees are replaced far more often than hips.

The knee is "a large joint," explains Douglas Jackson, medical director of the Southern California Center for Sports Medicine at Memorial Medical Center in Long Beach, Calif. "But it's one of the ones that wears out earliest in most people" because of the tremendous stresses and strains created by the range of human activities, from sprinting to just plain standing.

The biggest malady is osteoarthritis. Injuries and hereditary weakness can trigger the condition, but the most common cause is simply time: the cumulative stresses and strains of daily movement, which eventually grind down the knee's cartilage "padding" and allow bones to rub against one another. In the worst cases, nearby connective tissue and muscles can be damaged.

The first rung of the therapeutic ladder is exercise, which can only provide general strengthening of the joint. Non-steroidal or analgesic pain relievers such as Motrin are the second level, providing temporary relief. The next level usually involves the injection of steroids, but these substances cause side effects in many people. Painful and expensive knee surgery used to be the next step, but now many doctors are recommending viscosupplementation as at least a temporary alternative.

The treatment involves replacing synovial fluid, the natural substance in the knee joint that helps absorb shocks, dissipate loads and lubricate the knee's components against wear. After about 30 years, the concentration of the material that gives synovial fluid its elasticity, called hyaluronic acid, begins to decrease steadily, which is one of the causes of

osteoarthritis.

In viscosupplementation, a physician removes abnormal synovial fluid and replaces it with lubricants Synvisc, made and marketed by Biomatrix of Ridgefield, N.J., or Hyalgan, marketed in the U.S. by Sanofi-Synthelabo Inc. of New York, and produced in Italy by Fidia Pharmaceutical. Both substances consist mainly of hyaluronic acid, which ultimately is derived from chicken combs (which happen to contain significant amounts of the material).

A treatment with Synvisc requires a series of three weekly injections, while Hyalgan requires five. Because of its higher molecular weight, or density, lab-synthesized Synvisc lingers longer in the joint, up to a month; more natural Hyalgan, which is extracted directly from rooster combs, dissipates within two to three days.

That said, the palliative effects of both substances extend for weeks and months. Hyalgan was the first formula to be used in viscosupplementation, but Synvisc in the past year or so has captured the majority of the market for the procedure — mainly, doctors say, because patients would rather get three shots than five.

(It hasn't hurt, of course, that Biomatrix has been running a large direct-to-patient advertising campaign for Synvisc, with 60-second TV commercials and local newspaper ads in 20 major cities. This, in addition to national magazine spots that the company has been buying off and on since last summer.)

The cost of viscosupplementation, doctors say, is a bit more than the cost of a six-month supply of anti-inflammatory drugs — but only a fraction of the \$20,000 to \$30,000 cost of knee replacement. Many doctors require insurance-company pre-certification of the procedure or require patients to fill prescriptions for the lubricant themselves, then bring it to the physician for injection.

Who should try the therapy? Viscosupplementation works best on knees where some cartilage remains because the procedure "improves nutrition to the cartilage," says Arnold Scheller, chief of sports medicine at New England Baptist Hospital in Boston. "And by improving nutrition, it improves the ability of the cartilage to . . . withstand stress and to have a normal gliding mechanism, or certainly decreased friction."

Relief of pain and increase of mobil-

ity typically range "anywhere from 30% to 60%" for an "average duration of nine months to 12 months" at a time, says Michele Hooper, a rheumatologist at Case Western Reserve University in Cleveland. And if viscosupplementation has worked for a patient once, she says, there's a high likelihood that it will provide significant relief in second and even third applications. An accompanying exercise program and analgesic pain medication further enhance results.

In a significant number of individuals, however, osteoarthritis is so advanced or injuries or previous surgeries have taken such a toll that there's no cartilage left, leaving knee joints "bone-on-bone" — with little potential to benefit from viscosupplementation. "At that level, it isn't possible to do away with the need for knee replacement in most cases," says Cornell's Dr. Windsor. "They want the pain to go away, not a slight decrease in symptoms, so generally their expectations aren't fulfilled by using" injection therapy.

In that regard, the efficacy of Synvisc and Hyalgan has been "less impressive than when I originally heard about them," says Brian J. Cole, medical director of Rush Cartilage Restoration Center at Chicago's Rush Presbyterian/St. Luke's Medical Center. "Higher-grade patients haven't done as well in terms of reduction of swelling and pain relief. If you wait too long, it just doesn't have as much of a positive effect."

The right knee, for instance, of Rod Burns was damaged by football injuries when he was a child. Now, at age 30, the business-development manager for a San Francisco-based company is taking Hyalgan injections "as a stop-gap" on the way to eventual joint replacement. But the injections haven't enabled him to play sports again. "I had expectations — not unrealistic ones — that my mobility would be a little more heightened after the injections," he says. "And at the length of them and the cost, you expect some results."

Some orthopedic surgeons are even more critical. Viscosupplementation is akin to "used-car dealers putting sawdust in the crankcase to make the car run smoothly until you got it home," says Dr. Wayne Goldstein, president of the Illinois Bone & Joint Institute and chief of orthopedics at Lutheran Gener-

al Hospital in Park Ridge, Ill.

"I do not believe there is a scientific basis for this treatment," says the specialist in knee-replacement surgery. "If the patient reaches the point where bone rubs on bone, they are putting off the inevitable, which is progression, loss of range of motion and loss of muscle mass. This may actually make the results of a knee replacement worse."

And yet, anecdotally and in numbers surprising to many doctors, viscosupplementation is helping some people with bone-on-bone cases or with other pre-existing damage to the knee. Among his 400 viscosupplementation patients so far, says Devon Goetz, a joint-replacement specialist at Des Moines Orthopedic Surgeons in Des Moines, Iowa, about 10% to 20% of bone-on-bone sufferers have found relief with the procedure.

Doctors say two things might be at work here. One is that, for reasons not yet fully understood, the benefits of Synvisc and Hyalgan clearly linger for as much as a year "even though it is metabolized in the body sometimes within half a day," says Paul Enker, co-director of the Total Joint Replacement Program at Northshore University Hospital in Glen Cove, N.Y. Some physicians say the lubricant also may play a role in actually restoring or at least preserving the levels of cartilage in the knee, similar to the effects noted from taking nutritional supplements, including glucosamine and chondroitin.

Some of that mystery may be at work for Trish Harrison, for example. The 54-year-old businesswoman has had osteoarthritis since her late 30s. Even after surgery on her right knee in the early 1990s, she found herself needing a cane to walk. "Every night I had constant pain and swelling, and the knee looked like it had a basketball on it," recalls Ms. Harrison, a Rochester, N.Y., resident.

In 1998, a few years after she switched from an orthopedic surgeon to Dr. Hooper, who looks at the body more holistically, Ms. Harrison had viscosupplementation. And to her surprise, the outcome has been "very successful. The knee hasn't gone back to everyday swelling for more than two years."

She has been able to resume an active life, which involves serving as director of the lunch program at an elementary school, conducting all the retail-staff training for the local Lord &

Taylor stores and, this year, starting her own errand-running business offering services ranging from picking up groceries to writing thank-you notes.

"I still think I'll probably have to have my knee replaced by my 60th birthday," Ms. Harrison says.

"But I just don't want to put myself through that yet. It's a tough, tough surgery and hard to recuperate from. It isn't something to be jumped into lightly, and I'm holding my own. I just want to buy as many years out of what I've got before I go messing."

#### From Rest to Replacement

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Mr. Buss is a writer in Rochester Hills, Mich. He can be reached at [En-core@wsj.com](mailto:En-core@wsj.com)  
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Doctors like to treat most cases of osteoarthritis and complications from knee surgery with a therapy ladder that starts with simple inactivity and ends with knee replacement. Here are the steps along the way:

**Staying off the knee:** This used to be the first prescribed treatment. But for quite some time, doctors have realized that the knee does little to repair or strengthen itself if simply left alone. And today's active 50-plusers basically don't want to be idle.

**Stabilizing braces:** New, lightweight, easy-to-fasten braces can be used to support and stabilize the knee, allowing it to rest, says the Johns Hopkins Medical Letter. But overreliance on a brace can weaken knees, the letter says, and decrease range of motion.

**Controlled exercise:** The first and perhaps biggest benefit of this stratagem is that it often leads to weight loss, which directly benefits the stress-bearing joint. Exercise specifically to build up knee muscles can be a big help, of course. Fortifying thigh muscles, taking some pressure off the knees, also is often a part of this approach. Walking, cycling and swimming are three of the favored activities.

**Ordinary and exotic pain relievers:** There's aspirin, Tylenol and other common medicines that may provide some relief and even exotic balms like heat creams that dilate blood vessels around the knee and give you a few hours of relief, and pepper creams that block the substance that gives you the pain message at your nerve endings. This tack works fine for many patients for a long while.

**Nonsteroidal anti-inflammatory agents:** For more serious pain, doctors recommend these agents, which include, for example, prescription-strength doses of Advil and Motrin. They can do a lot of good, but many people have adverse reactions to them, including gastrointestinal bleeding and liver distress.

**Nutritional supplements:** Lots of knee-pain sufferers swear by orally consumed over-the-counter products that include high dosages of substances called glucosamine and chondroitin sulfate, which may halt the deterioration of - or even help rebuild - cartilage.

**Steroid injections:** These are the agents of serious attempts to relieve pain. They clearly decrease inflammation in the joint. But some doctors say the palliative effect of steroids doesn't last long enough to be worthwhile for many patients. And there's evidence that steroids soften and degrade the cartilage, which actually accelerates the underlying problems in the knee.

**Viscosupplementation:** This form of injection therapy involves replacing the natural fluid inside the knee joint with one of two polymers. It provides significant relief to a majority of patients who have mild to moderate osteoarthritis and some relief to more serious cases, though people in the bone-on-bone stage of the disease generally benefit little, if at all.

**Reparative surgery:** Surgeons often can do things short of knee replacement to try to repair the inside of the joint, including arthroscopic surgery, an outpatient procedure that involves making two or three small incisions around the knee. Tiny instruments are then inserted to repair tears or remove fragments of chipped bone and

cartilage.

Knee replacement: Costly and painful to recuperate from, this is the therapy of last resort, involving resurfacing of the bone and balancing of ligaments. But once accomplished, this open-knee surgery, which requires hospitalization, usually allows the patient to resume vigorous, if still limited, levels of physical activity.