

MAYO CLINIC HEALTH LETTER

Reliable Information for a Healthier Life

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Total knee replacement

Regaining mobility

The arthritis-related pain in your knees has steadily worsened over the years. Now, walking even a few blocks is almost unbearable, getting out of a chair causes you to wince, and your knees have a dull ache, even in bed.

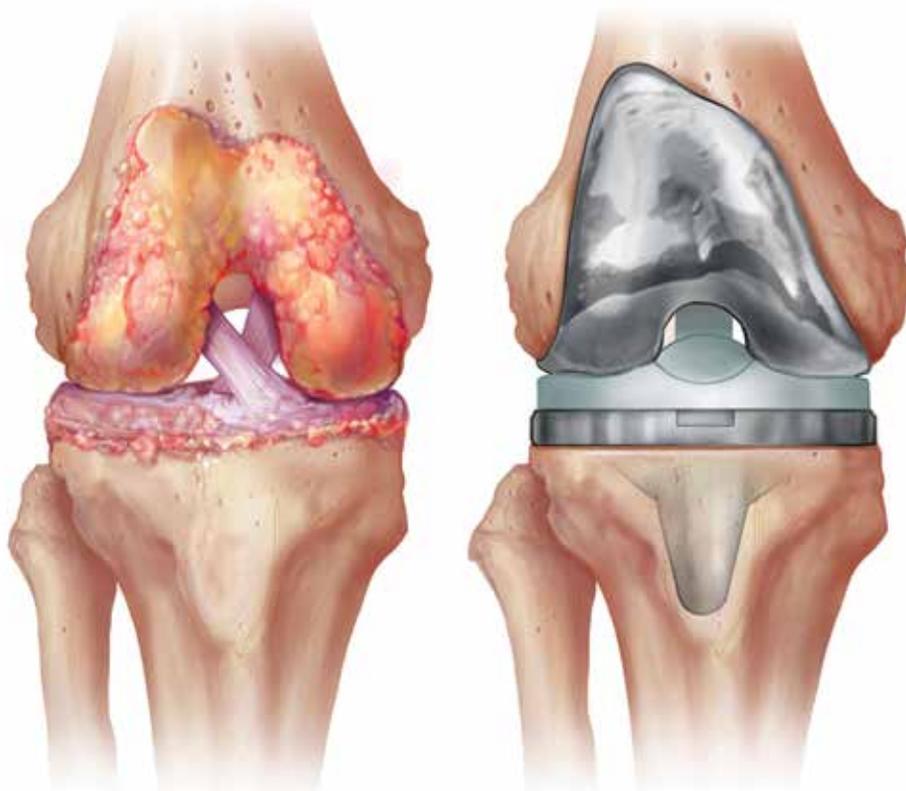
It's time to discuss your knee pain with your doctor. When it comes to knee arthritis, it's best to optimize non-surgical pain relief steps and get full mileage out of your natural knees.

However, knee replacement may be an important option when these pain-relieving options are no longer working.

About 700,000 knee replacements are performed in the U.S. each year — a number that's on the rise. If you're in reasonably good health, there's no age limit for knee replacement. Older adults in their 70s, 80s and beyond can successfully receive new knees.

Grinding away

Normally, joint surfaces in your knees are covered by a smooth, cushiony substance (cartilage). Two rounded pieces of thick, rubbery cartilage called the menisci provide cushioning of bone ends in the joint. A thin tissue lining



Osteoarthritis, left, is marked by a loss of cartilage and sometimes bone of the surface of the knee joint. Total knee replacement, right, can improve pain and function.

(synovium) also covers some joint surfaces and releases a fluid that lubricates the knee. This allows the ends of your leg bones — and the underside of your kneecap — to move against each other in a smooth, nearly frictionless manner.

Osteoarthritis, due to the wear and tear that occurs mostly with age, rheumatoid arthritis — which is immune related — and injury can all cause deterioration or deformity of the knee joint. Over 95 percent of total knee replacements are performed due to joint damage caused by osteoarthritis.

Pain with osteoarthritis often gradually worsens over time. The knee may begin to catch, lock or stick — or make creaking or grinding noises — with movement. Vigorous activity tends to cause symptoms to flare, and pain may also be worse when you try to move after sitting or resting. Walking, climbing stairs or getting out of a chair may become increasingly painful. Eventually, you may feel moderate to severe pain even at rest or at night.

There are several steps you can take to help ease pain or slow the progression of osteoarthritis. These steps include losing excess weight — even a fairly small amount can help — low-impact exercise, physical therapy, knee bracing, using a walking aid, taking non-narcotic pain-relieving medications, and receiving education and counseling related to joint care and pain management. Injections into the knee joint are sometimes recommended. These may include inflammation-suppressing corticosteroids, viscosupplementation — a molecule is injected that's part of the normal lubricating synovial fluid — or, in certain cases, stem cell injections in an attempt to stimulate the cartilage cells to repair themselves.

Time to act?

Total knee replacement may be considered when knee pain related to joint degeneration significantly impairs your day-to-day activities. It may be painful to walk even a few blocks, get out of chairs or climb stairs.

Before moving ahead, factors that are usually addressed include:

■ *Pinpointing the diagnosis* — An orthopedic surgeon will thoroughly review your health and the condition of your knee by taking a medical history, performing a physical exam, and reviewing imaging and other tests before making a recommendation for total knee replacement. Importantly, identification and management of any nonarthritis causes of knee pain could change the course of care.

■ *A review of nonsurgical care* — Managing knee arthritis with the tips above can sometimes provide enough relief to allow a return to fairly normal day-to-day activities. This could help you avoid or postpone surgery.

■ *Your overall health* — Total knee replacement is a major surgical procedure. Poor health may limit your surgical options. With less than optimal health, steps may need to be taken — such as getting diabetes under better control, stopping smoking or losing weight — to improve the balance of risk to benefit.

■ *Weighing benefits against surgical risks* — Complications related to knee replacement surgery are uncommon, but can include infection, blood clot development, knee stiffness or pain.

Planning for surgery

Preparation for surgery involves your surgeon determining the needs of the procedure, including the size and type of implant. There are many makes and models of implants and numerous surgical techniques. However, there isn't much evidence that one type is better than another, and what's best is typically related to your circumstances and your surgeon's experience.

The approach to anesthesia is another consideration. General anesthesia, in which you are put to sleep, is one option, as is sedation plus a nerve block that numbs your body from the waist down.

The surgery generally takes less than two hours. Damaged cartilage —

and some bone — is removed to prepare the joint surfaces for the new knee joint components. The new metal and plastic implants are positioned, aligned and installed to restore near frictionless joint movement. Before the incision is closed, the surgeon tests the new joint for smooth, even function and balance.

Rehab

Typically, you can expect to spend one to three nights in the hospital after surgery. Postoperative goals include:

■ Pain management, which is often achieved with a mix of knee injections, nerve blocks to numb the leg, and oral or intravenous pain medications.

■ Prevention of blood clots in the legs, which involves having you walk as soon as possible, using clot-reducing drugs and wearing compression devices on your lower legs to promote circulation.

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- Prevention of infection with antibiotics.
- Physical therapy, which may begin the day of surgery or the day after. This often includes exercises for strength, to improve range of motion, and to promote circulation.

After leaving the hospital, most people are able to go home. Others transition to a rehabilitation facility for a few more days. Either way, your care team will help you develop a plan for pain management and rehabilitation for the weeks of recovery ahead. This includes selecting an assistance device for walking — such as a walker, cane or crutches — that fits your body size and needs. These are typically used for four to eight weeks after surgery.

The rehabilitation plan will continue to focus on range of motion and strengthening. It also will include walking and a gradual return to daily tasks and activities. It's important that activity and exercise become part of your daily routine, but also that you take a gradual approach and let your new knee be your guide to how quickly you can progress.

Sticking with your rehabilitation plan typically allows for a return to most nonstrenuous tasks — such as light housework, driving and shopping — within three to six weeks. Your physical fitness level before surgery may influence how quickly you return to activities.

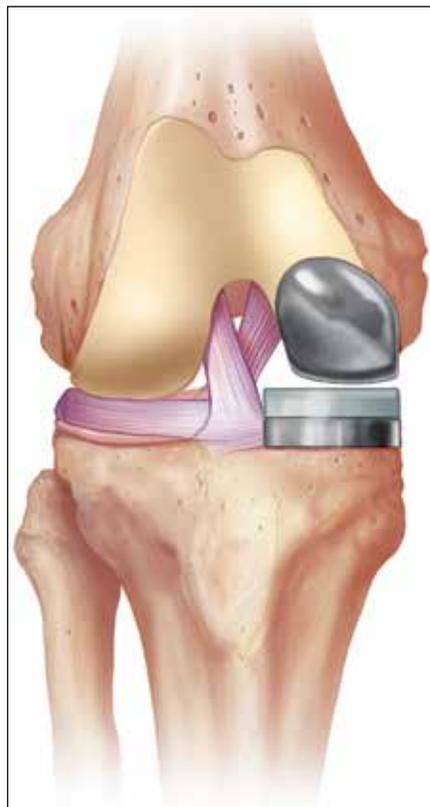
Back at it

Once you've recovered, you can resume a variety of low-impact activities, such as walking, swimming, playing golf, biking, yardwork and gardening. Higher impact activities such as jogging, tennis, or sports involving contact or jumping may not be suited for your new knee. Talk to your doctor about the best activities for you.

Infection around the implant is rare, but can occur even years after the surgery. Contact your doctor immediately if you have a fever higher than 100 F, shaking chills or increased knee

pain with both activity and rest. Preventive antibiotics are recommended before dental work for the first year after surgery, and longer in selected people.

Most knee replacements can be expected to last 15 to 20 years. People who are more active with moderately intense, low-impact activities don't have an increased risk of wearing out their implant early. In fact, limited evidence suggests that being active may reduce the risk of requiring a revision surgery to fix a worn implant. □



Partial knee replacement

When osteoarthritis damages only part of a knee, a partial knee replacement may be an option.

Partial knee replacement is a simpler surgery than total knee replacement, with a shorter recovery period. It can be an option for appropriately selected people. However, it may be associated with a higher risk of needing future revision surgery.

Health tips

Coming home after surgery

Returning home after surgery can be stressful, but taking action beforehand can make your recovery smoother. Here's what to do:

- *Arrange for extra hands* — You'll likely need help due to limited mobility, strength and endurance. Ask family members or friends to help with routine tasks. If no one is readily available, ask your medical team for a referral to a trained caregiver who can come to your home.

- *Create a recovery space* — Arrange a central living area on one floor with a stable chair or recliner that has a firm seat cushion and back, or a hospital bed if necessary. Include a footstool to elevate your legs. Have a small table or rolling cart nearby, so you can easily retrieve water, medications or other items. Consider wearing a fanny pack that can hold your phone or eyeglasses. Leave extra space around your chair or bed, so you can get in and out while using a walker, cane or crutches.

- *Declutter* — Remove from common walkways loose carpet, throw rugs, cords and any other objects that might trip you.

- *Make your bathroom user-friendly* — Consider getting a toilet-seat riser with arm rests. Install safety bars or a secure handrail. A nonskid chair or bench also can be useful.

Hospitals often have people specifically trained to help with home recovery after surgery. In some cases, they'll come to your home to do a safety assessment and make recommendations. □

News and our views

Advances in emergency stroke care

When it comes to emergency treatment of a suspected stroke, the saying “Time is brain” has become an important slogan. Prompt treatment of a stroke is critical, but advances in emergency care for certain kinds of strokes have extended the window of time when something can be done — while also decreasing the risk of disability after recovery.

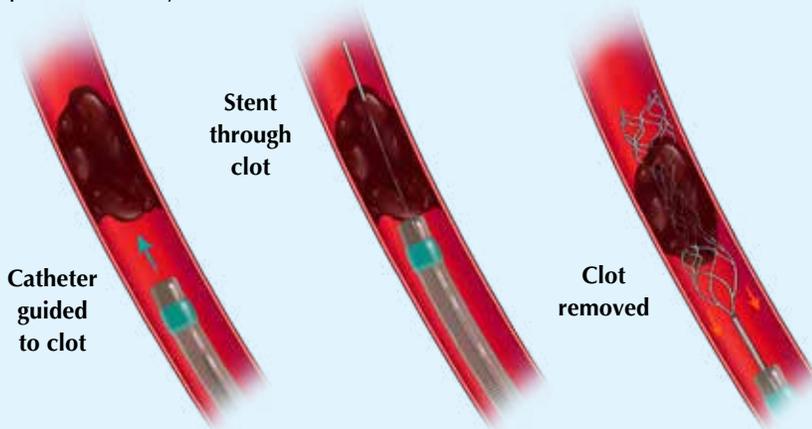
The most common cause of a stroke is a blood clot that’s blocking blood flow to part of the brain (ischemic stroke). This deprives brain cells of oxygen and nutrients, and within a few minutes of a blockage, brain cells start to die. Stroke signs and symptoms such as face drooping, arm weakness and speech difficulty often occur. If they do, it’s critical to call for immediate emergency medical help.

When a blood clot is the cause of your stroke, the first attempt at treatment is often a potent clot-dissolving drug called tissue plasminogen activator (TPA). This can be administered up to four and a half hours after the start of stroke symptoms, and the quicker it can be appropriately given, the better. Unfortunately, TPA drugs aren’t always able to clear clots, or the time window may have closed. Aside from this clotbuster, treatment options were limited until a few years ago.

Recent advances in the ability of doctors to guide a tube (catheter) to the site of a clot in a larger artery — and use a stent to clear away the clot to restore blood flow — have dramatically changed the acute management of strokes. TPA is still often administered as soon as possible in those with a stroke caused by a blood clot. If the clot is located in certain larger arteries leading to the brain, mechanical clot removal may be attempted alone or in addition to TPA. Mechanical clot removal can be safely completed within six hours of the start of stroke symptoms, but the sooner the better.

In five recently published studies, mechanical clot removal in select patients nearly doubled the odds that a person would recover from the stroke to the level of maintaining functional independence. Attempting mechanical clot removal didn’t add serious risk of complications.

Mayo Clinic doctors say this major advance in emergency stroke care is very helpful for larger clots in the larger arteries leading to the brain, which are often more resistant to the clot-dissolving drugs than are smaller clots in smaller arteries. The doctors also emphasize that suspected stroke symptoms must be treated as a medical emergency to preserve as much brain function as possible. Every second counts. □



Immunotherapy

Fighting cancer from within

What if a powerful tool against cancer lies right within your body? That’s the premise of immunotherapy, a broad term for cancer therapy that uses your body’s own immune system to fight cancer cells.

Your immune system continually conducts surveillance to guard against what it considers to be foreign substances. For example, when your immune system detects harmful bacteria or a virus, it mobilizes certain cells and produces specific proteins (antibodies) that attack and destroy the invaders.

Cancer cells are harmful, but your immune system doesn’t always recognize them as such. As a result, cancer cells can sometimes proliferate unrestrained. Scientists speculate that if your immune system could consistently recognize cancer as foreign, it might be able to fight cancer in the same way as it would fight an infection.

Fighting strategies

Ideally, your immune system would recognize and destroy cancer cells as foreign invaders. This process is hampered by the high degree of “self” antigens that camouflage cancer cells. “Self” antigens are proteins that signal to the immune system that the cells the proteins are attached to are normal or part of the self. In addition, developing cancers often evolve strategies that can blunt the immune response. Researchers are trying to dissect and exploit the complex interactions between cancer and the immune system in a way that, hopefully, will allow doctors to eventually target every type of cancer. Commonly explored areas so far include:

- *Nonspecific immune stimulation* — This approach seeks to produce a stronger response against cancer by enhancing the activity of specialized white blood cells called T cells.

The two agents most often used to stimulate T cells are interleukin-2 and interferon-alpha, which are both approved to treat melanoma — the most serious type of skin cancer — and renal cell carcinoma, a type of cancer that affects the kidneys. Other agents include lenalidomide (Revlimid) and pomalidomide (Pomalyst) for multiple myeloma and bacille Calmette-Guérin (BCG), derived from a type of bacteria, for bladder cancer.

■ **Immune checkpoint blockade** — T cells can generate powerful immune reactions, but they go through an elaborate signaling process before being fully unleashed. Normally, built-in checkpoints inhibit T cell activation in a way that minimizes damage to healthy tissue. However, cancer cells may impair the function of these checkpoints by blocking the activation of the immune system.

To counteract this, researchers have developed antibodies that can restore the normal function of immune checkpoints and allow T cells to respond to invading tumor cells.

An early example of an immune checkpoint blocker is the antibody ipilimumab (Yervoy), which blocks the activity of a key checkpoint protein known as cytotoxic T lymphocyte-associated protein 4 (CTLA4) and is approved to treat advanced melanoma.

More recently, checkpoint blockers targeting the proteins PD-L1 and PD-1 have been approved to treat a wide variety of cancers and can result in long-term control of cancers in about 1 in 5 people who receive them. Some examples include the drugs nivolumab (Opdivo), pembrolizumab (Keytruda), atezolizumab (Tecentriq), avelumab (Bavencio) and durvalumab (Imfinzi).

■ **Adoptive cell transfer** — In some cases, T cells recognize and target cancer cells as harmful, but there simply aren't enough T cells to slow down or destroy the growing tumor. Using an extracted sample of the T cells that have infiltrated the tumor, scientists select the ones with the strongest antigen

recognition capabilities and grow them in large numbers in a laboratory. These T cells are then activated and infused back into the bloodstream. The now massive amounts of activated T cells can help shrink or destroy the tumor.

The challenge lies in obtaining enough T cells from the tumor, which aren't always extractable and may not grow well in a lab. A way around this is to obtain T cells from a blood sample, where they're more plentiful. These peripheral blood T cells are genetically engineered to produce tumor-recognizing proteins called chimeric antigen receptors (CARs). CAR T cells are produced in the laboratory and then reinfused into the bloodstream. Once they find and attach themselves to the tumor cells, the T cells are activated to destroy the tumor cells.

Researchers are working on ways to more precisely target CAR T cells against cancer cells. For example, investigators are looking into the use of advanced genome-editing tools to fine-tune CAR T cells so that they become more efficient in recognizing and killing cancer cells.

■ **Vaccines** — The idea of a vaccine is to give your body a tiny, harmless taste of a particular disease, with the goal of training your immune cells to recognize and eliminate it if it should come around again. A cancer vaccine is different from the polio or measles vaccine in that it's designed to treat a disease you already have rather than prevent something you might get in the future. The vaccine exposes the immune system to the tumor antigens in a fresh context and provides an opportunity to re-educate immune cells to recognize the tumor antigen as harmful.

A cancer treatment vaccine called sipuleucel-T (Provenge) is approved to treat some forms of advanced prostate cancer. Treatment vaccines are being explored for other types of cancer too, such as brain, lung and breast cancers. The challenge with tailor-made vaccines is that they're typically complex and costly to produce.

■ **Oncolytic virus therapy** — This fairly recent type of immunotherapy uses genetically modified viruses to infect and kill cancer cells. As the cancer cells die, they release antigens, which activate the immune system to seek out and destroy all cancer cells expressing those same antigens. A genetically modified herpes simplex virus called talimogene laherparepvec (Imlygic) has been approved to treat melanoma that can't be surgically removed. Other therapeutic viruses also are being tested.

Predicting a response

So far, cancer immunotherapy seems to work well for some people, but not for others. A key issue is determining who might benefit the most from it. For example, is there a particular DNA signature that makes some people more responsive than others to immunotherapy? If so, what's that signature and how can we begin to customize cancer therapy to individuals so that each person is receiving the best treatment? Genetic analysis of cancer tissue samples can now sometimes provide quick and very specific answers to these questions.

Additionally, it's important to know that many of these drugs can be expensive and cause side effects. Common side effects include fatigue, rash and diarrhea. Also, unleashing the immune system can lead to unpredictable and sometimes even life-threatening effects. If a reaction occurs, the immunotherapy drug is discontinued and other medications, such as corticosteroids, may be used to suppress the immune system. Have a thorough discussion of possible side effects with your doctor before initiating immunotherapy. Also, it's wise to check with your insurance regarding coverage.

Many scientists think cancer immunotherapy represents a long but exciting road to a new understanding of how cancer develops and an opportunity to develop sophisticated tools to stop it in its tracks. □

Vitamin D

Do you need a supplement?

Are you getting enough vitamin D? Interest in vitamin D, traditionally known for its role in bone health, has risen rapidly in the past few years, fueled by a variety of studies that have associated lack of vitamin D with illnesses ranging from cancer to depression. Popular media outlets tell you to watch for evidence of vitamin D deficiency, such as muscle weakness, excessive crankiness and greater sensitivity to pain. Testing vitamin D levels has become more common.

So is it time to stock up on vitamin D supplements? Maybe, but maybe not. A close look at the science reveals that many of these recent reports have had mixed results and their conclusions need further review. According to the National Academy of Medicine, there's solid evidence to support benefits of vitamin D for bone health but not much else. And if you're in good health, more vitamin D may not be all that helpful and getting too much can be harmful.

Sunny D

Vitamin D is an essential nutrient that your body requires primarily to build strong bones. It does this by helping your body absorb and maintain adequate levels of two other nutrients important to bone health, calcium and phosphate. Vitamin D also appears to influence insulin production and your immune system.

You get most of your vitamin D from sunlight. When ultraviolet (UV) rays hit your skin — particularly midday — it triggers production of vitamin D. People in climates with more sunlight tend to get more exposure than do those in climates with less sunlight.

Certain foods — fortified foods, such as milk and cereal, and fatty fish, such as salmon, tuna and mackerel — also provide vitamin D. Chemical

reactions in your liver and kidneys transform vitamin D into forms that your body can use.

In general, adults should consume 600 international units (IU) of vitamin D a day. That goes up to 800 IU a day for those older than 70. National survey data indicate that most Americans don't get enough vitamin D through their diets. However, the data also indicate that average blood levels of vitamin D are above what's considered necessary for good bone health for most people. This implies that the majority of American adults get enough vitamin D, most likely through sun exposure.

Painful deficiency

Severe and prolonged vitamin D deficiency is known to cause bone mineralization disorders such as rickets in children and osteomalacia in adults. Conditions such as these can lead to soft bones, aching muscles, painful movement and fractures. Vitamin D deficiency may also contribute to osteoporosis.

Although numerous studies have reported results associating vitamin D deficiency with various other diseases and conditions — such as fatigue, depression, chronic pain, heart disease, autoimmune disorders, infections, metabolic issues and cancer — clinical trials of vitamin D supplements in people with these conditions have generally failed to show benefit. This implies that a lack of vitamin D probably isn't causing these conditions. Some experts argue that rather than being a cause of these kinds of illnesses, vitamin D deficiency may be a biological marker for them, signaling the presence of inflammatory processes related to the disease or condition.

Who's at risk?

Adults who may not get enough vitamin D generally fail to do so due to one or more of the following reasons:

- **Chronic condition** — Conditions that affect your absorption or processing of vitamin D can affect circulating levels of the vitamin. For example,

having conditions such as inflammatory bowel disease or celiac disease or having had bariatric surgery can affect your intestine's ability to absorb vitamin D. Obesity appears to drive down, or perhaps dilute, levels of circulating vitamin D. Chronic kidney or liver problems can interfere with the conversion of vitamin D into its active circulating forms, as can certain drugs such as anticonvulsants and glucocorticoids.

- **Reduced skin synthesis** — People with darker skin are at greater risk of vitamin D deficiency because greater amounts of melanin in the skin reduce the skin's ability to produce vitamin D from sunlight. Aging also decreases the efficiency of vitamin D synthesis. Sunscreen, clothing and other UV protective measures that block skin's exposure to the sun help prevent skin cancer but also reduce production of vitamin D.

- **Limited sun exposure** — People who spend most of their time indoors generally have low levels of vitamin D. The amount of sun exposure needed for adequate vitamin D production is uncertain, but most estimates are no more than 15 minutes a day between 10 a.m. and 3 p.m., three times a week. However, this must be balanced against your risk of skin cancer.

Do you need a supplement?

Most healthy American adults have adequate levels of vitamin D. But if you fall into a risk category, talk to your doctor about whether you need a supplement. Generally, a blood test isn't necessary, because taking the recommended amount of vitamin D as a supplement will ensure adequate levels in most people. Even 600 IU a day will correct a deficiency fairly quickly.

However, taking too much vitamin D — such as 10,000 IU daily for weeks to months — can overly increase your absorption of calcium, leading to problems such as kidney stones and damage to your heart and blood vessels. The National Academy of Medicine recommends an upper limit of 4,000 IU a day, to be safe. □

Headaches and spinal fluid leaks

An emerging problem

You've had headaches for years. You usually start the day fine, but by lunchtime, the pressure-like pain has begun and is growing in intensity. You've sought out plenty of treatment options, but nothing has truly helped. At this point, you're trying to live with the pain as best you can by taking medications and reducing stress.

Headaches come in a variety of types — such as migraine, tension or cluster headaches — with a variety of characteristics. A lesser known cause of headache pain occurs with low levels of cerebrospinal fluid — a fluid that surrounds, cushions and protects the brain and spinal cord. Low fluid levels can be caused by a temporary leak that occurs when the membrane holding the fluid (dura) is punctured, such as after a lumbar puncture, during surgery or with an epidural injection to numb part of the body. But cerebrospinal fluid (CSF) leaks also can occur spontaneously, typically along the spinal column, and aren't always temporary.

Doctors have known about spontaneous CSF leaks for some time. However, modern imaging techniques and attentive research have changed doctors' understanding of the problem. A spontaneous cerebrospinal fluid leak is recognized as a more common cause of headaches than previously thought.

Brain sag

Cerebrospinal fluid not only protects the brain, but the pressure of the fluid inside the dura also helps keep the brain suspended in place. This is similar to the way that a yolk is suspended in an egg white.

When cerebrospinal fluid leaks from the dura and fluid volume

decreases, the brain may sag, pulling on pain-sensitive structures that also support the brain. This is believed to be the main mechanism that causes the headache pain, which can range from a dull ache to severe pain.

The classic characteristic of CSF leak headaches is that they occur when you're upright — often within a few minutes — and are relieved when you lie down.

However, recent research and diagnostic technology has revealed that this is far from the entire story.

CSF leak headaches also may cause a variety of sometimes contradictory symptoms:

- Pain may become a lingering daily headache, or it may not obviously correspond to being upright or lying down.
- Rarely, a headache may start in a sudden, thunderclap manner that's similar to what occurs with a stroke caused by a burst blood vessel.
- With slower leaks, a headache may be absent in the morning then emerge in the late morning or early afternoon after you have been up and about, and intensify until you lie flat again. Intermittent headaches, which may be due to intermittent leaking, also can occur.
- Pain similar to the pain of a pressure headache can occur on both sides of the head, but can sometimes be throbbing and occur only on one side of the head. The headaches can occur in the front or back of the head, or can be felt all over the head. Focused pain can become more widespread as the day goes on.
- Bearing down, such as with coughing or straining, can trigger or aggravate the pain.

Other symptoms related to brain or spinal cord sagging may include neck or back pain, nausea or dizziness, ringing in the ears (tinnitus), and hearing or vision changes. People who are double-jointed or who have very stretchy skin — suggestive of a disorder of connective tissues — may have an increased risk of a CSF leak and low-pressure headaches.

Pinpointing

CSF leak headaches appear to represent a fairly small percentage of all headaches. Also, not all headaches that occur when you're upright are CSF leak headaches. In addition, the recognized scope of a CSF leak as a possible cause of headaches is relatively new, and may not be considered during diagnosis of headache pain.

A number of tests are aimed at confirming the presence of a leak or pinpoint its location. The search starts with an MRI with intravenous contrast dye. A test called a myelogram, which involves injecting a contrast into your cerebrospinal fluid, is often necessary to find the precise site of the leak, though often treatment can begin even without knowing the site of the leak.

If a CSF leak is diagnosed, initial conservative therapies — such as bed rest and increased fluid and caffeine intake — are given a trial run, with many people recovering completely.

If conservative therapies aren't effective, the recommended treatment is often an epidural blood patch. This involves injecting your own blood — or a mixture of your blood and a special type of glue — into the space just outside the dura where the leak is believed to be. The injection has the immediate effect of increasing the pressure of your cerebrospinal fluid, with the hoped-for add-on effect of sealing the leak.

With a blood patch, there's a reasonably good chance of the leak being sealed and achieving long-term relief. However, it's common to need more than one blood patch, and some people notice cumulative improvement in symptoms, even if full relief isn't achieved. If this proves ineffective, an operation to stitch shut or seal the leak may be an option.

Unfortunately, a small number of people with CSF leak headaches don't respond to treatment. Most people either get better with therapy or achieve enough relief that the headaches are manageable and they are able to do most of their usual activities. □

Second opinion

Q I've heard a stubbed toe can lead to gangrene. Is that true? What are the signs of gangrene, and how can it be avoided?

A Gangrene — which refers to tissue death caused by a severe shortage of blood supply — occurs in lower extremities, such as the toes, more commonly than other parts of the body. It tends to happen more often among people with peripheral artery disease (PAD), a common circulatory problem in which narrowed arteries reduce blood flow to the limbs. People with diabetes and PAD are especially vulnerable to complications such as gangrene because — in addition to poor blood circulation — they often have decreased sensation in their feet due to nerve damage. If an injured toe goes unnoticed and blood supply is inadequate to help heal the wound, tissue death may occur.

Gangrenous tissue typically becomes discolored, ranging from pale red or brown to black and purplish. The skin looks dry, hard and shriveled, and there's a clear line separating the dead tissue from healthy tissue. If an infection is present, the area may look swollen and ooze and blister. There's often a foul-smelling odor.

These signs and symptoms require immediate care, as they can quickly lead to loss of limbs and even death — at times quickly — due to sepsis. Treatment may involve taking antibiotics for infection, re-establishing blood flow to the area and removing the dead tissue.

See a doctor if you have leg pain or numbness, sores that won't heal on your feet or legs, or changes in the

color of the skin around your legs or feet. PAD often accompanies diabetes and coronary artery disease, and is strongly associated with smoking.

If you have diabetes, maintain careful control of your blood glucose level and take good care of your feet. Always wear protective footwear that properly accommodates your feet. Do a daily check for redness, calluses and wounds. If you find any of these problems, treat your feet promptly and adjust your activity. If you're a smoker, stop. Regular exercise and a healthy diet can keep PAD, diabetes and heart disease in check, thus minimizing your risk.

Q My wife has developed some cognitive impairment, and I'm concerned that one or more of the numerous drugs she's taking might be making it worse. Can drugs do that?

A Yes, there are many drugs that can affect cognitive function in older adults with mild cognitive impairment or a form of dementia such as Alzheimer's disease. In addition, some drugs can affect cognitive function in older adults who don't have pre-existing cognitive impairment.

Drugs with a sedative effect — such as opioid pain medication or sleeping pills, particularly those that are longer acting or in the benzodiazepine class — can cause confusion and impair mobility and cognitive function.

Drugs that have an anticholinergic (an-tee-koh-lin-UR-jik) effect also can be a problem. These drugs can affect a diverse range of involuntary functions including tear and saliva production, digestion, urination, mucus secretion,

and slowing of the heart rate. In addition, there's a well-documented link between anticholinergic use and cognitive changes such as memory impairment or confusion in older adults.

Major categories of drugs that commonly have anticholinergic effects include tricyclic antidepressants, anti-nausea medications, certain anti-tremor drugs used with Parkinson's disease, benzodiazepines used for anxiety or sleep, older antihistamines — which are found in nonprescription medications — muscle relaxants and drugs for urinary incontinence and some anti-diarrheal drugs.

The best way to check for drugs that may be affecting cognition is to have a thorough discussion about drugs you take with your doctor or pharmacist. □

Have a question or comment?

We appreciate every letter sent to Second Opinion but cannot publish an answer to each question or respond to requests for consultation on individual medical conditions. Editorial comments can be directed to:

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