



DIAGNOSING AND TREATING COMPLEX REGIONAL PAIN SYNDROME

It's unknown why this autoimmune disease strikes some and not others. And, while there is no cure, there are many treatments to reduce the pain the disease causes.

By Ronale Tucker Rhodes, MS

When Deborah Norris was a young mother, she and her husband and two kids were active; they went “biking, hiking, to the beach, skating at the local roller rink and played chase.” But, in 1992, after she had arthroscopic surgery on her knee, Deborah says she felt “the worst pain I’ve ever experienced.” It began after a second surgery to clean out what her surgeon thought was an infection that occurred after the first. While recovering, she was unable to tolerate anyone touching her knee or that side of her leg. “I was swollen from my knee to my ankle, and the skin was so shiny, you could see your reflection it,” explains Deborah. “It was either a bright red, or at times, it changed to a purplish blue. Physical therapy kept my mobility to a point, but I still needed a cane to walk. Gone were my carefree hiking days! At that point, I was spending most of my days flat on my back with my leg raised to help the swelling or doing exercises for mobility.” Fortunately, after only three months, a doctor

diagnosed Deborah with reflex sympathetic dystrophy, known today as complex regional pain syndrome (CRPS) — an early diagnosis for this disease. Unfortunately, there is no cure.

What Is CRPS?

CRPS is an uncommon form of chronic pain in which high levels of nerve impulses are sent to an affected site, usually an arm or a leg.^{1,2} What causes CRPS isn’t clearly understood, but it typically develops after a forceful trauma to an arm or a leg (such as a crush injury, fracture or amputation), surgery, stroke or heart attacks, infections and even emotional stress.³ And, it is believed that CRPS does not have a single cause, but instead results from multiple causes that produce similar symptoms.² Why these injuries can trigger CRPS is also not well understood. One theory is that it may be due to a dysfunctional interaction between an individual’s central and peripheral

nervous systems and inappropriate inflammatory responses (an immune system correlation), thus disrupting the healing process.³ What is known is that the pain is out of proportion to the severity of the initial injury, if any.¹ Knowing this, it is believed there are two ways to reduce the risk of developing CRPS. First, studies have shown that those taking vitamin C after a wrist fracture have a lower risk of CRPS than those who don't take vitamin C. Second, some research suggests that people who get out of bed and walk around soon after a stroke (early mobilization) lower their risk of CRPS.⁴

There are two similar types of CRPS, called CRPS-I and CRPS-II (previously known as causalgia), both of which have the same symptoms and treatments. Individuals with confirmed nerve injuries have CRPS-II, while individuals without confirmed nerve injury are classified as having CRPS-I.⁵ About 90 percent of patients with CRPS have CRPS-I.³

CRPS can strike anyone at any age, and while it affects both men and women, it is more common in women. The average age of individuals with the disease is approximately 40. And, while CRPS is rare in the elderly, it is not uncommon in children, although not before age 5 and only very rarely before age 10.⁴

The jury is out on how common CRPS is in the general population. To date, there have been only two studies conducted. The first, conducted by Sandroni et al. in 2003, reported that CRPS-I is rare with only 5.46 new cases per 100,000 annually that were associated with frequent spontaneous resolution. The conclusions of this study were controversial, however, because 90 percent of the individuals in the study received physical therapy and nearly half received sympathetic blocks and pharmacological intervention. The second study was conducted by de Mos et al. in 2007. When based on clinical diagnoses confirmed by the original treating physicians, this study reported the incidence was 26.2 new cases per 100,000 annually, a figure that is 4.2 times higher than the first study. And, even when restricted to those cases in which detailed specialist evaluation data were available to make independent diagnoses, this second study reported an incidence of 16.8 new cases per 100,000 annually, nearly three times higher than the first study.⁶

Symptoms of CRPS

The main symptom of CRPS is prolonged and intense pain that, in some cases, may be constant, and in others, may come and go. The pain may consist of continuous burning or throbbing; sensitivity to touch or cold; swelling; changes in skin temperature, color and texture; changes in

hair and nail growth; joint stiffness, swelling and damage; muscle spasms, weakness and loss; and decreased ability to move an affected body part. CRPS also can spread from one part of the body to another.⁷ This is the case for Deborah. Her pain began in her left leg on which she had knee surgery, but now it has spread to her right leg and hand and to the right side of her face.

Fortunately for Deborah, she was diagnosed in three short months. This is not the case for most, which can cause complications. Not diagnosing and treating CRPS early may cause the disease to progress to more disabling signs and symptoms, including tissue wasting (atrophy) and muscle tightening (contracture).⁸

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Diagnosing CRPS

CRPS can't be diagnosed with any test. However, testing is important to rule out the cause of pain from other conditions such as arthritis syndromes, Lyme disease, generalized muscle diseases, a clotted vein or small nerve fiber polyneuropathies, all of which require different treatment.⁵ Generally, doctors will diagnose CRPS based on a physical examination that reveals a higher-than-expected amount of pain from an injury, a change in appearance of an affected area and no other cause of pain or altered appearance. Doctors will also look at the patient's medical history of earlier injury to affected areas.² In addition, some tests can provide clues as to whether a person has CRPS. These include a bone scan that can help detect bone changes, sympathetic nervous system tests such as thermography that measures the skin temperature and blood flow of affected limbs, an MRI that can show a number of tissue changes, and X-rays that can reveal a loss of minerals from bones that often occurs later in the stages of this disease.⁹ CRPS is often associated with excess bone resorption, a process in which certain cells break down the bone and release calcium into the blood.⁵

Treating CRPS

There are many different treatments for CRPS that work for some and don't work for others. Rehabilitation therapy is often used to help keep a patient's painful body part moving to improve blood flow and lessen the circulatory symptoms, as well as to improve flexibility, strength and function. It can also help to treat the secondary profound psychological symptoms, including depression, anxiety or post-traumatic stress disorder, that are associated with CRPS and that heighten the perception of pain.⁵ Before Deborah found a physician who prescribed medications to lessen her pain, she said there were times when she felt she understood why people commit suicide. "I knew I couldn't because I love my husband and children too much to leave them like that, but when you're the only one awake at 2:00 a.m., and your pain is intolerable, you get quite depressed," she explained.

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While there are no drugs that are specifically approved to treat CRPS, there are several that have been shown to be effective, particularly when used in the early stage of the disease. These include non-steroidal anti-inflammatory drugs (aspirin, ibuprofen and naproxen), corticosteroids (prednisolone and methylprednisolone) in the early stages, drugs initially developed to treat seizures or depression, botulinum toxin injections, opioids (oxycontin, morphine, hydrocodone, fentanyl and vicodin), N-methyl-D-aspartate receptor antagonists (dextromethorphan and ketamine), nasal calcitonin for deep bone pain and topical local anesthetic creams and patches.⁵ Deborah lived in extreme pain from CRPS for five years before she located a doctor who was willing to prescribe pain medication, which allowed her to go back to teaching elementary school full time for 10 years. Of course, there were still bad times for which she had to find coping mechanisms. But, her doctor also prescribed an antidepressant, which greatly helped her.

Other treatments that can help to relieve the pain associated with CRPS include sympathetic nerve blocks that provide temporary pain relief; spinal cord stimulation to provide a tingling sensation in the painful area; neurostimulation delivered near injured nerves, outside the membranes of

the brain and within the parts of the brain that control pain (a recent option involves the use of magnetic currents applied externally to the brain called repetitive transcranial magnetic stimulation); intrathecal drug pumps that deliver pain-relieving medications, typically opioids and local anesthetic agents such as clonidine and baclofen, directly into the fluid that bathes the spinal cord; and surgical sympathectomy to destroy some of the nerves.⁵ While surgical sympathectomy is somewhat controversial, Deborah undergoes the procedure approximately every six months, which eliminates the pain in her face. "It has to be done about every six months because nerves have a tendency to grow back," explains Deborah. "But, those months with no facial pain are like heaven."

There also are emerging treatments for CRPS, including low doses of ketamine given intravenously for several days to either reduce substantially or eliminate the chronic pain, hyperbaric oxygen to deliver more oxygen to the body's organs and tissues, and immune globulin (IG) infusions. In a small trial in Great Britain, 13 patients with CRPS who did not respond well to other treatments and who were given low-dose intravenous IG for six months to 30 months had a greater decrease in pain scores than those receiving saline during the following 14 days after infusion. Deborah, who is also diagnosed with common variable immune deficiency, was prescribed subcutaneous IG infusions weekly to see if it would reduce her pain. "At first I thought it did," said Deborah. "But, now, I'm not so sure. The one thing it does do, though, is make the rest of my body feel better and eliminate all the infections I get so easily."

Living with CRPS

Living day to day with pain is difficult enough, often affecting the mental health of patients with CRPS, which is why it's often a good idea for those with CRPS to see a psychologist or other professional to help them put things in perspective. Support groups also can help by sharing experiences and feelings with other people with CRPS. Add to that the difficulty of making family and friends understand what they're experiencing, and living with CRPS can seem almost unbearable. Deborah knows this all too well. Her limbs are no longer swollen, so she looks normal, but she is still in a lot of pain. "Usually when people ask how I am, I lie and say 'fine' because they won't understand the truth," explains Deborah. "And, it's hard to blame them. You might be screaming inside, but if people don't have the experience of a debilitating disease in their own life, they can't relate." Her advice: It helps to have a

significant person in your life who understands your illness and believes you. I'm very fortunate to have a great, compassionate husband who's also my best friend. My children (now 31 and 34) get it, but still at times underestimate the amount of pain I'm in. But, my husband knows just by reading my body signs — the curl of my fingers, the constant wiggling of my feet. That person makes the biggest difference in how you're able to cope. Being understood is so important!"

Deborah also offers some additional advice. First, patients should find a doctor who is not suspicious of their pain. Instead, they should look for a doctor who is understanding and willing to be on their team. Second, they should find an outside interest or a hobby that they can focus on. "I've been very lucky because I'm a watercolor artist, and when I paint, I can 'lose' myself and set my pain aside," she says. "It's sort of like meditating." Deborah also has other interests, including a puppy to train and care for. "I got a puppy when I found it necessary to retire from teaching six years ago," adds Deborah. "My dad had just died, and I felt sorry for myself sitting at home with no job to make demands on me and command my focus, and [I was] in pain. My Maltipoo puppy, Daisy, took time to train, to care for and has become a therapy dog. Now, she and I are able to go to facilities for the elderly and other places to visit people, or to the library where children read to her. Being active not only takes your mind off of your pain, it helps you to personally feel like you are valuable."

Research in Progress

While there are significant discrepancies in CRPS incidence, applying the most conservative incidence figures in the study by de Mos et al. to current U.S. census bureau population estimates, it is expected that there will be more than 50,000 new cases of CRPS-I annually. And, although that number on a percentage basis does not indicate that CRPS is common in the general population, it does represent a substantial number of patients who will develop CRPS every year with significant quality of life consequences. This, then, demonstrates the importance of continued epidemiological investigations, as well as continued research to more aggressively treat the disease and lessen its symptoms.

Researchers at the National Institute of Neurological Disorders and Stroke, part of the National Institutes of Health, are involved in many different studies concerning CRPS. Using an animal model of the disorder, they hope to better understand the neuroinflammatory basis of CRPS

and to identify the relevant inflammatory signaling pathways that lead to the development of post-traumatic CRPS such as what occurs following limb trauma when having the limb placed in a cast. They also hope to identify specific cellular and molecular changes in sensory neurons following peripheral nerve injury to better understand the processes that underlie neuroplasticity (the brain's ability to reorganize or form new nerve connections and pathways following injury or death of nerve cells). This could provide targets for new drug therapies that could improve recovery following regeneration. Last, they are studying children with CRPS to investigate neuroplasticity and the biological processes that cause CRPS to occur, with the hope of developing more effective therapies and accelerated recoveries for both adults and children.⁵

For now, however, life has to go on for CRPS patients despite the pain. "I'm 21 years older than when I found out about my disease," says Deborah. "But, I'm also 21 years wiser. I use my time better even though it takes me longer to do everything. Although I know life would be great if I didn't have pain or need to do weekly three-plus-hour infusions, I'm perfectly happy being me. And, for those times that get me down, I have skills to help me climb right back out!" ■

RONALE TUCKER RHODES, MS, is the editor of *IG Living magazine*.

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