

SARCOIDOSIS AND THE NERVOUS SYSTEM



FOUNDATION FOR
SARCOIDOSIS RESEARCH

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What Is Neurosarcoidosis?

Sarcoidosis is an inflammatory disease that can affect almost any organ in the body. It causes heightened immunity, which means that a person's immune system, which normally protects the body from infection and disease, overreacts and damages the body's own tissues. The classic feature of sarcoidosis is the formation of granulomas, microscopic clumps of inflammatory cells that group together (and look like granules, hence the name). When too many of these clumps form in an organ they can interfere with how that organ functions.

In the United States, sarcoidosis most commonly affects people's lungs, but the disease can also affect many other organs and systems. (In Japan, for example, sarcoidosis frequently affects the heart.) One of the systems it can affect is the nervous system, which includes the brain, spinal cord, and nerves throughout the body. When sarcoidosis affects this system, it is called neurosarcoidosis. (For more information about

sarcoidosis in general, request the Foundation for Sarcoidosis Research brochure, **Sarcoidosis and the Body**. See **For More Information**, page 15, for contact information.)

Researchers think that neurosarcoidosis affects between 5 and 10 percent, maybe even 15 percent, of sarcoidosis patients. (See **Who Gets Neurosarcoidosis?** page 5) Its symptoms can include seizures, behavior and mood changes, vision problems, and paralysis. Other nervous system diseases can cause these symptoms, too, so having them doesn't necessarily mean that you have neurosarcoidosis. If you have been having nervous system problems, see your doctor. They can be serious. If you do have neurosarcoidosis, it is best to diagnose and treat it early.

In many cases, sarcoidosis will go away on its own within several years. Some people with neurosarcoidosis will recover completely. In other people, sarcoidosis and related nervous system symptoms are chronic, lasting a long time or even a lifetime.

What Nervous System Problems Are Caused by Sarcoidosis?

Experts refer to the nervous system as having two parts: the central nervous system (CNS) and the peripheral nervous system (PNS). This distinction makes it easier to think about how the nervous system functions. The CNS is your brain and spinal cord. It is your body's operations center, supervising and coordinating the actions of the rest of your body. The nerves outside the CNS are the peripheral nervous system (PNS). These nerves relay instructions and information between your brain and your muscles, skin, blood vessels,

and organs. Together, the CNS and the PNS control muscle movement, such as walking, talking, and swallowing, as well as involuntary actions, such as the beating of your heart or the production of hormones that help you digest food.

Although many people with neurosarcoidosis notice symptoms, some people will feel nothing. Nervous system symptoms can come on all at once or develop gradually.

Neurosarcoidosis symptoms might include

- *facial palsy*, sometimes called Bell's palsy, which is the most common nervous system symptom. It means that you have drooping and/or paralysis of the muscles on one side of your face. Although the palsy can be temporary, it requires immediate evaluation and possibly treatment to avoid long-term complications.
- *headaches*
- *eye pain and redness*
- *blurry or double vision*
- *blindness*
- *vomiting*
- *weakness, numbness, tingling, and/or pain in the face, arms, and/or legs*
- *arm and/or leg paralysis*
- *seizures*, which are usually a sign of the chronic type of neurosarcoidosis
- *behavior and mood changes, irritability, memory loss, and hallucinations*, which are rare

The problems caused by neurosarcoidosis can include

- *nerve inflammation and damage*, particularly of the cranial nerves. These are 12 important pairs of nerves that start at the bottom of your brain (rather than at your spinal cord, like other nerves). Some cranial nerves control muscles or internal organs. Others deliver sensory information, such as visual input, to your brain. Nerve inflammation and damage leads to many of the symptoms described in the list above.
- *peripheral neuropathy*, a condition that impairs your nerves' ability to transmit messages between your brain and spinal cord and the rest of your body. It can cause the weakness and numbness described in the list of symptoms above. Peripheral neuropathy tends to occur in more advanced cases and is a sign of chronic neurosarcoidosis.
- *masses of granulomas in the meninges, or, more rarely, in the brain*, which can cause some of the symptoms described in the list above, such as headaches, vision problems, and muscle weakness. These masses can also cause
 - *meningitis*, which means inflammation of the *meninges*, the membranes that surround your brain and spinal cord. Chronic meningitis can be a sign of the chronic type of neurosarcoidosis.
 - *hydrocephalus*, the term for excess cerebrospinal fluid in your skull. It might occur with or after meningitis.
 - *neuroendocrine disorders*, which affect how your nervous and endocrine systems interact. (The endocrine system

makes and secretes hormones.) When sarcoidosis damages an area at the base of your brain called the hypothalamus, it can lead to neuroendocrine disorders, such as hypopituitarism (an underactive pituitary gland) and diabetes insipidus (an uncommon condition in which your kidneys are unable to conserve water).

- *coma*, which is rare

Who Gets Neurosarcoidosis?

Like sarcoidosis in general, neurosarcoidosis can affect men and women of any age and race. Sarcoidosis usually strikes between the ages of 20 and 40, but research suggests that neurosarcoidosis symptoms might appear later. Experts can't predict who is at risk specifically for neurosarcoidosis, but we know that in the United States, sarcoidosis overall is most common in African Americans and people of European – particularly Scandinavian – descent.

No one knows what causes sarcoidosis or neurosarcoidosis. Some research suggests that bacteria, viruses, chemicals, or a combination of factors might trigger sarcoidosis, especially in people who are genetically predisposed to it. Researchers don't know why some sarcoidosis patients develop neurosarcoidosis symptoms and others don't.

How Do Doctors Diagnose Neurosarcoidosis?

Nervous system symptoms are not usually the first or only sign of sarcoidosis. If you already know that you have sarcoidosis when you start having nervous system symptoms, that's a big clue that

you should talk to your doctor about screening for neurosarcoidosis. Sometimes neurosarcoidosis is the only sign of sarcoidosis, however. When this is the case, it's hard to diagnose. You will probably need to undergo a lot of testing and see some specialists before your doctor will be able to rule out other conditions.

Early diagnosis and treatment, if you need treatment, are the keys to preventing the potentially serious effects of neurosarcoidosis. Only a few people who have nervous system symptoms are at risk for the most serious effects, such as paralysis or blindness, but these *are* risks. Some primary care doctors can diagnose and treat sarcoidosis, but it is probably best to work with a sarcoidosis specialist, a neurologist, or both to get the screening you need for nervous system complications. An ophthalmologist or neuro-ophthalmologist might be helpful if you have vision or eye problems related to neurosarcoidosis.

There is no one test that a doctor can use to diagnose neurosarcoidosis, and there are no official guidelines that tell doctors how to screen patients for the condition. Most of the tests your doctor might use to check for neurosarcoidosis are described below. Although these tests are not specific for neurosarcoidosis, the ones that your doctor recommends, taken together, can give a more complete picture of your risk for nervous system complications.

Imaging Technology

A number of sophisticated imaging tools are available today that can detect nerve inflammation and damage. Most of the

technologies a doctor might use to get a better look at your brain, meninges, and spinal cord are described below in alphabetical order.

Computed tomography: Computed tomography (CT) draws on x-ray technology that you are probably already familiar with. A traditional x-ray examination uses a stationary machine that points radiation beams at part of your body to produce a two-dimensional image. CT scanning also uses x-rays, but the machine rotates around you. A special computer then assembles the resulting x-ray image “slices” into a highly detailed picture of the inside of your body. Whereas a traditional x-ray image shows only bones clearly, a CT scan can show organs, glands, tissues, tumors, and blood vessels, as well. The amount of radiation exposure you receive from x-rays during a CT scan is generally considered safe. During some tests the doctor will give you a contrast agent, which is a liquid that makes parts of your body show up better in the image.

Gallium scans: A gallium scan is a type of nuclear imaging. It’s a nuclear technology because you are injected with a small amount of a radioactive tracer, in this case gallium. A special computer and a special camera that detects radioactivity will create a picture of the way your body absorbs the gallium. Places where your blood flow pattern is normal will look different from places where your blood flow is enhanced. And enhanced blood flow is often a sign of inflammation. Therefore, the parts of your body affected by sarcoidosis will tend to appear “lit up.” Gallium is radioactive, and you are exposed to a higher dosage than you would receive during

most standard x-ray examinations. The scans are generally considered safe, though, and side effects are rare.

Magnetic resonance imaging: Like CT scanning, magnetic resonance imaging (MRI) produces highly detailed pictures of your brain and other organs. Unlike CT scanning, however, MRI technology uses radio frequencies and a magnetic field, not radioactivity, to produce these images. Before some scans, the doctor might give you an injection of a contrast agent called gadolinium, which makes abnormal tissue stand out more clearly against normal tissue. It has been particularly helpful in detecting nervous system abnormalities in people who have neurosarcoidosis. Doctors also use MRI to assess your response to treatment. Anyone with a heart pacemaker or an automatic implantable defibrillator cannot undergo MRI scanning due to the strong magnetic field involved.

Positron Emission Tomography: Positron emission tomography (PET) scanning detects changes in the body's chemical activities. As with a gallium scan, you are injected with a radioactive tracer, in this case a kind of fluoride, before the test. The tracer travels through your bloodstream, accumulating in areas that show increased chemical activity. Since areas of inflammation often show such activity, PET scanning can help doctors determine whether an organ is healthy or inflamed. It can also help your doctor identify a good spot to biopsy if an organ biopsy seems necessary.

Laboratory Tests

Your doctor might want to perform laboratory tests on a sample of your cerebrospinal fluid, which is the fluid that surrounds your brain and spinal cord. In about 80% of people with neurosarcoidosis, this fluid contains elevated protein levels and higher-than-normal numbers of white blood cells called lymphocytes. These findings are not specific to neurosarcoidosis. They are just clues that can help your doctor when combined with other findings. Your doctor might also check your cerebrospinal fluid to assess whether you have tuberculosis, fungal infections, cancer, or multiple sclerosis.

The procedure that doctors use to get a sample of cerebrospinal fluid is called a lumbar puncture, or a spinal tap. The procedure is usually low risk, although it can be briefly uncomfortable and some people get headaches afterwards.

Biopsies

A biopsy that shows evidence of granulomas in any of your tissues is probably the best indication that you have sarcoidosis. Only rarely do doctors recommend a biopsy of your brain or spinal cord to check for neurosarcoidosis. These procedures are more invasive, with a greater risk of complications, than most other organ biopsies. Doctors usually prefer to rely on nervous system signs plus biopsy evidence of granulomas from other organs, such as the lungs.

Lung Biopsy

Sometimes a lung biopsy will show evidence of granulomas even in sarcoidosis patients who only outwardly show nervous system symptoms. The most common type of lung biopsy used to

diagnose sarcoidosis is a transbronchial or bronchial lung biopsy. You are usually given local anesthesia for this procedure so that a long tube, called a bronchoscope, can be inserted through one of your nostrils or mouth and into your lungs. After the tube is positioned, a pincer-like tool is passed through the tube to collect several lung tissue samples. As uncomfortable as this sounds, the procedure is usually painless when anesthesia is used. It is very low-risk when performed by an experienced doctor.

Brain Biopsy

In rare cases, a biopsy of your brain, meninges, or spinal cord tissue might be necessary. It can rule out a brain tumor or other dangerous conditions when your symptoms don't lead to a clear diagnosis. The doctor will probably choose the area to be biopsied using one of the imaging techniques described above. Usually, a surgeon will perform an open brain biopsy. They cut a small hole in your skull and remove a sample of the brain tissue beneath it. The skull section is then replaced and fastened back in place. This procedure is done under general (full) anesthesia.

Nerve or Muscle Biopsy

If your symptoms involve your muscles and/or your peripheral nerves, such as those in your arms and legs, your doctor might suggest a nerve or muscle biopsy. These are usually done under local anesthesia. In some procedures, the doctor uses a needle to extract the tissue. In others, the doctor will make a small incision to remove the sample.

Diagnostic Tests for Neurosarcoidosis

- Cerebrospinal fluid tests
- Computed tomography (CT)
- Gallium scan
- Magnetic resonance imaging (MRI)
- Positron emission tomography (PET)
- Lung biopsy
- Nerve or muscle biopsy
- Brain biopsy, rarely

How Is Neurosarcoidosis Treated?

In mild cases, neurosarcoidosis might not require treatment. Most of the time, however, treatment is necessary. Nerves heal slowly, so your doctor might recommend that you take medications for a long time.

Ideally, doctors prescribe treatments that have been proven effective in large clinical trials. But neurosarcoidosis is relatively rare, so there are no trials comparing various drugs with each other or with placebo treatment. As a result, doctors base their treatment recommendations on smaller studies and on their experience treating other patients.

Corticosteroids

Corticosteroid medications are the first-line treatment for neurosarcoidosis that requires treatment. Corticosteroids are also called glucocorticoids or steroids. These medications are powerful drugs that can slow, stop, or even prevent nervous system injury by reducing the inflammation caused by sarcoidosis. Commonly prescribed types include cortisone, prednisone, and prednisolone.

Most doctors will prescribe a moderate to high dosage of corticosteroids initially. They usually try to reduce the dosage gradually as your symptoms are brought under control. High dosages of steroids and/or long-term treatment can cause serious side effects. These include mood swings, weight gain, acne, difficulty sleeping at night, and, when taken for a long time, disorders such as osteoporosis, osteonecrosis, diabetes, high blood pressure, cataracts, and glaucoma. They can also lower your resistance to infection. Most people with chronic neurosarcoidosis, which is the kind that does not go away, will need ongoing corticosteroid therapy for a long time, possibly a lifetime. As a result, doctors try to prescribe the lowest dosage that suppresses nervous system inflammation. (For more information about steroids and bone loss, request the Foundation for Sarcoidosis Research brochure, **SOS: Your Bones Need Your Help**. See **For More Information**, page 15, for contact information.)

Other Medications

For people who cannot take corticosteroids, or for people whose nervous system symptoms are not brought under control by steroids, doctors might prescribe any of a number of other treatments that suppress the immune system and reduce inflammation. These include methotrexate, azathioprine, cyclophosphamide, and the antimalarial drugs chloroquine and hydroxychloroquine. In addition, doctors have reported that infliximab, a treatment given by infusion, shows some promise in relieving the symptoms of sarcoidosis that affect the spinal cord when other medications do not work. Doctors have also reported that the drug mycophenolate mofetil has some promise for

treating neurosarcoidosis when other medications do not work. Unfortunately, because of the rarity of neurosarcoidosis, these two treatments have not been well studied.

Doctors can prescribe pain medicine to treat the pain associated with inflammation of the peripheral nerves or certain skin nerves due to sarcoidosis. Some doctors have prescribed antiepileptic medications to treat people who have seizures caused by neurosarcoidosis.

Radiation

In some cases, doctors have used targeted radiation to treat masses of granulomas in the brain. These masses either did not respond to prior treatment or were in regions of the brain that made surgery difficult.

Surgery

Rarely, brain or spine surgery might be necessary to remove masses formed by granulomas. In cases of hydrocephalus, inserting a shunt can relieve the pressure of excess cerebrospinal fluid in the skull.

What Should I Expect?

Sarcoidosis can take many forms and affect many different organs. Some people have mild disease while others have severe complications. Some people have a form that goes away after several years. Others have sarcoidosis for a lifetime. If you have neurosarcoidosis, there are certain patterns of involvement that might help your doctor predict the severity of your disease. If central nervous symptoms appear early on, it could be a sign that your case of neurosarcoidosis might respond well to treatment and eventually

resolve. Peripheral neuropathy, masses of granulomas in the brain, seizures, and chronic meningitis that occur later in the course of disease, however, are often signs of chronic neurosarcoidosis that is hard to treat. Keep in mind that these patterns are just clues. Your doctor cannot use them to predict the severity or persistence of your disease with certainty.

Because you might not notice many outward signs of neurosarcoidosis, and because it is hard for doctors to detect, if you have sarcoidosis and you experience any nervous system symptoms at all, it is important to find a doctor who understands neurosarcoidosis. And, if sarcoidosis has affected other parts of your body, as well, it's important to have a good health care team with wide expertise in all of your affected body systems.

If you are diagnosed with neurosarcoidosis, you will need to visit your team of doctors regularly, and you will have frequent laboratory and imaging tests to monitor your treatment's progress. You might be on certain drugs for a long time, even a lifetime. However, most people who receive an early and accurate diagnosis of neurosarcoidosis can lead active lives, even if they have a chronic form that is hard to treat.

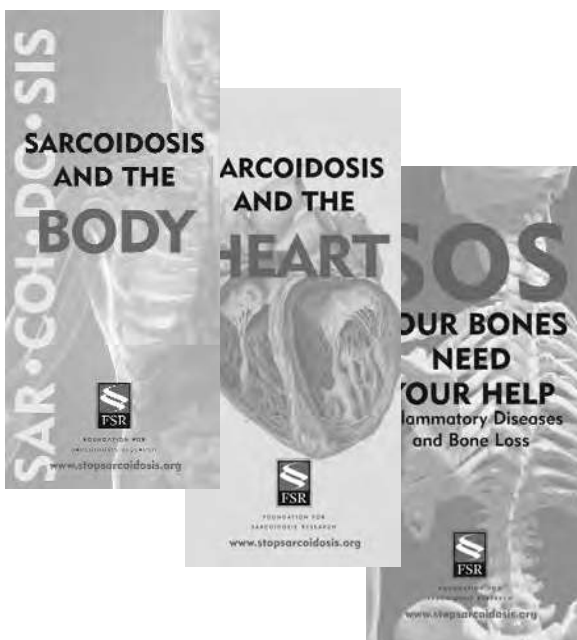
What Research Is Being Done?

Research is underway to improve the diagnosis and treatment of sarcoidosis and to find new medicines that are as effective as corticosteroids but have fewer side effects. In addition, genetic researchers are trying to find out how people become predisposed to develop sarcoidosis in the first place and why people of different races are affected differently.

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