Melbourne Respiratory & Sleep Services

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# SARCOIDOSIS

**Introduction**
Sarcoidosis is a disorder that causes tiny nodules (granulomas) of inflamed tissue to develop in the body's organs. These nodules can join together, forming larger nodules that interfere with normal body functions such as breathing. Sarcoidosis almost always involves the lungs, but it can also affect the skin, eyes, nose, muscles, heart, liver, spleen, bowel, kidney, testes, nerves, lymph nodes, joints, and brain. Granulomas in the lungs can cause narrowing of the airways and inflammation and scarring (fibrosis) of lung tissue.

**Causes**
The cause of sarcoidosis is not known. One theory suggests that it develops when a genetically susceptible person is exposed to specific environmental agents. Although the specific agents are unknown, several organisms, including viruses and bacteria, have been suggested as possible causes.

Noninfectious chemicals in the environment, including beryllium, aluminum, and zirconium, can cause lung disease that has features similar to sarcoidosis.

**Risk Factors**
Sarcoidosis occurs throughout the world, affecting both sexes and all races and ages. It is most commonly found in people between 20 and 40 years old. In a small percentage of cases, more than one family member is affected. Black people are three to four times more likely to have sarcoidosis, and may have more severe disease than people who are Caucasian. Sarcoidosis rarely occurs in children.

**Signs And Symptoms**
Sarcoidosis frequently causes mild symptoms and resolves on its own. In approximately half of all patients, the condition is detected before any symptoms develop. The most common signs of lung involvement are cough, shortness of breath, and chest pain. The chest pain is usually no more than a vague tightness of the chest, but can occasionally be severe and similar to the pain of a heart attack. Affected individuals may also experience fatigue, weakness, fever, and weight loss.

Other organs in the body can also be affected. The signs and symptoms in these organs depend upon the site and extent of organ involvement (eg. involvement of the lungs can cause breathlessness or coughing). The following organ systems are commonly involved.

Skin — Skin lesions of different types can occur on the face, neck, arms, legs, or trunk. These lesions range from subtle, painless rashes to deep scars. People with more severe disease involving the internal organs often have more severe skin lesions.
Eyes — Involvement of the eyes can cause inflammation of different eye structures, including the iris, retina, or cornea. Glaucoma, cataracts, and blindness are late complications of untreated sarcoidosis. Because some sarcoidosis-related eye problems do not cause symptoms, it is important that all patients with sarcoidosis have an annual eye examination that includes an examination while the eyes are dilated.

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Kidney — Abnormalities in the way the body handles calcium can occur and, if untreated, it may rarely lead to kidney failure. Small nodules (granulomas) may also develop in the kidney, leading to abnormal kidney function. Patients with sarcoidosis should have kidney function testing (usually with blood and/or urine tests) as part of their initial evaluation and follow up testing.

Heart — Nodules may develop in the heart, interfering with its electrical conduction system. This can result in abnormal heart rhythms and even death. An electrocardiogram (also referred to as an ECG or EKG) can generally detect abnormalities in the heart's electrical conduction. Damage and scarring of the lung and lung blood vessels (called pulmonary hypertension) rarely makes it more difficult for the heart to pump blood through the lungs. This condition can lead to failure of the heart's right ventricle.

Nervous system — Neurologic involvement affects approximately 5 percent of patients with sarcoidosis, and may be the first sign of the condition. In the late stages of the disease meningitis, or inflammation of the membranes covering the base of the brain, can cause impaired function of certain brain structures, including the pituitary gland, in addition to facial weakness or paralysis. The disease may also affect the nerves in the arms and legs, resulting in muscle weakness, numbness or tingling, and pain.

Musculoskeletal system — Ten to fifteen percent of people have musculoskeletal involvement, resulting in joint pain and swelling, changes in bone structure, or muscle discomfort and pain.

Reproductive system — Sarcoidosis can affect the male reproductive system, particularly the testes, and may cause male infertility. The disease rarely affects the female reproductive system. Sarcoidosis does not increase the risk of complications during pregnancy; however, the disease may worsen after the birth of the child. Therefore, a chest x-ray is recommended for women with sarcoidosis within 6 months after delivery.

Other organs — Enlargement of lymph nodes, especially those in the chest, occurs frequently. The liver or spleen can also be affected. Involvement of the spleen may lead to anemia and other blood abnormalities.

**Diagnosis**

Since there is no single test that confirms a diagnosis of sarcoidosis, the diagnosis is based upon multiple factors, including signs and symptoms, abnormalities on chest X-ray (or CT scan), and microscopic examination of one or more specimens from involved tissues or organs. In addition, the diagnostic process often involves tests that help to rule out other conditions, including tuberculosis, which share some features with sarcoidosis.

A biopsy involves removing a small sample of tissue from an affected tissue or organ. This test is usually recommended to identify a granuloma. Samples can be obtained from lung tissue with a procedure called bronchoscopy. A biopsy may also be done on an affected lymph node, skin nodule, salivary gland, or the tear gland near the eye.

Once the diagnosis of sarcoidosis is confirmed, other tests may be needed to determine the extent and severity of the disease. This may include imaging tests such as an MRI and/or PET scan to determine if there is evidence of the disease in the eyes, heart, or other organs.

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**Treatment**

Because the cause of sarcoidosis is not known, there is no specific treatment. Some medications are effective in suppressing symptoms, and these are discussed below. Fortunately, many individuals with sarcoidosis require no treatment since the nodules (granulomas) gradually resolve and leave behind few, if any, signs of inflammation or other complications.

There are many questions about the best time to start treatment for sarcoidosis and how long it should be continued. Treatment is usually recommended in patients with worsening lung problems, especially shortness of breath and cough. Other reasons for treatment include signs of decreased lung function (as determined by pulmonary function testing), or difficulty functioning due to fever, weakness, fatigue, joint pain, nervous system changes, disfiguring skin disease, or disease affecting the upper airway. Sarcoidosis affecting the eyes, heart, or kidneys is treated even when symptoms are mild because of the potentially serious risk of complications when these systems are involved.

Current treatment is focused on improving symptoms, suppressing inflammation, reducing the impact of the granulomas, and preventing the development of lung fibrosis.

Steroids

Steroids (usually prednisone ) are particularly effective in reducing inflammation, and are typically the first line treatment. In patients with mild disease, such as skin lesions, eye inflammation, or cough, topical steroid therapy with creams, eye-drops, or inhalers may be sufficient to control the disease.

When necessary, oral steroids are generally taken for 6 to 12 months. A relatively high dose is usually recommended at first, followed by a slow taper to the lowest effective dose. Relapses may occur after steroid treatment has ended, although this usually responds to repeated treatment with steroids. Patients who improve and remain stable for more than one year after steroid treatment have a low risk of relapse.

Signs of sarcoidosis, especially cough and shortness of breath, generally improve with steroid therapy. However, there are potentially serious side effects of long-term steroids, and the benefits must be weighed against the risks. These include Increased appetite, weight gain, acne, fluid retention, trembling, mood swings, and difficulty sleeping. If steroids are taken for long periods of time, particularly if high doses are used, there is an increased risk of developing diabetes, thinning of the skin, easy bruising, a "cushingoid" appearance (widening of the face and a hump in the back), thinning of the bones, body hair growth, cataracts, high blood pressure, stomach ulcers, avascular necrosis (a serious joint problem), and infections. Because of the risk of these side effects, most patients are tapered off of steroids as soon as possible.

Researchers continue to examine the role of steroids in the treatment of sarcoidosis. The biggest question is what effect these drugs have on the long-term course of the disease.

Other medication

Other medications may be recommended for people who cannot tolerate steroids, do not respond, want to avoid steroid side effects, or prefer to use a lower dose of steroids.

Methotrexate reduces inflammation and suppresses the immune system and may allow for a lower dose of steroids to be used.

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Other drugs, including cyclophosphamide and azathioprine , are commonly used in conjunction with steroids if the condition is worsening despite treatment.

Cyclophosphamide works by suppressing the immune system. There are serious concerns about the toxic effects of cyclophosphamide, especially cancer, which have restricted its use to patients with the most severe disease.

Some antimalarial medications (particularly hydroxychloroquine ) have been used to treat sarcoidosis affecting the skin or lungs.

Colchicine , a medication commonly used to treat gout, is sometimes prescribed for the treatment of sarcoidosis-related arthritis. Colchicine is an anti-inflammatory medication that helps to relieve pain and swelling.

Nonsteroidal anti-inflammatory agents (including ibuprofen ) may help reduce inflammation and relieve joint pain, swelling, and fever, although they are not recommended for the treatment of sarcoidosis affecting the lungs.

Methotrexate , hydroxychloroquine , and azathioprine are discussed in detail in a separate topic review. ( See "Patient information: Disease modifying antirheumatic drugs (DMARDs)" ).

Tumor necrosis factor antagonists

Tumor necrosis factor antagonists are medications that were originally designed for treatment of rheumatoid arthritis. They work by interfering with the production of proteins involved in inflammation. Drugs in this class include etanercept (Enbrel®) and infliximab (Remicade®). Both of these TNFa inhibitors have undergone preliminary study as treatments for sarcoidosis, although neither are currently recommended as routine treatments.

Anti-TNF medications may be used alone or in combination with other DMARDs, NSAIDs, and/or steroids. All anti-TNF treatments must be injected.

**Long-Term Outcome**

In many patients, sarcoidosis resolves on its own or does not progress. In other patients, sarcoidosis may progress over many years and involve many organs. However, the overall death rate from sarcoidosis is less than five percent. Death most commonly results from progressive lung scarring, sometimes complicated by right heart failure or bleeding from the lungs. Sarcoidosis involving the heart may also be fatal.

**Where To Get More Information**

Your healthcare provider is the best source of information for questions and concerns related to your medical problem. Because no two patients are exactly alike and recommendations can vary from one person to another, it is important to seek guidance from a provider who is familiar with your individual situation.

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A number of web sites have information about medical problems and treatments, although it can be difficult to know which sites are reputable. Information provided by the National Institutes of Health, national medical societies and some other well-established organizations are often reliable sources of information, although the frequency with which they are updated is variable.

National Library of Medicine (www.nlm.nih.gov/medlineplus/sarcoidosis.html )
National Heart, Lung, and Blood Institute
(www.nhlbi.nih.gov/health/dci/Diseases/sarc/sar_whatis.html )
American Lung Association (www.lungusa.org )
Foundation for Sarcoidosis Research (www.stopsarcoidosis.org )
The Arthritis Foundation (ww2.arthritis.org/conditions/DiseaseCenter/sarcoidosis.asp)