SARCOIDOSIS

What Is Sarcoidosis?

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 people in the United States, sarcoidosis most commonly affects the lungs and lymph nodes, but the disease can and usually does affect other organs, too, including (but not limited to) the skin, eyes, liver, salivary glands, sinuses, kidneys, heart, the muscles and bones, and the brain and nervous system.

Sarcoidosis is often serious and can even be life-threatening, especially if you don't know you have it. People who have any of the organ symptoms described below (see **How Can Sarcoidosis Affect the Body?** page 3) should discuss them with their doctor because early diagnosis and treatment of sarcoidosis can help relieve symptoms, reduce inflammation, and stop or minimize organ damage.

Who Gets Sarcoidosis?

Sarcoidosis can affect people of any age, race and gender. Mostly, though, the disease strikes adults between the ages of 20 and 40. In the United States, it is most common in African Americans and people of European – particularly Scandinavian – descent. Among African Americans, the most affected U.S. group, the estimated lifetime risk of developing sarcoidosis might be as high as 2 percent. The disease is slightly more common in women than in men.

Sarcoidosis affects the lungs and lymph nodes in most people who have the disease. It also tends to affect other organs more often in some groups than in others. For example, African Americans and the Japanese are more likely than whites to have eye involvement; painful skin lumps affect more Northern Europeans; the Japanese are the most likely to have heart problems.

What Causes Sarcoidosis?

No one knows exactly what causes sarcoidosis, but it is probably due to a combination of factors. Some research suggests that bacteria, viruses or chemicals might trigger the disease. Although such triggers might not affect most people, it is possible that in someone with the right genetic predisposition they provoke the immune system to develop the inflammation associated with sarcoidosis.

The fact that a person is more likely to develop the disease if someone in his or her close family has the disease strongly suggests that genetics plays a role. Researchers have not discovered the genes for sarcoidosis yet, but it seems likely that more than one gene is involved.

How Can Sarcoidosis Affect the Body?

Sarcoidosis is unpredictable, and it affects people differently. Some people have a mild form of the disease. Others, particularly African Americans, tend to have more severe forms. In many cases, sarcoidosis will go away on its own within several years, but in others the disease is chronic, lasting a long time or a lifetime. With the chronic type of sarcoidosis, symptoms might stay the same for years or they might get progressively worse over time without treatment.

In up to half of all cases, doctors spot the disease when their patients come in for a chest x-ray. In about one-third of cases, people visit the doctor because they have a fever, feel tired or fatigued, have lost weight, or just because they feel poorly. Others might see their doctors for a cough, trouble breathing, swollen lymph nodes, rashes, or some of the other symptoms described below. Some people with sarcoidosis may not notice any symptoms at all.

LUNGS

The lungs are the most commonly affected organ in sarcoidosis. Ninety percent or more of people with sarcoidosis have lung involvement, whether they have symptoms or not.

Common lung symptoms are

- *dry coughing*
- *trouble breathing*, *wheezing*, or *pain with breathing*
- *chest pain*, *tightness*, *or discomfort*
- *coughing up blood*, which is rare, especially in the early stages of sarcoidosis

Some of the lung problems caused by sarcoidosis – usually only in the most serious cases – can include

- *interstitial lung disease* (also called *pulmonary fibrosis*), which occurs when inflammation causes scar tissue to form on the lungs, leading to reduced oxygen levels in the blood and shortness of breath
- *fibrocystic disease*, which is an advanced form of lung disease that causes scars that block airways
- *pulmonary hypertension* (also called *pulmonary arterial hypertension*), which is high blood pressure in the arteries of the lungs caused by scar tissue that narrows or blocks them. The hypertension makes the heart work harder to pump blood through the vessels, which can weaken the heart muscle and hinder its ability to deliver oxygen to the lungs.
- *bronchiectasis*, which makes the airways in your lungs unable to clear out mucus. The mucus then builds up, creating an environment where bacteria will grow. Over time, the airways become inflamed, stretched out, and scarred, making it harder for the lungs to move air through them.
- *aspergilloma*, which is a clump of fungus that forms in healed lung scars and enlarged airways. It can cause bleeding in the lungs.

LYMPH NODES

Sarcoidosis affects the lymph nodes in up to 90 percent of people with the disease. Lymph nodes are glands found throughout the body that make and store white blood cells. When sarcoidosis inflammation targets these glands, they become enlarged. Swollen lymph nodes can be uncomfortable, but they rarely cause medical problems unless they press on organs or blood vessels.

Most commonly, it's the lymph glands in the chest that are affected, but this can be hard to detect without an x-ray. Some of the other places you might notice enlarged lymph nodes (they appear as swollen lumps) include

- your *neck*
- under your *chin*
- in your *armpit*
- in your *groin*

Unlike when you have a cold or the flu, swollen lymph nodes in these areas are not usually tender.

SPLEEN

The spleen is a large organ on the left side of the body under the ribs that produces and filters red blood cells and some types of white blood cells. Along with the lymph nodes, the spleen is part of the lymphatic system, which regulates blood cells and plays a role in immunity.

Sarcoidosis of the spleen does not usually cause symptoms. If you do notice some, they might include

- *pain* on your upper left side under your ribs
- *a sensation of pressure* in the same area
- *feeling tired*

Some of the problems sarcoidosis might cause when it affects the spleen include

- *spleen enlargement* (also called *splenomegaly*), which occurs when inflammation and the formation of granulomas cause the spleen to swell
- *anemia*, which means that your blood does not contain enough healthy red blood cells to carry sufficient oxygen to your body's tissues. It can make you feel tired.
- *leukopenia*, which means that you do not have enough white blood cells circulating through your body. It makes you prone to infections.
- *thrombocytopenia*, which means your body does not have enough of the circulating blood platelets necessary for blood clotting

LIVER

Between 50 and 80 percent of people with sarcoidosis develop granulomas in the liver. The disease rarely causes serious liver problems, however, and most people do not even realize it when their livers are affected.

If you have liver symptoms, they might include

- *fever*
- *feeling tired or fatigued*
- *itchy skin*
- *jaundice*, which causes your skin and eyes to look somewhat yellow
- *pain* on your upper right side under your ribs

The liver problems caused by sarcoidosis might include

- *liver enlargement* (also called *hepatomegaly*), which occurs when inflammation and granulomas on the liver cause it to swell.
- *abnormal liver enzyme levels*, which is a common problem, but not usually a serious one
- *portal hypertension*, a rare complication defined as high blood pressure in the main blood vessel that carries blood to the liver. When pressure on this vein prevents normal blood flow, the blood must return to the heart through other blood vessels. They become swollen and fragile due to the extra load.
- *cirrhosis*, a rare condition that occurs when inflammation and granulomas scar the liver.

HEART

Researchers estimate that sarcoidosis of the heart, or cardiac sarcoidosis, affects more than 10 percent of people with sarcoidosis in the United States, and perhaps as many as 25 percent. Because heart problems can be very serious, everyone who has sarcoidosis should be screened for cardiac sarcoidosis. (For more information about cardiac sarcoidosis, request the Foundation for Sarcoidosis Research brochure, **Sarcoidosis and the Heart.** For the FSR's contact information, see **For More Information,** inside back cover.)

Some people with heart involvement might notice symptoms, but many people will feel nothing, even in late-stage disease.

If you have heart symptoms, they might include

- *irregular heartbeats*, which can feel like palpitations and/or skipped beats
- *shortness of breath*, *coughing*, *chest tightness*, and/or *wheezing*, although these can be a sign of lung problems, too
- *swelling in the legs*, which usually occurs only in late-stage sarcoidosis of the heart
- *feeling lightheaded* or *fainting*

The problems caused by cardiac sarcoidosis can include

- *arrhythmias*, which are abnormal heartbeats or rhythms
- *heart blocks*, which block the electrical impulses that regulate the heart rate, impairing blood flow to the rest of the body.
- *heart failure*, which means your heart is unable to pump enough blood through the body, causing blood and fluid to back up in the lungs and elsewhere
- *pericarditis*, which, although rare, can cause inflammation of the covering of the heart, as well as chest pains
- *heart valve problems*, which can prevent your blood from flowing through your heart correctly
- *heart attacks*, which are rare but can occur when a blockage prevents blood and oxygen from reaching part of the heart

BRAIN AND NERVOUS SYSTEM

Sarcoidosis affects the brain and nervous system in up to 15 percent of cases. Although it can affect almost any part of the nervous system, the cranial nerves, which are important nerves at the base of the brain, are commonly involved. (For more information about sarcoidosis and the nervous system, request the Foundation for Sarcoidosis Research brochure, **Sarcoidosis and the Nervous System**. For the FSR's contact information, see **For More Information,** inside back cover.)

Brain and nervous system symptoms can 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 on one side of your face.
- *headaches*
- *eye pain* and *redness*
- *blurry* or *double vision*
- *blindness*
- *weakness*, *numbness*, *tingling*, and/or *pain in your face*, *arms* and/or *legs*
- *arm* and/or *leg paralysis*
- *seizures*
- *behavior and mood changes*, *irritabilty*, *memory loss*, and *hallucinations*, which are rare

The problems caused by sarcoidosis of the nervous system can include

- *nerve inflammation* and/or *damage*, which can result in many of the symptoms described above, depending on which nerves are affected. (For example, facial palsy is a result of damage to a nerve or nerves at the base of the brain.)

- *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 above.
- *masses of granulomas in the meninges, or, more rarely, in the brain,* which can cause the headaches, vision problems, and muscle weakness described above. These masses can also cause
  - *meningitis*, which means inflammation of the *meninges*, the membranes that surround your brain and spinal cord.
  - *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).
- *coma*, which is rare

SKIN

Roughly a quarter of people with sarcoidosis will develop skin problems related to the disease. If you have one of these skin problems, it can be a clue to how serious your case of sarcoidosis is.

Skin problems might include

- *erythema nodosum*, which causes raised, red, and tender bumps to form on the skin,

usually on the front of your legs. Nearby joints are often swollen and painful. Erythema nodosum usually goes away on its own in 6 to 8 weeks, even without treatment. Having it is a good sign that you might have the type of sarcoidosis that also goes away on its own after a few months or years.

- *lupus pernio*, an uncommon skin condition that causes hard, reddish-purplish bumps to form on your cheeks, nose, lips, and/or ears. These bumps do not go away on their own and often come back when treatment is stopped. They are usually associated with chronic sarcoidosis. In some cases, the sores are disfiguring and can damage underlying cartilage and bone.
- *other bumps on or under the skin*, *rashes*, *sores*, *scaling*, and/or *changes in old scars or tattoos* that do not go away and are rarely painful or itchy. These skin problems are also associated with the kind of sarcoidosis that lasts a long time.

BONES, JOINTS, AND MUSCLES (MUSCULOSKELETAL SYSTEM)

Sarcoidosis affects the bones and joints in up to one-third of people who have the disease. Granulomas can even form in the bone marrow, a problem that occurs in up to 10 percent of cases. Muscle symptoms are somewhat less common than bone symptoms.

Musculoskeletal symptoms you might notice include

- *early-onset arthritis*, which is joint pain, stiffness, and/or swelling that usually occurs

in the first 6 months of the disease, begins suddenly in one or both of the ankles and/or feet, and sometimes involves the knees, toes, fingers, wrists, and/or elbow joints. It often accompanies erythema nodosum (described in SKIN, above), and it usually goes away on its own in a few weeks or months.

- *late-onset arthritis*, which usually occurs 6 months or more after sarcoidosis develops, is less painful and affects fewer joints than early-onset arthritis (usually the knees and/or ankles, or sometimes the fingers or toes), and is often associated with chronic skin symptoms (described in SKIN, above) rather than erythema nodosum. This type of arthritis can last a long time or a lifetime, or it may come and go, but it usually does not go away for good without treatment like early-onset arthritis does. It can cause permanent joint damage and should be treated even when it is not painful.
- *bone cysts*, which are rare
- *muscle aches or muscle pain* (also called *myalgia*)
- *muscle weakness*

Problems caused by musculoskeletal sarcoidosis can include

- *permanent bone and joint damage* from the formation of granulomas and cysts on the bones or from chronic arthritis. Such damage is rare, but when it does occur, it often affects the hands.

- *bone thinning* (also called *low bone density* or *osteopenia*), which occurs when microscopic holes develop in the bones, making them weaker and more prone to fracture
- *chronic myopathy,* a general term for muscle weakness or muscle disease that lasts a long time or a lifetime. It is uncommon, but when it does occur, it is more likely to affect women.

EYES

Sarcoidosis affects the eyes of a quarter or more people with the disease. In many cases, these problems go away on their own within a year. Most eye problems are treatable.

Eye symptoms can include

- *burning, itching,* and/or *pain*
- *dryness*
- *tearing*
- *red eyes*
- *vision problems,* such as seeing black spots or having blurred vision
- *sensitivity to light*
- *small, pale yellow bumps on the eye*

Eye problems caused by sarcoidosis might include

- *uveitis*, the most common eye problem, which means inflammation of the middle membrane – or the uvea – of the eye
- *dry eye syndrome* (also called *keratoconjuctivitis*) which occurs when the tear ducts are blocked by inflammation
- *tear gland enlargement* (also called lacrimal *gland enlargement*), which occurs when the tear glands are swollen by

inflammation and granulomas
- *glaucoma*, *cataracts*, and *blindness*, which are rare but serious problems that can occur if uveitis goes untreated

KIDNEYS AND URINARY TRACT

Sarcoidosis rarely attacks the kidneys directly. However, sarcoidosis can cause the body to overproduce vitamin D, which in turn causes the body to absorb too much calcium and can lead to kidney stones. Although they are uncommon in sarcoidosis, kidney stones can be painful when they break loose from the kidney and pass into the bladder, so it is a good idea to ask your doctor to check you for excess calcium before kidney stones have the chance to develop.

Kidney and urinary tract symptoms that you might notice include

- *pain in your back or side*, just under your ribs, which can be caused by large kidney stones
- *an increased urge to urinate*, which is also caused by kidney stones

Kidney problems caused by sarcoidosis might include

- *too much calcium in your blood* (also called *hypercalcemia*), which occurs in roughly 10 percent of people with sarcoidosis
- *too much calcium in your urine* (also called *hypercalciuria*), which occurs in roughly one-third of people with sarcoidosis
- *kidney stones*, which are fairly uncommon
- *loss of kidney function* or *kidney failure* due to too high calcium levels in the blood or urine

SALIVARY GLANDS

Sarcoidosis causes enlargement of the saliva glands in some people. This inflammation is sometimes painful and can cause dryness in the mouth. It can also make your cheeks look swollen. These symptoms are not serious, and they are usually treatable.

SINUSES

Sarcoidosis can also cause inflammation of the sinuses (called sinusitis). Symptoms include a runny nose, stuffiness, and sinus pain or headache. The sinusitis associated with sarcoidosis is often chronic and can be very troublesome, although it is rarely serious. Medication can relieve some of the symptoms.

How Does Sarcoidosis Affect Mental Health?

It is probably no surprise that long-term illness can cause emotional problems along with the physical ones. Research shows that more than half of people with sarcoidosis symptoms also show signs of clinical depression. Among the most likely to be depressed are people who have severe disease, who have limited access to medical care, or who have trouble paying for medical care. Being a woman is also a risk factor.

Depression can affect your work, your studies, how well you sleep, and even your appetite. Persistent feelings of sadness, emptiness, and anxiety are all signs of depression that you should talk to your doctor about. Certainly if you are having suicidal thoughts you should tell your doctor.

Depression is treatable. Medications and/or talk therapy are often helpful.

How Do I Find a Doctor Who Treats Sarcoidosis?

Some primary care and family doctors can diagnose and treat sarcoidosis, but people who do not have the kind of sarcoidosis that goes away on its own – and quickly – might want to see a specialist, too.

Your doctor might be able to refer you to a local sarcoidosis specialist, or you can contact a nearby academic medical center or hospital and ask for the department that cares for people who have sarcoidosis. A few U.S. hospitals have centers dedicated specifically to sarcoidosis, but in most places the department that handles sarcoidosis will have a broader scope. In some centers it will be the pulmonary and critical care department; in others it might be the internal medicine or rheumatology department.

You might need to see other specialists, too, depending on which of your organs are affected and how seriously. In many cases, treating sarcoidosis requires a team approach that includes you, your primary care doctor, and one or more specialists. Specialists include pulmonologists, who treat lungs; cardiologists, who treat the heart; rheumatologists, who treat many bone and joint problems; gastroenterologists and hepatologists, who treat the liver; endocrinologists and urologists, who treat different kidney and hormone problems; ophthalmologists, who treat eye problems; and dermatologists, who treat skin problems.

How Is Sarcoidosis Diagnosed?

Early diagnosis is the key to preventing the potentially damaging effects of sarcoidosis. Only a few people who have sarcoidosis are at risk for the most serious medical problems, such as organ failure, heart attacks, or death, but these are risks.

There is no one laboratory test that will diagnose sarcoidosis for certain. Instead, doctors rely on a variety of different tests and procedures to screen you for the disease. For a confirmed diagnosis of sarcoidosis, a patient must meet the following three criteria:

- your signs and symptoms must be explained by the disease
- *other* diseases must have been excluded as the cause of your signs and symptoms
- there should be microscopic evidence (such as from a tissue biopsy) of granulomas

Once the sarcoidosis diagnosis is confirmed, your team of doctors should assess the extent and severity of disease, gauge whether your case is likely to progress or remain stable, and determine whether treatment is necessary.

INITIAL EXAM

Initially, as with most medical problems, a doctor will probably conduct a physical examination and ask about your medical history. Your doctor also might draw blood and take a urine sample in order to test for various health conditions.

CHEST X-RAYS

If your doctor suspects sarcoidosis, he or she will probably order a chest x-ray to see if you have lung inflammation. Alternatively, the doctor might suspect you have sarcoidosis after looking at a

chest x-ray that you had done for some other reason. Although more than 90% of people with sarcoidosis will have abnormal x-rays, many other diseases can cause abnormal x-rays, too, so a chest x-ray alone is not enough to diagnose sarcoidosis.

The Five X-ray Stages of Sarcoidosis

Stage 0 describes normal lung x-rays with no changes
Stage I describes x-rays that show enlarged lymph nodes but otherwise clear lungs
Stage II describes x-rays that show enlarged lymph nodes and shadows in the lungs
Stage III describes x-rays that do not show enlarged lymph nodes but do show shadows in the lungs
Stage IV describes x-rays that show permanent scarring of the lung tissue (also called fibrosis)

Doctors use a five-stage scale to classify chest x-rays that show changes suspected to be due to sarcoidosis. (See **The Five X-ray Stages of Sarcoidosis**, above.) In general, the higher the stage, the more severe the lung problems. In many cases, if you have low-stage x-rays (stage I or stage II), your sarcoidosis will go away on its own in a few months or a few years. (See WHAT SHOULD I EXPECT? page 37.)

BIOPSIES

Unless you have severe lung damage that makes a biopsy dangerous, or unless it seems fairly certain that you have the type of sarcoidosis that goes away on its own quickly and without treatment, your doctor will likely recommend a lung or lymph node biopsy to look for granulomas if there are abnormalities on your chest x-ray.

Transbronchial Lung Biopsy: 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 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.

Skin, Lip, or Lymph Node Biopsies: The doctor might also recommend a skin or lip biopsy, if those areas appear to be affected, or a lymph node biopsy, if you have swollen glands that are close to the surface of the skin and therefore easy to biopsy.

The bronchoscope used for lung biopsies can also be used to biopsy tissue from enlarged lymph nodes in the chest. This procedure uses a needle-sized tool to look for evidence of granulomas when sarcoidosis is suspected in those lymph nodes.

Surgical Lung Biopsy: If the transbronchial biopsy is inconclusive and other areas are not obviously affected (or if obviously affected areas are not easy to biopsy) then your doctor might propose a surgical biopsy of lung tissue or enlarged lymph nodes in your chest. These biopsies are usually done under general (full) anesthesia because they are more invasive than transbronchial biopsies and require an incision directly into the neck or chest. They tend to be associated with more complications than

transbronchial biopsies, but they are still considered to be low-risk procedures.

LABORATORY AND OTHER TESTS

Many people with sarcoidosis overproduce *vitamin D* and/or a chemical called *angiotensin-converting enzyme*. Both problems can be detected by laboratory tests that measure biological markers in blood or urine samples. However, overproduction of these chemicals is associated with other medical problems, too, so the tests can't be used to confirm a sarcoidosis diagnosis.

Other laboratory tests your doctor might order include *white blood cell, red blood cell,* and *platelet counts* to check for anemia and other blood problems (see SPLEEN in **How Can Sarcoidosis Affect the Body?** page 5); *liver enzyme tests* (see LIVER in **How Can Sarcoidosis Affect the Body?** page 6), and *creatinine* and *blood urea nitrogen tests*, both of which measure kidney function.

More than two-thirds of people who have early sarcoidosis and receive an injection of a substance called *Kveim-Siltzbach reagent* will develop granulomas at the injection site about 4 to 6 weeks later. This diagnostic test is only available at a very few medical centers, however.

IMAGING TECHNOLOGY

In addition to x-ray images, a number of sophisticated imaging tools are available today that can detect inflammation and tumors not only in the lungs but in other parts of the body, as well. Computed tomography (CT) scans and magnetic resonance imaging (MRI) are probably the most commonly available of these technologies.

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. Unlike MRI, CT can be used to scan people who have heart pacemakers or implanted defibrillators.

Magnetic Resonance Imaging: Like CT scanning, magnetic resonance imaging (MRI) produces highly detailed pictures of your organs. Unlike CT scanning, however, MRI technology uses radio frequencies and a magnetic field, not radioactivity, to produce these images. The doctor performing the MRI might give you an injection of a contrast agent to enhance the image's detail. Magnetic resonance imaging is used to look for signs of sarcoidosis in your brain, spinal cord, heart, bones, and sometimes other organs. 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.

Nuclear Imaging: Some imaging technologies are "nuclear" because you are injected with a small amount of a radioactive compound called a tracer. A special computer and a special camera that detects radioactivity will create a picture of the way your body absorbs the tracer, which allows doctors to see how well blood flows through your organs. 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. Even though radioactivity is involved, the scans are generally considered safe, and side effects are rare. Nuclear imaging is sometimes used to help diagnose cardiac sarcoidosis. Usually, you are first given an exercise test, which increases your heart rate. This way, the computer can capture images of your heart's blood flow pattern after exercise and again at rest. The tracers used to check for cardiac sarcoidosis include thallium or technetium sestamibi. Some doctors have found that a total body scan with gallium, another radioactive tracer, can help diagnose sarcoidosis in general.

Positron Emission Tomography: Positron emission tomography (PET) scanning detects changes in the body's chemical activities. As with nuclear imaging tests, you are injected with a radioactive tracer, usually 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 is often used to help diagnose cardiac sarcoidosis or to find a good spot to biopsy.

OTHER LUNG TESTS

In addition to imaging scans and lung biopsies, your doctor might recommend several other lung tests and procedures to look for granulomas or to identify the extent of lung damage.

Lung Function Tests: These tests measure how well your lungs are working, and they provide your doctor with a baseline measurement against which disease progression or improvement can be measured in the future. The two most frequently used tests for sarcoidosis are the **spirometer test,** which uses a machine to measure how fast you can exhale breath from your lungs, and the **diffusion capacity test,** which involves breathing in very small amounts of carbon monoxide gas for a breath or two, then measuring the difference between the amount of the gas that you inhaled vs. the amount you exhaled. The spirometer detects whether you have trouble moving air in and out of your lungs and the capacity test assesses how fast gas travels from your lungs to your blood.

Fiberoptic Bronchoscopy: During this procedure, a tube like the one used in a transbronchial lung biopsy, a bronchoscope, is inserted through one of your nostrils and into your lungs under local anesthesia. This tube has a light on the end that allows the doctor to look inside your lungs for scarring and inflammation in your airways.

Bronchoalveolar Lavage: During this procedure, a salt-water solution is injected through a bronchoscope into your lungs and then the fluid is syphoned back out. The cells that come up with the fluid can be examined to determine which type of inflammatory cell they are. The fluid can also be tested for biochemical markers of inflammation.

OTHER HEART TESTS

In addition to the imaging techniques described above (see IMAGING TECHNOLOGY, this section) a number of other tests are sometimes used to help diagnose cardiac sarcoidosis. Electrocardiography and Holter monitoring are probably the simplest and most widely available tools for initial evaluations of your heart rhythm. Heart biopsies are invasive. They are rarely used today to diagnose cardiac sarcoidosis.

Electrocardiography: An electrocardiograph test monitors your heart's electrical activity, producing an electrocardiogram (an ECG, or EKG, for short), which is a graph of your heart rhythm and blood flow pattern over a certain period of time. Up to 50 percent of people with sarcoidosis will produce an ECG that shows some abnormalities, however, so further testing might be necessary to determine whether any abnormalities that show up on your ECG are serious.

Holter Monitoring: Like an electrocardiograph test, a Holter monitor records your heart's electrical activity, but over a longer period – usually one or two days – so your doctor can check for irregular heartbeats. With Holter monitoring, you wear or carry with you a monitor that is attached to electrodes on your chest. The device then produces a report that your doctor can compare against the symptoms and activities you reported over the time period that you wore the monitor. As with ECGs, Holter monitor reports pick up a lot of abnormalities, and it is often unclear which ones are important without further testing.

Echocardiography: This technology uses high-frequency sound waves, also called ultrasound, to produce two-dimensional images

of the heart. (It is the same technology that doctors use with pregnant women to look at the developing fetus.) The image can help doctors identify problems with your heart valves and the chambers of your heart, so if the ECG or the Holter monitor report showed an abnormality, your doctor might use an echocardiograph test to learn more about that abnormality. However, echocardiograms might be better at picking up signs of late-stage cardiac sarcoidosis than early heart complications. Some doctors are beginning to use new, more sensitive ultrasound methods to look at the heart, but these are not yet widely available.

For more information about cardiac sarcoidosis, request the Foundation for Sarcoidosis Research brochure, **Sarcoidosis and the Heart.** (For the FSR's contact information, see **For More Information,** inside back cover.)

OTHER BRAIN AND NERVOUS SYSTEM TESTS

Doctors usually rely on your symptoms and imaging scans to diagnose sarcoidosis of the brain and nervous system. Magnetic resonance imaging, CT scans, gallium scans, and PET scans are all used to check for neurosarcoidosis. (See IMAGING TECHNOLOGY, this section.)

Cerebrospinal Fluid Tests: In about 80 percent of people with sarcoidosis of the nervous system, the cerebrospinal fluid, which surrounds your brain and spinal cord, contains elevated protein levels and higher-than-normal numbers of white blood cells called lymphocytes. These findings are not specific to sarcoidosis of the nervous system. They are just clues that can help your doctor when combined with other findings. Doctors use a lumbar puncture (a spinal tap) to obtain the fluid. The procedure is usually low risk.

Brain Biopsy: Only rarely do doctors recommend

brain biopsies. They are more invasive, with a greater risk of complications, than most other organ biopsies. In some cases, though, a biopsy of your brain, meninges, or spinal cord tissue might be necessary. These procedures can rule out a brain tumor or other dangerous conditions when your symptoms don't lead to a clear diagnosis. Usually, a surgeon will perform an open brain biopsy, cutting a small hole in your skull to remove a sample of the brain tissue beneath. The skull section is then replaced and fastened back in place. The procedure is done under 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.

(For more information about sarcoidosis and the nervous system, request the Foundation for Sarcoidosis Research brochure, **Sarcoidosis and the Nervous System.** For the FSR's contact information, see **For More Information**, inside back cover.)

EYE TESTS

A *routine eye examination* performed by an ophthalmologist is recommended for anyone with suspected sarcoidosis. It is a good idea to schedule them annually for several years after your diagnosis, and routinely as recommended thereafter.

If your doctor suspects you have the kind of long-lasting uveitis that sarcoidosis can cause, he or she might refer you to an ophthalmologist for *fluorescence angiography*. In this test, orange fluorescent dye is injected into one of your veins, usually in your arm, and – after the dye has a chance to circulate through your bloodstream – a special camera is then used to take pictures of the back of your eye. A light on the camera causes any of the dye that collects in the eye to glow, making it possible to see the blood vessels of the eye and any areas where they are blocked or leaking.

How Is Sarcoidosis Treated?

Many people with sarcoidosis will not require any treatment at all. As noted earlier, sarcoidosis is often mild and usually goes away on its own within several years without causing serious damage. (See **How Can Sarcoidosis Affect the Body?** page 3.) However, estimates suggest that in up to 30 percent of people, the disease lasts a long time or a lifetime. It can also worsen over time.

Removing granulomas is not an option. Surgery does not treat the underlying problem that causes the granulomas. In fact, granulomas can form around surgical scars.

CORTICOSTEROIDS

Corticosteroid medications are considered the first line of treatment for sarcoidosis that requires treatment. Corticosteroids are also called glucocorticoids or steroids. These medications are powerful drugs that can slow, stop, or even prevent organ damage by reducing the inflammation caused by sarcoidosis. Commonly prescribed types include cortisone, prednisone, and prednisolone. Corticosteroids can be taken

alone or in combination with other sarcoidosis medicines.

Most doctors will prescribe a moderate to high dosage of corticosteroids initially, but they will try to reduce the dosage gradually as symptoms are brought under control because high dosages of corticosteroids and/or long-term treatment can cause serious side effects. These side effects include mood swings, weight gain, acne, difficulty sleeping at night, and, when taken for a long time, problems such as osteoporosis, diabetes, high blood pressure, cataracts, glaucoma, and other serious conditions. Many people with chronic sarcoidosis will need corticosteroid therapy for a long time, possibly a lifetime, so the lowest dosage that still suppresses inflammation is desirable. (For more information about corticosteroids and bone loss, request the Foundation for Sarcoidosis Research brochure, **SOS: Your Bones Need Your Help.** For the FSR's contact information, see **For More Information,** inside back cover.)

In addition to prescribing corticosteroids in pill form to treat the whole body, doctors sometimes prescribe corticosteroid *injections* for skin sarcoidosis and corticosteroid *eye drops* for uveitis. Various studies have tested using corticosteroid *inhalers* to treat sarcoidosis lung problems, but results have been mixed. In some cases they were found to be no better than taking a placebo.

For people who cannot take corticosteroids, or when a combination drug treatment approach is warranted, doctors might prescribe any of a host of other medications that suppress the immune system and reduce inflammation, such as antimalarial medicines and immunosuppressant drugs.

IMMUNOSUPPRESSANT DRUGS

As their name implies, immunosuppressant drugs suppress the immune system. While that might not seem like a good idea, in a disease like sarcoidosis – where the immune system is *overactive* – suppressing the immune system can help control symptoms, reduce inflammation, and prevent organ damage.

Methotrexate (Rheumatrex, Trexall): Methotrexate was first used widely to treat cancer, and, in lower dosages, it is used today to treat inflammatory diseases such as psoriasis, rheumatoid arthritis, and lupus. It has been an effective treatment for some people with sarcoidosis, and one group of researchers recently found that two-thirds of sarcoidosis patients responded to methotrexate treatment alone, while 80 percent responded when it was combined with low-dosage corticosteroids. Methotrexate has side effects. It can cause nausea, mouth sores, and/or hair loss, and, because it weakens your immune system, it can also increase your risk of getting infections. Rarely, methotrexate causes an allergic reaction in the lungs, but that reaction stops when you stop taking the drug. One serious potential side effect of methotrexate is liver damage, but your doctor can check your liver function regularly with various laboratory tests to make sure it is functioning properly. Most doctors recommend that you stop drinking alcohol while taking methotrexate because alcohol might increase the risk of liver damage. Women who are pregnant or breastfeeding should not take methotrexate because it can harm the baby. Taking folic acid supplements or eating more folic acid in your diet can alleviate some of the side effects of methotrexate.

Leflunomide (Arava): Leflunomide is prescribed mainly for rheumatoid arthritis. It is being studied in a number of autoimmune and inflammatory diseases, including psoriatic arthritis and systemic lupus erythematosus. One small study of 32 patients has concluded it might be an effective sarcoidosis treatment. Sometimes it is prescribed alone for sarcoidosis, and sometimes it is prescribed in combination with other drugs, including methotrexate. Side effects of leflunomide can include diarrhea, nausea, rashes, and hair loss. Because it weakens your immune system, it can also increase your risk of getting infections. Like methotrexate, a serious potential side effect of leflunomide is liver damage, but your doctor can check your liver function regularly with various laboratory tests to make sure it is functioning properly. Most doctors recommend that you stop drinking alcohol while taking leflunomide. Women who are pregnant or breastfeeding should not take this drug. It can cause birth defects, and it stays in your body for a long time, even after you stop taking it. Therefore, both women and men who plan to have a child in the next few years should discuss the risks with their doctor before beginning treatment. For women, pregnancy must be avoided not only during treatment but for up to 2 years after treatment. Both women and men might want to consider a prescription drug regimen that helps eliminate leflunomide from the body.

Azathioprine (Azasan, Imuran): Azathioprine is most commonly used to prevent the rejection of kidney transplants and to treat inflammatory diseases such as rheumatoid arthritis and inflammatory bowel disease. Azathioprine appears to be roughly as effective as methotrexate in treating sarcoidosis. The side

effects of azathioprine include upset stomach, stomach pain, mouth sores, muscle aches, flu-like symptoms, yellowing of the skin or eyes, and blurred vision. Like methotrexate, azathioprine can increase your risk of getting infections. Women who are pregnant or breastfeeding should not take this drug.

Mycophenolate mofetil (CellCept): This drug was first used widely as a treatment for people who had received organ transplants. Today, doctors often prescribe it to treat a number of autoimmune and inflammatory diseases, including rheumatoid arthritis and lupus nephritis. Several very small studies have shown it to be effective in treating sarcoidosis. Side effects can include sore throat, fever, tiredness, tingling or burning in one part of the body, and weakness. Mycophenolate might increase your susceptibility to infection and your risk of developing certain types of cancer. Women who are pregnant or breastfeeding should not take this drug.

Cyclophosphamide (Cytoxan, Neosar): Cyclophosphamide is best known as a cancer treatment, but it is sometimes prescribed for sarcoidosis. It is very toxic, however, so most doctors only prescribe it when other medications have not worked and a person's symptoms are very serious. Preliminary and case studies have shown that cyclophosphamide appears to be effective for some people with sarcoidosis and is perhaps particularly useful in cases where brain and nervous system symptoms have not responded to other treatments. Its side effects can include nausea, weight loss, hair loss, acne, darkened and thickened skin, mouth blisters, and fatigue. Taking the drug increases your risk of developing infections and certain cancers, particularly bladder cancer. Women who are

pregnant or breastfeeding should not take cyclophosphamide.

BIOLOGIC RESPONSE MODIFIERS (TNF BLOCKERS)

Biologic response modifiers – or biologics, for short – are a new class of medicines derived from natural, living sources. For example, they can be proteins, sugars, acids, tissues, cells, or cell parts. All three of the biologics listed below are from a category called tumor necrosis factor (TNF) blockers. Like the immunosuppressant drugs described above, they suppress the immune system. But unlike those drugs, they target a *specific* part of the immune system – in this case a protein in your body called TNF – instead of the whole immune system. TNF plays a role in triggering inflammation during immune responses. TNF blockers are proteins that recognize and bind to these molecules, inhibiting their inflammatory effect. Produced using cutting-edge technologies from natural sources, biologics are often much more expensive than chemically synthesized conventional drugs.

Infliximab (Remicade): Infliximab was first used to treat Crohn's disease, a granulomatous inflammatory bowel disease. It has since been approved for several other inflammatory diseases, including rheumatoid arthritis. It is delivered by infusion in a medical setting. Researchers recently found infliximab to be effective in reducing symptoms and improving lung function in people who were on other treatments for sarcoidosis, but these results came from short-term studies. Infliximab can cause a variety of side effects, including chest pain, fever, hives, trouble breathing, nausea, headache, abdominal pain, and sore throat. It also increases the risk of

infection and slightly increases the risk of certain types of cancer. More large-scale research is needed before the value of infliximab as a sarcoidosis treatment becomes clear. Tell your doctor if you are pregnant, plan to become pregnant, or are breastfeeding. Infliximab has not been studied in pregnant women.

Etanercept (Enbrel): Like infliximab, etanercept is a TNF blocker, but it has not been studied as much as a treatment for sarcoidosis. It is delivered by injection, not infusion, and you can give it to yourself at home. It was first used to treat rheumatoid arthritis and has since been approved for a variety of other inflammatory diseases. Researchers have tested it, too, in small studies of people with various sarcoidosis symptoms, but results to date have been mixed and less promising than for infliximab. Etanercept can cause many of the same side effects as listed above for infliximab. It, too, increases the risk of infection and slightly increases the risk of certain types of cancer. Tell your doctor if you are pregnant, plan to become pregnant, or are breastfeeding. Etanercept has not been studied in pregnant women.

Adalimumab (Humira): The TNF-blocker adalimumab has not been studied as much as infliximab as a treatment for sarcoidosis. Like etanercept, it is delivered by injection, and you can give it to yourself at home. Adalimumab has been approved to treat rheumatoid arthritis and several other types of arthritis. Its value as a treatment for sarcoidosis is unknown because it has not been tested in clinical trials with people with sarcoidosis, but some doctors prescribe it for their sarcoidosis patients. It can cause many of the same side effects as described above for infliximab and etanercept. It also increases the

risk of infection and might slightly increase the risk of certain types of cancer. Tell your doctor if you are pregnant, plan to become pregnant, or are breastfeeding. Adalimumab has not been studied in pregnant women.

ANTIMALARIAL DRUGS

Hydroxychloroquine (Plaquenil) and **chloroquine** (Aralen) are best known as malaria treatments, but they are also sometimes used to treat inflammatory diseases such as rheumatoid arthritis and lupus. As a treatment for sarcoidosis, these drugs are most likely to be effective in people who have skin symptoms and a high level of calcium in their blood. Antimalarial drugs can irritate the stomach. They can also cause serious eye problems, particularly chloroquine. If you take chloroquine, you should have your eyes examined every 3 months. If you take hydroxychloroquine, you should have them examined at least every 6 months. In most cases, hydroxychloroquine and chloroquine are not recommended during pregnancy.

ANTI-INFLAMMATORY DRUGS

The three drugs described below are not from the same class of medicines. They are not particularly similar in how they work in your body. They are grouped together below because each has an anti-inflammatory effect and each has been used to treat small numbers of people with sarcoidosis.

Thalidomide (Thalomid) is used to treat certain skin problems, and researchers have been interested to see if thalidomide improves sarcoidosis. In very small studies it was effective in some people who had severe skin involvement. Side effects associated with thalidomide include drowsiness, dizziness, slowed heartbeats, rashes,

and numbness or tingling in the hands or feet. More studies are needed to determine whether thalidomide might be useful for treating sarcoidosis. The drug will cause severe birth defects, so women who are pregnant, who are thinking of becoming pregnant, or who are at risk for becoming pregnant should not take it. Women who are breastfeeding also should not take thalidomide.

Pentoxifylline (Trental) is used to reduce leg pain caused by poor blood circulation. Because of its anti-inflammatory effects, researchers are interested to see if pentoxifylline is useful as a combination treatment that allows for a lower dosage of corticosteroids. Pentoxifylline's side effects include dizziness, headaches, nausea, and stomach discomfort. More studies are needed to determine whether pentoxifylline has a role in sarcoidosis treatment. Tell your doctor if you are pregnant, plan to become pregnant, or are breastfeeding. Pentoxifylline has not been studied in pregnant women.

Tetracyclines, such as minocycline and doxycycline, are antibiotic medicines used to control a variety of infections and acne. Very small studies have shown that they might also improve the *skin* symptoms of sarcoidosis. No clinical studies have shown that these drugs improve sarcoidosis that affects the lungs or any other organs. The side effects of tetracyclines include increased sensitivity to the sun, stomach cramps, and diarrhea. More research on the efficacy of tetracyclines for sarcoidosis is needed. These drugs are not recommended during the last half of pregnancy or if you are breastfeeding.

Organ-Specific Treatments

Depending on how sarcoidosis affects you, you might need to treat specific symptoms of the disease on their own, with medications besides corticosteroids or the corticosteroid alternatives mentioned above. Below are a few of the most common treatments for various types of sarcoidosis.

LUNG TREATMENTS

If the drugs mentioned above do not control your lung symptoms, your doctor might prescribe other medications, including antifungal and antibiotic treatments. He or she might also recommend that you take medicines to open up the airways in the lungs or that you undergo a procedure to mechanically open up blocked airways. Some people with severe lung disease and blockages will need supplemental oxygen therapy, and in the most serious cases, your doctor might recommend lung transplantation, although this is rare.

HEART TREATMENTS

In addition to the medicine you take for sarcoidosis generally, if you have cardiac sarcoidosis your doctor might prescribe an anti-arrhythmia medication to correct irregular heartbeats or to improve your heart's pumping ability. For people with serious arrhythmias or heart blockages, a pacemaker or an automatic implantable defibrillator might also be necessary. Doctors rarely recommend heart transplantation and do so only in the most severe cases of cardiac sarcoidosis, when the heart is failing and has been damaged irreversibly.

BRAIN AND NERVOUS SYSTEM TREATMENTS

The brain and nervous system problems associated with sarcoidosis can be serious, and if

corticosteroids or the above-mentioned drugs do not improve them, your doctor might prescribe several other drugs in combination. In rare cases, brain or spine surgery may be necessary to remove masses formed by granulomas or to relieve the pressure of hydrocephalus (fluid in the skull). In some cases, doctors have used targeted radiation to treat masses of granulomas in the brain that either did not respond to prior treatment or were too hard to reach surgically. Doctors can prescribe pain medicine to treat the pain associated with sarcoidosis inflammation of the peripheral nerves or certain skin nerves.

EYE TREATMENTS

Corticosteroid eye drops are the most common treatment for eye symptoms. Surgery might be necessary in the most advanced cases of eye damage, but this is rare.

SKIN TREATMENTS

Most cases of erythema nodosum will go away on their own and do not require treatment. For chronic skin problems and lupus pernio, your doctor might prescribe corticosteroid injections if you are not already taking corticosteroid pills. Injections might provide temporary relief.

SPLEEN AND BLOOD TREATMENTS

If your white blood cell, red blood cell, and/or platelet counts have dropped, your doctor might prescribe medications or supplements to try and normalize these counts.

What Should I Expect?

If you are diagnosed with sarcoidosis, you will need to visit your doctor or team of doctors regularly, and you will have frequent laboratory

and imaging tests to monitor your treatment's progress. If you have the chronic type of sarcoidosis that doesn't resolve on its own, you might be on certain drugs for a long time, even a lifetime, and you might also have to use certain medical devices or undergo various medical procedures.

Doctors can sometimes predict whether you will have temporary or long-term sarcoidosis based on your symptoms. Certain groups of symptoms seem to go with certain types of sarcoidosis. There are, of course, exceptions to the rule, but, in general, people who develop early and painful arthritis, erythema nodosum, and swollen lymph nodes in both the right and left sides of the lungs (a group of symptoms collectively known as Löfgren's syndrome) have a high remission rate. People with sarcoidosis who develop arthritis after 6 months, who have lupus pernio or other chronic skin problems (not erythema nodosum), and who develop uveitis that does not go away are more likely to have the chronic form of sarcoidosis.

The five x-ray stages of sarcoidosis can also help predict outcome. Stage I sarcoidosis goes away on its own 55 to 90 percent of the time, and even when it doesn't, disease symptoms often stabilize. Stage II sarcoidosis resolves on its own in 40 to 70 percent of people, and stage III disease resolves in 10 to 20 percent of people. Stage IV sarcoidosis does not go away on its own. Of course, even when sarcoidosis resolves on its own it can leave behind permanent tissue or organ damage, so treatment and follow-up sometimes might still be necessary.

Most people who receive an early and accurate diagnosis can lead active lives if they receive competent care and ongoing, effective treatment

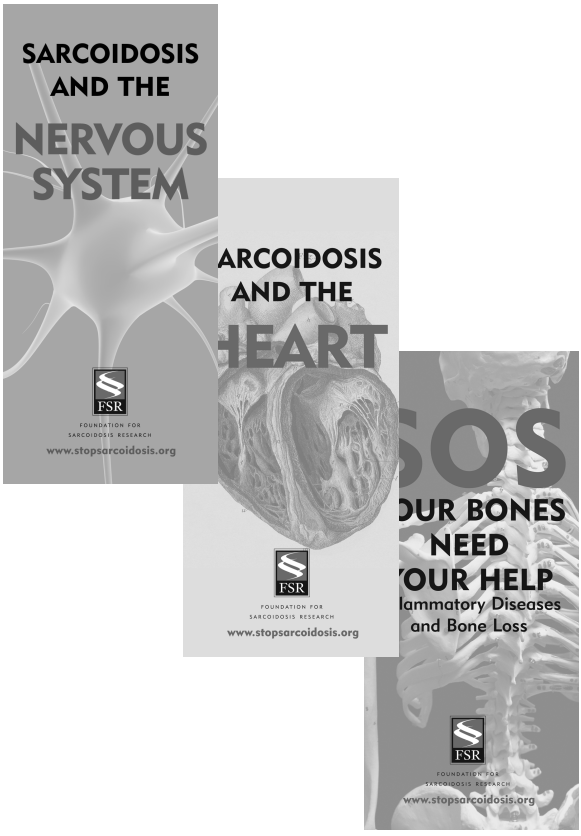
to prevent or halt organ damage. Managing the side effects of your medications and making common-sense lifestyle changes – such as quitting smoking, adopting healthy eating habits, and getting enough exercise – are also crucial for staying healthy when you have sarcoidosis.

Factors Associated With Chronic Sarcoidosis

- lupus pernio
- being over 40-years-old when disease develops
- chronic uveitis
- being African American
- advanced x-ray stage, progressive lung involvement
- bone cysts
- heart involvement
- peripheral neuropathy, seizures, and masses of granulomas on the brain
- hypercalcemia
- arthritis that occurs more than 6 months after disease develops
- pulmonary sarcoidosis
- aspergilloma

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.



Other Publications from FSR

The Foundation for Sarcoidosis Research offers a range of educational brochures for patients and professionals. Single copies are available for free by calling 866-358-5477 or visiting FSR online at www.stopsarcoidosis.org.

Sarcoidosis and the Nervous System:
Neurosarcoidosis

Sarcoidosis and the Heart: Cardiac Sarcoidosis

Your Bones Need Your Help:
Inflammatory Diseases and Bone Loss