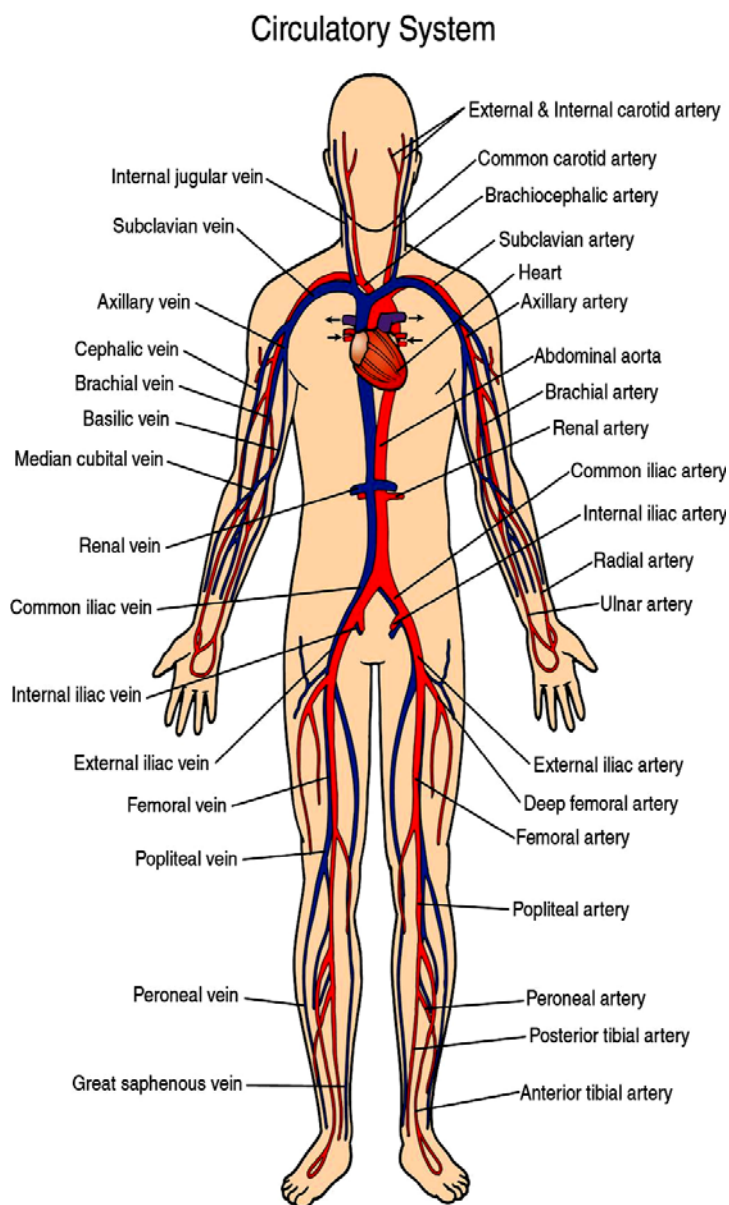


What Is Small-Vessel Vasculitis?



❖ What is vasculitis?

Vasculitis is a disease that inflames blood vessels throughout the body. The word "vasculitis" is formed from the root word "vas" which means vessel. The suffix "itis" means inflammation. This inflammation causes damage to vessel linings. Such damage can cause the vessel to close partially or close completely. Blocking the blood supply to organs and tissues prevents them from functioning normally. Symptoms of vasculitis appear when the organs cannot function well. The drawing below shows how the blood vessels are spread over the body. So, you may have problems anywhere in the body.

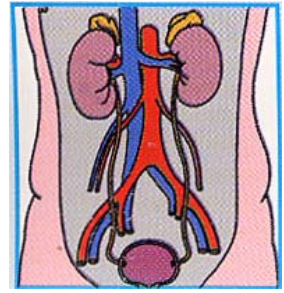


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Vasculitis may be triggered by the immune system mounting an autoimmune response. This means that your body's immune system turns against itself. This is similar to transplant patients' immune systems which sometimes reject transplanted organs. Autoimmune disease results from the immune system mistaking "self" as "nonself."

There are many types of vasculitis, and different parts of the body may be affected. Parts of the body that might be affected include kidney, lung, skin, sinus/nose, trachea, nerves, gastrointestinal tract, and eyes. Some of the types of vasculitis will be described in more detail in this booklet.

Your vasculitis may be a short-term illness and may be cured by treatment. Or, your vasculitis may be a chronic disease that you will have to manage the rest of your life. If your disease is chronic, you may have long periods when it seems to go away. This is called "remission." But you will always be at risk for it to return. You must be seen by your doctor at regular intervals to evaluate your health because your disease may return

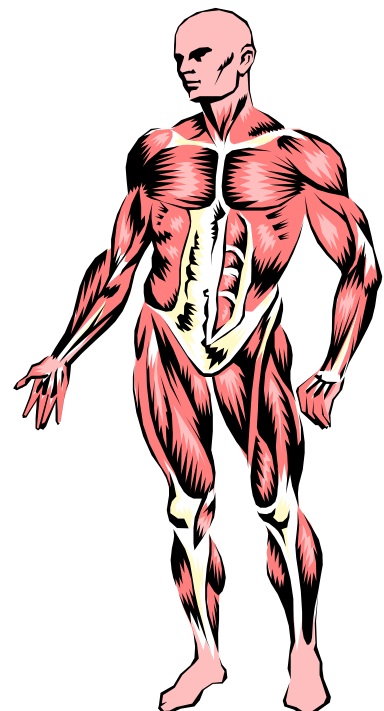


The types of vasculitis described in this booklet are:

- Microscopic polyangiitis (microscopic polyarteritis)
- Wegener's Granulomatosis
- Churg-Strauss syndrome
- Organ-Limited Disease (meaning that vasculitis affects only one organ or body site)

❖ **When was vasculitis first diagnosed?**

The first patient with a diagnosis of vasculitis was reported in medical books in 1852. In 1866, specimens from the patient were studied under the microscope. It was seen that nodules which could be felt under the skin were inflamed blood vessels. Since then, different forms of small and medium vessel vasculitis have been described by a number of physicians. Often the same disease was called by several names because the clinical symptoms are similar for different types of vasculitis. Even today, vasculitis is hard to label accurately because the symptoms for the different types are similar. Improved diagnostic tests make finding the specific type of vasculitis easier.



There are similar features for all types of small

vessel vasculitis. However, some have special characteristics. Patients with Churg-Strauss syndrome often have asthma. Patients with microscopic polyangiitis often have skin, lung, and kidney disease. Patients with Wegener's Granulomatosis often have destructive nose, sinus, and lung disease.

❖ **How does vasculitis affect your body?**

Many types of vasculitis are systemic, meaning they affect the entire body. Vasculitis may affect organs such as the:

- kidneys (renal)
- lungs(pulmonary/lower respiratory)
- sinus, ears, nose, airway (upper respiratory)
- stomach and intestines (gastrointestinal)
- eyes (ocular)
- muscles and bones (musculo-skeletal)
- nervous system (neurologic)

❖ **What are the symptoms of vasculitis?**

More patients become ill in the late fall, winter, and early spring than in the summer. Most patients first experience a flu-like illness with fever, aches and reduced appetite. They may also have pain in muscles and joints or weight loss. However, symptoms vary from person to person. You may have some or all of the symptoms, or you may have different ones at different times.

This disease affects your entire body. You feel constantly tired, your joints may ache and at times may even swell. You may feel the need to sleep many hours at a time.

Ear: If your ears are involved, you may have a hearing problem or hearing loss because of ear inflammation.

Eyes: If your eyes are involved, you may have red eyes that hurt.
Gastrointestinal Tract: If your stomach and intestinal tract are involved, you may have pain in your stomach or blood in your stool or urine.

Joints: If your joints are involved, the pain and/or swelling may travel to different parts of your body. Only a few joints may be involved or there may be several.

Kidney: If your kidneys are involved, you may not even know there is a problem. One of the warning signs of kidney problems is if your urine turns brown, tea-colored, or even red. This indicates leakage of blood through the inflamed kidneys into the urine.

Lung: You may not know you have lung disease or you may just have a cough. Your doctor may first think you have pneumonia and treat you with antibiotics that don't make you better. If you start coughing up blood, you need to see a doctor immediately.

Nose: If your nose is involved, you may have a "runny nose" that becomes worse, usually caused by sinus drainage.

Trachea: If your trachea or airway is involved, you may have shortness of breath.

❖ **What causes vasculitis?**

Doctors and scientists are coming closer to understanding what causes vasculitis. It does not seem to be hereditary. Possible factors include viruses, environmental exposures or a combination of these and other factors, but no one knows for sure.

All types of small-vessel vasculitis are related. Now an animal model proves that myeloperoxidase (MPO-ANCA) can cause vasculitis. What are ANCA? ANCA cause neutrophils and monocytes (white blood cells) to damage blood vessels.

ANCA are autoantibodies found in small-vessel vasculitis: Anti-Neutrophil Cytoplasmic Antibodies. These words mean that there is an antibody to the cytoplasm of neutrophils. ANCA are present in microscopic polyangiitis, Wegener's Granulomatosis and Churg-Strauss syndrome.

Let's look at the meaning of these words:

Anti- means "against."

Neutrophils are a type of white blood cell containing granules filled with potent chemicals that fight infection. These chemicals play a key role in acute or inflammatory reactions.

Cytoplasmic refers to the part of the cell outside the nucleus or center of the cell.

Autoantibodies are proteins secreted by a type of immune cell that recognizes foreign substances.

ANCA are used to help in the diagnosis of small-vessel vasculitis. ANCA react to two chemicals inside normal neutrophils. These two chemicals are called myeloperoxidase (the protein that makes pus green) and proteinase 3 (an enzyme that chews up elastic tissue).

You may have one of two types of ANCA:

1. ANCA directed against myeloperoxidase- called myeloperoxidase ANCA which is sometimes referred to as "MPO-ANCA."
2. ANCA directed against proteinase 3-called proteinase 3 ANCA which is sometimes referred to as "PR3-ANCA."

ANCA levels are sometimes related to the severity of your disease. For example, at the time of your diagnosis, your ANCA level may be high. After treatment it may be negative or lower.

Is vasculitis contagious?

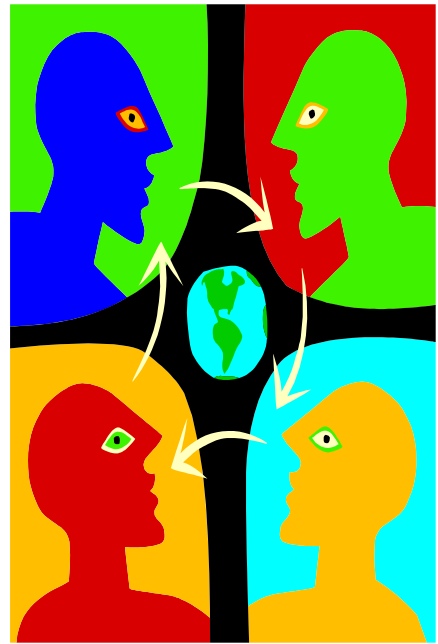
No. Vasculitis can not be caught by other people.

Is vasculitis hereditary?

Vasculitis does not seem to "run in families."

Who gets vasculitis?

Vasculitis has an incidence rate of 20 people per million. It affects mostly middle age to older people, with a median age at diagnosis of 55, although very young children (age 2) and much older people (age 90) have the disease as well. Incidence of vasculitis is much more frequent in whites than in minorities. Most forms of the disease are rare, and affect men and women equally. One type of vasculitis, called microscopic polyarteritis, is extremely rare.



Is vasculitis similar to cancer?

No. Although you may take cancer drugs such as cyclophosphamide (Cytosan) or methotrexate that are given to cancer patients, your disease is not a form of cancer. Cancer involves the uncontrolled growth of immature cells and is not related to vasculitis. Vasculitis is an inflammation of blood vessels caused by an autoimmune reaction. Immunosuppressive drugs such as cyclophosphamide (Cytosan) or methotrexate are given to control the inflammation.

Is vasculitis similar to AIDS?

No. In fact, vasculitis is the opposite of AIDS since the immune system is overactive in vasculitis. The immune system is deficient in AIDS.

Diagnosis

Vasculitis is uncommon, but there are now tests that can help your doctor tell if you have vasculitis and what type you may have. Many forms of vasculitis have similar symptoms. It is important that your doctor conduct tests to know which type you have so that you can get the best treatment for your type of vasculitis.

One test, a blood test, can detect an autoantibody present in some forms of vasculitis. Autoantibodies are antibodies (cell proteins) directed against the body's own parts—cells or cell components in specific organs. Autoantibodies may produce disease, and also serve as markers for the disease.

ANCA are autoantibodies found in small vessel vasculitis. It stands for Anti-Neutrophil Cytoplasmic Antibodies. These words mean that there is an antibody to the cytoplasm of neutrophils (white blood cells). It is present in microscopic polyangiitis, Wegener's granulomatosis, and Churg-Strauss syndrome.

Let's look at the meaning of these words:

Anti- means "against."

Neutrophils are a type of white blood cell containing granules filled with potent chemicals that fight infection. These chemicals play a key role in acute or inflammatory reactions.

Cytoplasmic refers to the part of the cell outside the nucleus or center of the cell.

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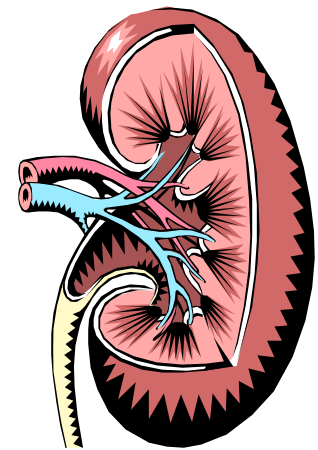
1. ANCA directed against myeloperoxidase, called myeloperoxidase ANCA, is sometimes referred to as "p-ANCA" (perinuclear).
2. ANCA directed against proteinase 3, called proteinase 3 ANCA, is sometimes referred to as "c-ANCA" (cytoplasmic).

ANCA levels are sometimes related to the severity of your disease. For example, at the time of your diagnosis, your ANCA level may be high. After treatment, it may be negative or lower.

How does your doctor determine what organs are being affected by vasculitis?

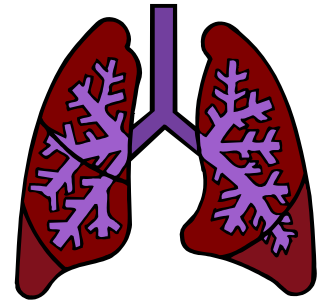
Your doctor will use a combination of results from your physical examination and laboratory tests. She or he will pay special attention to examining your skin, joints, lungs, ears, nose and throat, and kidney function.

To tell if your kidney is involved, your doctor may measure your creatinine level in your blood. Creatinine is a protein that is released in the blood. By measuring your creatinine level, your doctor measures your kidney function. The lower the creatinine level, the better your kidney function.



Your doctor may want to look at your urine to check it for blood or proteins leaking from the kidney. Your kidneys filter blood, removing toxins and water. They do so through tiny filters called glomeruli that keep blood products and protein in the blood stream, but remove toxins. When your kidney is damaged by vasculitis, these filters become inflamed. This condition is called glomerulonephritis. These inflamed glomeruli no longer act as effective filters, allowing red blood cells and protein normally found in the blood, to escape in your urine. This leakage is something that your doctor can examine under the microscope.

Your doctor may listen to your chest with a stethoscope to hear if your lungs are injured. A chest x-ray or CT scan of your lungs may be ordered to find smaller areas of damage to the upper respiratory tract.



Your doctor may look inside your nose to see if there are areas of inflammation. Your doctor may refer you to an ENT (Ear, Nose, and Throat) specialist to look at your entire upper respiratory tract using a small tube called a fiberoptic endoscope.

A biopsy may be performed. A small piece of tissue is taken to examine for disease. The most common sites for biopsies are nose, sinus, kidney, and lung. A biopsy can help your doctor determine the extent of your disease. This information will be used to establish the diagnosis and decide the type and length of treatment that will be best for you.

❖ Treatment

The treatment you will receive is based on:

- the type of vasculitis you have
- the severity of your disease
- how many of your organ systems are affected

Your doctor will take blood samples and conduct other tests to help determine the best type of treatment and medicines for you. The goal of the treatment is to stop the inflammation so that organ damage can be minimized. Another goal of treatment is not to overtreat, to avoid infections. Treatment is a balancing act: too little and flares can occur; too much and infections and other complications can occur.

You may be treated with one or more of the following drugs or procedures:



1. *Corticosteroids* such as prednisone or methylprednisolone (Medrol) work by controlling inflammation and suppressing the immune system.

2. *Immunosuppressive drugs* such as cyclophosphamide (Cytosan), cyclosporin azathioprine (Imuran) or mycophenolate mofetil (CellCept) suppress the immune system..

Methotrexate is an immunosuppressive drug, but is not used for patients with kidney disease. There are new immuno-suppressive drugs being developed that may help your disease. Talk with your doctor about all these medicines.

3. *Antibiotics* such as trimethoprim/sulfisoxazole (Septra or Bactrim) may stop recurrences, especially in the nose.

4. *Plasmapheresis* is a method of cleansing the blood. It may help if a patient has had bleeding in the lung and those with kidney failure. During plasmapheresis, blood is taken from the patient, the plasma separated from the blood cells in a machine, and the blood cells put back in the patient's blood system.

Getting a second opinion



Because vasculitis is rare, it is important that you see a specialist who can diagnose your disease, recommend and give you the correct treatment, and watch your clinical condition on a long-term basis. Some of the specialists you might see include a *nephrologist* who specializes in kidney diseases, a *rheumatologist* who specializes in connective tissue diseases, a *pulmonologist* who specializes in lung diseases or an *otorhinolaryngologist* - sometimes called an ENT specialist - who specializes in ear, nose, and throat diseases.

Why will you need to be cared for by several different doctors?

Vasculitis can affect many organ systems in your body. So you may need to be cared for by several specialists who can coordinate your treatment.

Preparing for Treatment

Being told that you have a rare disease can be stressful and may seem overwhelming. You will receive much information about treatment options from your health care team. When you are learning about these choices and need to make a decision, take someone with you such as a family member or a friend to the appointment. That way, someone else can help you take notes and ask questions. It is hard to remember everything you're being told. Having someone along can help you.

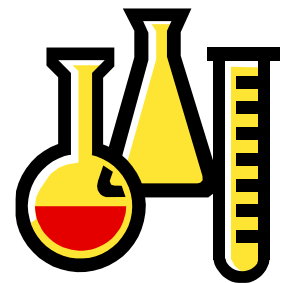
Here are some questions you may want to ask your doctor and other health care team members.

- What is my diagnosis?
- What stage is my disease?
- What are my treatment choices? Which do you recommend for me? Why?
- What are the chances that the treatment will be successful?
- What are the risks and side effects of treatment?
- How long will my treatment last?
- Will I have to change my normal activities?
- What will my treatments cost?

There are pages at the end of this booklet so you may write down the answers when you talk with your doctor.

Methods of Treatment

You may receive several medicines for your disease. Corticosteroids may be given intravenously (IV) or in pill form. Other drugs, such as cyclophosphamide- (Cytosan) or methotrexate, may be given orally by mouth as pills or intravenously (IV) on a periodic basis.



Side Effects of Treatment

The different medicines you are given to treat your illness may cause side effects. Some of the more common side effects for each drug are described below. You may have none of the side effects or some or several. Each person is different. Call your doctor for advice if you have any unusual symptoms.



CellCept: Bone marrow effects can include a temporary drop in white blood cells, platelets and red blood cells. This means you are at risk for infection and bleeding. While taking this medicine you are at an increased risk for catching an infection. Stay away from people who have any sickness and from crowded areas

Cytosan: Bone marrow effects can include a temporary drop in white blood cells, platelets and red blood cells. This means you are at risk for infection and bleeding. This usually occurs a few weeks after your treatment. Nausea and vomiting can occur several hours after you get your medicine and can last up to 24 hours. You can take anti-nausea medications to prevent this from happening. To help prevent damage to your bladder, drink 8-10 glasses of fluids a day starting one day before your treatment and up to three days after it. Your hair may thin as a result of taking the medicine, but will grow back after you finish. Treatment with cytosan can cause sterility or decreased sex hormones in both men and women. You may want to talk to your doctor about change of life symptoms or decreased sex drive.

Imuran: Bone marrow effects can include a temporary drop in white blood cells, platelets and red blood cells. This means you are at risk for infection and bleeding. While taking this medicine you are at an increased risk for catching an infection. Stay away from people who have any sickness and from crowded areas. You may bleed more easily. So, you will need to be very careful with razors, toothbrushes, knives and nailcutters. Sometimes, Imuran may cause nausea and vomiting. Taking it after meals and at bedtime may help lessen these effects. Anti-nausea medicine can relieve your symptoms. You may feel more tired than usual.

Methotrexate: You may have nausea and vomiting after your treatment. Anti-nausea medicine can relieve your symptoms. You may have sores in your mouth. Because your blood counts are decreased, you are more likely to get infections. Some signs to look for are: fever, chills, a sore that is red, swollen, or not healing as usual; severe cough or cough producing yellow sputum; sore throat. You may also experience bleeding in your gums or nose, or in your urine or bowel movement.

Predisone: Prednisone may cause weight gain, sodium and fluid retention, increased appetite and possible mood swings. Low potassium levels can occur and may cause muscle cramps. You may have gastrointestinal tract effects such as ulcers or bleeding. This drug may increase blood pressure and blood sugar and the risk of osteoporosis (brittle bones).

Septra/ Bactrim: This medicine may cause your skin to be sensitive to the sun. Wear protective clothing and use a sunscreen or sunblock product. If you develop symptoms such as difficulty in breathing, tightness of the chest, swelling of eyelids, face, or lips or develop a rash or hives, tell your doctor immediately.

Clinical Trials

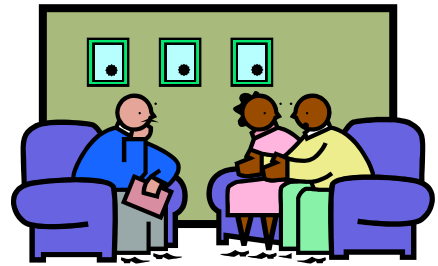
There are clinical trials of new drugs. New combinations of drugs currently used to treat vasculitis are being tested. One of the difficulties in conducting clinical trials is the lack of a central registry for patients and a standardized classification of the different types of vasculitis.

Support for Vasculitis Patients

A diagnosis of a rare, chronic disease can be difficult to handle. You may feel isolated since your disease is not one many people will know. You may react to your diagnosis in many ways or feel differently about it at different times.

Sometimes talking to someone about your concerns can help. A friend, a family member, a counselor or therapist, or a minister can listen to your thoughts and help you find ways to cope.

Sometimes just talking to someone else who has your disease can help. Knowing that others share your struggle can make you feel less isolated. Ask your doctor or nurse if they know someone with whom you can talk. Research is starting to show that for some illnesses, taking part in a support group can help participants cope better with their disease. There are support groups for some types of vasculitis. Ask your doctor or nurse if there is a support group in your state or region.



What will happen after you finish treatments?

Following your first treatment phase, you may have long periods of remission. You will continue visiting your doctor to make sure you are disease-free and to monitor you for possible side effects of medications.

What if I have a relapse or flare?

Recurrence is typical of any chronic illness. You may have tests to determine if your illness is a recurrence of the vasculitis or symptoms of some other illness. If it is a recurrence, you and your doctor will choose the best way to treat it. Your therapy may involve taking some of the same medicines you took when you were first treated for your disease.

What about the future for patients with vasculitis?

As research advances continue, the causes of vasculitis may be discovered or less toxic therapies may be developed.

Scientists have developed an experimental animal model system that resembles the human disease and from this system they hope to determine the causes and treatments of small vessel vasculitis.

What is the outlook for patients with vasculitis?

The outlook for vasculitis patients improved greatly with cytoxan therapy. Patients now routinely go into remission and live long, productive lives. Doctors continue to strive for the perfect balance of therapy-great efficiency and less toxicity. Recurrences are always possible, but treatment can reverse them. Much of the medical literature, before 1980 contains statistics before cytoxan became the standard therapy. One point to keep in mind is that statistics come from analysis of large groups of patients. You are an individual.

Resources

National Organization for Rare Diseases - a national group that serves as a clearinghouse for information about a number of rare diseases. Members receive a periodic newsletter and organize an annual national meeting. For more information, write NORD, P.O. Box 8923, Fairfield, CT 06812 or Internet: <http://www.rarediseases.org/>

Wegener's Granulomatosis Association - an international group for this disease. Members receive a periodic newsletter and organize an annual national meeting. For more information, please call 1-800-27WGSG(9474) or write: Wegener's Granulomatosis Support Group, Inc., P.O. Box 28660, Kansas City, MO 64188-8660 or Internet: <http://www.wgassociation.org>

National Kidney Foundation- a national group that seeks to improve the care and treatment of those afflicted with diseases of the kidney and urinary tract through advances in disease detection, diagnosis and treatment. For more information, write National Kidney Foundation, 30 East 33rd Street, New York, New York 10016 or call 1-800-622-9010 or Internet: <http://www.kidney.org>

Arthritis Foundation- a national group to support research to find the cure for and prevention of arthritis and to improve the quality of life for those affected by arthritis. For more information, write the national office at 1330 West Peachtree St., Atlanta, GA, 30309, or call (404) 872- 7100. Internet: <http://www.arthritis.org>

or for more information contact:

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