

# *Vasculitis: Attack of the Leukocytes*

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## **What is vasculitis?**

Vasculitis is an inflammation of the blood vessels. Inflammation is a condition in which tissue is damaged by the white blood cells that enter it. White blood cells (also called leukocytes) are composed of several different types of cells, including monocytes, macrophages, lymphocytes and neutrophils. Each of these cells has specialized functions. The cells circulate throughout the body in blood and lymphatic fluid, and they also reside in bone marrow and most other body tissues.

Ordinarily, this army of leukocytes provides our body's major defense against infection, or the invasion by any dangerous substances. However, leukocytes can also damage normal tissue once they invade it and are instructed by cell signals to release molecules that damage surrounding material.

In many conditions that cause inflammation of the skin or other organs, the white blood cells that are the marker of inflammation gather around blood vessels, but do not penetrate into those vessels. That is not vasculitis. In true vasculitis, leukocytes penetrate into blood vessel walls, where they cause inflammation.

Vasculitis can affect very small blood vessels (capillaries), medium size blood vessels (arterioles or venules), or large blood vessels (arteries or veins). Several things can happen to an inflamed blood vessel. If it is a small vessel, it may break and produce tiny areas of bleeding in the tissue. These areas will appear as small, red or purple dots on the skin. If a larger vessel is inflamed, it may swell and produce a nodule which can be felt if the blood vessel is close to the skin surface. The inside of the vessel tube (the lumen) may become narrowed so that blood flow is reduced, or the lumen may become totally closed (usually by a blood clot which forms at the site of inflammation and narrowing).

If blood flow is reduced or stopped, the tissues which receive blood from that vessel can be damaged with varying degrees of severity. For example, a person with vasculitis of a medium sized artery in the hand may develop a cold bluish finger which hurts whenever it is used; occasionally this can progress to black-colored gangrene.

## **What causes vasculitis?**

Vasculitis can be caused by (1) direct infection of the blood vessel walls, or (2) an immune or allergic reaction in the vessel walls. The first cause, infection, is rare. When it occurs, bacteria, viruses or fungi literally infect the blood vessel. White blood cells move in to destroy the infectious agents and damage the blood vessel in the process. This is a serious condition and requires prompt antibiotic treatment.

The second cause of vasculitis, an immune reaction, is more common. Some infectious agents, particularly the hepatitis B and C viruses, produce vasculitis which is more like the

immune reaction type than the direct infection type. Substances which produce allergic or immune vasculitis reactions are called “antigens.” They cause the body to make proteins called “antibodies” which bind to the antigen for the purpose of getting rid of it. Antigen and antibody bound together are called “immune complexes.”

Two primary ways in which immune complexes destroy antigens are: (1) by attracting white blood cells to digest the antigen, and (2) by activating other body substances, particularly complement proteins, to help destroy the antigens. Most immune complexes, after they serve their good functions, are removed from the circulation by several types of leukocytes that “clean up” the remains of bacteria, viruses, and dead cells.

Unfortunately, some immune complexes do not serve their purpose of destroying dangerous antigens. Instead, they remain too long in the body, circulate in the blood and deposit in tissues. Such immune complexes commonly accumulate in blood vessel walls, where they cause inflammation.

Another way that infection can cause vasculitis is by inducing immune complexes that contain antigens from the bacteria or virus, and antibodies directed against those antigens. A good example of this is the vasculitis that results from hepatitis B or C infections in the liver. In some people infected with these viruses, the disease caused by the vasculitis is more serious than damage to the liver (hepatitis); but in most people the liver damage is more serious.

Many individuals have low-grade infection with these hepatitis viruses and so develop little damage to any tissues—not enough to be clinically important. Probably many infectious agents can cause this “allergic” type of vasculitis, where the antigens provided by the bacteria and viruses persist long after the infectious agents have died, and those antigens are capable of driving persistent undesirable immune responses in joints or skin or other tissues.

The antigens causing the immune complexes are often not known in the type of vasculitis that is caused by lupus, or by other conditions such as drug reactions, rheumatoid arthritis, connective tissue diseases or collagen vascular diseases, polyarteritis nodosa (PAN), Wegener’s granulomatosis, and giant cell (temporal) arteritis.

In some cases, the immune complexes contain DNA antigens and anti-DNA antibodies, or Ro (also called SS-A) antigens and anti-Ro antibodies. A recently discovered antibody, ANCA (anti-neutrophil cytoplasm antibody), can cause vasculitis in some individuals, especially in association with Wegener’s granulomatosis and some types of kidney vasculitis. The ANCA probably binds to the surface of the white blood cells, called neutrophils, and signals those cells to release proteins (enzymes, for example) that damage surrounding tissue.

Your physician may wish to measure several of the antibodies and antigens that can form harmful immune complexes by ordering special blood tests to detect them.

### **Symptoms of vasculitis**

Vasculitis can cause many different symptoms, depending upon what tissues are involved and the severity of the tissue damage. Some patients are not ill but notice occasional red spots on

their skin. Others are very ill with systemic symptoms and major organ damage. The following is a list of symptoms based on the tissues in which vasculitis occurs:

- **Systemic symptoms:** Fever, generally feeling bad (malaise), muscle and joint pain, poor appetite, weight loss, and fatigue. This set of complaints can occur in many illnesses and is not specific to vasculitis.

- **Skin:** Red or purple dots (petechiae), are usually most numerous on the legs. When the spots are larger, about the size of the end of a finger, they are called “purpura.” Some look like large bruises. These are the most common vasculitis skin lesions, but hives, itchy lumpy rash, and painful or tender lumps can occur. Areas of dead skin can form ulcers (especially around the ankles), small black spots at the ends of the fingers or around the fingernails and toes (nail fold infarcts), or more rarely, gangrene of fingers or toes.

- **Joints:** Aching in joints and arthritis with pain, swelling and heat in joints. Deformities resulting from this arthritis are rare.

- **Brain:** Vasculitis in the brain can cause many problems, from mild to severe, including headaches, behavioral disturbances, difficulty thinking or remembering, confusion, seizures, and strokes. Of course, many other conditions can cause each of these symptoms, so the opinion of a physician will be critical in helping determine whether vasculitis or some other disturbance in blood vessels (like arteriosclerosis), or some condition unrelated to blood vessels, is causing the problem.

- **Peripheral nerves:** Peripheral nerve symptoms may include numbness and tingling (usually in an arm or a leg, or in areas which would be covered by gloves or socks), loss of sensation, or loss of strength (especially in the feet or hands).

- **Intestines:** Inadequate blood flow in the intestines can cause cramps, abdominal pain and bloating. If areas in the wall of the intestine are badly damaged, blood will appear in the stool. If the intestinal wall develops a hole (called a perforation), surgery may be required to repair the hole or remove a small part of intestine that has perforated.

- **Heart:** Vasculitis in the coronary arteries is unusual in vasculitis, especially vasculitis associated with lupus. If it occurs, it can cause a feeling of heaviness in the chest during exertion (angina), which is relieved by rest. Heart attacks can result but are extremely rare in vasculitis.

- **Lungs:** Vasculitis in this tissue can cause pneumonia-like attacks with chest X-ray changes that look like pneumonia, and symptoms of fever and cough. Occasionally, inflammation can lead to scarring of lung tissue with chronic shortness of breath.

- **Kidneys:** Vasculitis is not common in kidneys of people with lupus, even those who have lupus nephritis. It may not cause any symptoms, although most patients with renal vasculitis have high blood pressure.

- **Eyes:** Vasculitis involving the small blood vessels of the retina can occur in lupus. The retina is a tissue at the back of the eye which contains cells that have to be activated to form a visual image. Sometimes, vasculitis of the eyes causes no symptoms. Usually, however, there is visual blurring which comes on suddenly and stays; a person may even lose a portion of his or her vision. In other non-lupus types of vasculitis, such as temporal arteritis, there may be sudden loss of part or all of the vision in one eye, usually accompanied by severe headache.

### **Consulting your physician**

If you suspect that you or a friend or relative has vasculitis, you should consult a physician as soon as possible. Remember, vasculitis can be very mild and of little importance, or very severe

and life-threatening—or any degree in between. Therefore, an expert should help you decide: (a) if you have vasculitis, (b) how serious it is, and (c) if and how it should be treated.

Doctors trained in many different specialties are taught to recognize and treat vasculitis. These include rheumatologists, general internists, pediatricians, dermatologists, hematologists, nephrologists, gastroenterologists, infectious disease experts, pulmonologists, cardiologists, geriatricians, neurologists, and ophthalmologists.

### **Diagnosing vasculitis**

The diagnosis of vasculitis is based on a person's medical history, current symptoms, a complete physical examination, and the results of specialized laboratory tests.

Blood abnormalities which often occur when vasculitis is present include an elevated sedimentation rate, anemia, a high white blood count, and a high platelet count. In a small group of patients, particularly those with Wegener's granulomatosis, tests for ANCA may be positive.

Blood tests can also be used to identify immune complexes or antibodies that cause vasculitis in the circulation and to measure whether complement levels are abnormal. These tests take several days to complete. The physician may also order a urine analysis.

If there are any symptoms that suggest heart involvement, tests that may be ordered include EKG, ECHO cardiogram, stress tests, and heart scans.

For lung symptoms, the physician may order a chest X-ray, obtain blood from an artery to measure the oxygen content, and schedule a pulmonary function test. Routine and specialized CT scans of the lungs are often helpful in identifying areas that are inflamed, and occasionally a biopsy of such an area will be recommended. Its purpose is to establish the diagnosis of vasculitis and distinguish it from other causes of inflammation, particularly infection. A pulmonary function test uses a specialized machine to measure how well the lungs handle air and oxygen as you breathe into it.

If there are abdominal symptoms, the physician may order ultrasound or CAT scans of the organs in the abdomen, or other special X-rays to see the intestines.

For brain symptoms, CAT scans and magnetic resonance images (MRI) are frequently useful. Occasionally your physician may want to order a spinal tap (lumbar puncture) to be sure that symptoms are not due to infection in the central nervous system.

Sometimes, inflammation in medium and large-size arteries or veins can be seen by injecting dye into them and viewing the outlines of the blood vessels on X-ray. This procedure is called an "angiography," or "MR angiogram." It can be done in most areas of the body.

The diagnosis is most firmly made by seeing vasculitis in involved tissue. This is done by taking a biopsy of the involved tissue and examining that tissue under a microscope. Your physician may suggest this procedure.

Finally, it may be important for your physician to consult with other medical specialists about your case. For example, if your physician is a rheumatologist and you have visual complaints which could be indicative of vasculitis, you may be referred to an ophthalmologist. However, it is very important that one physician be in charge of your case, coordinating your care and helping you with decisions.

### **Treating vasculitis**

The choice of treatment for your vasculitis depends on the severity of the vasculitis, your general health, and your past reactions (positive and negative) to medications. Many cases of vasculitis do not require treatment. For example, a few spots on the skin now and then (if not combined with other symptoms) may not require any treatment. Most physicians recommend cortisone-type medications, such as prednisone, prednisolone, or methylprednisolone (Medrol) as the initial treatment for potentially dangerous vasculitis.

Some people with severe vasculitis, or vasculitis that does not respond well to cortisone-type drugs, will need to be treated with cytotoxic drugs. These medications kill the cells that cause inflammation in the blood vessels. The two most frequently used are azathioprine (Imuran) and cyclophosphamide (Cytoxan). They are usually used in combination with prednisone and are often effective in treating vasculitis.

Recently there has been considerable research into the benefits of using a mild chemotherapy anti-inflammatory medication, called methotrexate, and the value of inhibiting a pro-inflammatory protein called TNF $\alpha$  (tumor necrosis factor alpha).

Experimental procedures that have been helpful in treating some cases of vasculitis include: plasmapheresis; intravenous gamma globulin; and the use of cyclosporin, a medication used to prevent organ rejection in transplant patients. Experimental therapies change frequently. Your physician can provide you with current information.

### **Outcome**

There are various outcomes for people suffering from vasculitis. A small number of people have severe vasculitis involving major organ systems. In these cases, damage can occur so rapidly that treatment does not have time to work, or the condition may be resistant to treatment. An attack of vasculitis can be fatal or permanently disabling for individuals so affected.

For the vast majority of people with vasculitis, treatment is very effective. The vasculitis may disappear only to reoccur later and require treatment again; or it may be suppressed but never really go away, so that some ongoing treatment is always required.

But for many patients, vasculitis, especially if confined to the skin, may be annoying but never life-threatening. For those individuals, life can be normal—or close to it.

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