

What is Cryoglobulinemia?

Cryoglobulinemia is a rare form of vasculitis, which is an inflammation of the blood vessels. Inflammation of blood vessels may result in narrowing of the vessel, which can block or slow down blood flow to vital organs and tissues.

With cryoglobulinemia, abnormal blood proteins called cryoglobulins clump together at cold temperatures, restricting blood flow and causing damage to skin, muscles, nerves, and other organs—especially the kidneys. More rarely, it can affect the heart, brain, and gastrointestinal tract.

Vasculitis is also classified as an autoimmune disorder—a disease which happens when the body’s natural defense system mistakenly attacks healthy tissue. Factors that may trigger the autoimmune process include:

- Genetics
- Medications
- Infections and viruses
- Environmental factors such as pollutants

Causes

The cause of cryoglobulinemia is not fully understood. More than 90 percent of cases are associated with chronic hepatitis C infections, so treating the hepatitis is a major goal of treatment.

Cryoglobulinemia is also associated with other underlying inflammatory diseases, including lupus erythematosus, rheumatoid arthritis, Sjögren’s syndrome, and blood cancers such as lymphoma.

Who Gets Cryoglobulinemia?

The disease appears to affect females more than males at a ratio of 3:1. Cryoglobulinemia most frequently affects adults over the age of 50.

Symptoms

The symptoms of cryoglobulinemia vary depending on the organ systems affected. Some people may have no symptoms but are noted to have elevated cryoglobulin levels, which is detected in a blood test. When symptoms are present, they typically include the following:

- Rash with red spots and/or purplish discoloration from bleeding under the skin, mostly affecting the lower legs; hives may develop, as well as open sores (ulcers) and loss of tissue (necrosis)
- Severe fatigue
- Joint pain
- Numbness, tingling and/or burning sensation of the extremities, especially hands and feet, caused by nerve damage
- Muscle pain and weakness
- Discoloration of hands in cold temperatures
- Swollen lymph nodes
- Abdominal pain
- Kidney damage*
- Headaches or strokes
- Chest pain and congestive heart failure, which include difficulty breathing, swelling of the legs

*Note: A patient can have kidney damage without having symptoms; therefore, patients with vasculitis of any form should have regular urine tests.

Diagnosis

In diagnosing cryoglobulinemia, your doctor will consider a number of factors, including a detailed medical history and physical examination, as well as:

- **Blood test:** to detect the presence and type of cryoglobulins in the blood, hepatitis C virus, and the presence of abnormal blood cell counts
- **Urinalysis:** to look for blood in the urine, which can indicate kidney involvement
- **Imaging studies:** chest X-ray; computed tomography scans of the lungs; magnetic resonance angiography, computed tomography angiography, or angiograms (images of the arteries), as indicated
- **Nerve conduction and needle tests (EMG)** of the arms and legs
- **Biopsy:** surgical removal and examination of tissue from an affected blood vessel or organ; bone marrow, skin, liver or kidney biopsy may be ordered, depending on the organ involvement and any co-existing disease

Treatment

Treatment for cryoglobulinemia depends on organs affected, symptom severity, and the underlying conditions. When the co-existing condition is treated, the symptoms of cryoglobulinemia typically improve.

For mild cases, doctors may suggest avoiding cold temperatures and treating pain with over-the-counter anti-inflammatory drugs, along with regular check-ups to monitor the disease.

For moderate and severe cases, treatments may include the following:

- **Antiviral medications** are usually prescribed for those with hepatitis C virus (HCV); if doctors determine that HCV is the cause of the cryoglobulinemia, you will likely be referred to a hepatologist (liver specialist).
- **Immunosuppressive drugs** are the mainstay of treatment for severe disease where vital organs are affected. Corticosteroids such as prednisone, and immunosuppressants such as azathioprine and cyclophosphamide, are widely used.
- **Biologic drugs** such as rituximab is a common treatment option for this condition (biologic drugs are complex proteins that target certain parts of the immune system to control inflammation).
- **Plasmapheresis** is an option when patients have life-threatening or organ-threatening cryoglobulinemia. This procedure filters clumps of cryoglobulins from the blood plasma, helping to prevent cryoglobulins from blocking the arteries and restricting blood flow to organs.

Relapses can occur, so follow-up care is essential.

Side Effects of Treatment

The medications used to treat cryoglobulinemia have potentially serious side effects, such as:

- Lowering your body's ability to fight infection
- Potential bone loss (osteoporosis), among others

Therefore, it's important to see your doctor for regular checkups. Medications may be prescribed to offset side effects.

Infection prevention is also very important. Talk to your doctor about getting a flu shot, pneumonia vaccination, and/or shingles vaccination, which can reduce your risk of infection.

Patients on immunosuppressants should be monitored regularly for side effects.

Relapse

Regular doctor visits and ongoing monitoring are important in detecting relapses and preventing ongoing complications. If your symptoms return, or you develop new ones, report them to your doctor as soon as possible.

Your Medical Team

Effective treatment of cryoglobulinemia may require the coordinated efforts and ongoing care of a team of medical providers and specialists. In addition to a primary care provider, you may need to see the following specialists:

- Rheumatologist (joints, muscles, immune system)
- Dermatologist (skin)
- Hematologist (blood disorders)
- Nephrologist (kidney disease)
- Hepatologist (liver)
- Cardiologist (heart)
- Neurologist (brain/nervous system)
- Others as needed

The best way to manage your disease is to actively partner with your health care providers and get to know the members of the health care team.

It may be helpful to keep a health care journal to track your medications, symptoms, test results and notes from doctor appointments in one place.

To get the most out of your doctor visits, make a list of questions beforehand and bring along a supportive friend or family member, if necessary, to provide a second set of ears and take notes.

Remember, it is up to you to be your own advocate. If you have concerns with the treatment plan, be sure to speak with the medical team. It is always your right to seek a second opinion.

Living with Cryoglobulinemia

Living with cryoglobulinemia can be challenging at times. Fatigue, pain, emotional stress, and medication side effects can take a toll on your sense of well-being. This can affect relationships, work and other aspects of your daily life. Sharing your experience with family and friends, connecting with others through a support group, or talking with a mental health professional can help.

Outlook

The outlook for cryoglobulinemia depends on the presence of underlying diseases, the extent of organ damage, and how you respond to treatment. Some people don't have symptoms and may not need treatment.

For those with moderate to severe disease, appropriate and timely treatment can reduce symptoms, flare-ups, and prevent long-term complications. If permanent damage to nerves or internal organs has not occurred, long-term prognosis is excellent. Because kidney disease is an outcome in some cases of cryoglobulinemia, ongoing monitoring of kidney function is important.

For cryoglobulinemia associated with HCV, effective antiviral therapy usually prevents recurrence of vasculitis.

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