
Cryoglobulinaemia Factsheet

Author
Dr Laurence Knott

Peer Reviewer
Dr Neil Basu & Dr David Kluth

Cryoglobulinaemia is abnormality of the immune system which can sometimes result in vasculitis . Cryoglobulins are formed when the proteins which fight infection (also known as immunoglobulins or antibodies) clump together when exposed to cold. Because of their size, cryoglobulins can block off and cause inflammation of the blood vessels. The skin, kidneys and peripheral nerves (the nerves supplying the arms, legs, hands and feet) are most often affected.

There are three different types of cryoglobulinaemia which tend to involve the three major forms of immunoglobulin (IgA, IgM and IgG) to varying degrees:

Type 1:

The cryoglobulins in this type are composed of one type of immunoglobulin. It is sometimes referred to as a monoclonal or simple type of cryoglobulinaemia., The immunoglobulin involved is usually IgM but occasionally one of the other two forms are involved - IgA or IgG. Type 1 cryoglobulinaemia often occurs in people who have a lymphoproliferative disorder (a condition in which cells called lymphocytes are produced in larger than normal numbers).

Type 2:

The cryoglobulins in this type are made up of two different immunoglobulins, usually IgG and IgM. It often occurs in patients with hepatitis C virus infection.

Type 3:

The cryoglobulins in this type are also made up of two different immunoglobulins, usually IgM and either IgG or IgA. Type 3 occurs in people with hepatitis C virus but also in people with other chronic autoimmune conditions (e.g.Sjogren's syndrome and systemic lupus erythematosus).

Type 1 is referred to as a single cryoglobulinaemia and types 2 and 3 are called mixed cryoglobulinaemias. About a quarter of people with cryoglobulinaemia have type 1, a quarter have type 2, and half have type 3.

Who gets cryoglobulinaemia?

All types of cryoglobulinaemia are rare. Even the commonest forms - the mixed types - only affect about 1 in 100,000 people. The mixed types are commoner in Southern Europe than in Northern Europe. It usually occurs between the ages of 40 and 60 and is three times commoner in women than in men. Between two and 15 people in a 100 who have cryoglobulinaemia also develop inflammation of the blood vessels (vasculitis).

What causes cryoglobulinaemia?

The cause of cryoglobulinaemia is not fully understood. Hepatitis C virus infection is thought to be a cause in many people. Genetic factors (i.e. features inherited from your parents) and the way you react to the environment are also thought to be involved.

What are the symptoms of cryoglobulinaemia?

If you have Type 1 cryoglobulinaemia you may get acrocyanosis (a blue discolouration of the hands or feet) and retinal haemorrhage (bleeding into the tissue lining the back wall of the eye). You may also get Raynaud's phenomenon (pain and paleness of the fingers and toes when exposed to trigger factors such as cold) and arterial thrombosis (blood clots in the arteries).

If you have type 2 or 3 cryoglobulinaemia, you may develop arthralgia (pains in the joints) of the fingers, toes, knees and ankles, kidney problems, liver problems or purpuric papules (red spots) on the legs.

Late on in the condition, some people get cancer of the liver or lymphatic system. (the structures that circulate tissue fluid around the body).

How is cryoglobulinaemia diagnosed?

Cryoglobulins may be found in a cooled sample of your blood. Other tests may detect that your white cell count is raised, your kidneys are not working properly or that you have the features of hepatitis C liver infection. If you have type 2 or 3 cryoglobulinaemia, rheumatoid factor, a substance usually seen in people with rheumatoid arthritis, may be found. Complements – small proteins that help immunoglobulins fight infection – may be at low levels.

Other tests you may need depending on your symptoms are a chest x-ray, scans, heart tests, angiography (x-rays of blood vessels after dye has been injected), tests on the nervous system and removal of a small piece of tissue (biopsy) from the skin, kidney or liver.

What is the treatment for cryoglobulinaemia?

You may not need any treatment if cryoglobulins are found in your blood but you get no symptoms. If you have another condition that has caused the cryoglobulinaemia that illness will need treating. Anti-inflammatory medicines may be helpful if you have joint pains and tiredness. Your immune system may become overactive and you may need medicines to help calm it down. Steroids such as prednisolone are commonly prescribed for this purpose, but additional drugs are commonly required. Medicines such as cyclophosphamide, rituximab and azathioprine have been successfully employed.

What does the future hold for people with cryoglobulinaemia?

The outcome (prognosis) of cryoglobulinaemia varies considerably from person to person. Much will depend on what if any underlying condition has caused the cryoglobulinaemia in the first place. People with kidney or liver problems, lymphoproliferative conditions or cancers tend to have a worse outlook.

Further reading

Ferri C. Mixed cryoglobulinemia. Orphanet J Rare Dis. 2008 Sep 16;3:25. doi: 10.1186/1750-1172-3-25. Review.
<http://www.ncbi.nlm.nih.gov/pubmed/18796155>

Tritch A et al, Cryoglobulinaemia, Medscape 2012.
<http://emedicine.medscape.com/article/329255-overview#a0101>

Motyckova G et al Laboratory testing for cryoglobulins. Am J Hematol. 2011 Jun;86(6):500-2. doi: 10.1002/ajh.22023. Review.
<http://www.ncbi.nlm.nih.gov/pubmed/21594887>

Terrier B et al, Management of noninfectious mixed cryoglobulinemia vasculitis: data from 242 cases included in the CryoVas survey, Blood Journal, 2012 119: 5996-6004
<http://211.144.68.84:9998/91keshi/Public/File/45/119-25/pdf/Blood-2012-Terrier-5996-6004.pdf>