



Cryopyrin-Associated Autoinflammatory Syndrome

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Fast Facts

- CAPS includes three diseases related to a defect in the same gene. These diseases differ in the systems involved and in the severity of the disease.
- The major symptoms include fever, hive-like rash, joint pain and swelling, red eyes, hearing loss and central (brain) nerve problems.
- Treatments that block interleukin-1, an important molecule involved in the inflammatory process, are very effective. To prevent permanent damage, treatment needs to be started early in life.
- The disease is not contagious.

What are CAPS?

Cryopyrin-associated autoinflammatory syndrome (CAPS) includes three diseases related to a defect in the same gene. The three diseases differ in the organs involved and in the severity of the disease.

- Neonatal Onset Multisystem Inflammatory Disease (NOMID), also called Chronic Inflammatory Neurological Cutaneous Articular Syndrome (CINCA) in Europe
- Muckle-Wells syndrome
- Familial cold autoinflammatory syndrome

NOMID is the most severe of the CAPS and causes fever with inflammation in multiple organs. Newborn babies can have signs of infection (e.g., fever, rash) but no infection is found. The rash resembles hives, but is not itchy. Patients can have chronic meningitis (inflammation of the membranes surrounding the brain) resulting in headache, blindness, or hearing loss and other neurologic problems. The eyes often appear as bulging, and children often have episodes of vomiting. After 1 year of age, 50 percent of patients develop joint pain and swelling. There can be growth delay; children with NOMID are often very short. Not all children have all of these symptoms.

In Muckle-Wells syndrome, patients develop episodic fever, rash, red eyes, joint pain and severe headaches with vomiting. Episodes last from 1-3 days. Deafness or partial hearing loss often develops by teenage years.

In familial cold autoinflammatory syndrome, exposure to cold (including air-conditioning) and—perhaps—other environmental triggers causes a hive-like rash. Patients also can develop fever, chills, nausea, severe thirst, headaches and joint pain. Episodes usually last up to 1 day.

Who gets it?

All the CAPS are very rare, found in about one in 500,000 to 1,000,000 people. Familial cold autoinflammatory syndrome is more common in the United States, and Muckle-Wells syndrome is more common in Europe. NOMID is present around the world, and usually starts shortly after birth. Muckle-Wells syndrome may start later in life. Males and females are both affected, and all ethnic groups can be affected.

What causes the disease?

CAPS are genetic diseases. CAPS is inherited as an autosomal dominant disease (in which a mutation in only one copy of the gene inherited from one parent is sufficient to cause disease). That means that one of the parents may be ill with CAPS, or that the gene mutation developed in the sick child. A genetic defect is found by traditional methods in only 50-60 percent of patients with NOMID, 65-75 percent in patients with Muckle-Wells syndrome and in nearly all patients with familial cold autoinflammatory syndrome. The gene mutation causes a defect in a protein called cryopyrin, which has an important role in controlling inflammation.

How is it diagnosed?

CAPS is suspected by the symptoms and signs found by the physician on physical examination. The diagnosis may be confirmed by a genetic test, although occasionally the genetic test may be normal. Other tests may include skin biopsy (examining a small sample of the skin) of the rash, an eye examination, hearing tests, lumbar puncture (obtaining fluid from the spine) and imaging of the brain and inner ears by magnetic resonance imaging (MRI).

How is CAPS treated?

Until recently there was no effective treatment. Patients were treated with medications such as nonsteroidal anti-inflammatory drugs (ibuprofen or naproxen), steroids or methotrexate to reduce symptoms. Exciting research has shown that medications that target interleukin-1 are very effective in treating CAPS. These medications include anakinra (*Kineret*), rilonacept (*Arcalyst*) and canakinumab (*Ilaris*). Treatment must continue throughout life, as there is no known cure.

Other treatments include physical therapy, splints and other aids to treat joint deformities if they occur. Surgery is occasionally needed. Hearing aids are needed for children with deafness.

Living with the disease

Untreated patients suffer from frequent episodes, decreasing the quality of life. Families experience emotional and financial stress taking care of a chronically ill child, and patients can miss a lot of school. Prior to the discovery of effective treatment, patients with familial cold autoinflammatory syndrome usually needed to live in a place with mild weather, a place that is not too cold but also not so hot that there is a constant need for air-conditioning.

The outcome of NOMID used to be such that many patients developed severe joint deformities and neurologic damage, mainly to the ears and eyes. There also were cases of death from brain damage. New treatments may allow children to lead near-normal lives.

Untreated patients may develop a complication of inflammation called amyloidosis. Amyloid is a protein that deposits in certain organs in children with chronic inflammatory disease. The most common organ involved is the kidney, but amyloid can deposit in the intestines, skin and heart. Eventually, amyloid causes a loss of function, especially of the kidneys. This is another reason to continue life-long treatment, even when the child is feeling better.

Points to remember

- CAPS includes three very rare diseases related to a defect in the same protein: cryopyrin.
- The major symptoms include fever; hive-like rash; joint pain and swelling; red eyes; and symptoms of the nervous system, including headaches and deafness.
- Treatments to block interleukin-1 are very effective, and, if started early, may prevent organ damage.

To find a rheumatologist

For more information about rheumatologists, [visit www.rheumatology.org](http://www.rheumatology.org).

For a listing of rheumatologists in your area, [click here](#).

For additional information

The American College of Rheumatology has compiled this list to give you a starting point for your own additional research. The ACR does not endorse or maintain these websites, and is not responsible for any information or claims provided on them. It is always best to talk with your rheumatologist for more information and before making any decisions about your care.

Muckle-Wells syndrome

<http://ghr.nlm.nih.gov/condition=mucklewellssyndrome>

Neonatal onset multisystem inflammatory disease

<http://ghr.nlm.nih.gov/condition=neonatalonsetmultisysteminflammatorydisease>

Familial cold autoinflammatory syndrome

<http://ghr.nlm.nih.gov/condition=familialcoldautoinflammatorysyndrome>

The Rheumatology Research Foundation

www.rheumatology.org/Foundation

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Written by Philip Hashkes, MD, MSc, Shaare Zedek Medical Center and the Hebrew University, Jerusalem, and reviewed by the American College of Rheumatology Communications and Marketing Committee.

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