

# **Familial Cold Auto-Inflammatory Syndrome (FCAS): Fact Sheet**

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## **What It Is**

Familial Cold Auto-Inflammatory Syndrome (FCAS), also known as Familial Cold Urticaria (FCU), is a rare, inherited inflammatory disorder characterized by frequent, recurrent episodes of rash, fever/chills, joint pain, fatigue, eye pain/redness, and other signs/symptoms of systemic inflammation triggered by exposure to cooling temperatures. Onset of FCAS occurs during infancy and early childhood and persists throughout the patient's life.

FCAS is one of the Cryopyrin-Associated Periodic Syndromes (CAPS) most often caused by mutations in the CIAS1/NLRP-3 gene. These syndromes are characterized by unpredictable attacks of fever/chills, fatigue, and eye pain/ redness associated with rash and joint pain.

FCAS shares symptoms, and should not be confused with, acquired cold urticaria, a more common condition mediated by different mechanisms that usually develop later in life and are rarely inherited.

## **Causes and Symptoms**

FCAS is generally caused by mutation in a gene identified as the cold-induced auto-inflammatory syndrome 1 (CIAS1) gene, more recently named the Nod-Like Receptor Protein-3 (NLRP-3) gene. The mutation in the CIAS1/NLRP-3 gene causes increased activity of cryopyrin, a protein that regulates inflammation in the body. The increased activity of cryopyrin results in an overproduction of a protein known as interleukin-1 $\beta$ , which leads to symptoms of inflammation such as recurrent rash, fever/chills, joint pain, fatigue, and eye pain/redness.

## **FCAS Characteristics**

Patients with FCAS experience debilitating symptoms such as recurrent rash, fever/chills, joint pain, fatigue, and eye pain/redness.

Other symptoms may include profuse sweating, drowsiness, headache, extreme thirst, blurred vision, watering eyes, and nausea.

Symptoms occur within hours after exposure to cooling temperatures. In most cases, a rash will occur within a few hours, followed by a fever and joint pain. Episodes usually resolve within 24 hours if further exposure to cooling temperatures is avoided.

## **Incidence and Prevalence**

FCAS appears to be a very rare disease. Since FCAS is a newly discovered condition, the actual incidence and prevalence of the disease is difficult to determine at this time.

## **Living with FCAS**

The symptoms associated with FCAS can cause many patients to become incapacitated. A lack of effective treatments causes patients to utilize a variety of remedies in an attempt to alleviate symptoms, including additional sleep, warming treatments, and, in some cases, moving to warmer climates to reduce the frequency of attacks. FCAS can continue to be a problem, even in warm climates, because signs and symptoms can be triggered even by minor exposure to cooling temperatures such as air conditioning or a cool breeze.

## **Diagnosis & Treatment**

Diagnosis of FCAS is determined through an evaluation of a patient's symptoms. Confirmation of the diagnosis can sometimes be achieved through DNA gene analysis and the identification of a CIAS1/NLRP-3 mutation. Not all patients however, have a detectable genetic mutation, making accurate symptom evaluation critical.

Some of the common criteria that distinguish FCAS from other hereditary periodic fevers include:

- Recurrent, intermittent episodes of fever and rash that primarily follow exposure to cooling temperatures
- Family history of the disease
- Age of onset of less than 6 months of age
- Duration of most attacks is generally up to 24 hours
- Presence of eye pain/redness associated with attacks

While there are no medications currently indicated for the treatment for FCAS, non-steroidal anti-inflammatory drugs are sometimes used to try to alleviate joint pain. In addition, high doses of corticosteroids have been tried, but may cause short- and long-term side effects. There are currently no therapies approved by the U.S. Food and Drug Administration for the treatment of CAPS.