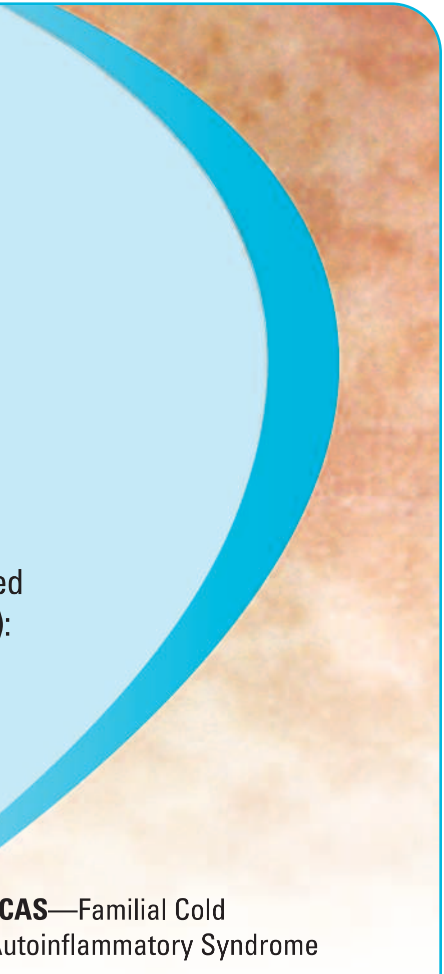


Facts
About CAPS

Your Guide to Learning About Cryopyrin-Associated Periodic Syndrome (CAPS):

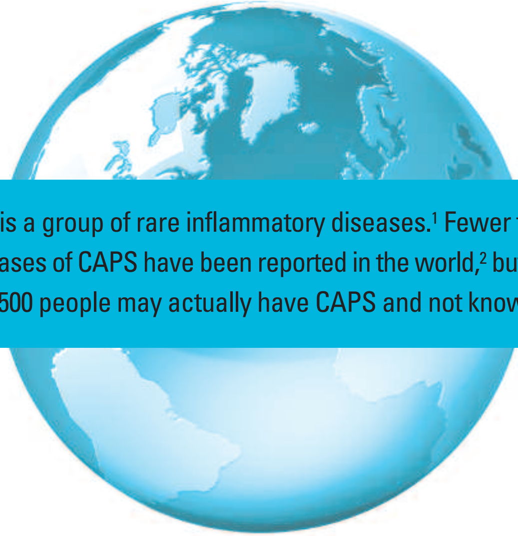
- **FCAS**—Familial Cold Autoinflammatory Syndrome
- **MWS**—Muckle-Wells Syndrome
- **NOMID/CINCA**—Neonatal-Onset Multisystem Inflammatory Disease, also known as Chronic Infantile Neurological Cutaneous Articular Syndrome

What Is CAPS?

CAPS stands for Cryopyrin-Associated Periodic Syndrome. It is the name given to a group of 3 different diseases.

These 3 diseases are:

- **FCAS**, which stands for Familial Cold Autoinflammatory Syndrome
- **MWS**, which stands for Muckle-Wells Syndrome
- **NOMID/CINCA**, which stands for Neonatal-Onset Multisystem Inflammatory Disease, also known as Chronic Infantile Neurological Cutaneous Articular Syndrome



CAPS is a group of rare inflammatory diseases.[1] Fewer than 1000 cases of CAPS have been reported in the world,[2] but more than 5500 people may actually have CAPS and not know it.[3]

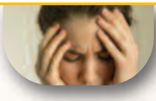
The symptoms of all 3 types of CAPS are a result of the body's reaction to inflammation.[4] The body responds to inflammation with soreness and swelling.

Some people may not know that they have CAPS,[4] but their symptoms will make them aware that something is wrong. If you think you may have CAPS after reading this brochure, you should see a doctor.

If the doctor diagnoses you with CAPS, he will provide treatment to address the inflammation and any symptoms that may follow.

Please see page 14 for the meanings of key words that you may not know in this booklet.

The Facts on FCAS



FCAS stands for Familial Cold Autoinflammatory Syndrome. It can also be called FCAIS or FCU, which stands for Familial Cold Urticaria.

Symptoms of FCAS are less severe than the other 2 types of CAPS,[4] but they can still seriously limit the decisions you make in your day-to-day life about what you can or cannot do.[5] These symptoms include:

- A rash that keeps coming back[4]
- Fever[4]
- Feeling weak or tired[4]
- Pain in the joints[4]
- Headache[4]
- Chills[4]
- Sore or red eyes[6]
- Pain in the muscles[4]

Noticing Symptoms

People with FCAS usually start having symptoms from birth. Occasionally, symptoms may start later in childhood.[4]

Symptoms of FCAS can begin after a person is exposed to cold temperature.[4] For example, being in an air-conditioned room, eating cold foods, or swimming in cool water can bring on symptoms.

A rash will usually start 1 to 2 hours after being exposed to the cold. Other symptoms may start 4 to 6 hours after being exposed to the cold.[7]

There may be some days when symptoms are not felt, but they always come back. These symptoms may get worse throughout the day. Most symptoms last up to 24 hours, although some can last longer.[4]

Some people may not know that they have FCAS.[4] If you think you do, you should see your doctor.

It is important to be diagnosed and get treatment from your doctor. Treatment can help relieve symptoms and, in some cases, may eliminate them.

Rash in FCAS

FCAS Can Disrupt Your Life

In most cases, people that have FCAS know that something is wrong. It is clear to them from their symptoms that they need to see a doctor and find out what is going on with their health.

The symptoms of FCAS can seriously impact your day-to-day activities. Thirty people with FCAS were surveyed to see how FCAS had disrupted their everyday lives before they were treated.[5]

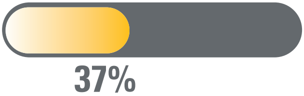
Here is what they said[5]:

- Almost all people with FCAS have had to give up most of their time spent outside

- Many people with FCAS said they have had to cancel plans with friends and family

- Many people with FCAS said that, even if they could work, it was still hard

- More than a third of the people with FCAS have had to leave their jobs



The symptoms of FCAS can strongly affect daily life. There are a number of treatments, however, that can help relieve symptoms and, in some cases, may eliminate them.

Please see page 10 for some of these treatments.

The Facts on MWS

MWS stands for Muckle-Wells Syndrome. MWS was first recognised in a family in the early 1960s by 2 doctors named Thomas James Muckle and Michael Vernon Wells.[8] Since then, doctors have learned much more about MWS.

The symptoms of MWS listed below in **orange** are similar to FCAS symptoms, but they occur more often and may last longer.[4] The symptoms in **green** are additional symptoms that someone with MWS may have.

- A rash that keeps coming back[4]
- Fever[4]
- Feeling weak or tired[4]
- Pain in the joints[4]
- High protein levels in the kidneys[6]
- Headache[4]
- Chills[4]
- Sore or red eyes[6]
- Pain in the muscles[4]
- Gradual loss of hearing[4]

Noticing Symptoms

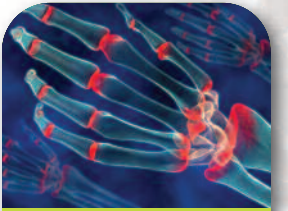
Like FCAS, people with MWS usually start having symptoms from birth. Occasionally, symptoms may start later in childhood.[4]

Symptoms can occur without any obvious reason. Only a few things have been linked to starting or making symptoms of MWS worse. For example, symptoms can begin after a person is exposed to cold temperature, feels stressed, or when the body is tired.[4]

There may be some days when symptoms are not felt, but they always come back. These symptoms may start anytime after being set off. Most symptoms last 1 to 2 days, although some can last longer.[4]

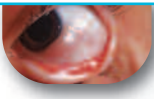
Some people may not know that they have MWS,[4] but their symptoms will make them aware that something is wrong. If you think you have MWS, you should see your doctor.

It is important to be diagnosed and get treatment from your doctor. Treatment can help relieve symptoms and, in some cases, may eliminate them.



Pain in the joints in MWS

The Facts on NOMID



NOMID stands for Neonatal-Onset Multisystem Inflammatory Disease. NOMID can also be called CINCA, which stands for Chronic Infantile Neurological Cutaneous Articular Syndrome.

NOMID/CINCA is the most severe type of CAPS.[4] The symptoms of NOMID/CINCA listed below in **green** are similar to MWS symptoms, but they are felt all the time.[4] The symptoms in **blue** are additional symptoms that someone with NOMID/CINCA may have.

- A rash that keeps coming back[4]
- Fever[4]
- Feeling weak or tired[4]
- Pain in the joints[4]
- High protein levels in the kidneys[6]
- Swelling of the knees[6]
- Headache[4]
- Chills[4]
- Sore or red eyes[6]
- Pain in the muscles[4]
- Gradual loss of hearing[4]
- Gradual loss of eyesight[4]
- Mental difficulties[4]

Noticing Symptoms

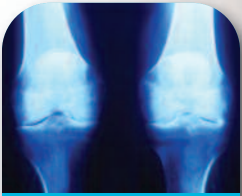
People with NOMID/CINCA almost always start having symptoms from birth.[4] A doctor may diagnose NOMID/CINCA quickly in a newborn because symptoms are often more noticeable than in FCAS or MWS.[9,10]

NOMID/CINCA can be disabling[1] and, without treatment, some cases may result in death.[11] Treatment can help symptoms to some degree, but they never completely go away.[4]

It is clear to parents of children with NOMID/CINCA how much they suffer. From the moment they are born, it is a constant battle to keep NOMID/CINCA from getting worse.

For patients with all types of CAPS, but especially for those who need support for NOMID/CINCA, there are organisations that can help.

Please see page 13 for some informative Web sites.



Swelling of the knees in NOMID/CINCA

Why Haven't I Heard of CAPS?

CAPS is rare.[1] Fewer than 1000 cases of CAPS have been reported in the world,[2] but more than 5500 people may actually have CAPS and not know it.[3] Because CAPS is so rare, most doctors will not have seen a patient with CAPS.[10]

Milder symptoms, such as headache and fever, can appear to be due to other things.[4,6] It can take some time before a doctor begins to think about CAPS because it is not something he or she sees every day.[4]

Even those who have milder symptoms of CAPS may think their symptoms are due to the flu. So, they may not visit the doctor to ask about these symptoms.[4]

If you think you have CAPS, you should talk to your doctor. Bring this booklet with you so that you can remember the symptoms you want to talk to your doctor about.

It is important to be diagnosed and get treatment from your doctor. Treatment can help relieve symptoms and, in some cases, may eliminate them.

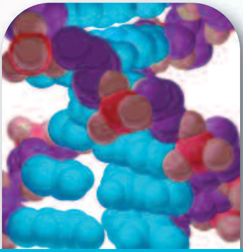
How Does Someone Get CAPS?

CAPS is usually passed on from one parent to the child through the genes.[4] So, it is likely that someone who has CAPS got it from a parent.

Just because someone in your family has CAPS doesn't mean that you do too.[6]

Some people can have CAPS without anyone else in their family having it. However, for most, CAPS can be traced back in their family for many generations.[6]

If someone in your family has CAPS, you should talk to your doctor.



How Do I Know If I Have CAPS?

Any of the symptoms of the 3 types of CAPS can range from extremely uncomfortable to disabling in severe cases.[4,5] Even if they are mild and don't seem to always be there, it is important to bring these symptoms to a doctor's attention.

Think about the answers to these questions:

- Do you get frequent rashes, fevers, or headaches?
- Do you feel a strong reaction to cold temperature?
- Do you always feel like you have the flu?
- Does your body ache constantly?
- Have you felt the same aches since you were a child?
- Do your aches seem to be getting worse?
- Have any of your family members or relatives ever suffered similar symptoms?
- Do any of your family members or relatives have CAPS?

Talk to your doctor about your answers to these questions. Details about your symptoms and your family history will help the doctor make the correct diagnosis.

Bring this booklet along with you to help you remember what you want to talk about.

It is important to be diagnosed and get treatment from your doctor. Treatment can help relieve symptoms and, in some cases, may eliminate them.

If you do have CAPS, your doctor will arrange to treat the symptoms with one of the medications available.

Current Treatments for CAPS

There is no cure yet for the cause of CAPS. However, based on the type of CAPS that you have and how bad your symptoms are, your doctor may suggest any of the following current treatment options to attempt to manage the symptoms of CAPS.

These treatments may be used alone or in combination, depending on the doctor's advice*:

- NSAIDs (nonsteroidal anti-inflammatory drugs) may be used for FCAS, MWS, and some NOMID/CINCA patients[4,9]
- Antihistamines may be used for FCAS patients[5]
- Steroids may be used for FCAS, MWS, and NOMID/CINCA patients[1,5]
- Immunosuppressants/immunomodulators may be used for MWS and NOMID/CINCA patients[1,12]

Although these treatments may be helpful, certain symptoms may not be relieved and others may not be relieved for long. This is because these treatments target only the symptoms while working to reduce inflammation overall.

*Remember: follow only your doctor's advice about treatment.

Future Treatments for CAPS

Research continues in the search to find a more complete treatment for CAPS that addresses more than just the symptoms. Targeted treatments are in development at this time for medications that will actually target the underlying cause of the inflammation and symptoms of CAPS.

Researchers believe these medications may have the ability to treat the inflammation in CAPS better and help stop symptoms from becoming worse. These medications are not yet approved, but they are being studied in clinical trials.

When Will New Treatments Be Approved?

Before a drug can be approved to be used, it has to go through clinical trials to show that it works. People who take part in these trials volunteer if their doctors think that it is a right match.

By participating in these trials, patients have the opportunity to receive medication for their disease that may not be available to the public yet.

Sometimes a person in a trial is given the actual drug being studied. Sometimes they are given a different drug that is already approved to treat the symptoms. At other times, a placebo is given.

Every trial needs a certain number of people to take part in it. Some trials can be as short as 1 month, while others can last 1 year or more.

There is no cost to take part in a trial. All drugs and doctor visits are free.

If your doctor diagnoses you with CAPS, you can ask him or her about how you can join any of these ongoing trials.

What Else Can I Do?

If you have FCAS or MWS, your doctor may also suggest these actions to ease your symptoms[4]:

- Keep warm with a hot beverage, warm bath, or layers of clothing
- Cut back on heavy exercise
- Avoid things that cause you stress on a regular basis

In some serious cases, these changes may not help. CAPS sufferers who get cold easily and find their symptoms becoming worse may consider living somewhere where the weather is warmer.[4] This can help relieve symptoms.

Where Else Can I Find Information?

There are support groups and organisations online that offer information about CAPS. The main goal is to help people understand these diseases and help improve the lives of people with CAPS.

Visit any of the sites below to learn more:

- CAPS Family Network—http://www.capsfamilynetwork.com
- The NOMID Alliance—http://www.nomidalliance.net
- The Genetics Home Reference Guide—http://ghr.nlm.nih.gov
- The Portal for Rare Diseases and Orphan Drugs—http://www.orpha.net
- National Organization for Rare Disorders (NORD)—http://www.rarediseases.org/
- International Society of Systemic Auto-Inflammatory Diseases (ISSAID)—http://fmf.igh.cnrs.fr/ISSAID/
- Centre de Référence des Maladies Auto-Inflammatoires—http://asso.orpha.net/CEREMAI/index.html

By browsing the Internet, you may come across other Web sites that support CAPS and allow people with CAPS to share their experiences. However, your doctor's advice is the best advice to follow.

Key Words

Antihistamines: drugs commonly used to treat allergies.
Articular: having to do with the joints in your body.
Autoinflammatory: inflammation in the body that occurs on its own without infection or injury.
Chronic: constant or frequent symptoms that keep coming back.
Clinical trials: studies used to determine if a new drug is approved.
Cutaneous: having to do with the skin.
Diagnose: a doctor confirms that you have an illness.
Disease: an illness that is set apart from others by the symptoms you may feel. It may also be called a *syndrome*.
Genes: when an illness is passed on through the genes, it means you can get it from your family or relatives. For example, if your parents have brown hair, you will likely have brown hair. Likewise, if your parents have CAPS, you are likely to also have CAPS.
High protein levels: proteins are the building blocks for all the parts of your body. For example, they make up the cells that act as your body's natural defence. Small amounts of protein may normally be found in your kidneys. But high protein levels in your kidneys may suggest an infection and should be treated by your doctor at once.
Immunosuppressants/immunomodulators: drugs commonly used to reduce inflammation.
Infantile: having to do with a baby, usually before walking age.
Inflammation: the body's natural defence to protect itself against infection or injury. In CAPS patients, inflammation occurs without infection or injury.
Inflammatory disease: an illness that is caused by inflammation. CAPS is a specific type of inflammatory disease called an autoinflammatory disease. See *autoinflammatory* definition above.
Neonatal: having to do with a newborn baby.
Neurological: having to do with the brain, the spine, and the nerves in your body.
Orphan drug: medicine that treats a rare disease.
Placebo: a treatment that has no medicine but is given in place of an actual treatment, usually as part of a clinical trial.
Rare disease: an uncommon illness that affects very few people in the world.
Steroids: drugs commonly used to treat a range of conditions, from irritation of the skin to joint pain.
Symptoms: a description of the way you are feeling due to a specific illness.
Syndrome: a group of symptoms that describe a specific illness. It may also be called a *disease*.
Urticaria: skin rash caused by inflammation.

References

1. Farasat S, Aksentijevich I, Toro JR. Autoinflammatory diseases: clinical and genetic advances. *Arch Dermatol*. 2008;144(3):392-402.
2. Data on file. Novartis Pharmaceuticals Corporation.
3. Durrant KLW, Goldbach-Mansky R, Hoffman H, Leslie K, Rubin B. CAPS: cryopyrin-associated periodic syndromes. San Francisco, CA: The NOMID Alliance; 2008.
4. Hoffman HM. Hereditary immunologic disorders caused by pyrin and cryopyrin. *Curr Allergy Asthma Rep*. 2007;7(5):323-330.
5. Stych B, Dobrovolny D. Familial cold auto-inflammatory syndrome (FCAS): characterization of symptomatology and impact on patients' lives. *Curr Med Res Opin*. 2008;24(6):1577-1582.
6. Shinkai K, McCalmont TH, Leslie KS. Cryopyrin-associated periodic syndromes and autoinflammation. *Clin Exp Dermatol*. 2007;33(1):1-9.
7. Familial Cold Autoinflammatory Syndrome (FCAS). The NOMID Alliance Web site. http://www.nomidalliance.net/subpage1.html. Accessed April 13, 2009.
8. Muckle TJ, Wells M. Urticaria, deafness and amyloidosis: a new heredo-familial syndrome. *QJM*. 1962;31:235-248.
9. Boschan C, Witt O, Lohse P, Foeldvari I, Zappel H, Schweigerer L. Clinical report: neonatal-onset multisystem inflammatory disease (NOMID) due to a novel s331r mutation of the CIAS1 gene and response to interleukin-1 receptor antagonist treatment. *Am J Med Genet*. 2006;140A:883-886.
10. Gattorno M, Federici S, Pelagatti MA, et al. Diagnosis and management of autoinflammatory diseases in childhood. *J Clin Immunol*. 2008;28 (suppl 1):S73-S83.
11. Prieur AM, Griscelli C, Lampert F, et al. A chronic infantile neurological cutaneous and articular (CINCA) syndrome: a specific entity analysed in 30 patients. *Scand J Rheumatol Suppl*. 1987;66:57-68.
12. Watts RA, Nicholls A, Scott DGI. Case report: the arthropathy of the Muckle-Wells syndrome. *Br J Rheumatol*. 1994;33(12):1184-1187.

What Is CAPS?

This booklet is your guide for all you need to know about CAPS. In it, you will learn what CAPS is, who gets CAPS, and what causes CAPS, as well as facts about CAPS symptoms and treatments.

If you think you or a family member has CAPS, here are some questions that may be used to help talk to a doctor:

- Do you get frequent rashes, fevers, or headaches?
- Do you feel a strong reaction to cold temperature?
- Do you always feel like you have the flu?
- Does your body ache constantly?
- Have you felt the same aches since you were a child?
- Do your aches seem to be getting worse?
- Have any of your family members or relatives ever suffered similar symptoms?
- Do any of your family members or relatives have CAPS?

Bring this booklet to the doctor's office to help remember what to address.

It is important that you speak with your doctor to see if you are suffering from CAPS. Your doctor can provide treatment to help relieve symptoms and, in some cases, eliminate them.

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