CONDITION

Autoinflammatory diseases

Learn how autoinflammatory diseases cause repeated inflammation, how doctors diagnose them, and which treatments and follow-up may help.

WHAT IT IS
Group of disorders causing untriggered inflammation

BODY SYSTEM
Immune system

MAIN SYMPTOMS
Repeated fevers, skin rashes, joint pain, abdominal pain

WHAT CAUSES IT
Immune dysfunction, sometimes inherited

HOW IT IS DIAGNOSED
Clinical pattern, blood tests, sometimes genetic testing

MAIN TREATMENT
Inflammation-controlling medicines

CAN IT BE CURED?
No, medicines manage ongoing inflammation

IS IT AN EMERGENCY?
Sometimes, with difficulty breathing

LONG-TERM OUTLOOK
Variable, with organ damage if uncontrolled

Overview

Autoinflammatory diseases are a group of disorders in which the immune system causes inflammation without an appropriate trigger. The inflammation may occur in repeated attacks, called flares, or remain active for long periods.

These conditions mainly involve the innate immune system , the body's rapid first line of defense against infection and injury. In contrast, autoimmune diseases usually involve the adaptive immune system mistakenly targeting specific cells or tissues. The two groups can overlap, so the distinction is not always exact.

Some autoinflammatory diseases are caused by a change in a single gene. These are called monogenic autoinflammatory diseases . Examples include familial Mediterranean fever, cryopyrin-associated periodic syndromes, tumor necrosis factor receptor-associated periodic

syndrome, and mevalonate kinase deficiency.

Other conditions involve several genes along with environmental or immune factors. Examples include systemic juvenile idiopathic arthritis, adult-onset Still disease, and periodic fever, aphthous stomatitis, pharyngitis, and cervical adenitis syndrome, commonly called PFAPA.

Autoinflammatory diseases are important because repeated inflammation can affect the joints, skin, eyes, hearing, kidneys, and other organs. Some conditions begin in infancy or childhood, but symptoms may first appear in adulthood. The pattern, severity, and long-term risks differ greatly among diseases.

Many autoinflammatory diseases can be managed with medicines that control specific inflammatory pathways. Identifying the condition can also help doctors plan monitoring, assess relatives when appropriate, and reduce the risk of organ damage.

Symptoms

Symptoms may occur in predictable attacks, irregular flares, or ongoing periods of inflammation. Attacks can last from hours to weeks, depending on the condition. Some people feel well between episodes, while others have continuing fatigue, pain, or inflammation.

Common features include:

Certain patterns may suggest a particular disease. Familial Mediterranean fever can cause short attacks of fever with severe abdominal, chest, or joint pain. Cryopyrin-associated periodic syndromes may cause a hive-like rash, headaches, joint symptoms, and inflammation triggered by cold in some people. Mevalonate kinase deficiency may involve fever, swollen lymph nodes, abdominal symptoms, and mouth ulcers.

Symptoms alone cannot confirm an autoinflammatory disease. Infection, autoimmune disease, cancer, medication reactions, and other conditions can cause similar problems.

A fever during a known flare is not automatically harmless. Seek emergency care for difficulty breathing, severe chest pain, confusion, a seizure, fainting, blue or gray lips, a stiff neck with severe illness, or signs of a serious allergic reaction. Prompt medical assessment is also important for severe dehydration, rapidly worsening symptoms, or fever in someone taking a medicine that weakens immune defenses.

- Repeated or unexplained fevers
- Skin rashes, hives, or painful skin lesions
- Joint pain, swelling, or stiffness

- Muscle pain
- Abdominal pain, vomiting, or diarrhea
- Chest pain caused by inflammation around the lungs or heart
- Headaches or eye redness
- Mouth ulcers, sore throat, or swollen neck glands
- Fatigue and reduced appetite

Causes and risk factors

Inflammation is normally a protective response. In autoinflammatory disease, signaling systems that start or stop inflammation do not work as they should. Some conditions involve an overactive inflammasome , a group of proteins inside cells that helps produce inflammatory signals such as interleukin-1.

Inherited gene variants can disrupt these pathways. Depending on the disease, one altered copy of a gene may be enough to cause symptoms, or a person may need altered copies from both parents. A new genetic change can also occur in a child even when neither parent has the condition. In some disorders, only a portion of the body's cells carries the change, which is called mosaicism.

Having a gene variant does not always predict when symptoms will begin or how severe they will become. Some variants have uncertain effects, and a negative genetic test does not rule out every autoinflammatory disease.

Risk patterns depend on the specific condition. Familial Mediterranean fever is more common among people with ancestry from regions around the Mediterranean, including people of Armenian, Arab, Turkish, North African Jewish, or Sephardic Jewish ancestry. However, it can occur in any population.

Flares may happen without a clear reason. In some people, infections, stress, cold exposure, lack of sleep, physical exertion, menstruation, or medical procedures appear to trigger episodes. These triggers do not cause the underlying disease.

Diagnosis

There is no single test for all autoinflammatory diseases. Diagnosis usually combines the symptom pattern, physical examination, family history, laboratory results, and sometimes genetic testing. A rheumatologist or clinical immunologist often coordinates the evaluation.

Children may see a pediatric rheumatologist.

A detailed history is especially useful. Your clinician may ask when attacks began, how long they last, which symptoms occur together, whether you are completely well between episodes, and whether relatives have similar problems. Keeping a diary of fever readings, symptoms, possible triggers, and photographs of rashes can help reveal a pattern.

Blood tests during a flare may include a complete blood count and tests of inflammation, such as C-reactive protein and erythrocyte sedimentation rate. Serum amyloid A may be measured in selected cases because persistent elevation can be linked to a complication called AA amyloidosis.

Doctors may also order:

Testing often needs to rule out infection before inflammation-suppressing treatment is started. Depending on the symptoms, evaluation may also address inflammatory bowel disease, immune deficiency, blood disorders, cancer, medication reactions, and other causes of repeated fever.

Genetic results require careful interpretation. A clearly disease-causing variant may support the diagnosis, but a variant of uncertain significance does not prove that a person has the condition. Genetic counseling can explain what a result may mean for the patient and their relatives.

- Kidney and liver function tests
- Urine tests for blood or protein
- Tests for infection or autoimmune disease
- Imaging or examination of affected organs
- Genetic testing for suspected inherited syndromes

Treatment and management

Treatment depends on the specific disease, affected organs, flare frequency, and test results. The main goals are to control symptoms, reduce inflammation between attacks, prevent organ damage, and support daily activities.

Colchicine is the standard long-term treatment for most people with familial Mediterranean fever. It can reduce attacks and helps prevent AA amyloidosis. Treatment response and side effects require medical monitoring. Patients should not change or stop colchicine without discussing it with their clinician.

Medicines that block interleukin-1, including anakinra and canakinumab, are important treatments for several autoinflammatory diseases. They may be used for cryopyrin-associated periodic syndromes and selected cases of familial Mediterranean fever, tumor necrosis factor receptor-associated periodic syndrome, mevalonate kinase deficiency, or Still disease. These medicines affect immune signaling and can increase the risk of infection, so screening and ongoing monitoring are needed.

Other treatments may include nonsteroidal anti-inflammatory drugs like ibuprofen or naproxen for pain and fever, short courses of corticosteroids like prednisone or hydrocortisone for certain flares, or medicines that block other inflammatory signals. Tumor necrosis factor, interleukin-6, or Janus kinase inhibitors may be considered for particular conditions. Long-term corticosteroid use is generally limited when possible because it can cause significant adverse effects.

Management may also involve:

Antibiotics like amoxicillin or doxycycline do not treat autoinflammatory inflammation unless a bacterial infection is also present. Fever should not automatically be assumed to be a flare, particularly when it has an unusual pattern or occurs while taking an immune-modifying medicine.

- A written plan for recognizing and treating flares
- Physical activity or physical therapy suited to joint symptoms
- School or workplace support during unpredictable attacks
- Vaccination planning before and during immune-modifying treatment
- Genetic counseling for inherited conditions
- Mental health support when chronic symptoms affect mood or daily life

Complications

Uncontrolled inflammation can cause complications, although the risks differ by disease. One important complication is AA amyloidosis . In this condition, an inflammatory protein builds up in organs, most often the kidneys. Early signs may include protein in the urine, while advanced disease can impair kidney function.

Chronic joint inflammation may cause reduced movement or joint damage. Some cryopyrin-associated periodic syndromes can lead to hearing loss, eye inflammation, or inflammation around the brain and spinal cord. Persistent inflammation in children can affect growth and participation in school or activities.

Repeated illness can also disrupt sleep, education, employment, relationships, and emotional well-being. Effective inflammation control and regular monitoring can lower several of these risks.

Follow up

Routine follow-up is important even when symptoms are controlled. The schedule depends on the condition and treatment. Visits may review flare frequency, daily functioning, medication use, side effects, growth in children, and any new organ symptoms.

Monitoring may include blood counts, liver and kidney tests, inflammatory markers, and urine testing for protein. People receiving immune-modifying medicines may need infection screening and medication-specific monitoring. Hearing, eye, joint, or neurologic assessments may be appropriate for certain diseases.

Contact your usual clinical team promptly if attacks become more frequent, symptoms change from their usual pattern, treatment stops working, or medication side effects develop. Fever, cough, painful urination, unusual weakness, or other possible infection symptoms should be reported promptly when taking medicine that suppresses immune activity.

Emergency symptoms are different from routine follow-up concerns. Seek immediate care for trouble breathing, severe or persistent chest pain, confusion, seizures, fainting, severe dehydration, or a rapidly worsening illness. Tell emergency clinicians about the autoinflammatory condition and all current medicines, but do not assume that a new fever is caused by the condition.

Sources

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