CONDITION

Chronic granulomatous disease

Learn how chronic granulomatous disease affects infection-fighting immune cells, including its symptoms, diagnosis, preventive care, treatment, and follow-up.

WHAT IT IS
Rare inherited immune system disorder

BODY SYSTEM
Immune system

MAIN SYMPTOMS
Repeated infections, fever, cough, skin abscesses

WHAT CAUSES IT
Inherited harmful gene change

HOW IT IS DIAGNOSED
DHR flow cytometry and genetic testing

MAIN TREATMENT
Preventive antimicrobial treatment

CAN IT BE CURED?
Sometimes, stem cell transplant can cure

IS IT AN EMERGENCY?
Sometimes, with severe difficulty breathing

LONG-TERM OUTLOOK
Lifelong specialist care with curative transplant for selected patients

Overview

Chronic granulomatous disease, or CGD, is a rare inherited disorder of the immune system. It affects certain white blood cells called phagocytes, which normally surround and kill bacteria and fungi.

In CGD, phagocytes cannot make the normal "oxidative burst" used to destroy some germs. An oxidative burst is a rapid release of germ-killing chemicals inside the cell. As a result, people with CGD are more likely to develop serious or repeated bacterial and fungal infections.

CGD can also cause excessive inflammation. The immune system may form clusters of inflammatory cells called granulomas. These clusters can damage tissue or block parts of the digestive or urinary tract. Some people develop inflammation resembling inflammatory bowel disease.

The condition is often identified during childhood, but milder forms may not be diagnosed until adolescence or adulthood. The age at diagnosis and severity vary according to the genetic change and how much immune-cell function remains.

CGD requires lifelong specialist care. Preventive medicines, early treatment of infections, and attention to environmental exposures can greatly reduce health risks. A hematopoietic stem cell transplant, also called a bone marrow transplant, can cure the underlying immune defect in selected patients.

Symptoms

Symptoms vary widely. Some people have frequent infections beginning in infancy, while others have fewer problems and receive a diagnosis later in life.

Infections may affect the lungs, skin, lymph nodes, liver, bones, or bloodstream. They may return after treatment or be unusually difficult to clear. Common signs include:

Pneumonia is an important concern. Fungal pneumonia may develop after exposure to heavy amounts of mold, such as when handling mulch, compost, hay, or decaying leaves.

Inflammation can occur even when no active infection is found. Granulomas may narrow the stomach outlet, bowel, or urinary tract. This may cause vomiting, constipation, abdominal swelling, painful urination, or difficulty passing urine. CGD-related bowel inflammation may cause chronic diarrhea, abdominal pain, or rectal bleeding.

CGD does not usually cause an increased number of routine viral illnesses. However, any illness can be harder to evaluate in someone who also has a higher risk of bacterial or fungal infection.

- Fever, chills, unusual tiredness, or poor appetite
- Ongoing cough, shortness of breath, or chest discomfort
- Painful or swollen lymph nodes
- Skin sores, boils, or abscesses containing pus
- Abdominal pain, diarrhea, blood in the stool, or poor weight gain
- Bone pain, swelling, or reduced movement
- Repeated mouth sores or gum inflammation

Causes and risk factors

CGD is caused by a harmful change in a gene involved in the NADPH oxidase system. This

system allows phagocytes to produce the chemicals needed to kill certain bacteria and fungi.

The most common form is X-linked CGD, caused by a change in the `CYBB` gene on the X chromosome. It mainly affects people with one X chromosome. A parent who carries the gene change may pass it to a child.

Other forms are autosomal recessive. These occur when a person inherits two altered copies of a CGD-related gene, usually one from each parent. Genes associated with these forms include `CYBA`, `NCF1`, `NCF2`, `NCF4`, and `CYBC1`.

A person can have CGD without a previously known family history. A gene change may be new in that person, or other relatives may carry the change without having been diagnosed.

People who carry an X-linked `CYBB` change usually have a mixture of normally functioning and affected phagocytes. Some carriers develop mouth ulcers, skin symptoms, joint pain, fatigue, or autoimmune-like inflammation. Serious infections are uncommon but can occur, particularly when only a small proportion of phagocytes function normally.

CGD increases susceptibility to particular germs. Important examples include Staphylococcus aureus , Serratia marcescens , Burkholderia cepacia complex, Nocardia species, and Aspergillus fungi. Other organisms can also cause infection, so laboratory testing is important.

Environmental exposure does not cause CGD. However, breathing in large amounts of fungal material from compost, mulch, construction dust, barns, or decaying vegetation can raise the risk of severe fungal infection in someone who has the condition.

Diagnosis

CGD may be considered when a person has repeated deep infections, infections caused by unusual organisms, liver or skin abscesses, fungal pneumonia, or granulomatous inflammation. A family history of CGD or unexplained severe infections can also prompt testing.

The main screening test is the dihydrorhodamine, or DHR, flow cytometry test. A laboratory stimulates a sample of white blood cells and measures their oxidative burst. The pattern can show whether phagocytes are functioning normally and may help distinguish X-linked CGD, autosomal recessive CGD, and some carrier states.

An older test called the nitroblue tetrazolium, or NBT, test may still be used in some settings. DHR testing generally provides more detailed information.

Genetic testing can identify the specific gene change. This confirms the diagnosis in many cases and helps with family testing, genetic counseling, and transplant planning. Test results should be interpreted by clinicians familiar with immune disorders because other conditions

can occasionally produce unusual oxidative-burst results.

When an infection is suspected, evaluation may include blood tests, cultures, imaging, or a sample from the affected tissue. A culture attempts to grow and identify the germ so treatment can be targeted. In some cases, a biopsy is needed to distinguish infection from inflammation.

Relatives may be offered testing after a diagnosis is confirmed. A genetic counselor can explain inheritance, carrier testing, and reproductive testing options without assuming what choices a family should make.

Treatment and management

Care is usually coordinated by a clinical immunologist or infectious disease specialist with experience in CGD. Other specialists may be involved for lung, liver, bowel, or inflammatory complications.

Preventive antimicrobial treatment is central to long-term care. Many people take an antibacterial medicine and an antifungal medicine on a regular schedule. Trimethoprim-sulfamethoxazole is commonly used for bacterial prevention, while an azole antifungal like fluconazole or terbinafine may be used to prevent fungal infection. The specific medicines depend on age, allergies, prior infections, drug interactions, and laboratory results.

Interferon gamma-1b may be offered to reduce the risk of serious infections. Practice varies among countries and treatment centers. It is given by injection and can cause flu-like symptoms, among other side effects. A specialist can explain whether it is appropriate in a particular situation.

Suspected infections need prompt assessment. Treatment may involve antibiotics or antifungal medicines, sometimes given through a vein and continued for an extended period. Samples should be collected for culture when possible. An abscess may need image-guided drainage or surgery, but some CGD liver abscesses require a more specialized approach.

Inflammatory complications can be difficult to separate from infection. Corticosteroids or other medicines that reduce immune activity may help selected inflammatory problems, but they can also make an untreated infection worse. These treatments require specialist supervision, often together with antimicrobial therapy.

Hematopoietic stem cell transplantation replaces the blood-forming cells that produce defective phagocytes. It is an established curative treatment for CGD. The decision involves the person's health, infection history, organ damage, donor options, and transplant-center experience. Transplantation also has important risks, including severe infection,

graft-versus-host disease, infertility, and failure of the donated cells to establish themselves.

Gene therapy aims to correct a person's own blood-forming stem cells. It remains available mainly through specialized research programs and is not routine treatment.

Daily precautions can reduce exposure without requiring complete isolation. People with CGD are generally advised not to handle mulch, compost, hay, or decaying plant material. A care team can provide practical guidance about gardening, construction sites, farm environments, swimming, pets, travel, food safety, and vaccines.

Vaccination plans should be reviewed with the immunology team. Many routine vaccines remain useful, but certain live bacterial vaccines, including the BCG tuberculosis vaccine, can cause infection in CGD and are generally avoided.

Complications

Repeated or severe infections can damage the lungs, liver, bones, skin, or other organs. Possible complications include chronic lung changes, liver abscesses, bone infection, bloodstream infection, and reduced liver blood flow.

Inflammation can cause colitis, bowel narrowing, urinary obstruction, or granulomas in other tissues. Persistent digestive symptoms may affect nutrition, growth, and quality of life.

Medicines used for prevention and treatment can also cause problems. Depending on the drug, these may include allergic reactions, changes in blood-cell counts, liver or kidney injury, nerve symptoms, or interactions with other medicines. Some antifungal drugs require laboratory monitoring and careful review of other prescriptions and supplements.

Living with an uncommon lifelong condition can affect school, work, travel, relationships, and emotional health. Support from mental health professionals, social workers, patient organizations, and other families affected by CGD may be helpful.

Follow up

Regular follow-up is important even when a person feels well. Visits may include a review of infections, bowel or urinary symptoms, medication use, environmental exposures, growth in children, and emotional well-being.

Blood tests may be used to monitor blood-cell counts and liver or kidney function. Some medicines need additional monitoring. The care team should know about all prescription drugs, nonprescription products, and supplements because interactions can change antimicrobial

levels or side effects.

A written illness plan can explain whom to call, where to seek care, and which tests may be needed. Tell any clinician evaluating an illness that CGD is present, even if the symptoms initially appear mild.

Contact the CGD care team promptly for fever or a new sign of infection. The team should provide a personal fever threshold and instructions. New cough, chest pain, shortness of breath, painful swelling, an abscess, persistent vomiting, worsening diarrhea, blood in the stool, or trouble urinating also needs timely medical advice.

Seek emergency care for severe difficulty breathing, blue or gray lips, confusion, fainting, inability to wake normally, signs of shock, or rapidly worsening illness. These are different from stable concerns that can be discussed at a scheduled follow-up visit.

Sources

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