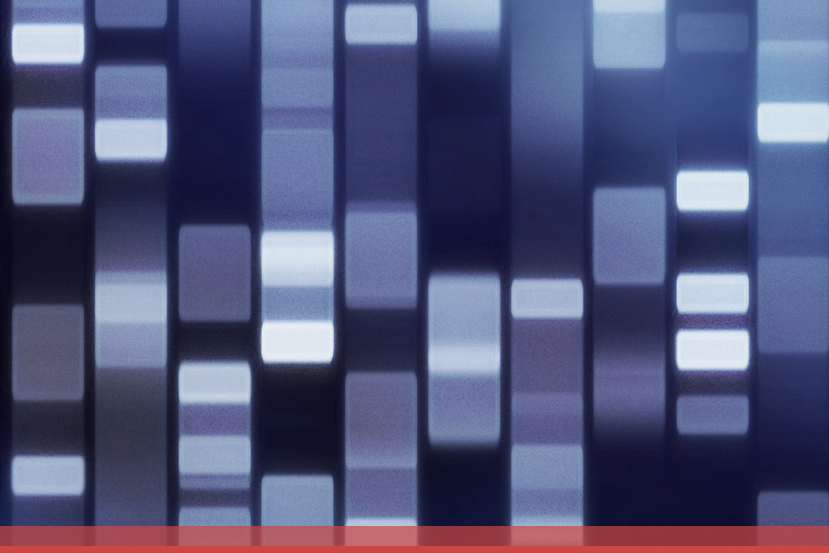
CGD ASSOCIATION OF AMERICA



WHAT IS CGD?

A QUICK RESOURCE FOR PATIENTS TO DISCUSS WITH THEIR MEDICAL PROVIDERS

Chronic Granulomatous Disease (CGD) is a rare, inherited genetic disorder that prevents the immune system from fighting specific types of bacteria or fungus infections. In CGD, white blood cells (phagocytes or neutrophils) are unable to make hydrogen peroxide to kill certain types of bacteria and fungi. Patients with CGD are highly prone to infections with these organisms in the lungs (pneumonias), lymph nodes, liver or bones. These infections can be life-threatening. CGD can also cause excessive inflammation and autoimmune problems, particularly inflammatory bowel disease.

CAUSES OF CGD

CGD is caused by defects in an enzyme, NADPH Oxidase, which is essential for proper functioning of the immune system. These defects are linked to any of one of five different genes that make subunit components of the NADPH Oxidase. The most common genetic form of CGD, affecting about 70 percent of patients, is caused by a defect that is inherited via the X chromosome. Therefore it mostly affects males. The other forms of CGD are caused by defects on other chromosomes and can affect both males and females equally.

SYMPTOMS OF CGD

The immune system of a patient with CGD does not work properly, leaving the body prone to bacterial and fungal infections, such as *staphylococcus aureus*, *serratia marcescens*, *burkholderia cepacia*, *nocardia* species, and organisms from the *aspergillus* species. However, response to viral infections is normal in patients with CGD.

CGD may involve any organ system or tissue of the body, but infections are usually found in the skin, lungs, liver, lymph nodes, gastrointestinal tract, bones, and occasionally the brain. Wounds may also have trouble healing and an inflammatory condition known as granuloma may develop. Pneumonia caused by a fungus such as aspergillus is a red flag for CGD. Infection b y normally non-pathogenic bacteria is also a red flag for CGD. A person with CGD will often show signs of an immunodeficiency at a very young age. Symptoms include, but are not limited to:

- Granulomas (small areas of tissue inflammation), often located in the lung or gastrointestinal tract (which can cause chronic inflammatory bowel disease that closely resembles Crohn's Disease or ulcerative colitis)
- Abscesses (collections of pus) in the lungs, liver, spleen, bones, or skin
- Swollen lymph nodes or lymphadenitis
- Continuous diarrhea, bloody diarrhea, or abdominal pain
- Prolonged or "yo-yo" fevers with no clear indication as to origin
- Frequent respiratory and skin infections as well as severe acne

DIAGNOSING CGD

CGD is usually diagnosed in childhood. If there is a family history of CGD or a child presents symptoms, physicians should test for CGD by ordering one of the two diagnostic tests below, which can determine X-linked, autosomal, and recessive forms of CGD:

- **Dihydrorhodamine** (DHR) test can determine NADPH-oxidase activity and can be performed on a very small sample of blood using a flow cytometer to measure the production of oxidants by individual blood neutrophils.
- **Nitroblue tetrazolium** test (NBT) can determine NADPH-oxidase activity. It is less commonly used than the DHR test.

In addition, genetic testing can determine the specific gene mutation and is useful to establish the genetic inheritance pattern and aid in family counseling.

REFERRING PATIENTS WITH CGD TO SPECIALISTS/PHYSICIANS

While each patient with CGD is different due to individual levels of NADPH-oxidase activity and form of CGD (as well as other unrelated health or environmental issues) it is recommended that patients be seen and, if necessary, managed proactively by a team of qualified specialists/physicians, who work in concert with a primary care physician. These can include (but are not limited to):

- **Immunologist:** to order NBT or DHR tests to diagnose for CGD, determine level of oxidative burst/severity of CGD, prescribe CGD prophylaxis, and monitor for infection
- **Gastroenterologist:** to look for symptoms of inflammatory bowel disease e.g., pain and continuous diarrhea and bloody diarrhea
- **Dermatologist:** to assess skin/cystic acne and prescribe oral antibiotics or treatment with Accutane in severe cases

TREATMENT & MANAGEMENT OF CGD

Avoiding infection in patients with CGD involves a combination strategy that typically includes prophylactic antibacterial agents, antifungal agents, and immunomodulation via interferon-gamma (IFN-γ) therapy (CGD prophylaxis) and avoidance of exposure to bacteria and fungi. Bacteria and fungi exposures are prevalent in daily life, but there are measures one can take to reduce exposure risk. People with CGD should avoid dirt, construction areas, caves, grass cuttings, decaying leaves, dust, garden mulch, fresh water (lakes, ponds, rivers), jacuzzis/hot tubs, and potting soil.

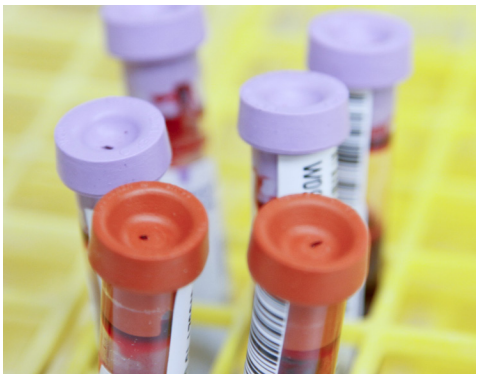
TREATMENTS TO MANAGE CGD

- Antibacterial and antifungal drugs, which are vital for preventing and treating infections. Commonly prescribed medications: trimethoprim-sulfamethoxazole (combination), also known as Bactrim®, and an antifungal medication such as itraconazole, voriconazole, or posaconazole
- Steroids, such as prednisone or methylprednisolone, can be used to control inflammation
- Interferon-gamma injections may help decrease the severity and frequency of infections

CURATIVE OPTIONS

- Bone marrow transplant has improved to a level where it has become a more standard curative treatment for patients whose CGD has led to severe challenges.
- Gene therapy is an experimental clinical treatment and is not yet a standard of care. A CGD patient's blood stem cells are collected and a healthy version of the gp91-phox gene is inserted into the stem cells. The patient with CGD undergoes chemotherapy before the cells are intravenously infused. After recovery from chemotherapy and the corrected cells have engrafted, the stem cells are potentially able to produce new white blood cells that can fight off infection.

No course of action, whether CGD treatment/prophylaxis or curative option, is without risks. It is important to encourage patients with CGD and their families to educate themselves in order to select the path that is right for them.



For more information about CGD, please visit the CGD Association of America website: **www.cgdaa.org**. We would also be happy to put you in touch with members of our CGDAA Medical Advisory Board for additional guidance.

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