CGDSociety

Supporting families affected by chronic granulomatous disorder

An introduction to **chronic granulomatous disorder**

If you are reading this booklet, then you or someone in your family has been diagnosed with chronic granulomatous disorder (CGD).

This leaflet provides an overview of CGD and its treatment, answering some of the questions you may have following diagnosis. More detailed information is available in our guide for patients and families and on our website at **www.cgdsociety.org**

Summary

CGD is a rare disorder of the immune system that can lead to serious and repeated infections. Having CGD can result in complications due to inflammation at various sites in the body.

In recent years the management and treatment of CGD have been transformed by the development of new drugs and improved knowledge among medical professionals. The condition is manageable and, provided that sensible precautions are followed, normal life is possible for most people with CGD.

The major advances in bone marrow transplant as a successful cure for CGD and the work on gene therapy hold great promise for those affected.

What is CGD?

CGD affects the way neutrophils, a type of white blood cell, work. Neutrophils 'eat' germs (bacteria and fungi) and then use special proteins, called enzymes, to kill them. Neutrophils from people with CGD can 'eat' the bacteria and fungi, but cannot kill certain types. This is because people affected by CGD are born without one or more of the killing enzymes in their neutrophils. The rest of their immune system functions normally.

CGD is usually diagnosed in childhood but in some cases people may not be diagnosed until adulthood, despite showing symptoms earlier.

How do you get CGD?

CGD is an inherited condition, which means it is passed from parents to their children. You do not catch it, you are born with it. This has implications for family planning.

Most people with CGD (about six in every ten) are male. The disease occurs because the affected gene, which tells neutrophils how to kill organisms, has a mistake in it (mutation) and doesn't work properly.

The gene for one type of CGD (which affects only males) is carried on the X chromosome (X-linked). Males, who have one X and one Y chromosome, inherit their X chromosome from their mother. The mother, despite carrying one of the faulty genes on her X chromosome, is usually well (since she has another X chromosome without the faulty gene). If a mother carries the faulty gene on one X chromosome she is referred to as an X-linked carrier and for every pregnancy there is a one in two chance that a son will have CGD and a one in two chance that a daughter will be a carrier.

There is another, less common type of CGD, called autosomal recessive CGD. This type affects both males and females. In this type of CGD one affected gene is inherited from the father and one from the mother. Neither parent will have a history of having had recurrent or unusual infections typical of CGD.

There are different forms of autosomal recessive CGD depending on which part of the enzyme protein is affected (see Table 1). In very rare cases, CGD can happen in a family due to new genetic changes occurring at conception.

Table 1. The types and inheritance of different forms of CGD

Protein affected	% of CGD patients	Genetic inheritance	Patients affected
Gp91	Approx 60%	X-linked inheritance	Males only
p22	Approx 5%	Autosomal recessive	Both sexes
p47	Approx 30%	Autosomal recessive	Both sexes
p67	Approx 5%	Autosomal recessive	Both sexes
p40	Rare	Autosomal recessive	Both sexes

The health of X-linked carriers of CGD

In general, X-linked female carriers of CGD are healthy but some may suffer from recurrent infections, excessive tiredness, mouth ulcers or recurrent light-sensitive rashes. Some carrier mothers may also have a diagnosis of systemic lupus erythematosus (SLE). These health problems will be monitored by a medical team.

There has been no evidence of health complications arising in the carriers of autosomal recessive forms of CGD.

Is there a diagnostic test?

Diagnostic tests for CGD use one of two special blood tests. These are the nitroblue tetrazolium (NBT) test or the dihydrorhodamine (DHR) test. Both work in a similar way: they check if someone's blood cells are producing the killing enzymes that fight infection. People with CGD will have abnormal neutrophils on either test. These tests can also be used to check for female carriers of the X-linked type of CGD.

Once these tests have confirmed the diagnosis, it is usual to look for the precise mistake in one of the genes that causes CGD. This can help with the screening of relatives.

Is there more testing after diagnosis?

Once CGD is diagnosed, doctors may need to do further X-rays, blood and urine tests, depending on the person's symptoms. They will also do baseline blood tests when the person is healthy, so they can compare results if the patient gets ill and find out what might be causing problems. It's vital that people with CGD have regular blood tests so that any problems can be found and treated early.

How is CGD treated?

The mainstay of keeping well when you have CGD is preventing infection. Taking daily antibacterial and antifungal medicines is the single most important factor in keeping CGD patients well.

Remember, taking antibiotics and antifungals everyday helps to prevent infection and keep people with CGD well.

The antibiotic Co-trimoxazole (Bactrim, Septrin) taken every day prevents many of the bacterial infections that patients with CGD are susceptible to. Daily antifungal medicines, such as Itraconazole (also called Sporonox), help prevent fungal infections caused by the fungi Aspergillus.

Some patients may also be offered interferon gamma as a preventative against infection. It is more commonly used in the United States, whereas in the UK and Europe it is not generally used.

What type of infections can occur?

Infections can include abscesses, enlarged lymph glands, unusual pneumonias and bone infections. People with CGD may also get chronic inflammation, including swollen gums or bowel inflammation. The bowel inflammation can behave like inflammatory bowel disease and sometimes needs specific long-term treatment.

Remember, infections in CGD need to be treated quickly before they become more serious.

Is there a cure for CGD?

At present, the only cure is a bone marrow transplant (BMT), also known as a haematopoietic stem cell transplant. The principle behind BMT is that stem cells can be taken from a healthy tissue-matched individual and grafted into a patient with CGD to provide a lifelong source of normally functioning cells. It is the preferred treatment option for most patients with CGD.

BMT is not without risk, so it is not undertaken lightly. However, recent experience shows that the risks in the long term are similar (or even better) than not having a transplant, and a successful transplant dramatically improves quality of life. BMT will usually be discussed when the patient has a suitable tissue match.

Researchers are investigating the possible use of gene therapy. To date, research and clinical trials have concentrated on developing gene therapy medicine for X-linked CGD and the p47 form of CGD. The aim here is to put a normal gene for CGD into the CGD patient's bone marrow cells, then to transplant those engineered cells back into the patient in order to try to cure CGD. This will allow the bone marrow to produce cells, such as neutrophils, that are now able to work properly.

Gene therapy does not currently result in a permanent cure and the corrected white blood cells tend to disappear over a few weeks or months. However, short-term correction of the CGD defect has led to clearance of life-threatening infections that were resistant to other means of treatment. Gene therapy has therefore been used as a 'rescue' therapy in those patients who are too sick to have a BMT, but for whom temporary correction of some neutrophil function may assist in fighting a serious infection.

Gene therapy is a relatively new branch of medicine. Research is ongoing to improve the outcomes of gene therapy for CGD with the intention that it offers an alternative, permanent cure when BMT is not a viable option.

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About the CGD Society

The Chronic Granulomatous Disorder Society (CGD Society) is the leading global charity dedicated to promoting an understanding of CGD and providing support to affected individuals and their families.

Our website **www.cgdsociety.org** provides medical information and practical advice on living with CGD. It is free to become a member of the CGD Society. Please go to **www.cgdsociety.org/register/**.

If we can be of any help, please contact us at **hello@cgdsociety.org** or on **0800 987 8988**, where you can leave a message.

Our charity is reliant on voluntary donations. To make a donation, please go to **www.cgdsociety.org/donate**.