

CGD Society

Supporting families affected by
chronic granulomatous disorder

Chronic granulomatous disorder

A guide for patients
and families

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Disclaimer



Introduction

If you are reading this booklet, then you or someone in your family is affected by chronic granulomatous disorder (CGD).

Approximately four to six babies in every million are born with CGD, although symptoms of the condition may not appear until after three months of age. Owing to advances in the diagnosis and treatment of CGD, most people who have the condition can live a full life. Some of the first people to be diagnosed with CGD are working, raising families and leading relatively normal lives.

Doctors and medical literature often refer to the condition as chronic granulomatous *disease*. People with CGD, however, prefer the term chronic granulomatous *disorder*. Their rationale is that you cannot catch CGD, you are born with it. We will use 'disorder' throughout this booklet.

People with CGD cannot fight bacterial or fungal infections effectively. This is because they have a faulty bone marrow gene, which means that some of their white blood cells, called phagocytes, do not work properly. Consequently, people with CGD are prone to more frequent and serious infections than people who do not have the genetic fault described.

This booklet is produced in collaboration with the CGD Society Medical Advisory Panel. It is designed to help you understand more about CGD and to answer some of the questions often asked by those affected and the parents and guardians of children who have received a diagnosis.

The content of this booklet should not replace advice from medical professionals involved in your care.

What is CGD?

CGD is a rare genetic disorder that affects the immune system.

The human immune system is made up of a complex network of specialised cells and organs that protect us from becoming ill. It works to kill germs, such as viruses, fungi and bacteria, that get into our bodies and make us sick. If any part of this network has a fault, it interferes with our general state of health and ability to fight off infection.

CGD is just one of over 300 different primary disorders of the immune system, which are known collectively as primary immunodeficiencies. The word 'primary' indicates that the disorders are caused by an inbuilt genetic or biochemical defect and not by a secondary cause, such as a virus or chemotherapy.

The genetic fault in CGD affects special white blood cells called phagocytes (pronounced *fag-o-sites*) that are made by the bone marrow. Phagocytes are the vital cells that help kill bacteria and fungi. In CGD, the phagocytes do not work properly, so people affected by the disorder are more susceptible to fungal and bacterial infections. Sometimes, these infections can be serious or even life threatening.

Phagocytes and CGD

The killing process in phagocytes is triggered whenever they encounter bacteria or fungi.

The phagocytes will surround and engulf (or 'eat') the invading bacteria or fungi (this is also known as phagocytosis) and then attack them with chemicals that are very similar to bleach. In fact, phagocytes can be described as 'mini bleach factories' because they produce toxic oxygen-containing substances, such as hydrogen peroxide, and a form of oxygen called superoxide. In effect, these chemicals disinfect the cell and kill the invading bacteria or fungi. During this process the phagocytes show a sudden intake of oxygen, which is called the 'respiratory burst'.

In CGD patients, the phagocytes, while able to engulf the invading bacteria or fungi, cannot produce the bleach-like chemicals to kill them. This means that people with the condition are at risk of developing serious, potentially life-threatening, bacterial and fungal infections.

Infection can take the form of abscesses, enlarged lymph glands, unusual pneumonias and bone infections. People with CGD may also experience chronic inflammation, which can, for instance, result in swollen gums or, where there is chronic inflammation in the bowels, in chronic diarrhoea.

Problems may also be caused by granulomas, from which the condition derives its name 'granulomatous'. Granulomas are large clusters of white blood cells at sites of infection or other inflammation. They form in an attempt by the body to isolate and 'wall off' areas of infection.

Granulomas can be troublesome and painful if they form in the walls of narrow tubes, where they can cause obstruction. For example, in the urinary tract, granulomas can block the flow of urine from the bladder or kidneys. In the digestive tract (the part of the body that breaks down and absorbs food), granulomas can cause problems with swallowing.

What are phagocytes?

'Phagocytic' (from the Greek word *phagein*, 'to eat') is a general term that is used to describe any white blood cell in the body that can surround and ingest microorganisms into tiny membrane packets in the cell. The membrane packets (called phagosomes) are filled with digestive enzymes and other antimicrobial substances.

Discover some more facts about phagocytes on page 52.

How do phagocytes kill bacteria and fungi?

When bacteria or fungi need to be killed, genes 'switch on' an enzyme called NADPH oxidase (PHOX). This action triggers the production of a chemical 'bleach' to destroy bacteria or fungi after phagocytes have ingested them.

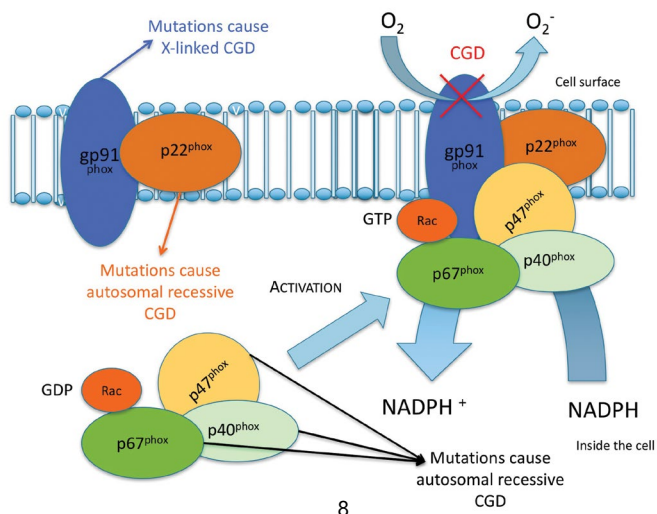
The initial step in this process involves the production of a superoxide anion (a free oxygen radical), followed by several other reactions that produce hydrogen peroxide, hydroxyl radical and hypochlorite (bleach). These chemicals are toxic to bacteria and fungi, and help phagocytes to kill them.

What happens in CGD?

In CGD, one of the five essential proteins that make up NADPH oxidase is either missing or defective (see Figure 1 and Table 1). The five proteins have different roles in the system. If one protein does not work properly, then the whole system breaks down and oxygen is not activated. As a result, phagocytes are unable to kill bacteria or fungi normally.

There are more than 410 known possible defects in the phox enzyme complex that can lead to CGD. The result in every case, however, is infection and inflammation.

Figure 1 CGD is caused by mutations in the enzyme NADPH oxidase



The enzyme affected in CGD is NADPH oxidase. This enzyme is responsible for the respiratory burst that makes the oxygen radical (O⁻), leading to the killing of bacteria and fungi. Mutations in any one of the five proteins of this enzyme (known as gp91^{phox}, p47^{phox}, p67^{phox}, p22^{phox} and p40^{phox}) cause CGD.

Table 1 The proteins and genes affected in CGD and their inheritance

Protein	Gene	Genetic inheritance	% of those affected by CGD	Groups affected
gp91 ^{phox}	CYBB	X-linked inheritance	65%	Males only
p47 ^{phox}	NCF-1	Autosomal recessive	25%	Both sexes
p67 ^{phox}	NCF-2	Autosomal recessive	5%	Both sexes
p22 ^{phox}	CYBA	Autosomal recessive	5%	Both sexes
p40 ^{phox}	NCF-4	Autosomal recessive	Rare	Both sexes

How is CGD diagnosed?

CGD would be suspected in a person who has certain severe or recurrent bacterial or fungal infections or enlarged lymph nodes, among other common symptoms (see page 14). In some families there may already be a family history of CGD.

CGD is usually diagnosed in childhood, with most symptoms appearing by three years old. About 95 per cent of people with CGD are diagnosed before the age of five. However, some people may not be diagnosed until adulthood, despite showing symptoms earlier.

To confirm diagnosis, the doctor will request a blood sample to test for a defect in the respiratory burst of the blood cells. The tests that are used to diagnose CGD are the DHR (dihydrorhodamine) (flow cytometry) test and the NBT (nitroblue tetrazolium) test. Both tests are reliable and work in a similar way. They check to see if the white blood cells can produce the bleach-like chemicals (reactive oxygen species) that fight infection. People with CGD cannot produce these chemicals.

If blood cells are fighting infection as they should do, the DHR test will change the fluorescence of dihydrorhodamine. A machine called a flow cytometer can detect this change. In the NBT test, the colour of the cell being tested will change, and this can be detected through a microscope.

Skill is needed to interpret the results of both tests, so it is best that experts perform them. Other tests may be carried out to assess how efficient an individual's cells are at killing bacteria.

Doctors may suggest carrying out an NBT and a DHR test on female members of the family to see if they are carriers of the X-linked form of CGD, as this may have implications for their children and their own health (see *The genetics of CGD*, page 14).

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 that the results can be compared when the person with CGD is ill and the cause of the problem detected. It is vital that people with CGD have regular blood tests, so that any problems can be found and treated early.

Doctors will also want to establish what the precise mutation is by looking at the affected person's DNA, using genetic analysis. This is done in special laboratories and helps further define the type of CGD present, how it is inherited, how it might affect the individual's health and what therapy may be offered. Genetic counselling will be offered to the affected person and their family.

How does the doctor make a diagnosis?

The doctor will ask for a blood sample to do one of two tests: either an NBT test or a DHR test. It is best that these tests are done in well-recognised laboratories, with staff who are experienced in interpreting the results.

What germs cause infection in CGD?

People with CGD can fight viral infections as normal (e.g. the common cold and chicken pox). It is bacteria and fungi (moulds) that cause infection in CGD.

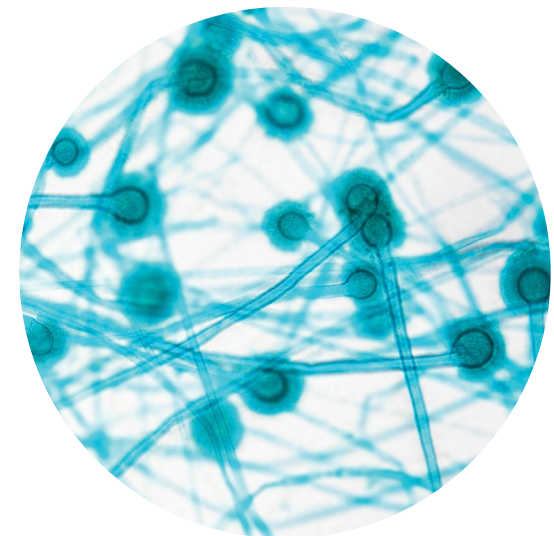
Bacteria that most commonly cause problems in CGD are:

- *Staphylococcus aureus*
- *Salmonella*
- *Klebsiella*
- *Aerobacter*
- *Serratia*
- *Pseudomonas (Burkholderia) cepacia*
- *Actinomyces*
- *Nocardia*
- *Mycobacteria*.

Fungi that cause problems in CGD include:

- Fungi from the Aspergillus family, most commonly *Aspergillus fumigatus* and sometimes *Aspergillus nidulans*
- *Scedosporium apiospermum*
- *Chrysosporium zonatum*.

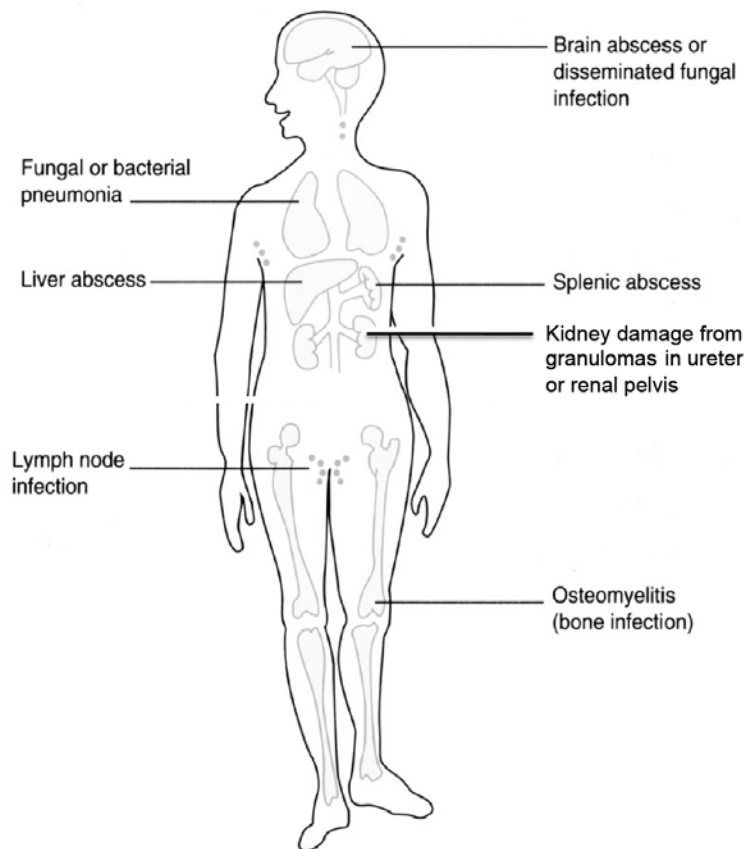
Fungi from the Aspergillus family (pictured right) can cause infection in CGD.



What infections affect people with CGD?

Bacteria and fungi can cause infections virtually anywhere in the body but commonly target the lungs, lymph nodes, skin, liver, intestines, nostrils, mouth, blood stream (septicaemia) and bones in the arms and legs (see Figure 2).

Figure 2 Common sites of infection and granuloma formation in CGD



Common signs and symptoms of these infections are abscesses, diarrhoea, boils, sore skin around or inside the nose, oozing or scaly skin and scalp rashes, ulcer-like sores, sores near the anus, local areas of pain and tenderness, swollen lymph nodes, fever and a persistent cough (see page 14). Infection is treated with antibiotics and/or antifungal medicines.

When the infection is severe, antibiotics may need to be given intravenously (into a vein) and often it is necessary to continue giving these over a long period of time. When this happens, patients may need to have a special tube inserted in their neck or chest (often called a central, PICC or Hickman® line), which allows long-term medications to be given into a vein. This tube can also be used for the frequent blood tests that patients on these medicines often need. The tubes can sometimes cause problems, however, and so should be removed once the immediate need for it has passed.

People with CGD often find that they lose their appetite during long-term treatment. This sometimes means that they need extra nutrition, which can be taken in the form of milkshake drinks or given via a special feeding tube inserted in the nose or stomach. Occasionally patients may need to be fed intravenously through a central line, for a short time.

Where can I find more information on treating infections?

See *Keeping well when you have CGD*, on page 24.

How often do infections occur?

CGD patients who take preventative antibiotics have, on average, one serious infection every 3–4 years, although this varies from person to person. Sometimes this can involve periods of time in hospital.

Many people affected by CGD also have frequent minor infections. About half of those affected have chronic inflammation of the gums (gingivitis) and three quarters have frequent ulcer-like sores in the mouth. Although these infections are not life threatening, they can be annoying and uncomfortable.

What are the symptoms of CGD?

The common symptoms of CGD are:

- severe or repeated bacterial or fungal infections; these might disappear with treatment but keep coming back, or the medicines prescribed might have little effect
- enlarged lymph nodes – hard lumps at the back of the ears or in the groin area
- abscesses or boils containing pus, anywhere on the body
- pneumonia
- persistent diarrhoea, with or without blood
- difficulty or pain when urinating
- failing to gain weight or grow normally as an infant.

The genetics of CGD

How do you get CGD?

CGD is an inherited disorder, which means that it is passed from parents to their children.



Most cells in the body contain over 20,000 genes that are grouped together on chromosomes (long strings of genes). Each gene contains a code that can be translated by the cell to make a certain protein. The type of protein that is made will determine a particular characteristic of a person (e.g. eye colour, blood type, production of phagocytes). A pair of genes – one inherited from each parent – governs each characteristic.

There are, however, a few characteristics that are governed by only one gene, rather than by a pair of genes. These characteristics are controlled by genes on the X and Y chromosomes that determine the sex of a person.

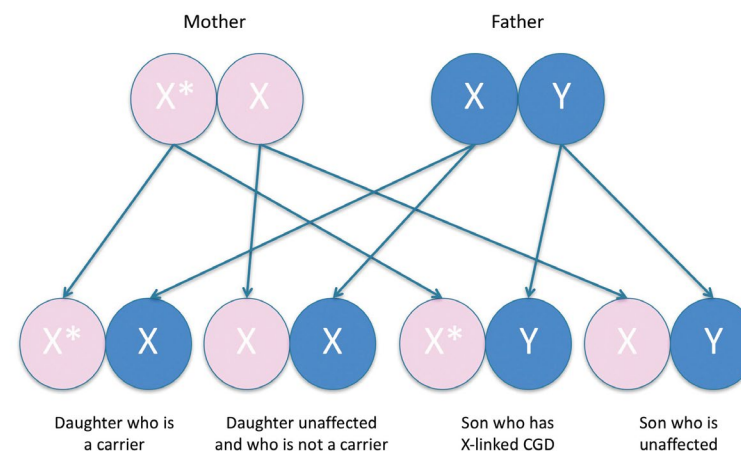
X-linked CGD

Females have two X chromosomes and no Y chromosomes. Males have one X chromosome and one Y chromosome. In about 65 per cent of cases, the defective gene that causes CGD is located on the X chromosome. Because the gene is found on the so-called sex chromosomes, the disorder is said to be sex- or X-linked.

Females inherit one of their mother's two X chromosomes and their father's only X chromosome. The CGD gene is a recessive gene, so females who inherit only one copy of the defective gene (from either parent) do not develop CGD, because normal phagocytes are produced from the gene on the other 'good' X chromosome (see Figure 3). These females may be called X-linked carriers, because they do not have CGD but, owing to the fact that they still have a defective gene in all their cells, they can pass the disorder on to their children. X-linked carriers seem to be prone to mouth ulcers and certain types of skin rashes (see page 21).

Males inherit one of their mother's two X chromosomes and their father's only Y chromosome. If a male inherits a faulty X chromosome from his mother, he will develop CGD. Because of this, there are more males with CGD than females.

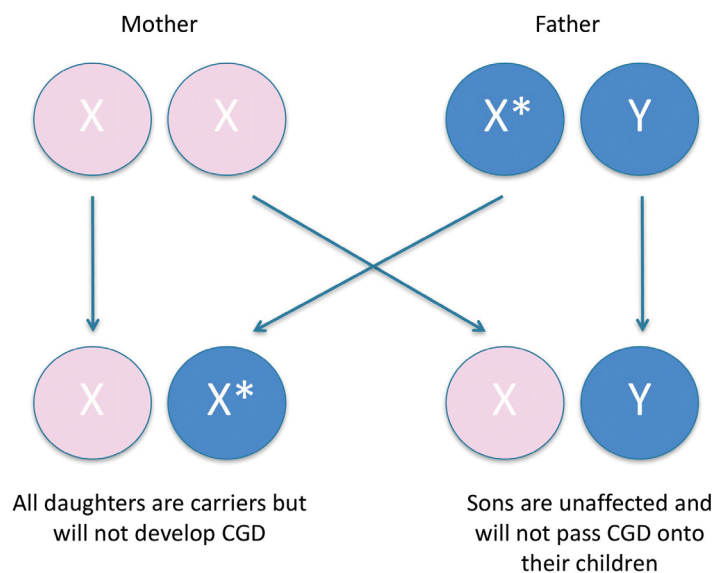
Figure 3 X-linked inheritance from a carrier mother



A mother who is a carrier of X-linked CGD carries the defective gene on her X chromosome. For every pregnancy, there is a 50 per cent chance of giving birth to a son who is affected by CGD or a daughter who is a carrier of CGD.

A father who has CGD passes on his defective X chromosome only to his daughters, who will all be carriers but will not develop CGD as they have one fully working active X chromosome inherited from their mother (see Figure 4).

Figure 4 Inheritance from a father with X-linked CGD



Remember

If you have X-linked CGD, all your daughters will become carriers of X-linked CGD.

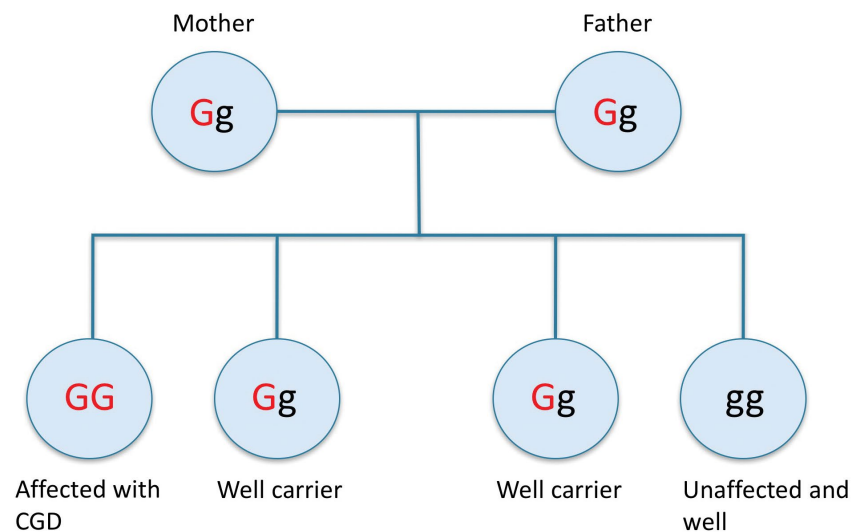
Autosomal recessive CGD

CGD is also caused by defective genes on chromosomes other than the sex chromosomes (i.e. on chromosomes that are called autosomes).

People have two of each autosome in their body, including those with the CGD genes. One autosome comes from their mother and one comes from their father. As long as one autosome works normally, the person won't develop CGD. This is because neutrophils (a key type of phagocyte that kills bacteria and fungi) need only one good copy of the gene to work well. However, the person will be a carrier. Carriers of autosomal recessive CGD do not have any associated health problems.

For a child to have autosomal recessive CGD, he or she must have two defective genes – one from each parent (see Figure 5). In autosomal recessive CGD, both males and females are affected.

Figure 5 Autosomal recessive inheritance



G = defective autosomal gene for CGD g = 'good' copy of the autosomal gene

In very rare cases, CGD can happen in a family due to new genetic changes occurring at conception.

Planning a family when you have CGD

Pregnancy and CGD

Women with CGD can become pregnant and have babies without adverse effects on their health. However, more care and management may be needed because some of the drugs used to prevent and treat infections in CGD can be passed from a pregnant woman to her baby and may cause birth defects or miscarriage. Because of this, it is recommended that women with CGD discuss their plans for having a baby with their doctor prior to becoming pregnant. The doctor will be able to prescribe medicines that are equally effective in treating infections, safe to use during pregnancy and will not harm the baby.



It is important that women consult their medical team and do not come off their antibiotics or antifungal drugs without medical advice.

Remember

If you have CGD and want to start a family, it is best to discuss your plans with a doctor. When this is not possible, women should inform their doctor as soon as they know they are pregnant.

The temptation may be to stop taking medication that prevents infection, but doing so could put both the mother and baby at risk. Any potential infection and the treatment it may entail are potentially more harmful than taking appropriate preventative medication.

Prenatal testing for CGD

People who have CGD or a family member who is affected by the disorder may want to consider the likelihood of any children they may have inheriting CGD. Genetic testing is done through blood tests and analysis of family history. CGD patients and families often find that a hospital genetic counselling service offers valuable guidance and advice on family issues.

A prenatal test on tissue (chorionic villus sampling, CVS) or fluid (amniocentesis) from the womb during early pregnancy can show whether the baby will have CGD.

Free fetal DNA testing can be done during the first nine weeks of pregnancy. This determines the sex of the baby, and only a sample of the mother's blood is needed. Some hospitals may offer this test to carriers of X-linked CGD.

A technique called pre-implantation gender determination (PIGD), which involves using IVF (in vitro fertilisation) treatment, can be used to enable couples to choose the sex of their baby, which may be crucial, especially in cases of X-linked CGD.

A hospital genetic counselling service is the best source of advice and information about this technique and can refer couples to a centre that offers a PIGD service.

How likely are people with CGD to have children with CGD?

Both men and women can pass CGD on to their children. The chance of a child of a CGD parent also developing the disorder varies considerably with the type of CGD involved (X-linked or autosomal recessive) and also depends on whether the other parent has any genetic links with CGD.

X-linked CGD and having children

When a man affected with X-linked CGD has children with a non-carrier mother (either X-linked or autosomal recessive CGD) any sons will not be affected by CGD and will not be carriers (see Figure 4). Any daughters will all be X-linked CGD carriers but will not have CGD.

When an X-linked carrier mother has children with a non-carrier father any daughters will be either healthy or carriers of X-linked CGD. Any sons will be either healthy or have X-linked CGD (see Figure 3).

When a man affected by X-linked CGD has children with a woman who is an X-linked carrier of CGD any daughters will be X-linked CGD carriers. Furthermore, for every daughter there is a 50 per cent chance of her having CGD because she may inherit from her parents both faulty CGD genes carried on the X chromosome. For every son there is a 50 per cent chance of developing CGD.

Remember

You can get genetic counselling if you or someone in your family is affected by CGD.

Autosomal recessive CGD and having children

It would be extremely unlikely that an individual with autosomal recessive CGD would go on to have a child with CGD. However, all the children of individuals with autosomal recessive CGD would be carriers of CGD but not affected by the condition.

A carrier could have a child with CGD if their partner carried the same genetic defect, which would, again, be very unlikely indeed, unless the parents of the child are close family members.

There are very many connotations involved and it is best to consult a genetic counsellor who can advise individuals and families based on their particular circumstances.

Being a carrier of CGD

Females who carry a defective CGD gene on one of their X chromosomes are referred to as X-linked carriers and may have sons with X-linked CGD, the most common form of CGD. Both males and females can carry a gene for the autosomal recessive form of CGD. They are referred to as autosomal recessive carriers.

Female carriers of X-linked CGD are diagnosed by a simple blood test, either the nitroblue tetrazolium test (NBT) or the dihydrorhodamine test (DHR), and/or by genetic analysis (see page 9). NBT and DHR tests will show a mixture of normal and abnormal white blood cells – some that can produce chemicals called reactive oxygen species and others that cannot. Carrier status should be considered on a case-by-case basis.

Are there any health problems associated with being a carrier?

In general, X-linked carriers are healthy but there have been reports of some associated health complications. In some cases, X-linked carriers get recurring mouth ulcers (known as aphthous ulcers or canker sores) or regular skin infections. Doctors may prescribe prophylactic antibiotics to prevent and treat these problems. Fatigue is another common symptom.

There is increasing evidence that occasionally X-linked carriers may also be at risk of developing lupus-like symptoms. The symptoms are referred to as 'lupus-like' because when standard tests for lupus are done, the results are negative.

Lupus-like symptoms include skin rashes, increased sensitivity to the sun, joint pains, severe fatigue and headaches. Sometimes there may be inflammation of internal organs, such as the lungs, heart, nervous system and kidneys. These symptoms should be taken seriously. Research into why and how lupus-like symptoms occur in X-linked carriers is ongoing.

X-linked carrier mothers with lupus-like symptoms who are worried should discuss their concerns with their family GP. It is important to tell the GP that there is a known link between the symptoms experienced and being an X-linked carrier, and an associated health risk, as he or she may not be aware of this. The recommendation is for those affected to be referred to a rheumatologist and/or other relevant specialists for treatment of the lupus-like symptoms regardless of the results of a test for lupus.

To date there is no evidence of health complications arising in carriers of the autosomal recessive form of CGD.

Where can I find more information about being a carrier of X-linked CGD?

Please visit the CGD Society website or request a copy of our booklet for carriers of X-linked CGD.

How are people with CGD looked after?

CGD is a rare condition, so do not be surprised if some doctors and nurses are unfamiliar with it.

Medical advice

It is important that people affected with CGD have a good point of reference at their local hospital who can be consulted when advice is needed. This can be a local doctor or a paediatrician who can access advice from an immunologist familiar with CGD. Another important source of advice for families affected in the UK is the CGD Society clinical nurse specialist (see page 23).

Your GP should refer you to the local children's or adult hospital. For many people this referral is likely to be to a clinical immunologist. If you live a long way from a hospital with a paediatric or adult immunologist, then you should also get help to identify a link doctor at your local hospital, for example, a general paediatrician for children.

It is a good idea to have regular appointments with your hospital doctors to monitor your health and to make sure that any problems, for example with drug levels or side effects, are picked up early.

For families living outside of the UK, the CGD Society can help you to find doctors who know about CGD. We can also answer general medical queries through our helpline: hello@cgd-society.org.

Shared care

CGD consultants in the UK offer a system of 'shared care'. This system means that you see your local consultant regularly *and* make an annual visit to the CGD consultant.

The CGD consultant has the advantage of seeing a larger number of affected patients and will know about new developments in treatment. The CGD consultant will be able to provide an overview of how to manage the condition and will liaise with the local consultant or other specialist, such as a gastroenterologist, to whom you may be referred, on treatment options. Regular outpatient review (every six months if you are well) is recommended, using this shared care system between local and specialist centres. Doctors will want to weigh you and do a range of blood tests to help monitor your state of health.

How is shared care arranged?

In the UK you need to ask your local consultant to refer you to a specialist centre, or your child to a paediatric CGD specialist. You could contact the CGD clinical nurse specialist if you feel you need some advice about this. (Please see page 53 for contact details.)

The consultants will keep your GP informed. Your GP's support is important and you will need their help with repeat prescriptions, vaccinations and home visits, if these are necessary.

What does the CGD Society clinical nurse specialist do?

The CGD Society clinical nurse specialist (CNS) offers support and clinical advice to patients and families across the UK and acts as a resource for local healthcare professionals, such as hospital doctors, GPs and district nurses.

If you have any concerns, need advice or want to chat things through, the CNS is happy to be contacted by telephone. See page 53 for contact details. The CNS makes home visits, can help in arranging appointments for UK specialist clinics and can accompany you to regional clinics.

Keeping well when you have CGD

The mainstay of keeping well when you are affected by CGD is preventing infection.

People with CGD have to take medicines every day to prevent and ward off infection (see page 26). This is because, in CGD, the white blood cells do not work properly to fight bacterial and fungal infection and the body needs an extra boost to do this. Consequently, it is very important for people with CGD to take daily antibiotic and antifungal medication (known as prophylaxis) as a preventative measure against infection. In the USA, interferon (IFN) gamma is used to prevent infections but it is not generally used in Europe.

Although antibiotic and antifungal medications do not provide an absolute guarantee against infection, taking them regularly means that the body is in better shape to 'put up a fight', so the infection should not be as serious and recovery should be quicker.

Antibiotics

Antibiotics are medicines for treating and preventing infections caused by bacteria.

Co-trimoxazole (also called Septrin) is the antibiotic most commonly used in CGD for preventing infection (see page 26). Co-trimoxazole is used because it gives wide-ranging protection against a number of bugs that can cause problems in CGD and is generally well tolerated. It is quite unusual for CGD patients to find that they do not tolerate Co-trimoxazole but if this does happen it is possible for your doctor to prescribe another, similar antibiotic.

Antifungals

Antifungal medicines are taken to prevent and treat fungal infections. The antifungal medication currently recommended to prevent infection in CGD is Itraconazole (also called Sporonox; see page 28) as it is effective in preventing fungal infections caused by the fungi *Aspergillus*. Itraconazole is also relatively well tolerated.

A few people find that Itraconazole gives them abdominal pain or diarrhoea. In these situations, changing the dose or the way the medicine is taken is usually sufficient, and this should be discussed with your doctor. Regular liver function checks, in the form of blood tests, are advised if Itraconazole is taken.

Keep taking the medicines even if you or your child is well. It may be tempting to stop taking your medicines, especially if you are feeling well. This can be particularly true of young people, who sometimes think that stopping their medication means that they will be able to forget all about having CGD.

But the times when you feel especially well, or the young person you care for feels well, are when medicines are working effectively. Stopping the medicines means running the risk of an infection.

Remember

Taking antibiotics and antifungals daily helps to prevent infection and keeps you well.



Medicines that need to be taken daily to prevent infection

Taking daily antibacterial and antifungal prophylaxis is the single most important factor in keeping well when you have CGD.

Antibiotic medicines for CGD

Co-trimoxazole (Septrin) is the antibiotic most commonly used to prevent serious bacterial infection. It is taken by mouth as a tablet or in the form of liquid medicine. Co-trimoxazole tablets are round and white. Table 2 gives recommended daily doses of Co-trimoxazole.



Table 2 Recommended daily doses of Co-trimoxazole

Age range	Co-trimoxazole prophylaxis (as a single daily dose)
0–6 months	120mg
6 months–5 years	240mg
6–12 years	480mg
over 12 years	960mg (can be taken as 2 × 480mg tablets)

Adult and paediatric liquid suspensions are available containing 480mg (adult) or 240mg (paediatric) of Co-trimoxazole in every 5ml.

Tips for taking Co-trimoxazole (Septrin)

- **Take it with or after food and with plenty of water.** Do not worry if you or your child cannot always manage this. Just make sure that you or they drink plenty of fluids during the day to help the kidneys flush the drug out and that the full dose is taken.

- **Consider other antibiotics you may be taking.** If you or your child is taking any other antibiotics, such as Ciprofloxacin or Flucloxacillin, it may not be necessary to carry on taking the Co-trimoxazole as well. However, you should restart the Co-trimoxazole as soon as the other course of antibiotics is finished. Always check with your doctor or nurse before stopping any medication.
- **You can divide the dose for your convenience.** The dose you are prescribed can be taken all in one go once a day or divided into morning and evening doses, whichever is more convenient. For instance, if you are prescribed one tablet twice a day and you take 480mg tablets, you are taking 960mg each day. You can either take it twice a day, or both tablets just once a day.

Side effects of Co-trimoxazole (Septrin)

- **Nausea, vomiting, skin rashes and headaches.** These are the most common side effects.
- **Bone marrow problems.** Co-trimoxazole can make some patients' bone marrow work less effectively. This can lead to anaemia and bruising or bleeding more easily. Tell your doctor if you or your child feels more tired than usual or if there is excessive bruising or bleeding. Your doctor will be able to check for bone marrow problems with a simple blood test.
- **Increased sensitivity to sunlight.** Taking Co-trimoxazole can make people more sensitive to the sun. Anyone taking it should use SPF25 or higher sun protection cream when they are in the sun.

Antifungal medicines for CGD

Itraconazole (Sporonox) is the most commonly taken antifungal for CGD.

The recommended dose is based on the weight of the person taking the medication and is usually 5mg/kg daily. It may be given in higher doses to treat particular infections.

Itraconazole is taken by mouth as a capsule or liquid. Capsules contain 100mg of Itraconazole and the liquid contains 100mg in every 10ml.

Sometimes people with CGD struggle to absorb Itraconazole through their gut, especially if it is in capsule form, so they may need to take a higher dose. Doctors who are concerned about this may do a blood test to check the level of Itraconazole in the person's system.

It is easier to absorb liquid Itraconazole than the capsule form, but the liquid is more likely to cause diarrhoea and/or abdominal pain in some people. It also tastes very bitter.

Tips for taking Itraconazole (Sporonox)

- **Take capsules with food.** This can help them to be absorbed. Taking Itraconazole with an acidic drink, such as fruit juice, squash or a fizzy drink, can also aid absorption. The capsules should not be split and taken as granules as this prevents the drug from being absorbed properly.
- **Take liquid on an empty stomach.** Ideally, Itraconazole liquid should be taken an hour before or after food. Just before bed can be a good time. It is best to take the liquid with water or weak squash (not milk, as this counts as food). Getting children to take the bitter-tasting Itraconazole can be difficult but it is important that they do, so make any necessary adjustments to our advice to make this happen.

Side effects of Itraconazole (Sporonox)

- **Stomach problems.** These can include nausea, indigestion, diarrhoea, abdominal pain and constipation.
- **Headaches, dizziness and menstrual problems, such as bleeding between periods.** These are less common side effects.

Side effects of both Co-trimoxazole and Itraconazole

- **Abnormal liver function.** Itraconazole, and occasionally Co-trimoxazole, can cause certain liver enzymes to increase. This is rare and reversible. It is easy for a doctor to monitor this with a simple blood test called a liver function test. Doctors generally do routine liver function tests every 6 to 12 months for people with CGD. However, this will vary from person to person.
- **Diarrhoea.** Co-trimoxazole and Itraconazole can cause diarrhoea. Itraconazole – especially the liquid form – is the most likely culprit. Tell your doctor if you/your child has diarrhoea that does not go away.
- **Allergic reactions.** Although it is rare, some people with CGD have allergic reactions to their medication, ranging from mild to severe. Signs of a mild reaction can include skin rashes, itching, a high temperature, shivering, a flushed face, dizziness and a headache. If you/your child experiences any of these symptoms, report them to your doctor or nurse.

Signs of a severe allergic reaction include chest pain and difficulty breathing. Call for an ambulance straight away if you or your child with CGD experiences either reaction.

The use of Co-trimoxazole and Itraconazole needs to be reviewed in the case of pregnancy.

What if you get ill?

Despite taking preventative medicines, people with CGD will sometimes get ill with infections.

When infection occurs, it is important to treat it quickly. People with CGD may need longer courses of treatment than average to treat infections. Sometimes they may need higher doses or a combination of medications. If you have an infection, you should always request that expert help is sought through a CGD specialist centre or by contacting the CGD Society clinical nurse specialist.

Not sure? Don't panic!

Help is always at hand! Contact your consultant, the CGD Society clinical nurse specialist or, outside the UK, the medical professional who looks after you or your child.

Treating infections

Infections in CGD need to be treated promptly with appropriate antibiotics or antifungal agents where necessary. These may need to be given via an intravenous drip to ensure that they work quickly and effectively. The particular combination of antibiotics and antifungals will depend on the type of infection and where it is in the body.

Remember

Infections in CGD need to be treated quickly, before they progress and become more serious.

Antibiotics

It is vital that doctors put people with CGD on antibiotics quickly if they have an infection, even if the exact cause of the infection is unknown. This is because an acute infection may progress quickly into very serious illness if it is not treated promptly.

If the cause of an infection is unknown, doctors will likely prescribe a broad-spectrum antibiotic that fights a range of bugs. This can then be

changed for an antibiotic that treats a specific bug if the exact cause of infection is identified.

A 'safety-first' approach should always be adopted for patients with CGD and this should outweigh the risk of developing resistance to antibiotics.

Antifungals

Amphotericin B (Ambisome) is the most common medication used to treat fungal infections if someone has CGD. It is given once a day through an intravenous drip and is often used in combination with oral antifungal medicines.

A number of other antifungal drugs, including Voriconazole and Caspofungin, may be alternatives. Other medications are in development. It can sometimes be difficult to get rid of fungal infections and they often need to be treated for many weeks or even months.

Steroids

For certain infections, particularly liver abscesses, taking steroids in combination with antibiotics can help with treating the infection and reduce the need for surgery. Steroids can have side effects, including weight gain and weakening of bones, but these are less of a problem with relatively short-term treatment.

Interferon gamma

Interferon (IFN) gamma is sometimes used in CGD as a preventative against infection. It is more commonly used as a preventative medicine in the USA, whereas in the UK and Europe it is generally reserved for use in difficult infections or complications, when it is used in conjunction with antibiotics and other treatments. This is because the exact way in which IFN works is not yet known and its usefulness in preventing infection is not certain, particularly when compared with the use of preventative antibiotics. IFN is also less user-friendly as it has to be given by injection, usually three times a week, and can cause flu-like symptoms in many of the people who receive it.

White cell transfusions

A white cell transfusion is the process of giving someone with CGD normal white cells from a healthy donor to fight infection. Doctors use white cell transfusions only occasionally, usually to treat serious or very difficult infections that are not responding to other treatments.

White cell transfusions can cause allergic reactions in some patients, similar to standard blood transfusions. Allergic reactions are more likely to happen if a person has had transfusions of white cells in the past. This is because after your body is exposed to something 'foreign' once, your immune system recognises and fights it more strongly the next time. Reactions of this type may complicate the possibility of having a successful bone marrow transplant.

Transfusions can also be difficult because it is not clear how many white cells people with CGD need to receive in order to fight an infection. It can also be difficult sometimes to get enough matched white cells from donors. Hence, white cell transfusions are used rarely and with caution.

Surgery

Occasionally antibiotics, even in combination with steroids, are not sufficient to clear an infection. In some situations, surgery can be very effective in curing infection; for example, removal of an abscess.

Inflammation and CGD

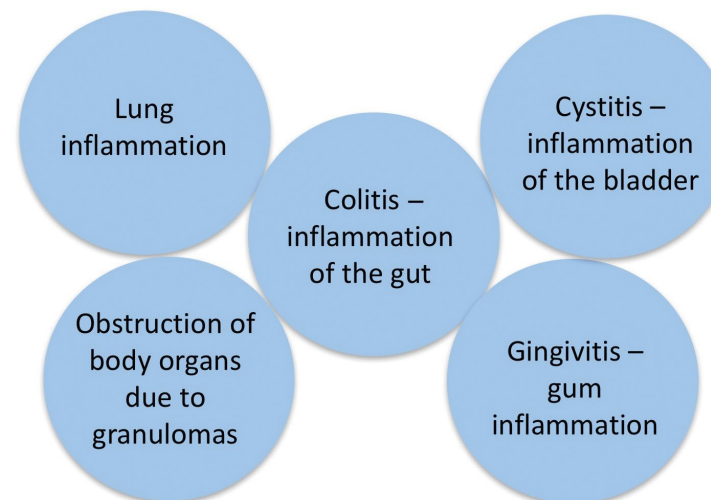
In CGD, some of the health complications that people have are due to inflammation rather than infection (see Figure 6).

The most common problem is colitis. Colitis is inflammation of the large bowel – the last and lower part of your digestive system. Symptoms of colitis are diarrhoea, weight loss, failure to thrive (children not putting on weight as they normally would) and perianal disease involving sores around the anus.

Sometimes doctors can misdiagnose colitis as Crohn's disease. Doctors often recommend referral to a gastroenterologist for the investigation and treatment of colitis in CGD.

Sometimes problems are caused by granulomas. These are nodules of immune cells that form into tight ball-like structures and may cause obstruction in the gut or urinary tract. Symptoms include difficulty swallowing (obstruction of the oesophagus), vomiting (obstruction of the gastric outlet), abdominal pain (obstruction of the bowel) and difficulty passing urine (obstruction of the ureter). Granulomas can also affect the lungs.

Figure 6 Inflammatory complications in CGD



Less common inflammatory complications are chorioretinitis (inflammation of the eye; see page 45), pericardial effusion (fluid around the heart) and fulminant muller pneumonitis (a serious pneumonia caused by exposure to high levels of fungi contained in compost and organic matter and which can be a source of both infection and inflammation).

Inflammatory problems are treated with anti-inflammatory medicines, including steroids. Steroids are only given if they are necessary and only after doctors have established that the problem is not caused by an infection. They are generally used with caution in CGD and preferably after discussion with a specialist centre involved in your care because of specialists' knowledge of the history of the infections you or your child may have had. Occasionally surgery may be required; for example, for very inflamed sections of bowel.

Fulminant mulch pneumonitis, with symptoms including cough and shortness of breath, can be prevented by taking precautions to avoid fungal infection. However, when fulminant mulch pneumonitis occurs, it is a serious emergency, requiring antifungal and steroid treatment.

Bone marrow transplantation

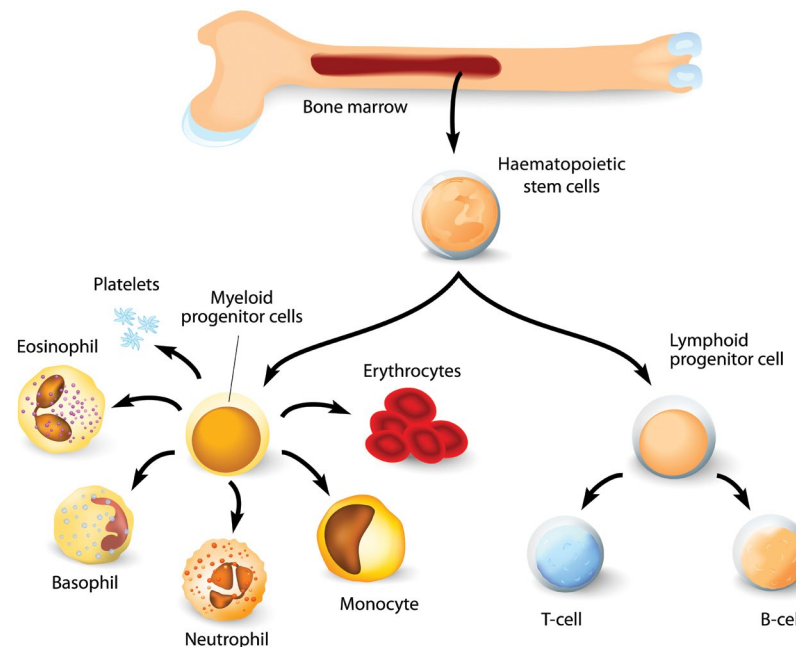
Bone marrow transplantation (BMT), also known as a haematopoietic stem cell transplant (HSCT), is currently the only cure for CGD and is the preferred treatment option for most patients with the disorder.

Bone marrow is the soft, spongy tissue found in the centre of bones. It is responsible for producing the three main types of blood cells: red blood cells, white blood cells (including phagocytes, such as neutrophils that are affected in CGD) and platelets. All of these start off as immature cells called stem cells. Stem cells mature in the bone marrow and are then slowly released into the blood stream.

A bone marrow or stem cell transplant involves collecting healthy cells from a matched donor and introducing them into the person with CGD. These new healthy stem cells then start to make fully functioning white blood cells capable of fighting infection.

Successful transplants for CGD result in resolution of infection and colitis, and in children and adolescents who have remaining growth potential, it allows them to 'catch up' on their growth. Research has also shown that post-BMT, quality of life for children with CGD improves to levels similar to those of healthy young people.

Figure 7 How blood cells are made



The person with CGD receives bone marrow (or sometimes stem cells collected from the umbilical cord blood of babies are used) from a donor who shares the same 'tissue type' as them and is therefore called a 'match'. Two types of match are normally considered. The first is a perfectly matched related donor, who is usually a sibling. The second is a well-matched, unrelated donor. Occasionally, a less well-matched (mis-matched) donor may be considered.

To allow for the growth and development of these new cells, the patient has to undergo 'conditioning'. This involves giving several powerful medicines, called chemotherapy. Chemotherapy works to:

- 'make space' for the new stem cells
- suppress the immune system in order to encourage acceptance of the new cells.

Having a BMT involves a long stay in hospital (on average 6–8 weeks), during which time the patient is looked after in an isolation room on a transplant ward. This ward will have more restrictions on visiting, diet and hygiene than a general ward. This is because during transplant the patient's immune system is weakened and a few extra precautions are necessary to protect them from infection.

Over the last few years there has been significant progress in BMT techniques and recent results for CGD are extremely good. Survival and cure are now equivalent with either a matched sibling or a well-matched, unrelated donor and extend to rates of 85–90 per cent in specialist centres designated to transplant patients with a primary immunodeficiency.

While transplantation is generally best tolerated in childhood, successful outcomes are possible in young people and adults, using new transplantation techniques. However, BMT is not without risk.

The main risks are infection and Graft-versus-Host disease (GvHD). In GvHD, the new bone marrow from the donor may recognise the patient's cells as 'foreign' to it and react against them. GvHD can cause problems with the skin, liver and bowels.

Doctors have made the following general recommendations about BMT for CGD.

- BMT should be considered soon after a diagnosis of CGD. This is because better outcomes are usually achieved if those affected do not have a history of serious infections or inflammatory problems. This means that doctors will want to test siblings to see if they are a tissue match. If siblings are not a tissue match, then doctors can start to find a well-matched, unrelated donor. Doctors are also able to give appropriate counselling over a period of time to help people



Thomas had a BMT in 2012 when he was 11 months old.



Tom had a BMT using an unrelated donor in 2011 when he was 17 years old.

make the decision about whether or not to proceed with a BMT once a suitable donor is found.

- BMT should be done in a specialist centre that has experience of transplanting people with primary immunodeficiency. This is because the doctors will know about CGD and be able to give good-quality, up-to-date advice about the risks and benefits of this treatment.

In spite of increased success rates, BMT is not suitable for all people affected with CGD and you should discuss the suitability and individual risk factors for you and your family with doctors and nurses involved in your care.

Finally, it is important to remember that although a person's CGD may be cured by BMT, CGD can still be inherited by any future offspring.

Need more information on BMT?

The CGD Society website has a wealth of information on BMT, including patient and expert perspectives, and family experiences.

Gene therapy

Unfortunately, BMT is not a treatment option for all people affected by CGD. To address this, researchers and clinicians have been developing an alternative treatment using gene therapy. This 'genetic' medicine has already been used to treat people with CGD and clinical trials have taken place in Europe and the USA.

In gene therapy, the aim is to correct the defect in the CGD patient's own cells by giving them a healthy copy of the gene affected. For example, to treat X-linked CGD, a copy of the CYBB gene that makes the protein gp91phox is used. The cells are then able to produce the normal protein (NADPH oxidase) that is necessary to fight infection.

Gene therapy uses the ability of viruses to infect cells to carry the corrective gene into the patient's stem cells. The virus used is inactivated, made safe and engineered, so that once it infects the patient's stem cells its DNA code makes the healthy gene in the correct way and in the right cells – phagocytes. The engineered viruses used in gene therapy are referred to as vectors.

This 'mini-gene' transplant uses a procedure very similar to that for BMT. The patient's bone marrow stem cells are removed, mixed with the CGD gene therapy vector and given back to the patient (see Figure 8). As in BMT, people need to receive chemotherapy conditioning before gene therapy. This is important because doctors want to eliminate as many of the existing cells carrying the genetic defect that they can, prior to giving back the gene-corrected cells.

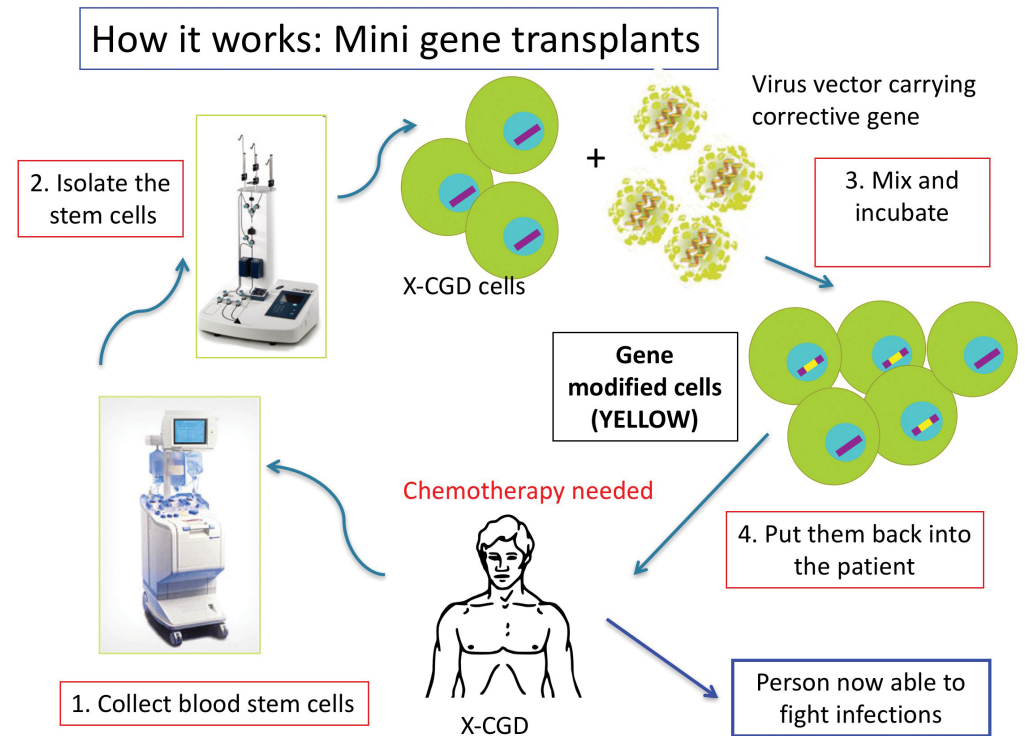
One advantage of gene therapy is that it uses the patient's own cells, so reduces the chance of the patient developing GvHD. Patient clinical trials involving over 12 people affected by CGD have already shown that this treatment can work. Short-term correction of the CGD defect has helped to save lives and led to the clearance of life-threatening infections that were resistant to other conventional means of treatment.

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

Gene therapy for CGD

Find out more information on the CGD Society website, at www.cgdsociety.org/whatiscgd/treatment#genetherapy

Figure 8 The steps involved in gene therapy



Recognising and preventing infection

CGD patients will suffer colds and other viral infections just like any other person and their immune system will respond normally. It can be difficult, therefore, to differentiate between infections that are 'normal', especially in a child, and those that are a result of CGD. It is difficult to determine which infections are a real cause for concern and which are not, particularly when you are first diagnosed with CGD.

If you are not sure, always ask!

It is extremely important that doctors are contacted immediately if a patient with CGD develops an infection, so that treatment can be started early. People with CGD and their families should be on the look out for the following signs of infection:

- A fever of 38°C or above
- Frequent/persistent headaches
- Warm, tender or swollen areas
- Loss of appetite
- Hard lumps
- Weight loss
- Sores with pus or rashes
- Pain or difficulty urinating
- Persistent diarrhoea
- Difficulty swallowing food
- A persistent cough or chest pain
- Vomiting shortly after eating, on a more or less consistent basis
- Night sweats.

How do I know if I need to consult the doctor?

If in doubt, contact your consultant or the CGD Society clinical nurse specialist (if you live in the UK) to share your concerns and ask for advice.



When a CGD-related infection is suspected, it is best treated early. Treatment is often intravenous and while it can be a little upsetting for the patient and their family, it is worthwhile to prevent the infection taking hold. It may also reduce the length of the treatment period. Intravenous treatment often requires a hospital stay. Sometimes the patient is able to leave the hospital during the day and return for overnight infusions. In some instances, drugs can be given at home.

All spots and abscesses containing pus should be investigated. Your doctor may want to take a sample of the pus and send it to the laboratory to identify the bacteria causing the infection.

Occasionally, a sample of tissue (biopsy) is taken from an infected area (usually using a fine, needle-like tube) to trace the cause of an infection. Sometimes infected tissue must be removed or drained if the infection does not respond to antibiotics, so drainage tubes may be inserted in the person's chest, abdomen or other sites. This usually involves a hospital stay.

Your doctor may want to do other tests, such as an ultrasound, an X-ray, a CT scan or an MRI scan, to investigate a suspected infection.

If your doctor is not sure of a diagnosis or treatment, encourage him or her to contact the CGD Society clinical nurse specialist or a relevant centre of excellence that may be able to help. You can also contact the CGD Society – please see page 53 for details.

How do you prevent getting infections?

Taking your daily medication and keeping all recommended vaccinations up to date (except those that involve live bacteria, such as BCG and salmonella) are the most important ways to prevent infection.

Some simple precautions can also help to reduce your chances of getting an infection.

- Do not work or play with or around mulch, hay, wood chips, thick grass clippings, other garden waste or firewood that has dry rot or old fungi on it. This will help to avoid inhalation of high levels of fungi, which can cause sudden, severe respiratory problems and infections.
- Stay out of barns, caves, sheds and other dusty or damp areas because there may be fungal spores present. Remember, fungus + CGD = serious health problems.
- Practise good oral hygiene. Brush your teeth twice daily and use mouthwash to reduce the occurrence of gingivitis.
- Wash all cuts and scrapes thoroughly with soap and water and follow with antiseptic. Remember to look out for signs of infection. Any redness, swelling, warmth on touch or pus should be reported to a doctor or nurse immediately.
- Always wear shoes or sandals outside.
- Choose playgrounds with a plain dirt or gravel surface; wood chips harbour fungi.
- Avoid re-potting plants, because mould often grows in soil.
- Do not enter buildings that are being built or renovated, because the dust that is generated during construction work harbours fungi. Only enter once the site has been thoroughly cleaned. The demolition phase rather than the rebuilding phase carries the highest risk.
- Ask someone else to rip up or replace carpets or ceramic tiles. If you are moving, clean the rooms of your new home thoroughly with disinfectant (bleach) before living in them. Do not sleep in your new home until this has been done.
- If you use a vapouriser, empty it daily and wash it with bleach to prevent mould accumulating.
- If you have fresh cut flowers, add a teaspoon of bleach to the water to prevent mould and algae.

- It is fine to have some pets but do not use wood shavings as bedding. Make sure your pets are up to date on all recommended immunisations. Keep their water bowls and bedding clean.
- Some pets, including turtles and lizards (iguanas), carry salmonella. Avoid these animals if you have CGD.
- Do not swim in rivers or lakes. Even if the water looks clean, it is full of bacteria. Swimming in a clean, chlorinated pool or in safe, unpolluted seawater is fine.
- Fever, especially if accompanied by a cough, should always be reported immediately.

Looking at the list of precautions, you might think that there are lots of 'do not's', but keeping active and enjoying life is important for health and good mental well-being.

Families find it best to concentrate on the activities they can do rather than those they cannot. Accentuate the positive rather than dwell on the negative. Interests and activities, such as cycling, fencing, ten-pin bowling, tennis, golf, badminton, swimming and walking, and visits to play parks with gravel surfaces, youth clubs, cinemas and art centres, are some examples of things that families can do together. In a family with affected and non-affected siblings, you may need to keep a balance by allowing each child to take part in suitable activities at different times.

Some parents and affected individuals may decide that participating in contact sports, such as football or rugby, is not a good idea because of the risk of being cut or scratched and getting an infection. Others may decide differently. Everyone has a different perspective on managing the risk of infection. Your doctor and nurses can talk this over with you.

Remember

If you do get an infection, complete the full course of prescribed antibiotics, even if the symptoms have disappeared, so that the infection does not reoccur.

What vaccinations are recommended?

It is important that people with CGD keep their vaccinations up to date.

Childhood vaccines

Children with CGD should be fully immunised. The only immunisation that adults and children with CGD should *not* have is the BCG vaccine, which protects against tuberculosis. All other vaccines can be given, including those for polio; tetanus; measles, mumps and rubella (MMR); pneumococcus and meningitis C. Children will be given their vaccines at school; adults can go to their GP practice nurse.

Flu vaccine

Flu is a virus, so people with CGD can fight it off as well as anybody else. People with CGD can have problems with bacterial chest infections associated with flu, however, so anyone with CGD over six months old should have the seasonal flu vaccine every year. It is safe to have the nasal (live) flu vaccine.

All vaccines can cause adverse reactions and side effects. Your doctor or nurse will tell you about the possible side effects of each immunisation you have. Common side effects for all vaccines include a sore arm and redness or swelling at the injection site. Reactions and side effects are no more common in CGD patients than anyone else. Talk to your doctor or CGD nurse if you have these. Serious reactions are rare.



Living with CGD



Smoking, drugs and alcohol

If you are an adult with CGD you should not drink to excess or smoke, as these can impair the immune system further and interfere with the way the preventative medicines work. Smoking marijuana is dangerous because of the risk of inhaling mould spores found in this plant, which can cause a serious type of fungal pneumonia.

Oral hygiene

Oral hygiene is very important in CGD because it is easy for infection to enter through the mouth, so regular dental appointments are recommended. People with CGD can have persistent gingivitis (gum inflammation) and get mouth ulcers. Brushing your teeth twice a day and using a mouthwash (containing chlorhexidine gluconate) regularly helps to keep gum inflammation at bay.

People with CGD should take antibiotic cover for all dental procedures that are likely to cause bleeding as this can allow bacteria to enter the blood stream. This should be discussed with your dentist and doctor before going ahead with dental work.

A course of antibiotics should be taken before and after dental treatment. Doctors may recommend the tablet form of Ciprofloxacin: 7.5mg/kg for a child and 500mg for an adult. This will be given before the procedure, followed by two doses, 12 hours apart, in the 24 hours following the procedure.

Eye health and CGD

Some people affected by CGD may have chorioretinitis. This condition is inflammation of the choroid: the thin, pigmented, vascular coat of the eye and retina of the eye. It is not known why chorioretinitis occurs, and the lesions that result do not appear to interfere with vision in the majority of people with CGD. However, doctors recommend that people with lesions should be assessed every 1–2 years to monitor eye health.

Those without lesions at diagnosis should be assessed every 2–3 years by an ophthalmologist.

Can you live a normal life with CGD?

Yes, absolutely! Having CGD does not mean you cannot live as 'normal' a life as anyone else – going on holiday, travelling, going to college or university, getting a job, having a career, getting married and having a family. However, those affected and their families should expect, and be prepared for, frequent and sometimes long stays in hospital that may interfere with school or work.

If needed, children with CGD can often be tutored at home or in hospital to help keep up with their education. Teenagers with CGD who are planning to go to university or college may find it helpful to choose one located close to a medical centre that has doctors who are used to treating CGD, so that treatment and advice is easily accessible.

Planning a holiday?

If you are going on holiday, visit the CGD Society's website for some practical tips that will help you plan ahead.

Can CGD affect the growth and development of children?

Some children with CGD grow and develop more slowly than their peers. They may not be as tall as other children of their age and they may reach puberty later.

This can be a worry for teenagers, although many children with CGD are likely to catch up with their growth later on, often continuing to grow after their peers have stopped and achieving a reasonable adult height. There is the possibility that children who have received prolonged courses of steroids or who have been very unwell for a long time, may not reach a similar height to their parents when they get older.

For more specialist advice, a referral to an endocrinologist (a doctor who specialises in growth and the way hormones work) may be appropriate. This should be discussed with your CGD consultant. The endocrinologist can further advise whether special treatments, such as growth hormone, should be considered.

Maintaining a healthy weight with CGD

Sometimes it may be difficult for children who have CGD to put on weight or maintain their weight. This is referred to as failure to thrive.

Failure to thrive may occur because the child's body is burning extra calories to fight off infections. The child may also have inflammation of the gut, meaning that they cannot absorb the nutrients from food as well as healthy children.

Your child's doctor will carefully monitor your child's weight and, if needed, may recommend specialist nutritional advice and referral to a dietician. They might also refer your child to a gastroenterologist – a doctor specialising in the health of the gut – or an endocrinologist. These specialists should work in cooperation with your child's CGD specialist.

Adults with CGD may also experience problems maintaining their weight, for much the same reasons as children. Some adults often report reduced appetite and interest in food. Again, advice from a dietician as to how to increase calorie intake will help. If you lose weight suddenly, then an underlying infection may be the cause and you should seek medical help.

The emotional impact of CGD

Life with CGD sometimes isn't plain sailing. It can affect the whole family. Frequent episodes of being unwell, coping with serious infections and long stays in hospital, as well as the psychological issues involved in managing a complex condition, while, at the same time, trying to maintain a 'normal' life with family and friends, can take its toll.

Feeling afraid, 'stressed out', angry, frustrated or depressed is not uncommon. Sometimes it may be difficult to talk about these emotional issues for a variety of reasons, including stigma, fear of being judged and fear of managing your own emotions. It is important that those affected talk to a hospital social worker and/or a clinical psychologist, who can arrange support for them.

Sometimes parents of children with CGD may feel guilty about passing on the disorder (although no one is at fault because genetic conditions just happen) or blame themselves for the infections the child has. Parents are also often torn between the needs of their child with CGD and the needs of their other children or the demands of their jobs. All these feelings can cause stress and are normal.

How does having CGD make children feel?

Living with CGD can sometimes have a big impact on a child's life and expose them to stresses that other people might not even consider. Feelings of isolation, exclusion, 'feeling different' and that no one is ever going to understand, are common. A range of issues can occur, including not wanting to go to school because of difficulties with friends and teachers; a fear of needles and feelings of anger, frustration and sadness.

Seeking help in coping with these problems is important. Feeling good mentally makes such a difference to coping with the health challenges that CGD presents. Help can be found through a GP, who can refer you on to a counsellor or psychologist. Talking to someone (e.g. your relatives or the doctors and nurses involved in your care or to someone who is also affected by CGD) can be valuable.

Want to talk to someone else with CGD?

Contact the CGD Society and we should be able to put you in contact with someone who can chat to you about it all.

How does CGD affect other brothers and sisters?

Sometimes brothers and sisters of children with CGD may become jealous of the attention given to the affected child. They may feel resentful and become increasingly demanding and dependent.

They should be encouraged to talk about their feelings and worries. Family counselling can help sort out these and other problems within the family. Clinical psychologists who are used to working with children and families can help to suggest ways of talking with children about their illness, or to siblings, and strategies that parents can use to address difficulties, such as problems taking medicine or demanding behaviour. Talk this over with your doctor.

How to cope with CGD?

Remember, you are not alone. Joining a support group and talking to other families that are affected by CGD or other chronic conditions can be a real help. The CGD Society runs a buddying scheme and can help link you up with people in a similar position to yours. Joining a Facebook group is also a good way of forming bonds with others (see page 55).

Relaxation techniques, such as meditation, visual imagery and therapeutic massage, can reduce physical and mental stress and help those affected to think positively. Many hospitals offer recreational therapy, such as crafts or playing musical instruments, that can make hospital stays more pleasant and help relieve boredom.

If you are finding things difficult, then talk to your GP or your CGD consultant. They may be able to refer you to a psychologist or counsellor.

You can also refer yourself to the psychological services in your area through a service called IAPT (Improving Access to Psychological Therapies). Please visit www.iapt.nhs.uk/services for more information. Your GP surgery will also have details of what help is available to you.

What other information is available?

Many CGD patients and their families find it beneficial to keep informed about the advances made in understanding and treating CGD. Please see the section *Further support* (page 53) for a list of organisations that may be helpful.

Summary

CGD is a rare disorder of the immune system that can lead to serious and repeated infections. It can result in chronic complications owing 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.

Advances in bone marrow transplantation as a successful cure for CGD, and research into gene therapy, hold great promise for those affected.

Key facts

About CGD

- CGD stands for chronic granulomatous disorder.
- CGD is a rare condition and affects more boys than girls.
- You cannot catch CGD; you are born with it. CGD is a genetic disorder inherited through your genes.
- CGD is caused by slight changes in the make-up of your DNA, known as a mutation.
- CGD affects the ability of the immune system to function effectively.
- CGD makes those affected vulnerable to infection from some bacteria and fungi but not from viruses.
- CGD is caused by DNA mutations in an enzyme called NADPH oxidase. This enzyme is present in white blood cells, known as phagocytes. The role of phagocytes is to find, eat and kill germs.
- In CGD, not having fully working NADPH oxidase means that people with the condition cannot produce a respiratory burst and cannot produce the normal cellular 'bleach' to kill germs.
- People with CGD have to take antibiotics and antifungal medicines every day to protect against infection and to keep well.
- Having CGD also means having to take some simple precautions to reduce the risk of infection.
- Infections need to be treated quickly.
- CGD can be cured by bone marrow transplantation.
- Gene therapy for X-linked CGD and p47phox CGD is under development.

About phagocytes

- Phagocytes are a type of white blood cell.
- We have lots of phagocytes in our body. One litre of human blood contains about six billion phagocytes.
- Phagocytes circulate in the blood but can also move into the tissues of the body to do their work.
- Phagocytes are crucial in fighting infections by finding, eating and killing germs. They can also call on other phagocytes to assist.
- Phagocytes also keep tissues healthy by removing dead and dying cells that have reached the end of their life cycle. Phagocytes in the human spleen and liver dispose of over 10,000,000,000 old blood cells a day.
- Phagocytes kill germs by surrounding and ingesting them and breaking them down.
- There are different types of phagocytes and they perform different functions in the body.
- There are two main types of phagocytes that you might read about in connection with CGD. These are:

Neutrophils (sometimes referred to as granulocytes or polymorphonuclear leukocytes (PMNs)). Neutrophils are the first responders to bacterial or fungal infections. They are short-lived, lasting only about three days in body tissues, and represent 50–70 per cent of all circulating white blood cells.

Monocytes. Monocytes represent 1–5 per cent of all circulating white blood cells. When they enter body tissues they can live a long time. Over time they develop slowly into other, more specialised phagocytes known as macrophages and dendritic cells. These are cells that coordinate with other cells of the immune system to fight infection.

Further support

The CGD Society

CGD Society
PO Box 454
Dartford
DA1 9PE
Helpline: 0800 987 8988
Email: hello@cgdsociety.org
Website: www.cgdsociety.org

If you or your doctor is unfamiliar with CGD, please contact the CGD Society and we will do our best to ensure that you are put in touch with someone who can answer your query.

The CGD Society is working hard to improve the outlook for patients. It is free to join the Society and members receive regular e-newsletters. To find out more, please visit www.cgdsociety.org.

CGD Society clinical nurse specialist for patients in the UK

Helen Braggins
Telephone: + 44 (0)20 7405 9200 ext. 5024
Email: helen.braggins@gosh.nhs.uk

Other booklets available from the CGD Society:

- Bone marrow transplantation: A guide for families
- Key questions to ask when considering a BMT
- A guide for female carriers of X-linked CGD
- A short guide to CGD for medical professionals
- BMT questions

Specialist centres for CGD in the UK

Paediatric care

Great North Children's Hospital, Newcastle upon Tyne, United Kingdom

Consultant: Professor Andrew Gennery
Institute of Cellular Medicine
Paediatric Immunology Department
Great North Children's Hospital
Queen Victoria Road
Newcastle upon Tyne
NE1 4LP
Telephone: +44 (0)191 282 5234
Fax: +44 (0)191 273 0183

Great Ormond Street Hospital for Children, London, United Kingdom

Consultant: Professor David Goldblatt
Clinical Immunology Department
Great Ormond Street Hospital
Great Ormond Street
London
WC1N 3JH
Telephone: +44 (0)20 7829 8834

Adult care

The Royal Free London Hospital, London, United Kingdom

Consultant: Dr David Lowe
Clinical Immunology Department
The Royal Free London Hospital
Pond Street
London
NW3 2QG
Telephone: +44 (0)20 7794 0500

CGD support groups

National groups

Korea / Dae Han Min Guk: Chronic Granulomatous Disease
<http://cafe.daum.net/cgd.cafe>

Spain / España: Ayuda GC <http://idd007ai.eresmas.net/index.html>

United Kingdom: CGD Society www.cgdsociety.org

United States: Chronic Granulomatous Disease Association
www.cgdassociation.org

United States: Immune Deficiency Foundation
<https://primaryimmune.org>

Facebook groups

In English

CGD: www.facebook.com/groups/4773993378

CGD Society:
www.facebook.com/pages/CGDSociety/296241460441934?fref=ts

Chronic Granulomatous Disease Group:
www.facebook.com/groups/307915108014/

Living with CGD: www.facebook.com/groups/6214046732/

Living with Chronic Granulomatous Disorder:
www.facebook.com/groups/16319443986/

Those Affected By CGD: www.facebook.com/groups/20845768071/

En español

Enfermedad Granulomatosa Crónica:
www.facebook.com/groups/48263844699/

Gc La Granulomatosa Crónica: www.facebook.com/AyudaGC



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.