A Guide for Female X-linked CGD Carriers

CGDSociety
Supporting families affected by chronic granulomatous disorder

About chronic granulomatous disorder

Chronic granulomatous disorder (CGD) prevents the immune system from fighting off certain infections.

People with CGD carry a faulty gene, which means that some white blood cells don't work properly. As a result, people affected by CGD tend to get frequent bacterial and fungal infections, and need to take daily medication to stay healthy. Even if they take this medication, problems can still arise. This could lead to serious illnesses and prolonged periods in hospital.

CGD affects around six to eleven in a million people, depending on the part of the world you live in.

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Introduction

CGD is a genetic disorder, meaning it is caused by a faulty gene. CGD can be inherited, which means the faulty gene is passed from one generation to the next. Alternatively, the faulty gene can sometimes develop in someone whose parents do not have or carry CGD. This is called a 'de novo' genetic variation. There are two types of CGD: '**autosomal recessive CGD**' and '**X-linked CGD**'. Both types of CGD are inherited in different ways.

Some people are **affected** by CGD (which means they have the disease), while others are only a '**carrier**' of CGD. Being a carrier of CGD means that you have the faulty gene that causes CGD, and that you can pass it on to your children. However, being a carrier means that you do not **have** CGD.

This guide is created to inform you about **female X-linked CGD** carriers. It was developed because female X-linked CGD can experience specific health issues, and may have questions about their condition and how it impacts their family.

The first section of the booklet will explain the difference between '**autosomal recessive CGD**' and '**X-linked CGD**', and how these two types of CGD are inherited.

This guide then provides information about testing for X-linked CGD carrier status, health problems that are associated with being an X-linked CGD carrier, and how to manage them. This guide also provides information about the implications that being an X-linked carrier can have on family planning.

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Inheritance of CGD and being a carrier

There are two ways people can inherit CGD from their parents. One way is called '**autosomal recessive**' inheritance and the other way is '**X-linked**' (also known as '**sex-linked**') inheritance.

Autosomal recessive CGD

What is an autosomal recessive disease?
Every person has two copies of each gene in their body: one copy they received from their father, and one copy they received from their mother. When we talk about an '**autosomal recessive**' disease, this means that a person only has the disease if they inherit copies of the faulty gene from **both** parents.

Who can get autosomal recessive CGD?
Autosomal recessive CGD develops when someone inherits **two** faulty copies of a gene from their parents (one from their mother, and one from their father). The genes that may lead to autosomal recessive CGD are: CYBA, CYBC1, NCF1, NCF2 and NCF4.

Both males and females can have autosomal recessive CGD. Someone who has autosomal recessive CGD may experience health problems.

What is an autosomal recessive CGD carrier?

People can also be '**carriers**' of autosomal recessive CGD. A carrier is someone who has inherited only **one** faulty copy of a gene from **one** parent, and therefore does not **have** the disease. A carrier can, however, pass down the faulty copy to their son or daughter. Both males and females can be carriers of autosomal recessive CGD. To date, there has been no evidence of health complications due to being an autosomal recessive CGD carrier.

How is autosomal recessive CGD inherited?

When both parents are carriers of autosomal recessive CGD, there is a 1 in 4 chance that the child inherits a faulty copy from each parent and therefore has CGD. There is also a 2 in 4 (or 50%) chance that the child inherits one faulty copy, and therefore becomes a carrier of CGD. **Figure 1** shows the inheritance pattern of autosomal recessive CGD.

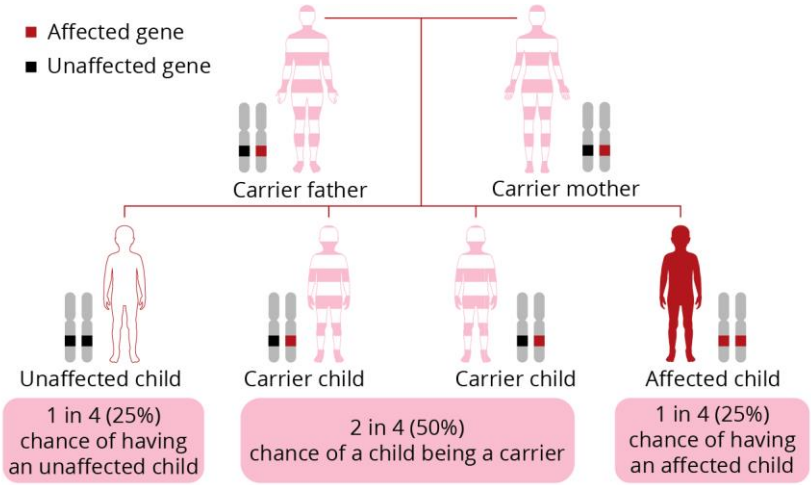

Figure 1. *The inheritance pattern of autosomal recessive CGD*

X-linked CGD

What is an X-linked disease?

When we talk about an '**X-linked disease**', this means that the faulty gene is found on the '**X-chromosome**', which is a so-called '**sex chromosome**'. Females have two X-chromosomes in their cells (sometimes labelled XX), while males have one X-chromosome and one Y-chromosome (sometimes labelled XY).

Who can get X-linked CGD?

X-linked CGD is caused by a mistake in the *CYBB* gene, which can be found on the X-chromosome. Males are most often affected by X-linked CGD.

X-linked CGD males

If males have X-linked CGD, the faulty gene is present on their **only** X-chromosome. As a result, a man with X-linked CGD can experience serious symptoms of CGD.

X-linked CGD carrier females

If a woman has a faulty copy of the *CYBB* gene on one X-chromosome, the copy on the other X-chromosome is almost always healthy. As a result, any CGD symptoms they may experience are likely **mild**, or they will have no symptoms at all. However, the severity and the type of symptoms they may experience can differ from one person to another. We call females who have only one copy of the faulty gene '**X-linked CGD carriers**'.

How is X-linked CGD inherited?

Both males and females can pass a faulty copy of the gene on to their children. Worthy of note is that a father can only pass the faulty copy on to a daughter, and not a son. The inheritance pattern of a father with X-linked CGD is presented in **Figure 2**. X-linked CGD is, however, most often passed on from the mother. The inheritance pattern of a female X-linked CGD carrier is presented in **Figure 3**.

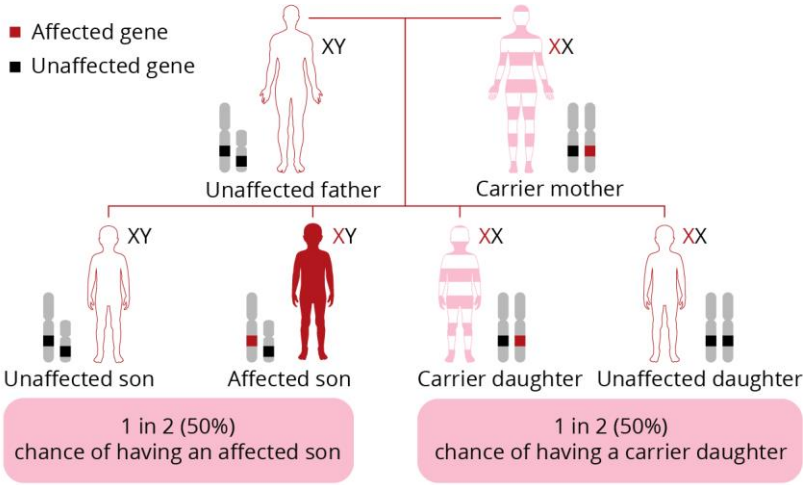

Figure 2. *The inheritance pattern of X-linked CGD when the mother is an X-linked CGD carrier and the father is not a carrier*

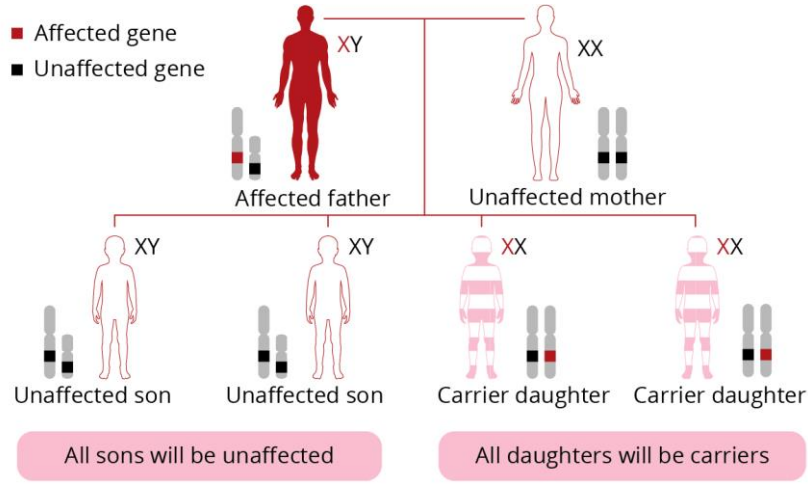

Figure 3. *The inheritance pattern of X-linked CGD when the mother is unaffected and the father has X-linked CGD*

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Testing for being an X-linked CGD carrier

To determine whether you are an X-linked CGD carrier, you can get a simple blood test to look at the function of your white blood cells or at whether you carry a genetic variation. If you would like to get a test, you should discuss this with your doctor. Your doctor will help you to get the test, and will help you understand the results.

The **functional blood tests** used for X-linked CGD carriers are the same as those used for diagnosing CGD. These are the '**nitroblue tetrazolium**' (**NBT**) test and the '**dihydrorhodamine**' (**DHR**) test. The NBT and DHR tests check if your white blood cells are producing a protein called '**NADPH oxidase**'. NADPH oxidase normally makes it possible for white blood cells to fight infections. However, in CGD, NAPDH oxidase does not work properly.

The NBT and DHR test results for an X-linked CGD carrier normally show a mix of white blood cells. There are some healthy white blood cells (which make NADPH oxidase that kills bacteria and fungi) and unhealthy white blood cells (whose NAPDH oxidase does not work well). The mix of healthy and unhealthy cells may differ from one X-linked CGD carrier to another and may change over time. This, and how it affects the health of X-linked CGD carriers, is still being researched.

Overall, the DHR test is generally more accurate than the NBT test. This is because the NBT test result can sometimes look normal in X-linked CGD carriers when it should not be.

The **genetic blood test** looks at the genes that can cause CGD, to see whether these genes are healthy or faulty. For a genetic test you will usually only need to provide a bit of blood. Your blood is then taken to a laboratory and analysed, after which the doctor will discuss the results with you.

Why would a female need to test for X-linked CGD carrier status?

There are a few reasons why a female would be tested for X-linked CGD carrier status. These include the following:

1. **She has a mother that is an X-linked CGD carrier** – If a mother is an X-linked CGD carrier, there is a 50% chance that her daughter is also a carrier.

2. **She has a father or brother with X-linked CGD** – If a female's father or brother is affected by CGD, there is a 50% chance that she is a carrier of X-linked CGD.

3. **She has a child (usually a son) that is suspected of having CGD** – If a mother's child is suspected of having CGD, a doctor may choose to test for carrier status to help with the diagnosis of the child.

4. **Her carrier status needs to be determined for family planning** – If a female is considering having a child,

determining her carrier status can be beneficial for both genetic counselling as well as for her own health. This is discussed in more detail in the section called '**Family planning**'.

5. **Her carrier status needs to be determined for blood stem cell donation** – This occurs when a female is being considered as a stem cell donor for someone with CGD.

6. **She is experiencing significant symptoms associated with CGD** – X-linked CGD carriers can experience symptoms of CGD to varying degrees. However, this is unlikely to be the reason for a female to be tested for X-linked carrier status. The symptoms which X-linked CGD carriers can experience are presented below in the **X-linked CGD carrier health problems** section.

7. Her doctor wants to **rule out other diseases** (this is called a '**differential diagnosis**').

In the UK, if a doctor thinks a female older than 16 years of age may be an X-linked CGD carrier, she may be tested. The test for X-linked CGD carrier status will be done with her consent. Testing for carrier status can also happen at a younger age than 16, for example when someone is experiencing significant symptoms or when they are being considered as a bone marrow transplant donor for a sibling. The decision to test a girl for X-linked carrier status at a younger age is made on a case-by-case basis, under the guidance of the medical team.

Having a daughter identified as an X-linked CGD carrier will have implications for when she wants to start a family of her own. If the mother is an X-linked CGD carrier and the father is not affected by

X-linked CGD, for each pregnancy there is a one in two (50%) chance that a son will be affected by CGD. There is also a one in two (50%) chance that a daughter will be an X-linked CGD carrier. You should discuss with your medical team when and how to approach discussing the test results with your daughter.

Coping with the news of being an X-linked CGD carrier

Feelings that may arrive after receiving the news
Being told you are an X-linked CGD carrier may have come as a shock to you, and you may still be coming to terms with the news. A new diagnosis can be daunting. This may especially be the case with a diagnosis that may affect any children you have, or you might have in the future. Remember, being a carrier of X-linked CGD isn't down to anything that you did or did not do. It is not your fault or anyone else's. Genetic conditions just happen by **chance**.

Studies have shown that X-linked CGD carriers have higher **anxiety** levels than the general population. They may also have higher anxiety levels than parents with other conditions. The reasons for feeling anxious may be to do with being tested yourself, getting your children tested or having to talk about the condition. You may also feel anxious about the uncertainty of your own future and you children's futures. There may be anger towards family members if CGD is not talked about as a matter that affects your family.

The emotional effects may lead to feelings of sadness or depression. Be aware of the warning signs of stress, tension,

anxiety and depression, and recognise when and how they are impacting your life.

Key symptoms to look out for are:

- Feeling irritated
- Poor sleep and concentration
- Losing enjoyment in things you do or experience

Generally, carries of X-linked CGD may feel **tired**. If you have a child who has CGD, caring for them may be burdensome. Additionally, some X-linked CGD carriers may experience symptoms of their condition, which is further explained in the section '**X-linked CGD carrier health problems**'. Tiredness can also come from the emotions that you feel about being an X-linked CGD carrier.

Coping with your feelings

Once you know that you are an X-linked CGD carrier, you can start to develop ways to **cope** with your feelings. This may be by distracting yourself by having 'me' time to do something new or something you enjoy. Relaxation and meditation techniques may also help reduce feelings of anger and anxiety. Other self-help approaches include the online resource **Mood Gym**. There are also organisations which you can easily contact for support with your mental health. In the UK, two such organisations are **Mind** and the **Mental Health Foundation**.

Reaching out for support
If the impact on your daily life and wellbeing is severe and you cannot function as you normally do, you should **seek help**. Make sure your GP knows how you are feeling. Your GP may be able to refer you to a clinical psychologist for counselling, which can help you to feel better.

Remember, **you don't have to feel like you're facing this alone**. The CGD Society is here to provide you with information, help and support should you need it.

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X-linked CGD carrier health problems

In general, X-linked CGD carriers are healthy. However, some people who are X-linked carriers may develop **symptoms of CGD** and **associated health problems**. In extreme cases, the symptoms can be as severe as those experienced by people with CGD. Such extreme cases are rare. Researchers are working hard to learn more about the health of X-linked CGD carriers.

In 2017, the largest study of its kind involving 81 X-linked CGD carriers was conducted. This study identified health problems that X-linked CGD carriers experience. Many X-linked CGD carriers reported that they experienced one or more health problems or symptoms. These are described in **Table 1**.

In some X-linked CGD carriers it has been observed that some symptoms tend to be **more significant in older carriers** than younger carriers. In particular, fatigue and joint pains seem to become worse. However, research needs to be done to properly investigate how symptoms change with age and the reasons why this might happen.

Symptom	How many people experienced this symptom
Infections	
A history of significant infections, with most people having recurrent swelling or lumps on the skin ('skin abscesses')	
Enlargement of the lymph nodes, usually due to infection ('lymphadenitis'). Lymph nodes are small bean-shaped structures that make an immune response to harmful things like bacteria	
Skin problems	
Being highly sensitive to the sun ('photosensitivity')	
A butterfly-shaped rash on the face ('Malar rash')	
Pimples ('acne'), redness in the face ('rosacea'), or an irritated skin ('dermatitis')	
Flaky skin ('psoriasis') or a skin condition that can be caused by infection ('erythema multiforme')	
Gut ('gastrointestinal') problems	
Gut problems (overall)	
Stomach pain or diarrhoea	
Bleeding from the anus	
Irritable bowel syndrome (IBS)	
Respiratory problems	
Lung infection ('pneumonia')	
Fatigue	
Fatigue	
Autoimmune problems	
Joint pain ('arthritis')	
Mouth ulcers ('aphthous ulcers' or 'canker sores')	
Temporary changes in the colour of your fingers and toes when you are cold, anxious or stressed ('Raynaud's phenomenon')	

Table 1. *Health problems and symptoms experienced by X-linked CGD carriers in a 2017 study*

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Lupus and its link to X-linked CGD carriers

There is increasing evidence that some female X-linked CGD carriers experience symptoms of a condition called '**lupus**'. Some carriers might have a lupus diagnosis, while other may experience '**lupus-like symptoms**' without receiving a diagnosis. In both of these cases, it is important that symptoms are taken **seriously** by your GP and that they are managed appropriately.

What is lupus?
Lupus is an '**autoimmune condition**'. This means that in people with lupus, the immune system mistakenly attacks the body's own healthy tissues. It does this in much the same way as it would attack an infection. When this happens, it causes inflammation in various parts of the body. This can result in symptoms such as skin rashes and joint pain.

There are two forms of lupus:

1. **Discoid lupus erythematosus** (also called '**discoid lupus**'), which is largely confined to the skin.

2. **Systemic lupus erythematosus** (also called '**systemic lupus**'), which affects the joints, heart, blood, lungs and kidneys.

What symptoms of lupus should I look out for?
The most common symptoms of lupus are skin rashes which are very sensitive to the sun (sometimes referred to as '**photosensitive rashes**'), fatigue and joint pain. Photosensitive rashes usually develop on parts of the body that are exposed to the sun such as the face, wrists, hands, and chest.

Other symptoms can also include headaches, mouth ulcers and temporary changes in the colour of your fingers and toes when you are cold, anxious or stressed (this is known as '**Raynaud's phenomenon**'). In Raynaud's phenomenon, your skin on your fingers and toes may become white or blue in colour.

For people with systemic lupus, more severe symptoms may include inflammation of internal organs such as the lungs, heart, nervous system and kidneys. However, this is very rare in carriers of X-linked CGD.

How is lupus diagnosed?
A GP can diagnose lupus by looking at the symptoms that people have and the results of blood tests. The blood tests for lupus look for particular types of '**autoantibodies**' in your body. Your immune system makes these autoantibodies when it mistakes parts of your own body as 'harmful invaders'. This is what happens in lupus, and these autoantibodies attack your cells and tissues, including your joints and skin. One of the most common blood tests for lupus is called an **anti-nuclear antibodies (ANA) test**. This test looks for '**anti-nuclear antibodies**', which are a specific type of autoantibody.

However, the ANA test and other blood tests can show a negative result in some people who do actually have lupus, especially discoid lupus. This seems to be particularly true for X-linked CGD carriers.

How serious are lupus and lupus-like symptoms?
For many people, lupus-like symptoms are no more than a nuisance. Others who have troublesome symptoms may benefit from the approaches used to manage symptoms of lupus. Systemic lupus can be a more unpredictable condition and should be carefully monitored by a rheumatologist and/or immunologist (often in a special lupus clinic).

To find out more about how symptoms of lupus can affect X-linked CGD carriers, visit the CGD Society website at **https://cgdsociety.org** or get in touch via **hello@cgdsociety.org**.

If you are an X-linked CGD carrier and think you may have lupus-like symptoms, **consult your GP**. Your GP may refer you for screening tests and an assessment by a rheumatologist or immunologist. Lupus-like symptoms need to be taken seriously. If they're significant, you should be referred to a rheumatologist, dermatologist and/or immunologist and given appropriate medications to manage your symptoms. It is important that your healthcare providers understand that there is a known link between lupus-like symptoms and being an X-linked CGD carrier. If you have any concerns, discuss them with your GP and care team.

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Dealing with symptoms

There are ways in which you can **treat and manage** the symptoms that you may experience. Because people have different symptoms, the treatment approach and the medications given can be slightly different for every person.

Managing infections

Doctors may prescribe '**prophylactic antibiotics**' that aim to prevent infections. Antibiotic prophylaxis is when antibiotics are given as a precaution and as preventative treatment, since people with CGD and X-linked CGD carriers are at higher risk of infections.

Managing mouth ulcers

Mouth ulcers can be treated but may keep coming back. Treatment for mouth ulcers involves relieving the associated symptoms (such as irritation and pain). Treatment is adapted to each person depending on the severity of the problems and their age. There are over the counter treatments to manage associated symptoms, which may be recommended by your local pharmacy. These may include numbing sprays or gels, mouthwashes, and painkillers.

Recommendations for preventing and dealing with mouth ulcers

1. **Maintain good oral (mouth) hygiene and use a mouthwash.** The best way to avoid mouth ulcers is by brushing your teeth twice a day and using an alcohol-free, anti-bacterial mouthwash containing chlorhexidine, such as Corsodyl. Please be aware that using Corsodyl over a long period of time can cause teeth to discolour and the tongue to feel too sensitive, so you may need to stop using it for a while, then restart. If you want to know more about Corsodyl, you can talk to your dentist.

2. When you develop a mouth ulcer, **continue to clean your teeth and mouth gently**, even if it is painful. Use an alcohol-free, anti-bacterial mouthwash containing chlorhexidine, such as Corsodyl.

3. **If the ulcers are painful you can use a sore mouth gel**, such as Bonjela, or the pharmacist's own brand equivalent. Some gels are not suitable for children, so make sure you read the instruction leaflet carefully. Alternatively, you can try Difflam mouth spray to numb the pain or take painkillers such as paracetamol. Bonjela and Difflam can be bought over the counter which means that you can get them at your local pharmacy. If the pain is very severe, your doctor may give you stronger painkillers.

4 **Your doctor may prescribe medication that contains a steroid**, as it is the most effective treatment for difficult-to-treat, painful or frequent mouth ulcers. Steroids work by reducing inflammation, swelling and irritation in the mouth which is associated with ulcers. The steroid helps ulcers heal quicker although it doesn't stop new ones occurring. Steroid treatments include:

- **Corlan**, ('hydrocortisone hemisuccinate') pellets. You put the pellet next to or on the ulcer. If you want to find out more about Corlan, you can visit **https://www.nhs.uk/medicines/hydrocortisone-buccal-tablets/** or talk to your GP.

- **Betamethasone**, 500 mg soluble tablets dissolved in 15 ml of water to make a mouth rinse, used four times daily for a few minutes. This can be a very useful approach if there are many ulcers in the mouth. If you want to find out more about betamethasone tablets you can visit **https://www.nhs.uk/medicines/betamethasone-tablets/** or talk to your GP.

- **Topical 'tetracyclines'**, may reduce the severity of an ulcer. Tetracyclines are medications that can help with bacterial infections. An example is Doxycycline, 100 mg in 10 ml of water used as a month rinse four times daily. This treatment is only used for people older than 12 years of age.

Talk to your doctor

When the ulcers just won't go away, talk to your doctor or specialist nurse if you're concerned. There may be an underlying minor infection causing them that may need treating with antibiotics.

Recent research suggests that mouth ulcers tend to worsen if you have '**iron deficiency anaemia**'. Iron deficiency anaemia is caused by a lack of iron in the blood and is not uncommon in females who have periods. Research into the link between iron deficiency anaemia and mouth ulcers has been done, but a clear link has not yet been documented in CGD or X-linked CGD carriers. However, it has been found that in X-linked CGD carriers, mouth ulcers improve when iron deficiency anaemia is treated.

You can **talk to your GP** about getting a blood test to check if you have iron deficiency anaemia. Usually, the blood test which your GP will perform is called a '**full blood count**' **(FBC)** test. If you have iron deficiency anaemia you will typically be prescribed iron tablets by your GP to replace the iron that is missing from your body. Overall, if you have mouth ulcers, it is worth checking if you have iron deficiency anaemia.

Managing sun sensitivity

Being extra sensitive to the sun means you may burn more easily or get skin rashes or blisters. Our **sun safety tips** include:

- Wear a high factor sun cream (SPF 50 upwards) or sun block. Reapply it every couple of hours. Sun cream may be available on prescription. You can talk to your doctor about this for more information
- Put sun cream on your hands, feet, face, ears, and neck – common places to miss!
- Avoid the sun when it is at its strongest – between midday and 3pm
- Drink plenty of water to avoid dehydration
- The sun can get through clothes, so wear clothes with an SPF, or dark clothes (which protect the skin more than lighter clothes)
- The sun reflects off water, making it more intense. Be particularly careful if you are swimming or on a boat trip
- Wear a hat, sunglasses, and T-shirt
- Moisturise your skin after you've been in the sun

Managing lupus-like symptoms
People who have skin rashes and joint pain are usually treated with creams (often containing steroids) or anti-inflammatory medicines. Some people find that anti-malarial drugs, such as **hydroxychloroquine**, are also effective in treating the symptoms of lupus. Hydroxychloroquine may help with preventing severe recurrent mouth ulcers and sun-sensitive skin rashes, and possibly in reducing the feelings of tiredness. A doctor must prescribe hydroxychloroquine specifically for you.

People who have more serious complications that are associated with systemic lupus may be treated with **steroid tablets** or **immunosuppressants**. Immunosuppressants are drugs that alleviate symptoms by damping down the immune system. When these medicines are prescribed, your doctor will want to review your health regularly through blood tests and check-ups.

Skin rashes associated with lupus are often very sensitive to the sun. The section above called '**Managing sun sensitivity**' provides tips on how to deal with this. In cold weather, people who have problems with Raynaud's phenomenon should keep warm and wear thick gloves and socks or tights.

Managing fatigue
Fatigue tends to come and go, so it's best to try and get some rest when you are not feeling good and make the most of days when you are.

07

Family planning

X-linked CGD carrier females can become pregnant and have babies, and may not experience any adverse effects to their health. If you are an X-linked CGD carrier, your children may inherit the faulty gene. The inheritance patterns of CGD are explained in the section '**Inheritance of CGD and being a carrier**' at the start of this guide.

Before getting pregnant

If you are an X-linked CGD carrier it is worth discussing with your doctor your plans for starting a family. Your doctor may refer you to a hospital **genetic counselling service** that will offer valuable guidance and advice on family planning issues. If this is not possible, you should inform your doctor as soon as you know you are pregnant.

During the pregnancy

If you are affected by any health problems associated with being an X-linked CGD carrier or taking medication to relieve symptoms, your doctor will take these into account in the management of your pregnancy.

Pregnancy can alleviate or worsen problems for many conditions,

and any health problems will be **carefully monitored** as your pregnancy progresses.

Does my child have CGD?
There are options available to determine if you are carrying a child affected by CGD. These include:

1. **Cell-free fetal DNA testing**, which can be done from the 9th week of pregnancy. Only a sample of the mother's blood is needed for this test. The test can determine the sex of the baby. The chances of a baby inheriting CGD are discussed under the section '**Inheritance of CGD and being a carrier**'. Some hospitals may offer this to X-linked CGD carriers. In the UK, the family clinic at Great Ormond Street Hospital in London can offer this service to families.

2. **Diagnostic prenatal testing** during early pregnancy using tissue ('**chorionic villus sampling**') or fluid ('**amniocentesis**') from the womb:

   Chorionic villus sampling (CVS) is usually done between the 11th and 14th week of pregnancy. This test involves removing a small sample of cells from the '**placenta**'. The placenta is the organ which links the mother's blood supply with the blood supply of the unborn baby. Usually, a needle is inserted through the mother's

tummy to remove the sample of cells from the placenta.

Amniocentesis is usually done between the 15th and 20th weeks of pregnancy. This test involves removing a small sample of cells from the '**amniotic fluid**'. The amniotic fluid is the fluid that surrounds the unborn baby in the '**amniotic sac**' in the womb. To remove the sample of cells, a long, thin needle is inserted through the mother's abdominal wall into the amniotic sac.

Your doctor should explain what these tests involve and what the possible benefits and risks are. You do not have to take any of these tests when they are offered to you. You should discuss with your doctor which of these tests may be best for you.

In vitro fertilisation

Some people may opt to have '**in vitro fertilisation**' **(IVF)** treatment. With IVF, an egg is taken from the woman's ovaries and is fertilised with sperm from a partner or sperm donor in a laboratory. Then, the fertilised egg ('**embryo**') is put into the woman's womb. With IVF, it is possible to see whether an embryo has CGD or not before it is placed into the womb.

If, for any reason, you choose to have IVF treatment you should discuss your X-linked CGD carrier status with your doctor. Your doctor can also provide information on the criteria for NHS-funded IVF.

08

Research and X-linked CGD carriers

Research into the possible health problems that X-linked CGD carriers may experience is still in the early stages. The CGD Society is working hard to raise awareness of these health problems in X-linked CGD carriers and to encourage more research in this area.

Below we have listed several studies that examine the health of X-linked CGD carriers of interest. Most of these research papers are free to access and read. For some you may need to pay a subscription or a one-off fee to gain access. These papers have been indicated with this icon:

'**Abnormal apoptosis in chronic granulomatous disease and autoantibody production characteristic of lupus**'. Sanford AN, Suriano AR, Herche D, Dietzmann K, Sullivan KE. Rheumatology (Oxford). 2006 Feb; 45(2): 178–81.

This study can be found **here**. This study found a link between developing lupus and the inability of X-linked CGD carriers' white blood cells to die when they should, and be cleared away by other cells in a normal, coordinated way.

'**Health-related quality of life and emotional health in X-linked carriers of chronic granulomatous disease in the United Kingdom**'. Battersby AC, Braggins H, Pearce MS, McKendrick F, Campbell M, Burns S, Cale CM, Goldblatt D, Gennery AR. *Journal of Clinical Immunology*, 2019 Feb; 39(2): 195–199.

This study can be found **here.** The study found that over 40% of the 61 X-linked CGD carriers surveyed had experienced moderate or greater levels of anxiety, with only a third having levels equivalent to those of the general population. The high anxiety scores were strongly associated with high levels of depression, low self-esteem, the presence of joint or bowel symptoms and higher levels of fatigue. X-linked CGD carriers were found to have lower quality of life scores than CGD patients in the areas of vitality (feeling active and energised), emotional wellbeing and mental health.

'**Clinical manifestations of disease in X-linked carriers of chronic granulomatous disease**'. Battersby AC, Cale CM, Goldblatt D, Gennery AR. *Journal of Clinical Immunology*, 2013 Nov; 33(8): 1276–84.

This study can be found **here.** It investigates the published literature about symptoms that X-linked CGD carriers may experience.

'**Inflammatory and autoimmune manifestations in X-linked carriers of chronic granulomatous disease in the United Kingdom**'. Battersby AC, Braggins H, Pearce MS, Cale CM, Burns SO, Hackett S, Hughes S, Barge D, Goldblatt D, Gennery AR. *Journal of Allergy and Clinical Immunology*, 2017 Aug; 140(2): 628–630.

'**X-linked carriers of chronic granulomatous disease: illness, lyonization, and stability**'. Marciano BE, Zerbe CS, Falcone EL, Ding L, DeRavin SS, Daub J, Kreuzburg S, Yockey L, Hunsberger S, Foruraghi L, Barnhart LA, Matharu K, Anderson V, Darnell DN, Frein C, Fink DL, Lau KP, Long Priel DA, Gallin JI, Malech HL, Uzel G, Freeman AF, Kuhns DB, Rosenzweig SD, Holland SM. *Journal of Allergy and Clinical Immunology*, 2018 Jan; 141(1): 365–371.

The first study can be found **here**, and the second study can be found **here**. The two studies above showed that some X-linked CGD carriers have similar problems with infection, inflammation and autoimmunity as seen in people with CGD. The studies underline the recommendation that the health of X-linked CGD carriers who experience symptoms should be managed proactively (before they occur or become severe) and reviewed by suitably qualified specialist doctors.

'**Cutaneous and other lupus-like symptoms in carriers of X-linked chronic granulomatous disease: incidence and autoimmune serology**'. Cale CM, Morton L, Goldblatt D. Clinical and Experimental Immunology, 2007 Apr; 148(1): 79–84.

This study can be found **here**. This research found that symptoms of photosensitivity, skin rashes, joint pains, fatigue and mouth ulcers are common in X-linked CGD carriers. It recommends that symptoms should be taken seriously, and that GPs should consider referring patients to a rheumatologist or dermatologist so appropriate treatment can begin. It's likely that tests for lupus will be negative but this should not influence diagnosis and treatment of people who have 'lupus-like' symptoms.

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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 **https://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 **The CGD Society - Membership Registration** to become a member.

If we can be of any help, **please contact us:**

0800 987 8988

hello@cgdsociety.org

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

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My notes

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Acknowledgements

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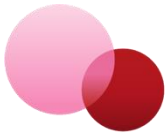

CGDSociety

Supporting families affected by chronic granulomatous disorder