FACTSHEET

Chronic granulomatous disease

What is chronic granulomatous disease?

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

Children with CGD may have one or more of the following:

Individuals with CGD are usually healthy at birth, but go on to develop recurrent infections, infections which are often difficult to treat or infections caused by unusual organisms, such as fungi, in the first few months or years of life. Although infection of any part of the body can occur, the places in the body affected most are the skin, lungs, lymph nodes, liver and bones. Typical infections include:

- Abscesses (collection of pus) of the skin, liver or lymph nodes
- Osteomyelitis (infection of the bone)
- Pneumonia (lung infection)

Five organisms are responsible for the majority of infections in CGD. These include

- *Staphylococcus aureus, Burkholderia cepacia, Serratia marcescens* (types of bacteria)
- *Nocardia species, Aspergillus species* (types of fungi)

Individuals with CGD often have gingivitis (recurrent bleeding gums), and tend to have poor wound healing. Good dental hygiene is therefore very important in those with CGD.

Another problem for patients with CGD is that, while they can't kill some germs, they can produce a lot of inflammation. This is a normal part of the response to infection and can itself be more serious than the triggering infection itself. Due to this, CGD patients with infections usually receive a cortisone type drug (e.g. prednisolone) to fight the inflammation as well as receiving antibiotics. Often low dose prednisolone is continued for a long time. Children with CGD often have inflammation of their bowel which is very similar to Crohn's disease. When children with inflammatory bowel disease have abscesses or leakage around the back passage they will usually be tested for CGD.

How do you get CGD?

CGD is an inherited disease. You do not catch it, you are born with it. Most children with CGD (5 of every 6) are boys. The disease occurs because the affected gene, which tells neutrophils how to kill organisms, has a mistake in it (mutation) and doesn't work properly. The gene for one type of CGD (which affects only boys) is carried on the X chromosome ("X-linked"). The boys, who have one X and one Y chromosome, inherit their X chromosomes from their mother. The mother, despite carrying one of the faulty genes on her X chromosome, is usually well (since she has another X chromosome

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without the faulty gene). Rarely some mothers may themselves have had a history of recurrent infections or had a history of mouth ulcers or recurrent light-sensitive rash. Some carrier mothers may also have a diagnosis of SLE. If a mother carries the gene on one X chromosome, then half her sons on average will have CGD and half her daughters will be carriers. There is another, less common type of CGD, called autosomal recessive CGD, which can affect both boys and girls. In this type of CGD one affected gene is inherited from the father and one from the mother (neither parent will have a history themselves of having had recurrent or unusual infections typical of CGD).

Is there a test for CGD?

We can test for CGD using one of two special blood tests. These are the nitroblue tetrazolium (NBT) test or the dihydrorhodamine (DHR) test). Children with CGD will have abnormal neutrophils on either test.

These tests can also be used to check whether the mother is a carrier of the X-linked type of CGD.

Once these tests have confirmed the diagnosis, it is common to look for a mistake in one of the genes which causes CGD, which can help with screening of relatives.

Can CGD be diagnosed during pregnancy?

Antenatal diagnosis in pregnancy is possible, usually by doing a test called a chorionic villous biopsy to look for the gene. This test can only be done if the exact mutation (gene mistake) in the family has already been identified. An alternative test is to take a blood sample directly from the umbilical cord of the baby in the womb and then perform a nitroblue tetrazolium (NBT) or dihydrorhodamine (DHR) test on the fetal blood.

What is the outlook for affected children?

With modern care, children affected by CGD are living into adult life. The severity of the disease varies, which means some children have lots of infections and others have very few. Life expectancy in children who are less severely affected may be normal. Risks associated with CGD do not go away and adults with CGD continue to be at risk of life-threatening complications of the disease.

Can CGD be treated?

The antibiotic cotrimoxazole (Bactrim, Septrin) has improved things enormously for children with CGD. Taken every day, it prevents many of the bacterial infections patients with CGD are susceptible to, and is recommended in all patients with CGD. Some patients with CGD may also be placed on daily anti-fungal therapy, such as itraconazole. Most children will be recommended to have injections of interferon gamma on a long term basis to prevent infections. Interferon gamma is given three times a week by injection under the skin with a very small needle. Some individuals may complain of "flu-like" symptoms when starting the therapy, although most children tolerate the injections well.

Can it be cured?

The only possibility of cure at the moment is to perform a bone marrow transplant. Bone marrow transplantation (BMT) can be a dangerous procedure and may even be fatal, so it is not undertaken lightly but recent experience shows that the risks in the long term are similar (or even better) than not having a transplant and a successful transplant dramatically improves quality of life. BMT will usually be discussed when the patient has a tissue matched sibling and is increasingly being offered to other patients.

Scientists have been interested in the possibility of using gene therapy (putting normal gene for CGD into the CGD patient's bone marrow cells then transplanting those engineered cells back into the patient) in order to try to cure CGD. However gene therapy does not currently result in a permanent cure and the corrected white blood cells tend to disappear over a few weeks or months. It can be used as a "rescue" therapy in those who are too sick to have a bone marrow transplant, but in whom temporary correction of some neutrophil function may assist in fighting a serious infection, and improving the health of the individual, so that in the future bone marrow transplant may be feasible if a match is found. However, this process is not currently available in Australia and if it were to be considered, the patient would need to travel overseas.

Research programs are advancing rapidly, and it is hoped that in the future there may be more help or a cure for sufferers of the disease.

For more information:
IDF Immune Deficiencies Foundation Australia

www.idfa.org.au

Remember:

The antibiotic cotrimoxazole (Bactrim, Septrin) has improved lifestyle greatly for children with CGD.