



Great Ormond Street Hospital for Children NHS Trust: Information for Families

Severe chronic neutropenia

This leaflet explains severe chronic neutropenia and what to expect when your child comes to Great Ormond Street Hospital for treatment.

What is Severe Chronic Neutropenia (SCN)?

SCN affects the white cells in the blood, but does not affect other blood cells.

There are two main types of white cells: neutrophils, which fight bacterial infection and lymphocytes, which fight viral infection. Children with SCN have very few neutrophils in their blood and so are at an increased risk of bacterial infection.

There are four major types of SCN: congenital, cyclical, idiopathic and autoimmune. More information about each follows:

Congenital neutropenia

Congenital neutropenia is a very rare disease with around 650 people worldwide known to have the condition. In general it affects between one or two people per million population and seems to be more common in Caucasian (white) people.

The exact cause is uncertain. We do know that in some cases it is an inherited disease and that it can run in families. In other cases, it can occur for no completely understood reason. Examination of the bone marrow (effectively the blood cell factory) of children with SCN shows that there appears to be a block in the growth of neutrophils. Normal neutrophil 'parent' cells can be seen, but the division and growth of these cells appears to stop before mature neutrophils are formed. The reasons behind this problem are being investigated both in our laboratories and in others around the world.

When congenital neutropenia occurs as an isolated problem, it is known as Kostmann's syndrome. But it can also be present with other symptoms, for example in Schwachman-Diamond syndrome and Glycogen Storage disease type 1b. Children are born with congenital neutropenia and it is usually recognised soon after birth. Your child will be particularly susceptible to fever and infections, some may be recurrent and severe. Congenital neutropenia does not get better alone but can be controlled.



Cyclical neutropenia

Cyclical neutropenia is extremely rare, it occurs because of changing rates of cell production by the bone marrow. This causes the number of neutrophils to fluctuate from zero to near normal over a period of about 21 days. Periods of severe neutropenia normally occur at approximately three-week intervals and last for three to six days. Severe infections are more likely to occur during times of low neutrophil count. Mouth ulcers in a three weekly cycle are typical of this sort of neutropenia.

Idiopathic neutropenia

This form of neutropenia may develop in children or adults and is diagnosed when the disorder cannot be attributed to any other disease or chemotherapy. Idiopathic neutropenia can develop in response to an illness, a virus or chemical exposure. Unlike congenital forms of neutropenia, children with idiopathic may have had normal blood cell counts in the past and their neutropenia may spontaneously resolve. Idiopathic neutropenia is estimated at two to four cases per million population.

Autoimmune neutropenia

This is the most common form of neutropenia in childhood. In this disorder the body makes antibodies against its own neutrophils. The body then thinks that its own neutrophils are enemies and tries to destroy them. Autoimmune neutropenia is diagnosed by a blood test detecting autoimmune antibodies. This type of neutropenia is most common in infants and young children. Serious infections are uncommon. Children usually 'grow out' of this disorder within two years of diagnosis.

How is SCN diagnosed?

Blood tests and then a bone marrow biopsy (which involves taking a small sample of the bone marrow for examination under a microscope) will generally help to decide which sort of neutropenia your child has. Blood tests will reveal the level of neutrophils circulating in your child's blood.

A normal neutrophil count in children is roughly between 1.5 and 7 billion cells per litre of blood. In conversation, the 'billion cells per litre' is dropped and the level of neutrophils is generally referred to as 1.5 and 7. When your child has a neutrophil count of less than 0.5, he or she is said to have severe neutropenia.

What problems can SCN cause?

When your child has severe neutropenia, the risk of bacterial infection increases and this increase is more rapid when the neutrophil count is below 0.2. Most infections occur in the ears, skin or throat and to a lesser extent, the chest. These infections can be very serious and your child will need antibiotics to clear them up.

Because your child's defences are weakened, he or she is likely to become seriously unwell more quickly than a child with a normal neutrophil count. If your child has a temperature above 38.5°C for more than two hours or 39°C once unwell and appears listless without any obvious reason, you should get in touch with your local hospital immediately. Most have 'direct access' for neutropenic children. This means they can be admitted straight to the ward



without going via your GP. The doctors on the ward at GOSH will also be happy to provide advice over the telephone.

How is SCN treated?

The first line of treatment is to give children antibiotics just in case (prophylaxis) but some children manage just by having antibiotics when they are unwell.

However, children with congenital neutropenia usually require treatment with granulocyte colony stimulating factors (G-CSFs). This is the main option of treatment with congenital neutropenia and can significantly improve the quality of your child's life. G-CSFs are artificial versions of natural hormones that drive the bone marrow to produce neutrophils. Giving G-CSF pushes the development of neutrophils in the bone marrow and allows these cells to mature and come out into the bloodstream to prevent and treat bacterial infection. Many children with congenital neutropenia need G-CSFs every day to keep them free of dangerous infections. Some only need to boost their neutrophils when they get a severe infection.

G-CSFs are given by an injection just under the skin using a very small needle. To make this less painful, a local anaesthetic cream can be applied to the site half an hour before the injection is due. You will need to give your child these injections at home. Before you leave the hospital, the ward staff will ensure that you and your child feel comfortable and confident about these injections.

For more information about G-CSFs, please see our leaflet.

What is the outlook for children with congenital neutropenia?

While there is no cure for congenital neutropenia, giving G-CSFs can raise your child's neutrophil count making him or her less prone to infections and therefore feeling in better health generally.

Unfortunately there appears to be a risk that children with congenital neutropenia develop leukaemia or myelodysplasia (effectively a pre-leukaemia). This was recognised before the use of G-CSF therapy, but is being seen more often now. The most likely explanation for this is that before G-CSF therapy, many children died of infections before living long enough to develop leukaemia, rather than the G-CSF itself being to blame.

In other conditions with neutropenia where G-CSF has been used (that is, cyclical, autoimmune and idiopathic), this increase in leukaemia has not been described. It seems that this problem only affects children with congenital neutropenia. Children therefore have annual bone marrow tests to look for early signs of leukaemia. As with most cancers, the earlier the disease is diagnosed, the better the outlook for the child.

For children with very severe disease, a bone marrow transplant may be considered.

Your child should receive the usual childhood immunisations (these are not dangerous for your child). There is no reason why your child should not live an active life at school and home, and there are no particular activities your child should avoid.



Support Groups

There is no support group in the UK specifically for SCN, but the Primary Immunodeficiency Association can offer help and advice.

Primary Immunodeficiency Alliance
Alliance House
Caxton Street
London SW1H 0QS
Helpline: 0845 603 9158
(Mon - Thurs 7pm - 10pm)
Website: www.pia.org.uk

You can also contact the Severe Chronic Neutropenia International Registry:

Severe Chronic Neutropenia UK Registry
Department of Paediatric Haematology
& Oncology
St James' University Hospital
Leeds LS9 7TF

Two organisations outside the UK have websites:

Neutropenia Support Association Inc.
(Canada)

www.neutropenia.ca

Neutropenia Support Australia

www.neutropenia.com.au

They do not contain a lot of information at present, but may be worth visiting in the future.

Notes

Compiled by the Haematology department
in collaboration with the Child and Family Information Group

Great Ormond Street Hospital for Children NHS Trust
Great Ormond Street
London WC1N 3JH

www.goshfamilies.nhs.uk www.childrenfirst.nhs.uk