Children's Cancer and Leukaemia Group | the EXPERTS in CHILDHOOD CANCER

Neuroblastoma in children

An information guide for parents, carers and families

The purpose of this guide is to give information about neuroblastoma to help you understand more about the type of cancer your child has.

Information in this guide should be used to support professional advice specific to your child's diagnosis. If you have any questions, it is important to ask your child's medical team.

What is neuroblastoma?

Around 100 children in the UK are diagnosed each year with neuroblastoma. Most children who have this cancer are younger than five years old. Neuroblastoma is the second most common solid tumour in children after brain tumours and makes up 6% of the total number of childhood cancer diagnoses.

Neuroblastoma develops from the cells left behind from a baby's development in the womb. The cells that it develops from are called neuroblasts.

Neuroblastoma starts from either the adrenal gland or from nervous tissue that runs alongside the spinal cord in the neck, chest, abdomen or pelvis. The adrenal glands are found above the kidneys and release hormones to maintain blood pressure, and enable us to respond to stress.

Causes of neuroblastoma

The exact cause of neuroblastoma is not known. It is not infectious and cannot be passed on to other people. It is important to remember that nothing you have done has caused your child's cancer.

Signs and symptoms

The symptoms vary, depending on where your child's tumour is. Symptoms may include:

- swollen tummy
- constipation
- difficulty weeing
- breathlessness or difficulty swallowing
- visible lump
- small, blue-coloured lumps in the skin
- leg weakness or unsteadiness
- reduced leg movements
- jerky eye and muscle movements
- non-specific symptoms of tiredness, pallor, loss of appetite, weight loss, bone pain and general discomfort

How it is diagnosed

A variety of tests and investigations are needed to diagnose neuroblastoma. These may include a biopsy, blood and bone marrow tests, x-rays, CT or MRI scans, and an MIBG scan. These tests will help to confirm the diagnosis, to find the original site of the tumour and to see whether it has spread. Any tests and investigations that your child needs will be explained to you.

Urine test – Nine out of ten children with neuroblastoma will have the substances, vanillylmandelic acid (VMA), or homovanillic acid (HVA), in their urine. These are sometimes called 'tumour markers'. Measuring VMA and HVA can help to confirm the diagnosis. VMA and HVA levels will be checked during and after treatment.

MIBG (nuclear medicine) scan – Most children will have an MIBG (meta-iodo-benzyl guanidine) scan. Attaching a small amount of radioactive iodine to the MIBG makes neuroblastoma tissue show up on the scanner. Some children have neuroblastoma that does not take up MIBG and a FDG-PET scan may be needed instead.

Biopsy – A small sample of cells is taken from the tumour during an operation under a general anaesthetic. The biology and genetics of these cells are looked at. The presence of a certain amount of a 'marker' called MYCN (known as MYCN amplification) can suggest that the neuroblastoma may be an aggressive type. In this situation, the treatment needs to be more intensive.

Staging

The 'stage' of a cancer is a term used to describe its size and whether it has spread beyond its original site. Knowing the particular type and stage helps doctors to decide on the most appropriate treatment.

The staging system below is commonly used:

- **Stage 1 (INRG stage L1)** – the tumour is in one place, and can be removed completely by an operation.
- **Stage 2 (INRG stage L1)** – the tumour is in one area and has not spread. It may be larger than Stage 1 and more difficult to remove completely by an operation.
- **Stage 3 (INRG stage L2)** – the tumour has not spread but it may be large and have grown from one side of the child's body to the other. This type of tumour is usually difficult to safely remove with surgery alone.
- **Stage 4 (INRG stage M)** – the tumour may be any size, but cells have broken away and spread to other parts of the body. Depending on age, children with Stage 4 are likely to need more intensive treatment.
- **Stage 4s (INRG stage MS)** – most often found in babies, under one year old. The cells may have spread, but often behave less aggressively than in an older child. As well as a primary tumour, the liver, skin, lymph nodes and bone marrow may be affected but not bones, lungs or brain.

Treatment

Treatment for neuroblastoma depends on the age of your child, the size and position of the tumour, risk factors shown on scan images, the tumour biology (including the MYCN status) and whether the cancer has spread. Based on these features, your child's neuroblastoma will be classified as **very low, low intermediate, or high-risk** disease and treatment will be planned accordingly.

Surgery

If the tumour is at an early stage and there is no evidence that it has spread to the lymph nodes or any other parts of the body, an operation to remove it, or as much of it as possible, will be undertaken. If the tumour is too large or in too difficult a position to remove safely, chemotherapy will be given to shrink it before surgery.

Chemotherapy

If the tumour has already spread or is identified as high-risk, intensive chemotherapy is needed. Chemotherapy is the use of anti-cancer drugs to destroy cancer cells. It is usually given as an infusion into a vein. Your child's doctor will discuss with you the type and amount of chemotherapy needed.

High-dose chemotherapy with stem cell rescue

If your child has high-risk neuroblastoma, they are likely to have high dose chemotherapy with peripheral blood stem cell rescue. High-dose chemotherapy wipes out any remaining neuroblastoma cells but also wipes out the body's bone marrow, where blood cells are made. To prevent the problems this causes, stem cells (blood cells at their earliest stages of development) are collected from your child's blood before the chemotherapy is given. These stem cells are frozen and stored until required. After high-dose chemotherapy, the stem cells are given back to your child through their central line. They make their way into the bone marrow, where they grow and develop into mature blood cells.

Radiotherapy

External beam radiotherapy may be given if the neuroblastoma is high-risk, or has spread to several parts of the body. This uses high-energy rays to destroy cancer cells, while doing as little harm as possible to normal cells. External beam radiotherapy is given from a machine outside the body. Internal radiotherapy may sometimes be given using radioactive MIBG.

Radioactive MIBG is similar to the MIBG used in an MIBG scan to diagnose a neuroblastoma, but uses higher doses of radioactivity to kill the cancer cells.

Immunotherapy

Immunotherapy (monocolonal antibodies) can encourage a patient's immune system to destroy some types of cancer cells while causing little harm to normal cells. Children with high-risk neuroblastoma, are usually given immunotherapy using an antibody called anti-GD2 (dinutuximab-beta). Evidence shows that anti-GD2 monoclonal antibodies can reduce the risk of relapse or delay the timing of relapse. Each course of dinutuximab beta is given over 10 days and some children can be at home for parts of each course. The treatment has side effects, which your doctor will discuss in detail.

Dinutuximab-beta is combined with a medicine taken by mouth called retinoic acid, which is similar to vitamin A. This medicine helps to stop cancer cells growing and helps them to transform into non-cancerous cells.

Younger children

Children under 18 months old with neuroblastoma often have 'low-risk' tumours, and as long as there is no MYCN amplification, their outlook is excellent.

Children with Stage 4S disease often get better with very little or no treatment at all. These tumours can regress spontaneously or after chemotherapy, which is only given if the tumour is causing symptoms. They disappear completely or develop into a non-cancerous (benign) tumour, called a ganglioneuroma. Ganglioneuromas are usually harmless and do not need any treatment.

Side effects during treatment

Treatment for neuroblastoma can cause side effects, and your child's doctor will discuss these with you before the treatment starts. Side effects will depend on the part of the body being treated and what treatment is used. Most side effects are short-term and gradually disappear once treatment stops.

Side effects can include:

- feeling sick (nausea) and being sick (vomiting)
- temporary hair loss
- tiredness
- low blood count leading to an increased risk of infection and bruising and bleeding (sometimes blood and/or platelet transfusions are needed)
- a sore mouth and tummy
- diarrhoea

Radiotherapy can make your child feel tired, and the skin in the treated area may go red or get darker.

Clinical trials

Many children have their treatment as part of a clinical research trial or study. Trials and studies are carried out to try to improve our understanding of the best way to treat an illness. There are better results for curing children's cancers compared with just a few years ago because of clinical trials. The European research group for neuroblastoma is called SIOPEN (www.siopen.org).

Your child's medical team will talk to you about taking part in a clinical trial, and will answer any questions you have. Taking part is completely voluntary, and you'll be given plenty of time to decide if it's right for your child. You may decide not to take part, or you can withdraw from a trial at any stage. Your child will still receive the best treatment available.

National treatment guidelines

Sometimes, clinical trials are not available for your child's tumour. In this case, your doctors will offer the most appropriate treatment, using guidelines which have been agreed by experts across the UK. Children's Cancer and Leukaemia Group (CCLG) is an important organisation which helps to produce these guidelines.

Donating to a tissue bank

Neuroblastoma is a rare disease and more research is needed to help doctors develop better treatment for the future. Your child's hospital team will offer you the opportunity to anonymously donate tissue left over from tests carried out, for example, a biopsy or bone marrow test, to the tissue bank. This sample of tissue can then be used by scientists to learn more about neuroblastoma and how best to treat it. This is voluntary, and you will have plenty of time to decide if you wish to take part.

Late side effects

Months or years later, some children may develop late side effects from the treatment they have had. These may include a reduction in bone growth, hearing problems, a change in the way the heart, lungs and kidneys work, a risk of infertility and a small increase in the risk of developing another cancer in later life. For more information please visit www.cclg.org.uk/living-beyond-cancer.

Your child's doctor or nurse will talk to you about possible late effects and will keep a close eye on possible long-term side effects in follow-up clinics.

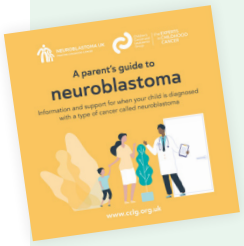
Follow-up care

Once treatment has finished, the doctors will monitor your child closely with regular appointments to be sure that the cancer has not come back and there are no complications. After a while, you will not need to visit the clinic so often. If you have specific concerns about your child's condition and treatment, it's best to discuss them with your child's doctor, who knows their case in detail.

Your feelings

It's devastating to hear that your child has cancer and you may feel overwhelmed but there are many professionals and organisations to help you through this difficult time. You may have many feelings, such as fear, guilt, sadness, anger, and uncertainty. These are all normal reactions and are part of the process that many parents go through.

It's not possible to address in this guide all of the feelings you may have. However, the CCLG booklet 'A parent's guide to children and young people with cancer' talks about the emotional impact of caring for a child with cancer and suggests sources of help and support. Your child may have a variety of powerful emotions throughout their experience of cancer. The Parent's Guide discusses these further and talks about how you can support your child.



The CCLG booklet 'A parent's guide to neuroblastoma' is available FREE of charge from your child's hospital

All CCLG booklets and leaflets can be downloaded or ordered from our website:

www.cclg.org.uk/publications

USEFUL ORGANISATIONS

Children's Cancer and Leukaemia Group (CCLG) publishes a variety of free resources to order or download
www.cclg.org.uk

Young Lives vs Cancer offers practical support to children and young people with cancer and to their families
www.younglivesvscancer.org.uk

Macmillan Cancer Support offers support and advice to those affected by cancer
www.macmillan.org.uk

SIOPEN European research group for neuroblastoma clinical trials
www.siopen.net

Neuroblastoma UK offers parents help and support
www.neuroblastoma.org.uk

Solving Kids' Cancer offers parents help and support
www.solvingkidscancer.org

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Children's Cancer and Leukaemia Group (CCLG) is a leading national charity and expert voice for all childhood cancers.

Each week in the UK and Ireland, more than 30 children are diagnosed with cancer. Our network of dedicated professional members work together in treatment, care and research to help shape a future where all children with cancer survive and live happy, healthy and independent lives.

We fund and support innovative world-class research and collaborate, both nationally and internationally,to drive forward improvements in childhood cancer. Our award-winning information resources help lessen the anxiety, stress and loneliness commonly felt by families, giving support throughout the cancer journey.

Our work is funded by donations. If you would like to help, text 'CCLG' to 70085 to donate £3. You may be charged for one text message at your network's standard or charity rate. CCLG (registered charity numbers 1182637 and SC049948) will receive 100% of your donation.

If you have any comments on this factsheet, please contact us at publications@cclg.org.uk