



# About Neuroblastoma

## Overview

If your child has been diagnosed with neuroblastoma or you are worried about it, you likely have a lot of questions. Learning some basics is a good place to start.

- [What Is Neuroblastoma?](#)

## Research and Statistics

See the latest estimates for new cases of neuroblastoma in the US and what research is currently being done.

- [Key Statistics About Neuroblastoma](#)
- [What's New in Neuroblastoma Research?](#)

# What Is Neuroblastoma?

Cancer starts when cells in the body begin to grow out of control and crowd out normal cells. Cells in nearly any part of the body can become cancer, and can spread to other areas of the body. To learn more about how cancers start and spread, see [What Is Cancer?](#)

The types of cancers that develop in children are often different from the types that develop in adults. To learn more about , see [What Are the Differences Between Cancers in Adults and Children?](#)

Neuroblastoma starts in certain very early forms of nerve cells, most often found in an embryo or fetus. (The term **neuro** refers to nerves, while **blastoma** refers to a cancer that affects immature or developing cells). This type of cancer occurs most often in infants and young children. It is rare in children older than 10 years.

To understand neuroblastoma, it helps to know about the sympathetic nervous system, which is where these tumors start.

## The sympathetic nervous system

The brain, spinal cord, and the nerves that reach out from them to all areas of the body are all part of the nervous system. The nervous system is needed for thinking, sensation, and movement, among other things.

Part of the nervous system also controls body functions we are rarely aware of, such as heart rate, breathing, blood pressure, digestion, and other functions. This part of the nervous system is known as the **autonomic nervous system**.

The **sympathetic nervous system** is part of the autonomic nervous system. It includes:

- Nerve fibers that run along either side the spinal cord.
- Clusters of nerve cells called **ganglia** (plural of ganglion) at certain points along the path of the nerve fibers.
- Nerve-like cells found in the medulla (center) of the adrenal glands. The adrenals are small glands that sit on top of each kidney. These glands make hormones (such as adrenaline [epinephrine]) that help control heart rate, blood pressure, blood sugar, and how the body reacts to stress.

The main cells that make up the nervous system are called **nerve cells** or **neurons**. These cells interact with other types of cells in the body by releasing tiny amounts of chemicals (hormones). This is important, because neuroblastoma cells often release certain chemicals that can cause symptoms (see [Signs and Symptoms of Neuroblastoma](#)).

## Neuroblastomas

Neuroblastomas are cancers that start in early nerve cells (called **neuroblasts**) of the sympathetic nervous system, so they can be found anywhere along this system.

- Most neuroblastomas begin in sympathetic nerve ganglia in the abdomen, about half of these start in the adrenal gland.
- Most of the rest start in sympathetic ganglia near the spine in the chest or neck, or in the pelvis.

- Rarely, a neuroblastoma has spread so widely by the time it is found that doctors can't tell exactly where it started.

Some neuroblastomas grow and spread quickly, while others grow slowly. Sometimes, in very young children, the cancer cells die for no reason and the tumor goes away on its own. In other cases, the cells sometimes mature on their own into normal ganglion cells and stop dividing (this makes the tumor a benign ganglioneuroma).

## Other autonomic nervous system tumors in children

Not all childhood autonomic nervous system tumors are malignant (cancerous). However, there may be tumors that have both non-cancerous and cancerous cells within the same tumor.

- **Ganglioneuroma** is a benign (non-cancerous) tumor made up of mature ganglion and nerve sheath cells.
- **Ganglioneuroblastoma** is a tumor that has both malignant and benign parts. It contains neuroblasts (immature nerve cells) that can grow and spread abnormally, similar to neuroblastoma, as well as areas of more mature tissue that are similar to ganglioneuroma.

Ganglioneuromas are usually removed by surgery and looked at carefully with a microscope to be sure they don't have areas of malignant cells (which would make the tumor a ganglioneuroblastoma). If the final diagnosis is ganglioneuroma, no other treatment is needed. If it's found to be a ganglioneuroblastoma, it's treated the same as a neuroblastoma.

- [References](#)

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## Key Statistics About Neuroblastoma

Neuroblastoma is by far the most common cancer in infants (less than 1 year old). It accounts for about 6% of all cancers in children. There are about 800 new cases of neuroblastoma each year in the United States. This number has remained about the same for many years.

The average age of children when they are diagnosed is about 1 to 2 years. In rare cases, neuroblastoma is detected by ultrasound even before birth. Nearly 90% of cases are diagnosed by age 5. Neuroblastoma is rare in people over the age of 10 years.

In about 2 of 3 cases, the disease has already spread to the lymph nodes or to other parts of the body when it is diagnosed.

Statistics related to survival are discussed in [Survival Rates for Neuroblastoma Based on Risk Groups](#).

Visit the [American Cancer Society's Cancer Statistics Center](#) for more key statistics.

- [References](#)

American Cancer Society. *Cancer Facts & Figures 2018*. Atlanta, Ga: American Cancer Society; 2018.

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## What's New in Neuroblastoma

# Research?

Important research into neuroblastoma is being done right now in many university hospitals, medical centers, and other research institutions around the world. Each year, scientists find out more about what causes the disease and how to improve treatment.

## Genetics of neuroblastomas

Researchers now have better tests to look for changes in the genes of neuroblastoma cells. Researchers might know that a change has happened on a certain chromosome (a strand of DNA inside the cell, which contains its genes), but they still need to know more about that gene or what part of a gene has been affected. There are a few different ways that genes change in neuroblastoma:

- Sometimes there are extra copies of the same gene (called **amplification**) on a chromosome.
- Sometimes a chromosome can have missing pieces of DNA (called **deletions**) or extra pieces of DNA (called **gains** or additions), which can affect which genes the chromosome has.

Understanding the gene changes in neuroblastoma helps researchers understand which neuroblastomas are likely to be cured with less intense treatment, and which will need more aggressive treatment. More aggressive neuroblastoma tumors are often called high-risk neuroblastomas, while tumors that tend to be easier to treat are called low- or intermediate-risk neuroblastomas. Some of these gene changes are being used now to help cancer care teams determine a child's neuroblastoma [stage](#) and [risk group](#). Other gene changes might help researchers find new treatments that work on certain types of neuroblastoma cells.

Here are some specific DNA and gene changes currently being studied:

- DNA changes on the short arm of chromosome 6 (6p22) are more likely to be seen in neuroblastomas that grow more aggressively.
- Neuroblastoma cells in older children are more likely to have changes in the *ATRX* tumor suppressor gene. Tumors with this gene change tend to grow more slowly, but they are also harder to cure. This may help explain why older children tend to have high-risk neuroblastoma while younger children tend to have low- or intermediate-risk neuroblastoma and do better.
- Changes in or having more than one copy (amplification) of the *ALK* and *MYCN*

genes are features used to help decide a child's risk group. Some drugs might work well against neuroblastomas with *ALK* gene changes. Some scientists also are studying how *ALK* gene changes might be related to extra copies of the *MYCN* gene in neuroblastoma cells.

## Treatment

Survival rates for neuroblastoma have gotten better as doctors have found ways to improve on current treatments, but survival rates for children with high-risk neuroblastoma are not as good as they are for children with low- or intermediate-risk disease. Most research studies about high-risk neuroblastoma (more aggressive and hard to treat tumors) focus on finding the best combinations of chemotherapy drugs, stem cell transplant regimens, immunotherapies and other new treatments to try to cure more children. Current studies of low- and intermediate-risk neuroblastoma are trying to figure out if children can get less treatment and still do as well.

### Chemotherapy

The search continues for the best combinations of chemotherapy drugs to treat neuroblastoma.

Several chemotherapy drugs that are already used to treat other cancers, such as topotecan, irinotecan, and temozolomide, are now being studied in combination with other kinds of therapies for use against high-risk neuroblastoma or neuroblastoma that has come back.

Other studies are looking to see if children with low- or intermediate-risk neuroblastoma can be treated with less (or even no) chemotherapy. The goal is to still have the same good results, but with fewer side effects from treatment.

### Stem cell transplants

Doctors are also trying to improve the success rate for children with aggressive neuroblastoma with high-dose chemotherapy and stem cell transplants, using different combinations of chemotherapy, radiation therapy, retinoids, and other treatments. A recent clinical trial looked at whether giving two stem cell transplants to children with high-risk neuroblastoma works better than giving just one stem cell transplant. The long-term improvement in survival for children who received two transplants is not yet clear, but early results show that two stem cell transplants, followed by certain kinds of immunotherapy works better than one stem cell transplant . Other studies are looking to

see if using stem cells donated from another person (an **allogeneic stem cell transplant**) might help some children with hard-to-treat tumors. More research will be done to confirm these results. If you have questions about this, talk with your doctor.

## **Retinoids**

Retinoids such as 13-*cis*-retinoic acid (isotretinoin) have reduced the risk of recurrence after treatment in children with high-risk neuroblastoma, especially when they are given with certain immunotherapy treatments. Giving 13-*cis*-retinoic acid in combination with different types of chemotherapy drugs, immunotherapies called monoclonal antibodies, and targeted drugs is being studied in a number of clinical trials to help determine the combinations that might work the best.

## **Targeted drugs**

Knowing what makes neuroblastoma cells different from normal cells could lead to new approaches to treating this disease. Newer drugs that target neuroblastoma cells more specifically than standard chemo drugs are now being studied in clinical trials. For example, doctors are now studying medicines that target the pathways inside neuroblastoma cells that help them grow, such as crizotinib (Xalkori) for the ALK pathway and alisertib (MLN8237) for the aurora A pathway.

Crizotinib is a drug that targets cells with changes in the *ALK* gene. Up to 15% of neuroblastomas have changes in this gene. In an early study, crizotinib was found to cause some neuroblastomas to shrink, although it's not clear how long this might last, or if giving this drug with certain chemotherapy drugs might work better. Other drugs that target cells with *ALK* changes are being developed. Some of these are approved for treating other cancers and are being studied to see if they work in neuroblastoma.

Some other drugs that work differently from standard chemo drugs are being studied in clinical trials against neuroblastoma as well. Examples include bortezomib, vorinostat,, temsirolimus, bevacizumab, nifurtimox, and DMFO.

## **Immunotherapy**

Immunotherapy is the use of medicines to help a patient's own immune system fight cancer. A few different kinds of immunotherapy are being used in neuroblastoma.

### **Anti-GD2 monoclonal antibodies**

The [monoclonal antibody](#) dinutuximab (Unituxin®), which targets GD2 on neuroblastoma cells, is now used routinely for children with high-risk neuroblastoma, to help immune system cells find and destroy the cancer cells.

Clinical trials are now testing the effectiveness of several other antibodies that target GD2:

- Hu14.18-IL2 is an antibody that is linked to interleukin-2 (an immune-boosting cytokine). Early results have found that this antibody/cytokine combination may help some children for whom other treatments are no longer working.
- Hu14.18K322A is a modified antibody that might work as well as other GD2 antibodies without some of the side effects.
- Hu3F8 is another modified antibody that targets GD2. It is being studied in combination with other treatments.

## Vaccines

Several cancer vaccines are also being studied for use against neuroblastoma. For these vaccines, injections of modified neuroblastoma cells or other substances are given to try to get the child's own immune system to attack cancer cells. These treatments are still in the early stages of clinical trials.

## CAR T-cell therapies

[CAR T-cell therapy](#) is a promising new way to get a patient's own immune cells called **T cells (a type of white blood cell)** to fight cancer by changing them in the lab so they can find and destroy cancer cells. The T cells used in CAR T-cell therapies get changed in the lab to spot specific cancer cells by adding a man-made receptor (called a **chimeric antigen receptor** or CAR). One early trial created CAR T-cells to target GD2 on neuroblastoma cells. Other clinical trials are studying using CAR T-cells that target other proteins on the outside of neuroblastoma cells. These are very new clinical trials and are ongoing or in the planning phase. Talk to your doctor about these trials if you have questions.

- [References](#)

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