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## 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?](#)<sup>1</sup>

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?](#)<sup>2</sup>

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](#)<sup>3</sup>).

### **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.

## Hyperlinks

1. [www.cancer.org/cancer/cancer-basics/what-is-cancer.html](http://www.cancer.org/cancer/cancer-basics/what-is-cancer.html)
2. [www.cancer.org/cancer/cancer-in-children/differences-adults-children.html](http://www.cancer.org/cancer/cancer-in-children/differences-adults-children.html)
3. [www.cancer.org/cancer/neuroblastoma/detection-diagnosis-staging/signs-and-symptoms.html](http://www.cancer.org/cancer/neuroblastoma/detection-diagnosis-staging/signs-and-symptoms.html)

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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](#)<sup>1</sup>.

Visit the [American Cancer Society's Cancer Statistics Center](#)<sup>2</sup> for more key statistics.

## Hyperlinks

1. [www.cancer.org/cancer/neuroblastoma/detection-diagnosis-staging/survival-rates.html](http://www.cancer.org/cancer/neuroblastoma/detection-diagnosis-staging/survival-rates.html)
2. <https://cancerstatisticscenter.cancer.org/>

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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](#)<sup>1</sup> and [risk group](#)<sup>2</sup>. 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](#)<sup>3</sup> 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](#)<sup>4</sup> 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.

## Hyperlinks

1. [www.cancer.org/cancer/neuroblastoma/detection-diagnosis-staging/staging.html](http://www.cancer.org/cancer/neuroblastoma/detection-diagnosis-staging/staging.html)
2. [www.cancer.org/cancer/neuroblastoma/detection-diagnosis-staging/risk-groups.html](http://www.cancer.org/cancer/neuroblastoma/detection-diagnosis-staging/risk-groups.html)
3. [www.cancer.org/cancer/neuroblastoma/treating/immunotherapy.html](http://www.cancer.org/cancer/neuroblastoma/treating/immunotherapy.html)
4. [www.cancer.org/treatment/treatments-and-side-effects/treatment-types/immunotherapy/car-t-cell1.html](http://www.cancer.org/treatment/treatments-and-side-effects/treatment-types/immunotherapy/car-t-cell1.html)

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# Neuroblastoma Causes, Risk Factors, and Prevention

## Risk Factors

A risk factor is anything that affects your chance of getting a disease such as cancer. Learn more about the risk factors for neuroblastoma.

- [Risk Factors for Neuroblastoma](#)
- [What Causes Neuroblastoma?](#)

## Prevention

The risk of many adult cancers can be reduced with certain lifestyle changes , but at this time there are no known ways to prevent most cancers in children.

The only known risk factors for neuroblastoma cannot be changed. There are no known lifestyle-related or environmental causes of neuroblastoma at this time.

- [Can Neuroblastoma Be Prevented?](#)

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# Risk Factors for Neuroblastoma

A risk factor is anything that affects your chance of getting a disease such as cancer. Different cancers have different risk factors.

Lifestyle-related risk factors such as body weight, physical activity, diet, and tobacco use play a major role in many adult cancers. But these factors usually take many years to influence cancer risk, and they are not thought to play much of a role in childhood cancers, including neuroblastomas.

No environmental factors (such as being exposed during the mother's pregnancy or in early childhood) are known to increase the chance of getting neuroblastoma.

## Age

Neuroblastoma is most common in very young children, but it is still rare even in this age group. It is very rare in people over the age of 10 years.

## Heredity

In about 1% to 2% of all neuroblastomas, children inherit an increased risk of developing neuroblastoma from a parent. But most neuroblastomas do not seem to be inherited.

Children with the **familial** form of neuroblastoma (those with an inherited tendency to develop this cancer) usually come from families with one or more members who had neuroblastoma as infants. The average age at diagnosis of familial cases is younger than the age for **sporadic** (not inherited) cases.

Children with familial neuroblastoma sometimes develop 2 or more of these cancers in different organs (for example, in both adrenal glands or in more than one [sympathetic ganglion](#)<sup>1</sup>). It's important to distinguish neuroblastomas that start in more than one organ from neuroblastomas that have started in one organ and then spread to others (metastatic neuroblastomas). When tumors develop in several places at once it suggests a familial form. This might mean that family members should consider genetic counseling and testing (see [Genetic Testing: What You Need to Know](#)<sup>2</sup>). Both familial and neuroblastoma that is not inherited can spread to other organs.

## Having birth defects (congenital anomalies)

Some studies have shown that children with birth defects might have an increased risk of developing neuroblastoma. Some of the link between birth defects and neuroblastoma might be related to changes in genes that happen during fetal development.

Genes are made of DNA, which is a chemical inside our cells. Genes are instructions that tell our body cells what to do. Fetal development, which happens in a mother's uterus, is also directed by genes that tell the cells how to grow and divide. If cell growth and development doesn't happen normally in the fetus, it can cause a birth defect. Changes in genes that happen during fetal development might contribute to a birth defect and increase the risk of some kinds of childhood cancers, like neuroblastoma. That doesn't mean all children with birth defects will get neuroblastoma. More research is needed to understand the relationship between birth defects and risk of childhood cancer. For more information about genes and causes of neuroblastoma, see [What Causes Neuroblastoma?](#)

## Hyperlinks

1. [www.cancer.org/cancer/neuroblastoma/about/what-is-neuroblastoma.html](http://www.cancer.org/cancer/neuroblastoma/about/what-is-neuroblastoma.html)
2. [www.cancer.org/cancer/cancer-causes/genetics.html](http://www.cancer.org/cancer/cancer-causes/genetics.html)

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# What Causes Neuroblastoma?

The causes of most neuroblastomas are not known. But researchers have found important differences between neuroblastoma cells and the normal neuroblasts (early forms of nerve cells) from which they develop. They have also found differences between neuroblastomas that are likely to respond to treatment and those that have a poor prognosis (outlook). These differences (known as [prognostic markers](#)<sup>1</sup>) are sometimes helpful in choosing the best treatment.

## How normal cells become neuroblastoma

Nerve cells and cells of the medulla (center) of the adrenal gland develop from neuroblasts in the fetus. These neuroblasts usually grow and change into mature nerve cells. Neuroblastomas develop when normal fetal neuroblasts do not become mature nerve cells or adrenal medulla cells. Instead, they continue to grow and divide.

Neuroblasts might not have matured completely in babies by the time they are born. Most of these eventually mature into nerve cells or simply die off and do not form neuroblastomas. Sometimes, neuroblasts remaining in very young infants continue to grow and then form tumors. Some can even spread to other parts of the body. But many of these tumors will still eventually mature into nerve tissue or go away on their own.

However, as children get older, it becomes less likely that these cells will mature and more likely that they will grow into a cancer. By the time neuroblastomas are large enough to be felt or cause symptoms, most can no longer mature on their own and will grow and spread unless treated.

The failure of some neuroblasts to mature and to stop growing is due to abnormal DNA inside the cells. DNA is the chemical in each of our cells that makes up our genes, which control how our cells function. The DNA inside our cells is in long string-like structures called chromosomes.

Some genes contain instructions for controlling when our cells grow, divide into new cells, and die:

- Certain genes that help cells grow, divide, or stay alive are called **oncogenes**.
- Genes that help keep cell division under control or cause cells to die at the right time are called **tumor suppressor genes**.

Cancers can be caused by DNA changes that turn on oncogenes or turn off tumor

suppressor genes. These gene changes can be inherited from a parent (as is rarely the case with childhood cancers), or they may happen during a person's lifetime as cells in the body divide to make new cells.

In most cases, neuroblastoma cells have chromosome changes (such as having too many or too few chromosomes or missing part of a chromosome) that are likely to affect certain genes. Scientists are still trying to determine which genes are affected by these chromosome changes, as well as how these changes affect the growth of neuroblastoma cells.

### Gene changes in neuroblastoma

In rare cases, neuroblastoma seems to occur because of gene changes inherited from a parent. Inherited changes in certain genes account for most cases of hereditary neuroblastoma:

- *ALK* oncogene changes account for most cases of inherited neuroblastoma.
- Changes in *PHOX2B*, a gene that normally helps nerve cells mature, account for a small number of inherited neuroblastomas.

Still, most neuroblastomas are not caused by inherited DNA changes. They are the result of gene changes that happen at some point during the child's development, sometimes before birth. What causes these gene changes is not known. These changes are found only in the child's cancer cells, so they will not be passed on to his or her children. For example, about 10% to 15% of sporadic (not inherited) neuroblastomas also have changes in the *ALK* gene. In many neuroblastomas the exact genes affected are not known.

Other gene changes seem to affect how quickly a neuroblastoma can grow. Here are some examples of gene changes in neuroblastoma cells and what they can mean about a child's neuroblastoma:

- Neuroblastoma cells sometimes have extra copies of an oncogene called *MYCN* amplification, which is often a sign that the tumor will grow quickly and be harder to treat.
- When the *NTRK1* gene (which makes the TrkA protein) is overactive in the cells of neuroblastomas, it can be sign that a child's neuroblastoma might have a better outlook.
- 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 younger children with neuroblastoma tend to do better long term than children who are older when they are diagnosed.

Researchers have found some of the gene changes that may lead to neuroblastoma, but it's still not clear what causes these changes. Some gene changes may be inherited. Some might have unknown outside causes, but others could just be random events that sometimes happen inside a cell, without having an outside cause. There are no known lifestyle-related or environmental causes of neuroblastomas at this time, so it's important to remember that there is nothing these children or their parents could have done to prevent these cancers.

## Hyperlinks

1. [www.cancer.org/cancer/neuroblastoma/detection-diagnosis-staging/staging.html](http://www.cancer.org/cancer/neuroblastoma/detection-diagnosis-staging/staging.html)

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# Can Neuroblastoma Be Prevented?



The risk of many adult cancers can be reduced with certain lifestyle changes (such as staying at a healthy weight or quitting smoking), but at this time there are no known ways to prevent most cancers in children.

The only known **risk factors** for neuroblastoma (age and heredity) cannot be changed. There are no known lifestyle-related or environmental causes of neuroblastomas at this time.

Some studies suggest that having mothers take prenatal multi-vitamins or folic acid might lower the risk of neuroblastoma, but further research is needed to confirm this. Getting care from a doctor during pregnancy is always an important thing to do for the health of your baby.

If there is a history of neuroblastoma in your family, you may want to talk with a [genetic counselor](#)<sup>1</sup> about your children's risks of developing the disease. It is important to remember, though, that familial neuroblastoma is very rare.

## Hyperlinks

1. [www.cancer.org/cancer/cancer-causes/genetics.html](http://www.cancer.org/cancer/cancer-causes/genetics.html)

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# Neuroblastoma Early Detection, Diagnosis, and Staging

## Detection and Diagnosis

Catching cancer early often allows for more treatment options. Some early cancers may have signs and symptoms that can be noticed, but that is not always the case.

- [Can Neuroblastoma Be Found Early?](#)
- [Signs and Symptoms of Neuroblastoma](#)
- [Tests for Neuroblastoma](#)

## Stages, Risk Groups, and Outlook (Prognosis)

After a diagnosis of neuroblastoma, the stage and risk group of the cancer provide important information about the anticipated response to treatment.

- [Neuroblastoma Stages and Prognostic Markers](#)
- [Neuroblastoma Risk Groups](#)
- [Neuroblastoma Survival Rates by Risk Group](#)

## Questions to Ask About Neuroblastoma

Here are some questions you can ask your child's cancer care team to help you better understand your child's diagnosis and treatment options.

- [Questions To Ask About Neuroblastoma](#)
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# Can Neuroblastoma Be Found Early?

Researchers have studied whether screening infants for neuroblastoma might find these tumors earlier and lead to better treatment results. Screening is testing for a disease, such as cancer, in people who don't have any symptoms. One way to screen for neuroblastoma is to test children's urine for certain substances made by neuroblastoma tumors. (For more information on this urine test, see [Tests for Neuroblastoma](#).)

Studies have not found neuroblastoma screening to be helpful. Testing infants when they were 6 months old did find many tumors that wouldn't have normally been diagnosed. But most of these tumors were of a type that probably would have gone away or matured into benign (non-cancerous) tumors on their own. These tumors probably would never have caused any problems. The screening didn't lower the number of cancers found at advanced stages or save lives.

What's more, finding tumors that would never cause serious problems may needlessly frighten parents and can lead to unnecessary tests and surgery in children whose tumors would have gone away or matured on their own if left alone.

For these reasons, most experts do not recommend screening for neuroblastoma in infants who are not at increased risk of the disease.

In rare instances, neuroblastoma is found before birth during an ultrasound, a test that uses sound waves to create an image of the internal organs of a fetus. Ultrasounds are usually done to estimate the age of a fetus, predict the date of birth, and look for certain common birth defects. Improvements in ultrasound technology or other tests may lead to more accurate prenatal (before birth) testing for this disease.

Neuroblastoma is sometimes found incidentally in young children without any symptoms during tests done to find other childhood diseases. These children will usually have a good outcome, and some may not even need treatment.

But most often, neuroblastoma is first detected because of [signs or symptoms](#) the child is having.

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## Signs and Symptoms of Neuroblastoma

Neuroblastoma can cause many different signs and symptoms. Common symptoms include:

- Lump or swelling in the child's abdomen or neck that doesn't seem to hurt
- Swelling of the legs or upper chest, neck and face
- Enlarged belly
- Problems breathing or swallowing
- Weight loss
- Not eating or complaining about feeling full
- Problems with bowel movements or urinating
- Pain in bones
- Lumps or bumps in the skin that may appear blue
- Drooping eyelid and small pupil (the black area in the center of the eye) in one eye
- Problems being able to feel or move parts of the body
- Eyes that appear to bulge and/or bruising around the eyes

The signs and symptoms that a child has might be different depending on where the tumor is, how large it is, how far it has spread, and if the tumor makes chemicals called hormones.

Many of the signs and symptoms above are more likely to be caused by something other than neuroblastoma. Still, if your child has any of these symptoms, check with your doctor so the cause can be found and treated, if needed.

## Signs or symptoms caused by the main tumor

**Tumors in the abdomen (belly) or pelvis:** One of the most common signs of a neuroblastoma is a large lump or swelling in the child's abdomen. The child might not want to eat (which can lead to weight loss). If the child is old enough, he or she may complain of feeling full or having belly pain. But the lump itself is usually not painful to the touch.

Sometimes, a tumor in the abdomen or pelvis can affect other parts of the body. For example, tumors that press against or grow into the blood and lymph vessels in the abdomen or pelvis can stop fluids from getting back to the heart. This can sometimes lead to swelling in the legs and, in boys, the scrotum.

In some cases the pressure from a growing tumor can affect the child's bladder or bowel, which can cause problems urinating or having bowel movements.

**Tumors in the chest or neck:** Tumors in the neck can often be seen or felt as a hard, painless lump.

If the tumor is in the chest, it might press on the superior vena cava (the large vein in the chest that returns blood from the head and neck to the heart). This can cause swelling in the face, neck, arms, and upper chest (sometimes with a bluish-red skin color). It can also cause headaches, dizziness, and a change in consciousness if it affects the brain. The tumor might also press on the throat or windpipe, which can cause coughing and trouble breathing or swallowing.

Neuroblastomas that press on certain nerves in the chest or neck can sometimes cause other symptoms, such as a drooping eyelid and a small pupil (the black area in the center of the eye). Pressure on other nerves near the spine might affect the child's ability to feel or move their arms or legs.

## Signs or symptoms caused by cancer spread to other parts of the body

About 2 out of 3 neuroblastomas have already spread to the lymph nodes or other parts of the body by the time they are found.

[Lymph nodes](#)<sup>1</sup> are bean-sized collections of immune cells found throughout the body. Cancer that has spread to the lymph nodes can cause them to swell. These nodes can sometimes be felt as lumps under the skin, especially in the neck, above the collarbone, under the arm, or in the groin. Enlarged lymph nodes in children are much more likely to

be a sign of infection than cancer, but they should be checked by a doctor.

Neuroblastoma often spreads to bones. A child who can talk may complain of bone pain. The pain may be so bad that the child limps or refuses to walk. If it spreads to the bones in the spine, tumors can press on the spinal cord and cause weakness, numbness, or paralysis in the arms or legs. Spread to the bones around the eyes is common and can lead to bruising around the eyes or cause an eyeball to stick out slightly. The cancer can also spread to other bones in the skull, causing bumps under the scalp.

If the cancer spreads to the bone marrow (the inner part of certain bones that makes blood cells), the child may not have enough red blood cells, white blood cells, or blood platelets. These shortages of blood cells can result in tiredness, irritability, weakness, frequent infections, and excess bruising or bleeding from small cuts or scrapes.

Rarely, large tumors can start to break down, leading to a loss of clotting factors in the blood. This can result in a high risk of serious bleeding, which is known as a **consumption coagulopathy** and can be life threatening.

A special widespread form of neuroblastoma (known as **stage 4S**) occurs, but only during the first few months of life. In this special form, the neuroblastoma has spread to the liver, to the skin, and/or to the bone marrow (in small amounts). Blue or purple bumps that look like small blueberries may be a sign of spread to the skin. The liver can become very large and can be felt as a mass on the right side of the belly. Sometimes it can grow large enough to push up on the lungs, which can make it hard for the child to breathe. Despite the fact that the cancer is already widespread when it is found, stage 4S neuroblastoma is very treatable, and often shrinks or goes away on its own. Almost all children with this form of neuroblastoma can be cured.

## Signs or symptoms caused by hormones from the tumor

Neuroblastomas sometimes release hormones (chemicals) that can cause problems with tissues and organs in other parts of the body, even though the cancer has not spread to those tissues or organs. These problems are called **paraneoplastic syndromes**.

Symptoms of paraneoplastic syndromes can include:

- Constant watery diarrhea
- Fever
- High blood pressure (causing irritability)

- Rapid heartbeat
- Reddening (flushing) of the skin
- Sweating

An uncommon set of symptoms is called the **opsoclonus-myoclonus-ataxia syndrome** or “dancing eyes, dancing feet.” The child has irregular, rapid eye movements (opsoclonus), twitch-like muscle spasms (myoclonus), and appears uncoordinated when standing or walking (ataxia). He or she might also have trouble speaking. For reasons that are not clear, neuroblastomas that cause this syndrome tend to be less life-threatening than other forms of the disease.

## Hyperlinks

1. [www.cancer.org/cancer/cancer-basics/lymph-nodes-and-cancer.html](http://www.cancer.org/cancer/cancer-basics/lymph-nodes-and-cancer.html)

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# Tests For Neuroblastoma

Neuroblastomas are usually found when a child is brought to the doctor because of signs or symptoms he or she is having. If a tumor is suspected, tests will be needed to confirm the diagnosis.



## Medical history and physical exam

If your child has signs or symptoms that might be caused by a neuroblastoma (or another tumor), the doctor will ask about the symptoms and how long they have been present. The doctor might also ask if there is any history of possible [risk factors](#)<sup>1</sup>, such as a family history of neuroblastoma.

The doctor will examine your child for possible signs of a neuroblastoma and other health problems. For example, the doctor may be able to see or feel an abnormal mass or swelling. The doctor might feel to see if the child has lumps or bumps under the skin and examine your child's eyes closely. They might also look at your child's blood pressure because sometimes neuroblastoma cells can make hormones that cause high blood pressure. Neuroblastomas can sometimes grow close to the spinal cord, which can affect movement and strength in the child's arms and legs, so the doctor will pay close attention to these.

Some signs that could be caused by neuroblastoma, such as fever and enlarged lymph nodes, are much more likely to be caused by an infection, so the doctor might look for other signs of infection at first.

## Lab and imaging tests

If the history and exam suggest a child might have a neuroblastoma (or another type of tumor), more [tests](#)<sup>2</sup> will be done. These could include blood and urine tests, imaging tests, and biopsies. These tests are important because many of the symptoms and signs of neuroblastoma can also be caused by other diseases, such as infections, or even other types of cancer.

### Blood and urine catecholamine tests

The body makes many different types of hormones. Sympathetic nerve cells normally release hormones called **catecholamines**, such as epinephrine (adrenaline) and norepinephrine, which enter the blood and eventually break down into smaller pieces, called **metabolites**. The metabolites normally pass out of the body in urine. When epinephrine and norepinephrine are broken down by the body, the two most common metabolites made are:

- Homovanillic acid (HVA)
- Vanillylmandelic acid (VMA)

Neuroblastoma cells can also make these catecholamines. These 2 catecholamine metabolites can be measured in blood and urine. In most cases, neuroblastoma cells make enough catecholamines to be detected by blood or urine tests. If neuroblastoma cells are making catecholamines, the amount of HVA and VMA in urine or blood will be higher than expected.

If neuroblastoma is suspected or has been found, your child's doctor will probably order [blood tests](#)<sup>3</sup> to check blood cell counts, liver and kidney function, and the balance of salts (electrolytes) in the body. A urinalysis (urine test) may also be done to further check kidney function.

## Imaging tests

[Imaging tests](#)<sup>4</sup> use x-rays, magnetic fields, sound waves, or radioactive substances to create pictures of the inside of the body. Imaging tests can be done for a number of reasons, including:

- To help find out if a suspicious area might be cancerous
- To learn how far cancer has spread
- To help determine if treatment has been effective

If neuroblastoma is highly suspected, the most common imaging test to have first is usually an MRI or CT scan. If your child is diagnosed with neuroblastoma, they will have an MIBG scan as well. Most children who have or might have neuroblastoma will have one or more of these tests, but might not need all of these tests.

Children with neuroblastoma are often very young, so it can be hard to do some of these tests because the child might need to hold very still. Depending on your child's age and the imaging test that they will have, they might get medicines that are a kind of anesthesia or sedation to help them keep still.

## ***Ultrasound (sonogram)***

[Ultrasound](#)<sup>5</sup> might be one of the first tests done in very young children if a tumor is suspected, because it is fairly quick and easy, it does not use radiation, and it can often give the doctor a good view inside the body, especially in the abdomen (belly). Ultrasounds are usually not done if the child has already had an MRI or CT scan.

For this test, your child lies on a table (or sits on your lap) while a small wand called a transducer is placed on the skin over the belly (which is first lubricated with gel). The wand gives off sound waves and picks up the echoes as they bounce off organs. The

echoes are converted by a computer into a black and white image on a screen. The test is not usually painful, but it might cause some discomfort if the transducer is pressed down hard on the belly.

Ultrasound is used most often to look for tumors in the abdomen. (It's not used to look in the chest because the ribs block the sound waves.)

### ***Magnetic resonance imaging (MRI) scan***

[MRI scans](#)<sup>6</sup> provide detailed images of soft tissues in the body. These scans are very helpful in looking at the brain and spinal cord. They may be slightly better than CT scans for seeing the extent of a neuroblastoma tumor, especially around the spine.

MRI scans use radio waves and strong magnets to create the images instead of x-rays, so there is no radiation. A contrast material called **gadolinium** may be injected into a vein before the scan to better see details.

MRI scans can take up to an hour. For most MRI machines, your child has to lie inside a narrow tube, which is confining and can be distressing. Newer, more open MRI machines may be an option in some cases, but they still require the child to stay still for long periods of time. The MRI machine also makes loud buzzing and clicking noises that may be disturbing. Younger children and children who will not be able to be still for a long period of time are often given medicine to help keep them calm or even asleep during the test.

### ***Computed tomography (CT or CAT) scan***

[CT scans](#)<sup>7</sup> are often used to look for neuroblastoma in the abdomen, pelvis, and chest.

Before the test, your child may be asked to drink a contrast solution and/or get an IV (intravenous) injection of a contrast dye. This helps better outline structures in the body.

Younger children or children that might not be able to hold still may be sedated (given medicine to make them sleepy) before the test to reduce movement and help make sure the pictures come out well.

**CT-guided needle biopsy:** CT scans can also be used to help guide a biopsy needle into a tumor. It is not as common for children to have a needle biopsy if neuroblastoma is suspected because the amount of the sample collected might not be enough for all of the tumor tests that are needed.

### ***MIBG scan***

This test is often an important part of finding out how far a child's neuroblastoma has spread. It is often done after a CT scan or MRI has already been done. This scan uses a form of the chemical meta-iodobenzylguanidine (MIBG) that contains a small amount of radioactive iodine. MIBG is similar to norepinephrine, a hormone made by sympathetic nerve cells. It is injected into a vein and travels through the blood, and in most patients it will attach to neuroblastoma cells anywhere in the body. Between 1 and 3 days later, the body is scanned with a special camera to look for areas that picked up the radioactivity. This helps doctors know where the neuroblastoma is and if it has spread to the bones and/or other parts of the body.

MIBG scans can be repeated after treatment to see if the tumors are responding well. It is also good to know if the tumor takes up the MIBG because in some cases, this radioactive molecule can be used at higher doses to treat the neuroblastoma (see [Radiation Therapy for Neuroblastoma](#)<sup>8</sup>). The thyroid gland can also absorb MIBG, so a medicine containing iodine is sometimes given before and during the test to protect the thyroid.

### ***Bone scan***

A [bone scan](#)<sup>9</sup> can help show if a cancer has spread to the bones, and can provide a picture of the entire skeleton at once. Neuroblastoma often causes bone damage, which a bone scan can find. This test used to be done routinely, but in many centers it has been replaced by use of MIBG or PET scans. This test might be done after an MIBG scan, depending on those results.

For this test, a small amount of low-level radioactive material (technetium-99) is injected into a vein. (The amount of radioactivity used is very low and will pass out of the body within a day or so.) The substance settles in areas of damaged bone throughout the skeleton over the course of a couple of hours. Your child then lies on a table for about 30 minutes while a special camera detects the radioactivity and creates a picture of the skeleton. Younger children may be given medicine to help keep them calm or even asleep during the test.

Areas of active bone changes attract the radioactivity and appear as “hot spots” on the skeleton. These areas may suggest cancer, but other bone diseases can also cause the same pattern. To help tell these apart, other imaging tests such as plain x-rays or MRI scans, or even a bone biopsy might be needed.

### ***Positron emission tomography (PET) scan***

For a [PET scan](#)<sup>10</sup>, a radioactive substance (usually a type of sugar related to glucose, known as FDG) is injected into the blood. The amount of radioactivity used is very low and will pass out of the body within a day or so. Because cancer cells in the body are growing quickly, they absorb large amounts of the radioactive sugar. After about an hour, your child will be moved onto a table in the PET scanner. He or she will lie on the table for about 30 minutes while a special camera creates a picture of areas of radioactivity in the body. Younger children may be given medicine to help keep them calm or even asleep during the test. The picture from a PET scan is not as detailed as a CT or MRI scan, but it can provide helpful information about the whole body.

Some newer machines can do a PET and CT scan at the same time (PET/CT scan). This lets the doctor compare areas of higher radioactivity on the PET scan with the more detailed appearance of that area on the CT scan.

### ***X-rays***

The doctor may order an x-ray of the chest or another part of the body as an early test if a child is having symptoms but it's not clear what might be causing them. But the pictures might not be good enough to spot tumors.

An MIBG scan or a bone scan is usually better for looking at the bones in the rest of the body and to see if neuroblastoma has spread to the bones.

A standard chest x-ray may be done if a child is having trouble breathing, but a CT or MRI scan of the chest can show more about the tumor size and location.

### **Biopsies**

Exams and imaging tests might strongly suggest a child has neuroblastoma, but a biopsy (removing some of the tumor for viewing under a microscope and other lab testing) is usually needed to be sure. During a biopsy, the doctor removes a piece of the tumor. The biopsy samples are sent to a lab, where they are viewed under a microscope by a pathologist (a doctor with special training in identifying cancer cells). Some neuroblastomas are easily recognized when looked at by experienced doctors. But some may be hard to tell apart from other types of children's cancers. In these cases, special lab tests must be done to show the tumor is a neuroblastoma.

In adults, biopsies are sometimes done using local anesthetic (numbing medicine), but in children they are more often done while the child is under general anesthesia (asleep). There are 2 main types of biopsies:

- [Incisional \(open or surgical\) biopsy](#)<sup>11</sup>: This type of biopsy is done by removing a piece of the tumor through an incision (cut) in the skin. For tumors deep in the body this may be done laparoscopically using long, thin surgical tools inserted through small cuts in the skin.
- **Needle (closed) biopsy**: For this type of biopsy, a thin, hollow needle is placed through the skin and into the tumor to remove a small sample. If the tumor is deep within the body, CT scans or ultrasound can be used to help guide the needle into the tumor. Needle biopsies are not usually helpful when a child might have neuroblastoma because the amount of tumor in the sample is often not large enough to have all the special tests that are needed.

Other lab tests on neuroblastoma samples can help determine how quickly the tumor might grow or spread in the body. What doctors learn about a child's neuroblastoma from these tests can help determine what treatments might work the best. Some of these tests are described in [Neuroblastoma Stages and Prognostic Markers](#).

### **Bone marrow aspiration and biopsy**

Neuroblastoma often spreads to the bone marrow (the soft inner parts of certain bones). If blood or urine levels of catecholamines are increased, then finding cancer cells in a bone marrow sample is enough to diagnose neuroblastoma (without getting a biopsy of the main tumor). If neuroblastoma has already been diagnosed by a biopsy done elsewhere in the body, bone marrow tests are done to help determine the extent of the disease.

A bone marrow aspiration and biopsy are usually done at the same time. In most cases the samples are taken from the back of both of the pelvic (hip) bones.

Even when the area is numbed with local anesthetic, these tests can be painful, so in most cases the child is also given other medicines to reduce pain or even be asleep during the procedure.

For a bone marrow **aspiration**, a thin, hollow needle is inserted into the bone and a syringe is used to suck out a small amount of liquid bone marrow.

A bone marrow **biopsy** is also done. A small piece of bone and marrow is removed with a slightly larger needle that is pushed down into the bone. Once the biopsy is done, pressure is applied to the site to help stop any bleeding.

Samples from the bone marrow are sent to a lab, where they are looked at and tested

for the presence of cancer cells. You can read more about testing tissue samples in [Testing Biopsy and Cytology Specimens for Cancer](#)<sup>12</sup>.

## Hyperlinks

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## Neuroblastoma Stages and Prognostic Markers

After someone is diagnosed with neuroblastoma, doctors will try to figure out if it has spread, and if so, how far. This process is called staging. The **stage** of a child's neuroblastoma describes how much cancer is in the body. Stage is used to help determine how serious the cancer is and how best to treat it.

For neuroblastoma, several other factors are looked at along with a child's stage to decide what **risk group** a child falls into. A risk group is an overall picture of how a child's neuroblastoma will respond to treatment and helps doctors select the treatments that might work the best. Doctors also use neuroblastoma risk groups when talking about survival statistics. For more information, see [Neuroblastoma Risk Groups](#)

There are two systems used for neuroblastoma staging today. The main difference between the two systems is whether the staging system can be used to help determine a child's risk group *before* treatment has started.

- The **International Neuroblastoma Risk Group Staging System (INRGSS)** uses results from imaging tests (such as CT or MRI and MIBG scan) to help decide a stage. The INRGSS can be determined before treatment has started.
- The **International Neuroblastoma Staging System (INSS)** uses results from the surgery to remove a child's tumor instead of imaging tests.

Since many children with neuroblastoma will have surgery as part of their treatment plan, the INSS does not work as well for assigning a risk group before some treatment has started. INRGSS is now being used to determine staging for most Children's Oncology Group studies, but some studies have results that will be published over the next few years that used INSS.

These staging systems can both be used to help make sure children with neuroblastoma get the treatments that are best for them. If your child has neuroblastoma and has not had surgery, you are most likely to hear about your child's



stage based on INRGSS. If your child has had a surgery, you may hear doctors talk about your child's stage using either system.

For more information about the physical exams, imaging tests, and biopsies used to help determine neuroblastoma stages, see [Tests for Neuroblastoma](#).

The stages and risk groups for neuroblastoma are complex and can be confusing. If you are unsure about what these mean for your child, ask your child's doctor to explain them to you in a way you can understand.

## International Neuroblastoma Risk Group Staging System (INRGSS)

The INRGSS was developed to help determine a child's stage and risk group before treatment has started. It has also helped researchers around the world compare results of studies to help figure out which treatments are the best. Before it was developed, researchers in different countries couldn't easily compare study results because of different staging systems. INRGSS uses [imaging tests](#) (usually a CT or MRI scan, and an MIBG scan), as well as exams and biopsies to help define the stage. The stage can then be used to help predict how resectable the tumor is – that is, how much of it can be removed with surgery.

The INRGSS uses image-defined risk factors (IDRFs), which are factors seen on imaging tests that might mean the tumor will be harder to remove. This includes things like the tumor growing into a nearby vital organ or growing around important blood vessels.

The INRGSS has 4 stages:

**L1:** A tumor that has not spread from where it started and has not grown into vital structures as defined by the list of IDRFs. It is confined to one area of the body, such as the neck, chest, or abdomen.

**L2:** A tumor that has not spread far from where it started (for example, it may have grown from the left side of the abdomen into the left side of the chest), but that has at least one IDRF.

**M:** A tumor that has spread (metastasized) to a distant part of the body (except tumors that are stage MS).

**MS:** Metastatic disease in children younger than 18 months with cancer spread only to skin, liver, and/or bone marrow. No more than 10% of marrow cells are cancerous, and

an MIBG scan does not show spread to the bones and/or the bone marrow.

## International Neuroblastoma Staging System (INSS)

Since the mid-1990s, most cancer centers have used the INSS to stage neuroblastoma. This system takes into account the results of surgery to remove the tumor. It cannot help doctors determine a stage before any treatment has started, so it doesn't work as well for children who don't need or cannot have surgery. In simplified form, the stages are:

**Stage 1:** The cancer is still in the area where it started. It is on one side of the body (right or left). All visible tumor has been removed completely by surgery (although looking at the tumor's edges under the microscope after surgery may show some cancer cells). Lymph nodes outside the tumor are free of cancer (although nodes enclosed within the tumor may contain neuroblastoma cells).

**Stage 2A:** The cancer is still in the area where it started and on one side of the body, but not all of the visible tumor could be removed by surgery. Lymph nodes outside the tumor are free of cancer (although nodes enclosed within the tumor may contain neuroblastoma cells).

**Stage 2B:** The cancer is on one side of the body, and may or may not have been removed completely by surgery. Nearby lymph nodes outside the tumor contain neuroblastoma cells, but the cancer has not spread to lymph nodes on the other side of the body or elsewhere.

**Stage 3:** The cancer has not spread to distant parts of the body, but one of the following is true:

- The cancer cannot be removed completely by surgery and it has crossed the midline (defined as the spine) to the other side of the body. It may or may not have spread to nearby lymph nodes.
- The cancer is still in the area where it started and is on one side of the body. It has spread to lymph nodes that are relatively nearby but on the other side of the body.
- The cancer is in the middle of the body and is growing toward both sides (either directly or by spreading to nearby lymph nodes) and cannot be removed completely by surgery.

**Stage 4:** The cancer has spread to distant sites such as distant lymph nodes, bone, liver, skin, bone marrow, or other organs (but the child does not meet the criteria for

stage 4S).

**Stage 4S (also called “special” neuroblastoma):** The child is younger than 1 year old. The cancer is on one side of the body. It might have spread to lymph nodes on the same side of the body but not to nodes on the other side. The neuroblastoma has spread to the liver, skin, and/or the bone marrow. However, no more than 10% of marrow cells are cancerous, and imaging tests such as an [MIBG scan](#) do not show cancer in the bones or the bone marrow.

**Recurrent:** While not formally part of the staging system, this term is used to describe cancer that has come back (recurred) after it has been treated. The cancer might come back in the area where it first started or in another part of the body.

## Prognostic markers

Prognostic markers are features that help predict whether the child’s outlook for cure is better or worse than would be predicted by the stage alone. Many of these prognostic markers are used along with a child’s stage to assign their risk group. The following markers are used to help determine a child’s prognosis:

- **Age:** Younger children (under 12-18 months) are more likely to be cured than older children.
- **Tumor histology:** Tumor histology is based on how the neuroblastoma cells look under the microscope. Tumors that contain more normal-looking cells and tissues tend to have a better prognosis and are said to have a **favorable histology**. Tumors whose cells and tissues look more abnormal under a microscope tend to have a poorer prognosis and are said to have an **unfavorable histology**.
- **DNA ploidy:** The amount of DNA in each cell, known as ploidy or the **DNA index**, can be measured using special lab tests, such as flow cytometry or imaging cytometry. Neuroblastoma cells with about the same amount of DNA as normal cells (a DNA index of 1) are classified as **diploid**. Cells with increased amounts of DNA (a DNA index higher than 1) are termed **hyperdiploid**. Neuroblastoma cells with more DNA are associated with a better prognosis, particularly for children under 2 years of age. DNA ploidy is not as useful for understanding a prognosis in older children.
- **MYCN gene amplifications:** *MYCN* is an oncogene, a gene that helps regulate cell growth. Changes in oncogenes can make cells grow and divide too quickly, as with cancer cells. Neuroblastomas with too many copies (amplification) of the *MYCN* oncogene tend to grow quickly and can be harder to treat.

- **Chromosome changes:** Tumor cells that are missing certain parts of chromosomes 1 or 11 (known as *1p deletions* or *11q deletions*) may predict a less favorable prognosis. Having an extra part of chromosome 17 (*17q gain*) is also linked with a worse prognosis. Understanding the importance of chromosome deletions/gains is an active area of neuroblastoma research, for more information see [What's New In Neuroblastoma Research?](#)<sup>1</sup>
- **Neurotrophin (nerve growth factor) receptors:** These are substances on the surface of normal nerve cells and on some neuroblastoma cells. They normally allow the cells to recognize neurotrophins – hormone-like chemicals that help the nerve cells mature. Neuroblastomas that have more of certain neurotrophin receptors, especially the nerve growth factor receptor called *TrkA*, may have a better prognosis.

Serum (blood) levels of certain substances can be used to help predict prognosis.

- Neuroblastoma cells release **ferritin**, a chemical that is an important part of the body's normal iron metabolism, into the blood. Patients with high ferritin levels tend to have a worse prognosis.
- **Neuron-specific enolase (NSE)** and **lactate dehydrogenase (LDH)** are made by some types of normal cells as well as by neuroblastoma cells. Increased levels of NSE and LDH in the blood are often linked with a worse outlook in children with neuroblastoma.
- A substance on the surface of many nerve cells known as **ganglioside GD2** is often increased in the blood of neuroblastoma patients. Although the usefulness of GD2 in predicting prognosis is unknown, it may turn out to be more important in treating neuroblastoma. (See [What's New in Neuroblastoma Research?](#)<sup>2</sup>)

## Hyperlinks

1. [www.cancer.org/cancer/neuroblastoma/about/new-research.html](http://www.cancer.org/cancer/neuroblastoma/about/new-research.html)
2. [www.cancer.org/cancer/neuroblastoma/about/new-research.html](http://www.cancer.org/cancer/neuroblastoma/about/new-research.html)

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# Neuroblastoma Risk Groups

Risk groups are used to help predict how likely it is that a child can be cured. For example, a child in a low-risk group can often be cured with limited treatment, such as surgery alone. Children in higher risk groups often need more intensive treatment to have the best chance of being cured. The risk groups included here are commonly accepted standard risk groups in the US. Other internationally used risk groups are being tested in clinical trials.

## Children's Oncology Group (COG) risk groups

The Children's Oncology Group (COG) uses the major prognostic factors discussed in the [staging section](#), combined with the INRGSS stage of the disease, to place children into 3 different risk groups: low, intermediate, and high. COG risk groups in the past used certain prognostics factors along with the INSS stage of the disease, and have transitioned to INRGSS more recently. Some study results that used INSS to determine a child's risk group have not been published yet, and these results will probably come out over the next few years. For that reason, you might hear about both staging systems.

These risk groups are based on what is now known about neuroblastoma and how it is treated. As new research provides more information, these risk groups may change over time. For example, in recent treatment recommendations the age cut-off for some of these categories has been revised from up to 12 months (365 days) to up to 18 months (547 days).

### Low risk

- All children who are Stage 1
- Any child who is Stage 2A or 2B and not yet 1 year old
- Any child who is Stage 2A or 2B, older than 1 year, whose cancer has **no** extra copies of the *MYCN* gene
- Any child who is Stage 2A or 2B, older than 1 year, whose cancer has extra copies of the *MYCN* gene **AND** has favorable histology (appearance under the microscope)
- Any child who is Stage 4S (not yet 1 year old), whose cancer has favorable histology, is hyperdiploid (excess DNA) and has **no** extra copies of the *MYCN* gene

### Intermediate risk

- Any child who is Stage 3, not yet 1 year old, whose cancer has **no** extra copies of the *MYCN* gene
- Any child who is Stage 3, older than 1 year old, whose cancer has **no** extra copies of the *MYCN* gene **and** has favorable histology (appearance under the microscope)
- Any child who is Stage 4, not yet 1 year old, whose cancer has **no** extra copies of the *MYCN* gene
- Any child who is Stage 4S (not yet 1 year old), whose cancer has **no** extra copies of the *MYCN* gene **and** has normal DNA ploidy (number of chromosomes) and/or has unfavorable histology

### High risk

- Any child who is Stage 2A or 2B, older than 1 year, whose cancer has extra copies of the *MYCN* gene and unfavorable histology
- Any child who is Stage 3, not yet 1 year old, whose cancer has extra copies of the *MYCN* gene
- Any child who is Stage 3, older than 1 year, whose cancer has extra copies of the *MYCN* gene
- Any child who is Stage 3, older than 18 months, whose cancer has unfavorable histology
- Any child who is Stage 4, whose cancer has extra copies of the *MYCN* gene regardless of age
- Any child who is Stage 4 and older than 18 months
- Any child who is Stage 4 and between 12 and 18 months old whose cancer has extra copies of the *MYCN* gene, unfavorable histology, and/or normal DNA ploidy (a DNA index of 1)
- Any child who is Stage 4S (not yet 1 year old), whose cancer has extra copies of the *MYCN* gene

### International Neuroblastoma Risk Group (INRG) classification

A newer risk group classification system, the International Neuroblastoma Risk Group (INRG) classification, is now being used to help researchers in different countries compare results and work together to find the best treatments. This system is based on the newer INRGSS staging system, which includes the image-defined risk factors (IDRFs), as well as many of the prognostic factors listed in the [staging section](#), such as:

- The child's age
- Tumor histology (how the tumor looks under the microscope)
- The presence or absence of *MYCN* gene amplification
- Certain changes in chromosome 11 (known as an 11q aberration)
- DNA ploidy (the total number of chromosomes in the tumor cells)

The INRG classification uses these factors to put children into 16 different pre-treatment groups (lettered A through R). Each pre-treatment group falls into 1 of 4 overall risk groups:

- Very low risk
- Low risk
- Intermediate risk
- High risk

This system will most likely be used in addition to the COG Risk Classification system in the United States.

## Hyperlinks

## References

Brodeur GM, Hogarty MD, Bagatell R, Mosse YP, Maris JM. Neuroblastoma. In: Pizzo PA, Poplack DG, eds. *Principles and Practice of Pediatric Oncology*. 7th ed. Philadelphia Pa: Lippincott Williams & Wilkins; 2016:772–792.

Cohn SL, Pearson AD, London WB, et al. The International Neuroblastoma Risk Group (INRG) Classification System: An INRG task force report. *J Clin Oncol*. 2009; 27: 289–297.

National Cancer Institute. Physician Data Query (PDQ). Neuroblastoma Treatment. 2017. Accessed at [www.cancer.gov/cancertopics/pdq/treatment/neuroblastoma/healthprofessional](http://www.cancer.gov/cancertopics/pdq/treatment/neuroblastoma/healthprofessional) on October 12, 2017.

<sup>1</sup>Pinto NR, Applebaum MA, Volchenboum SL, et al. Advances in risk classification and treatment strategies for neuroblastoma. *J Clin Oncol*. 2015; 30:3008-3017.

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## Neuroblastoma Survival Rates by Risk Group

Survival rates are a way to get an idea of the outlook for children with a certain type of cancer. Some parents might want to know the statistics for children in similar situations, but others might not find the numbers helpful, or may even not want to know them.

The 5-year survival rate refers to the percentage of children who live **at least** 5 years after their cancer is diagnosed. Of course, many children live much longer than 5 years (and many are cured).

In order to get 5-year survival rates, doctors have to look at children who were treated at least 5 years ago. Improvements in treatment since then may result in a better outlook for children now being diagnosed with neuroblastoma.

Survival rates are based on previous outcomes of large numbers of people who had the disease, but they cannot predict what will happen in any particular child's case. The risk group of a child's cancer is important in estimating their outlook. But many other factors can also affect a child's outlook, such as their age, the location of the tumor, and how well the cancer responds to treatment. Your child's doctor can tell you how the numbers below might apply to your child, as he or she knows your situation best.

### Survival by Children's Oncology Group (COG) risk group

**Low-risk group:** Children in the low-risk group have a 5-year survival rate that is higher than 95%.

**Intermediate-risk group:** Children in the intermediate-risk group have a 5-year survival rate of around 90% to 95%.

**High-risk group:** Children in the high-risk group have a 5-year survival rate around 40% to 50%.



## References

Maris JM. Recent advances in neuroblastoma. *N Engl J Med.* 2010;362:2202–2211.

Pinto NR, Applebaum MA, Volchenbom SL, et al. Advances in risk classification and treatment strategies for neuroblastoma. *J Clin Oncol.* 2015: 30;3008-3017.

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# Questions To Ask About Neuroblastoma

It is important to have open, honest discussions with your child's cancer care team. You should ask any question, no matter how minor it might seem. Among the questions you might want to ask are:

- What is the [stage](#) (extent) of the neuroblastoma?
- Which [1risk group](#) does my child's cancer fall into? What does this mean?
- What else can you tell about the cancer based on the lab tests?
- Do we need to have any other tests done before we discuss treatment?
- How much experience do you have treating this type of cancer?
- What other doctors will we need to see?
- What are our [treatment<sup>2</sup>](#) options?
- Does one type of treatment increase the chance of cure more than another?
- Are there any clinical trials we should consider?
- Which treatment do you recommend? Why?
- What should we do to be ready for treatment?
- How long will treatment last? What will it be like? Where will it be done?
- How will treatment affect our daily activities?
- How long will it take my child to recover from treatment?
- What are the possible [side effects<sup>3</sup>](#) from treatment? What can be done for them?
- Which side effects start shortly after treatment and which ones might develop later on?
- How might treatment affect my child's ability to learn, grow, and develop?
- Will treatment affect my child's ability to have children someday? Can we do anything about this?

- Will my child have a higher long-term risk of other cancers?
- What are the chances that the cancer will [come back](#)<sup>4</sup> after treatment? What would we do if this happens?
- What type of follow-up will my child need after treatment?
- Is there a support group for families who are coping with neuroblastoma or childhood cancer?

Along with these sample questions, be sure to write down some of your own. For instance, you might want to ask about getting a [second opinion](#)<sup>5</sup>. Keep in mind, too, that doctors are not the only ones who can give you information. Other members of your health care team, such as nurses and social workers, might have the answers you seek.

## Hyperlinks

1. [www.cancer.org/cancer/neuroblastoma/treating.html](http://www.cancer.org/cancer/neuroblastoma/treating.html)
2. [www.cancer.org/treatment/treatments-and-side-effects/physical-side-effects.html](http://www.cancer.org/treatment/treatments-and-side-effects/physical-side-effects.html)
3. [www.cancer.org/treatment/survivorship-during-and-after-treatment/understanding-recurrence.html](http://www.cancer.org/treatment/survivorship-during-and-after-treatment/understanding-recurrence.html)
4. [www.cancer.org/treatment/finding-and-paying-for-treatment/choosing-your-treatment-team/seeking-a-second-opinion.html](http://www.cancer.org/treatment/finding-and-paying-for-treatment/choosing-your-treatment-team/seeking-a-second-opinion.html)

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## Treating Neuroblastoma

If your child has been diagnosed with neuroblastoma, your child's treatment team will discuss the options with you. It's important to weigh the benefits of each treatment option against the possible risks and side effects.

### How is neuroblastoma treated?

The types of treatment used for neuroblastoma can include:

- [Neuroblastoma Surgery](#)
- [Chemotherapy for Neuroblastoma](#)
- [Radiation Therapy for Neuroblastoma](#)
- [High-Dose Chemotherapy/Radiation Therapy and Stem Cell Transplant for Neuroblastoma](#)
- [Retinoid Therapy for Neuroblastoma](#)
- [Immunotherapy for Neuroblastoma](#)

### Common treatment approaches

Treatment of neuroblastoma depends on the [risk group](#)<sup>1</sup> of the cancer, the child's age, and other factors, and might include more than one type of treatment.

- [Treatment of Neuroblastoma by Risk Group](#)

### Who treats neuroblastoma?

Children with neuroblastoma and their families have special needs. These needs can be met best by cancer centers for children, working closely with the child's primary care doctor. These centers have teams of specialists who understand the differences

between cancers in adults and those in children, as well as the unique needs of younger people with cancer. Treating neuroblastoma is complex and often requires the expertise of many different doctors, nurses, and other health professionals.

- [How to Find the Best Cancer Treatment for Your Child<sup>2</sup>](#)
- [Navigating the Health Care System When Your Child Has Cancer<sup>3</sup>](#)

## **Making treatment decisions**

Your child's cancer care team will discuss the treatment options with you. It's important to discuss these options and their possible side effects with your child's doctors so you can make an informed decision. It's also important to ask questions if there's anything you don't understand or are not sure about.

If time allows, getting a second opinion from another doctor experienced with your child's type of tumor is often a good idea. This can give you more information and help you feel more confident about the treatment plan you choose. If you aren't sure where to go for a second opinion, ask your doctor for help.

- [Questions To Ask About Neuroblastoma<sup>4</sup>](#)
- [How to Talk to Your Child's Cancer Care Team<sup>5</sup>](#)
- [Seeking a Second Opinion<sup>6</sup>](#)

## **Thinking about taking part in a clinical trial**

Today, most children and teens with cancer are treated at specialized children's cancer centers. These centers offer the most up-to-date-treatment by conducting clinical trials (studies of promising new therapies). Children's cancer centers often conduct many clinical trials at any one time, and in fact most children treated at these centers take part in a clinical trial as part of their treatment.

Clinical trials are one way to get state-of-the art cancer treatment. Sometimes they may be the only way to get access to newer treatments (although there is no guarantee that newer treatments will be better). They are also the best way for doctors to learn better methods to treat these cancers. Still, they might not be right for everyone.

If you would like to learn more about clinical trials that might be right for your child, start by asking the treatment team if your clinic or hospital conducts clinical trials.

- [Clinical Trials<sup>7</sup>](#)

## Considering complementary and alternative methods

You may hear about alternative or complementary methods that your doctor hasn't mentioned to treat your child's tumor or relieve symptoms. These methods can include vitamins, herbs, and special diets, or other methods such as acupuncture or massage, to name a few.

Complementary methods refer to treatments that are used *along with* your regular medical care. Alternative treatments are used *instead of* standard medical treatment. Although some of these methods might be helpful in relieving symptoms or helping people feel better, many have not been proven to work. Some might even be harmful.

Be sure to talk to your child's cancer care team about any method you are thinking about using. They can help you learn what is known (or not known) about the method, which can help you make an informed decision.

- [Complementary and Alternative Medicine](#)<sup>8</sup>

## Preparing for treatment

Before treatment, the doctors and other members of the team will help you, as a parent, understand the tests that will need to be done. The team's social worker will also counsel you about the problems you and your child might have during and after treatments such as surgery, and might be able to help you find housing and financial aid if needed.

- [When Your Child Has Cancer](#)<sup>9</sup>

## Help getting through cancer treatment

Your child's cancer care team will be your first source of information and support, but there are other resources for help when you need it. Hospital- or clinic-based support services can also be an important part of your care. These might include nursing or social work services, financial aid, nutritional advice, rehab, or spiritual help. For children and teens with cancer and their families, other specialists can be an important part of care as well.

The American Cancer Society also has programs and services – including rides to treatment, lodging, and more – to help you get through treatment. Call our National Cancer Information Center at 1-800-227-2345 and speak with one of our trained

specialists.

- [Finding Help and Support When Your Child Has Cancer](#)<sup>10</sup>
- [Find Support Programs and Services in Your Area](#)<sup>11</sup>

*The treatment information given here is not official policy of the American Cancer Society and is not intended as medical advice to replace the expertise and judgment of your cancer care team. It is intended to help you and your family make informed decisions, together with your doctor. Your doctor may have reasons for suggesting a treatment plan different from these general treatment options. Don't hesitate to ask him or her questions about your treatment options.*

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## Neuroblastoma Surgery

Surgery can be used both to help [diagnose](#)<sup>1</sup> neuroblastoma and to treat it. For smaller tumors that have not spread, surgery is often the only treatment that is needed.

### Surgical (open) biopsy

In many cases, doctors need to get a sample of the tumor to be sure it is a neuroblastoma before deciding which treatment might work best. Tumor samples are removed during a surgical biopsy to be looked at under a microscope and for other lab tests.

If the tumor is in the abdomen (belly), the surgeon might do the biopsy with a laparoscope. This is a long, thin tube with a tiny video camera on the end. It is put into the abdomen through a small incision to allow the surgeon to see inside. The surgeon then makes a second small incision to reach inside the abdomen with long, thin instruments and remove pieces of tumor.

### Surgery as treatment

After neuroblastoma is diagnosed, surgery is often used to try to remove as much of the tumor as possible. In some cases, surgery can remove the entire tumor and no additional treatments are needed.

During the operation, the surgeon looks carefully for signs of cancer spread to other organs. Nearby lymph nodes (small collections of immune system cells to which cancers often spread first) are removed and looked at under a microscope for cancer cells.

If possible, the surgeon will remove the entire tumor. This is less likely if the tumor is near vital structures or wrapped around large blood vessels. Even if some of the tumor is left behind, that doesn't always mean the tumor will come back. Whether chemotherapy and other treatments will be needed after surgery depends on the child's risk group.

If the tumor is very large, chemotherapy may be used before surgery to shrink the tumor and make it easier to remove.

### **Possible risks and side effects of surgery**

The risks from surgery depend on the location and extent of the operation and the child's health beforehand. Serious complications, although rare, can include problems with anesthesia, excess bleeding, infections, and damage to blood vessels, kidneys, other organs, or nerves. Complications are more likely if the tumor is large and growing into blood vessels or nerves. Most children will have some pain for a while after the operation, but this can usually be helped with medicines if needed.

### **Hyperlinks**

1. [www.cancer.org/cancer/neuroblastoma/detection-diagnosis-staging/how-diagnosed.html](http://www.cancer.org/cancer/neuroblastoma/detection-diagnosis-staging/how-diagnosed.html)

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Pinto NR, Applebaum MA, Volchenboum SL, et al. Advances in risk classification and

treatment strategies for neuroblastoma. *J Clin Oncol*. 2015; 30;3008-3017.

Speleman F, Park JR, Henderson TO. Neuroblastoma: a tough nut to crack. *Am Soc Clin Oncol Educ Book*. 2016; 35:e548-557. Accessed at <https://meetinglibrary.asco.org/record/50740/edbook#fulltext> on October 15, 2017.

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## Chemotherapy for Neuroblastoma

Chemotherapy (chemo) uses anti-cancer drugs, which are usually given into a vein. The drugs enter the bloodstream and travel throughout the body to reach and destroy cancer cells. This makes chemo useful for treating neuroblastoma that has spread to the lymph nodes, bone marrow, liver, lungs, or other organs.

Whether a child with neuroblastoma will get chemotherapy depends on their risk group. Some children with neuroblastoma are treated with chemo either before surgery (neoadjuvant chemotherapy) or after surgery (adjuvant chemotherapy). In other cases, especially when the cancer has spread too far to be removed completely by surgery, chemotherapy is the main treatment.

Chemo for neuroblastoma usually includes a combination of drugs. The main chemo drugs used include:

- Cyclophosphamide
- Cisplatin or carboplatin
- Vincristine
- Doxorubicin (Adriamycin)
- Etoposide
- Topotecan
- Busulfan and melphalan (sometimes used during stem cell transplant)
- Thiotepa (sometimes used during stem cell transplant)

The most common combination of drugs includes carboplatin (or cisplatin), cyclophosphamide, doxorubicin, and etoposide, but others may be used. For children in the high-risk group, more combinations are used, and some drugs are given at higher



doses, which may be followed by a [stem cell transplant](#) (described further on).

Doctors give chemo in cycles, which consist of treatment on a few days in a row, followed by time off to allow the body time to recover. The cycles are typically repeated every 3 or 4 weeks. The total length of treatment depends on which risk group the child is in – higher risk groups usually require longer treatment.

## Possible side effects of chemotherapy

Chemo drugs attack cells that are dividing quickly, which is why they work against cancer cells. But other cells in the body, such as those in the bone marrow (where new blood cells are made), the lining of the mouth and intestines, and the hair follicles, also divide quickly. These cells are also likely to be affected by chemo, which can lead to side effects.

The side effects of chemo depend on the type and dose of drugs given and the length of time they are taken. General side effects can include:

- Hair loss
- Mouth sores
- Loss of appetite
- Nausea and vomiting
- Diarrhea or constipation
- Increased chance of infections (from having too few white blood cells)
- Easy bruising or bleeding (from having too few blood platelets)
- Fatigue (from having too few red blood cells)

Most of these side effects tend to go away after treatment is finished. There are often ways to lessen these side effects. For example, drugs can be given to help prevent or reduce nausea and vomiting. Be sure to ask your child's doctor or nurse about medicines to help reduce side effects, and let him or her know if your child has side effects so they can be managed.

Along with the effects listed above, some drugs can have specific side effects. For example:

**Cyclophosphamide** can damage the bladder, which can cause blood in the urine. The risk of this can be lowered by giving the drugs with plenty of fluids and with a drug called mesna, which helps protect the bladder. These drugs can also damage the ovaries or testicles, which could affect fertility (the ability to have children).

**Doxorubicin** can cause heart damage. Doctors try to reduce this risk as much as possible by limiting the doses of doxorubicin and by checking the heart with an echocardiogram (an ultrasound of the heart) during treatment. This drug can also cause skin damage if it should leak out of the vein while it is being given.

**Cisplatin and carboplatin** can affect the kidneys. Giving plenty of fluids can help reduce this risk. These drugs can also affect hearing. Your child's doctor may order hearing tests (audiograms) during or after treatment.

**Vincristine** can damage nerves. Some patients may have tingling, numbness, weakness, or pain, particularly in the hands and feet.

Chemotherapy can also have some longer-term side effects. For example, some drugs can increase the risk of later developing another type of cancer (such as [leukemia](#)<sup>1</sup>). While this is a serious risk, it is not common, and the small increase in risk has to be weighed against the importance of chemotherapy in treating neuroblastoma. For more on the possible long-term effects of treatment, see [Late and Long-term Effects of Neuroblastoma and Its Treatment](#)<sup>2</sup>.

For more information on chemotherapy in general, see [Chemotherapy](#)<sup>3</sup>.

## Hyperlinks

1. [www.cancer.org/cancer/leukemia.html](http://www.cancer.org/cancer/leukemia.html)
2. [www.cancer.org/cancer/neuroblastoma/after-treatment/long-term-effects.html](http://www.cancer.org/cancer/neuroblastoma/after-treatment/long-term-effects.html)
3. [www.cancer.org/treatment/treatments-and-side-effects/treatment-types/chemotherapy.html](http://www.cancer.org/treatment/treatments-and-side-effects/treatment-types/chemotherapy.html)

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## Radiation Therapy for Neuroblastoma

Radiation therapy uses high-energy rays or particles to kill cancer cells. It is sometimes a necessary part of treatment, but because of the possible long-term side effects in children, doctors avoid using it when possible. Most children with neuroblastoma will not need radiation therapy. It is most common for radiation to be used in children with high-risk neuroblastoma after stem cell transplant. It might be used for children with low- and intermediate-risk neuroblastoma only if a child has life-threatening symptoms and needs emergency treatment to shrink the tumor.

Two types of radiation therapy can be used to treat children with neuroblastoma:

- External beam radiation therapy
- Radioisotope based radiation

### External beam radiation therapy

External radiation therapy focuses the radiation on the cancer from a source outside the body. This type of treatment might be used:

- To try to shrink tumors before surgery, making them easier to remove
- To treat larger tumors that are causing serious problems (such as trouble breathing) and do not respond quickly to chemotherapy
- As part of the treatment regimen after [stem cell transplant](#) in children with high-risk neuroblastoma to destroy neuroblastoma cells that remain behind. Radiation might involve the primary tumor area and other areas of the body that might have active disease seen on an [MIBG scan](#)<sup>1</sup>.

- To help relieve pain caused by advanced neuroblastoma

When radiation is aimed at the whole body, it is known as *total body irradiation* (TBI). Total body irradiation has been used in the past for children with high risk neuroblastoma before a stem cell transplant, but it is more common now for radiation only to be given after a stem cell transplant to the primary tumor site and any other areas of the body that might have active neuroblastoma cells.

Before treatments start, the radiation team takes careful measurements with [imaging tests](#)<sup>2</sup> such as MRI scans to determine the correct angles for aiming the radiation beams and the proper dose of radiation.

Radiation therapy is much like getting an x-ray, but the dose of radiation is much higher. Your child might be fitted with a plastic mold resembling a body cast to keep him or her in the same position during each treatment so that the radiation can be aimed more accurately.

The number of radiation treatments given depends on the situation. For each treatment session, your child lies on a special table while a machine delivers the radiation from a precise angle. The treatment is not painful. Each actual treatment lasts only a few minutes, but the setup time – getting your child into place for treatment – usually takes longer. Young children may be given medicine to make them sleep so they will not move during the treatment.

**Possible side effects:** Radiation therapy is sometimes an important part of treatment, but young children’s bodies are very sensitive to it, so doctors try to use as little radiation as possible to help avoid or limit any problems. Radiation can cause both short-term and long-term side effects, which depend on the dose of radiation and where it is aimed.

### **Possible short-term effects**

- Effects on skin areas that receive radiation can range from mild sunburn-like changes and hair loss to more severe skin reactions.
- Radiation to the abdomen (belly) can cause nausea or diarrhea.
- Radiation therapy can make a child tired, especially toward the end of treatment.

Radiation can also make the side effects of chemotherapy worse. Talk with your child’s doctor about the possible side effects because there are ways to relieve some of them.

## Possible long-term effects

- Radiation therapy can slow the growth of normal body tissues (such as bones) that get radiation, especially in younger children. In the past this led to problems such as short bones or a curving of the spine, but this is less likely with the lower doses of radiation used today.
- Radiation can affect the thyroid gland in the neck, causing it to make less thyroid hormone (hypothyroidism). Symptoms of hypothyroidism can vary greatly. In children, hypothyroidism can affect growth and development. Thyroid replacement medicine is usually all that's needed to manage hypothyroidism.
- Radiation that reaches the chest area can affect the heart and lungs. This does not usually cause problems right away, but in some children it may eventually lead to heart or lung problems as they get older.
- Radiation to the abdomen in girls can damage the ovaries. This might lead to abnormal menstrual cycles or problems getting pregnant or having children later on.
- Radiation can damage the DNA inside cells. As a result, radiation therapy slightly increases the risk of developing a second cancer in the areas that get radiation, usually many years after the radiation is given.

Close follow-up with doctors is important as children grow older so that any problems can be found and treated as soon as possible. For more on the possible long-term effects of treatment, see the section [Late and Long-term Effects of Neuroblastoma and Its Treatment](#)<sup>3</sup>.

## MIBG radiotherapy

As described in the section [Tests for Neuroblastoma](#)<sup>4</sup>, MIBG is a chemical similar to norepinephrine, which is made by sympathetic nerve cells. A slightly radioactive form of MIBG is sometimes injected into the blood as part of an imaging test to look for neuroblastoma cells in the body.

A more highly radioactive form of MIBG is also used to treat some children with advanced neuroblastoma, often along with other treatments. Once injected into the blood, the MIBG goes to tumors anywhere in the body and delivers its radiation. The child will need to stay in a special hospital room for a few days after the injection until most of the radiation has left the body. Most of the radiation leaves the body in the urine, so younger children might need to have a catheter in the bladder to help urine leave the body, usually for a couple of days.

**Possible side effects:** Most of the radiation from MIBG therapy stays in the area of the neuroblastoma, so most children do not have serious side effects from this treatment. MIBG therapy can sometimes cause mild nausea and vomiting. It can also make some children feel tired or sluggish. Some children might have swollen cheeks from the MIBG because it can affect the salivary glands. In rare cases it might cause high blood pressure for a short period of time.

## Hyperlinks

1. [www.cancer.org/cancer/neuroblastoma/detection-diagnosis-staging/how-diagnosed.html](http://www.cancer.org/cancer/neuroblastoma/detection-diagnosis-staging/how-diagnosed.html)
2. [www.cancer.org/cancer/neuroblastoma/detection-diagnosis-staging/how-diagnosed.html](http://www.cancer.org/cancer/neuroblastoma/detection-diagnosis-staging/how-diagnosed.html)
3. [www.cancer.org/cancer/neuroblastoma/after-treatment/long-term-effects.html](http://www.cancer.org/cancer/neuroblastoma/after-treatment/long-term-effects.html)
4. [www.cancer.org/cancer/neuroblastoma/detection-diagnosis-staging/how-diagnosed.html](http://www.cancer.org/cancer/neuroblastoma/detection-diagnosis-staging/how-diagnosed.html)

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# High-Dose Chemotherapy/Radiation

# Therapy and Stem Cell Transplant for Neuroblastoma

This type of treatment is often used in children with high-risk neuroblastoma who are unlikely to be cured with other treatments. Before the stem cell transplant, a child has usually had about 5 months of intense chemotherapy and might have had surgery to remove the tumor.

Giving higher doses of [chemotherapy](#) might be more effective in treating these cancers, but normally this can't be done because it would cause severe damage to the bone marrow, where new blood cells are made. This could lead to life-threatening shortages of blood cells.

Doctors can sometimes get around this problem by giving the high-dose treatments, then replacing the patient's bone marrow cells by giving them new blood-making cells (called **stem cells**). This is known as a **stem cell transplant** (SCT). Some children might have 2 stem cell transplants, called **tandem stem cell transplants**.

## Collecting stem cells before the transplant

For most children with neuroblastoma, their own stem cells are used for the transplant. These stem cells are collected in a process called **apheresis**.

To help prepare for stem cell collection, doctors give children a medicine called G-CSF that helps bone marrow make more white blood cells and helps stem cells move into the bloodstream.

G-CSF is usually started at the end of a regular cycle of chemotherapy and is given daily. Children often need blood tests every day once their blood cell counts start to increase (this is often about 7 to 10 days after their first dose of chemotherapy). Once part of the white blood cell count (known as the **absolute neutrophil count**, or **ANC**) reaches a certain level, the dose of G-CSF is increased until there are enough stem cells to collect. A special kind of central line will be placed so the stem cells can be collected using apheresis. The collection process is similar to donating blood, but instead of going into a collecting bag, the blood goes into a special machine that filters out the stem cells and returns the other parts of the blood back to the person's body. Apheresis can take 3 to 4 hours and your child will probably need to lie flat and hold still during the procedure. This process may be repeated over a few days. The stem cells are then frozen until the transplant.

## How the transplant is done

Typically, the child will be admitted to the SCT unit of the hospital on the day before the high-dose chemo begins. He or she will usually stay in the hospital until after the chemo and the stem cells have been given, and until the stem cells have started making new blood cells again (see below).

The child gets high-dose chemotherapy first. This destroys the cancer cells in the body, as well as the normal cells in the bone marrow. After high-dose chemotherapy, the frozen stem cells are thawed and given as a blood transfusion. The stem cells travel through the bloodstream and settle in the child's bone marrow.

Usually within a couple of weeks, the stem cells begin making new white blood cells. This is later followed by new platelet production and new red blood cell production. Until this happens, the child is at high risk of [infection](#)<sup>1</sup> because of a low white blood cell count, as well as bleeding because of a low platelet count. To help lower the risk of infection, the child stays in a special hospital room, and visitors must wear protective clothing. Blood and platelet transfusions and treatment with IV antibiotics may also be used to help prevent or treat infections or bleeding problems.

The child usually stays in the hospital room until part of the white blood cell count rises to a safe level. The child is then seen in an outpatient clinic almost every day for several weeks. Because platelet counts often take longer to return to a safe level, the child may get platelet transfusions as an outpatient. Patients may need to make regular visits to the outpatient clinic for about 6 months, after which time their regular doctors may continue their care.

A SCT is a complex treatment that can cause life-threatening side effects. If the doctors think your child can benefit from a transplant, the best place to have this done is at a nationally recognized cancer center where the staff has experience with the procedure and managing the recovery period.

### Possible side effects

The possible side effects from SCT are generally divided into early and long-term effects.

#### Early or short-term side effects

The early complications and side effects are basically the same as those caused by high-dose chemotherapy or radiation therapy and can be severe. They are caused by



damage to the bone marrow and other quickly growing tissues of the body, and can include:

- Low blood cell counts (with fatigue and increased risk of infection and bleeding)
- Nausea and vomiting
- Loss of appetite
- Mouth sores
- Diarrhea
- Hair loss
- Problems with liver

One of the most common and serious short-term effects is an increased risk for serious infections. Antibiotics are often given to try to prevent this. [Other side effects](#)<sup>2</sup>, like low red blood cell and platelet counts, might require [blood product transfusions](#)<sup>3</sup> or other treatments.

### **Late or long-term side effects**

Some complications and side effects can last for a long time or might not occur until months or years after the transplant. These can include:

- Radiation damage to the heart or lungs
- Problems with the thyroid or other hormone-making glands
- Problems with fertility
- Damage to bones or problems with bone growth
- Development of another cancer (including leukemia) years later

Be sure to talk to your child's doctor before the transplant to learn about possible long-term effects your child might have. For more on the possible long-term effects of this and other treatments, see the section, [Late and Long-term Effects of Neuroblastoma and Its Treatment](#)<sup>4</sup>.

For more information on stem cell transplants in general, see [Stem Cell Transplant for Cancer](#).<sup>5</sup>

### **Hyperlinks**

1. [www.cancer.org/treatment/treatments-and-side-effects/physical-side-effects/infections/infections-in-people-with-cancer.html](http://www.cancer.org/treatment/treatments-and-side-effects/physical-side-effects/infections/infections-in-people-with-cancer.html)

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5. [www.cancer.org/treatment/treatments-and-side-effects/treatment-types/stem-cell-transplant.html](http://www.cancer.org/treatment/treatments-and-side-effects/treatment-types/stem-cell-transplant.html)

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# Retinoid Therapy for Neuroblastoma

Retinoids are chemicals that are related to vitamin A. They are known as **differentiating agents** because they are thought to help some cancer cells mature (differentiate) into normal cells.

In children with high-risk neuroblastoma, treatment with a retinoid called *13-cis-retinoic acid* (isotretinoin) reduces the risk of the cancer coming back after high-dose chemotherapy and stem cell transplant. Most doctors now recommend 6 months of *13-cis-retinoic acid* after the transplant. This drug is taken as a capsule, twice a day for 2 weeks, followed by 2 weeks off.

Researchers are now trying to develop more effective retinoids and to define the exact role of this approach in treating neuroblastoma.

## Possible side effects

The most common side effect of 13-cis-retinoic acid is dry and cracked lips. Dry skin or eyes are also possible, as are nosebleeds, muscle and joint pains, and changes in the nails.

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# Immunotherapy for Neuroblastoma

Immunotherapy is the use of medicines to help a patient's own immune system recognize and destroy cancer cells more effectively. Several types of immunotherapy are now being studied for use against neuroblastoma (some of which are described in [What's New in Neuroblastoma Research?](#)<sup>1</sup>).

Monoclonal antibodies are man-made versions of immune system proteins that can be made to attack a very specific target. They can be injected into the body to seek out and attach to cancer cells.

A monoclonal antibody called **dinutuximab (Unituxin)** attaches to GD2, a substance found on the surface of many neuroblastoma cells. This antibody can be given together with cytokines (immune system hormones) such as GM-CSF and interleukin-2 (IL-2) to

help the child's immune system recognize and destroy neuroblastoma cells. This antibody is now part of the routine treatment for many children with high-risk neuroblastoma, often after a [stem cell transplant](#)<sup>2</sup>.

### **Possible side effects**

Side effects of dinutuximab treatment can include:

- Nerve pain (which can sometimes be severe)
- Leaking of fluid in the body (which can lead to low blood pressure, fast heart rate, shortness of breath, and swelling)
- Allergic reactions (which can lead to airway swelling, trouble breathing, and low blood pressure)
- Vomiting
- Diarrhea
- Infections

### **Hyperlinks**

1. [https://author-prod.cancer.org/content/launches/2017/10/17/2017\\_review-neuroblastoma-copyedit/content/launches/2017/10/17/2017\\_review-neuroblastoma/content/cancer/en/cancer/neuroblastoma/about/new-research.html](https://author-prod.cancer.org/content/launches/2017/10/17/2017_review-neuroblastoma-copyedit/content/launches/2017/10/17/2017_review-neuroblastoma/content/cancer/en/cancer/neuroblastoma/about/new-research.html)
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## Treatment of Neuroblastoma by Risk Group

Treatment for neuroblastoma is largely based on which [risk group](#)<sup>1</sup> a child is in. Generally older children, children with tumors that have spread throughout the body (high stage), or have unfavorable tumor features or extra copies of the *MYCN* gene will be considered high risk. Some infants with neuroblastoma that has spread throughout the body can still be considered low risk, especially if their tumor does not have extra copies of *MYCN* or other unfavorable features.

### Low risk

Children at low risk usually don't need very intensive treatment to cure the neuroblastoma. In fact, some children might not need to be treated at all because some of these neuroblastomas will mature or go away on their own. If a child is low risk and the tumor can easily be removed, [surgery](#) can often be their only treatment. Even if some neuroblastoma is left behind after surgery, the child can usually be watched carefully without further treatment because the remaining tumor will often mature or go away on its own.

If much of the tumor can't be removed, the tumor gets bigger after a surgery, or if a tumor is causing symptoms, [chemotherapy](#) (chemo) is typically given. A common chemo regimen is a combination of carboplatin, cyclophosphamide, doxorubicin, and etoposide. But other combinations may be used.

For those few children that have symptoms from a low-risk tumor that can't safely be treated right away with surgery, a short course of chemo might be given first. For example, if the tumor is pressing on the spinal cord or affecting breathing, chemo may be used to shrink the tumor to control the symptoms. A short course of [radiation therapy](#) usually is only used if the symptoms are not getting better with chemo, are life threatening, or are causing spinal cord compression.

Infants with stage 4S disease and no symptoms can often be watched carefully with no treatment, because these cancers typically mature or go away on their own. If the tumor causes problems such as an enlarged liver, which can be life-threatening for very young infants, chemo that is less intense may be used to shrink the tumor. Radiation therapy may be used if chemo doesn't shrink the liver right away.

Recent research has also shown that infants younger than 6 months with small adrenal tumors (which are assumed to be neuroblastomas) can often be watched closely without needing surgery or other treatments. Many of these tumors will mature or go away on their own, but if a tumor keeps growing or is causing symptoms, surgery or chemo might be used.

## Intermediate risk

Surgery is an important part of treatment for children at intermediate risk, but it is rarely enough on its own. Children are typically given 4 to 8 cycles (about 12 to 24 weeks) of chemotherapy before or after surgery. The chemo drugs used usually include carboplatin, cyclophosphamide, doxorubicin, and etoposide. If chemo is used first, surgery may then be done to remove any remaining tumor. Radiation therapy usually is only used if the tumor is not responding well to chemo or if a child's symptoms from the tumor require emergency treatment.

Doctors are looking at the possibility of observing infants and young babies with no symptoms and favorable tumor features instead of treatment with surgery and/or chemotherapy. In this approach, doctors watch the tumor closely using [imaging tests](#)<sup>2</sup> to make sure the tumor goes away or does not get bigger. If the tumor does get bigger or a child has symptoms, then treatment with chemotherapy will be started. Some studies have shown promising results using this approach, and more studies are being done now.

Children at intermediate risk who need chemotherapy are monitored closely to see how they respond after every 2 cycles (6 to 8 weeks). The total number of cycles depends on how well chemotherapy shrinks the tumor. Doctors hope that treating with chemotherapy based on a child's results can help children who have tumors that respond quickly get less chemotherapy..

## High risk

Children at high risk require more aggressive treatment, which often includes chemotherapy, surgery, radiation, stem cell transplant, immunotherapy and retinoid therapy. Treatment is often done in 3 phases:

- **Induction:** The goal of this phase is to get the cancer into remission by destroying or removing as much of it as possible. Treatment usually starts with chemotherapy, using alternating regimens of several drugs (typically cisplatin, etoposide, vincristine, cyclophosphamide, doxorubicin, and topotecan) given at higher doses than what is used for other risk groups. Surgery is usually done after induction to try to remove any tumors that are still visible.
- **Consolidation:** This phase uses more intensive treatment to try to get rid of any cancer cells that remain in the body. High-dose chemotherapy is given, followed by one or two stem cell transplants. A recent study showed that giving two stem cell transplants back to back (tandem stem cell transplant) was better than giving one stem cell transplant. Even though long-term results of this study are still being looked at, the short-term results were promising enough that some centers may give two stem cell transplants, followed by immunotherapy. Radiation is often given to the primary tumor site after stem cell transplant (even if the tumor was removed by surgery) and to any other parts of the body that might have active disease, based on [MIBG scan results](#)<sup>3</sup>.
- **Maintenance:** The goal of this phase of treatment is to try to lower the chance that the cancer will come back. The retinoid drug 13-cis-retinoic acid (isotretinoin) is often given for 6 months after other treatments are completed. Immunotherapy with the monoclonal antibody dinutuximab (Unituxin), along with immune-activating cytokines (GM-CSF and IL-2), is often given as well.

## Recurrent neuroblastoma

If neuroblastoma comes back after initial treatment, it is known as a [recurrence](#)<sup>4</sup> or relapse. Treatment of recurrent neuroblastoma depends on many factors, including the initial [risk group](#)<sup>5</sup>, where the cancer recurs, and what treatments have been used.

For low- and intermediate-risk neuroblastomas that recur in the same area where they started, surgery with or without chemotherapy may be effective.

For high-risk cancers or those that recur in distant parts of the body, treatment is usually more intense, and may include a combination of chemotherapy, surgery, and radiation therapy (such as MIBG radiotherapy). Chemotherapy might include drugs that weren't used during the initial treatment. Intensive treatment with high-dose chemotherapy followed by a stem cell transplant might be another option. Because these cancers can be hard to treat, clinical trials of newer treatments, such as monoclonal antibodies or new anti-cancer drugs, might be another reasonable option. See [What's New in](#)

## Neuroblastoma Research?<sup>6</sup>

### Hyperlinks

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## After Neuroblastoma Treatment

### Living as a Neuroblastoma Survivor

For many people, cancer treatment often raises questions about next steps as a survivor.

- [What Happens After Treatment for Neuroblastoma?](#)

### Cancer Concerns After Treatment

Neuroblastoma survivors are at risk for possible late effects of their cancer treatment. It's important to discuss what these possible effects might be with your child's medical team so you know what to watch for and report to the doctor.

- [Late and Long-Term Effects of Neuroblastoma and Its Treatment](#)
- 

## What Happens After Treatment for Neuroblastoma?

During treatment for neuroblastoma, the main concerns for most families are the daily aspects of getting through treatment and beating the cancer. After treatment, the concerns tend to shift toward the long-term effects of neuroblastoma and its treatment, and concerns about neuroblastoma coming back (recurrence).

It's certainly normal to want to put neuroblastoma and its treatment behind you and to get back to a life that doesn't revolve around cancer. But it's important to realize that follow-up care is a central part of this process that offers your child the best chance for recovery and long-term survival.

## Follow-up exams and tests

After treatment, the doctor will probably order follow-up tests, which may include lab tests and [imaging tests](#)<sup>1</sup> (MIBG scans, PET scans, ultrasound, CT scans, and/or MRI scans) to see if there is any tumor remaining. The tests done will depend on the [risk group](#)<sup>2</sup>, the size and location of the tumor, and other factors.

Because there is a chance that the cancer might return after treatment, it is very important to go to all follow-up appointments and to report any new symptoms to your child's doctor right away. The health care team will discuss a follow-up schedule with you, including which tests should be done and how often. Doctor visits, lab tests, and imaging tests to look for signs of [recurrence](#)<sup>3</sup> are done more often at first. If nothing abnormal is found, the time between tests can then be extended.

A benefit of follow-up care is that it gives you a chance to discuss any questions and concerns that arise during and after your child's recovery. For example, almost any cancer treatment can have side effects. Some might last for only a short time, but [others can last longer](#) or might not show up until months or even years later. It's important to report any new symptoms to the doctor right away so that the cause can be found and treated, if needed.

## Ask your child's doctor for a survivorship care plan

Talk with your child's doctor about developing a [survivorship care plan](#)<sup>4</sup>. This plan might include:

- A suggested schedule for follow-up exams and tests
- A schedule for other tests your child might need in the future, such as early detection (screening) tests for other types of cancer, or tests to look for long-term health effects from neuroblastoma or its treatment
- [late- or long-term side effects](#)<sup>5</sup> A list of possible from your child's treatment, including what to watch for and when to contact the doctor
- Diet and physical activity suggestions

## Keeping records of health insurance and your child's medical care

As much as you might want to put the experience behind you once treatment is done, it's very important to keep good records of your child's medical care during this time. Eventually, your child will grow up, be on his or her own, and have new doctors. It's important for them to be able to give the new doctors the details of their cancer diagnosis and treatment. Gathering the details soon after treatment may be easier than trying to get them at some point in the future.

Ask your cancer care team where and how to get this information. Learn more in [Keeping Copies of Important Medical Records](#)<sup>6</sup>.

It's also important to keep health insurance coverage. Tests and doctor visits can cost a lot, and even though no one wants to think of neuroblastoma coming back, this could happen.

## Can we lower the risk of neuroblastoma progressing or coming back?

If your child has (or has had) neuroblastoma, you probably want to know if there are things you can do that might lower the risk of it growing or coming back, such as eating a certain type of diet or taking nutritional supplements. Unfortunately, it's not yet clear if there are things you can do that will help.

As your child gets older, adopting healthy behaviors such as [not smoking](#)<sup>7</sup>, [eating well, getting regular physical activity](#)<sup>8</sup>, and staying at a healthy weight might help, but no one knows for sure. However, we do know that these types of behaviors can have positive effects on your child's health that can extend beyond their risk of neuroblastoma or other cancers.

### About dietary supplements

So far, no dietary supplements (including vitamins, minerals, and herbal products) have been shown to clearly help lower the risk of neuroblastoma progressing or coming back. This doesn't mean that there are no supplements that can help, but it's important to know that none have been proven to do so.

Dietary supplements are not regulated like medicines in the United States – they do not have to be proven effective (or even safe) before being sold, although there are limits on what they're allowed to claim they can do. If you're thinking about having your child take any type of nutritional supplement, talk to your child's health care team. They can help you decide which ones can be used safely while avoiding those that might be

harmful.

To learn more, see [Dietary Supplements: What Is Safe?](#)<sup>9</sup>

## Emotional and social issues in children with neuroblastoma

When a child is diagnosed with cancer, it is a crisis for the whole family. Younger children might not remember much about their experience after treatment completes, but getting through it and helping them cope can be a challenge. Older children might have difficulty being away from school, friends, and activities that they enjoy, in addition to dealing with treatment stresses. Most pediatric cancer centers have special support programs and services to help children with cancer during treatment and for many years after treatment ends.

Parents and other family members, especially siblings, can also be affected, both emotionally and in other ways. The family's situation should be evaluated by the treatment center as soon as possible. Some common family concerns include financial stresses, traveling to and staying near the cancer center, the need for family members to take time off from work, the possible loss of a job, and the need for home schooling. Social workers and other professionals at cancer centers can help families sort through these issues.

To learn more about helping children with neuroblastoma and their loved ones cope during and after treatment, see [Finding Help and Support When Your Child Has Cancer](#)<sup>10</sup>.

## Hyperlinks

1. [www.cancer.org/cancer/neuroblastoma/detection-diagnosis-staging/how-diagnosed.html](http://www.cancer.org/cancer/neuroblastoma/detection-diagnosis-staging/how-diagnosed.html)
2. [www.cancer.org/cancer/neuroblastoma/detection-diagnosis-staging/risk-groups.html](http://www.cancer.org/cancer/neuroblastoma/detection-diagnosis-staging/risk-groups.html)
3. [www.cancer.org/treatment/survivorship-during-and-after-treatment/understanding-recurrence.html](http://www.cancer.org/treatment/survivorship-during-and-after-treatment/understanding-recurrence.html)
4. [www.cancer.org/treatment/survivorship-during-and-after-treatment/survivorship-care-plans.html](http://www.cancer.org/treatment/survivorship-during-and-after-treatment/survivorship-care-plans.html)
5. [www.cancer.org/treatment/children-and-cancer/when-your-child-has-cancer/late-effects-of-cancer-treatment.html](http://www.cancer.org/treatment/children-and-cancer/when-your-child-has-cancer/late-effects-of-cancer-treatment.html)
6. [www.cancer.org/treatment/survivorship-during-and-after-treatment/be-healthy-after-treatment/keeping-copies-of-important-medical-records.html](http://www.cancer.org/treatment/survivorship-during-and-after-treatment/be-healthy-after-treatment/keeping-copies-of-important-medical-records.html)

7. [www.cancer.org/healthy/stay-away-from-tobacco.html](http://www.cancer.org/healthy/stay-away-from-tobacco.html)
8. [www.cancer.org/healthy/eat-healthy-get-active.html](http://www.cancer.org/healthy/eat-healthy-get-active.html)
9. [www.cancer.org/treatment/treatments-and-side-effects/complementary-and-alternative-medicine/dietary-supplements.html](http://www.cancer.org/treatment/treatments-and-side-effects/complementary-and-alternative-medicine/dietary-supplements.html)
10. [www.cancer.org/treatment/children-and-cancer/when-your-child-has-cancer/during-treatment/help-and-support.html](http://www.cancer.org/treatment/children-and-cancer/when-your-child-has-cancer/during-treatment/help-and-support.html)

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## Late and Long-Term Effects of Neuroblastoma and Its Treatment

Neuroblastoma can cause long-lasting side effects. Most of the long-term side effects depend on exactly what kind of treatment a child had, where the tumor was located, and how old the child was when treated. Children who received 3 or more kinds of treatment (surgery, radiation, chemotherapy, etc.) are more likely to have serious long-term side effects of treatment. For more information see [Late Effects of Childhood Cancer Treatment](#)<sup>1</sup>.

Because of major advances in treatment, most children treated for neuroblastoma are now surviving into adulthood. Doctors have learned that the treatment can affect children's health later in life, so watching for health effects as they get older has become more of a concern in recent years.

Neuroblastoma survivors are at risk for several possible late effects of their treatment. It's important to discuss what these possible effects might be with your child's medical team.

After treatment, the cancer care team will create a [Survivorship Care Plan](#)<sup>2</sup> describing the treatments given and what that tells you about your child's risk of late effects. The plan will also describe how the child should be monitored for these problems. Most children do not experience all the problems they might be at risk for, but it's important to find any problems that do come up early, so they can be treated effectively.

Late effects after neuroblastoma treatment can include:

- Hearing loss
- Problems with bones and muscles, like scoliosis (curving of the spine)
- Thyroid problems
- Problems with growth and development
- Fertility problems
- Neurological problems
- Second cancers, including leukemia
- Emotional or psychological issues

In very rare instances and for unknown reasons, in some children with neuroblastoma the body's immune system attacks the child's normal nerve tissue. This can lead to problems such as learning disabilities, delays in muscle development, language problems, and behavioral problems. This is called **opsoclonus myoclonus syndrome**.

Children whose tumors are in the neck or chest and who have problems with the eyes or with muscle twitches may need further treatment with corticosteroids, intravenous immunoglobulin (IVIG), or other drugs.

### Long-term follow-up guidelines

To help increase awareness of late effects and improve follow-up care of childhood cancer survivors throughout their lives, the Children's Oncology Group (COG) has developed long-term follow-up guidelines for survivors of childhood cancers. These guidelines are used to create a child's Survivorship Care Plan.

To learn more, ask your child's doctors about the COG survivor guidelines. You can also download them for free at the COG website: [www-survivorshipguidelines.org](http://www-survivorshipguidelines.org)<sup>3</sup>. The guidelines are written for health care professionals. Patient versions of some of the guidelines are available (as "Health Links") on the site as well.

### Hyperlinks

1. [www.cancer.org/treatment/children-and-cancer/when-your-child-has-cancer/late-effects-of-cancer-treatment.html](http://www.cancer.org/treatment/children-and-cancer/when-your-child-has-cancer/late-effects-of-cancer-treatment.html)
2. [www.cancer.org/treatment/survivorship-during-and-after-treatment/survivorship-care-plans.html](http://www.cancer.org/treatment/survivorship-during-and-after-treatment/survivorship-care-plans.html)
3. <http://www-survivorshipguidelines.org/>

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