



[cancer.org](https://www.cancer.org) | 1.800.227.2345

---

# 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](#)

# 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.

## 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.

Dome JS, Rodriguez-Galindo C, Spunt SL, et al. Pediatric solid tumors. In: Neiderhuber JE, Armitage JO, Doroshow JH, Kastan MB, Tepper JE, eds. *Abeloff's Clinical Oncology*. 5th ed. Philadelphia, PA. Elsevier: 1804-1847

Last Medical Review: March 19, 2018 Last Revised: March 19, 2018

---

## 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)

## 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.

Dome JS, Rodriguez-Galindo C, Spunt SL, et al. Pediatric solid tumors. In: Neiderhuber JE, Armitage JO, Doroshow JH, Kastan MB, Tepper JE, eds. *Abeloff's Clinical Oncology*. 5th ed. Philadelphia, PA. Elsevier: 1804-1847

Last Medical Review: March 19, 2018 Last Revised: March 19, 2018

---

# 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

1. [www.cancer.org/cancer/neuroblastoma/causes-risks-prevention/risk-factors.html](http://www.cancer.org/cancer/neuroblastoma/causes-risks-prevention/risk-factors.html)
2. [www.cancer.org/treatment/understanding-your-diagnosis/tests.html](http://www.cancer.org/treatment/understanding-your-diagnosis/tests.html)
3. [www.cancer.org/treatment/understanding-your-diagnosis/tests/understanding-your-lab-test-results.html](http://www.cancer.org/treatment/understanding-your-diagnosis/tests/understanding-your-lab-test-results.html)
4. [www.cancer.org/treatment/understanding-your-diagnosis/tests/imaging-radiology-tests-for-cancer.html](http://www.cancer.org/treatment/understanding-your-diagnosis/tests/imaging-radiology-tests-for-cancer.html)
5. [www.cancer.org/treatment/understanding-your-diagnosis/tests/ultrasound-for-cancer.html](http://www.cancer.org/treatment/understanding-your-diagnosis/tests/ultrasound-for-cancer.html)
6. [www.cancer.org/treatment/understanding-your-diagnosis/tests/mri-for-cancer.html](http://www.cancer.org/treatment/understanding-your-diagnosis/tests/mri-for-cancer.html)
7. [www.cancer.org/treatment/understanding-your-diagnosis/tests/ct-scan-for-cancer.html](http://www.cancer.org/treatment/understanding-your-diagnosis/tests/ct-scan-for-cancer.html)
8. [www.cancer.org/cancer/neuroblastoma/treating/radiation-therapy.html](http://www.cancer.org/cancer/neuroblastoma/treating/radiation-therapy.html)
9. [www.cancer.org/treatment/understanding-your-diagnosis/tests/nuclear-medicine-scans-for-cancer.html](http://www.cancer.org/treatment/understanding-your-diagnosis/tests/nuclear-medicine-scans-for-cancer.html)
10. [www.cancer.org/treatment/understanding-your-diagnosis/tests/nuclear-medicine-scans-for-cancer.html](http://www.cancer.org/treatment/understanding-your-diagnosis/tests/nuclear-medicine-scans-for-cancer.html)
11. [www.cancer.org/cancer/neuroblastoma/treating/surgery.html](http://www.cancer.org/cancer/neuroblastoma/treating/surgery.html)
12. [www.cancer.org/treatment/understanding-your-diagnosis/tests/testing-biopsy-and-cytology-specimens-for-cancer.html](http://www.cancer.org/treatment/understanding-your-diagnosis/tests/testing-biopsy-and-cytology-specimens-for-cancer.html)

## 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.

Dome JS, Rodriguez-Galindo C, Spunt SL, et al. Pediatric solid tumors. In: Neiderhuber JE, Armitage JO, Doroshow JH, Kastan MB, Tepper JE, eds. *Abeloff's Clinical Oncology*. 5th ed. Philadelphia, PA. Elsevier: 1804-1847.

Last Medical Review: March 19, 2018 Last Revised: March 19, 2018

# 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)

Last Medical Review: March 19, 2018 Last Revised: March 19, 2018

---

# 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 prognostic 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.

Last Medical Review: March 19, 2018 Last Revised: March 19, 2018

# 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.

Last Medical Review: March 19, 2018 Last Revised: March 19, 2018

---

## 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)

Last Medical Review: March 19, 2018 Last Revised: March 19, 2018

## Written by

The American Cancer Society medical and editorial content team  
([www.cancer.org/cancer/acs-medical-content-and-news-staff.html](http://www.cancer.org/cancer/acs-medical-content-and-news-staff.html))

Our team is made up of doctors and oncology certified nurses with deep knowledge of cancer care as well as journalists, editors, and translators with extensive experience in medical writing.

American Cancer Society medical information is copyrighted material. For reprint requests, please see our Content Usage Policy ([www.cancer.org/about-us/policies/content-usage.html](http://www.cancer.org/about-us/policies/content-usage.html)).

**cancer.org | 1.800.227.2345**