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 the Health Care Team About Neuroblastoma
Can Neuroblastoma Be Found Early?

Some neuroblastomas can be found early, before they start to cause any signs or symptoms.

For example, a small number of neuroblastomas are 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 often done during pregnancy to estimate the age of a fetus, predict the date of birth, and look for certain common birth defects.

Neuroblastoma is also sometimes found incidentally in young children without any symptoms during tests done to look for other childhood diseases or during regular medical checkups.

But most often, neuroblastoma is first detected because of signs or symptoms a child is having.

Screening for neuroblastoma

Screening is testing for a disease, such as cancer, in people who don’t have any symptoms. Screening can help find some types of cancer early, when they’re likely to be easier to treat.

Studies in several countries have looked at screening infants for neuroblastoma. Screening was done by testing the infants’ urine for certain chemicals made by neuroblastoma tumors. (For more on this urine test, see Tests for Neuroblastoma.) However, these studies did not find neuroblastoma screening to be helpful.

Screening did find many tumors that wouldn’t normally have been detected. But most of these tumors probably would have gone away or matured into benign (non-cancerous) tumors on their own, so they never would have caused any problems if they hadn’t been found. (See What Is Neuroblastoma? for more on this.) Screening didn’t lower the number of cancers found at advanced stages, nor did it lower the number of deaths from neuroblastoma.

Screening for neuroblastoma could have downsides as well. For example, finding tumors that would never cause serious problems might still needlessly frighten parents and lead to unnecessary tests and surgery in some children.

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

Screening might be recommended for infants who are at increased risk, such as those with a family history of neuroblastoma. Along with a urine test, this might also include genetic testing to look for changes in the ALK gene, which is often seen in cases of hereditary (familial) neuroblastoma.

Hyperlinks

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

References


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Signs and Symptoms of Neuroblastoma

Neuroblastoma can start in different places in the body. Neuroblastoma cells can also sometimes release chemicals called hormones, which can affect other parts of the body. Because of this, neuroblastoma can cause many different signs and symptoms.
Some of the more common symptoms can include:

- Lump or swelling in the child's belly that doesn't seem to hurt
- Swelling in the legs or in the upper chest, neck, and face
- Problems with breathing or swallowing
- Weight loss
- Not eating or complaining about feeling full
- Problems with bowel movements or urinating
- Pain in bones
- Lumps or bumps under the skin, which 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

Signs and symptoms might be different depending on where the tumor is, how large it is, how far it has spread, and if the tumor makes hormones.

Many of these signs and symptoms 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, they 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.

Tumors in the chest or neck 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), part of a condition known as Horner syndrome.

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**

Many neuroblastomas have already spread to the lymph nodes or other parts of the body by the time they are found.

**Spread to the lymph nodes:** Lymph nodes 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.

**Spread to bones:** 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 might also spread to other bones in the skull, causing bumps under the scalp.

**Spread to bone marrow:** If the cancer spreads to the bone marrow (the inner part of certain bones, where new blood cells are made), 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.

**Bleeding problems:** 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.

**Stage 4S (MS) neuroblastoma:** A special widespread form of neuroblastoma (known as stage 4S or stage MS) sometimes occurs, usually 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. While stage 4S neuroblastoma is already widespread when it is found, it is very treatable, and it 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**

Neuroblastoma cells sometimes release hormones 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**.

Signs and 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 opsoclonus myoclonus ataxia (OMA). This is thought to result from the body’s immune system attacking the normal nerve tissue. A child with this syndrome typically has irregular, rapid eye movements (opsoclonus) and twitch-like muscle spasms (myoclonus), and appears uncoordinated when standing or walking (ataxia). They might also have trouble speaking. Children who have this syndrome tend to have a better outlook when it comes to the neuroblastoma itself, although some children
might have long-term nervous system problems, even after the neuroblastoma has been treated. (For more on this, see Late and Long-Term Effects of Neuroblastoma and Its Treatment2.)

Hyperlinks


References


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Tests for Neuroblastoma

Neuroblastomas are usually found when a child is brought to the doctor because of signs or symptoms they are having. If a neuroblastoma (or another type of tumor) is suspected, tests will be needed to confirm the diagnosis.

If a neuroblastoma is found, other tests will then be needed to learn more about it.
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 are any possible risk factors\(^1\), such as a family history of neuroblastoma.

The doctor will examine your child for possible signs of a neuroblastoma or other health problems. For example, the doctor may feel the abdomen (belly) for any abnormal masses or swelling. The doctor might check for lumps or bumps under the skin and examine your child's eyes closely. They might also check child's blood pressure because sometimes neuroblastoma can 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 may 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.

If the history and exam suggest a child might have a neuroblastoma (or another type of tumor), more tests will be done. These could include:

- Blood and urine tests
- Imaging tests
- 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

Cells in the body make many different types of hormones. For example, 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 also often make these catecholamines, so these same metabolites can be detected in blood and urine. If the neuroblastoma cells are making catecholamines, the amount of HVA and VMA in urine or blood will be higher than expected.

If a child does have neuroblastoma, levels of HVA and VMA can also be followed during treatment to get an idea of how well it is working.

**Other blood and urine tests:** If neuroblastoma is suspected or has been found, your child’s doctor will probably order blood tests 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 help check kidney function.

**Imaging tests**

Imaging tests 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 cancer
• To learn how far cancer has spread
• To help determine if treatment is working

Most children who have or might have neuroblastoma will get one or more of these tests, but they might not need all of them.

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 the child’s age and the imaging test being done, they might get medicines to make them drowsy (or even asleep) to help them keep still.

**Ultrasound (sonogram)**

**Ultrasound** uses sound waves and their echoes to look inside the body. This 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 needed if the child has already had an MRI or CT scan.
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)**

*MRI scans* provide detailed images of soft tissues in the body. These scans 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.

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

*CT scans* combine many x-ray pictures to make detailed cross-sectional images of the inside of the body. These tests 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.

**CT-guided needle biopsy:** CT scans can also be used to help guide a biopsy needle into a tumor. But needle biopsies (described below) aren't often done 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 been done.

For this test, a form of the chemical meta-iodobenzylguanidine (MIBG) that contains a small amount of radioactive iodine is injected into the blood. MIBG is similar to norepinephrine, a hormone made by sympathetic nerve cells, 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). 

The thyroid gland can also absorb MIBG, so a medicine containing iodine is sometimes given before, during, and after the test to protect the thyroid.

**Bone scan**

A bone scan 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 can be seen on a bone scan. This test isn't often needed for neuroblastoma, because an MIBG scan can usually detect cancer spread to the bone. But if the MIBG scan doesn't find cancer in the bone and the doctor still suspects it might have spread there, a bone scan might be helpful.

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, a radioactive substance (usually a type of sugar called 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 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. They 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.

PET scans usually aren’t needed if an MIBG scan has been done. But a PET scan might be useful for some neuroblastomas, especially if the neuroblastoma cells do not
absorb MIBG.

**X-rays**

X-rays⁹ can be used to look at the bones, although they aren’t as good at showing other structures in the body.

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

In children with neuroblastoma, an MIBG, PET, or bone scan is usually better than an x-ray for looking at the bones in the rest of the body and to see if neuroblastoma has spread to the bones, but an x-ray test might still be helpful in some situations.

**Biopsies**

During a biopsy, a doctor removes one or more pieces (samples) from the tumor for testing.

Exams and imaging tests might strongly suggest a child has neuroblastoma, but a biopsy is usually needed to be sure. (Some very young infants with small adrenal tumors seen on an imaging test might not need a biopsy. Instead, the tumor might be watched closely with further imaging tests, as these tumors often mature or go away on their own.)

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**: This is the most common type of biopsy for neuroblastoma. It 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 inserted 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 enough to do all the special tests that are needed.

Once the biopsy samples have been removed, they are sent to a lab, where they are viewed under a microscope by a pathologist (a doctor with special training in identifying cancer cells). Special lab tests are often done on the samples as well to show if the tumor is a neuroblastoma.

If it is a neuroblastoma, lab tests can also help determine how quickly the tumor might grow or spread, as well as which treatments might work 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 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.

For a bone marrow **biopsy**, 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. 

Hyperlinks
2. www.cancer.org/treatment/understanding-your-diagnosis/tests/understanding-your-lab-test-results.html
4. www.cancer.org/treatment/understanding-your-diagnosis/tests/mri-for-cancer.html

References


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Neuroblastoma Stages and Prognostic Markers

If 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 neuroblastoma describes how much cancer is in the body.

(For neuroblastoma, several other factors are looked at along with a child's stage to decide what risk group a child falls into. Risk groups give an overall picture of how a neuroblastoma is likely to respond to treatment and, it helps doctors choose the treatments that might work 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. The main difference between them 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 scans) to help decide the stage. The INRGSS stage can be determined before treatment has started.
- The International Neuroblastoma Staging System (INSS) is based on the results from the surgery to remove a child's tumor instead of imaging tests.

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 surgery, you may hear doctors talk about your child's stage using either system.

The stages for neuroblastoma are complex and can be confusing. If you are unsure about what they 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 best. 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 divides neuroblastomas into 4 stages:

**L1:** The tumor 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:** The tumor 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 it has at least one IDRF.

**M:** The tumor 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.

### International Neuroblastoma Staging System (INSS)

The INSS 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 can't 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 near 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 near 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 it 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 can't 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).

Stage 4: The cancer has spread to distant parts of the body such as distant lymph nodes, bones, 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 cancer cells, and imaging tests such as an MIBG scan do not show cancer in the bone marrow.

Recurrent: While not a formal 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 prognosis (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:

- **Age:** Younger children (under 12-18 months) are more likely to have a better outcome than older children.
- **Tumor histology:** Tumor histology is 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. 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 a gene that normally helps regulate cell growth. Changes in the **MYCN** gene can turn it into an **oncogene**, which 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]?^2

- **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, which are hormone-like chemicals that help the nerve cells mature. Neuroblastomas that have more of certain neurotrophin receptors, especially the nerve growth factor receptor TrkA, may have a better prognosis.

Serum (blood) levels of certain substances can also 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.

- Increased levels of **lactate dehydrogenase (LDH)** in the blood is also linked with a worse outlook in children with neuroblastoma.
Hyperlinks

2. www.cancer.org/cancer/neuroblastoma/about/new-research.html

References


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Neuroblastoma Risk Groups

Risk groups are used to help predict how likely it is that a child with neuroblastoma can be cured (and therefore how intensive treatment might need to be). 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 are based on the stage (extent) of the cancer, as well as other factors that can affect a child’s prognosis (outlook), such as their age. (See Neuroblastoma Stages and Prognostic Markers.)

The risk groups included here are commonly accepted standard risk groups in the United States. Other internationally used risk groups are being tested in clinical trials.

**Children’s Oncology Group (COG) risk groups**

The Children’s Oncology Group (COG, the major group of doctors who treat childhood cancer in the US) risk group system was initially based on the International Neuroblastoma Staging System (INSS) staging system, but is now transitioning to using the International Neuroblastoma Risk Group Staging System (INRGSS), along with the major prognostic factors, all of which are described in Neuroblastoma Stages and Prognostic Markers. These are combined to place children into 3 different risk groups:

- Low risk
- Intermediate risk
- High risk

These risk groups are based on what is known about neuroblastoma and how it is treated. As new research provides more information, the 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 to up to 18 months.

**International Neuroblastoma Risk Group (INRG) classification**

The International Neuroblastoma Risk Group (INRG) classification is a newer system that 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 INRGSS staging system, which includes the image-defined risk factors (IDRFs), as well as many of the prognostic factors listed in Neuroblastoma Stages and Prognostic Markers, such as:

- The child’s age
- Tumor histology (how the tumor looks under the microscope)
- The presence or absence of MYCN gene amplification in tumor cells
- Certain changes in chromosome 11 (known as an 11q aberration) in tumor cells
• 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.

The risk groups for neuroblastoma are complex and can be confusing. If you are unsure about your child’s risk group and what it means, ask your child’s doctor to explain it to you in a way you can understand.

References


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. They can't tell you for sure if treatment will be successful, but they may help give you a better understanding of how likely this is.

What is a 5-year survival rate?

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).

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 can't predict what will happen in any particular child's case.

The survival rates below are based on the risk group of the child's cancer. The risk group, in turn, is based on the stage (extent) of the cancer, as well as other prognostic factors (such as the child's age). But other factors can also affect a child's outlook, such as 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 they know 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 of around 50%.

References


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Questions to Ask the Health Care Team About Neuroblastoma

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

**If a neuroblastoma has been diagnosed**

• What is the **stage** (extent) of the neuroblastoma? What does this mean?
• Which **risk group** does my child’s cancer fall into? What does this mean?
• What else can you tell about the cancer based on the tests that have been done?
• Do we need to have any other tests before we discuss treatment options?
• How much experience do you have treating this type of cancer?
• Do we need to see any other types of doctors?
• Who else will be on the treatment team, and what do they do?

When deciding on a treatment plan

• Does the neuroblastoma need to be treated? Why or why not?
• What are our treatment 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?
• Should we get a second opinion? How do we do that? Can you recommend a doctor or cancer center?
• How soon do we need to start treatment?
• 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 lives?
• How long will it take my child to recover from treatment?
• What are the possible side effects 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?

During and after treatment

Once treatment begins, you’ll need to know what to expect and what to look for. Not all of these questions may apply, but getting answers to the ones that do may be helpful.

• How will we know if the treatment is working?
• Is there anything we can do to help manage side effects?
• What symptoms or side effects should we tell you about right away?
• How can we reach you or someone on your team on nights, weekends, or
holidays?
- Who can we talk to if we have questions about costs, insurance coverage, or social support?
- What are the chances that the cancer will come back\(^5\) after treatment? What would we do if this happens?
- What type of follow-up will my child need after treatment?
- Do you know of any local or online support groups where we can talk to other 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 more information about recovery times so that you can plan your work or school schedules.

Keep in mind, too, that doctors aren’t the only ones who can give you information. Other members of your health care team, such as nurses and social workers, can answer some of your questions. To find more about speaking with your health care team, see *The Doctor-Patient Relationship*\(^6\).

**Hyperlinks**


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**Written by**


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