Treating Neuroblastoma

If your child has been diagnosed with neuroblastoma, the cancer care team will discuss treatment options with you. It’s important to consider both the benefits of each treatment option and the possible risks and side effects.

How is neuroblastoma treated?

Several types of treatment can be used for neuroblastoma:

- Neuroblastoma Surgery
- Chemotherapy for Neuroblastoma
- Radiation Therapy for Neuroblastoma
- High-dose Chemotherapy and Stem Cell Transplant for Neuroblastoma
- Retinoid Therapy for Neuroblastoma
- Immunotherapy for Neuroblastoma

Common treatment approaches

Treatment of neuroblastoma depends on the risk group 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 that can best be met by children’s cancer centers. 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 a team approach that includes many different doctors, nurses, and other health professionals.

- How to Find the Best Cancer Treatment for Your Child
- Navigating the Health Care System When Your Child Has Cancer

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 treating neuroblastoma 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 the Health Care Team About Neuroblastoma
- How to Talk to Your Child’s Cancer Care Team
- Seeking a Second Opinion

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
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 Integrative Medicine

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

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.
Neuroblastoma Surgery

Surgery can be used both to help diagnose 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 can be 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 the tumor.

Surgery to treat neuroblastoma

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 all (or almost all) of the 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 or other treatments will be needed after surgery depends on the child's risk group\(^2\).

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 of the tumor and the extent of the operation, as well as the child’s health beforehand. Serious complications, although rare, can include problems with anesthesia; excess bleeding; infections; and damage to blood vessels, kidneys or 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.

**More information about Surgery**

For more general information about surgery as a treatment for cancer, see [Cancer Surgery](#)

To learn about some of the side effects listed here and how to manage them, see [Managing Cancer-related Side Effects](#).

**Hyperlinks**

Chemotherapy for Neuroblastoma

Chemotherapy (chemo) is the use of 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, especially if it can’t all be removed with surgery.

When might chemotherapy be used?

Whether a child with neuroblastoma will get chemotherapy depends on their risk group, which is based on the stage (extent) and location of the cancer, the child’s age, and other factors.

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, chemo is the main treatment.

**Which chemo drugs are used for neuroblastoma?**

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

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

The most common combination of drugs includes cisplatin (or carboplatin), cyclophosphamide, doxorubicin, vincristine, and etoposide, but others may be used.

For children in the high-risk group, other drugs might be added as well, and some drugs might be given at higher doses. This may be followed by a stem cell transplant.

Doctors give chemo in cycles. Treatment is given for 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 can affect other cells in the body that are dividing quickly, 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 of chemo**
Side effects common to many chemo drugs include:

- Hair loss
- Mouth sores
- Loss of appetite
- Nausea and vomiting
- Diarrhea or constipation

Chemo can damage the bone marrow, where new blood cells are made. This can lead to low blood cell counts, which can result in:

- 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 them know if your child has side effects so they can be managed.

**Side effects of certain chemo drugs**

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. This drug can also damage the ovaries or testicles, which could affect fertility (the ability to have children).

**Doxorubicin** can damage the heart. 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** and **etoposide** can cause **nerve damage (neuropathy)**. 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**). 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**.

**More information about chemotherapy**

For more general information about how chemotherapy is used to treat cancer, see **Chemotherapy**.

To learn about some of the side effects listed here and how to manage them, see **Managing Cancer-related Side Effects**.

**Hyperlinks**


**References**


Radiation Therapy for Neuroblastoma

Radiation therapy uses high-energy rays or particles to kill cancer cells.

When might radiation therapy be used?

Radiation therapy is sometimes a necessary part of treatment, but because of the possible long-term side effects in young children, doctors avoid using it when possible.

Most children with neuroblastoma will not need radiation therapy. It is most commonly used in children with high-risk neuroblastoma, typically after a stem cell transplant. It might also be used for children with low- and intermediate-risk neuroblastoma, if a child has life-threatening symptoms and needs emergency treatment to shrink the tumor.

How is radiation therapy given?

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

- External beam radiation therapy
- MIBG radiotherapy

External beam radiation therapy

External radiation therapy uses a machine to focus a beam of radiation on the cancer
from a radiation 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 a stem cell transplant in children with high-risk neuroblastoma to destroy neuroblastoma cells that remain behind. Radiation might be given to the primary tumor area and other areas of the body that might have active disease seen on an MIBG scan\(^1\).
- To help relieve pain caused by advanced neuroblastoma

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

Before the radiation treatments start, the radiation team will take careful measurements with imaging tests\(^2\) such as MRI scans to determine the correct angles for aiming the radiation beams and the proper dose of radiation.

Your child might also be fitted with a plastic mold resembling a body cast to keep them 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. Radiation therapy is much like getting an x-ray, but the dose of radiation is much higher. 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 of external radiation therapy**

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.
Short-term effects

- Radiation can affect the skin in the area treated. Effects 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.

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 Late and Long-term Effects of Neuroblastoma and Its Treatment³.

MIBG radiotherapy

As described in Tests for Neuroblastoma⁴, 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. This is called an MIBG scan.

A more highly radioactive form of MIBG can also be used to treat some children with advanced neuroblastoma, often along with other treatments. Once injected into the blood, the MIBG goes to neuroblastoma cells anywhere in the body and delivers its radiation. (This type of radiation travels only a very short distance, so it doesn’t affect most healthy cells in the body.)

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 don't 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 treatment because it can affect the salivary glands. Rarely, it might cause high blood pressure for a short period of time.

**More information about radiation therapy**

To learn more about how radiation is used to treat cancer, see [Radiation Therapy](#).

To learn about some of the side effects listed here and how to manage them, see [Managing Cancer-related Side Effects](#).

**Hyperlinks**


References


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**High-dose Chemotherapy and Stem Cell Transplant for Neuroblastoma**

This type of treatment combines higher doses of chemotherapy (chemo) with a transplant to replace the bone marrow stem cells damaged by the chemo. It is often used in children with high-risk neuroblastoma who are unlikely to be cured with other treatments.

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 stem cells.
in the bone marrow, which make new blood cells. This could lead to life-threatening shortages of blood cells.

A stem cell transplant (SCT) can sometimes help doctors get around this problem by giving the high-dose chemo, then replacing the patient’s bone marrow cells by giving them new stem cells.

Before the stem cell transplant, a child is usually given about 5 months of intense chemotherapy and sometimes surgery to remove the tumor as well. Some children might get 2 stem cell transplants a few months apart, called tandem stem cell transplants
transplants

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 cancer center where the staff has experience with the procedure and managing the recovery period.

Collecting stem cells before the transplant

For most children with neuroblastoma, their own stem cells are collected and used for the transplant.

To help prepare for stem cell collection, doctors give a medicine called G-CSF (filgrastim), which helps the bone marrow make more stem cells and helps those cells move into the bloodstream.

G-CSF is usually started at the end of a regular cycle of chemo and is given daily. 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.

The child will have a special kind of central venous catheter put in place so the stem cells can be collected during a process called 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 child’s body. Apheresis can take a few 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 collected stem cells are then frozen until the transplant.

The high-dose chemo and transplant procedure
Typically, the child will be admitted to the SCT unit of the hospital on the day before the high-dose chemo begins. They 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 (typically at least several weeks).

The child gets high-dose chemo first. This destroys the cancer cells in the body, as well as the normal cells in the bone marrow. After the chemo, 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. Soon after, they will start making new red blood cells and platelets. Until new blood cells are made, the child is at high risk of infection 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 the ANC 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.

**Possible side effects**

A stem cell transplant can have both short-term and long-term side effects.

**Early or short-term side effects**

The early complications and side effects are usually caused by the high-dose chemo, and they can be severe. They are the result of 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
• Liver problems

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, like low red blood cell and platelet counts, might require blood product transfusions 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:

• 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 Late and Long-term Effects of Neuroblastoma and Its Treatment.

More information about stem cell transplant

To learn more about stem cell transplants, including how they are done and their potential side effects, see Stem Cell Transplant for Cancer.

For more general information about side effects and how to manage them, see Managing Cancer-related Side Effects.

Hyperlinks

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.

**References**


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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?¹), and some are now being used to treat it.

Anti-GD2 monoclonal antibodies

Monoclonal antibodies are lab-made versions of immune system proteins that can attach to a very specific target on cells in the body. These antibodies can be injected into the blood to seek out and attach to cancer cells.

Many neuroblastoma cells have large amounts of a substance called GD2 on their surfaces. Monoclonal antibodies that attach to GD2 can help the body’s immune system find and destroy these cancer cells.

Dinutuximab (Unituxin)

This monoclonal antibody is typically given together with cytokines (immune system hormones) such as GM-CSF and interleukin-2 (IL-2), as well as isotretinoin, to help the body’s immune system recognize and destroy neuroblastoma cells. It is typically used as part of the treatment for children with high-risk neuroblastoma², following a stem cell transplant.

This drug is given as an infusion into a vein (IV) over many hours, for 4 days in a row. This is done about once a month, usually for a total of about 5 cycles of treatment. Other medicines are given before and during each infusion to help with possible side effects such as pain or infusion reactions.

Possible side effects

Dinutuximab can cause side effects, some of which can be serious. Possible side effects include:

- Nerve pain (which can sometimes be severe)
- Leaking of fluid from small blood vessels (which can lead to low blood pressure, fast heart rate, shortness of breath, and swelling)
- Infusion reactions (which can lead to airway swelling, trouble breathing, and low
blood pressure)
• Eye and vision problems
• Fever
• Vomiting
• Diarrhea
• Itching
• Trouble urinating
• Infections
• Low blood cell counts
• Changes in mineral levels in the blood

Other side effects are possible as well. Talk to your child’s treatment team to learn more about the possible side effects and what can be done about them.

**Naxitamab (Danyelza)**

This monoclonal antibody is given together with the cytokine (immune system hormone) GM-CSF to help the body’s immune system recognize and destroy neuroblastoma cells.

Naxitamab can be used in patients who are at least one year old and who have high-risk neuroblastoma that is in their bones or bone marrow and that has come back or started to grow again after initially responding to treatment.

This drug is given as an infusion into a vein (IV) over 30 to 60 minutes on days 1, 3, and 5 of each 4-week cycle. Other medicines are given before and during each infusion to help with possible side effects such as pain or infusion reactions.

**Possible side effects**

Naxitamab can cause side effects, some of which can be serious. Possible side effects include:

• Nerve pain (which can sometimes be severe)
• Infusion reactions (which can lead to airway swelling, trouble breathing, and low blood pressure)
• Eye and vision problems
• Rapid heartbeat
• Fever
• Vomiting
- Cough
- Nausea
- Diarrhea
- Low blood pressure
- Itching
- Trouble urinating
- Infections
- Low blood cell counts
- Changes in mineral levels in the blood

Other side effects are possible as well. Talk to your child's treatment team to learn more about the possible side effects and what can be done about them.

**More information about immunotherapy**

To learn more about how drugs that work on the immune system are used to treat cancer, see [Cancer Immunotherapy](https://www.cancer.org/treatment/treatments-and-side-effects/treatment-types/immunotherapy.html)³.

To learn about some of the side effects listed here and how to manage them, see [Managing Cancer-related Side Effects](https://www.cancer.org/treatment/treatments-and-side-effects/physical-side-effects.html)⁴.

**Hyperlinks**


**References**


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**Treatment of Neuroblastoma by Risk Group**

Treatment for neuroblastoma is largely based on which risk group a child is in. Generally, younger children with smaller tumors are in the lower risk groups, while older children, children with tumors that have spread throughout the body, and children whose tumors have unfavorable features or extra copies of the MYCN gene are in the high-risk group. 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 (especially young infants with small tumors) 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 might be the only treatment needed. 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 surgery, or if the 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 who 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 might be used if the symptoms are not getting better with chemo, are life threatening, or are causing spinal cord compression.

Infants with stage 4S (MS)² 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.

Infants younger than 6 months with small adrenal tumors (which are assumed to be neuroblastomas) can often be watched closely with imaging tests, 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 isn’t needed unless the tumor is not responding well to chemo or if a child's symptoms from the tumor require emergency treatment.

Doctors are also studying 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 tests³ 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 now being done.

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

**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 (in the United States, typically cisplatin, etoposide, vincristine, cyclophosphamide, doxorubicin, and topotecan) given at higher doses than what is used for other risk groups.

Doctors are also studying the use of other treatments in this phase, such as targeted drugs for tumors with ALK gene mutations and MIBG radiotherapy for tumors that take up MIBG.

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 remaining cancer cells in the body. High-dose chemotherapy is given, followed by one or two stem cell transplants. Some research has suggested that giving two stem cell transplants back to back (tandem stem cell transplants) may be better than giving one stem cell transplant. This is now being studied further in clinical trials.

Radiation is often given to the primary tumor site after a stem cell transplant (even if the tumor was removed by surgery) and to any other parts of the body that might still have cancer, based on MIBG scan results.

**Maintenance:** The goal of this phase of treatment is to try to lower the chance that the cancer will come back. Treatment is typically given for about 6 months after
consolidation has been completed, and includes the retinoid drug 13-cis-retinoic acid (isotretinoin), as well as immunotherapy with a monoclonal antibody such as dinutuximab (Unituxin) and immune-activating cytokines (GM-CSF and IL-2).

Recurrent neuroblastoma

If neuroblastoma comes back after initial treatment, it is known as a recurrence or relapse. Treatment of recurrent neuroblastoma depends on many factors, including the initial risk group, 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. Other options might include intensive treatment with high-dose chemotherapy followed by a stem cell transplant, or treatment with the monoclonal antibody naxitamab (Danyelza).

Because these cancers can be hard to treat, clinical trials of newer treatments, such as other monoclonal antibodies, CAR T-cell therapy, or other new anti-cancer drugs, might be another reasonable option. To learn more, see What’s New in Neuroblastoma Research?

Hyperlinks

References


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