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 and Related Drugs 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.

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

- Surgical (open) biopsy
- Surgery to treat neuroblastoma
- Possible risks and side effects of surgery
- More information about Surgery

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[3].

To learn about some of the side effects listed here and how to manage them, see Managing Cancer-related Side Effects[4].

Hyperlinks

1. www.cancer.org/cancer/types/neuroblastoma/detection-diagnosis-staging/how-diagnosed.html
2. www.cancer.org/cancer/types/neuroblastoma/detection-diagnosis-staging/risk-groups.html
3. www.cancer.org/cancer/managing-cancer/treatment-types/surgery.html
4. www.cancer.org/cancer/managing-cancer/side-effects.html

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Park JR, Hogarty MD, Bagatell R, et al. Chapter 23: Neuroblastoma. In: Blaney SM, Adamson PC, Helman LJ, eds. *Pizzo and Poplack's Principles and Practice of Pediatric Oncology*. 8th ed. Philadelphia Pa: Lippincott Williams & Wilkins; 2021.

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Chemotherapy and Related Drugs for Neuroblastoma

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.

- 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 exampa hed. There are oftenffe2 plsed chance of infectionmpa3

Tests will be done to check blood counts before and during treatment.

Liver problems:

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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

– 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

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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 ffec 9 gho35 4s A44.

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 Treatment[3].

MIBG radiotherapy

As described in Tests for Neuroblastoma[4], 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[5].

To learn about some of the side effects listed here and how to manage them, see Managing Cancer-related Side Effects[6].

Hyperlinks

1. www.cancer.org/cancer/types/neuroblastoma/detection-diagnosis-staging/how-diagnosed.html
2. www.cancer.org/cancer/types/neuroblastoma/detection-diagnosis-staging/how-diagnosed.html
3. www.cancer.org/cancer/types/neuroblastoma/after-treatment/long-term-effects.html
4. www.cancer.org/cancer/types/neuroblastoma/detection-diagnosis-staging/how-diagnosed.html
5. www.cancer.org/cancer/managing-cancer/treatment-types/radiation.html
6. www.cancer.org/cancer/managing-cancer/side-effects.html

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High-dose Chemotherapy and Stem Cell Transplant for Neuroblastoma

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[3] 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[4] 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.

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[7].

For more general information about side effects and how to manage them, see Managing Cancer-related Side Effects[8].

Hyperlinks

1. www.cancer.org/cancer/types/neuroblastoma/detection-diagnosis-staging/risk-groups.html
2. www.cancer.org/cancer/managing-cancer/treatment-types/stem-cell-transplant/types-of-transplants.html
3. www.cancer.org/cancer/managing-cancer/making-treatment-decisions/tubes-lines-ports-catheters.html
4. www.cancer.org/cancer/managing-cancer/side-effects/low-blood-counts/infections.html
5. www.cancer.org/cancer/managing-cancer/treatment-types/blood-transfusion-and-donation.html
6. www.cancer.org/cancer/types/neuroblastoma/after-treatment/long-term-effects.html
7. www.cancer.org/cancer/managing-cancer/treatment-types/stem-cell-transplant.html
8. www.cancer.org/cancer/managing-cancer/side-effects.html

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Retinoid Therapy for Neuroblastoma

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

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

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

Possible side effects

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 neuroblastoma[2], 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[3].

To learn about some of the side effects listed here and how to manage them, see Managing Cancer-related Side Effects[4].

Hyperlinks

1. www.cancer.org/cancer/types/neuroblastoma/about/new-research.html
2. www.cancer.org/cancer/types/neuroblastoma/detection-diagnosis-staging/risk-groups.html
3. www.cancer.org/cancer/managing-cancer/treatment-types/immunotherapy.html
4. www.cancer.org/cancer/managing-cancer/side-effects.html

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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 tests[3] to make sure the tumor goes away or does not get bigger. If the tumor does gets 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:

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