

CHAPTER 2A

FACTS ABOUT NEUROBLASTOMA AND RELATED TREATMENTS



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Neuroblastoma (PDQ®): Treatment Patient Version

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General Information About Neuroblastoma

Key Points for This Section

- [Neuroblastoma is a disease in which malignant \(cancer\) cells form in nerve tissue of the adrenal gland, neck, chest, or spinal cord.](#)
- [Possible signs of neuroblastoma include bone pain and a lump in the abdomen, neck, or chest.](#)
- [Tests that examine many different body tissues and fluids are used to detect \(find\) and diagnose neuroblastoma.](#)
- [Certain factors affect prognosis \(chance of recovery\) and treatment options.](#)

Neuroblastoma is a disease in which malignant (cancer) cells form in nerve tissue of the adrenal gland, neck, chest, or spinal cord.

[Neuroblastoma](#) often begins in the [nerve tissue](#) of the [adrenal glands](#). There are two adrenal glands, one on top of each [kidney](#) in the back of the upper [abdomen](#). The adrenal glands produce important [hormones](#) that help control heart rate, [blood](#) pressure, blood sugar, and the way the body reacts to stress. Neuroblastoma may also begin in the chest, in nerve tissue near the spine in the neck, or in the [spinal cord](#).

Neuroblastoma most often begins during early childhood, usually in children younger than 5 years. It sometimes forms before birth but is usually found later, when the tumor begins to grow and cause symptoms. In rare cases, neuroblastoma may be found before birth by fetal ultrasound.

By the time neuroblastoma is diagnosed, the cancer has usually metastasized (spread), most often to the lymph nodes, bones, bone marrow, liver, and skin.

Possible signs of neuroblastoma include bone pain and a lump in the abdomen, neck, or chest.

The most common symptoms of neuroblastoma are caused by the tumor pressing on nearby tissues as it grows or by cancer spreading to the bone. These and other symptoms may be caused by neuroblastoma or by other conditions. A doctor should be consulted if any of the following problems occur:

- Lump in the abdomen, neck, or chest.
- Bulging eyes.
- Dark circles around the eyes ("black eyes").
- Bone pain.
- Swollen stomach and breathing problems in infants.
- Painless, bluish lumps under the skin in infants.
- Weakness or paralysis (loss of ability to move a body part).

Less common signs of neuroblastoma include the following:

- Fever.
- Shortness of breath.
- Feeling tired.
- Easy bruising or bleeding.
- Petechiae (flat, pinpoint spots under the skin caused by bleeding).
- High blood pressure.
- Severe watery diarrhea.
- Jerky muscle movements.
- Uncontrolled eye movement.
- Swelling of the legs, ankles, feet, or scrotum.

Tests that examine many different body tissues and fluids are used to detect (find) and diagnose neuroblastoma.

The following tests and procedures may be used:

- Physical exam and history: An exam of the body to check general signs of health, including checking for signs of disease, such as lumps or anything else that seems unusual. A history of the patient's health habits and past illnesses and treatments will also be taken.
- Twenty-four-hour urine test: A test in which urine is collected for 24 hours to measure the amounts of certain substances. An unusual (higher or lower than normal) amount of a substance can be a sign of disease in the organ or tissue that produces it. A higher than normal amount of the substances homovanillic acid (HMA) and vanillyl mandelic acid (VMA) may be a sign of neuroblastoma.
- Blood chemistry study: A procedure in which a blood sample is checked to measure the amounts of certain substances released into the blood by organs and tissues in the body. An unusual (higher or lower than normal) amount of a substance can be a sign of disease in the organ or tissue that produces it. A higher than normal amount of the hormones dopamine and norepinephrine may be a sign of neuroblastoma.
- Cytogenetic analysis: A test in which cells in a sample of tumor tissue are viewed under a microscope to look for certain changes in the chromosomes.
- Bone marrow aspiration and biopsy: The removal of a small piece of bone and bone marrow by

inserting a needle into the hipbone or breastbone. A pathologist views both the bone and the bone marrow samples under a microscope to look for abnormal cells.

- Biopsy: The removal of cells or tissues so they can be viewed under a microscope to check for signs of cancer.
- X-ray: An x-ray is a type of energy beam that can go through the body and onto film, making a picture of areas inside the body.
- CT scan (CAT scan): A procedure that makes a series of detailed pictures of areas inside the body, taken from different angles. The pictures are made by a computer linked to an x-ray machine. A dye may be injected into a vein or swallowed to help the organs or tissues show up more clearly. This procedure is also called computed tomography, computerized tomography, or computerized axial tomography.
- Neurological exam: A series of questions and tests to check the brain, spinal cord, and nerve function. The exam checks a person's mental status, coordination, ability to walk normally, and how well the muscles, senses, and reflexes work. This may also be called a neuro exam or a neurologic exam.
- Ultrasound: A procedure in which high-energy sound waves (ultrasound) are bounced off internal tissues or organs and make echoes. The echoes form a picture of body tissues called a sonogram.
- Immunohistochemistry study: A procedure in which dyes or enzymes are added to a blood or bone marrow sample to test for certain antigens (proteins that stimulate the body's immune response).

Certain factors affect prognosis (chance of recovery) and treatment options.

The prognosis (chance of recovery) and treatment options depend on the following:

- Age of the child when diagnosed.
- Stage of the cancer.
- Where the tumor is in the body.
- Tumor histology (the shape, function, and structure of the tumor cells).

Prognosis is also affected by tumor biology. In neuroblastoma, tumor biology is described according to the following:

- The patterns of the tumor cells.
- How different the tumor cells are from normal cells.
- How fast the tumor cells are growing.
- The number of chromosomes in the tumor cells.
- How many copies of the N-myc gene there are.

The tumor biology is said to be favorable or unfavorable, depending on these factors. A favorable tumor biology means there is a better chance of recovery.

Stages of Neuroblastoma

Key Points for This Section

- After neuroblastoma has been diagnosed, tests are done to find out if cancer has spread from where it started to other parts of the body.
- The following stages are used for neuroblastoma:
 - Stage 1
 - Stage 2
 - Stage 3
 - Stage 4

- Treatment of neuroblastoma is based on risk groups.

After neuroblastoma has been diagnosed, tests are done to find out if cancer has spread from where it started to other parts of the body.

The process used to find out the extent or spread of cancer is called staging. The information gathered from the staging process helps determine the stage of the disease. For neuroblastoma, stage is one of the factors used to plan treatment. The following tests and procedures may be used to determine the stage:

- Bone marrow aspiration and biopsy: The removal of a small piece of bone and bone marrow by inserting a needle into the hipbone or breastbone. A pathologist views both the bone and the bone marrow samples under a microscope to look for signs of cancer.
- Lymph node biopsy: The removal of all or part of a lymph node. A pathologist views the tissue under a microscope to look for cancer cells. One of the following types of biopsies may be done:
 - Excisional biopsy: The removal of an entire lymph node.
 - Incisional biopsy or core biopsy: The removal of part of a lymph node using a wide needle.
 - Needle biopsy or fine-needle aspiration: The removal of a sample of tissue or fluid from a lymph node using a thin needle.
- CT scan (CAT scan): A procedure that makes a series of detailed pictures of areas inside the body, taken from different angles. The pictures are made by a computer linked to an x-ray machine. A dye may be injected into a vein or swallowed to help the organs or tissues show up more clearly. This procedure is also called computed tomography, computerized tomography, or computerized axial tomography.
- MRI (magnetic resonance imaging): A procedure that uses a magnet, radio waves, and a computer to make a series of detailed pictures of areas inside the body. This procedure is also called nuclear magnetic resonance imaging (NMRI).
- X-rays of the chest, bones, and abdomen: An x-ray is a type of energy beam that can go through the body and onto film, making a picture of areas inside the body.
- Ultrasound: A procedure in which high-energy sound waves (ultrasound) are bounced off internal tissues or organs and make echoes. The echoes form a picture of body tissues called a sonogram.
- Radionuclide scan: A procedure to find areas in the body where cells, such as cancer cells, are dividing rapidly. A very small amount of radioactive material is swallowed or injected into a vein and travels through the bloodstream. The radioactive material collects in the bones or other tissues and is detected by a radiation-measuring device.

The following stages are used for neuroblastoma:

Stage 1

In stage 1, the tumor is in only one area and all of the tumor that can be seen is completely removed during surgery.

Stage 2

Stage 2 is divided into stage 2A and 2B.

- Stage 2A: The tumor is in only one area and all of the tumor that can be seen cannot be completely removed during surgery.
- Stage 2B: The tumor is in only one area and all of the tumor that can be seen *may* be completely removed during surgery. Cancer cells are found in the lymph nodes near the tumor.

Stage 3

In stage 3, one of the following is true:

- the tumor cannot be completely removed during surgery and has spread from one side of the body to the other side and may also have spread to nearby lymph nodes; or
- the tumor is in only one area, on one side of the body, but has spread to lymph nodes on the other side of the body; or
- the tumor is in the middle of the body and has spread to tissues or lymph nodes on both sides of the body, and the tumor cannot be removed by surgery.

Stage 4

Stage 4 is divided into stage 4 and stage 4S.

- In stage 4, the tumor has spread to distant lymph nodes, the skin, or other parts of the body.
- In stage 4S, the following are true:
 - the child is younger than 1 year; and
 - the cancer has spread to the skin, liver, and/or bone marrow; and
 - the tumor is in only one area and all of the tumor that can be seen *may* be completely removed during surgery; and/or
 - cancer cells may be found in the lymph nodes near the tumor.

Treatment of neuroblastoma is based on risk groups.

For many types of cancer, stages are used to plan treatment. For neuroblastoma, treatment depends on risk groups. The stage of neuroblastoma is one factor used to determine risk group. Other factors are the age of the child, tumor histology, and tumor biology.

There are 3 risk groups: low risk, intermediate risk, and high risk.

- Low-risk and intermediate-risk neuroblastoma have a good chance of being cured.
- High-risk neuroblastoma may be difficult to cure.

Progressive/Recurrent Neuroblastoma

Progressive neuroblastoma is cancer that has progressed (continued to grow) during treatment. Recurrent neuroblastoma is cancer that has recurred (come back) after it has been treated. The cancer may come back in the same place or in other parts of the body.

Treatment Option Overview

Key Points for This Section

- There are different types of treatment for patients with neuroblastoma.
- Children with neuroblastoma should have their treatment planned by a team of doctors with expertise in treating childhood cancer.
- Four types of standard treatment are used:
 - Surgery
 - Radiation therapy
 - Chemotherapy
 - Watchful waiting

- Other types of treatment are being tested in clinical trials. These include the following:
 - Monoclonal antibody therapy
 - High-dose chemotherapy and radiation therapy with bone marrow transplant or stem cell transplant
 - Other drug therapy

There are different types of treatment for patients with neuroblastoma.

Different types of treatment are available for patients with neuroblastoma. Some treatments are standard (the currently used treatment), and some are being tested in clinical trials. Before starting treatment, patients may want to think about taking part in a clinical trial. A treatment clinical trial is a research study meant to help improve current treatments or obtain information on new treatments for patients with cancer. When clinical trials show that a new treatment is better than the standard treatment, the new treatment may become the standard treatment.

Clinical trials are taking place in many parts of the country. Information about ongoing clinical trials is available from the NCI Web site¹. Choosing the most appropriate cancer treatment is a decision that ideally involves the patient, family, and health care team.

Children with neuroblastoma should have their treatment planned by a team of doctors with expertise in treating childhood cancer.

Your child's treatment will be overseen by a pediatric oncologist, a doctor who specializes in treating children with cancer. The pediatric oncologist may refer you to other pediatric doctors who have experience and expertise in treating children with neuroblastoma and who specialize in certain areas of medicine. These may include the following specialists:

- Medical oncologist/hematologist.
- Pediatric surgeon.
- Radiation oncologist.
- Endocrinologist.
- Neurologist.
- Pediatric nurse specialist.
- Social worker.
- Rehabilitation specialist.

Some cancer treatments cause side effects that continue or appear years after cancer treatment has ended. These are called late effects. Late effects of cancer treatment include physical and mental problems and second cancers. Some late effects may be treated or controlled. It is important that parents of children who are treated for neuroblastoma talk with their doctors about the possible late effects caused by some treatments.

Four types of standard treatment are used:

Surgery

Surgery is usually used to treat neuroblastoma. Depending on where the tumor is and whether it has spread, as much of the tumor as possible will be removed. If the tumor cannot be removed, a biopsy may be done instead.

Radiation therapy

Radiation therapy is a cancer treatment that uses high-energy x-rays or other types of radiation to kill cancer cells. There are two types of radiation therapy. External radiation therapy uses a machine outside the body to send radiation toward the cancer. Internal radiation therapy uses a radioactive substance sealed in needles, seeds, wires, or catheters that are placed directly into or near the cancer. The way the radiation therapy is given depends on the type and stage of the cancer being treated.

Chemotherapy

Chemotherapy is a cancer treatment that uses drugs to stop the growth of cancer cells, either by killing the cells or by stopping the cells from dividing. When chemotherapy is taken by mouth or injected into a vein or muscle, the drugs enter the bloodstream and can reach cancer cells throughout the body (systemic chemotherapy). When chemotherapy is placed directly into the spinal column, an organ, or a body cavity such as the abdomen, the drugs mainly affect cancer cells in those areas (regional chemotherapy). The way the chemotherapy is given depends on the type and stage of the cancer being treated.

The use of two or more anticancer drugs is called combination chemotherapy.

Watchful waiting

Watchful waiting is closely monitoring a patient's condition without giving any treatment until symptoms appear or change.

Other types of treatment are being tested in clinical trials. These include the following:

Monoclonal antibody therapy

Monoclonal antibody therapy is a cancer treatment that uses antibodies made in the laboratory, from a single type of immune system cell. These antibodies can identify substances on cancer cells or normal substances that may help cancer cells grow. The antibodies attach to the substances and kill the cancer cells, block their growth, or keep them from spreading. Monoclonal antibodies are given by infusion. They may be used alone or to deliver drugs, toxins, or radioactive material directly to cancer cells.

High-dose chemotherapy and radiation therapy with bone marrow transplant or stem cell transplant

High-dose chemotherapy and radiation therapy with bone marrow transplant or stem cell transplant is a method of giving high doses of chemotherapy and radiation therapy and replacing blood-forming cells destroyed by the cancer treatment. Stem cells (immature blood cells) are removed from the blood or bone marrow of the patient or a donor and are frozen and stored. After chemotherapy and radiation therapy are completed, the stored stem cells are thawed and given back to the patient through an infusion. These reinfused stem cells grow into (and restore) the body's blood cells.

Other drug therapy

13-cis retinoic acid is a vitamin-like drug that slows the cancer's ability to make more cancer cells and changes how these cells look and act.

This summary section refers to specific treatments under study in clinical trials, but it may not mention every new treatment being studied. Information about ongoing clinical trials is available from the NCI Web site¹.

Treatment Options for Neuroblastoma

Low-Risk Neuroblastoma

Treatment of low-risk neuroblastoma may include the following:

- Surgery followed by watchful waiting.
- Watchful waiting alone for certain infants.
- Surgery followed by chemotherapy, when less than half of the tumor is removed or when serious symptoms cannot be relieved by surgery.
- Radiation therapy to treat tumors that are causing serious problems and do not respond quickly to chemotherapy.
- Low-dose chemotherapy.

Information about ongoing clinical trials is available from the NCI Web site¹.

Intermediate-Risk Neuroblastoma

Treatment of intermediate-risk neuroblastoma may include the following:

- Chemotherapy.
- Chemotherapy followed by surgery and/or radiation therapy.
- Radiation therapy to treat tumors that are causing serious problems and do not respond quickly to chemotherapy.

High-Risk Neuroblastoma

Treatment of high-risk neuroblastoma may include the following:

- High-dose chemotherapy followed by surgery to remove as much of the tumor as possible.
- Radiation therapy to the tumor site and, if needed, to other parts of the body with cancer.
- Bone marrow or stem cell transplant.
- Chemotherapy followed by 13-cis retinoic acid.
- A clinical trial of monoclonal antibody therapy after chemotherapy.
- A clinical trial of radiation therapy with radioactive iodine, alone or before stem cell transplant.
- A clinical trial of stem cell transplants.

This summary section refers to specific treatments under study in clinical trials, but it may not mention every new treatment being studied. Information about ongoing clinical trials is available from the NCI Web site¹.

Progressive/Recurrent Neuroblastoma

Patients First Treated for Low-Risk Neuroblastoma

Treatment for recurrent neuroblastoma that is found in one place in the body may include the following:

- Surgery followed by watchful waiting or chemotherapy.
- Chemotherapy.
- High-dose chemotherapy, bone marrow or stem cell transplant, and 13-cis retinoic acid.

Treatment for recurrent neuroblastoma that has spread to other parts of the body may include the following:

- Watchful waiting.
- Surgery followed by chemotherapy.

- Chemotherapy.
- High-dose chemotherapy, bone marrow or stem cell transplant, and 13-cis retinoic acid.
- A clinical trial of a new treatment.

Information about ongoing clinical trials is available from the [NCI Web site](#)¹.

Patients First Treated for Intermediate-Risk Neuroblastoma

For recurrent neuroblastoma that is found in one place in the body, treatment is usually surgery, with or without chemotherapy.

For recurrent neuroblastoma that has spread to other parts of the body, treatment is usually high-dose chemotherapy, bone marrow or stem cell transplant, and 13-cis retinoic acid.

Patients First Treated for High-Risk Neuroblastoma

Treatment of recurrent neuroblastoma in patients first treated for high-risk neuroblastoma may include the following:

- A clinical trial of chemotherapy followed by monoclonal antibody therapy.
- A clinical trial of radiation therapy with radioactive iodine, alone or before stem cell transplant.
- A clinical trial of stem cell transplants.

This summary section refers to specific treatments under study in clinical trials, but it may not mention every new treatment being studied. Information about ongoing clinical trials is available from the [NCI Web site](#)¹.

Changes to This Summary (12/16/2004)

The PDQ cancer information summaries are reviewed regularly and updated as new information becomes available. This section describes the latest changes made to this summary as of the date above.

Changes were made to this summary to match those made to the health professional version.

To Learn More

Call

For more information, U.S. residents may call the National Cancer Institute's (NCI's) Cancer Information Service toll-free at 1-800-4-CANCER (1-800-422-6237) Monday through Friday from 9:00 a.m. to 4:30 p.m. Deaf and hard-of-hearing callers with TTY equipment may call 1-800-332-8615. The call is free and a trained Cancer Information Specialist is available to answer your questions.

Web sites and Organizations

The [NCI Web site](#)² provides online access to information on cancer, clinical trials, and other Web sites and organizations that offer support and resources for cancer patients and their families. There are also many other places where people can get materials and information about cancer treatment and services. Local hospitals may have information on local and regional agencies that offer information about finances, getting to and from treatment, receiving care at home, and dealing with problems associated with cancer treatment.

Publications

The NCI has booklets and other materials for patients, health professionals, and the public. These

publications discuss types of cancer, methods of cancer treatment, coping with cancer, and clinical trials. Some publications provide information on tests for cancer, cancer causes and prevention, cancer statistics, and NCI research activities. NCI materials on these and other topics may be ordered online or printed directly from the [NCI Publications Locator](#)¹. These materials can also be ordered by telephone from the Cancer Information Service toll-free at 1-800-4-CANCER (1-800-422-6237), TTY at 1-800-332-8615.

LiveHelp

The NCI's LiveHelp service, a program available on several of the Institute's Web sites, provides Internet users with the ability to chat online with an Information Specialist. The service is available from 9:00 a.m. to 11:00 p.m. Eastern time, Monday through Friday. Information Specialists can help Internet users find information on NCI Web sites and answer questions about cancer.

Write

For more information from the NCI, please write to this address:

NCI Public Inquiries Office
Suite 3036A
6116 Executive Boulevard, MSC8322
Bethesda, MD 20892-8322

About PDQ

PDQ is a comprehensive cancer database available on NCI's Web site.

PDQ is the National Cancer Institute's (NCI's) comprehensive cancer information database. Most of the information contained in PDQ is available online at [NCI's Web site](#)². PDQ is provided as a service of the NCI. The NCI is part of the National Institutes of Health, the federal government's focal point for biomedical research.

PDQ contains cancer information summaries.

The PDQ database contains summaries of the latest published information on cancer prevention, detection, genetics, treatment, supportive care, and complementary and alternative medicine. Most summaries are available in two versions. The health professional versions provide detailed information written in technical language. The patient versions are written in easy-to-understand, nontechnical language. Both versions provide current and accurate cancer information.

The PDQ cancer information summaries are developed by cancer experts and reviewed regularly.

Editorial Boards made up of experts in oncology and related specialties are responsible for writing and maintaining the cancer information summaries. The summaries are reviewed regularly and changes are made as new information becomes available. The date on each summary ("Date Last Modified") indicates the time of the most recent change.

PDQ also contains information on clinical trials.

In the United States, about two-thirds of children with cancer are treated in a clinical trial at some point in their illness. A clinical trial is a study to answer a scientific question, such as whether one treatment is better than another. Trials are based on past studies and what has been learned in the laboratory. Each trial answers certain scientific questions in order to find new and better ways to help cancer patients. During treatment clinical trials, information is collected about new treatments, the risks involved, and how well they do or do not work. If a clinical trial shows that a new treatment is better than one currently being used, the new treatment may become "standard."

Listings of clinical trials are included in PDQ and are available online at [NCI's Web site](#)⁴. Descriptions of

the trials are available in health professional and patient versions. For additional help in locating a childhood cancer clinical trial, call the Cancer Information Service at 1-800-4-CANCER (1-800-422-6237), TTY at 1-800-332-8615.

The PDQ database contains listings of groups specializing in clinical trials.

The Children's Oncology Group (COG) is the major group that organizes clinical trials for childhood cancers in the United States. Information about contacting COG is available on the [NCI Web site](#)² or from the Cancer Information Service at 1-800-4-CANCER (1-800-422-6237), TTY at 1-800-332-8615.

The PDQ database contains listings of cancer health professionals and hospitals with cancer programs.

Because cancer in children and adolescents is rare, the majority of children with cancer are treated by health professionals specializing in childhood cancers, at hospitals or cancer centers with special facilities to treat them. The PDQ database contains listings of health professionals who specialize in childhood cancer and listings of hospitals with cancer programs. For help locating childhood cancer health professionals or a hospital with cancer programs, call the Cancer Information Service at 1-800-4-CANCER (1-800-422-6237), TTY at 1-800-332-8615.