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Neuroblastoma Causes, Risk Factors, and Prevention

Risk Factors

A risk factor is anything that affects your chance of getting a disease such as cancer. Learn more about the risk factors for neuroblastoma.

- [Risk Factors for Neuroblastoma](#)
- [What Causes Neuroblastoma?](#)

Prevention

The risk of many adult cancers can be reduced with certain lifestyle changes , but at this time there are no known ways to prevent most cancers in children.

The only known risk factors for neuroblastoma cannot be changed. There are no known lifestyle-related or environmental causes of neuroblastoma at this time.

- [Can Neuroblastoma Be Prevented?](#)

Risk Factors for Neuroblastoma

A risk factor is anything that affects your chance of getting a disease such as cancer. Different cancers have different risk factors.

Lifestyle-related risk factors such as body weight, physical activity, diet, and tobacco use play a major role in many adult cancers. But these factors usually take many years to influence cancer risk, and they are not thought to play much of a role in childhood cancers, including neuroblastomas.

No environmental factors (such as being exposed during the mother's pregnancy or in early childhood) are known to increase the chance of getting neuroblastoma.

Age

Neuroblastoma is most common in very young children, but it is still rare even in this age group. It is very rare in people over the age of 10 years.

Heredity

In about 1% to 2% of all neuroblastomas, children inherit an increased risk of developing neuroblastoma from a parent. But most neuroblastomas do not seem to be inherited.

Children with the **familial** form of neuroblastoma (those with an inherited tendency to develop this cancer) usually come from families with one or more members who had neuroblastoma as infants. The average age at diagnosis of familial cases is younger than the age for **sporadic** (not inherited) cases.

Children with familial neuroblastoma sometimes develop 2 or more of these cancers in different organs (for example, in both adrenal glands or in more than one [sympathetic ganglion](#)¹). It's important to distinguish neuroblastomas that start in more than one organ from neuroblastomas that have started in one organ and then spread to others (metastatic neuroblastomas). When tumors develop in several places at once it suggests a familial form. This might mean that family members should consider genetic counseling and testing (see [Genetic Testing: What You Need to Know](#)²). Both familial and neuroblastoma that is not inherited can spread to other organs.

Having birth defects (congenital anomalies)

Some studies have shown that children with birth defects might have an increased risk of developing neuroblastoma. Some of the link between birth defects and neuroblastoma might be related to changes in genes that happen during fetal development.

Genes are made of DNA, which is a chemical inside our cells. Genes are instructions that tell our body cells what to do. Fetal development, which happens in a mother's uterus, is also directed by genes that tell the cells how to grow and divide. If cell growth and development doesn't happen normally in the fetus, it can cause a birth defect. Changes in genes that happen during fetal development might contribute to a birth defect and increase the risk of some kinds of childhood cancers, like neuroblastoma. That doesn't mean all children with birth defects will get neuroblastoma. More research is needed to understand the relationship between birth defects and risk of childhood cancer. For more information about genes and causes of neuroblastoma, see [What Causes Neuroblastoma?](#)

Hyperlinks

1. www.cancer.org/cancer/neuroblastoma/about/what-is-neuroblastoma.html
2. www.cancer.org/cancer/cancer-causes/genetics.html

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Brodeur GM, Hogarty MD, Bagatell R, Mosse YP, Maris JM. Neuroblastoma. In: Pizzo PA, Poplack DG, eds. *Principles and Practice of Pediatric Oncology*. 7th ed. Philadelphia Pa: Lippincott Williams & Wilkins; 2016:772–792.

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What Causes Neuroblastoma?

The causes of most neuroblastomas are not known. But researchers have found important differences between neuroblastoma cells and the normal neuroblasts (early forms of nerve cells) from which they develop. They have also found differences between neuroblastomas that are likely to respond to treatment and those that have a poor prognosis (outlook). These differences (known as [prognostic markers](#)¹) are sometimes helpful in choosing the best treatment.

How normal cells become neuroblastoma

Nerve cells and cells of the medulla (center) of the adrenal gland develop from neuroblasts in the fetus. These neuroblasts usually grow and change into mature nerve cells. Neuroblastomas develop when normal fetal neuroblasts do not become mature nerve cells or adrenal medulla cells. Instead, they continue to grow and divide.

Neuroblasts might not have matured completely in babies by the time they are born. Most of these eventually mature into nerve cells or simply die off and do not form neuroblastomas. Sometimes, neuroblasts remaining in very young infants continue to grow and then form tumors. Some can even spread to other parts of the body. But many of these tumors will still eventually mature into nerve tissue or go away on their own.

However, as children get older, it becomes less likely that these cells will mature and more likely that they will grow into a cancer. By the time neuroblastomas are large enough to be felt or cause symptoms, most can no longer mature on their own and will grow and spread unless treated.

The failure of some neuroblasts to mature and to stop growing is due to abnormal DNA inside the cells. DNA is the chemical in each of our cells that makes up our genes, which control how our cells function. The DNA inside our cells is in long string-like structures called chromosomes.

Some genes contain instructions for controlling when our cells grow, divide into new cells, and die:

- Certain genes that help cells grow, divide, or stay alive are called **oncogenes**.
- Genes that help keep cell division under control or cause cells to die at the right time are called **tumor suppressor genes**.

Cancers can be caused by DNA changes that turn on oncogenes or turn off tumor

suppressor genes. These gene changes can be inherited from a parent (as is rarely the case with childhood cancers), or they may happen during a person's lifetime as cells in the body divide to make new cells.

In most cases, neuroblastoma cells have chromosome changes (such as having too many or too few chromosomes or missing part of a chromosome) that are likely to affect certain genes. Scientists are still trying to determine which genes are affected by these chromosome changes, as well as how these changes affect the growth of neuroblastoma cells.

Gene changes in neuroblastoma

In rare cases, neuroblastoma seems to occur because of gene changes inherited from a parent. Inherited changes in certain genes account for most cases of hereditary neuroblastoma:

- *ALK* oncogene changes account for most cases of inherited neuroblastoma.
- Changes in *PHOX2B*, a gene that normally helps nerve cells mature, account for a small number of inherited neuroblastomas.

Still, most neuroblastomas are not caused by inherited DNA changes. They are the result of gene changes that happen at some point during the child's development, sometimes before birth. What causes these gene changes is not known. These changes are found only in the child's cancer cells, so they will not be passed on to his or her children. For example, about 10% to 15% of sporadic (not inherited) neuroblastomas also have changes in the *ALK* gene. In many neuroblastomas the exact genes affected are not known.

Other gene changes seem to affect how quickly a neuroblastoma can grow. Here are some examples of gene changes in neuroblastoma cells and what they can mean about a child's neuroblastoma:

- Neuroblastoma cells sometimes have extra copies of an oncogene called *MYCN* amplification, which is often a sign that the tumor will grow quickly and be harder to treat.
- When the *NTRK1* gene (which makes the TrkA protein) is overactive in the cells of neuroblastomas, it can be sign that a child's neuroblastoma might have a better outlook.
- Neuroblastoma cells in older children are more likely to have changes in the *ATRX* tumor suppressor gene. Tumors with this gene change tend to grow more slowly,

but they are also harder to cure. This may help explain why younger children with neuroblastoma tend to do better long term than children who are older when they are diagnosed.

Researchers have found some of the gene changes that may lead to neuroblastoma, but it's still not clear what causes these changes. Some gene changes may be inherited. Some might have unknown outside causes, but others could just be random events that sometimes happen inside a cell, without having an outside cause. There are no known lifestyle-related or environmental causes of neuroblastomas at this time, so it's important to remember that there is nothing these children or their parents could have done to prevent these cancers.

Hyperlinks

1. www.cancer.org/cancer/neuroblastoma/detection-diagnosis-staging/staging.html

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Brodeur GM, Hogarty MD, Bagatell R, Mosse YP, Maris JM. Neuroblastoma. In: Pizzo PA, Poplack DG, eds. *Principles and Practice of Pediatric Oncology*. 7th ed. Philadelphia Pa: Lippincott Williams & Wilkins; 2016:772–792.

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Can Neuroblastoma Be Prevented?

The risk of many adult cancers can be reduced with certain lifestyle changes (such as staying at a healthy weight or quitting smoking), but at this time there are no known ways to prevent most cancers in children.

The only known **risk factors** for neuroblastoma (age and heredity) cannot be changed. There are no known lifestyle-related or environmental causes of neuroblastomas at this time.

Some studies suggest that having mothers take prenatal multi-vitamins or folic acid might lower the risk of neuroblastoma, but further research is needed to confirm this. Getting care from a doctor during pregnancy is always an important thing to do for the health of your baby.

If there is a history of neuroblastoma in your family, you may want to talk with a [genetic counselor](#)¹ about your children's risks of developing the disease. It is important to remember, though, that familial neuroblastoma is very rare.

Hyperlinks

1. www.cancer.org/cancer/cancer-causes/genetics.html

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Brodeur GM, Hogarty MD, Bagatell R, Mosse YP, Maris JM. Neuroblastoma. In: Pizzo PA, Poplack DG, eds. *Principles and Practice of Pediatric Oncology*. 7th ed. Philadelphia Pa: Lippincott Williams & Wilkins; 2016:772–792.

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