Neuroblastoma - Childhood - Risk Factors [1]

This section has been reviewed and approved by the Cancer.Net Editorial Board [2], 04/2016

ON THIS PAGE: You will find out more about the factors that increase the chance of developing this type of tumor. To see other pages, use the menu.

For most types of cancer, a “risk factor” is anything that increases a person’s chance of developing cancer. Although risk factors can influence the development of cancer, most do not directly cause cancer. Some people with several risk factors never develop cancer, while others with no known risk factors do.

For neuroblastoma, the term “risk factor” is more commonly used to describe the factors that are used to predict how the tumor will grow and how well treatment will work (see Stages and Groups [3]).

Neuroblastoma occurs more often in boys than in girls. So far, no environmental factors have been shown to increase the risk of developing neuroblastoma. Rarely, more than one member of a family is diagnosed with neuroblastoma.

Researchers have found inherited gene mutations (changes) that play a role in the development of neuroblastoma for children with a family history of the disease. Other genetic changes, called single-nucleotide polymorphisms (SNPs), may contribute to the development of neuroblastoma in children who do not have a family history.

Family history and genetic predisposition

Approximately 1% to 2% of children with neuroblastoma have a family history of the disease. Children with an inherited likelihood of neuroblastoma tend to develop the disease, on average, 9 to thirteen months earlier than other children with neuroblastoma. In children who have a

family history of neuroblastoma, the disease may occur in 2 or more organs.

Neuroblastoma tumors have been diagnosed in patients with congenital central hypoventilation syndrome (CCHS), a unique disorder of breathing control associated with Hirschsprung disease (HSCR). CCHS results from germline mutations, which is a mutation that may be passed directly from parent to child or may be a new mutation in the child, in the *paired-like homeobox (PHOX) 2B* gene. Mutations in the *PHOX2B* homeobox gene have also been found in patients with a family history of neuroblastoma, and in most cases are associated with HSCR and CCHS. *PHOX2B* mutations have also been detected rarely (< 2%) in DNA samples from neuroblastoma tumors in patients without any family history.

In most patients with a family history of neuroblastoma, germline mutations in the *anaplastic lymphoma kinase (ALK)* gene are detected. These mutations result in abnormal *ALK* activation. Identical activating *ALK* mutations have also been identified in DNA from neuroblastoma tumors in patients without a family history and in a subset of patients, *ALK* amplification is found in neuroblastoma tumors.

Neuroblastoma has also been diagnosed in several patients who are missing portions of chromosomes 1p and 11q that are thought to prevent tumor growth.

Genetic factors without a family history

The genetic factors that have a role in the development of neuroblastoma in patients who do not have a family history are not well understood. Common copy number variation of germline *NBPF23* has been shown to be associated with neuroblastoma. Genome-wide association studies, comparing germline genomic variables in patients with neuroblastoma to patients without neuroblastoma have identified a number of germline neuroblastoma SNPs that are associated with increased risk of developing neuroblastoma. These include SNPs within or upstream of these genes:

- *CASC15*
- *CASC14*
- *BARD1*
- *LMO1*
- *DUSP12*

- *HSD17B12*
- *DDX4/IL31RA*
- *HACE1*
- *LIN28B*
- Rare variants in *TP53*
- *NEFL*

However, these variants account for only a small portion of the risk for developing neuroblastoma. Read more about the genetics of cancer [4]. Learn more about this topic at the National Institute of Health's website for the National Human Genome Research Institute [5] (please note this link takes you to a separate website).

The next section in this guide is Symptoms and Signs [6]*. It explains what body changes or medical problems this disease can cause. Or, use the menu to choose another section to continue reading this guide.*

Links
[1] http://www.cancer.net/cancer-types/neuroblastoma-childhood/risk-factors
[2] http://www.cancer.net/about-us
[3] http://www.cancer.net/node/19429
[4] http://www.cancer.net/node/24864
[5] https://www.genome.gov/
[6] http://www.cancer.net/node/19427