Neurofibromatosis type 1

Neurofibromatosis type 1 is a condition characterized by changes in skin coloring (pigmentation) and the growth of tumors along nerves in the skin, brain, and other parts of the body. The signs and symptoms of this condition vary widely among affected people.

Beginning in early childhood, almost all people with neurofibromatosis type 1 have multiple café-au-lait spots, which are flat patches on the skin that are darker than the surrounding area. These spots increase in size and number as the individual grows older. Freckles in the underarms and groin typically develop later in childhood.

Most adults with neurofibromatosis type 1 develop neurofibromas, which are noncancerous (benign) tumors that are usually located on or just under the skin. These tumors may also occur in nerves near the spinal cord or along nerves elsewhere in the body. Some people with neurofibromatosis type 1 develop cancerous tumors that grow along nerves. These tumors, which usually develop in adolescence or adulthood, are called malignant peripheral nerve sheath tumors. People with neurofibromatosis type 1 also have an increased risk of developing other cancers, including brain tumors and cancer of blood-forming tissue (leukemia).

During childhood, benign growths called Lisch nodules often appear in the colored part of the eye (the iris). Lisch nodules do not interfere with vision. Some affected individuals also develop tumors that grow along the nerve leading from the eye to the brain (the optic nerve). These tumors, which are called optic gliomas, may lead to reduced vision or total vision loss. In some cases, optic gliomas have no effect on vision.

Additional signs and symptoms of neurofibromatosis type 1 include high blood pressure (hypertension), short stature, an unusually large head (macrocephaly), and skeletal abnormalities such as an abnormal curvature of the spine (scoliosis). Although most people with neurofibromatosis type 1 have normal intelligence, learning disabilities and attention deficit hyperactivity disorder (ADHD) occur frequently in affected individuals.

Frequency

Neurofibromatosis type 1 occurs in 1 in 3,000 to 4,000 people worldwide.

Causes

Mutations in the *NF1* gene cause neurofibromatosis type 1.

The *NF1* gene provides instructions for making a protein called neurofibromin. This protein is produced in many cells, including nerve cells and specialized cells surrounding nerves (oligodendrocytes and Schwann cells). Neurofibromin acts as a tumor suppressor, which means that it keeps cells from growing and dividing too

rapidly or in an uncontrolled way. Mutations in the *NF1* gene lead to the production of a nonfunctional version of neurofibromin that cannot regulate cell growth and division. As a result, tumors such as neurofibromas can form along nerves throughout the body. It is unclear how mutations in the *NF1* gene lead to the other features of neurofibromatosis type 1, such as café-au-lait spots and learning disabilities.

Inheritance Pattern

Neurofibromatosis type 1 is considered to have an autosomal dominant pattern of inheritance. People with this condition are born with one mutated copy of the *NF1* gene in each cell. In about half of cases, the altered gene is inherited from an affected parent. The remaining cases result from new mutations in the *NF1* gene and occur in people with no history of the disorder in their family.

Unlike most other autosomal dominant conditions, in which one altered copy of a gene in each cell is sufficient to cause the disorder, two copies of the *NF1* gene must be altered to trigger tumor formation in neurofibromatosis type 1. A mutation in the second copy of the *NF1* gene occurs during a person's lifetime in specialized cells surrounding nerves. Almost everyone who is born with one *NF1* mutation acquires a second mutation in many cells and develops the tumors characteristic of neurofibromatosis type 1.

Other Names for This Condition

- Neurofibromatosis 1
- NF1
- Peripheral Neurofibromatosis
- Recklinghausen Disease, Nerve
- von Recklinghausen Disease

Diagnosis & Management

Genetic Testing Information

- What is genetic testing?
  /primer/testing/genetictesting
- Genetic Testing Registry: Neurofibromatosis, type 1
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C0027831/

Research Studies from ClinicalTrials.gov

- ClinicalTrials.gov
  https://clinicaltrials.gov/ct2/results?cond=%22neurofibromatosis+type+1%22

Other Diagnosis and Management Resources

- GeneReview: Neurofibromatosis 1
  https://www.ncbi.nlm.nih.gov/books/NBK1109
- MedlinePlus Encyclopedia: Neurofibromatosis-1
  https://medlineplus.gov/ency/article/000847.htm

Additional Information & Resources

Health Information from MedlinePlus

- Encyclopedia: Neurofibromatosis-1
  https://medlineplus.gov/ency/article/000847.htm
- Health Topic: Neurofibromatosis
  https://medlineplus.gov/neurofibromatosis.html

Genetic and Rare Diseases Information Center

- Neurofibromatosis
  https://rarediseases.info.nih.gov/diseases/10420/neurofibromatosis
- Neurofibromatosis type 1
  https://rarediseases.info.nih.gov/diseases/7866/neurofibromatosis-type-1

Additional NIH Resources

- National Human Genome Research Institute
  https://www.genome.gov/14514225/
- National Institute of Neurologic Disorders and Stroke
  https://www.ninds.nih.gov/Disorders/All-Disorders/Neurofibromatosis-Information-Page

Educational Resources

- Boston Children's Hospital
  http://www.childrenshospital.org/conditions-and-treatments/conditions/n/neurofibromatosis
- Centre for Genetics Education (Australia)
  http://www.genetics.edu.au/publications-and-resources/facts-sheets/fact-sheet-45-neurofibromatosis-type-1
- Genetic Science Learning Center, University of Utah
  https://learn.genetics.utah.edu/content/disorders/singlegene/
- JAMA Patient Page
  https://jamanetwork.com/journals/jama/fullarticle/184901
- KidsHealth from the Nemours Foundation
  https://kidshealth.org/en/parents/nf.html

- MalaCards: neurofibromatosis, type i
  https://www.malacards.org/card/neurofibromatosis_type_i
- March of Dimes
  https://www.marchofdimes.org/baby/neurofibromatoses.aspx
- Merck Manual Consumer Version
  https://www.merckmanuals.com/home/children-s-health-issues/neurologic-disorders-in-children/neurofibromatosis
- Orphanet: Neurofibromatosis type 1
  https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=636
- Understanding NF1
  http://www.understandingnf1.org/
- Your Genes Your Health from Cold Spring Harbor Laboratory: Neurofibromatosis
  http://www.ygyh.org/nf/whatisit.htm

Patient Support and Advocacy Resources

- Children's Tumor Foundation (formerly the National Neurofibromatosis Foundation)
  http://www.ctf.org
- National Organization for Rare Disorders (NORD)
  https://rarediseases.org/rare-diseases/neurofibromatosis-type-1-nf1/
- Neurofibromatosis, Inc.
  https://www.nfnetwork.org/
- Resource list from the University of Kansas Medical Center
  http://www.kumc.edu/gec/support/neurofib.html

Clinical Information from GeneReviews

- Neurofibromatosis 1
  https://www.ncbi.nlm.nih.gov/books/NBK1109

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28Neurofibromatosis+1%5BMAJR%5D%29+AND+%28%28neurofibromatosis%5BTI%5D%29+AND+%281+OR+I%5BTI%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+180+days%22%5Bdp%5D

Catalog of Genes and Diseases from OMIM

- NEUROFIBROMATOSIS, TYPE I
  http://omim.org/entry/162200

Medical Genetics Database from MedGen

- Neurofibromatosis, type 1
  https://www.ncbi.nlm.nih.gov/medgen/18013

Sources for This Summary

- Arun D, Gutmann DH. Recent advances in neurofibromatosis type 1. Curr Opin Neurol. 2004 Apr; 17(2):101-5. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/15021234
- Baralle D, Mattocks C, Kalidas K, Elmslie F, Whittaker J, Lees M, Ragge N, Patton MA, Winter RM, ffrench-Constant C. Different mutations in the NF1 gene are associated with Neurofibromatosis-Noonan syndrome (NFNS). Am J Med Genet A. 2003 May 15;119A(1):1-8.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/12707950
- De Luca A, Bottillo I, Sarkozy A, Carta C, Neri C, Bellacchio E, Schirinzi A, Conti E, Zampino G, Battaglia A, Majore S, Rinaldi MM, Carella M, Marino B, Pizzuti A, Digilio MC, Tartaglia M, Dallapiccola B. NF1 gene mutations represent the major molecular event underlying neurofibromatosis-Noonan syndrome. Am J Hum Genet. 2005 Dec;77(6):1092-101. Epub 2005 Oct 26.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/16380919
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1285166/
- Friedman JM. Neurofibromatosis 1. 1998 Oct 2 [updated 2014 Sep 4]. In: Pagon RA, Adam MP, Ardinger HH, Wallace SE, Amemiya A, Bean LJH, Bird TD, Ledbetter N, Mefford HC, Smith RJH, Stephens K, editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2017. Available from http://www.ncbi.nlm.nih.gov/books/NBK1109/
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/20301288
- Hart L. Primary care for patients with neurofibromatosis 1. Nurse Pract. 2005 Jun;30(6):38-43. Review. Erratum in: Nurse Pract. 2005 Jul;30(7):4.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/15944472
- Hüffmeier U, Zenker M, Hoyer J, Fahsold R, Rauch A. A variable combination of features of Noonan syndrome and neurofibromatosis type I are caused by mutations in the NF1 gene. Am J Med Genet A. 2006 Dec 15;140(24):2749-56.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/17103458
- Kandt RS. Tuberous sclerosis complex and neurofibromatosis type 1: the two most common neurocutaneous diseases. Neurol Clin. 2003 Nov;21(4):983-1004. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/14743661
- Levine TM, Materek A, Abel J, O'Donnell M, Cutting LE. Cognitive profile of neurofibromatosis type 1. Semin Pediatr Neurol. 2006 Mar;13(1):8-20. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/16818171
- Reynolds RM, Browning GG, Nawroz I, Campbell IW. Von Recklinghausen's neurofibromatosis: neurofibromatosis type 1. Lancet. 2003 May 3;361(9368):1552-4. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/12737880
- Rose VM. Neurocutaneous syndromes. Mo Med. 2004 Mar-Apr;101(2):112-6. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/15119108
- Theos A, Korf BR; American College of Physicians; American Physiological Society. Pathophysiology of neurofibromatosis type 1. Ann Intern Med. 2006 Jun 6;144(11):842-9. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/16754926

- Tonsgard JH. Clinical manifestations and management of neurofibromatosis type 1. Semin Pediatr Neurol. 2006 Mar;13(1):2-7. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/16818170
- Ward BA, Gutmann DH. Neurofibromatosis 1: from lab bench to clinic. Pediatr Neurol. 2005 Apr; 32(4):221-8. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/15797177

Reprinted from Genetics Home Reference:
https://ghr.nlm.nih.gov/condition/neurofibromatosis-type-1

Reviewed: July 2012
Published: November 13, 2018

Lister Hill National Center for Biomedical Communications
U.S. National Library of Medicine
National Institutes of Health
Department of Health & Human Services