American Association of Neurological Surgeons

Neurofibromatosis

Patient Information

This resource, developed by neurosurgeons, provides patients and their families trustworthy information on neurosurgical conditions and treatments.

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Neurofibromatosis is a rare genetic disorder that causes typically benign tumors of the nerves and growths in other parts of the body. Some people with this disorder have barely noticeable neurological problems, while others are affected profoundly. There are two major types: **neurofibromatosis type I** (NF1) and **neurofibromatosis type II** (NF2).

NF1 manifests itself at birth or during early childhood. NF1 is characterized by multiple light brown (café-au-lait) spots concentrated in the groin and underarms and benign tumors under the skin. Enlargement and deformity of bones and curvature of the spine (**scoliosis**) may also be present. On occasion, people with NF1 may develop tumors in the brain, on the **cranial nerves** or involving the **spinal cord**.

NF2 may appear during childhood, adolescence or early adulthood. NF2 is primarily characterized by benign tumors of the nerves that transmit sound impulses and balance signals from the inner ears to the brain. Tumors commonly affect both the left and right ("bilateral") auditory (hearing) nerves.

A third, related, disorder, called **schwannomatosis**, has been recognized. While schwannomatosis may share many features with NF1 and NF2, current evidence suggests that it is a distinct genetic disease. This disorder is more frequently diagnosed in adults aged 30 and older.

Causes

NF1 is caused by mutations in the gene that controls production of a protein called neurofibromin (neurofibromin 1). This gene is believed to function as a tumor suppressor. In about 50 percent of people with NF1, the disorder results from gene mutations that occur for unknown reasons ("spontaneous mutation"). In others with the disorder, NF1 is inherited (**"autosomal dominant inheritance pattern,"** see below).

NF2 results from mutations in a different tumor-suppressing gene (neurofibromin 2, **merlin**). Some people with NF2 experience a gene mutation that occurs for unknown reasons ("spontaneous mutation"), while others inherit it from their parent(s) ("autosomal dominant inheritance pattern," see below).

While schwannomatosis is not well-understood, it is estimated that 85 percent of cases have no known cause ("spontaneous") and 15 percent are inherited.

Incidence and Prevalence

- NF1 occurs in approximately one out of every 3,500 births
- NF2 occurs in approximately one out of every 40,000 births
- Schwannomatosis occurs an estimated one out of every 40,000 births
- There is a 50-percent chance that each child of a parent with NF1 or NF2 will inherit the gene and develop NF1 or NF2 (respectively) — this is known as autosomal dominant inheritance pattern
- Tumors in these disorders are overwhelmingly benign; they may be/become malignant in 3 to 5 percent of all cases
- About one-third of people with NF notice no symptoms

Other Names

Neurofibromatosis Type I (NF1)

- Von Recklinghausen's Disease
- Von Recklinghausen's Phakomatosis
- Von Recklinghausen's Neurofibromatosis
- Neurofibroma, multiple
- Neurofibromatosis-pheochromocytoma-duodenal carcinoid syndrome
- Peripheral Neurofibromatosis

Neurofibromatosis Type II (NF2)

- Bilateral Acoustic Neurofibromatosis
- Vestibular Schwannoma Neurofibromatosis
- Central Neurofibromatosis

Diagnostic Criteria/Signs of NF1

- Family history of NF1
- Six or more café-au-lait spots on the skin
- Freckling under the arms or in the groin area
- Presence of pea-sized bumps (neurofibromas) on/just under the skin
- Larger areas on/under the skin that appear swollen (**plexiform neurofibromas**)
- Pigmented bumps on the eye's iris (Lisch nodules)
- Skeletal abnormalities, such as bowing of the legs (**tibial dysplasia**), thinning of the shin bone, scoliosis
- Tumor on the optic nerve that may interfere with vision

Café-au-lait spots are most common on the chest, back, pelvis, elbows and knees. These spots may exist at birth or appear during infancy. Between ages 10 and 15, flesh-colored growths of different sizes and shapes may begin to appear on the skin. There may be fewer than 10 of these growths or thousands of them.

Additional features may include an unusually large head (**macrocephaly**) and relatively short stature. Seizures may occur, learning disabilities, speech problems or hyperactivity may be experienced.

Diagnostic Criteria/Signs of NF2

- Bilateral vestibular schwannomas (VS), also called acoustic neuromas, are definitive signs of NF2
- Probable signs of NF2 include family history of NF2, unilateral VS or any two of the following: meningioma, glioma, schwannoma, juvenile posterior subcapsular lenticular opacity, juvenile cortical cataracts

Depending on the exact location and size of the VS, any of the following may occur, alone or in combination with:

- Balance problems
- Walking problems
- Dizziness
- Headache
- Hearing loss
- Facial weakness
- Numbness or pain
- Ringing in ears (tinnitus)

Diagnostic Criteria/Signs of Schwannomatosis

- Definitive signs (age 30 or older) include showing no evidence of vestibular tumors on an MRI, having no known NF2 mutation and having two or more schwannomas within, or between, layers of the skin (with at least one that is confirmed by tissue pathology)
- One pathologically confirmed schwannoma and a first-degree relative who meets the above criteria is also a definitive sign of schwannomatosis
- About one-third of people with schwannomatosis have segmental schwannomatosis, with tumors limited to one part of the body (such as an arm, leg or a region of the spine)

Treatment and Management

Children with NF1 should be checked for height, weight, head circumference, evidence of normal sexual development, signs of learning disability and/or behavioral issues. They should receive an examination of the skin for growths, spots, scoliosis, blood pressure, vision and screening for hearing loss. Any unusual growth patterns are generally investigated. Early or late onset of puberty also may indicate further study. Diagnostic evaluations such as blood tests and X-rays may be ordered if there are additional concerns. Healthy children with NF1 are usually examined at six or 12-month intervals.

Adults with NF1 generally have standard physical evaluations and an examination of the skin for growths, spots, scoliosis, blood pressure, vision and screening for hearing loss. Physicians should also be on the lookout for any new or enlarging mass or any new symptoms in general. Adults with NF1, who are otherwise healthy, usually have annual checkups.

There is no known treatment or cure for neurofibromatosis, nor for schwannomatosis. In some cases, growths may be removed surgically or reduced with radiation therapy. Surgery in these areas may cause further injury to nerves and additional neurological problems. The benefits of surgery should always be weighed against its risks. Likewise, in situations where radiation treatment is an option, the risks and benefits must be carefully considered.

Neurofibromatosis Resources

- **Acoustic Neuroma Association**
- **The British Columbia Neurofibromatosis Foundation**
- **Cedar-Sinai Medical Genetics-Birth Defects Center**
- **Children's Tumor Foundation: Ending Neurofibromatosis Through Research**
- **Neurofibromatosis Network**

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