

## Condition: Neurofibromatosis

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### Inheritance:

Autosomal Dominant.

### Genetic etiology:

NF1: mutation in *NF1* gene on chromosome 17; NF2: mutation in *NF2* gene on chromosome 22. The NF1 gene product is neurofibromin, a GTPase activating protein; the NF2 gene product is called merlin or schwannomin. Both the *NF1* and *NF2* genes function as tumor suppressors. A third disorder classified with the neurofibromatosis, schwannomatosis, is associated with *SMARCB1* mutations in a proportion of cases; *SMARCB1* encodes a chromatin remodeling protein.

### Frequency:

NF1: 1/3,000; NF2: 1/25,000; schwannomatosis frequency unknown.

### Clinical features:

All three disorders are associated with development of tumors of the nerve sheath. In NF1 these are neurofibromas, whereas in NF2 and schwannomatosis they are schwannomas. Other features of NF1 include café-au-lait spots, intertriginous freckling, skeletal dysplasia, optic glioma, learning disability, and increased risk of malignancy or vascular disease. NF2 is associated with bilateral vestibular schwannomas, schwannomas of other cranial and spinal nerves, meningiomas, ependymomas, and posterior subcapsular cataract. Schwannomatosis is associated with non-vestibular schwannomas and pain.

### Management:

Screening for associated tumors and other features and symptomatic treatment.

### Genetic counseling:

Affected individuals at 50% risk of transmitting a gene mutation; both familial and de novo cases occur. Genetic testing is available, though not all pathogenic mutations can be identified. Penetrance is complete for NF1 and NF2 but incomplete for schwannomatosis.