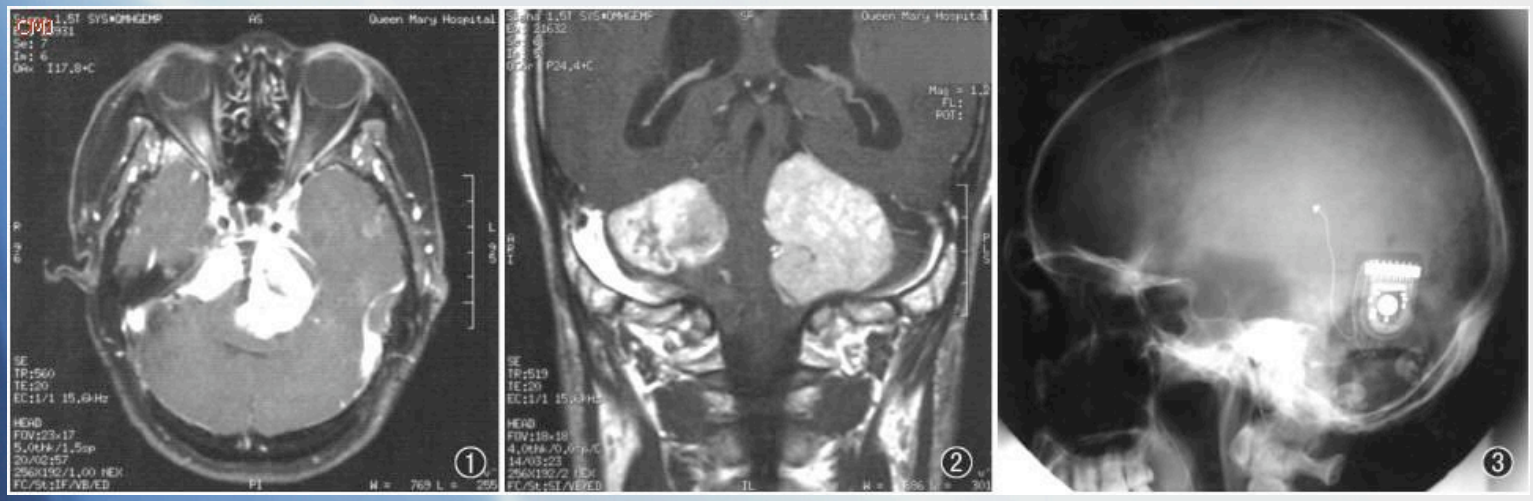
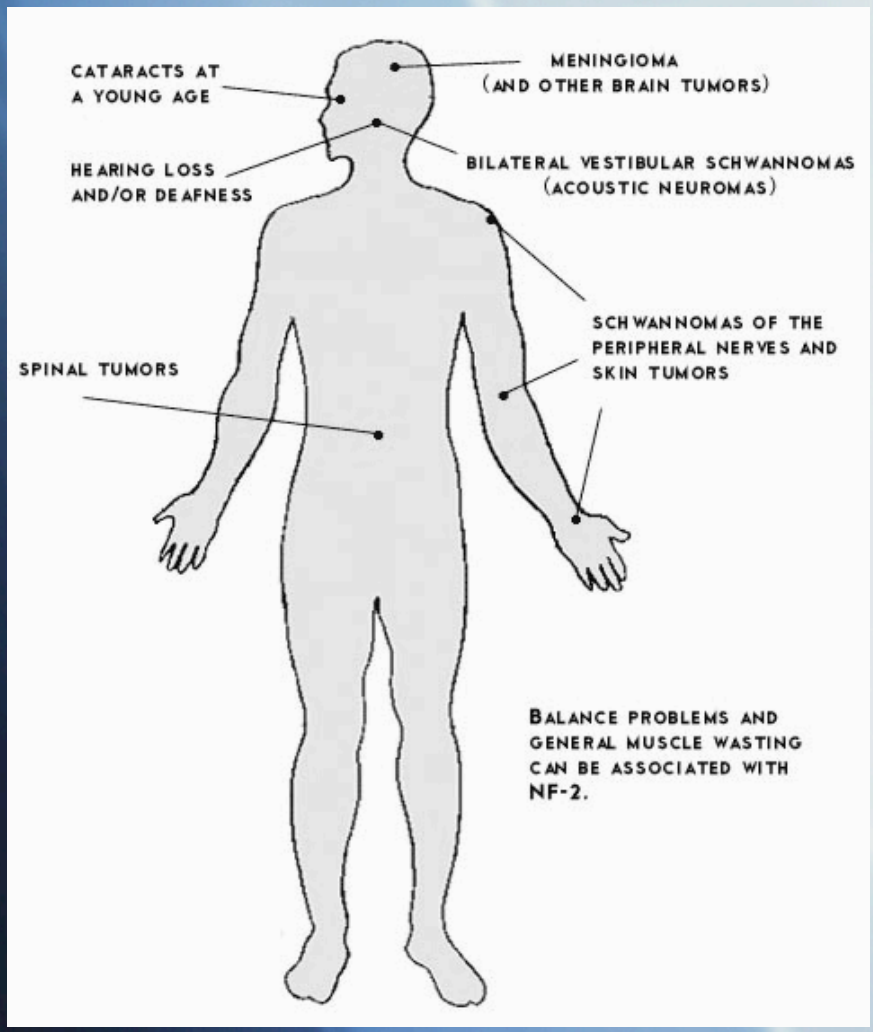
Neurofibromatosis, Type 2



www.cmj.org

Presentation

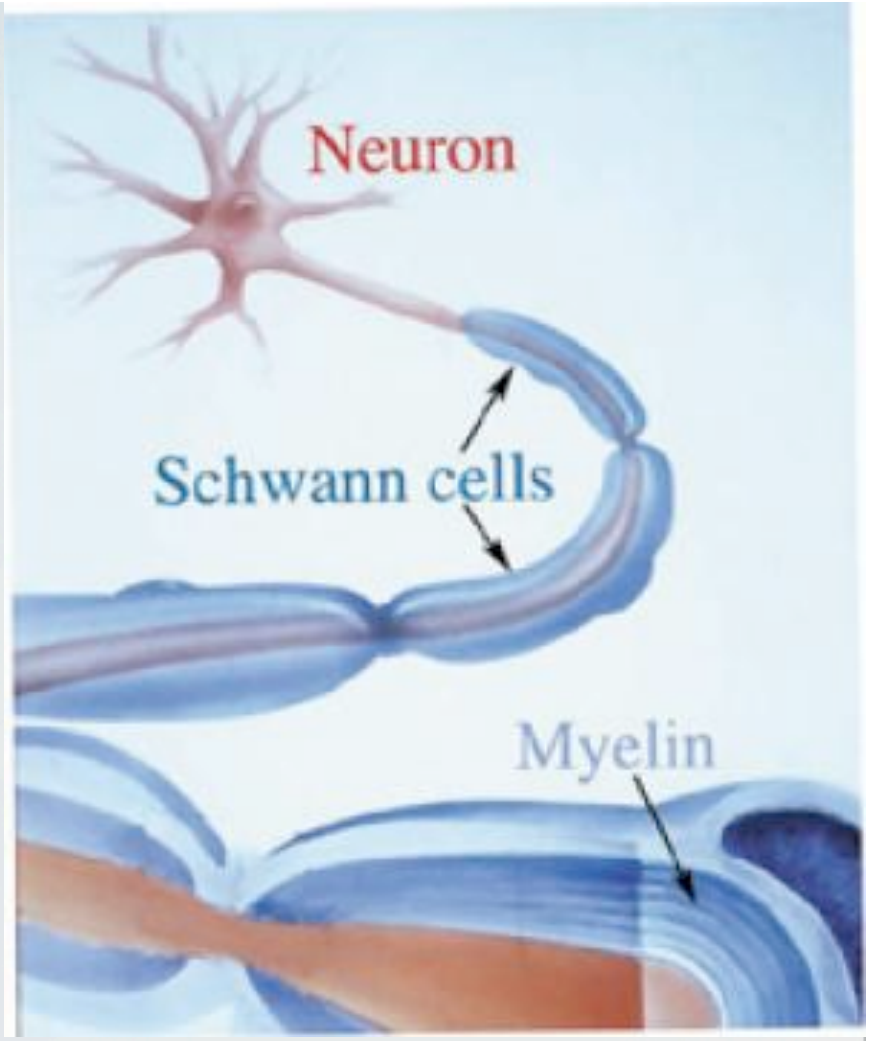


www.dallasnf.org

- Mean age of onset of 20 years
- Bilateral schwannomas of cranial nerve VIII
- Bilateral deafness
- Meningiomas
- Brain stem compression
- Hydrocephaly
- Ependymomas and astrocytomas of the spinal cord (rare)
- Blindness
- Two subsets
  - Gardner (mild)
  - Winshart (severe)

Schwann Cells

Responsible for forming myelin sheath around axons in central and peripheral nervous system.



http://www.sciencedaily.com/releases/2005/09/050902073203.htm

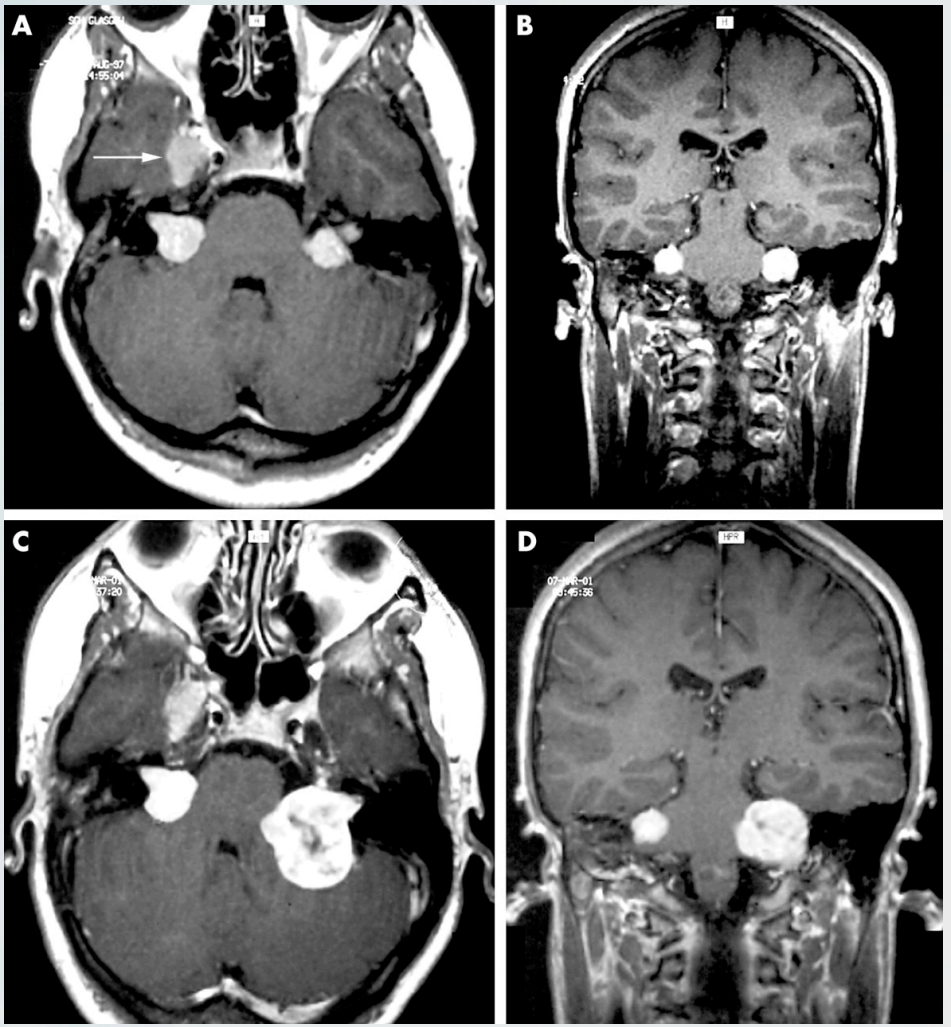
Bilateral vestibular schwannoma

A, B Typical NF2 tumors

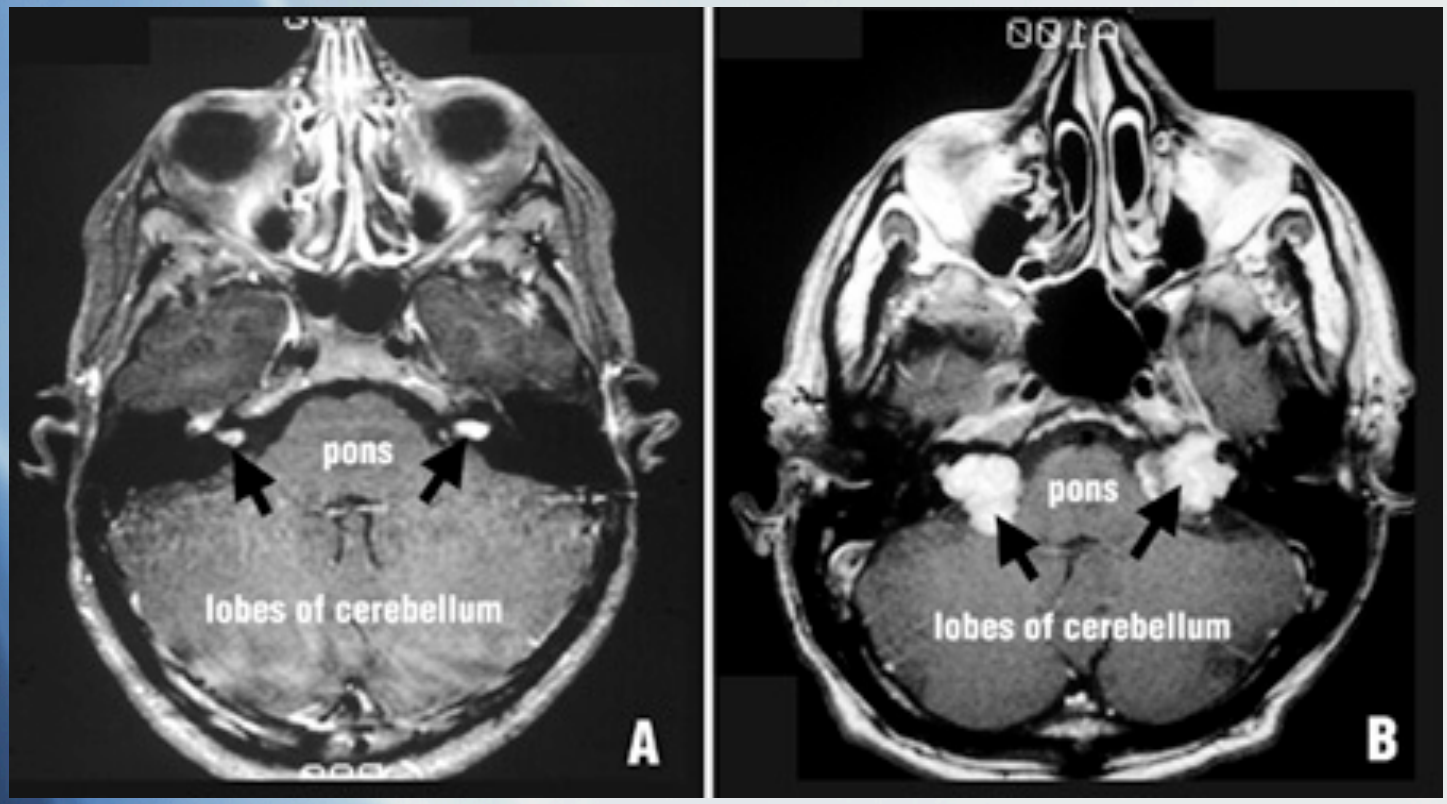
C, D same patient 4 years later

Rapid growth

brain stem compression



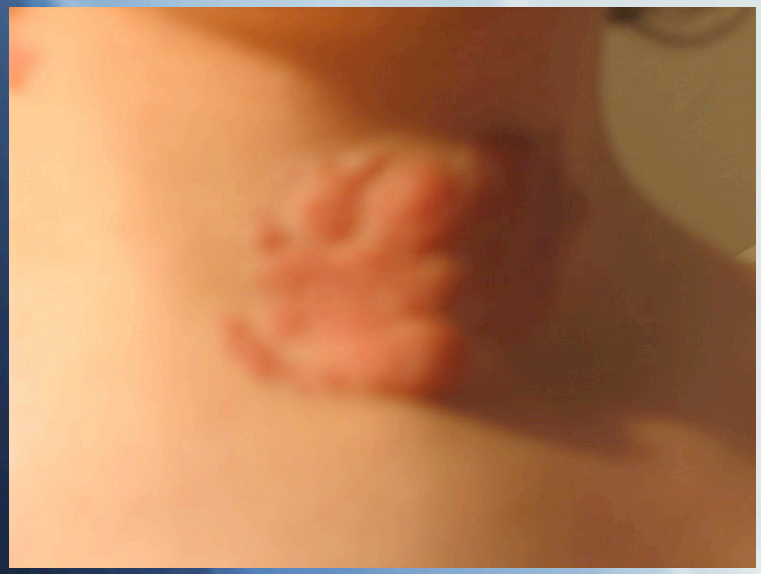
Overell, J et al. J Neurol Neurosurg Psychiatry 2004;75:iv53-iv59



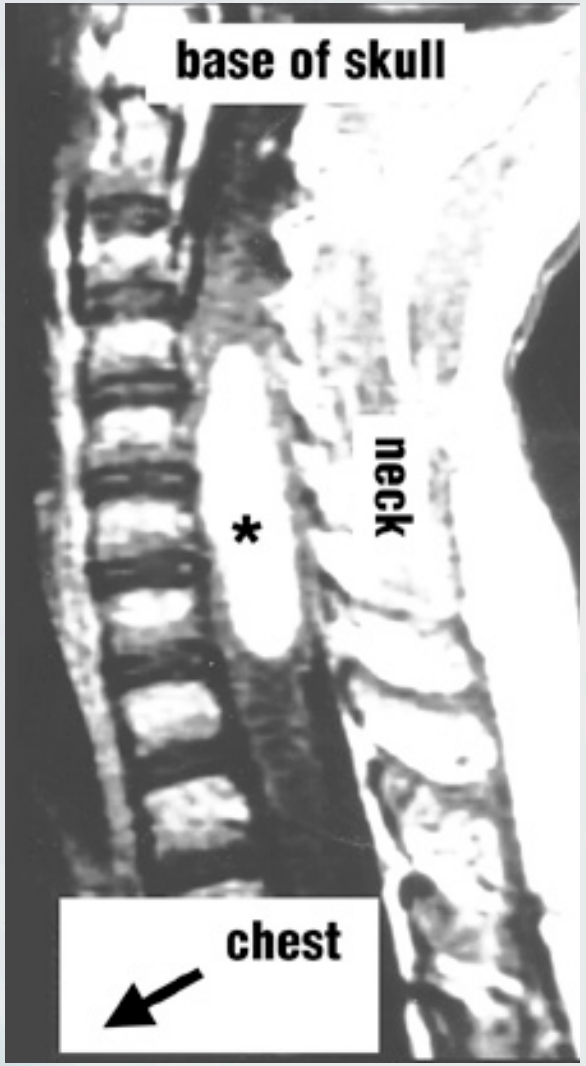
A 14 year old patient with manageable tumors and the 50 year old uncle with more advanced tumor involving the temporal bone and compressing the pons.

http://neurosurgery.mgh.harvard.edu/NFclinic/NF2.htm

Subdural schwannoma associated with NF 2

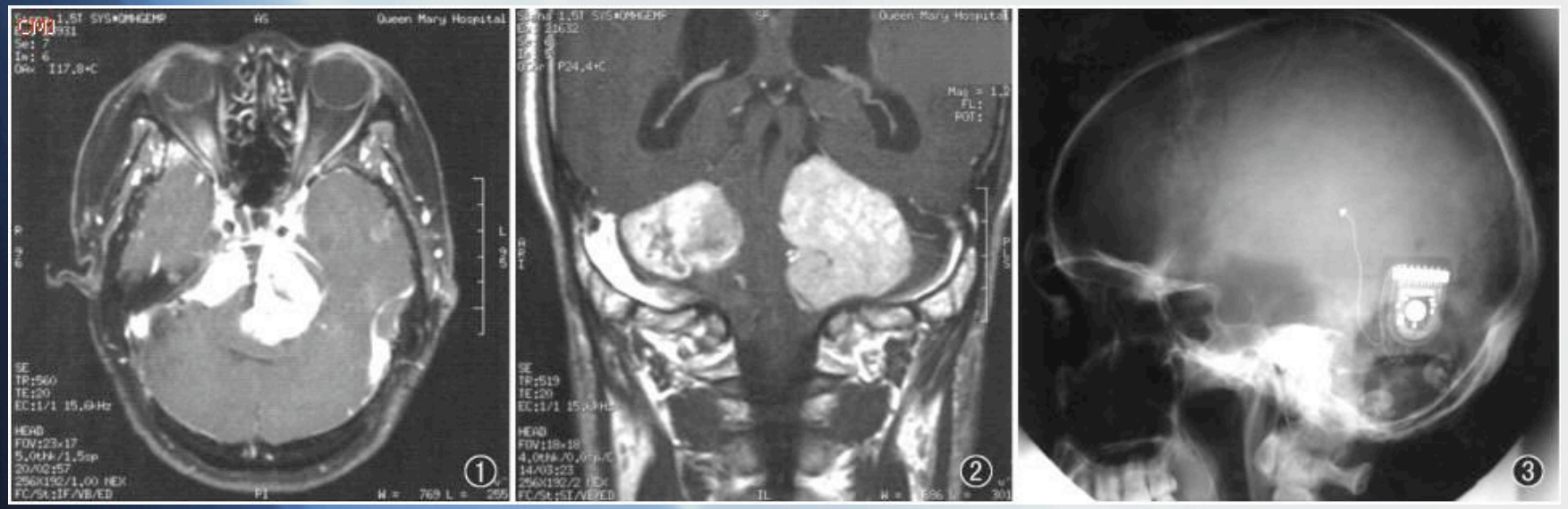


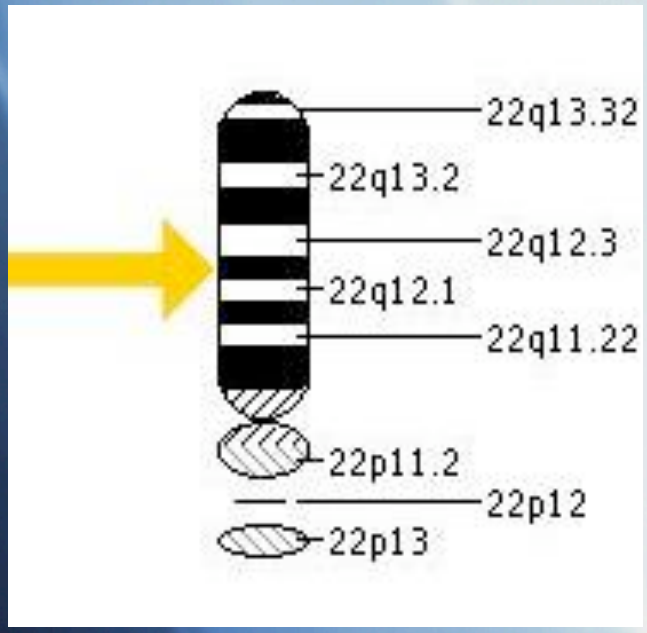
Ependymomas and astrocytomas of the spinal cord



http://neurosurgery.mgh.harvard.edu/NFclinic/NF2.htm

Treatment options
Hearing preservation
Observation without intervention
Stereotactic radiosurgery
Craniotomy
Radiation therapy
Non hearing preservation
Tumor resection
Auditory brain stem implant





http://ghr.nlm.nih.gov/gene=nf2

Genetic Information

Localized to chromosome 22
in 1993 at 22q12.2

Gene codes for structural protein
merlin

Cytoskeletal protein and
tumor suppressor gene

Autosomal dominant inheritance

95% penetrance

Type of Mutation	Number of People*	Number of Families
Nonsense	293	232
Frameshift deletion	159	128
Frameshift insertion	47	41
Indel	10	10
Splice donor site	174	88
Splice acceptor site	150	86
Missense	88	35
In-frame deletion	18	18
In-frame insertion	13	4
Large deletion	141	80
Large insertion	4	3
Chromosomal translocation	15	13
Total	1,112	738

Mutation types and frequencies

Highly diverse range of mutation

No single mutation or mutation type involved

Large deletions, frameshift deletions, and nonsense mutations responsible for most common and severe form

http://www.advocurenf2.org/01_nf2_mutation_types.html

Genomic information's influence on care

Screening available to identify at risk individuals allowing for thorough follow up over years

Genetic testing for definitive diagnosis

No breakthroughs in novel therapies

More focused and effective use of current therapies

References

http://www.dallasnf.org/whatisNF.html

http://neurosurgery.mgh.harvard.edu/NFclinic/NF2.htm

http://www.ncbi.nlm.nih.gov/entrez/dispomim.cgi?id=101000

http://www.ncbi.nlm.nih.gov/entrez/dispomim.cgi?id=607379

http://www.sciencedaily.com/releases/2005/09/050902073203.htm

http://www.cmj.org