CNS pathology
Third year medical students

Dr Heyam Awad 2019

Lecture 14: PNS tumors

Tumours of PNS

- Tumours arising from peripheral nerves can be benign or malignant

- Benign tumours include schwannoma and neurofibroma

- Malignant tumours include: malignant peripheral nerve sheath tumour. (MPNST)

Schwannoma

- Benign , encapsulated tumours that are composed of proliferation of Schwann cells.

- Can arise in soft tissue, internal organs, spinal roots or cranial nerves

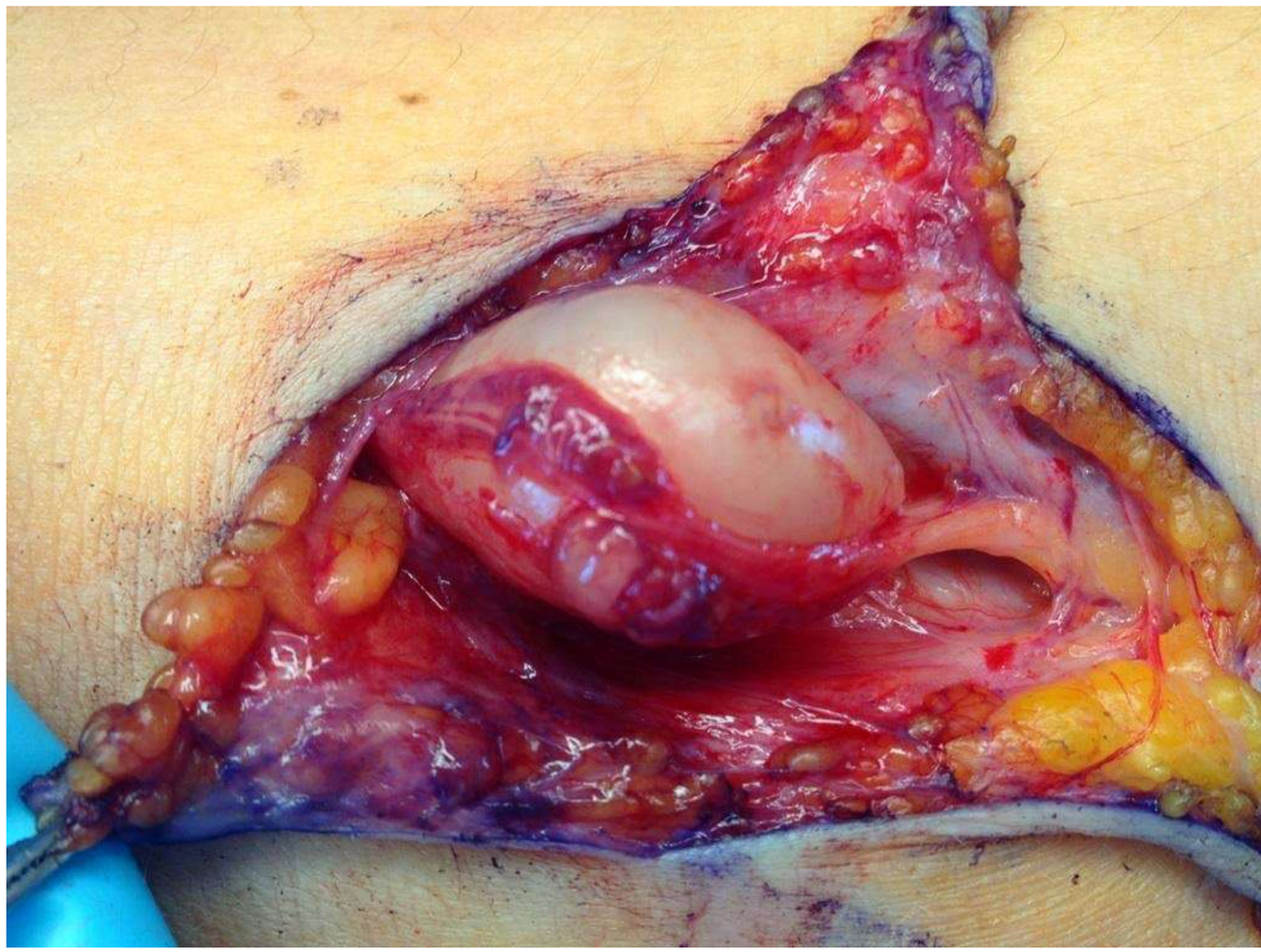
- *the most cranial nerve affected is the eighth cranial nerve which can result in hearing loss*.

- If affecting the 8th cranial nerve it is called acoustic neuroma or vestibular schwannoma.

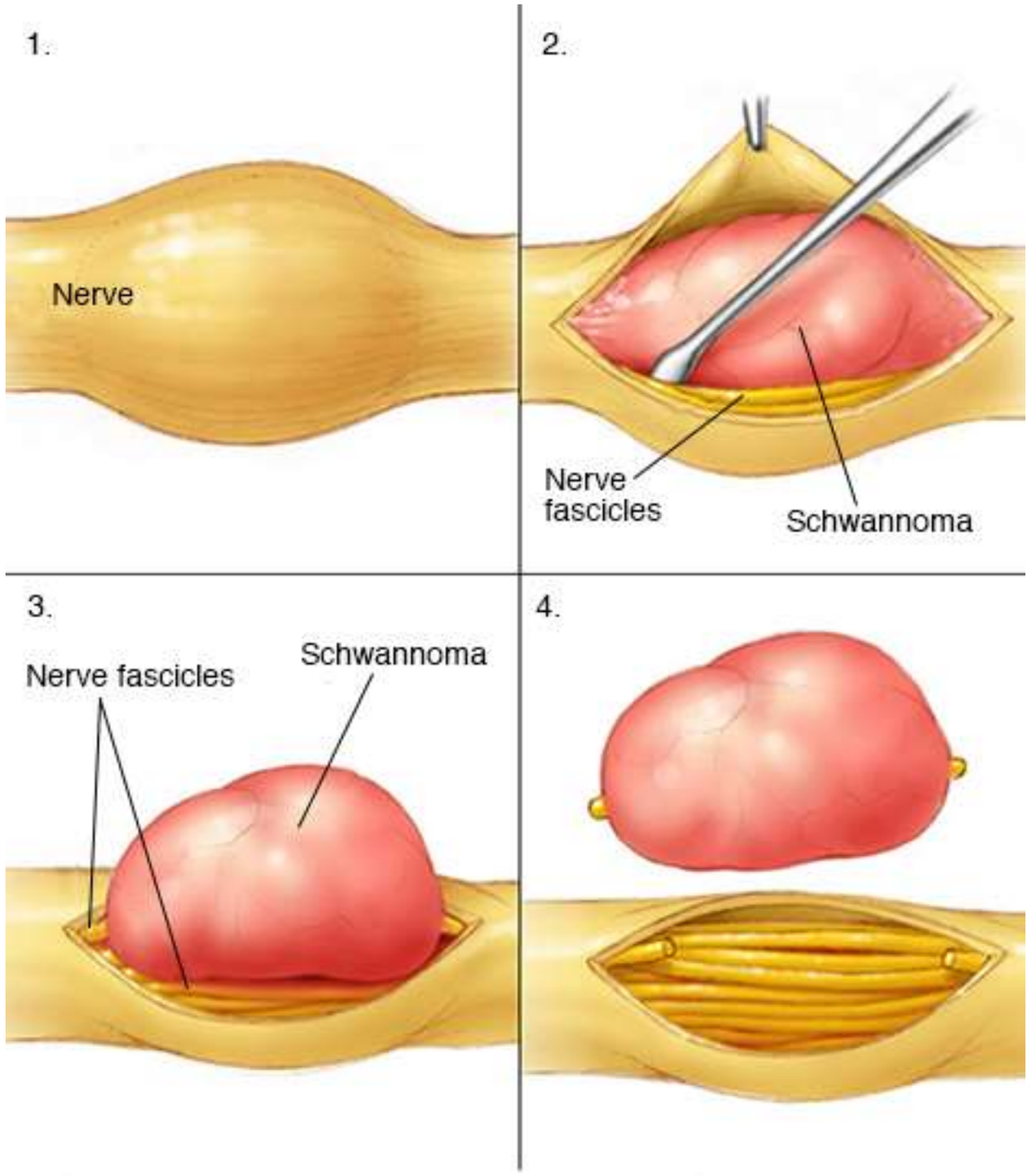
- Shwannomas can be sporadic or familial

Shwannoma

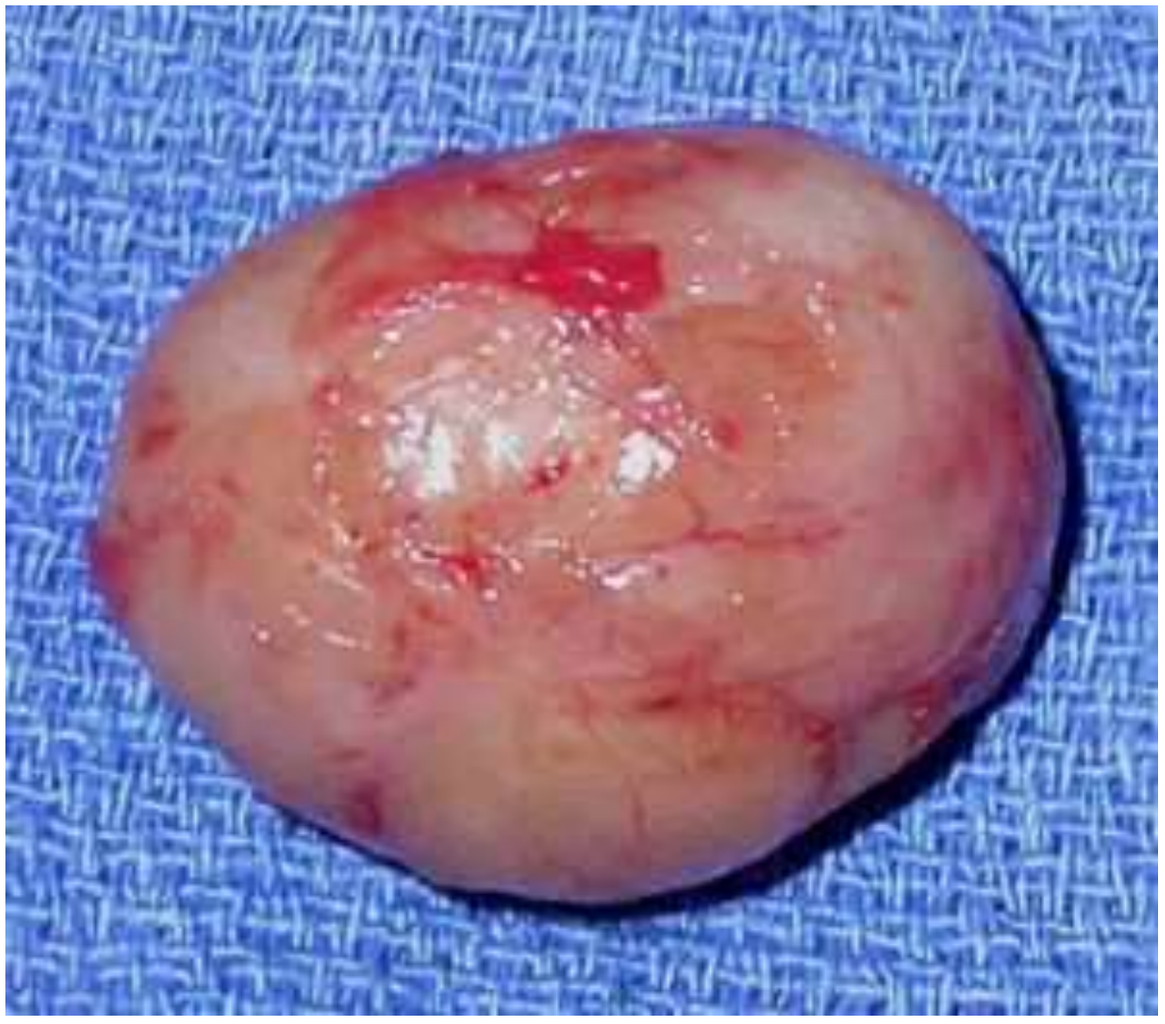
Note that the tumour is well circumscribed, encapsulated and abuts a nerve (as if it hugs the nerve but not actually arsing from it.. this is because it is a proliferation of Schwann cells that are adjacent to the nerve.)



Schwannoma



Schwannoma: note the encapsulation which makes it easy for full surgical removal the tumour



Familial schwannomas

- 10% of schwannomas are familial, these occur in association with **neurofibromatosis type 2.**

- Familial schwannomas are usually **multiple**.

- **the presence of bilateral vestibular schwannoma is a hallmark for NF 2**

- Patients with NF 2 can have **other CNS tumours** like meningiomas and ependymomas

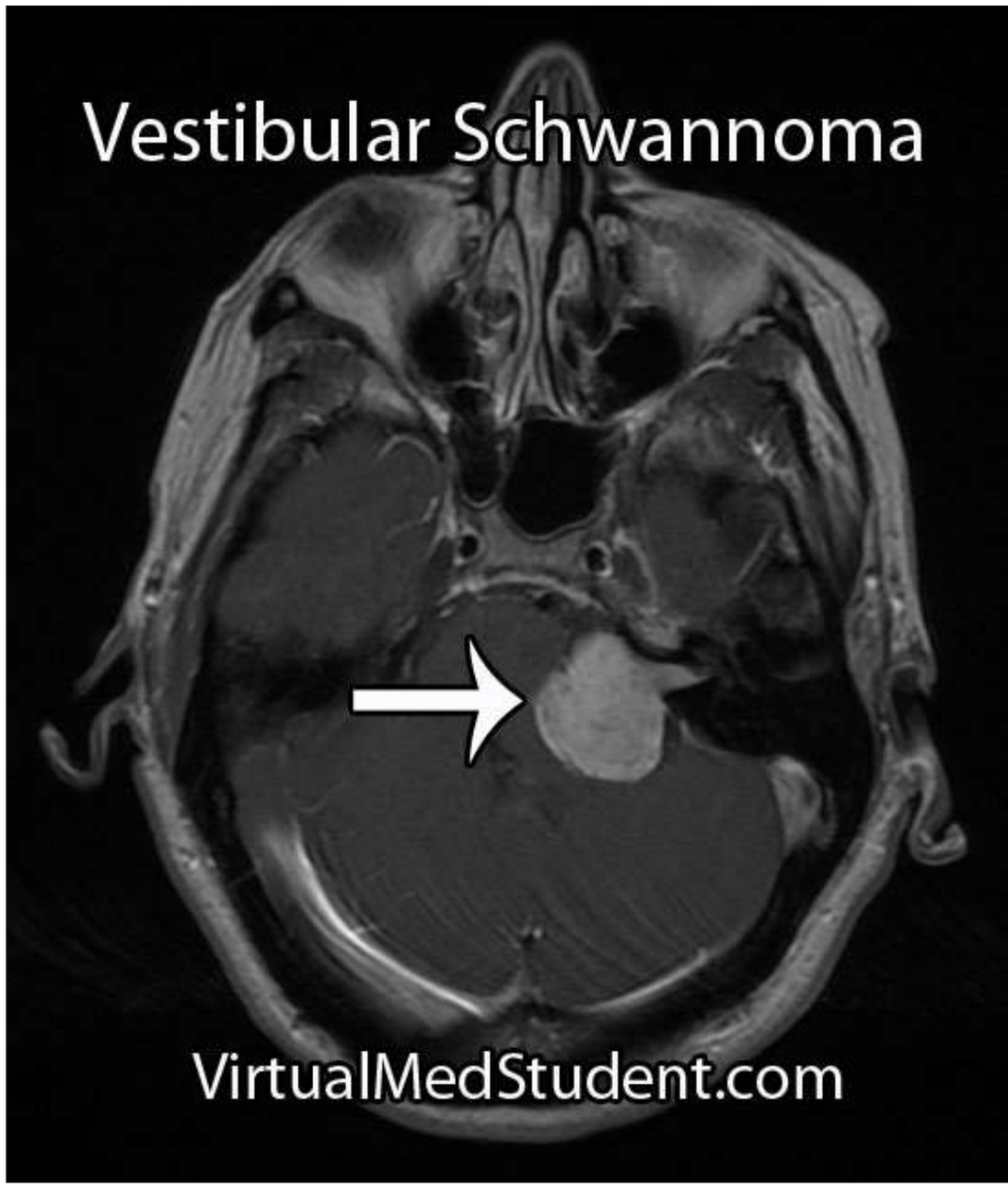
- ***<u>Although the syndrome is called neurofibromatosis, patients do not have neurofibromas!!!!</u>***

Vestibular schwannoma

- Note that vestibular schwannomas can be sporadic or familial.

- if a patient has bilateral vestibular schwannomas , this almost always means that the patient has NF 2

- Note: not all patients with NF2 will have bilateral schwannomas.



Genetic mutation in NF 2

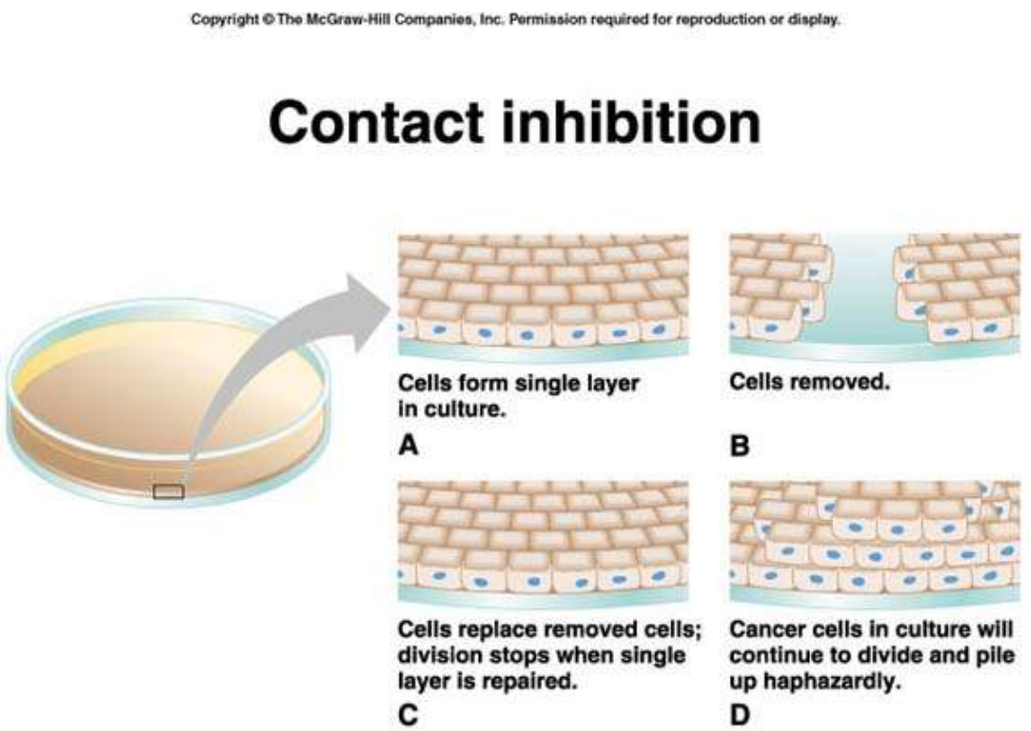
- NF2 is caused by loss of function mutation in **merlin** gene on chromosome 22.

- Merlin is a cytoskeletal protein that is a tumour suppressor gene by facilitating E cadherin mediated contact inhibition.

- **With mutated merlin contact inhibition is lost so tumours can proliferate.**

merlin protein and contact inhibition

- Please remember that contact inhibition is an important process to limit and regulate cell growth
- If contact inhibition is lost growth can go unchecked
- E cadherin is the most important factor causing contact inhibition
- Merlin protein facilitated contact inhibition
- if merlin is lost then contact inhibition is lost and tumours occur
- Loss of function mutation in merlin protein is the underlying genetic defect in NF2



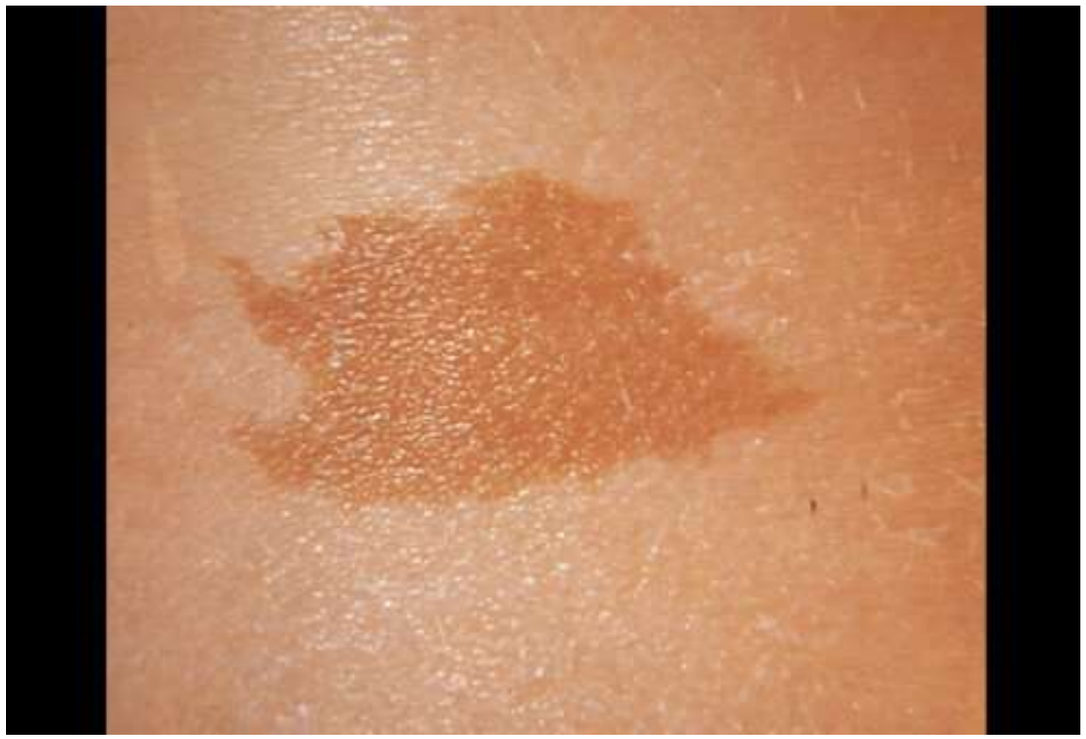
Neurofibroma

- Benign peripheral nerve sheath tumours.
- they are benign but not encapsulated
- Composed of proliferating Schwann cells admixed with other cells including mast cells and fibroblasts.
- Can be sporadic or familial (neurofibromatosis type 1= NF 1)

NF 1

- Autosomal dominant disorder caused by mutation in neurofibromin
- neurofibromin is a tumour supressor gene encoded on chromosome 17. It is a negative regulator of the Ras oncoprotein.
- Patients have multiple neurofibromas, malignant peripheral nerve sheath tumour, optic gliomas, and other glial tumours.
- Patients also have learning disability, seizures, pigmented nodules in the iris and pigmented skin lesions= cafe- au-lait spots.

Cafe-au-lait spots
the word means: coffee with milk, referring to the colour of the spots!



Neurofibromatosis 1: multiple neurofibromas

Malignant peripheral nerve sheath tumour MPNST

- Malignant tumours arising from Schwann cells
- 50% occur in the setting of NF 1
- Histologically: highly cellular, anaplastic, pleomorphic, and show necrosis and a high mitotic rate.

Traumatic neuroma

- if the ends of a cut nerve are not approximated, the regenerating axons might grow in a haphazard fashion, forming a mass called traumatic neuroma.

- So: traumatic neuromas are non-neoplastic masses related to a previous trauma and composed of a haphazard mixture of axons, Schwann cells and connective tissue.

- traumatic neuromas contain abnormal nerve bundles, so the mass is usually **painful.**

Question

- Which of the following patients least likely has neurofibromatosis type 2?
- A. A 30 year old patient suffering from decreased hearing acuity. he was found to have bilateral tumors of the 8th cranial nerves.
- B. A 43 year old woman having an ependymoma. 3 years ago she underwent surgical excision for a meningioma. her mother removed several tumours, all were reported as schwannomas.
- C. A 12 year old boy, who had a genetic test that revealed mutation in the merlin gene.
- D. A 24 year old woman suffering from multiple skin masses which were non-capsulated and composed of proliferation of Schwann cells admixed with fibroblasts and mast cells.

Explanation of the question

- the answer is D. the description of the lesions is that of a neurofibromas, and neurofibromas are not seen in NF 2

summary 1/2

- Traumatic neuromas are painful, non neoplastic proliferations of haphazardly arranged axons, Schwann cells and connective tissue, resulting after trauma.
- Neurofibroma is a benign non encapsulated tumour of Schwann cells mixed with fibroblasts and mast cells
- Schwannomas are benign encapsulated tumours of Schwann cells.
- Peripheral nerve sheath tumour is a malignant tumour of Schwann cells. Half of cases are familial (NF1)

summary 2/2

- NF 1 is an autosomal dominant syndrome characterised by multiple neurofibromas, PNST, gliomas and cafe au last skin lesions.

- NF 1 is caused by a mutation in neurofibromin, an inhibitor of Ras oncogene.

- NF 2 is characterised by multiple schwannomas (including acoustic schwannomas that can be bilateral), meningiomas and ependymomas BUT NOT NEUROFIBROMAS.

- NF 2 is caused by a mutation in merlin protein resulting in loss of contact inhibition.


THANK YOU