PIPADOR REVISION

MRCOG Part 1 Revision Notes

Neurofibromatosis and Neurocutaneous Syndromes

CELL BIOLOGY • LECTURE 122

VISUAL EXAMINATION REVISION NOTES

2026 Edition

MRCOG Part 1 Revision Notes

Lecture 122: Neurofibromatosis and Other Neurocutaneous Syndromes

Cell biology • Visual revision edition

COLOUR CODE USED THROUGHOUT THESE NOTES

NF1	NF2	TUBEROUS SCLEROSIS	VHL / PREGNANCY RISK	STURGE–WEBER / OTHER

LEARNING OBJECTIVES — tick off as you go

- ☐ Compare the genetics and pathways of NF1, NF2, TSC and VHL.
- ☐ Apply the NF1 diagnostic criteria and know its pregnancy issues.
- ☐ Recognise TSC, including antenatal cardiac rhabdomyomas.
- ☐ Screen for phaeochromocytoma in VHL and NF1 pregnancies.
- ☐ Know Sturge–Weber, ataxia-telangiectasia, incontinentia pigmenti and PHACE.

1 Overview

IN ONE LINE: *Inherited tumour-suppressor disorders (mostly AD, many de novo) that show in skin and nervous system first. Pregnancy can grow tumours, unmask phaeochromocytoma and complicate anaesthesia.*

Neurocutaneous syndromes (phakomatoses) — skin + nervous system + tumours

Disorder	Gene / protein	Inheritance	Frequency	Hallmarks
NF1	NF1 17q11 — neurofibromin (RAS brake)	AD, ~50% de novo	~1 in 3000	café-au-lait, freckling, neurofibromas, Lisch nodules
NF2 (NF2-SWN)	NF2 22q12 — merlin	AD	~1 in 25,000	BILATERAL vestibular schwannomas, meningiomas, cataract
TUBEROUS SCLEROSIS	TSC1 (hamartin) / TSC2 (tuberin) — mTOR brake	AD, ~2/3 de novo	~1 in 6000	seizures, angiofibromas, ash-leaf macules, cardiac RHABDOMYOMA
VON HIPPEL–LINDAU	VHL 3p25 — HIF breakdown	AD	~1 in 36,000	haemangioblastomas, clear-cell RCC, PHAEOCHROMOCYTOMA
STURGE–WEBER	GNAQ — SOMATIC mosaic	NOT inherited	~1 in 20–50,000	V1 port-wine stain + leptomeningeal angioma, glaucoma
ATAXIA-TELANGIECTASIA	ATM 11q22 — DNA damage kinase	AR	~1 in 40–100,000	ataxia, telangiectasia, immunodeficiency, cancer, ↑AFP

Common thread: most are TUMOUR-SUPPRESSOR disorders — the 'brakes' on RAS (NF1), mTOR (TSC) or HIF (VHL) are lost; a second hit in a cell → tumour.

Figure 1. Neurocutaneous syndromes at a glance.

MNEMONIC / MEMORY HOOK

'NF1 = 17 letters in neurofibromatosis; NF2 = 22 (chromosome 22)' — NF1 on 17q, NF2 on 22q. And **'tubers, ash-leaf, rhabdo' = TSC**.

2 Neurofibromatosis Type 1

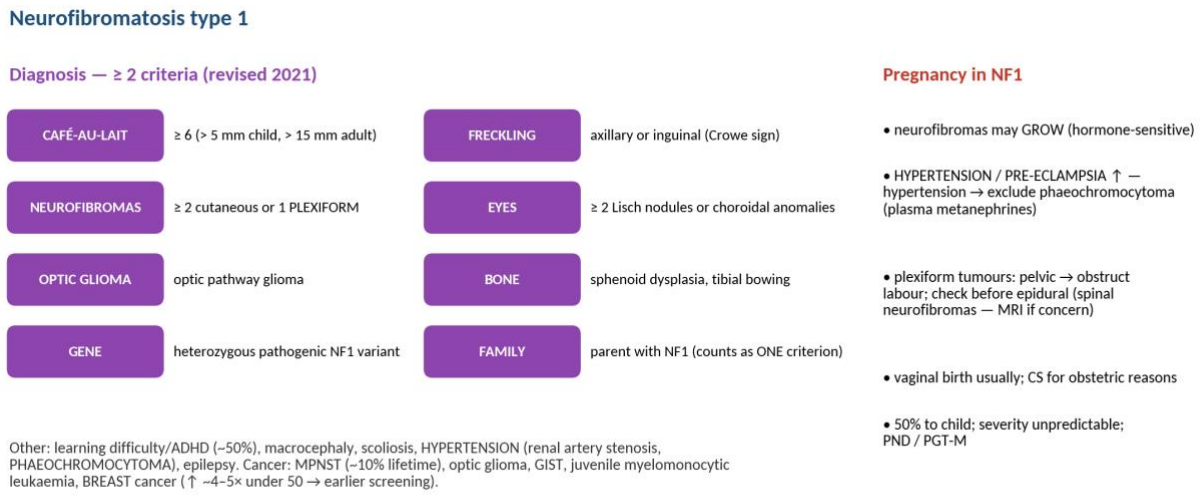


Figure 2. NF1 diagnosis and pregnancy.

3 Tuberous Sclerosis Complex

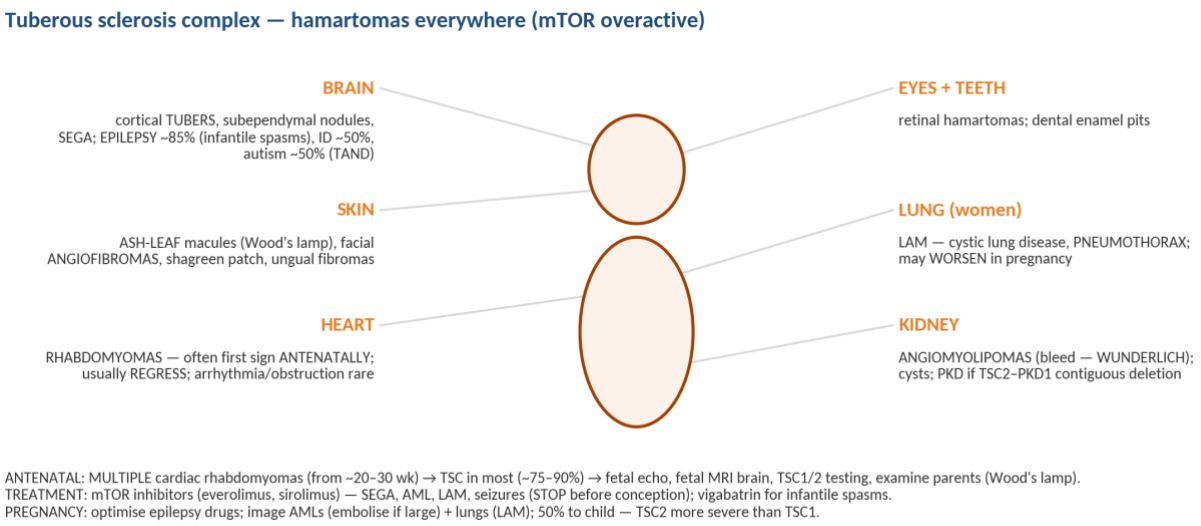


Figure 3. TSC.

4 VHL and NF2

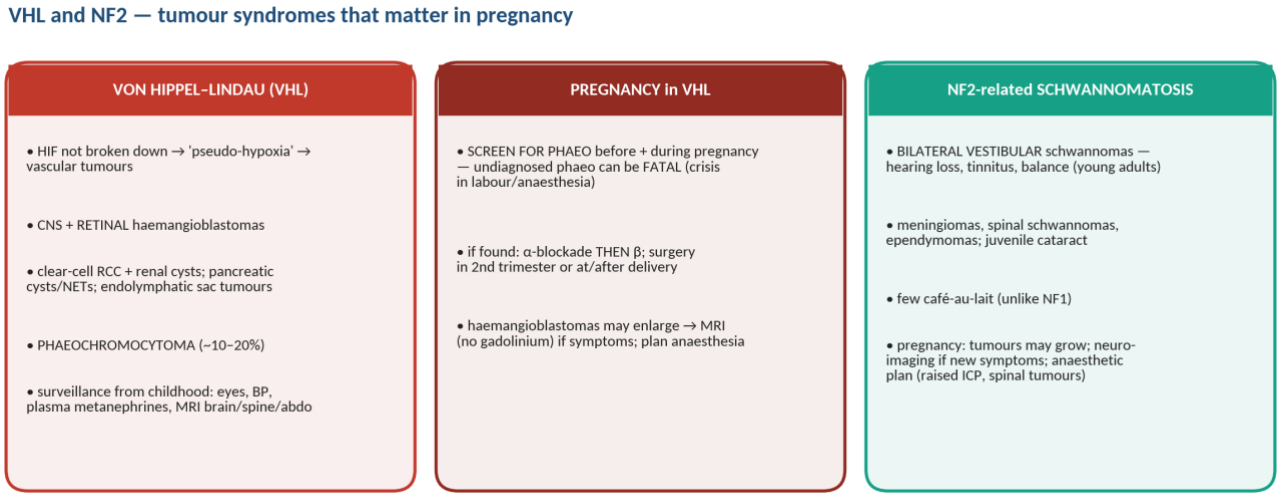


Figure 4. VHL and NF2.

5 Other Syndromes

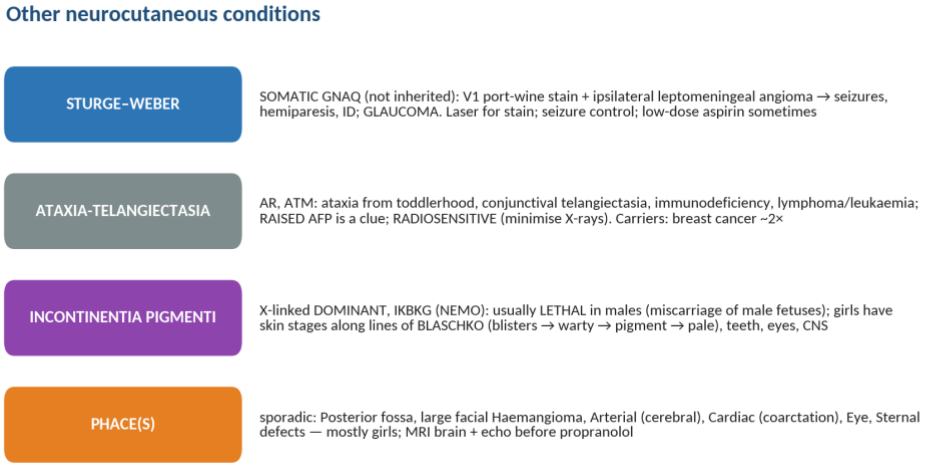


Figure 5. Other neurocutaneous conditions.

★ PEARL

Multiple fetal cardiac rhabdomyomas → tuberous sclerosis until proven otherwise (fetal MRI, TSC1/2, examine parents). They usually regress.

Hypertension in a pregnant woman with NF1 or VHL → exclude phaeochromocytoma (plasma metanephrines) — α-blockade before β.

6 MRCOG Exam Pearls — Last-Minute Page

Numbers to know

~1 in 3000 NF1	**~50%** NF1 de novo	**≥ 6** Café-au-lait macules	**~10%** MPNST lifetime (NF1)
~1 in 6000 TSC	**~85%** TSC epilepsy	**~10–20%** Phaeo in VHL	**~2×** Breast cancer in ATM carriers

HIGH-YIELD CHECKLIST

- ☐ NF1 17q11 neurofibromin (RAS); ~50% de novo; full penetrance, variable expression.
- ☐ NF1 criteria (2021): CALM, freckling, neurofibromas, Lisch, glioma, bone, gene, parent.
- ☐ NF1 pregnancy: tumour growth, hypertension/PE, phaeo, plexiform, epidural check.
- ☐ NF2 22q12 merlin: bilateral vestibular schwannomas.
- ☐ TSC1/TSC2 → mTOR; tubers, ash-leaf, angiofibroma, rhabdomyoma, AML, LAM.
- ☐ Antenatal multiple rhabdomyomas → TSC; everolimus stopped pre-conception.
- ☐ VHL 3p25 → HIF; haemangioblastoma, ccRCC, phaeo — screen in pregnancy.
- ☐ Sturge–Weber: somatic GNAQ, port-wine V1, glaucoma — not inherited.
- ☐ A-T: AR ATM, ↑AFP, radiosensitivity; carriers ↑ breast cancer.
- ☐ IP: X-linked dominant, male lethality; PHACE: haemangioma + coarctation.

Self-assessment — cover the right-hand column

Question	Answer
Protein encoded by NF1?	Neurofibromin (RAS GTPase-activating)
Pathognomonic feature of NF2?	Bilateral vestibular schwannomas
Iris hamartomas in NF1?	Lisch nodules
Fetal cardiac tumour suggesting TSC?	Rhabdomyoma (multiple)
Pathway overactive in TSC?	mTOR
Lung disease in women with TSC?	Lymphangioleiomyomatosis (LAM)
Tumour to exclude before/in pregnancy in VHL?	Phaeochromocytoma
Order of blockade for phaeochromocytoma?	α first, then β
Is Sturge–Weber inherited?	No — somatic GNAQ mosaicism
Blood clue in ataxia-telangiectasia?	Raised AFP

7 References

- Legius E et al. Revised diagnostic criteria for neurofibromatosis type 1 and Legius syndrome: an international consensus. Genet Med 2021.
- Northrup H et al. Updated international tuberous sclerosis complex diagnostic criteria and surveillance. Pediatr Neurol 2021.
- Maher ER et al. von Hippel–Lindau disease: a clinical and scientific review. Eur J Hum Genet 2011.