PIPADOR REVISION

MRCOG Part 1 Revision Notes

Duplications

CELL BIOLOGY • LECTURE 115

VISUAL EXAMINATION REVISION NOTES

2026 Edition

MRCOG Part 1 Revision Notes

Lecture 115: Duplications

Cell biology • Visual revision edition — the mirror of Lecture 114

COLOUR CODE USED THROUGHOUT THESE NOTES

DELETION (loss)	DUPLICATION (gain)	NORMAL / NEURO	MECP2 / X-LINKED	COUNSELLING / O&G

LEARNING OBJECTIVES — tick off as you go

- ☐ Explain how duplications arise and why they mirror deletions.
- ☐ Pair each recurrent microduplication with its reciprocal deletion.
- ☐ Describe dosage-sensitive genes: PMP22 (CMT1A/HNPP) and MECP2.
- ☐ Know the O&G relevance of CMT1A, HNPP and MECP2 duplication.
- ☐ Counsel on variable expressivity and incomplete penetrance.

1 Mechanisms and Mirror Syndromes

IN ONE LINE: *Unequal crossing over between look-alike repeats (NAHR) makes a deletion on one chromosome and the matching duplication on the other. Duplications are usually milder, less penetrant and more often inherited.*

- **Other mechanisms**: NHEJ and replication errors (non-recurrent); whole-chromosome gain = trisomy; partial trisomy from an unbalanced parental translocation. **Types**: tandem, inverted, insertional.

Mirror-image syndromes — NAHR makes a deletion AND its reciprocal duplication

	DELETION (loss)	DUPLICATION (gain)
22q11.2	DiGeorge/VCFS: conotruncal CHD, ↓Ca, cleft, schizophrenia	variable, often MILD; ~70% inherited from a near-normal parent
17p11.2	Smith–Magenis: sleep inversion, self-injury	Potocki–Lupski: hypotonia, FTT, autism traits, sleep apnoea
17p12 (PMP22)	HNPP: pressure palsies	CMT1A: demyelinating neuropathy
7q11.23	Williams: SVAS, ↑Ca, over-friendly	speech delay, ANXIETY, selective mutism; aortic DILATATION
16p11.2	autism, ID, OBESITY, macrocephaly	autism, ADHD, schizophrenia, UNDERWEIGHT, microcephaly
1q21.1	microcephaly, ID, cataracts, heart	MACROcephaly, autism, ID, schizophrenia
15q11–q13	PWS (paternal) / Angelman (maternal)	MATERNAL dup → autism, ID, seizures; paternal milder
Xq28 (MECP2)	loss-of-function: Rett (girls)	MECP2 duplication: severe in BOYS

Rule of thumb: duplications are usually MILDER and less penetrant than the matching deletion — more often inherited from a healthy-looking parent.

Figure 1. Reciprocal deletion/duplication pairs.

MNEMONIC / MEMORY HOOK

'Losing hurts more than gaining' — microduplications are usually milder than their reciprocal deletions (MECP2 in boys is the big exception).

2 Dosage-Sensitive Genes

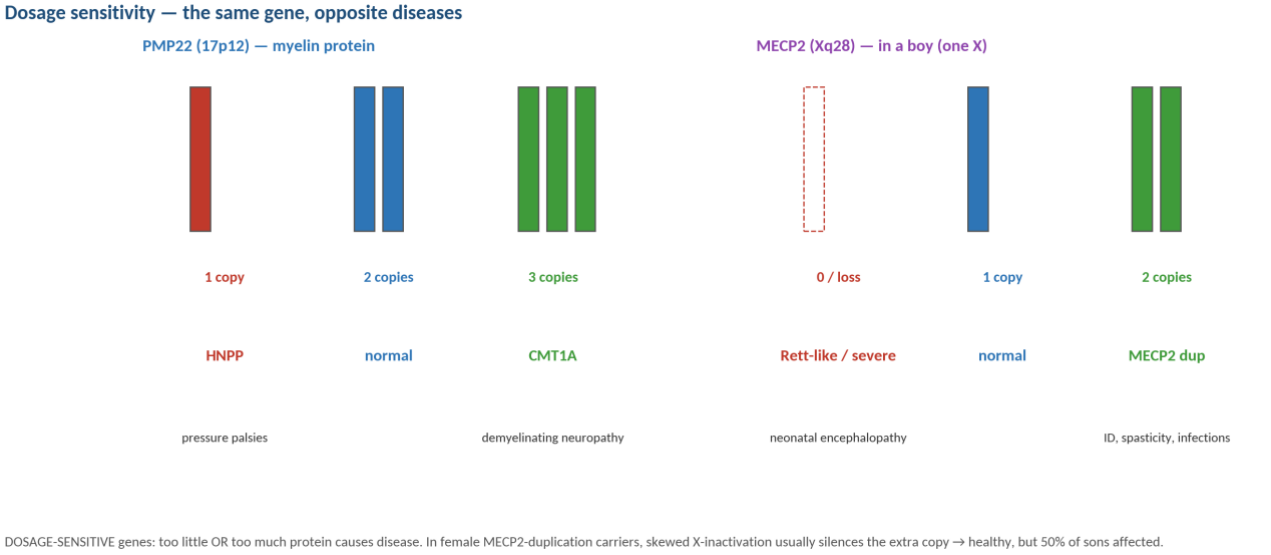


Figure 2. Dosage sensitivity: PMP22 and MECP2.

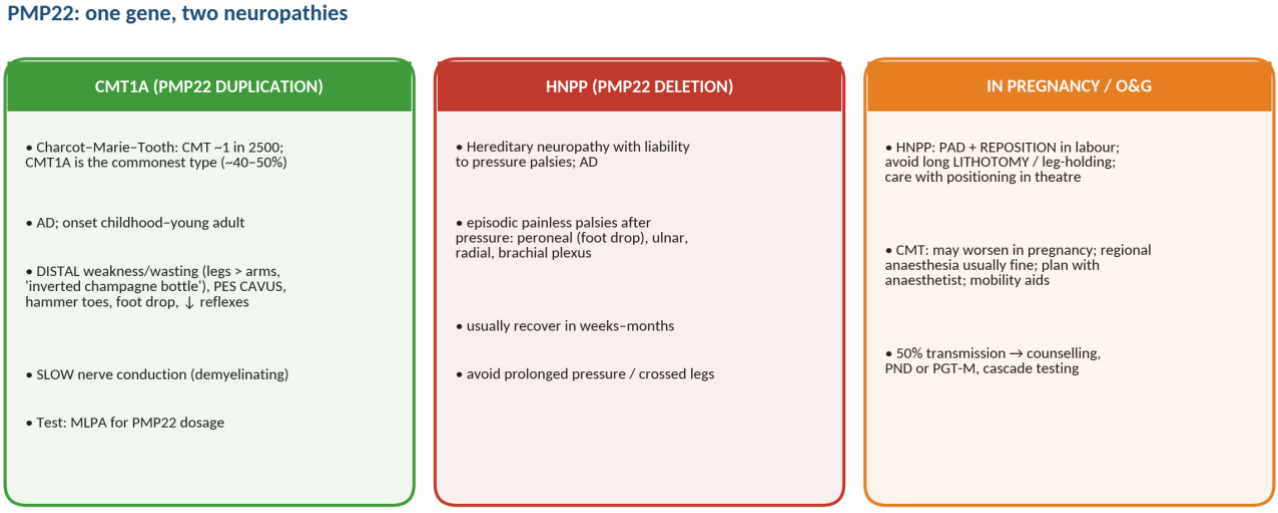


Figure 3. CMT1A and HNPP.

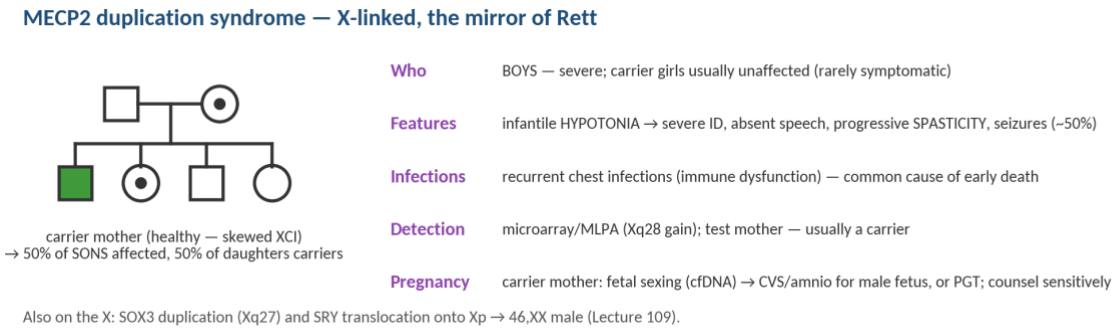


Figure 4. MECP2 duplication syndrome.

3 Counselling and Detection

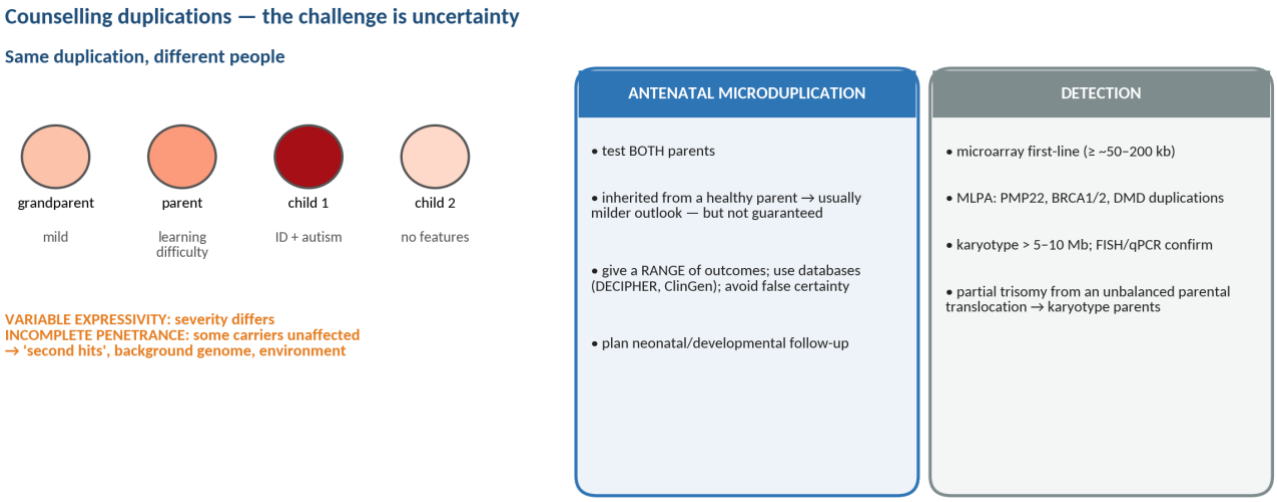


Figure 5. Variable expressivity, counselling and detection.

★ PEARL

PMP22: 3 copies = CMT1A (commonest CMT); 1 copy = HNPP (pressure palsies — careful positioning in labour). MLPA detects both.

MECP2 duplication: severe in boys; carrier mothers usually healthy (skewed XCI) with 50% of sons affected.

4 MRCOG Exam Pearls — Last-Minute Page

Numbers to know

~1 in 2500 CMT (all types)	**~40–50%** CMT that is CMT1A	**3 / 1** PMP22 copies: CMT1A / HNPP	**~70%** 22q11.2 dup inherited
50% Sons of MECP2 carrier	**~50%** MECP2 dup with seizures	**≥ 50–200 kb** Array resolution	**> 5–10 Mb** Karyotype resolution

HIGH-YIELD CHECKLIST

- ☐ NAHR → reciprocal deletion + duplication; NHEJ, replication errors.
- ☐ Duplications usually milder, variable, often inherited.
- ☐ 22q11.2 dup: variable, ~70% inherited.
- ☐ Potocki–Lupski = 17p11.2 dup (vs Smith–Magenis).
- ☐ 7q11.23 dup: speech delay, anxiety, aortic dilatation.
- ☐ 16p11.2 dup: underweight, autism, schizophrenia (del: obesity).
- ☐ Maternal 15q11–q13 dup: autism, seizures.
- ☐ CMT1A (PMP22 dup) vs HNPP (PMP22 del); MLPA.
- ☐ MECP2 dup: severe boys, carrier mothers; vs Rett.
- ☐ Counsel: test parents, range of outcomes, databases.

Self-assessment — cover the right-hand column

Question	Answer
Mechanism of recurrent microduplications?	NAHR between low-copy repeats
Reciprocal of Smith–Magenis?	Potocki–Lupski (17p11.2 dup)
Gene duplicated in CMT1A?	PMP22
Reciprocal deletion of CMT1A?	HNPP
Labour care point in HNPP?	Avoid prolonged pressure/lithotomy; pad and reposition
Who is affected by MECP2 duplication?	Mainly boys
Why are carrier mothers usually well?	Skewed X-inactivation
Weight with 16p11.2 duplication?	Underweight (deletion → obesity)
Test for PMP22 copy number?	MLPA
Key counselling issue for microduplications?	Variable expressivity and incomplete penetrance

5 References

- Gardner RJM, Amor DJ. Chromosome Abnormalities and Genetic Counselling. 5th ed. 2018.
- Pareyson D, Marchesi C. Diagnosis, natural history and management of Charcot–Marie–Tooth disease. Lancet Neurol 2009.
- Van Esch H. MECP2 duplication syndrome. GeneReviews (updated).