PIPADOR REVISION

MRCOG Part 1 Revision Notes

Mosaicism and Chimerism

CELL BIOLOGY • LECTURE 110

VISUAL EXAMINATION REVISION NOTES

2026 Edition

MRCOG Part 1 Revision Notes

Lecture 110: Mosaicism and Chimerism

Cell biology • Visual revision edition — links Lectures 94, 102, 103

COLOUR CODE USED THROUGHOUT THESE NOTES

MOSAIC / FETAL	PLACENTAL (CPM)	CHIMERISM / SOMATIC	UPD / IMPRINTING	LATE / DETECTION

LEARNING OBJECTIVES — tick off as you go

- ☐ Define mosaicism and chimerism and explain how timing shapes the phenotype.
- ☐ Describe the mechanisms, including trisomy and monosomy rescue.
- ☐ Manage a mosaic CVS result and understand confined placental mosaicism.
- ☐ Explain UPD (iso vs hetero) and the imprinting disorders.
- ☐ Recognise mosaic disorders, germline mosaicism, chimerism and detection methods.

1 Definitions and Mechanisms

IN ONE LINE: *Mosaic = one zygote, two or more cell lines (a post-zygotic event). Chimera = cells from two or more zygotes. The earlier the error, the more tissues — and possibly the gonads — it reaches.*

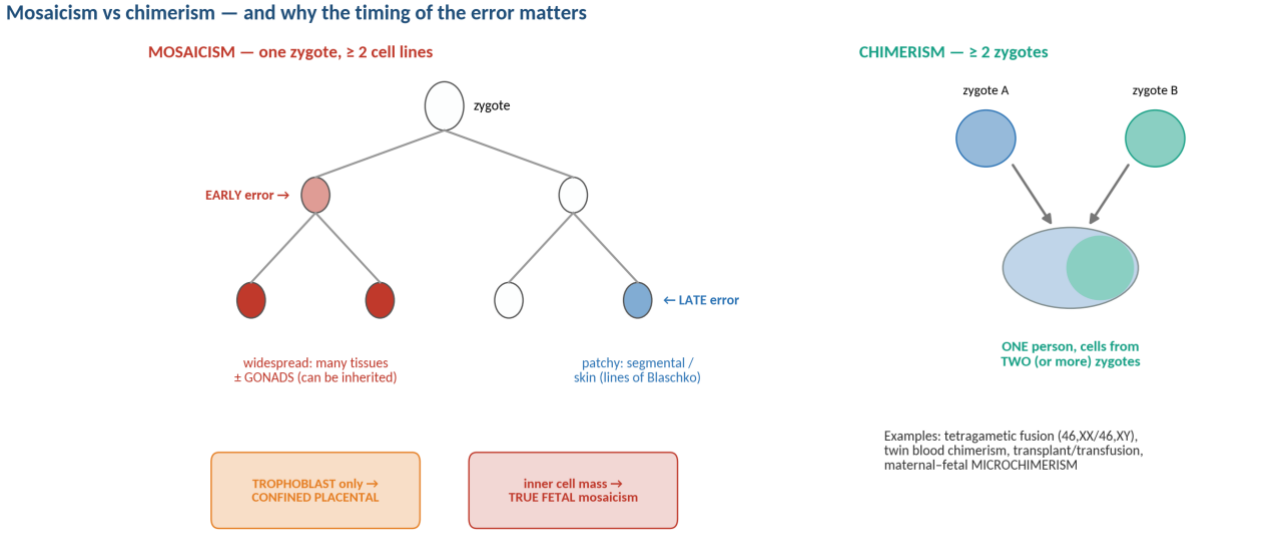


Figure 1. Mosaicism vs chimerism and timing.

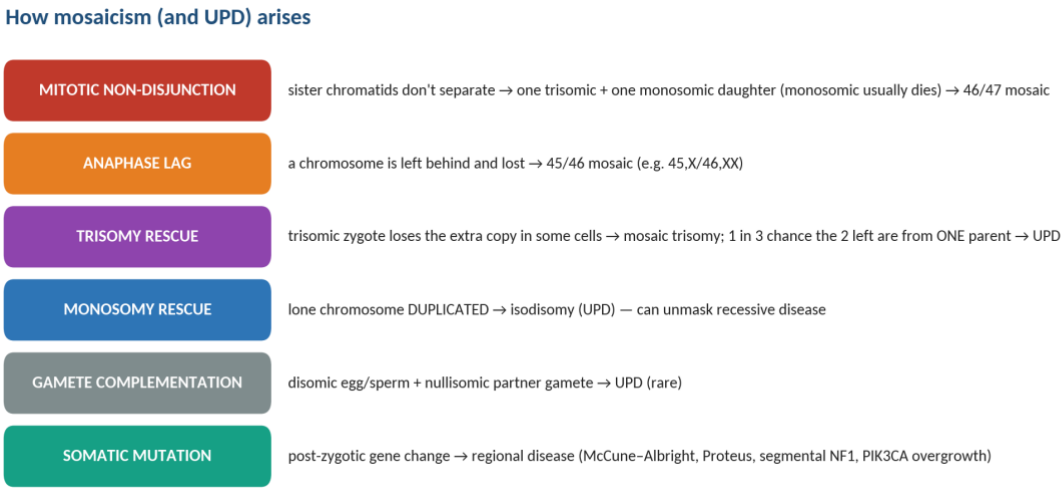


Figure 2. Mechanisms.

2 Mosaicism in Prenatal Diagnosis

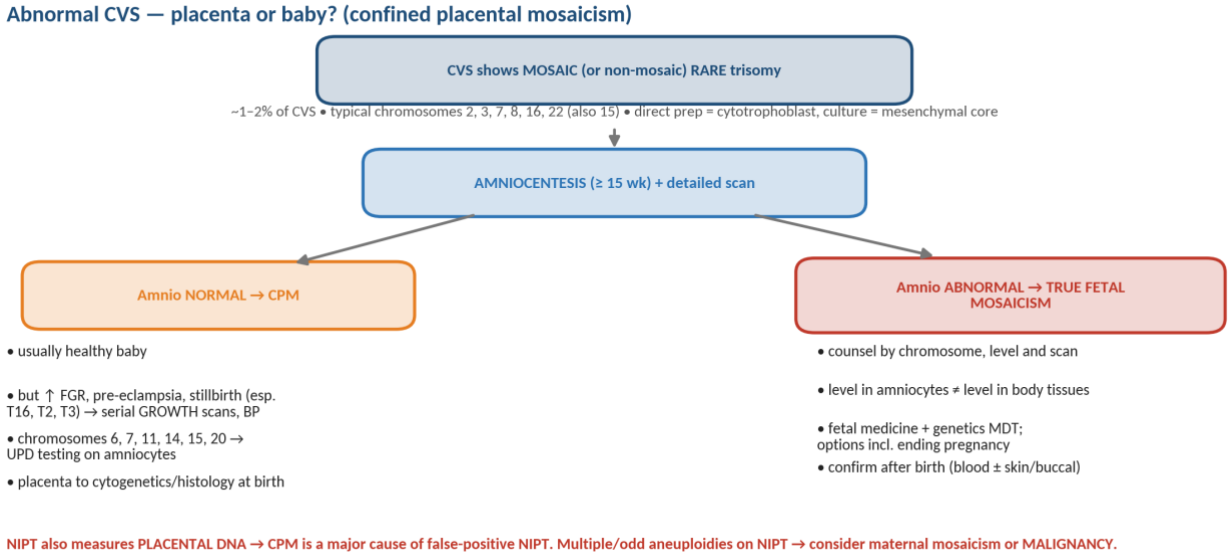


Figure 3. Abnormal CVS: placenta or baby?

MNEMONIC / MEMORY HOOK

'CVS sees the Placenta; Amnio sees the Person' — confirm any mosaic or unusual CVS result with amniocentesis.

3 Uniparental Disomy

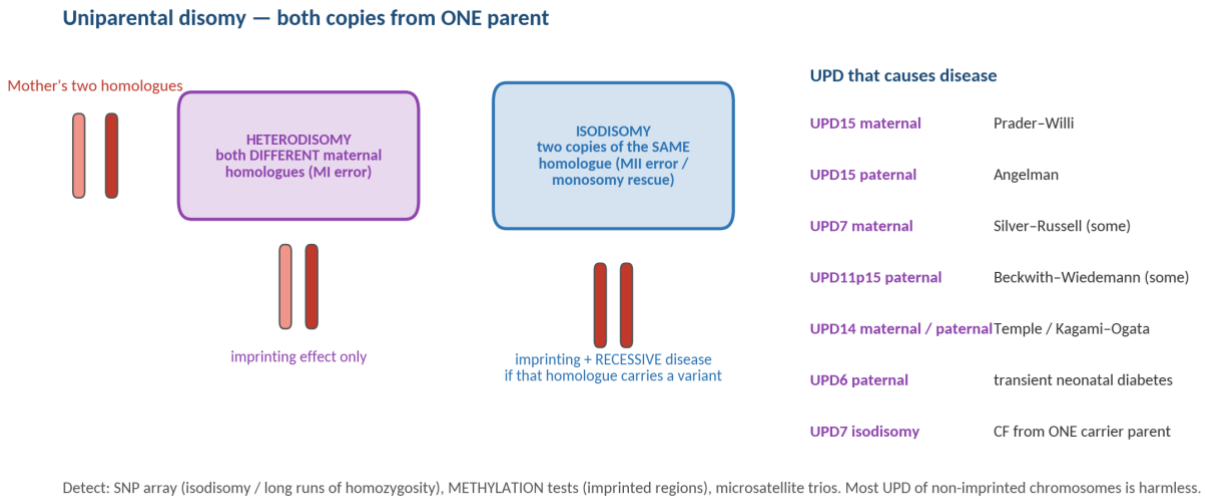


Figure 4. UPD — iso vs hetero and imprinting disorders.

4 Mosaic Disorders and Germline Mosaicism

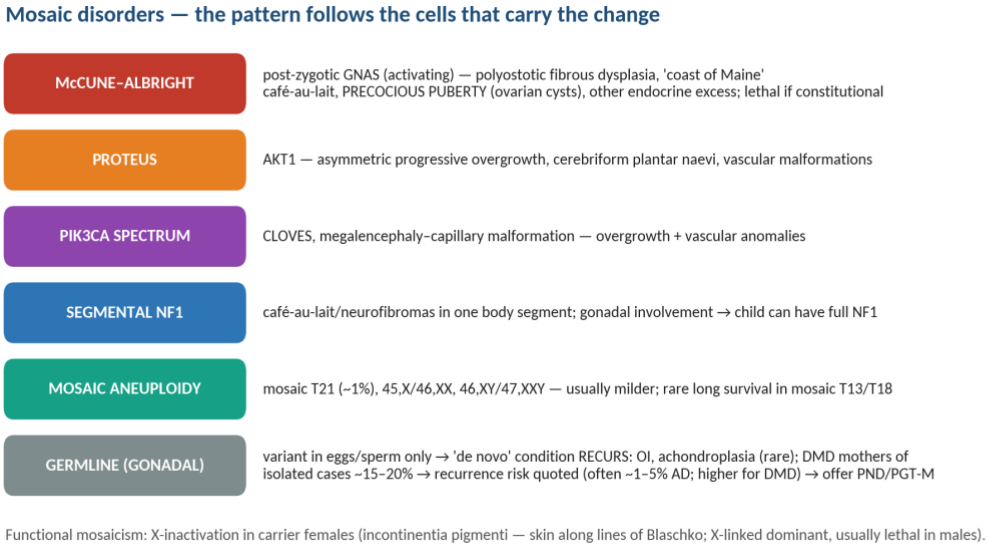


Figure 5. Mosaic disorders.

Germline mosaicism	Key points
What	Variant present in a parent's eggs/sperm but not (or barely) in their blood — parent clinically unaffected
Clue	'De novo' dominant (or X-linked) condition recurs in siblings
Recurrence	Quote condition-specific figures — often ~1–5% after an apparently de novo dominant variant (higher for some, e.g. OI type II); in DMD, mothers of isolated cases may have germline mosaicism (~15–20%) — so offer testing even if the mother's blood is negative
Action	Offer PND or PGT-M in future pregnancies; testing of parental sperm can sometimes refine risk

5 Chimerism, Detection and IVF

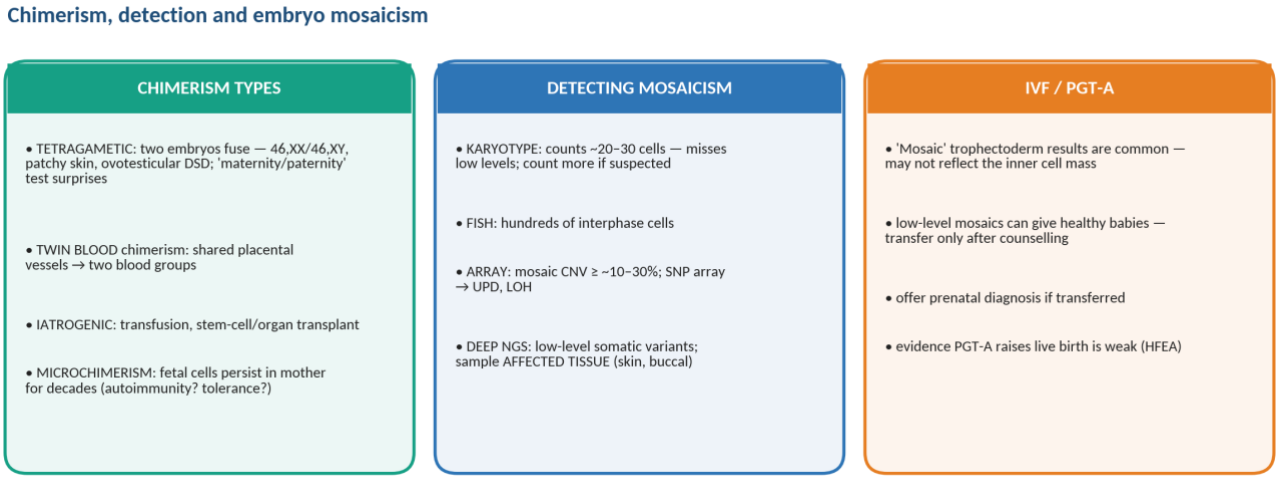


Figure 6. Chimerism, detection, PGT-A.

★ PEARL

CPM in ~1–2% of CVS → amnio. Normal amnio = usually healthy baby, but watch growth/BP and test UPD for imprinted chromosomes (e.g. 15).

Isodisomy (MII error/monosomy rescue) can unmask recessive disease; heterodisomy (MI error) causes imprinting effects only.

6 MRCOG Exam Pearls — Last-Minute Page

Numbers to know

~1–2% CVS with CPM	**1 in 3** Trisomy rescue → UPD	**~1%** Mosaic Down's	**~1–5%** Typical germline recurrence
15–20% DMD mothers' germline mosaicism	**10–30%** Array mosaic threshold	**20–30** Cells counted in karyotype	**15** Key chromosome for UPD testing

HIGH-YIELD CHECKLIST

- ☐ Mosaic = one zygote; chimera = ≥ 2 zygotes.
- ☐ Mitotic non-disjunction, anaphase lag, trisomy/monosomy rescue, somatic mutation.
- ☐ Early error → widespread ± gonads; late → segmental (Blaschko lines).
- ☐ CPM ~1–2% CVS (2, 3, 7, 8, 16, 22); amnio to confirm; growth scans.
- ☐ CPM causes false-positive NIPT; odd NIPT → think maternal malignancy.
- ☐ UPD: iso (MII/monosomy rescue) vs hetero (MI); imprinting 15, 7, 11p15, 14, 6.
- ☐ McCune–Albright (GNAS), Proteus (AKT1), PIK3CA, segmental NF1.
- ☐ Germline mosaicism → recurrence of 'de novo' disorders; PND/PGT-M.
- ☐ Chimerism: tetragametic, twin, transplant, microchimerism.
- ☐ Detect: karyotype, FISH, SNP array, deep NGS, affected tissue.

Self-assessment — cover the right-hand column

Question	Answer
Mosaicism vs chimerism?	One zygote vs two or more zygotes
CVS shows mosaic trisomy — next step?	Amniocentesis (+ detailed scan)
Pregnancy risks with CPM?	FGR, pre-eclampsia, stillbirth
Why test UPD after CPM of chromosome 15?	Trisomy rescue may leave two maternal/paternal 15s (PWS/AS)
UPD type that unmasks recessive disease?	Isodisomy
Mutated gene in McCune–Albright?	GNAS (post-zygotic activating)
Explanation for a 'de novo' disorder recurring in siblings?	Germline (gonadal) mosaicism
Skin pattern of late mosaicism?	Lines of Blaschko
Major cause of false-positive NIPT?	Confined placental mosaicism
Example of chimerism in pregnancy?	Fetal microchimerism in the mother

7 References

- Grati FR. Chromosomal mosaicism in human feto-placental development: implications for prenatal diagnosis. J Clin Med 2014.
- Gardner RJM, Amor DJ. Chromosome Abnormalities and Genetic Counselling. 5th ed. 2018.
- PGDIS / ESHRE good practice recommendations on mosaic embryo transfer (2021–2022).