PIPADOR REVISION

MRCOG Part 1 Revision Notes

FISH and Microarray

MOLECULAR BIOLOGY • LECTURE 94

VISUAL EXAMINATION REVISION NOTES

2026 Edition

MRCOG Part 1 Revision Notes

Lecture 94: FISH and Chromosomal Microarray

Molecular biology • Visual revision edition

COLOUR CODE USED THROUGHOUT THESE NOTES

KARYOTYPE	FISH	aCGH ARRAY	SNP ARRAY / IMPRINTING	DELETION / ABNORMAL

LEARNING OBJECTIVES — tick off as you go

- ☐ Compare karyotype, FISH, aCGH and SNP arrays — what each can and cannot detect.
- ☐ Describe FISH probe types and clinical uses.
- ☐ Explain how microarray works and how to read it.
- ☐ Recognise the main microdeletion syndromes.
- ☐ Explain UPD, imprinting and mosaicism; choose tests in prenatal, postnatal and oncology settings.

1 Choosing a Cytogenetic Test

IN ONE LINE: *Karyotype sees the big picture (incl. balanced rearrangements); FISH zooms in on a known target; microarray scans the whole genome for gains and losses — but can't see anything balanced.*

Which test sees what? (green = yes, yellow = partly, red = no)

	Aneuploidy	Balanced translocation	Microdeletion (< 5 Mb)	Triploidy	UPD / LOH	Low-level mosaicism	Point variant	Speed
Karyotype	✓	✓	✗	✓	✗	±	✗	1–3 wk
QF-PCR	✓	✗	✗	✓	✗	±	✗	24–48 h
FISH	±	±	✓	±	✗	✓	✗	1–3 days
aCGH array	✓	✗	✓	✗	✗	±	✗	~1–2 wk
SNP array	✓	✗	✓	✓	±	±	✗	~1–2 wk
Exome/genome	±	✗	±	✗	±	✗	✓	~2–3 wk

Resolution: karyotype ~5–10 Mb • FISH probe ~100–500 kb (targeted) • microarray ~50–200 kb genome-wide • sequencing to single base.
Arrays measure DOSAGE — so balanced rearrangements (no gain/loss) are invisible; SNP arrays add genotype → isodisomy, LOH, consanguinity, triploidy.

Figure 1. What each test detects.

- **Karyotype**: culture → arrest in metaphase (colcemid) → G-banding (trypsin + Giemsa) → count ~20 cells; resolution ~5–10 Mb; 1–3 weeks; still needed for **balanced** translocations/inversions and some mosaicism.

2 FISH

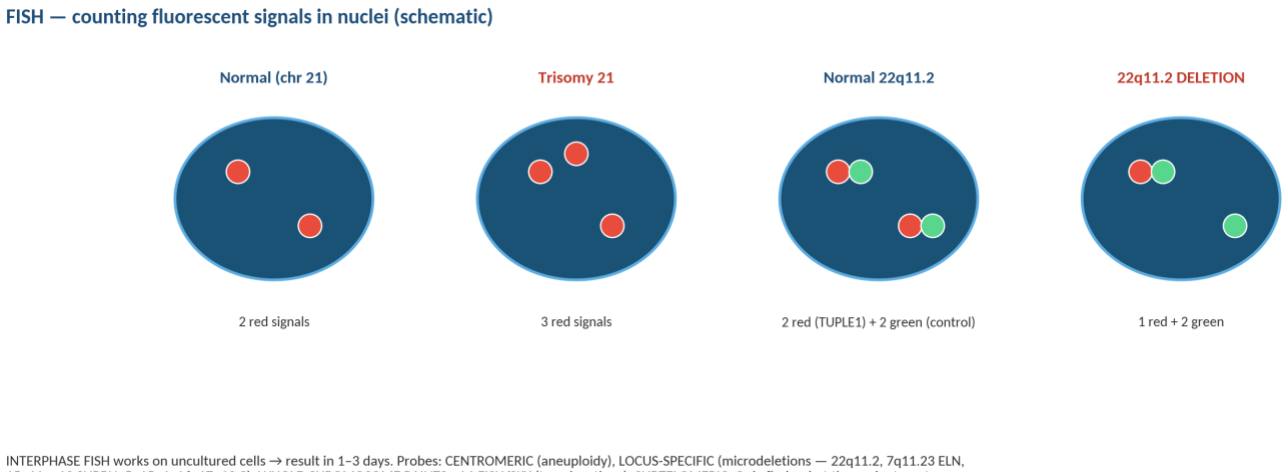


Figure 2. FISH signals.

Use	Probe / target
Rapid aneuploidy (13, 18, 21, X, Y)	Centromeric / locus-specific (largely replaced by QF-PCR in the UK)
22q11.2 deletion	TUPLE1/HIRA region
Prader–Willi / Angelman	SNRPN 15q11–q13 (detects deletions only — methylation testing preferred)
Williams / cri-du-chat / Wolf–Hirschhorn / Miller–Dieker	ELN 7q11.23 / 5p15 / 4p16.3 / 17p13.3
Oncology	BCR-ABL t(9;22) (CML), HER2 amplification (breast), ALK/ROS1 (lung), MYCN (neuroblastoma)

- **M-FISH / SKY**: every chromosome a different colour — complex translocations (mainly cancer/research).

3 Chromosomal Microarray

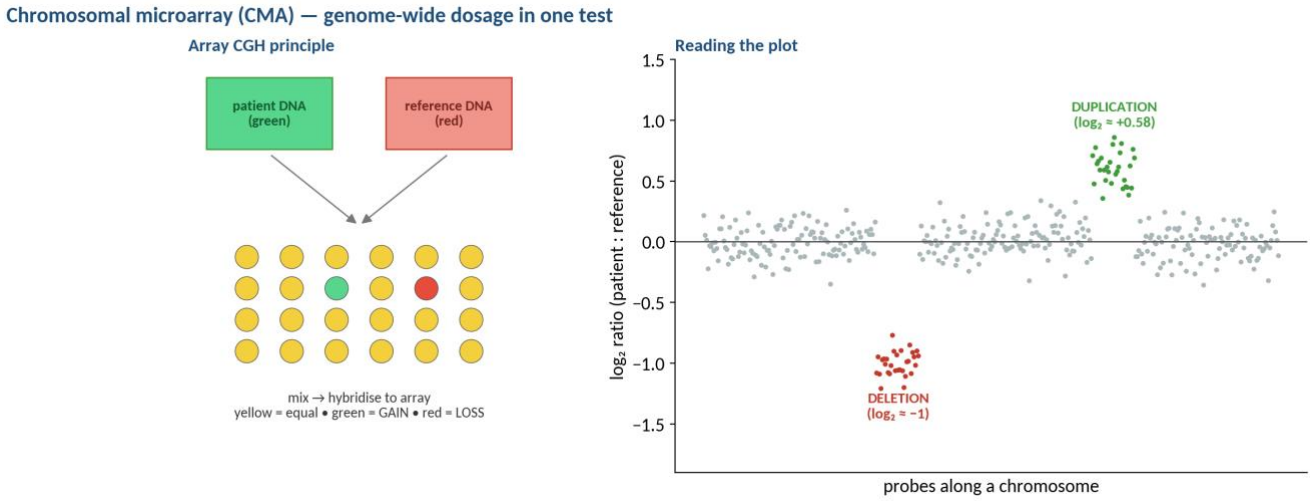


Figure 3. aCGH principle and plot.

Feature	Key points
aCGH	Patient vs reference DNA, two colours; copy number only

Feature	Key points
SNP array	Copy number + genotype → isodisomy UPD, long runs of homozygosity (consanguinity), triploidy, some mosaicism; misses heterodisomy
Resolution	~50–200 kb (platform-dependent) — ~100× better than karyotype
Misses	Balanced rearrangements, point variants, low-level mosaicism (< ~20%), triploidy (aCGH)
Yield	Postnatal ID/DD/anomalies: first-line (~15–20%). Prenatal structural anomaly with normal karyotype: +~6%
Problem	VUS and incidental findings (adult-onset, variable penetrance like 16p11.2) — counsel before testing

4 Microdeletion Syndromes

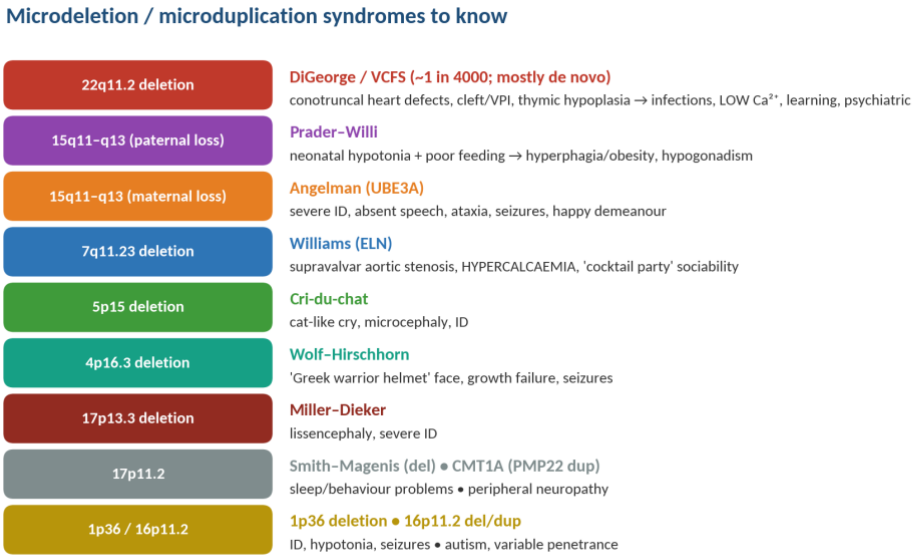


Figure 4. Key microdeletion syndromes.

MNEMONIC / MEMORY HOOK

'CATCH-22' for 22q11.2: Cardiac, Abnormal face, Thymic hypoplasia, Cleft palate, Hypocalcaemia — chromosome 22. (Clinicians now prefer '22q11.2 deletion syndrome'.)

5 UPD, Imprinting and Mosaicism

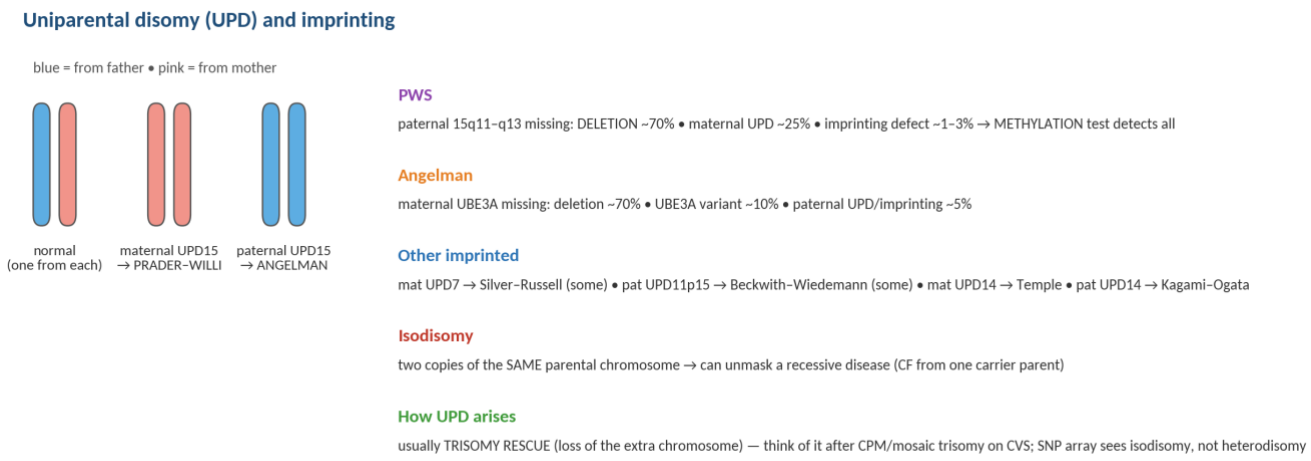


Figure 5. Uniparental disomy.

- **Confined placental mosaicism** (~1–2% of CVS) → confirm with amniocentesis; mosaic trisomy 15 (or 7, 11, 14) in the placenta should prompt **UPD testing** of the fetus (trisomy rescue).

6 In Practice

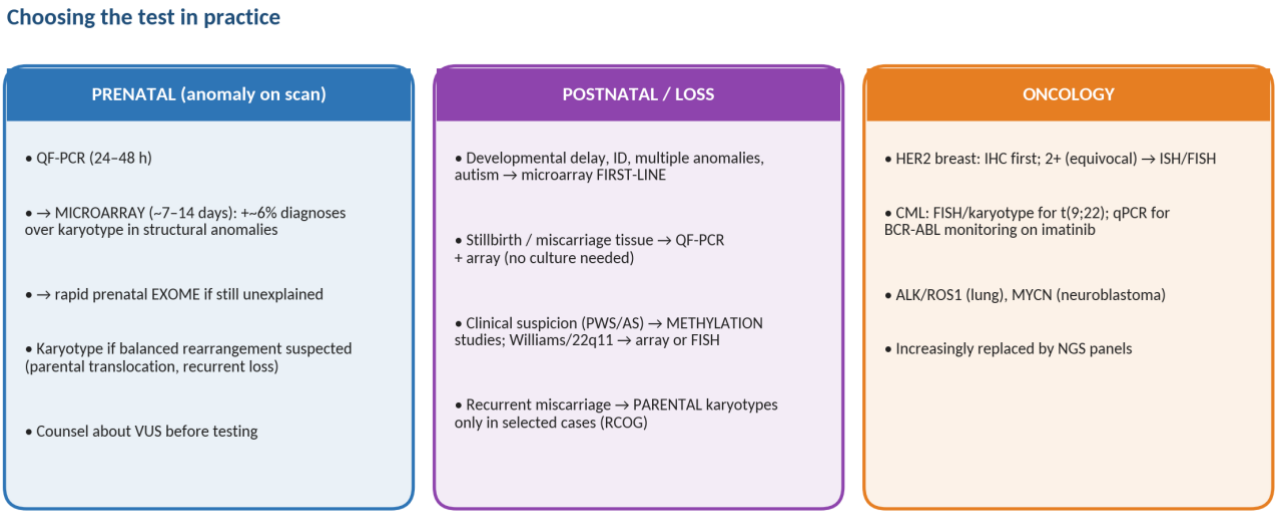


Figure 6. Choosing the test.

★ **PEARL**

Microarray can't see balanced translocations (no change in dosage) — use karyotype. SNP arrays add UPD (isodisomy), runs of homozygosity and triploidy.

Prader–Willi = missing paternal 15q11–q13 (often maternal UPD); Angelman = missing maternal UBE3A. Methylation test first for PWS.

7 MRCOG Exam Pearls — Last-Minute Page

Numbers to know

5–10 Mb Karyotype resolution	**50–200 kb** Microarray resolution	**1–3 days** Interphase FISH	**+~6%** Array yield over karyotype
~1–2% CPM at CVS	**> ~20%** Mosaicism array detects	**~1 in 4000** 22q11.2 deletion	**~70% / ~25%** PWS: deletion / mat UPD

HIGH-YIELD CHECKLIST

- ☐ Karyotype: G-banding, ~5–10 Mb, 1–3 wk, sees balanced rearrangements.
- ☐ FISH: targeted; centromeric, locus-specific, paints, subtelomeric; interphase = fast.
- ☐ aCGH: dosage only; SNP array: + UPD (iso), LOH, triploidy.
- ☐ Arrays miss balanced rearrangements, point variants, low mosaicism.
- ☐ Array first-line for DD/ID/anomalies; +~6% prenatally.
- ☐ 22q11.2, PWS/AS, Williams, cri-du-chat, Wolf–Hirschhorn, Miller–Dieker, Smith–Magenis, CMT1A.
- ☐ UPD: mat 15 PWS, pat 15 AS, mat 7 SRS, pat 11p15 BWS; trisomy rescue.
- ☐ Isodisomy can unmask AR disease.
- ☐ CPM ~1–2% CVS → amnio; CPM of imprinted chromosomes → UPD test.
- ☐ Oncology: HER2 IHC → ISH if 2+; BCR-ABL FISH, qPCR monitoring.

Self-assessment — cover the right-hand column

Question	Answer
Why can't microarray detect a balanced translocation?	There is no gain or loss of DNA
Which array type detects UPD?	SNP array (isodisomy)
Extra prenatal yield of array over karyotype?	~6% (structural anomalies)
FISH region for Williams syndrome?	ELN at 7q11.23
Calcium in 22q11.2 vs Williams?	Low in 22q11.2; high in Williams
Maternal UPD15 causes…	Prader–Willi syndrome
Best first test for suspected Prader–Willi?	Methylation analysis of 15q11–q13
Usual mechanism of UPD?	Trisomy rescue
HER2 IHC 2+ — next step?	In-situ hybridisation (FISH)
Abnormal CVS, normal scan — next step?	Amniocentesis (possible CPM)

8 References

- Wapner RJ et al. Chromosomal microarray versus karyotyping for prenatal diagnosis. N Engl J Med 2012.
- RCOG Green-top Guideline No. 17. Recurrent miscarriage. 2023.
- Gardner RJM, Amor DJ. Chromosome Abnormalities and Genetic Counselling. 5th ed. 2018.