PIPADOR REVISION

MRCOG Part 1 Revision Notes

Translocations

CELL BIOLOGY • LECTURE 112

VISUAL EXAMINATION REVISION NOTES

2026 Edition

MRCOG Part 1 Revision Notes

Lecture 112: Translocations

Cell biology • Visual revision edition — links Lectures 103, 104, 105

COLOUR CODE USED THROUGHOUT THESE NOTES

RECIPROCAL	ROBERTSONIAN	UNBALANCED / CANCER	BALANCED / HEALTHY	FISH / OTHER

LEARNING OBJECTIVES — tick off as you go

- ☐ Define reciprocal, Robertsonian and insertional translocations.
- ☐ Explain meiotic segregation in carriers (quadrivalent, trivalent).
- ☐ Quote recurrence risks, including translocation Down's.
- ☐ Know when to karyotype (RCOG 2023) and the reproductive options, incl. PGT-SR.
- ☐ Recognise cancer translocations and choose the right detection test.

1 Reciprocal Translocations

IN ONE LINE: *A balanced carrier is healthy (~1 in 500) but makes unbalanced eggs or sperm — causing miscarriage, or a child with partial trisomy/monosomy.*

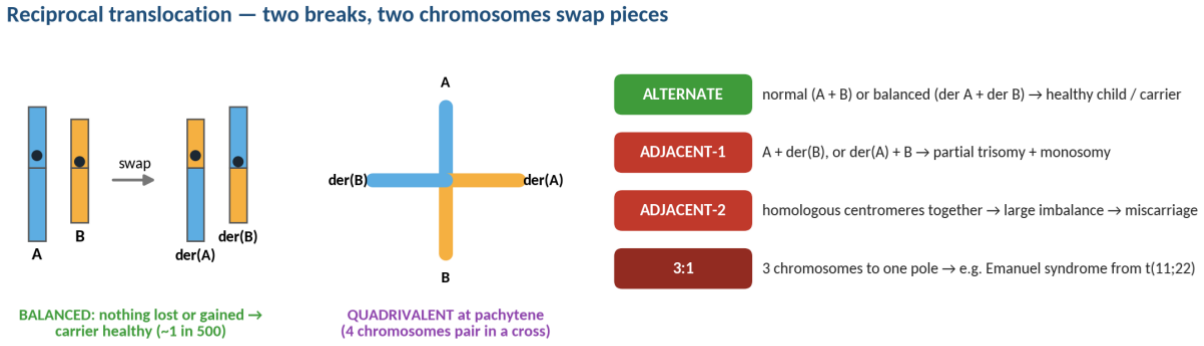


Figure 1. Reciprocal translocation and segregation.

Risk depends on	Key points
How found	Via an affected child → higher risk (often ~10–20%); via miscarriages only → lower (often ~1–5%) — large imbalances miscarry
Carrier's sex	Often higher when the MOTHER carries
Segments	Small imbalanced segments are more likely to survive to birth
t(11;22)	Commonest recurrent; 3:1 → +der(22) = Emanuel syndrome (female carrier risk a few %)
Insertional (3 breaks)	Highest liveborn risk — up to ~50%

2 Robertsonian Translocations

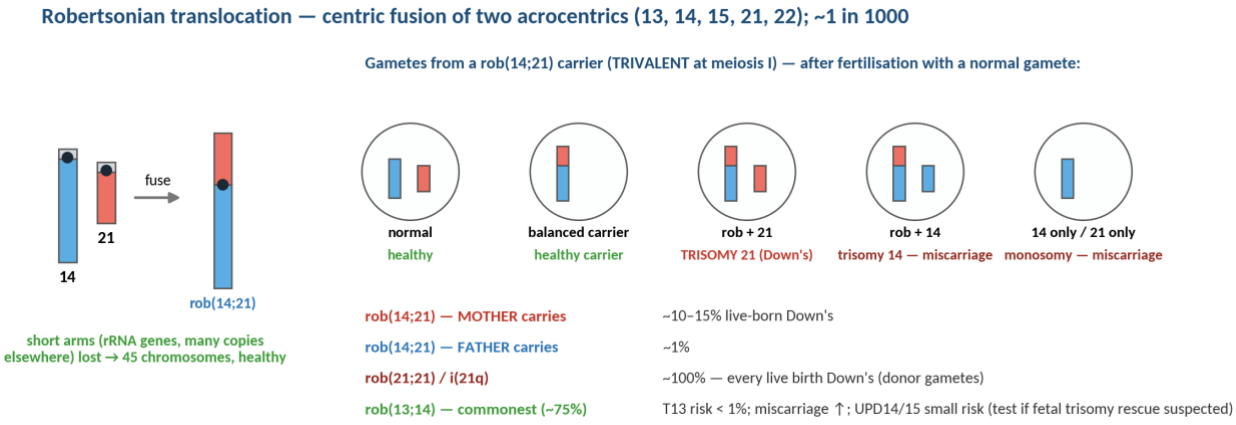


Figure 2. Robertsonian translocation and gametes.

MNEMONIC / MEMORY HOOK

'Mum Matters Most' — rob(14;21): ~10–15% if Mother carries, ~1% if father; rob(21;21) = every liveborn has Down's.

3 Clinical Pathway

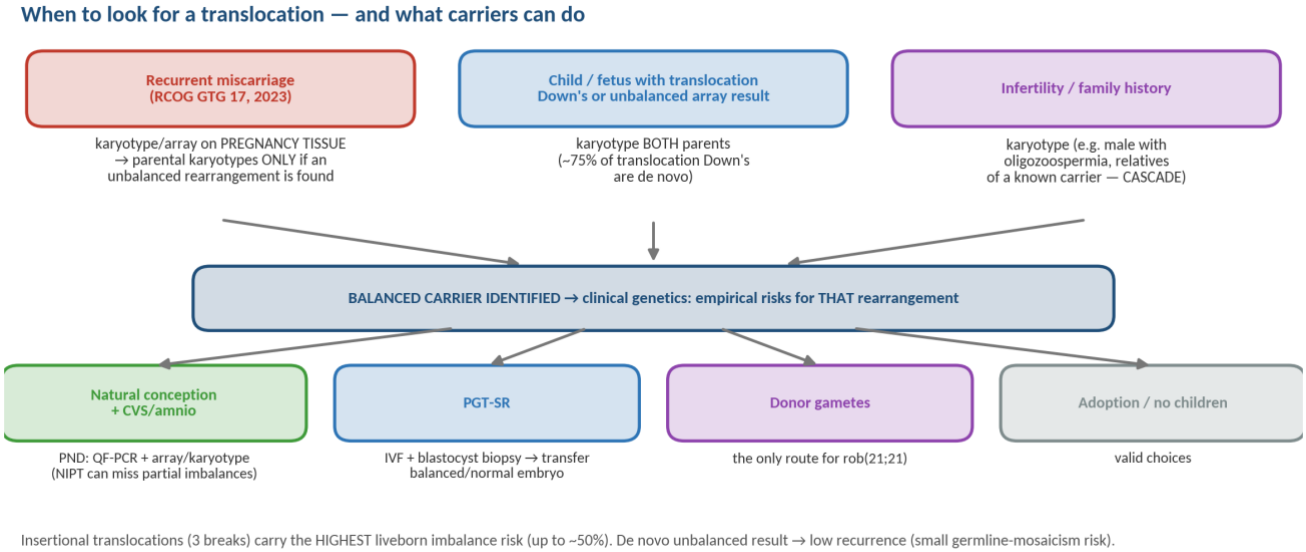


Figure 3. When to test and reproductive options.

- **PGT-SR**: IVF → blastocyst trophectoderm biopsy → NGS/array → frozen transfer of a normal/balanced embryo. Only a proportion of embryos are suitable; standard IVF success rates apply; most methods cannot tell normal from balanced.

4 Detection

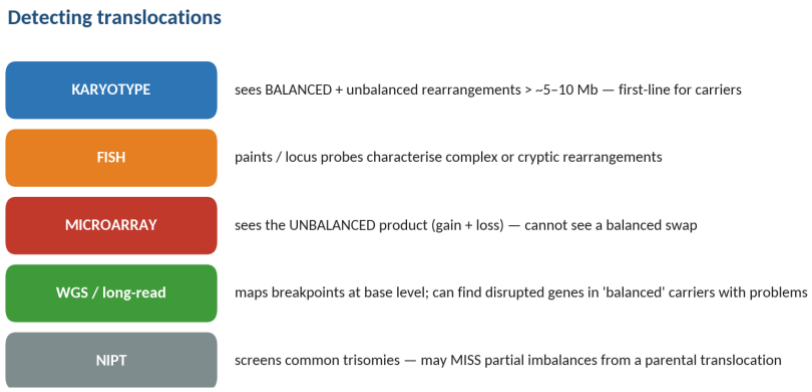


Figure 4. Detecting translocations.

5 Acquired Translocations in Cancer

ACQUIRED (somatic) translocations in cancer — in the tumour, NOT inherited

Translocation	Fusion / effect	Cancer	Targeted / use
t(9;22)(q34;q11)	BCR–ABL1 (Philadelphia)	CML, some ALL	imatinib & other TKIs; RT-qPCR monitoring
t(15;17)(q24;q21)	PML–RARA	acute promyelocytic leukaemia (DIC!)	ATRA + arsenic trioxide
t(8;14)(q24;q32)	MYC → IGH enhancer	Burkitt lymphoma	intensive chemo
t(14;18)(q32;q21)	IGH–BCL2 (anti-apoptosis)	follicular lymphoma	rituximab-based
t(11;14)(q13;q32)	CCND1–IGH (cyclin D1)	mantle cell lymphoma	BTK inhibitors etc.
t(X;18)(p11;q11)	SS18–SSX	synovial sarcoma	surgery ± chemo
t(11;22)(q24;q12)	EWSR1–FLI1	Ewing sarcoma	chemo + local therapy

In pregnancy: CML → avoid tyrosine kinase inhibitors (teratogenic, esp. 1st trimester); interferon-α or leukapheresis; MDT. Detect fusions by FISH or RT-PCR.

Figure 5. Cancer translocations.

★ PEARL

Karyotype sees balanced rearrangements; microarray sees only their unbalanced products. Translocation Down's → karyotype both parents (~25% inherited).

RCOG 2023: parental karyotypes for recurrent miscarriage ONLY if pregnancy tissue shows an unbalanced rearrangement.

6 MRCOG Exam Pearls — Last-Minute Page

Numbers to know

~1 in 500 Reciprocal carriers	**~1 in 1000** Robertsonian carriers	**~75%** Rob(13;14) share	**10–15% / ~1%** Rob(14;21) mother / father
~100% Rob(21;21)	**~75%** Translocation Down's de novo	**2 / 3** Breaks: reciprocal / insertional	**45** Chromosomes in Robertsonian carrier

HIGH-YIELD CHECKLIST

- ☐ Reciprocal: 2 breaks, balanced carrier healthy; quadrivalent.
- ☐ Alternate = balanced; adjacent-1/-2 and 3:1 = unbalanced.
- ☐ t(11;22) commonest; Emanuel syndrome via 3:1.
- ☐ Robertsonian: acrocentrics 13, 14, 15, 21, 22; 45 chromosomes; trivalent.
- ☐ Rob(14;21): mother 10–15%, father ~1%; rob(21;21) 100%.
- ☐ Rob(13;14) commonest; small UPD14/15 risk.
- ☐ RCOG 2023: karyotype parents only if POC unbalanced.
- ☐ Options: PND, PGT-SR, donor gametes, adoption; cascade testing.
- ☐ Karyotype vs array vs FISH vs WGS vs NIPT.
- ☐ BCR-ABL, PML-RARA, MYC-IGH, BCL2-IGH, CCND1-IGH, SS18-SSX, EWSR1-FLI1.

Self-assessment — cover the right-hand column

Question	Answer
Meiotic figure in a reciprocal carrier?	Quadrivalent
Segregation giving balanced gametes?	Alternate
Commonest recurrent reciprocal translocation?	t(11;22)(q23;q11.2)
Chromosomes involved in Robertsonian translocations?	Acrocentrics 13, 14, 15, 21, 22
Down's risk if father carries rob(14;21)?	~1%
Why does rob(21;21) always give Down's?	Every gamete is disomic or nullisomic for 21
Can microarray detect a balanced translocation?	No
Embryo test for carriers?	PGT-SR
When are parental karyotypes indicated in RM?	Unbalanced rearrangement in pregnancy tissue
Fusion gene in APL?	PML–RARA (t(15;17))

7 References

- RCOG Green-top Guideline No. 17. Recurrent miscarriage. 2023.
- Gardner RJM, Amor DJ. Chromosome Abnormalities and Genetic Counselling. 5th ed. 2018.
- ESHRE PGT Consortium good practice recommendations. 2020.