PIPADOR REVISION

MRCOG Part 1 Revision Notes

Mendelian Inheritance

GENETICS • LECTURE 78

VISUAL EXAMINATION REVISION NOTES

2026 Edition

MRCOG Part 1 Revision Notes

Lecture 78: Mendelian Inheritance

Genetics • Visual revision edition

COLOUR CODE USED THROUGHOUT THESE NOTES

AUTOSOMAL DOMINANT | AUTOSOMAL RECESSIVE | X-LINKED | MITOCHONDRIAL | COUNSELLING

LEARNING OBJECTIVES — tick off as you go

- ☐ Define the key genetic terms and Mendel's two laws.
- ☐ Recognise AD, AR, X-linked, Y-linked and mitochondrial patterns on a pedigree.
- ☐ Calculate recurrence risks with Punnett squares and Hardy–Weinberg.
- ☐ Explain penetrance, expressivity, heterogeneity, mosaicism, anticipation and imprinting.
- ☐ Apply to counselling, carrier screening and reproductive options.

1 Terms and Laws

IN ONE LINE: *Mendel: each person has two alleles; one goes into each gamete (SEGREGATION), and different genes sort independently (INDEPENDENT ASSORTMENT) — unless they are LINKED.*

Term	Meaning
Allele / locus	Version of a gene / its position on a chromosome
Homo- / hetero- / hemizygous	Two same / two different / only one copy (X genes in males)
Compound heterozygote	Two DIFFERENT faulty alleles at one locus (common in CF)
Penetrance	% of people with the genotype who show ANY disease
Expressivity	How SEVERELY it shows in those who are affected
Linkage	Close genes travel together; recombination frequency ≈ distance

2 Patterns of Inheritance

Pedigree symbols — generations in Roman numerals (I, II, III), individuals in Arabic numerals



Figure 1. Pedigree symbols.

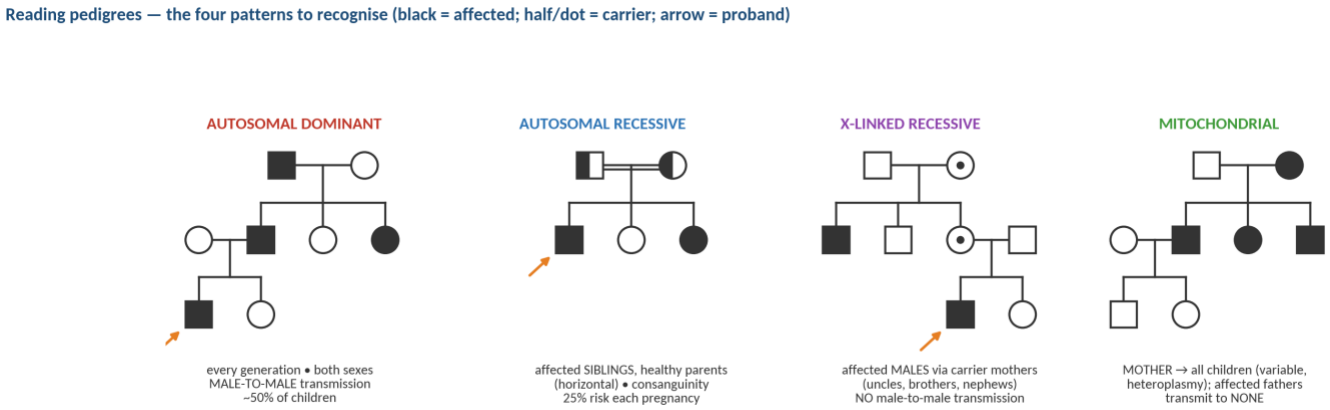


Figure 2. The four patterns.

Pattern	Clues	Examples
AD	Every generation; male-to-male; 50%	Huntington, Marfan, NF1, achondroplasia, BRCA1/2, myotonic dystrophy
AR	Affected sibs, healthy parents; consanguinity; 25%	CF, sickle cell, β-thalassaemia, CAH, SMA, Tay–Sachs, PKU, galactosaemia
X-linked recessive	Males via carrier mothers; no male-to-male; daughters of affected men are obligate carriers	Haemophilia A/B, DMD/Becker, G6PD, red–green colour blindness
X-linked dominant	Affected father → ALL daughters, NO sons; often lethal in males	X-linked hypophosphataemic rickets, Rett, incontinentia pigmenti
Y-linked	Father → all sons	AZF microdeletions (passed to sons via ICSI); SRY changes are usually new
Mitochondrial	Mother → all children (variable); never from father	LHON, MELAS, MERRF, Kearns–Sayre

- **Fragile X** (FMR1, CGG repeat) is X-linked but doesn't fit neatly: premutations expand when passed by a **mother**; about half of female full-mutation carriers are affected. Premutation carriers risk **premature ovarian insufficiency**.

3 Risk Calculation

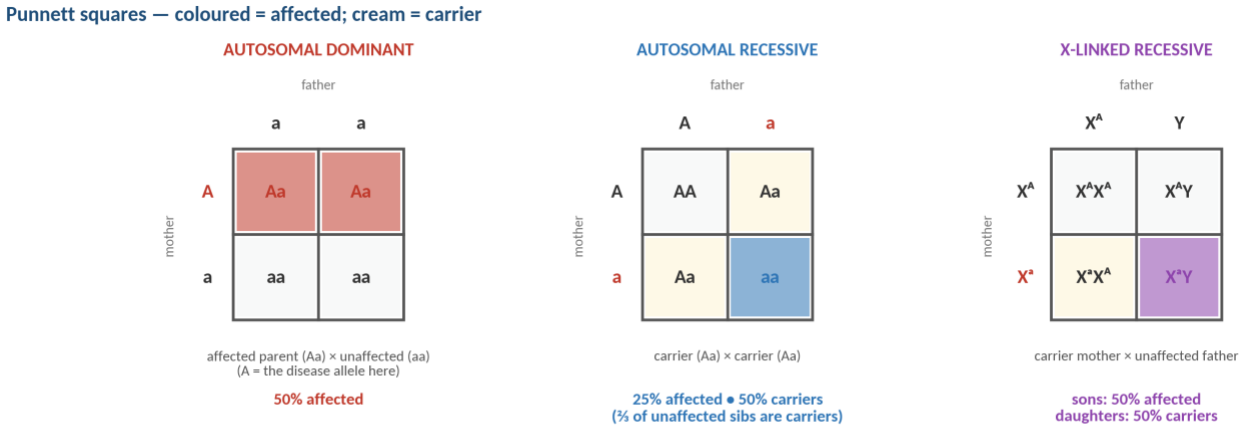


Figure 3. Punnett squares.

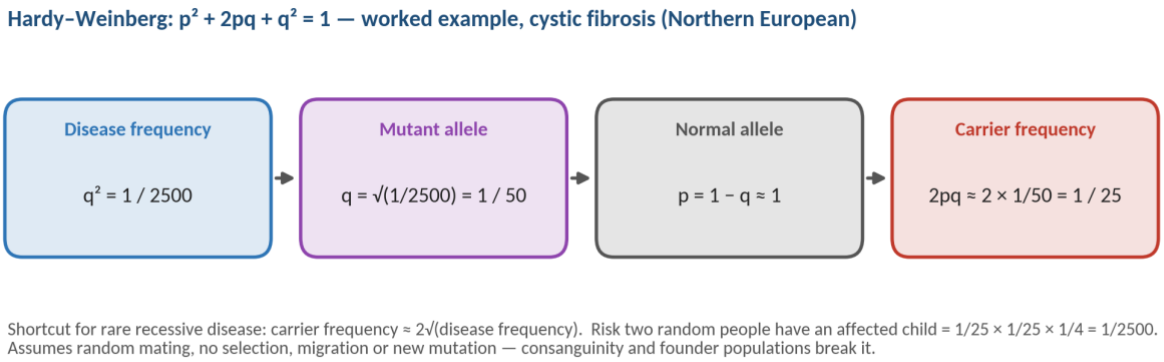


Figure 4. Hardy–Weinberg.

MNEMONIC / MEMORY HOOK

'Two-thirds trick': a healthy sibling of someone with an AR disease has a ⅔ chance of being a carrier (not ½) — the affected outcome is already excluded.

4 When Mendel Gets Complicated

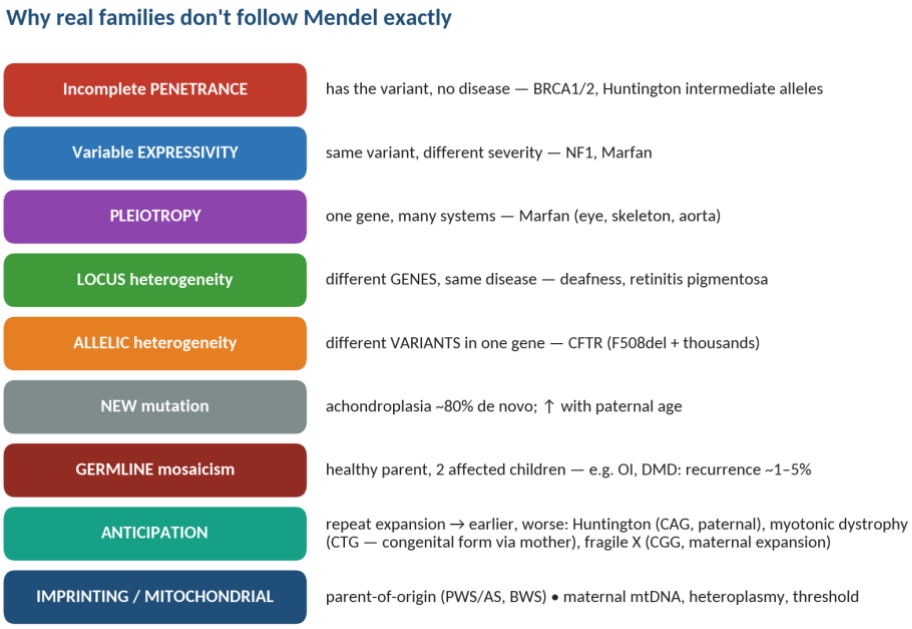


Figure 5. Modifiers of Mendelian patterns.

5 Counselling and Reproductive Options

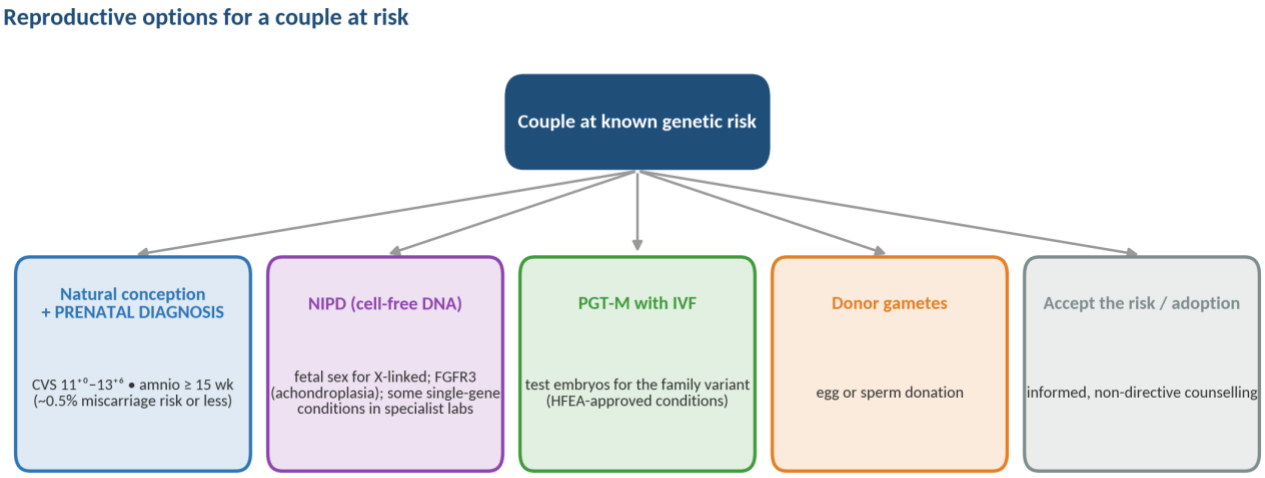


Figure 6. Reproductive options.

UK SCREENING

- **Antenatal sickle cell + thalassaemia** screening for all (family origin questionnaire; partner testing)
- **CF**: newborn bloodspot screening; carrier testing for relatives/partners — **not** routine population antenatal screening
- Ask about family origin and consanguinity sensitively; 3-generation family tree

CONSANGUINITY

- First cousins share ~1/8 of their genes
- Risk of a serious congenital/genetic problem roughly **doubles** (~2–3% → ~4–6%), mostly AR
- Offer carrier testing where a family condition is known

BRCA PENETRANCE (by ~80 y)

- **BRCA1**: breast ~70%, ovarian ~40–45%
- **BRCA2**: breast ~70%, ovarian ~15–20%
- Surveillance, risk-reducing mastectomy, **salpingo-oophorectomy** (BRCA1 ~35–40 y, BRCA2 ~40–45 y)

MITOCHONDRIAL DISEASE

- Heteroplasmy + threshold → hard to predict severity
- Many mitochondrial diseases are actually **nuclear-gene (Mendelian)**
- UK: **mitochondrial donation** licensed by the HFEA (Newcastle)

★ **PEARL**

Male-to-male transmission rules out X-linked inheritance. Affected father with ALL daughters affected and no sons → X-linked dominant.

CF carrier frequency ~1 in 25 (Northern Europe) — from Hardy–Weinberg with disease 1 in 2500.

6 MRCOG Exam Pearls — Last-Minute Page

Numbers to know

50% AD child risk	**25%** AR (carrier × carrier)	**⅔** Healthy sib is a carrier	**1 in 25** CF carriers
~80% Achondroplasia de novo	**~1/8** Genes shared by 1st cousins	**~70%** BRCA breast risk	**55–200** FMR1 premutation

HIGH-YIELD CHECKLIST

- ☐ Segregation + independent assortment; linkage is the exception.
- ☐ AD: vertical, male-to-male, 50%.
- ☐ AR: horizontal, consanguinity, 25%; healthy sib ⅔ carrier.
- ☐ XLR: no male-to-male; daughters of affected men are carriers.
- ☐ XLD: father → all daughters, no sons.
- ☐ Mitochondrial: maternal, heteroplasmy, threshold.
- ☐ Hardy–Weinberg: carriers ≈ 2√(disease frequency).
- ☐ Penetrance vs expressivity; locus vs allelic heterogeneity.
- ☐ De novo, germline mosaicism, anticipation (HD paternal, DM congenital maternal, FXS maternal).
- ☐ Options: PND (CVS/amnio), NIPD, PGT-M, donor gametes.

Self-assessment — cover the right-hand column

Question	Answer
Which pattern shows male-to-male transmission?	Autosomal dominant
Risk of an affected child, two carrier parents (AR)?	25%
Carrier chance of a healthy sib of a CF child?	⅔
CF carrier frequency if disease is 1 in 2500?	~1 in 25
Sons of a man with haemophilia — affected?	None (all daughters are carriers)
Define penetrance.	Proportion with the genotype who show the disease
Example of pleiotropy?	Marfan syndrome
What explains two affected children of healthy parents in an AD disease?	Germline (gonadal) mosaicism
Mechanism of anticipation?	Trinucleotide repeat expansion
UK population-wide antenatal genetic screening?	Sickle cell and thalassaemia

7 References

- Turnpenny P, Ellard S. Emery's Elements of Medical Genetics. 16th ed. 2021.
- NHS Sickle Cell and Thalassaemia Screening Programme — standards.
- Kuchenbaecker KB et al. Risks of breast, ovarian and contralateral breast cancer for BRCA1/2 carriers. JAMA 2017.