PIPADOR REVISION

MRCOG Part 1 Revision Notes

Prader–Willi and Angelman Syndromes

CELL BIOLOGY • LECTURE 119

VISUAL EXAMINATION REVISION NOTES

2026 Edition

MRCOG Part 1 Revision Notes

Lecture 119: Prader–Willi and Angelman Syndromes

Cell biology • Visual revision edition — links Lectures 87, 94, 110

COLOUR CODE USED THROUGHOUT THESE NOTES

PATERNAL	MATERNAL / HIGH RISK	PRADER–WILLI	ANGELMAN	LOW RISK / OTHER

LEARNING OBJECTIVES — tick off as you go

- ☐ Explain genomic imprinting at 15q11–q13 and why one region gives two syndromes.
- ☐ List the mechanisms and their frequencies for PWS and AS.
- ☐ Describe the clinical course of each syndrome.
- ☐ Use methylation testing first and know recurrence by mechanism.
- ☐ Recognise other imprinting disorders and the ART association.

1 Imprinting at 15q11–q13

IN ONE LINE: *Prader–Willi genes work only from DAD's chromosome 15; the Angelman gene (UBE3A) works only from MUM's (in neurons). Lose the paternal copy → PWS; lose the maternal copy → AS.*

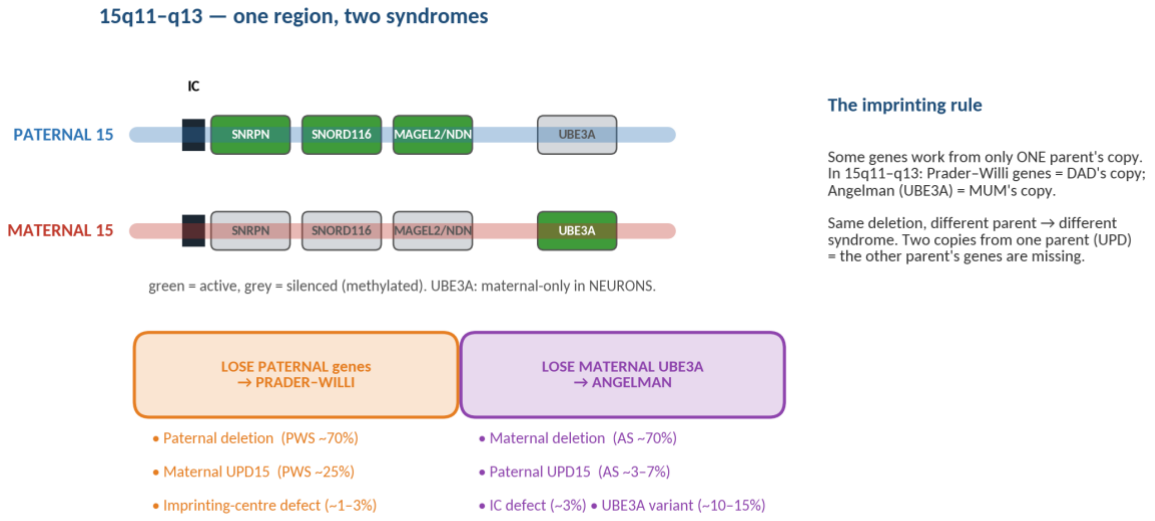


Figure 1. One region, two syndromes.

MNEMONIC / MEMORY HOOK

'Prader = Paternal missing; Angelman = mAternal missing' — and UPD of the OTHER parent's 15 does the same.

2 Prader–Willi Syndrome

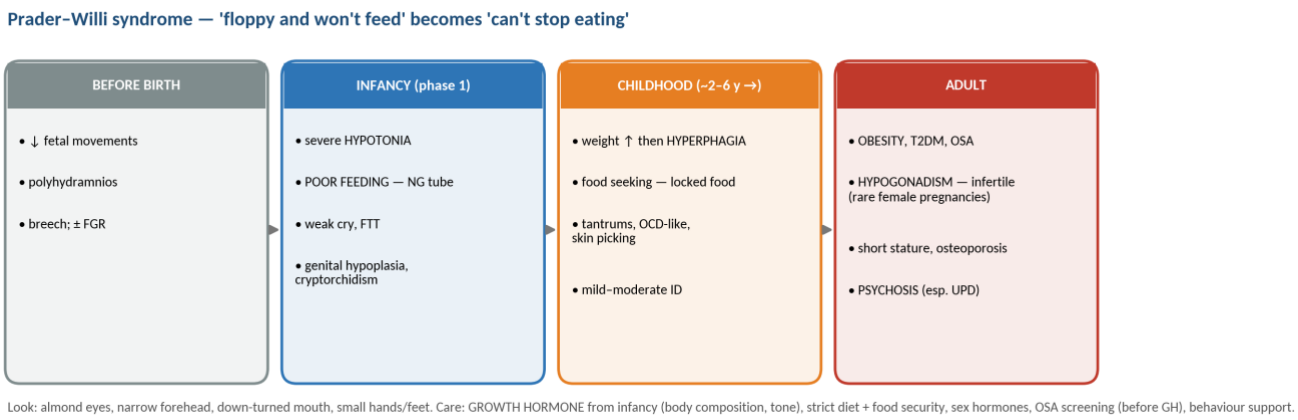


Figure 2. PWS through life.

3 Angelman Syndrome

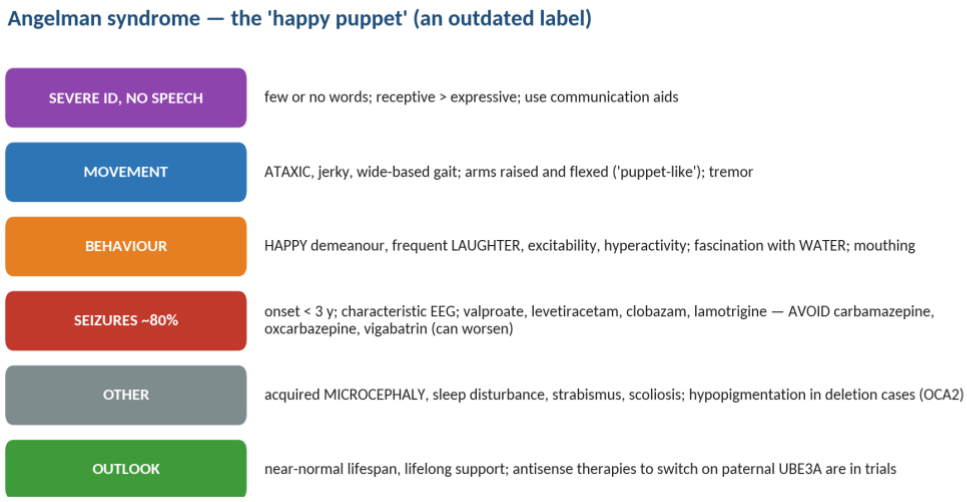


Figure 3. Angelman syndrome.

	Prader–Willi	Angelman
Missing	Paternal 15q11–q13	Maternal UBE3A
Infancy	Severe hypotonia, poor feeding	Delay, hypotonia; feeds OK
Later	Hyperphagia, obesity, hypogonadism	Normal weight; ataxia, laughter
Speech / IQ	Speaks; mild–moderate ID	Absent speech; severe ID
Seizures	Uncommon	~80%
Key test	Methylation	Methylation → UBE3A sequencing

4 Diagnosis and Recurrence

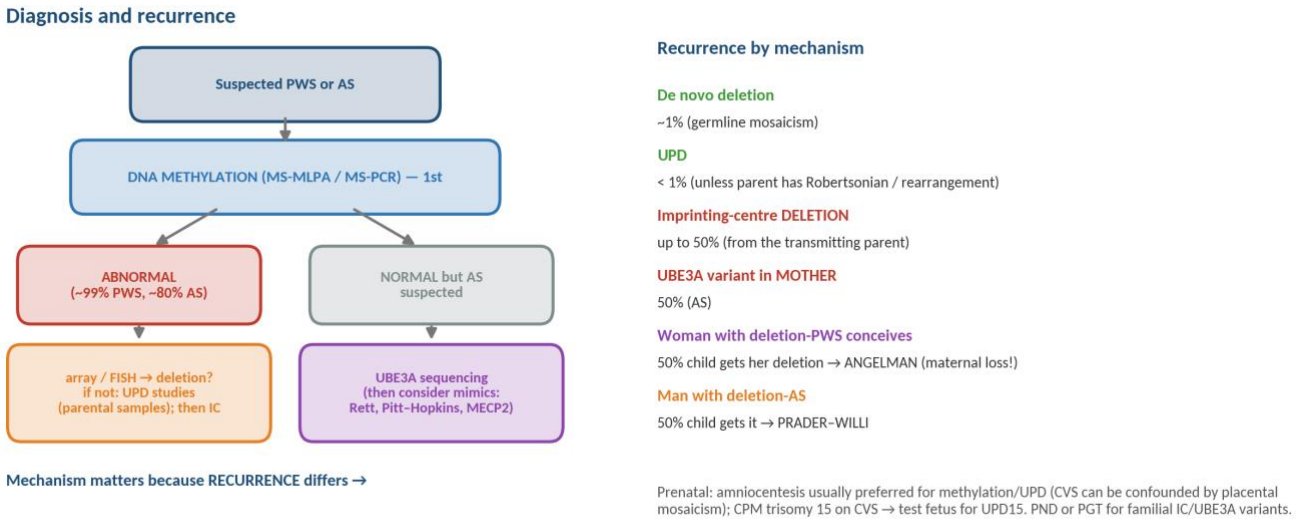


Figure 4. Testing pathway and recurrence.

5 Other Imprinting Disorders

Other imprinting disorders — and the ART link

Syndrome	Locus	Mechanisms	Features
BECKWITH-WIEDEMANN	11p15.5	IC2 (KvDMR1) LOSS of methylation ~50%; paternal UPD11 ~20%; CDKN1C ~5%; IC1 GAIN ~5%	OVERGROWTH, macroglossia, EXOMPHALOS, neonatal HYPOGLYCAEMIA, hemihypertrophy; Wilms/hepatoblastoma screening
SILVER-RUSSELL	11p15.5 / 7	IC1 (H19/IGF2) LOSS of methylation ~50%; maternal UPD7 ~10%	severe FGR, relative macrocephaly, triangular face, body asymmetry, feeding problems
TEMPLE / KAGAMI-OGATA	14q32	maternal UPD14 → Temple; paternal UPD14 → Kagami-Ogata	Temple: FGR, hypotonia, early puberty. KOS: polyhydramnios, BELL-SHAPED thorax ('coat-hanger' ribs), omphalocele
TRANSIENT NEONATAL DIABETES	6q24	paternal UPD6 / dup / maternal hypomethylation (PLAGL1)	FGR + neonatal diabetes, usually resolves by ~3 months; may recur later

ART (IVF/ICSI): relative risk of BWS (and SRS) raised ~3–5×, but ABSOLUTE risk remains low (< 1 in 1000) — mention in counselling; BWS surveillance if diagnosed.

Figure 5. Other imprinting disorders.

★ PEARL

Methylation testing first for both (detects deletion, UPD and IC defects). Normal methylation but AS suspected → UBE3A sequencing.

A woman with deletion-PWS who conceives passes her deletion to 50% — as a MATERNAL loss → Angelman. CPM trisomy 15 on CVS → test for UPD15.

6 MRCOG Exam Pearls — Last-Minute Page

Numbers to know

~70% Deletion (PWS and AS)	**~25%** Maternal UPD15 in PWS	**~3–7%** Paternal UPD15 in AS	**~10–15%** UBE3A variants in AS

~80%	~1%	Up to 50%	~3–5×
Seizures in AS	Recurrence (deletion)	IC deletion / UBE3A	BWS relative risk after ART

HIGH-YIELD CHECKLIST

- ☐ 15q11–q13: SNRPN/SNORD116 paternal; UBE3A maternal (brain); IC.
- ☐ PWS: paternal del ~70%, maternal UPD ~25%, IC ~1–3%.
- ☐ AS: maternal del ~70%, UBE3A ~10–15%, paternal UPD ~3–7%, IC ~3%.
- ☐ PWS: hypotonia/poor feeding → hyperphagia, obesity, hypogonadism; GH.
- ☐ AS: severe ID, no speech, ataxia, laughter, seizures; avoid carbamazepine.
- ☐ Methylation first; then array/UPD/IC; UBE3A if normal.
- ☐ Recurrence: deletion ~1%, UPD <1%, IC/UBE3A up to 50%.
- ☐ Prenatal: amnio preferred; CPM T15 → UPD15 test.
- ☐ BWS (IC2 LOM commonest), SRS (IC1 LOM, UPD7), Temple/KOS, TNDM.
- ☐ ART: BWS RR ~3–5×, absolute risk low.

Self-assessment — cover the right-hand column

Question	Answer
Loss of which parent's 15q11–q13 causes PWS?	Paternal
Gene responsible for Angelman?	UBE3A (maternal allele)
Second commonest cause of PWS?	Maternal UPD15
First-line test for both?	DNA methylation analysis
Next test if methylation normal but AS suspected?	UBE3A sequencing
Hallmark of PWS after age 2?	Hyperphagia and obesity
Hormone treatment from infancy in PWS?	Growth hormone
Recurrence if mother carries a UBE3A variant?	50%
Commonest BWS mechanism?	Loss of methylation at IC2 (KvDMR1)
CVS shows CPM trisomy 15 — what next?	Amnio + UPD15 testing

7 References

- Driscoll DJ et al. Prader–Willi syndrome. GeneReviews (updated).
- Dagli AI et al. Angelman syndrome. GeneReviews (updated).
- Brioude F et al. Beckwith–Wiedemann syndrome: international consensus. Nat Rev Endocrinol 2018.