PIPADOR REVISION

MRCOG Part 1 Revision Notes

Marfan, Ehlers–Danlos and Connective Tissue Disorders

CELL BIOLOGY • LECTURE 121

VISUAL EXAMINATION REVISION NOTES

2026 Edition

MRCOG Part 1 Revision Notes

Lecture 121: Marfan, Ehlers–Danlos and Other Connective Tissue Disorders

Cell biology • Visual revision edition — single-gene disorders begin

COLOUR CODE USED THROUGHOUT THESE NOTES

MARFAN / AORTA	VASCULAR EDS / HIGH RISK	HYPERMOBILE / CLASSICAL	OI / SKELETAL	LOWER RISK / SAFE

LEARNING OBJECTIVES — tick off as you go

- ☐ Compare the main heritable connective tissue disorders and their genes.
- ☐ Describe Marfan syndrome and its diagnosis (Ghent).
- ☐ Plan pregnancy in Marfan syndrome using aortic root thresholds.
- ☐ Distinguish vascular, hypermobile and classical EDS and their obstetric risks.
- ☐ Know osteogenesis imperfecta, Loeys–Dietz and achondroplasia in pregnancy.

1 Overview

IN ONE LINE: *Faulty structural proteins — fibrillin, collagens, TGF-β pathway — weaken aorta, arteries, skin, joints, bone or uterus. Pregnancy multiplies the vascular risk, especially in the third trimester and puerperium.*

Heritable connective tissue disorders at a glance — most are autosomal dominant (50% to each child)

Disorder	Gene	Inheritance	Key features	Pregnancy risk
MARFAN	FBN1 (fibrillin-1)	AD (~25% de novo)	aortic ROOT dilatation/dissection, ectopia lentis (UP), tall, arachnodactyly	HIGH if root ≥ 40–45 mm
LOEYS–DIETZ	TGFBR1/2, SMAD3, TGFB2/3	AD	aneurysms + TORTUOUS arteries everywhere, bifid uvula, hypertelorism	VERY HIGH — dissects at smaller sizes
VASCULAR EDS	COL3A1 (type III collagen)	AD	thin translucent skin, bruising, ARTERIAL, BOWEL + UTERINE rupture	HIGHEST — maternal death ~5–12%
CLASSICAL EDS	COL5A1/2	AD	very stretchy skin, wide atrophic 'cigarette-paper' scars, hypermobility	moderate: tears, wound healing
HYPERMOBILE EDS	unknown (clinical diagnosis)	AD	hypermobility (Beighton), dislocations, pain, POTS	low vascular risk; pain, fast labour
OSTEOGENESIS IMP.	COL1A1/2 (type I); some AR	mostly AD	fractures, BLUE sclera, dentinogenesis imperfecta, deafness	fractures, pelvis, fetal OI risk

Figure 1. At a glance.

2 Marfan Syndrome

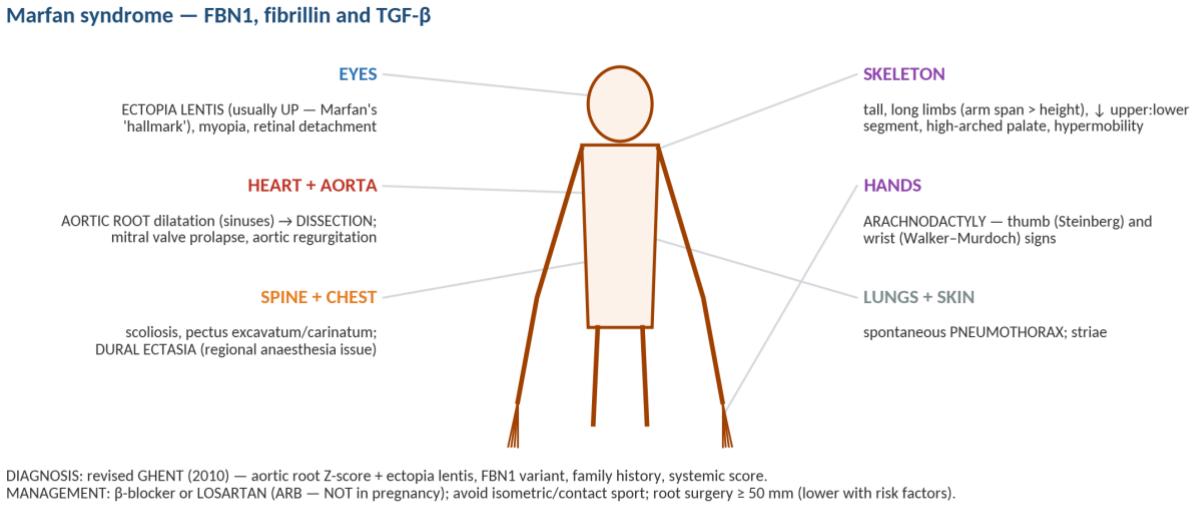


Figure 2. Marfan syndrome.

MNEMONIC / MEMORY HOOK

'Marfan lenses look UP, homocystinuria lenses look DOWN' — Marfan ectopia lentis is usually superotemporal.

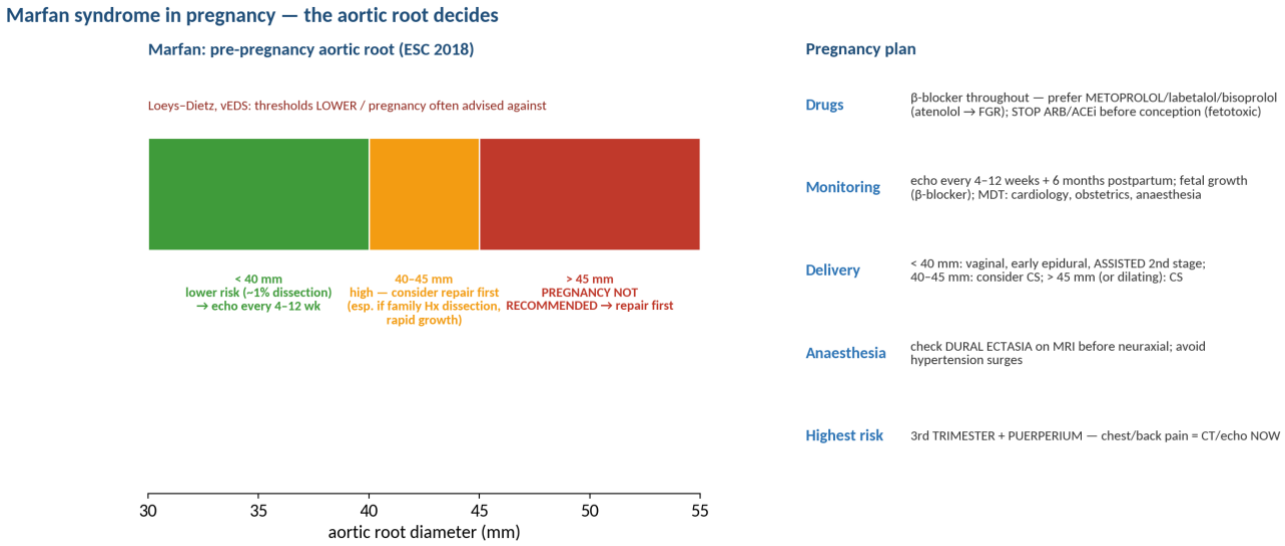


Figure 3. Marfan in pregnancy.

3 Ehlers–Danlos and Loeys–Dietz

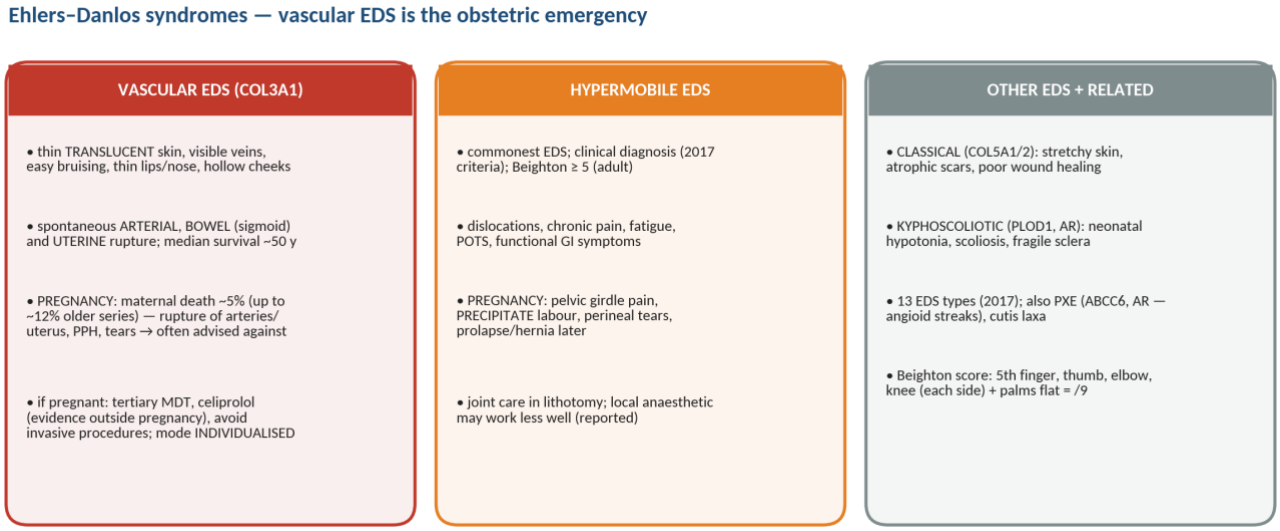


Figure 4. Ehlers–Danlos syndromes.

- **Loeys–Dietz** (TGFBR1/2, SMAD3, TGFB2/3): aneurysms and TORTUOUS arteries throughout, bifid uvula, hypertelorism; dissection at smaller diameters than Marfan → image the WHOLE arterial tree (MRA) before pregnancy; very high risk.

4 Skeletal Disorders

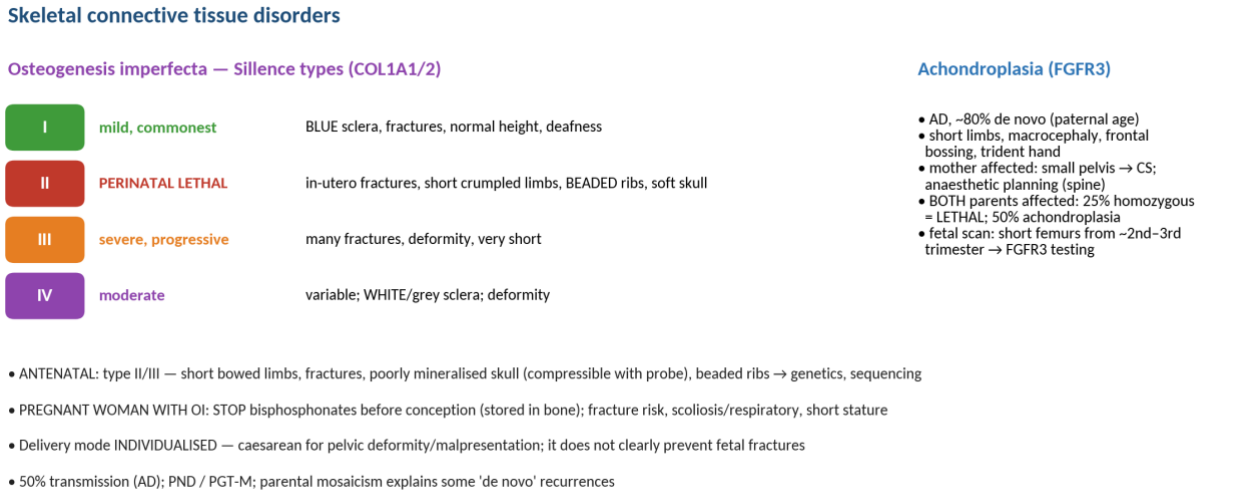


Figure 5. Osteogenesis imperfecta and achondroplasia.

★ PEARL

Marfan: root > 45 mm → pregnancy not recommended (repair first); 40–45 mm high risk. β-blocker throughout (avoid atenolol); stop ARB/ACEi before conception.

Vascular EDS (COL3A1): arterial, bowel and uterine rupture — maternal death ~5% or more; often advised against pregnancy; tertiary MDT if pregnant.

5 MRCOG Exam Pearls — Last-Minute Page

Numbers to know

~25% Marfan de novo	**< 40 mm** Marfan lower-risk root	**> 45 mm** Avoid pregnancy (Marfan)	**≥ 50 mm** Elective root surgery
~5–12% vEDS maternal death	**~50 y** vEDS median survival	**≥ 5 / 9** Beighton (adult hEDS)	**25%** Homozygous achondroplasia (2 affected parents)

HIGH-YIELD CHECKLIST

- ☐ Marfan FBN1 AD; ectopia lentis UP; aortic root; Ghent 2010.
- ☐ β-blocker/losartan; surgery ≥ 50 mm; no ARB in pregnancy.
- ☐ Pregnancy: < 40 / 40–45 / > 45 mm; echo 4–12 wk; 6 months postpartum.
- ☐ Delivery: assisted 2nd stage < 40 mm; CS > 45 mm; dural ectasia.
- ☐ Loeys–Dietz: tortuous arteries, bifid uvula — very high risk.
- ☐ vEDS COL3A1: arterial/bowel/uterine rupture; mortality ~5–12%.
- ☐ hEDS: Beighton, pain, POTS, precipitate labour, tears.
- ☐ Classical EDS COL5A1/2: stretchy skin, atrophic scars.
- ☐ OI COL1A1/2: Sillence I–IV; stop bisphosphonates pre-conception.
- ☐ Achondroplasia FGFR3: 80% de novo; CS for small pelvis; homozygous lethal.

Self-assessment — cover the right-hand column

Question	Answer
Gene in Marfan syndrome?	FBN1 (fibrillin-1)
Direction of lens dislocation in Marfan?	Usually upward
Root size above which pregnancy is not recommended?	> 45 mm
Drug class to stop before conception?	ARBs / ACE inhibitors
β-blocker to avoid because of FGR?	Atenolol
Anaesthetic issue in Marfan?	Dural ectasia
Gene in vascular EDS?	COL3A1
Most serious obstetric complication of vEDS?	Arterial/uterine rupture (maternal death)
OI type that is perinatal lethal?	Type II
Drug to stop before conception in OI?	Bisphosphonates

6 References

- Regitz-Zagrosek V et al. 2018 ESC Guidelines for the management of cardiovascular diseases during pregnancy. Eur Heart J 2018.
- Malfait F et al. The 2017 international classification of the Ehlers–Danlos syndromes. Am J Med Genet C 2017.
- Loeys BL et al. The revised Ghent nosology for the Marfan syndrome. J Med Genet 2010.