PIPADOR REVISION

MRCOG Part 1 Revision Notes

Renin–Angiotensin System

ENDOCRINOLOGY • LECTURE 178

VISUAL EXAMINATION REVISION NOTES

2026 Edition

MRCOG PART 1 REVISION NOTES | ENDOCRINOLOGY

178 Renin–Angiotensin System

Components and actions, pregnancy adaptation and angiotensin II refractoriness, pre-eclampsia and RAAS blockade

JG cells	ACE	AT_1	Refractory
Renin source (afferent arteriole)	Lung endothelium: Ang I → Ang II	Vasoconstriction, aldosterone	Vascular response to Ang II in pregnancy

■ KEY FACTS: Learning objectives

- Describe the components and regulation of the renin–angiotensin–aldosterone system and the actions of angiotensin II.
- Describe the RAAS in normal pregnancy, including angiotensin II refractoriness.
- Describe changes in pre-eclampsia, the uteroplacental RAS and the fetotoxicity of RAAS blockade.

178.1 The system

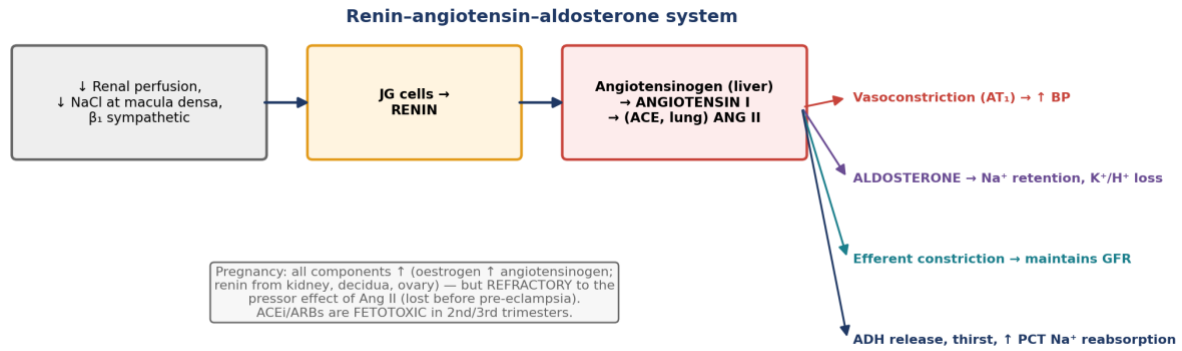


Figure 178.1 — The renin–angiotensin–aldosterone cascade

Component	Details
Renin	Aspartyl protease from juxtaglomerular cells (afferent arteriole). Released by: ↓ renal perfusion pressure (baroreceptor), ↓ NaCl at macula densa, β_1 sympathetic stimulation; inhibited by Ang II, ANP, high BP. Rate-limiting step
Angiotensinogen	α_2-globulin from the liver; ↑ by oestrogen (pregnancy, COC → BP), cortisol, thyroid hormones
ACE	On endothelium (especially lungs); converts Ang I → Ang II and degrades bradykinin (ACE-inhibitor cough, angio-oedema)
Angiotensin II	AT_1 receptor: arteriolar vasoconstriction, aldosterone, ADH and thirst, sympathetic facilitation, efferent arteriolar constriction (maintains GFR), PCT Na^+ reabsorption, cardiac/vascular remodelling. AT_2: opposing vasodilatory, anti-proliferative effects (fetal tissues)
Other peptides	Ang 1–7 (via ACE2, Mas receptor): vasodilatation — ↑ in normal pregnancy

178.2 RAAS in normal pregnancy

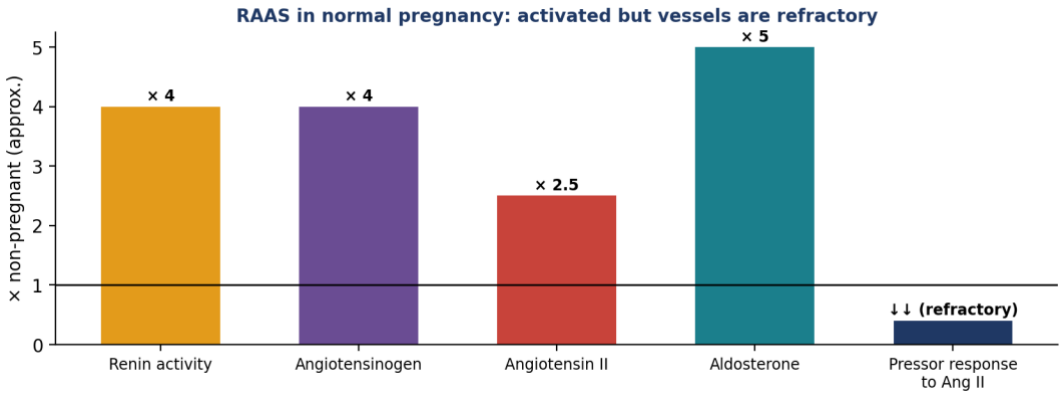


Figure 178.2 — RAAS components in pregnancy

- Early **systemic vasodilatation** (↓ SVR) → perceived arterial underfilling → **↑ renin**; oestrogen **↑ angiotensinogen**; extra-renal renin from **ovary (CL), decidua and chorion** (prorenin very high in early pregnancy).
- **Ang II and aldosterone ↑** → sodium and water retention → **plasma volume expansion** (Lecture 126); progesterone's natriuretic effect balances aldosterone; K^+ retained.
- **Refractoriness to the pressor effect of Ang II**: pregnant women need ≈ 2–3× the dose to raise BP — due to ↑ **prostacyclin and NO**, ↑ **Ang 1–7**, ↑ AT_2 expression, reduced AT_1 sensitivity (progesterone metabolites).

178.3 Pre-eclampsia

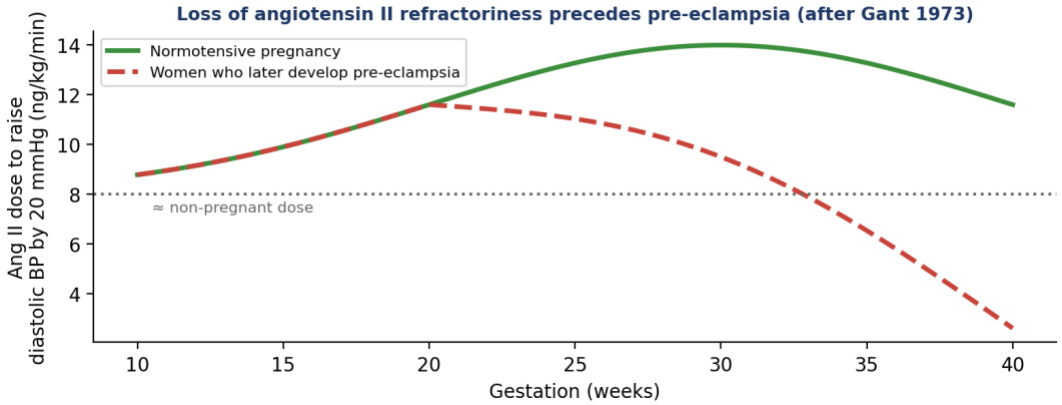


Figure 178.3 — Loss of angiotensin II refractoriness before pre-eclampsia

Feature	Pre-eclampsia vs normal pregnancy
Ang II sensitivity	↑ (refractoriness lost from ≈ 20–24 weeks — before hypertension)
Renin, Ang II, aldosterone	Lower than normal pregnancy (suppressed by hypertension/vasoconstriction)
AT_1 receptor autoantibodies (AT1-AA)	Agonistic autoantibodies — vasoconstriction, sFlt-1 release
AT_1–bradykinin B_2 heterodimers	↑ AT_1 sensitivity on platelets/vessels
Plasma volume	↓ (vs expanded in normal pregnancy)

178.4 Uteroplacental and fetal RAS

A local RAS in decidua, chorion and placenta regulates trophoblast invasion, angiogenesis and uteroplacental blood flow. The fetal RAS is essential for **renal development and fetal urine output** (Lecture 153).

■ **RED FLAGS**

- **ACE inhibitors and ARBs are contraindicated in the 2nd and 3rd trimesters**: fetal **renal tubular dysgenesis**, anuria → **oligohydramnios**, pulmonary hypoplasia, **skull hypoplasia**, limb contractures, neonatal hypotension and renal failure. Switch before or as soon as pregnancy is confirmed (labetalol, nifedipine, methyldopa).
- **Direct renin inhibitors** (aliskiren) and **spironolactone** (anti-androgenic) are also avoided. ACE inhibitors (enalapril, captopril) are compatible with **breastfeeding**.

178.5 Must-know summary

■ **EXAM TIP**

- Renin (JG cells) is rate-limiting — released by ↓ perfusion, ↓ macula densa NaCl, β_1.
- **Oestrogen ↑ angiotensinogen** (COC/pregnancy BP); ACE in lungs; ACE also degrades bradykinin.
- Ang II via **AT_1**: vasoconstriction, aldosterone, ADH, thirst, efferent constriction.
- Pregnancy: RAAS **activated** but **refractory to Ang II** (PGI_2, NO, Ang 1–7); lost early in pre-eclampsia.
- ACEi/ARB **fetotoxic** after the 1st trimester; safe in breastfeeding.

■ **MNEMONIC / MEMORY AID**

Renin release — 'Pressure low, Salt low, Sympathetic go'.