THE UNIVERSITY OF MELBOURNE

Melbourne Veterinary School

Structure and Function of the Kidney – Renal control of blood volume, sodium, chloride and potassium concentrations

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VETS30017 / VETS90125

Intended learning outcomes

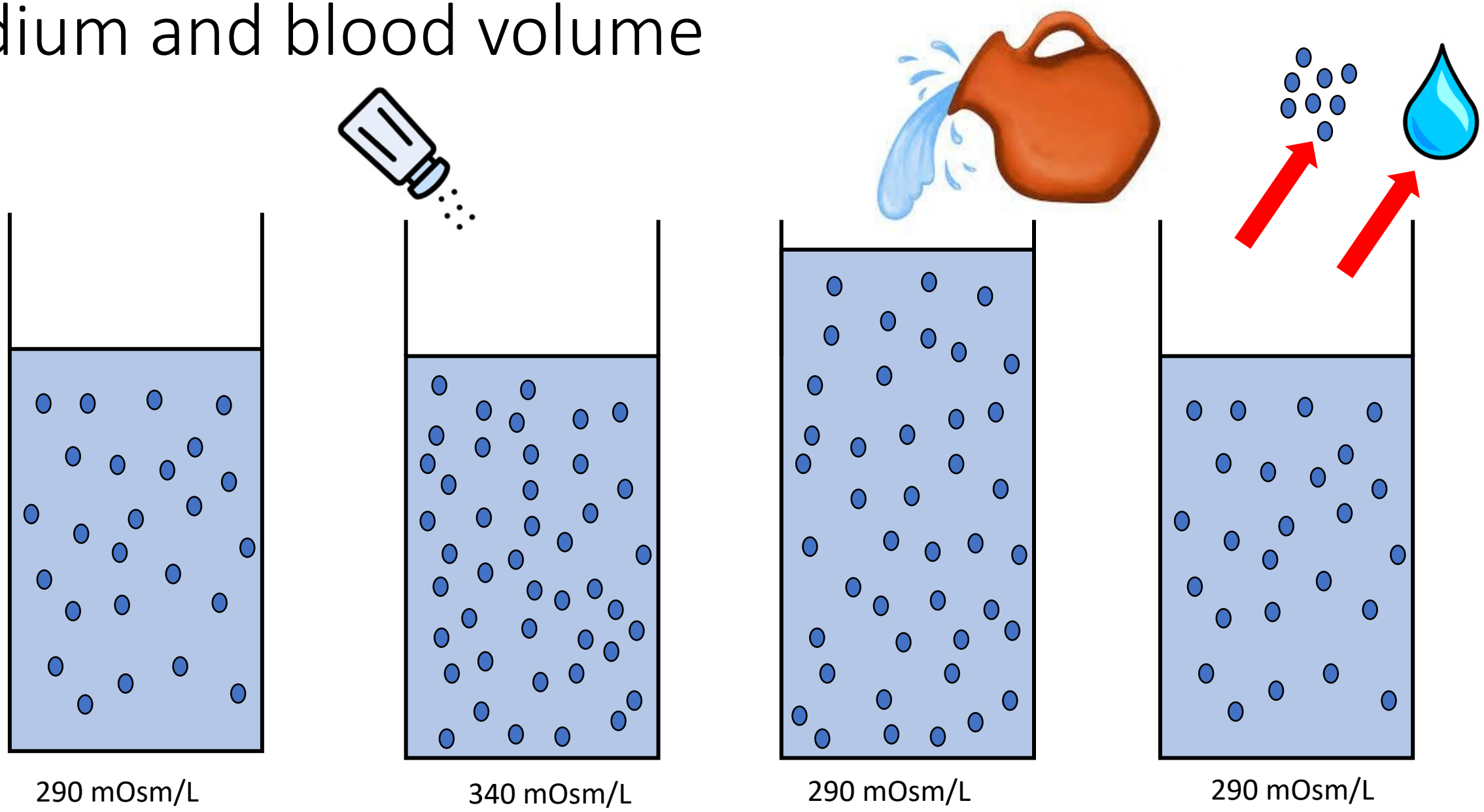
- Explain why changes in extracellular fluid are linked to sodium concentrations and water movement
- Describe the renin-angiotensin-aldosterone system (RAAS) and how it is regulated
- Discuss how sympathetic nerves, angiotensin II, aldosterone and natriuretic peptides regulate sodium secretion and reabsorption
- Describe the mechanisms and regulation of potassium secretion and reabsorption by the kidney

Sodium and blood volume

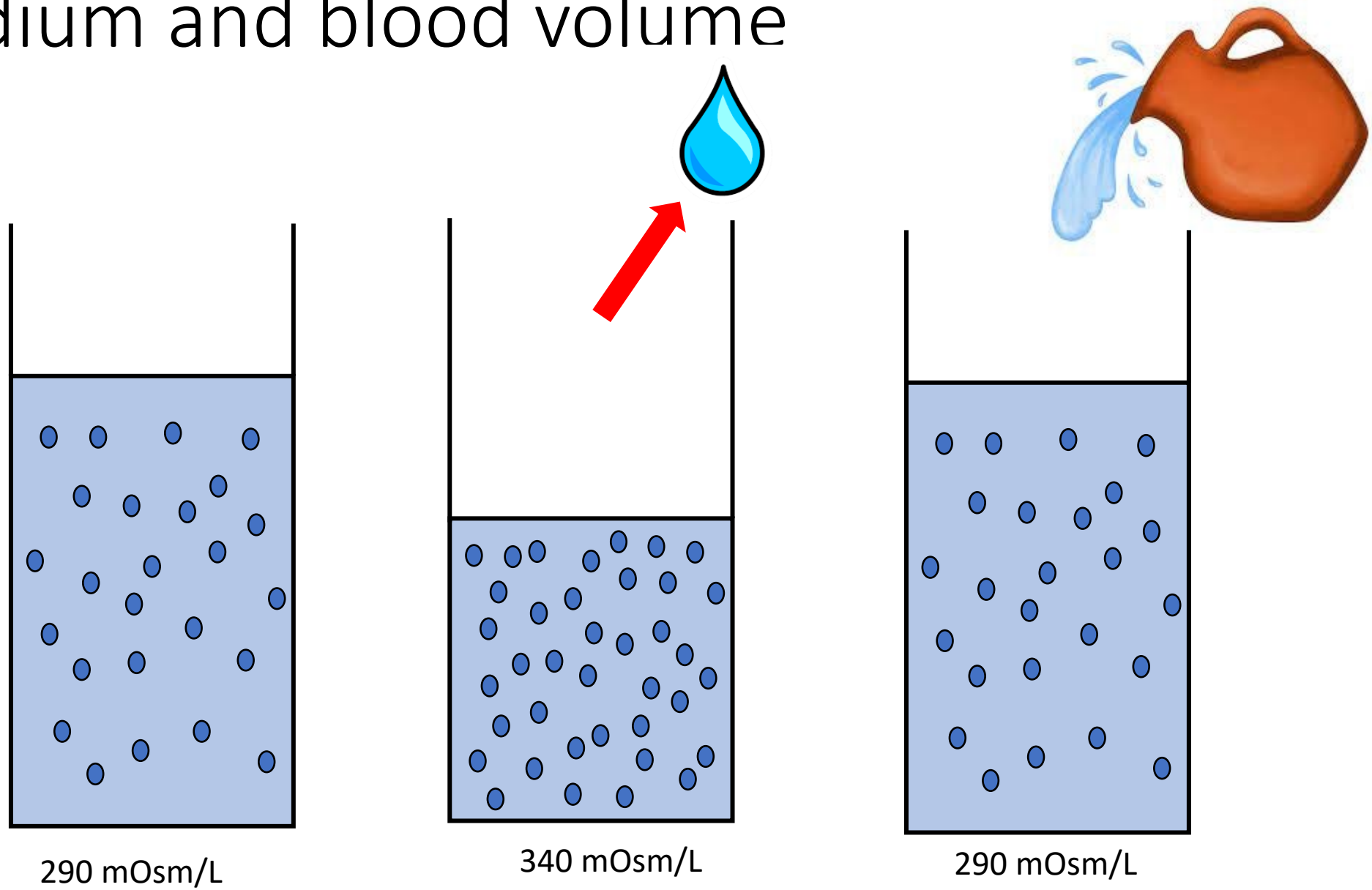
- Extracellular fluid
  - Main solutes Na^+ and Cl^-
  - ADH and thirst mechanisms keep these within a narrow range
  - Maintains plasma osmolarity within a narrow range
- Increase in Na^+ concentration in ECF
  - More water retained by kidneys
  - More water enters ECF through gut (drinking and absorption)
- Intracellular fluid
  - K^+ is main solute

Sodium and blood volume

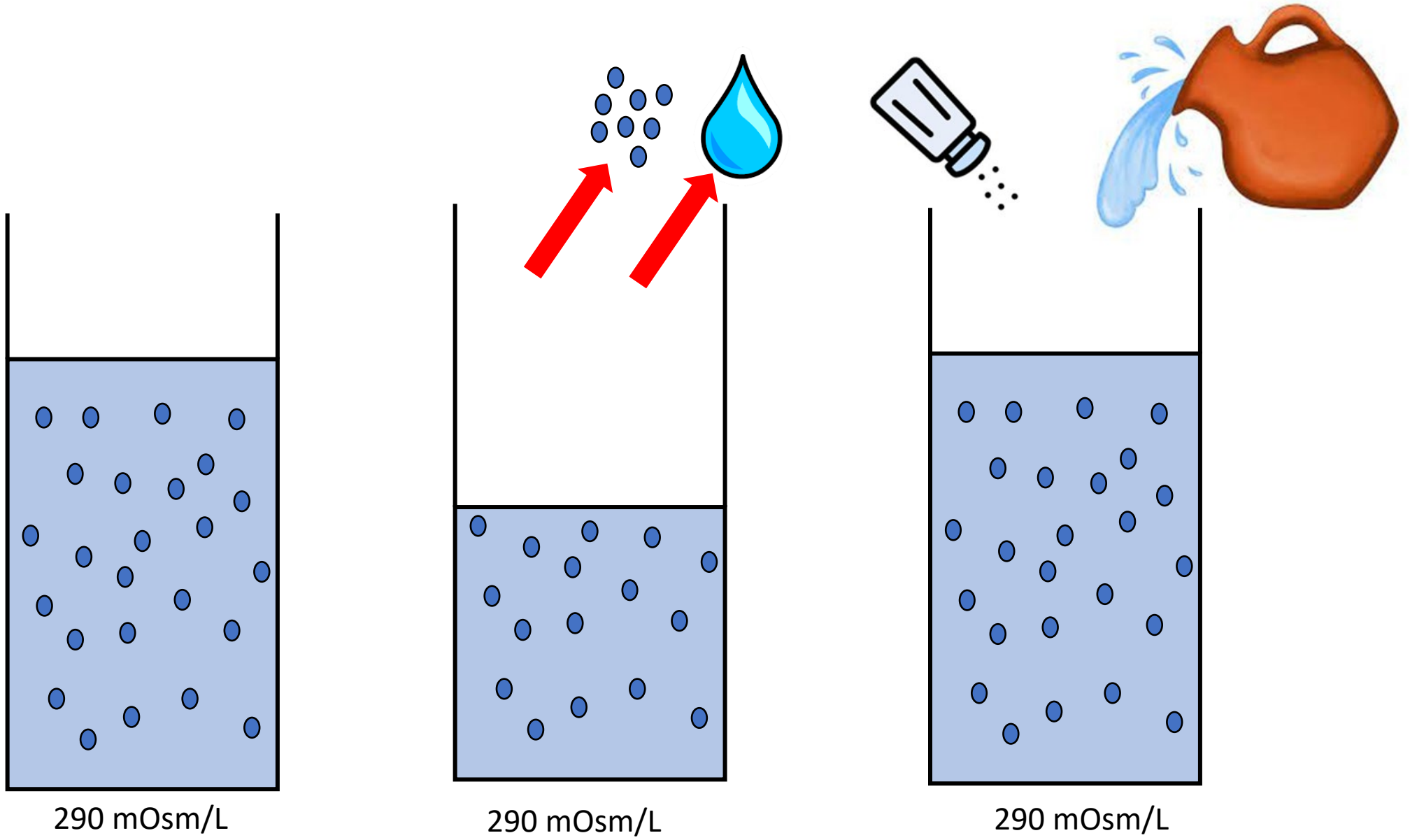
Sodium and blood volume



Sodium and blood volume

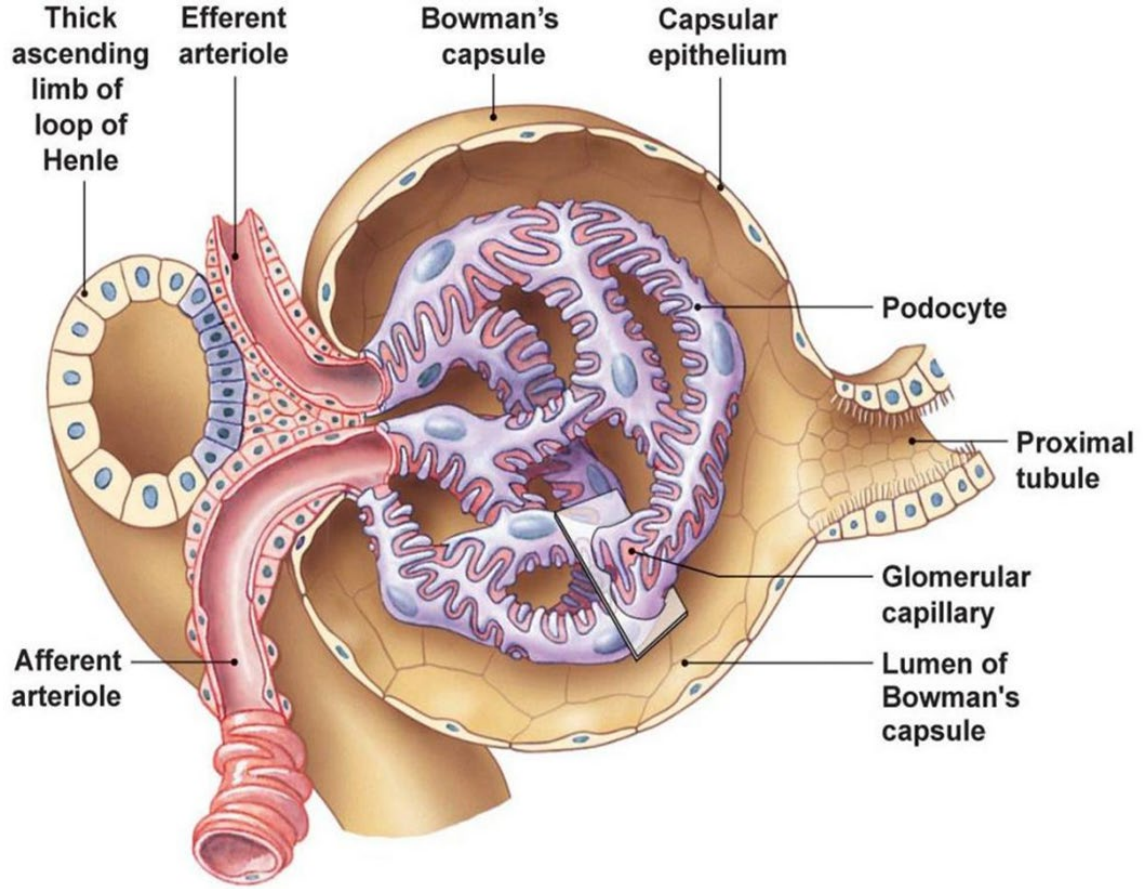


Sodium and blood volume



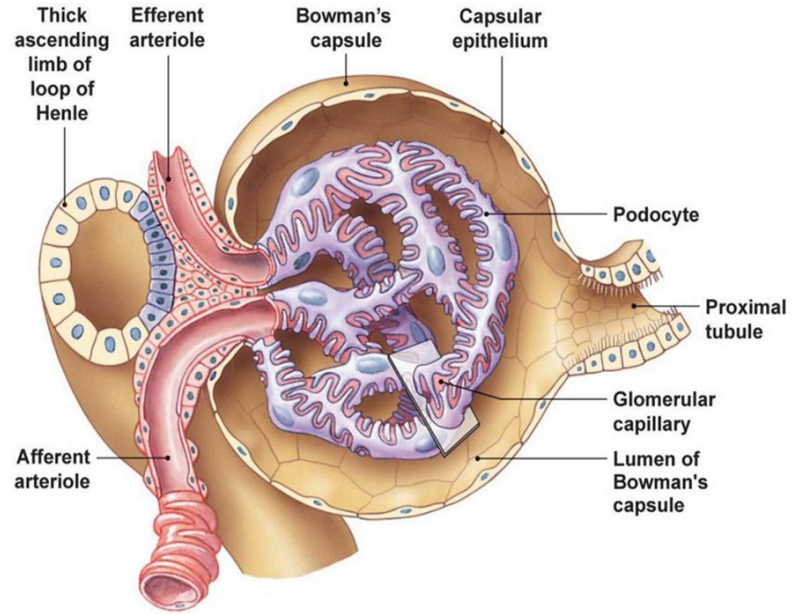
Sodium and blood volume

- How do things get back to normal?
- Detection of changes in blood volume/pressure by the kidneys
  - ↓ Na^+ in the distal tubule (macula densa)
  - ↓ pressure in the kidney detected by baroreceptors in the afferent arteriole
  - Sympathetic stimulation of the juxtaglomerular cells

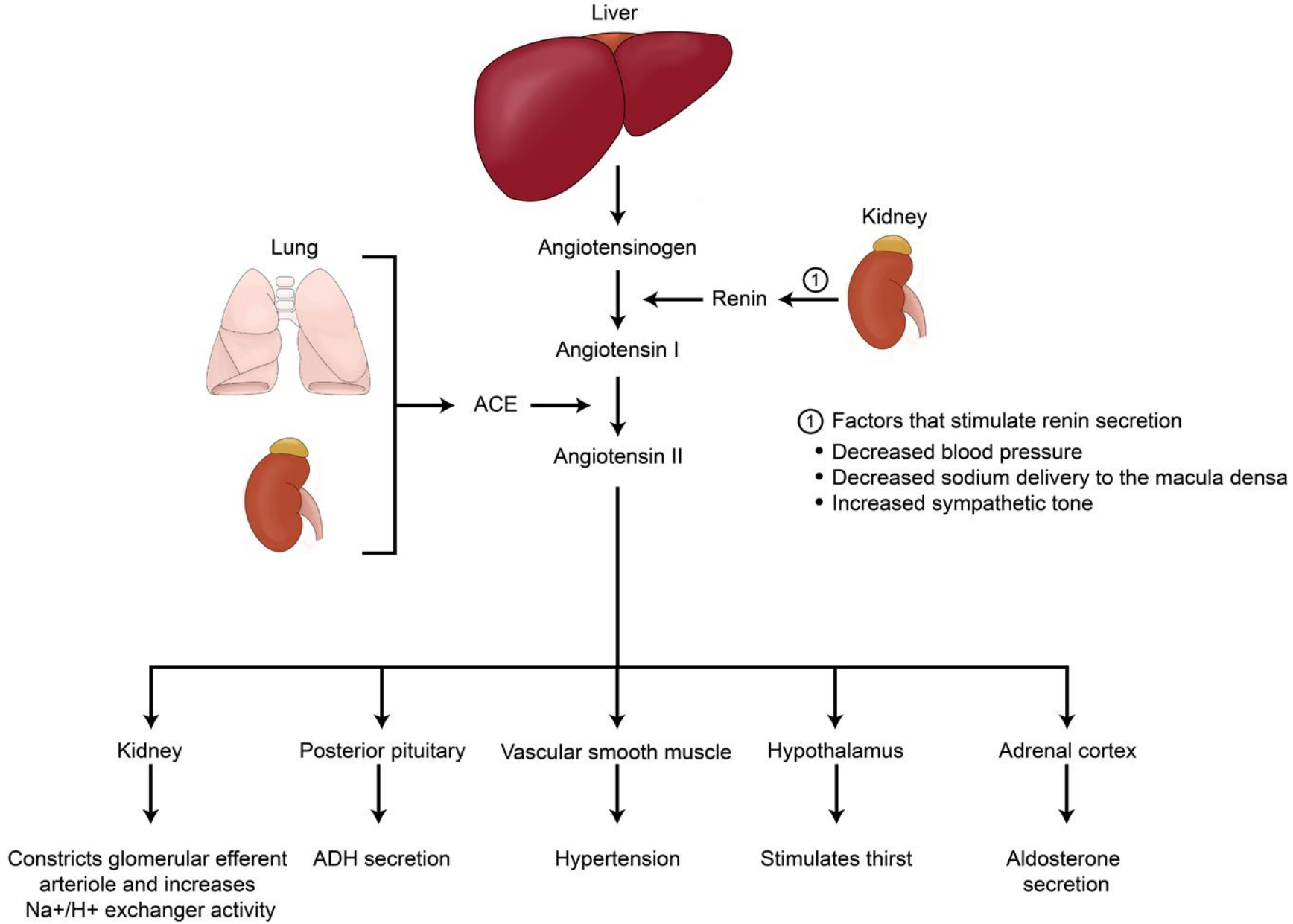


Renin-angiotensin-aldosterone system (RAAS)

- Renin
  - Secreted by juxtaglomerular cells in response to:
    - ↓ Na^+ in the distal tubule (macula densa)
    - ↓ pressure in the kidney detected by baroreceptors in the afferent arteriole
    - Sympathetic stimulation of the juxtaglomerular cells
  - Converts angiotensinogen (from liver) to angiotensin I
- Angiotensin Converting Enzyme (ACE)
  - Lungs (mainly)
  - Converts angiotensin I to angiotensin II
- Angiotensin II
  - Potent vasoconstriction, direct effect on kidneys
  - Preferential vasoconstriction of efferent arterioles in kidney (maintain GFR)
  - Stimulates release of aldosterone (adrenals)
- Aldosterone
  - ↑ sodium reabsorption

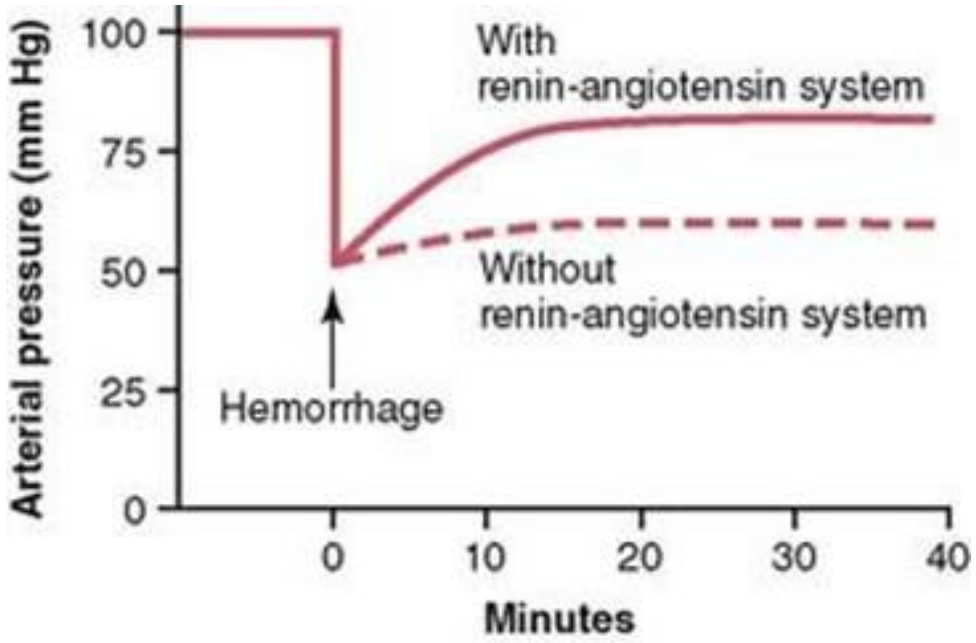


Renin-Angiotensin-Aldosterone System



Renin-angiotensin-aldosterone system (RAAS)

- Long term changes in BP, Na^+
- Takes ≈20 min to become fully activated (longer for aldosterone)
- Angiotensin II only lasts 1-2 min in the circulation
- Has a significant, long-lasting effect on BP



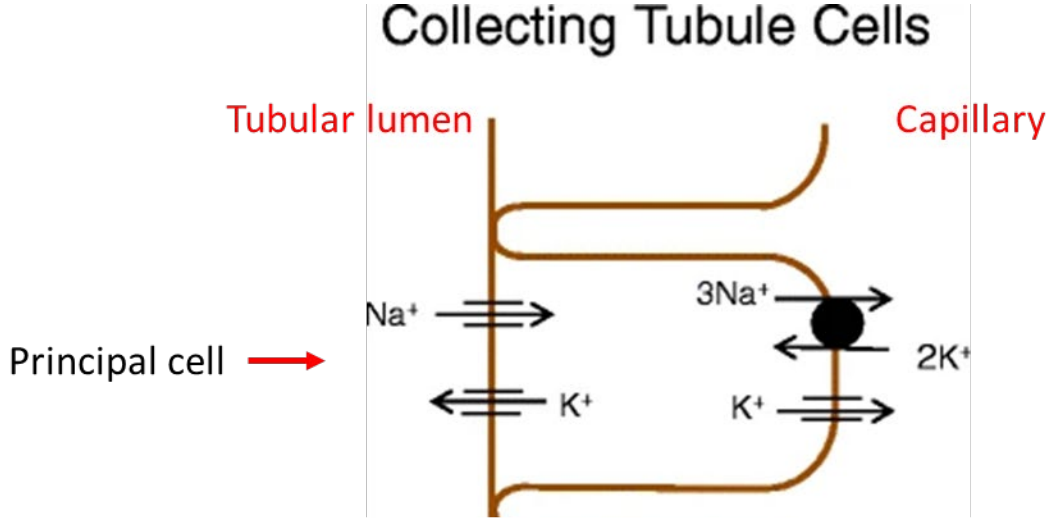
Guyton & Hall, 14th Ed. 2021

Angiotensin II

- Effects at multiple sites:
  - Proximal tubule to ↑Na^+ reabsorption (Na^+/H^+ exchange)
  - Constriction of efferent arteriole (maintain GFR)
  - Systemic constriction of arterioles (↑ peripheral vascular resistance)
  - Stimulates release aldosterone from adrenal cortex
  - Effects on brain:
    - Hypothalamus – stimulates thirst
    - Posterior pituitary – ADH release
    - Baroreceptors – prevent response to ↑BP

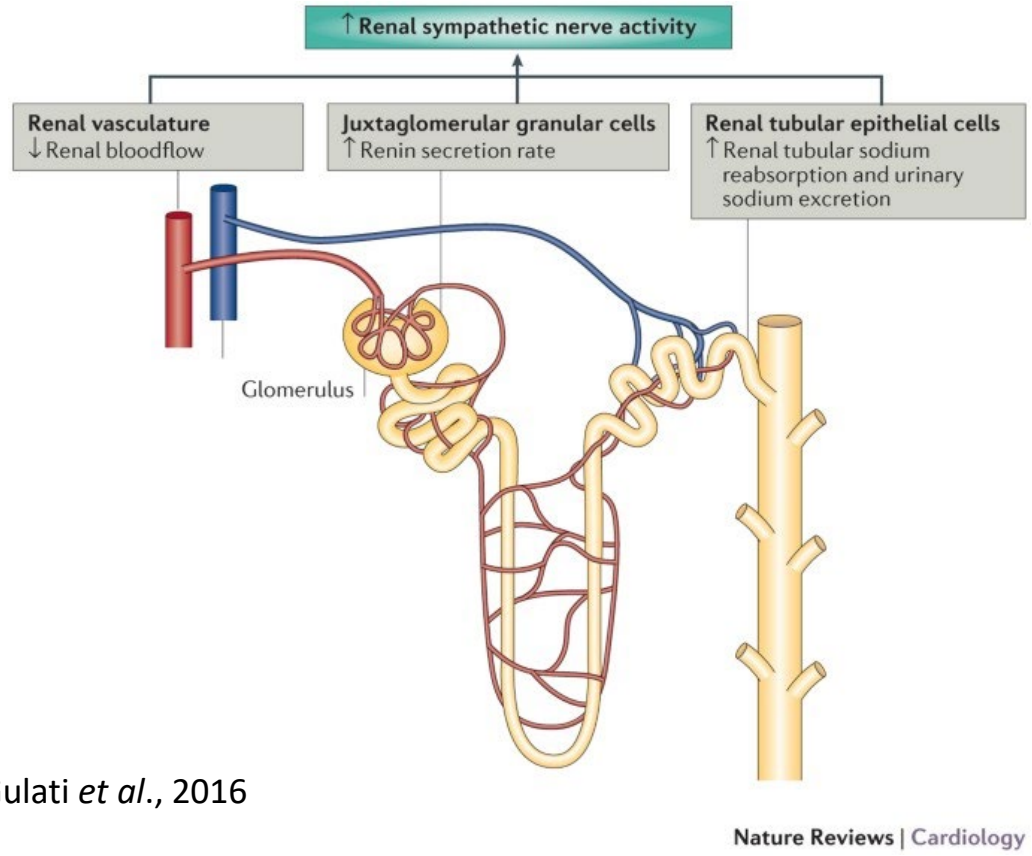
Aldosterone

- Na^+ reabsorption, K^+ secretion
- Principal cells in cortical collecting tubule
- Production stimulated by RAAS, also by ↑K^+ in ECF



Gattineni & Baum, 2015

Other mechanisms of blood volume & pressure maintenance; Na^+ excretion/reabsorption

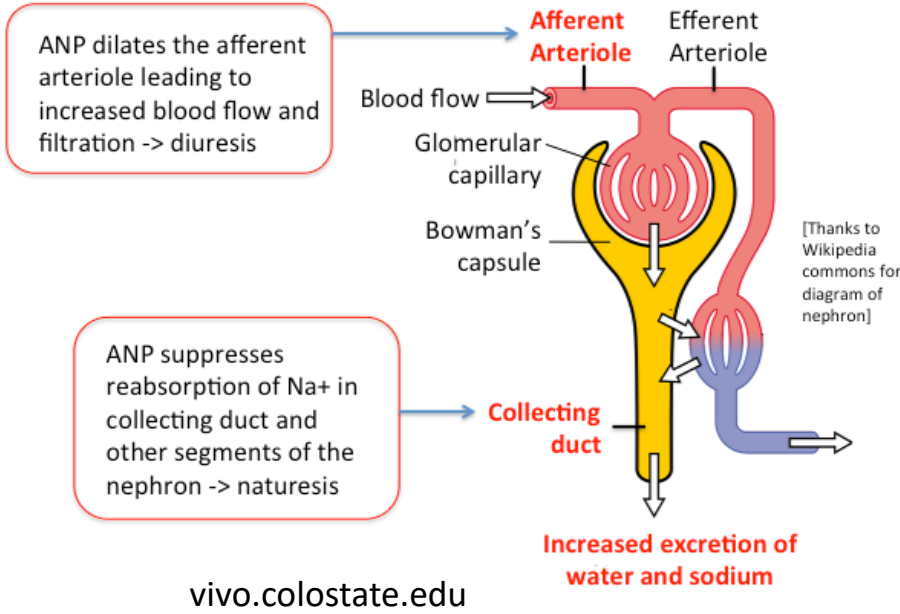


Gulati *et al.*, 2016

- Sympathetic nerves
  - Strong sympathetic stimulation → vasoconstriction and ↓ GFR
  - Any degree of stimulation → ↑ Na^+ reabsorption
    - Stimulation of α-adrenoceptors on tubular epithelial cells
  - ↑ renin and angiotensin II formation

Other mechanisms of blood volume & pressure maintenance; Na^+ excretion/reabsorption

- Natriuretic peptides
  - Atrial natriuretic peptide (ANP)
  - Produced by cardiomyocytes in response to stretching of atria when blood volume ↑
  - **OPPOSES** Na^+ and water reabsorption
    - Direct effect in renal tubules – Na^+/H^+ exchange inhibition
  - Inhibits renin secretion (therefore whole RAAS)
  - Dilates afferent arteriole → ↑ GFR



vivo.colostate.edu

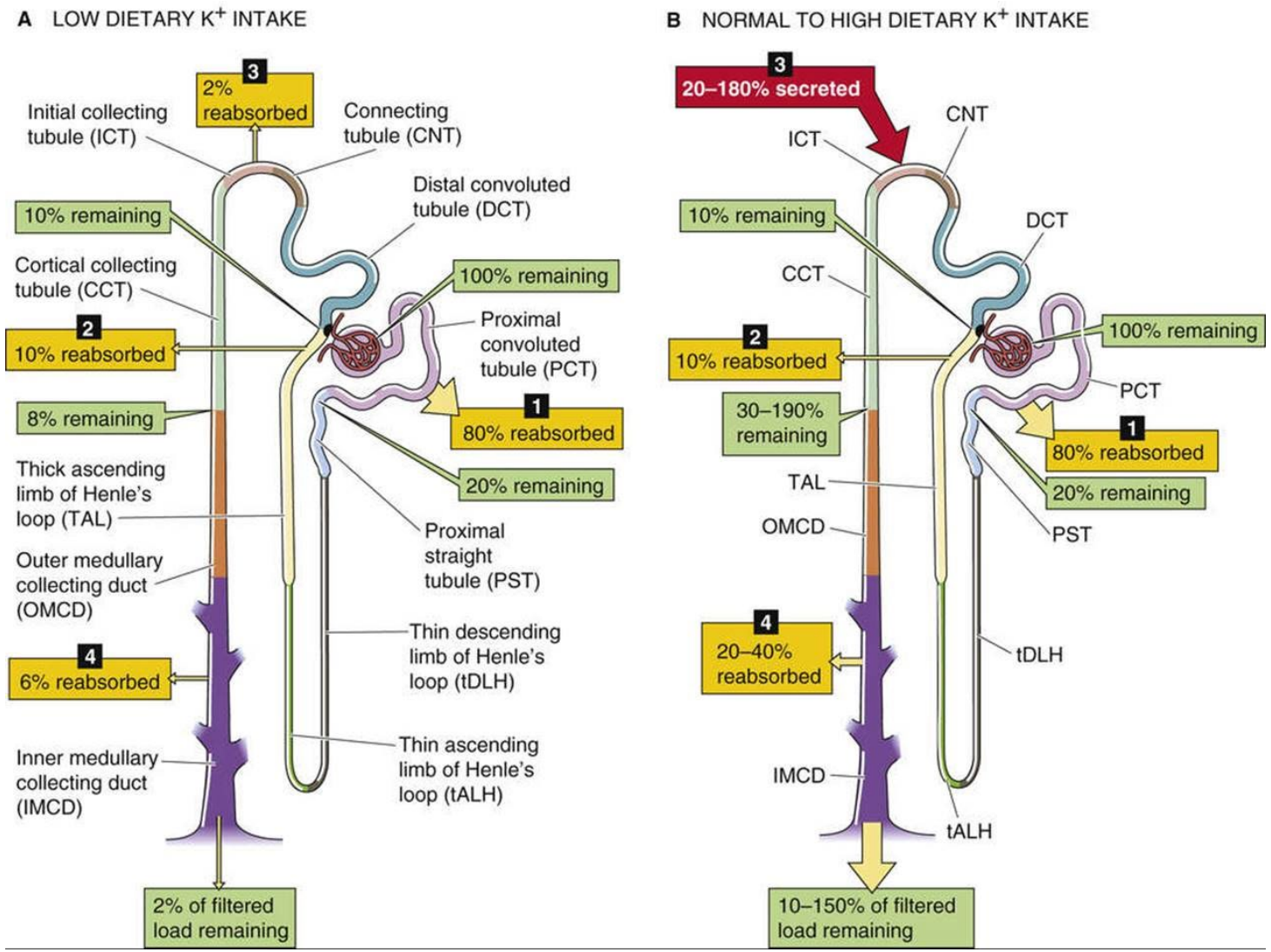
What could possibly go wrong?

- Congestive heart failure
- RAAS activated when BP decreased
- RAAS helpful in the early stages
- Blood volume increases to compensate for lack of CO, but heart can’t pump normally, so this becomes detrimental
- Too much sodium and water retention
- Inhibit ATII production by administering ACE inhibitors

Regulation of potassium reabsorption & secretion

- K^+ main intracellular ion
- Tightly regulated in response to dietary intake
- Plasma concentrations controlled mainly through reabsorption or secretion in the kidney

Regulation of potassium reabsorption & secretion

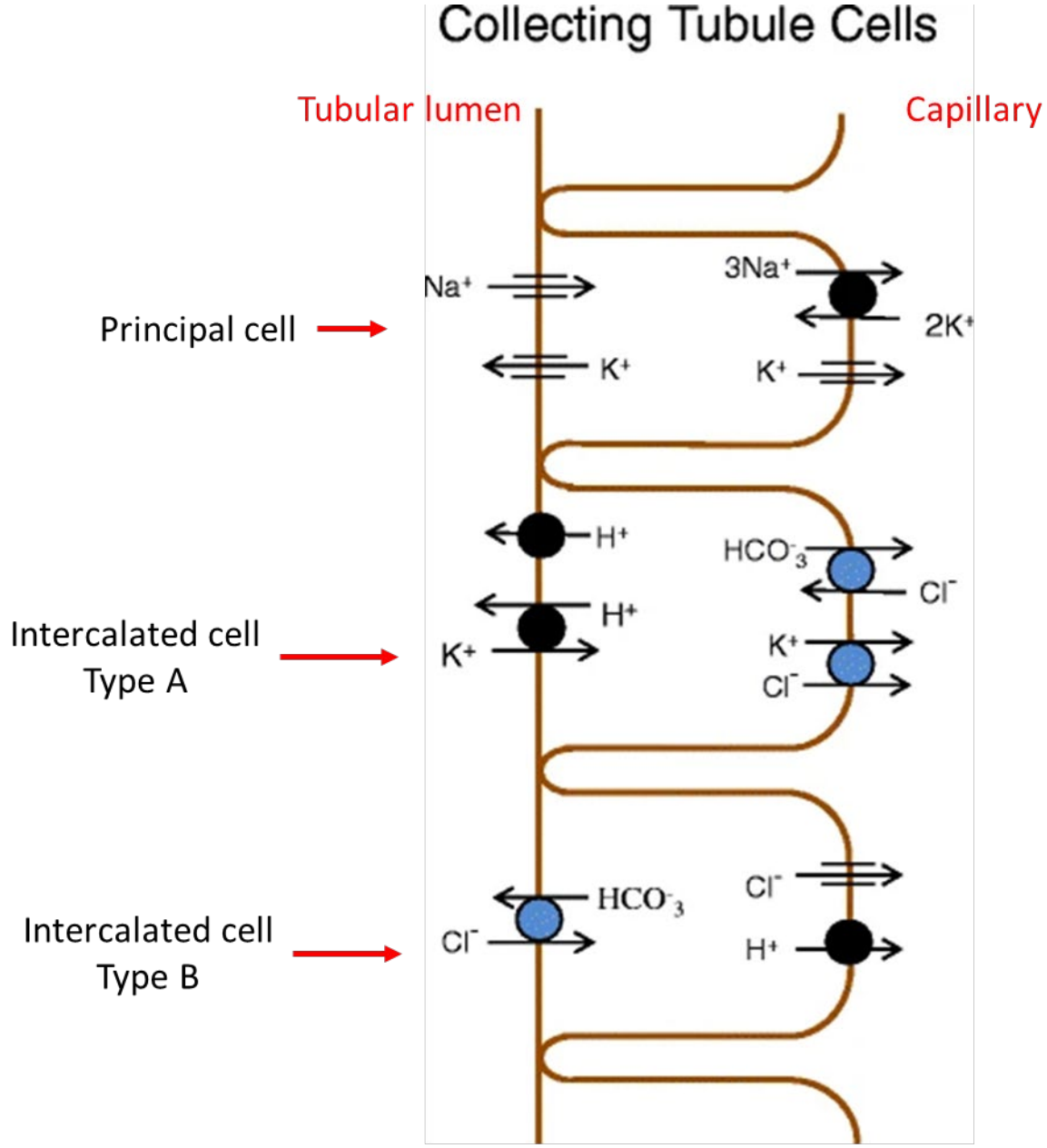


doctorlib.info/physiology/medical/197

- Reabsorption and secretion happen all along the nephron
- Main site of secretion
  - Cortical collecting tubule
- Main site of reabsorption
  - Inner medullary collecting duct

Regulation of potassium reabsorption & secretion

- Major role aldosterone
  - K^+ secretion, Na^+ reabsorption
  - ATII biggest stimulus for aldosterone release
  - Plasma K^+ concentration also important in aldosterone release
- Acidosis
  - ↓ K^+ secretion
  - Alteration K^+ channels, Na^+-K^+-ATPase
- Tubular flow rate
  - Alters electrochemical gradient
  - ↑ → ↑ K^+ secretion
- Intracellular K^+ concentration



Gattineni & Baum, 2015

What could possibly go wrong?

- 4 year old FN standard poodle
- History of vague intermittent signs
- Collapsed
- Plasma electrolyte concentrations:

Electrolyte	Value	Reference range
Sodium (mEq/L)	117	143-150
Potassium (mEq/L)	7.2	4.0-5.0
Chloride (mEq/L)	92	106-114

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