Renal physiology IV

Regulation of ECF volume and osmolarity
Micturition

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Handling of water 1

- plasma osmolarity = 300 mosm/l
- urine volume = 1-1,5 l/day normally
- can excrete 400 ml (obligatory) @ 1200 mosm/l – due to diarrhea or sweating
- or larger volumes @ 100 mosm/l (due to fluid intake)
- kidney can excrete small urine volumes of high osmolarity or large volumes with low osmolarity
- this ability depends on the “countercurrent” system and ADH

Handling of water 2

- renal plasma flow = 650 ml/min, 125 ml/min filtered, thus 19%
- filtrate iso-osmotic to plasma = 300 mosmol/l
- 66-75% reabsorbed in proximal tubule, secondary to solute reabsorption, stays iso-osmotic
- loops of Henlé in cortical nephrons: same as proximal, juxtamedullary nephrons
- collecting ducts: 11% water left, ADH increases reabsorption into hyperosmotic inner medulla
- the blood in the capillary beds is in osmotic equilibrium with surrounding interstitial fluid

Handling of water 3

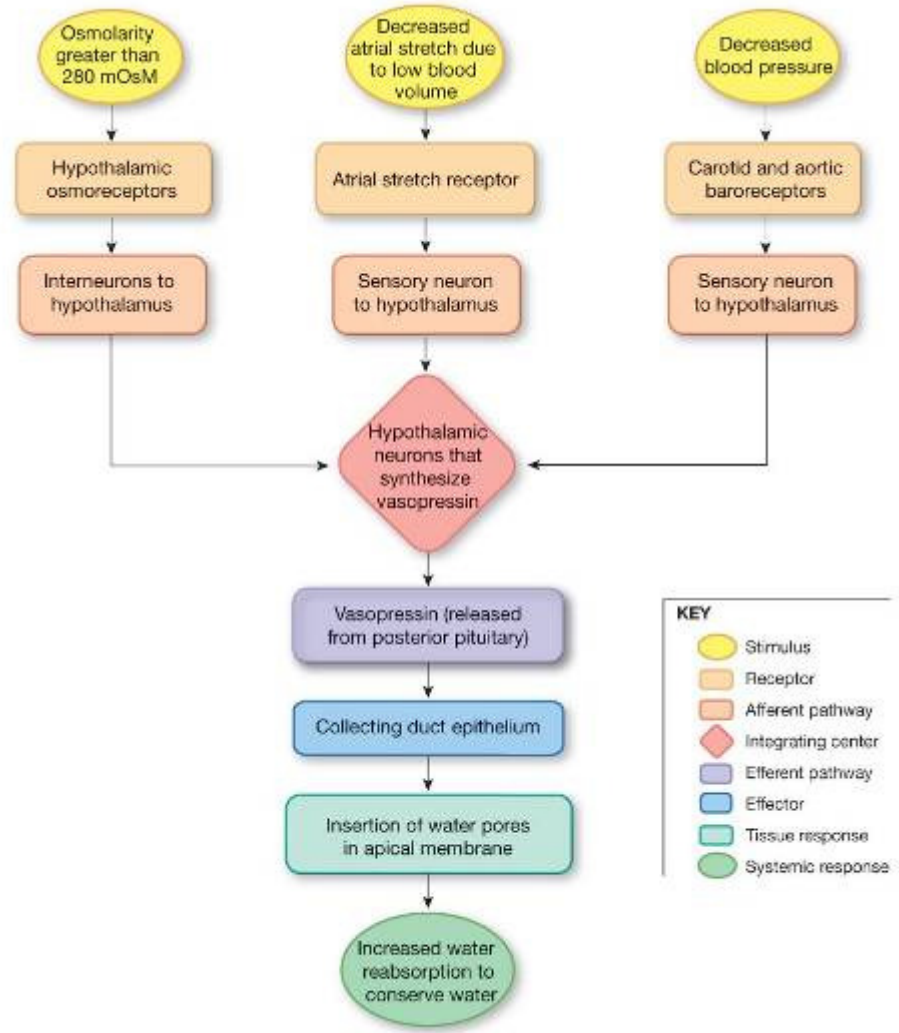
Hormones regulate water processing

- ADH
- aldosterone
- renin-angiotensin II system
- natriuretic hormone
- catecholamines
- prostaglandins

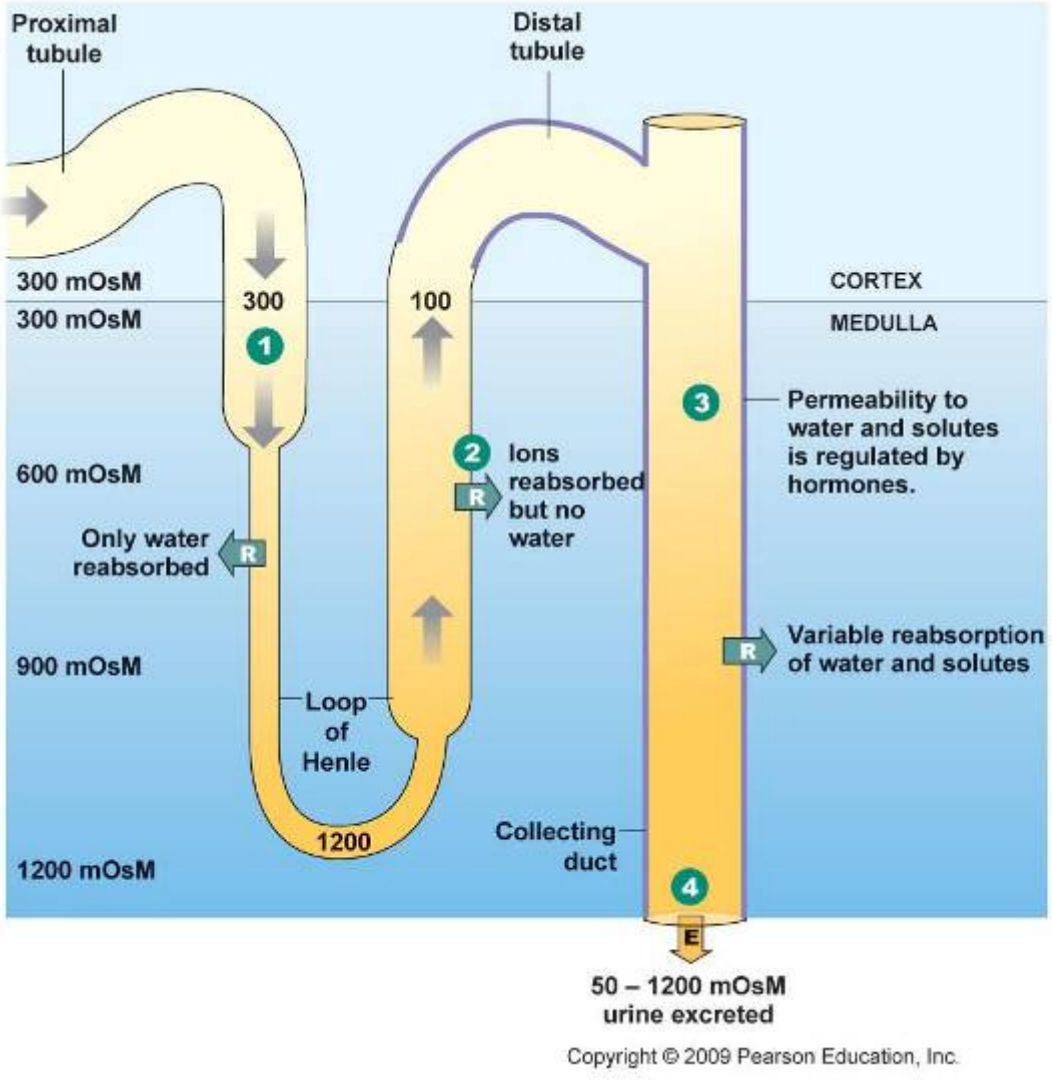
Antidiuretic hormone (ADH)

- hyperosmolality of ECF
- hypovolemia
- low blood pressure
  - cause ADH release from supra-optic nuclei in HT
  - ADH promotes synthesis of aquaporin – inserted into LM of collecting ducts – act as water channels
  - ADH increases urea permeability of medullary (not cortical) collecting ducts – helps to maintain medullary hyperosmolarity during water reabsorption

Factors affecting ADH release

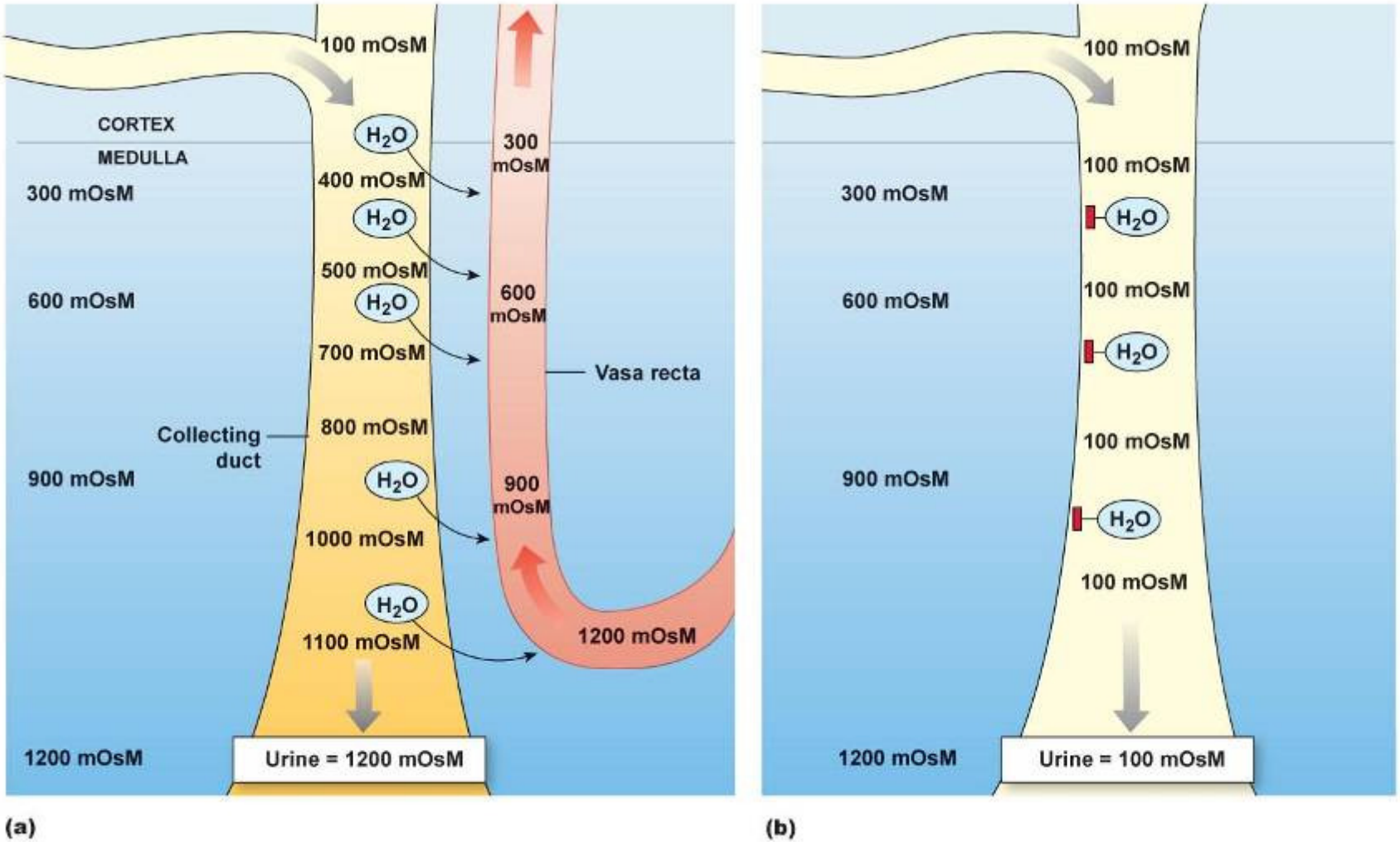


Summary of osmolarity changes as fluid flows through the nephron

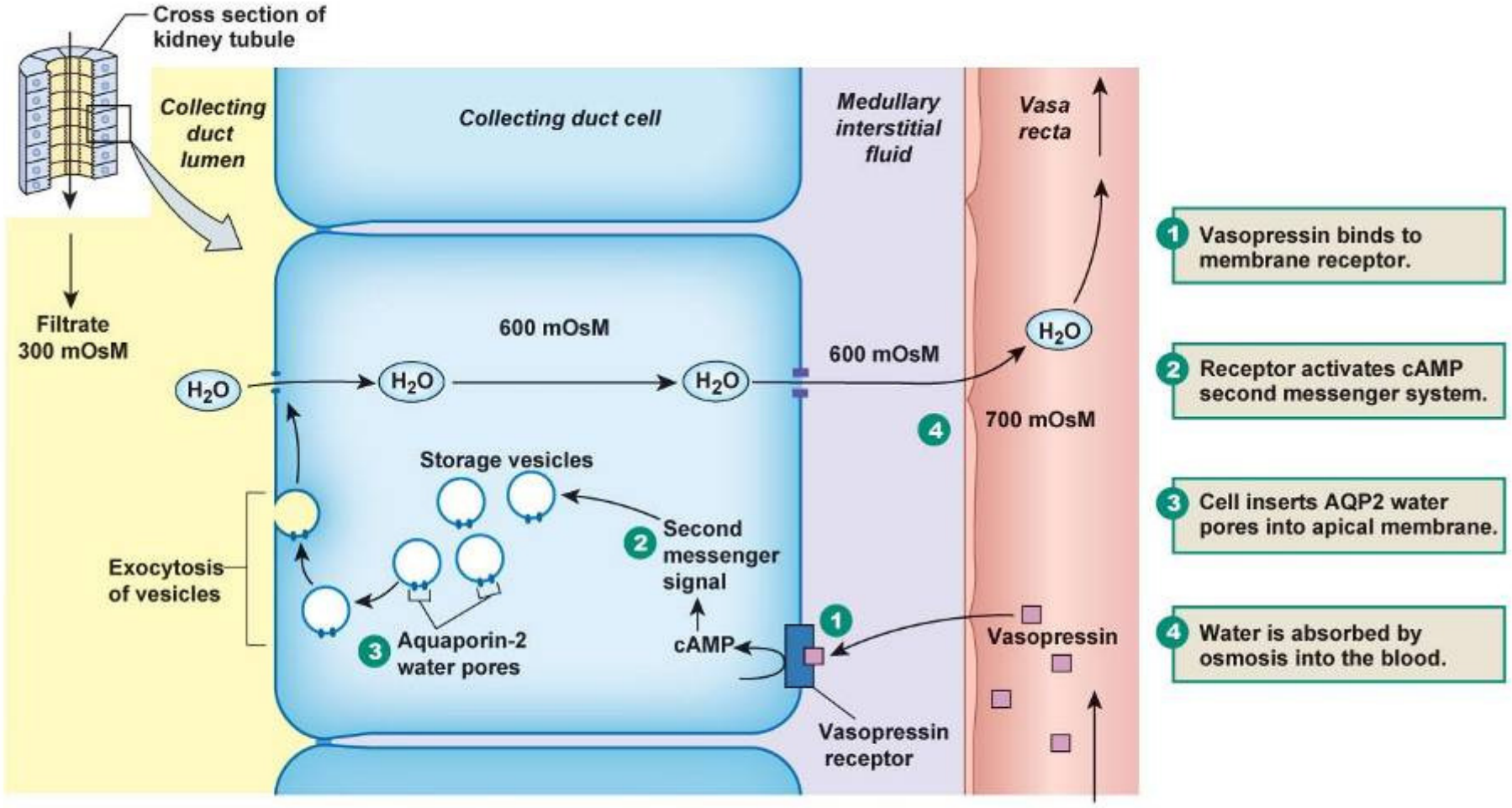


1. Isosmotic fluid leaving the proximal tubule becomes progressively more concentrated in the descending limb.
2. Removal of solute in the thick ascending limb creates hyposmotic fluid.
3. Hormones control distal nephron permeability to water and solutes.
4. Urine osmolarity depends on reabsorption in the collecting duct.

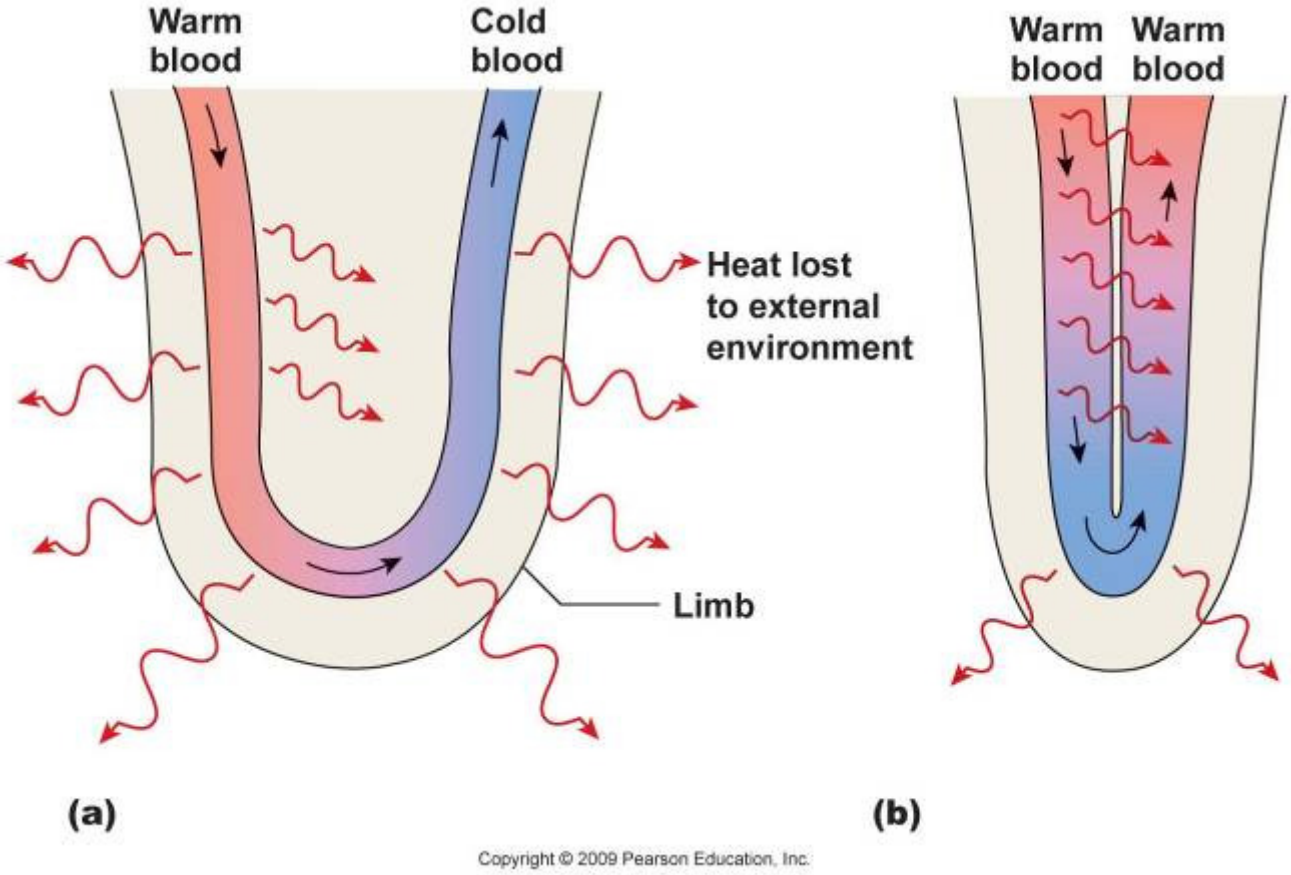
Water movement in the collecting duct in the presence and absence of ADH



ADH action mechanism

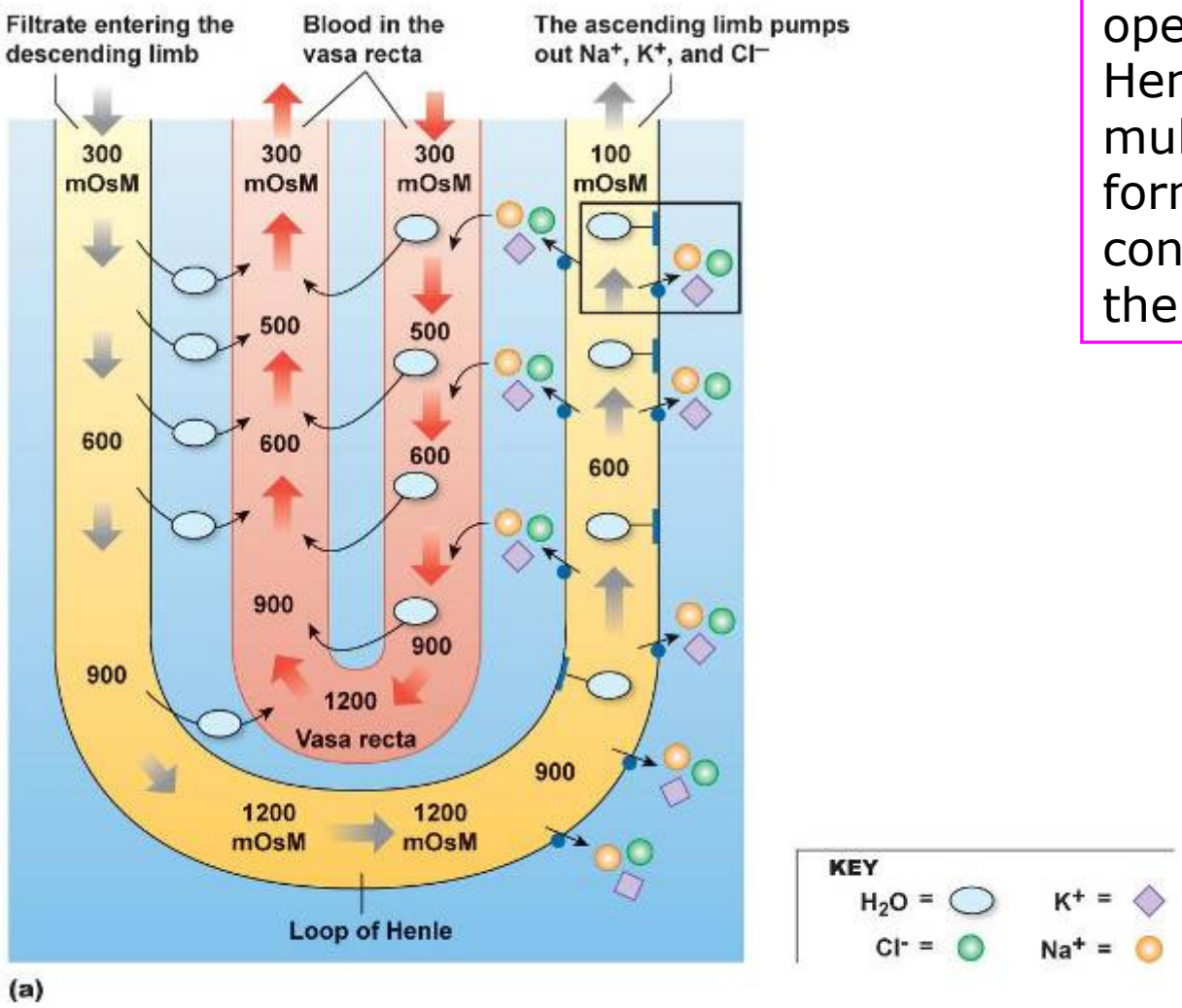


Concentrating of urine –
the countercurrent heat exchanger



the outflowing hot blood heats the inflowing cold blood – countercurrent system in juxtamedullary nephrons is analogous

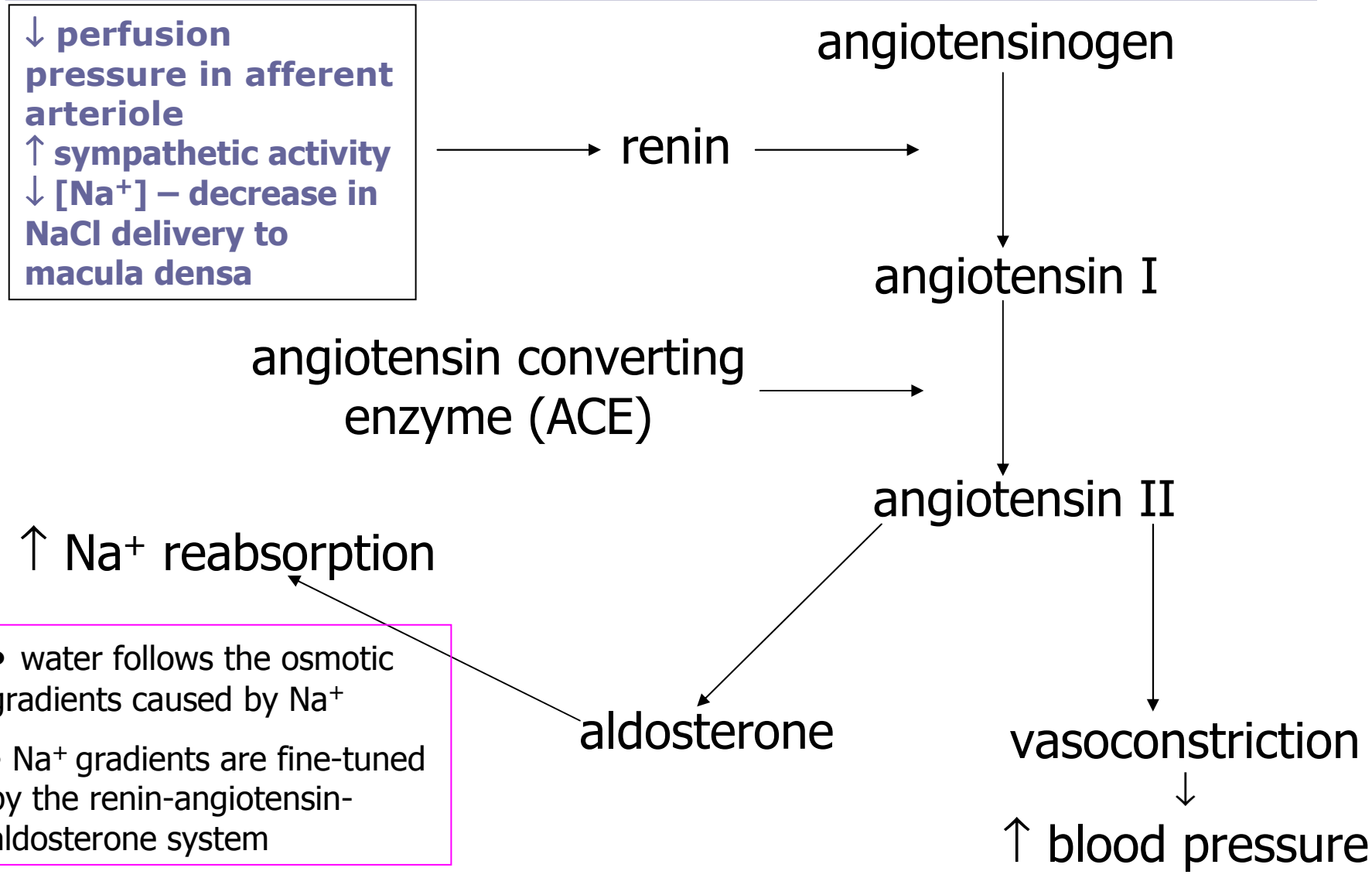
Countercurrent multiplier in the medulla of the kidney



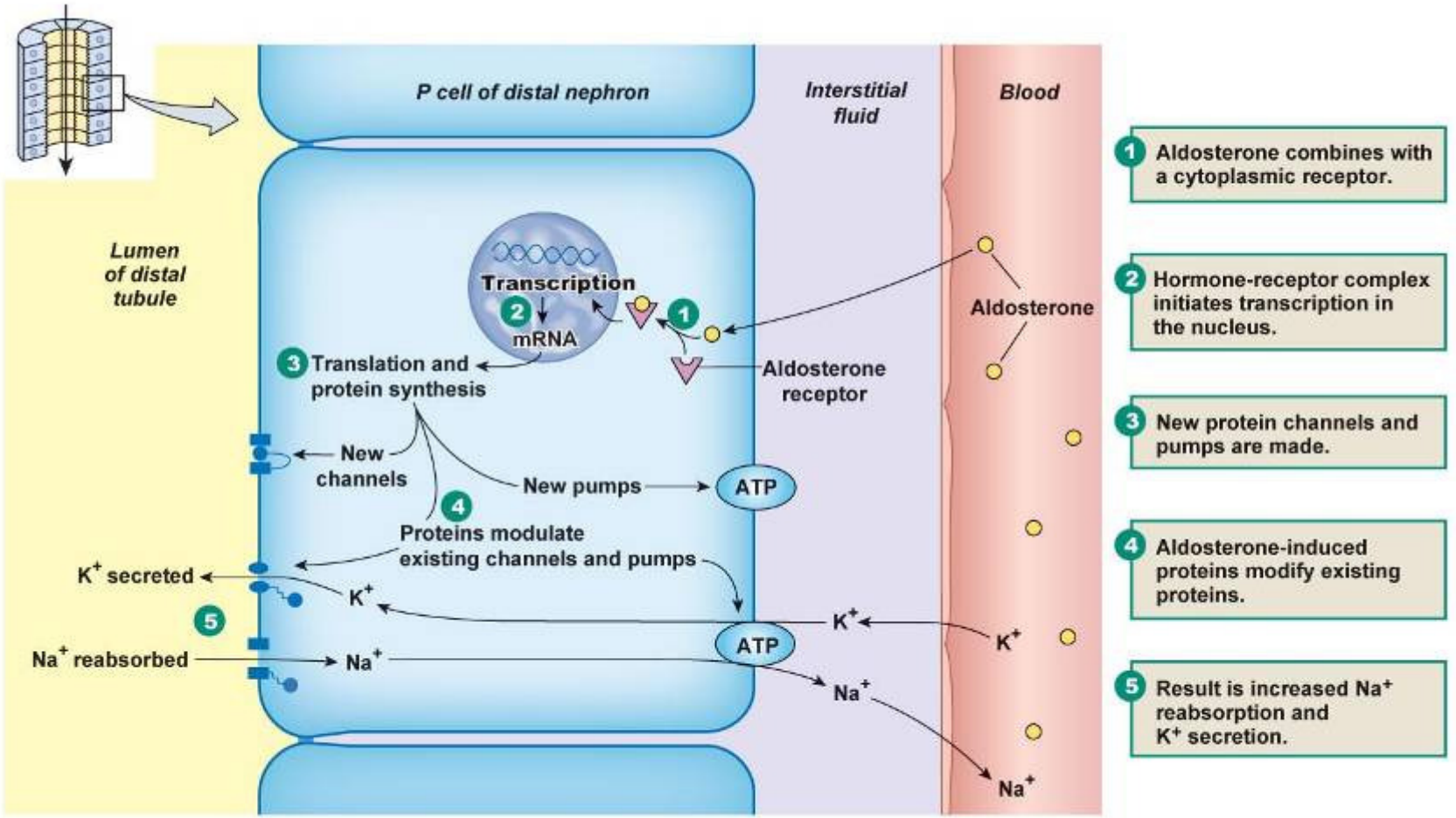
operation of the loops of Henlé as countercurrent multipliers and the formation of a concentrated urine in the presence of ADH

- the vasa recta act as countercurrent exchangers
- sluggish blood flow
- endothelium freely permeable to water
- water moves out of blood in inner medulla, moves back towards the cortex
- perfusion achieved, hypertonicity maintained

Handling of water is also determined by Na^+ balance
The renin-angiotensin system

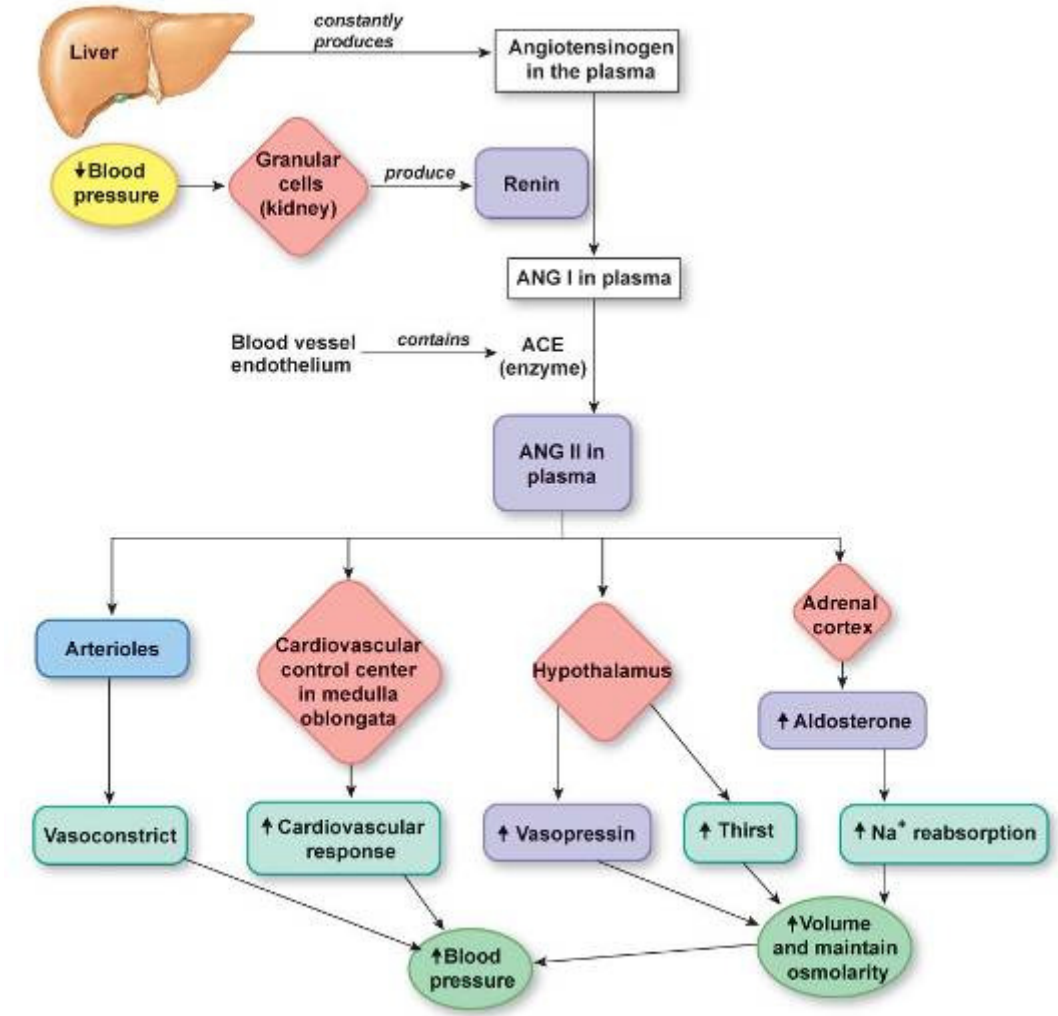


Aldosterone action in principal cells

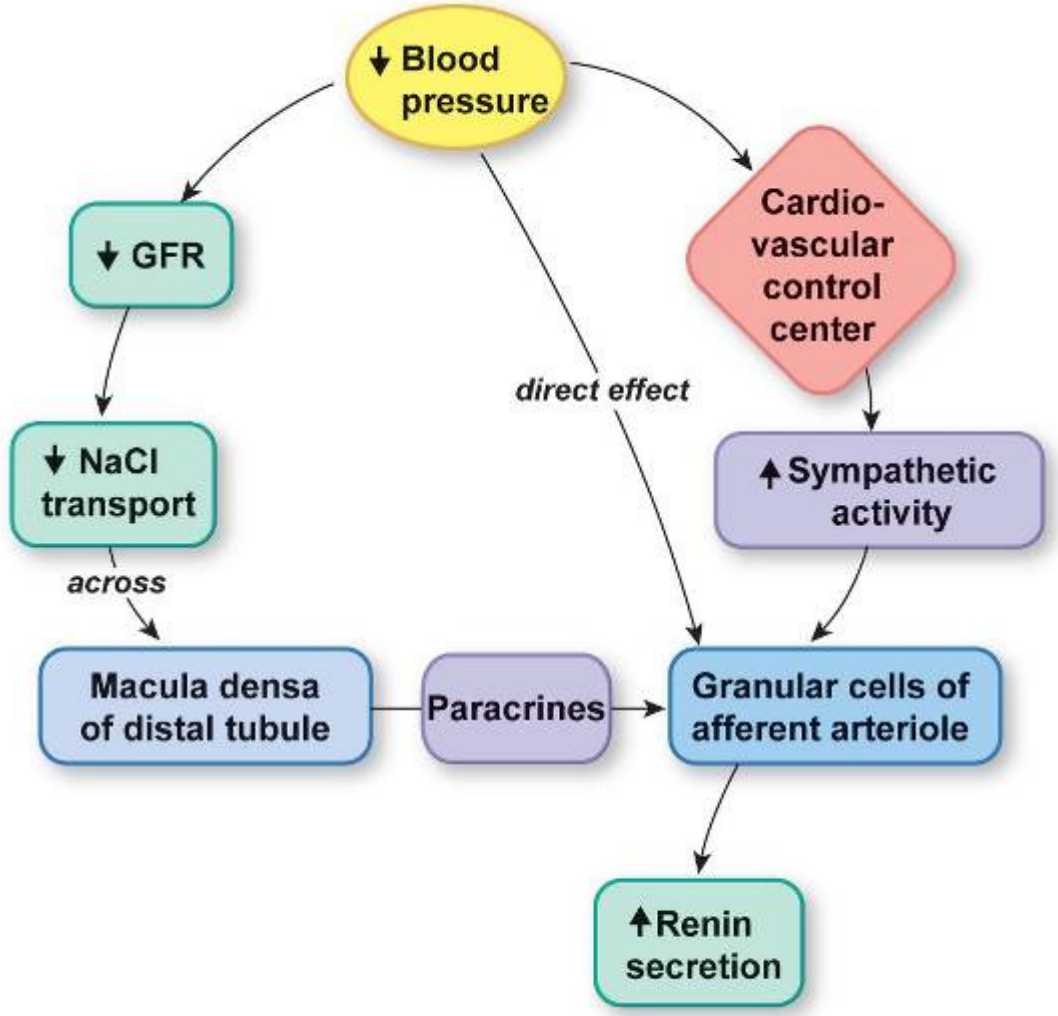


↑ synthesis of Na^+ channels, Na^+/K^+-pump and citric acid cycle enzymes

The renin-angiotensin pathway



Decreased blood pressure stimulates renin secretion

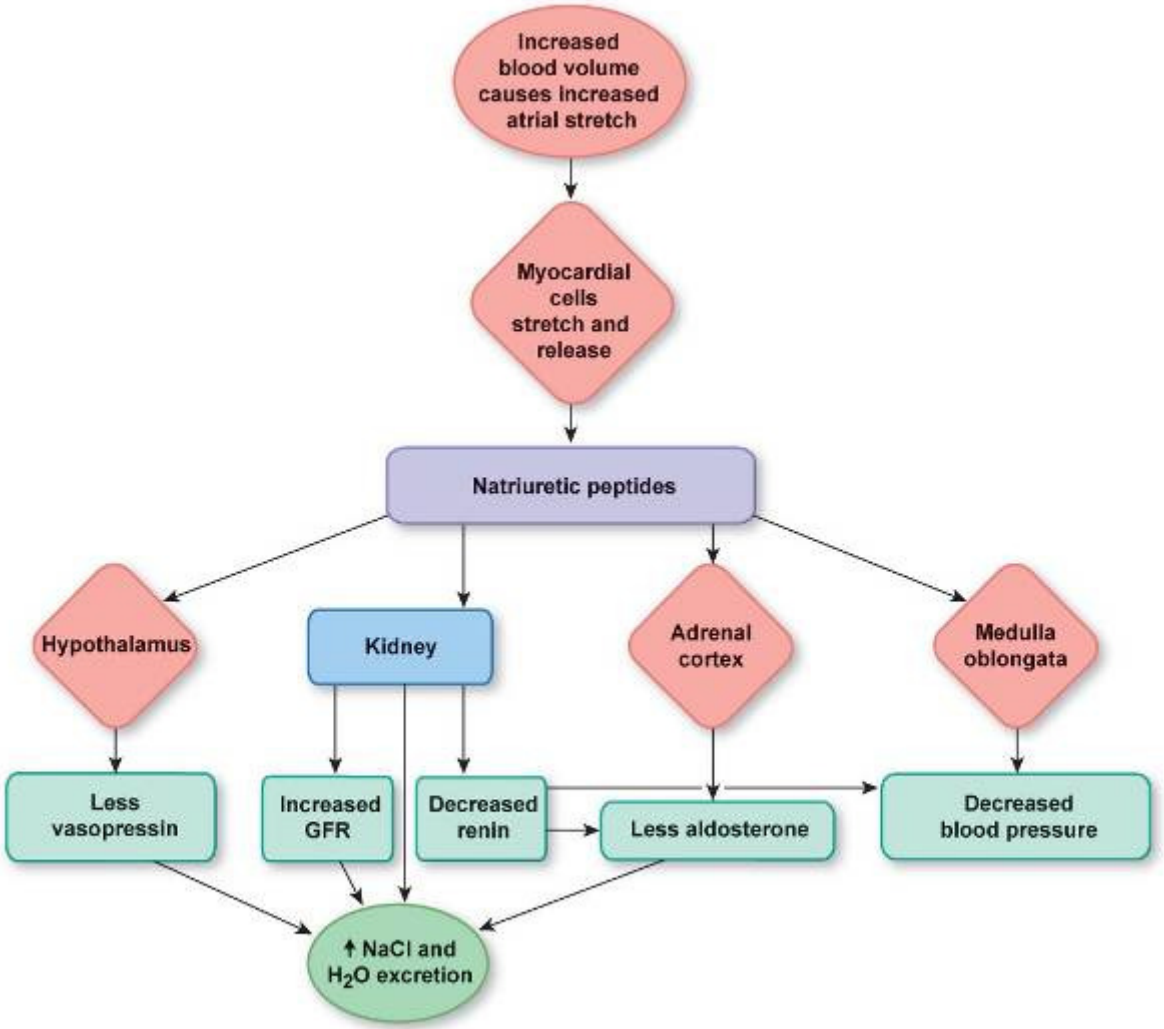


Regulation of ECF volume and osmolarity

- Renin-Angiotensin
  - Stimuli: low BP, renal perfusion pressure, osmolarity in distal tubule, sympathetic stimulation
  - Effects: direct and sympathetic-mediated vasoconstriction, ADH release, dipsogenic effect, aldosterone secretion, salt & water retention, salt appetite, cardiac output
  - Total effect: increase in blood volume and pressure
- Aldosterone
  - Stimuli: AT I & II, high ECF K^+, suppressed by ANP
  - Effects: salt & water retention, increase in ECF volume

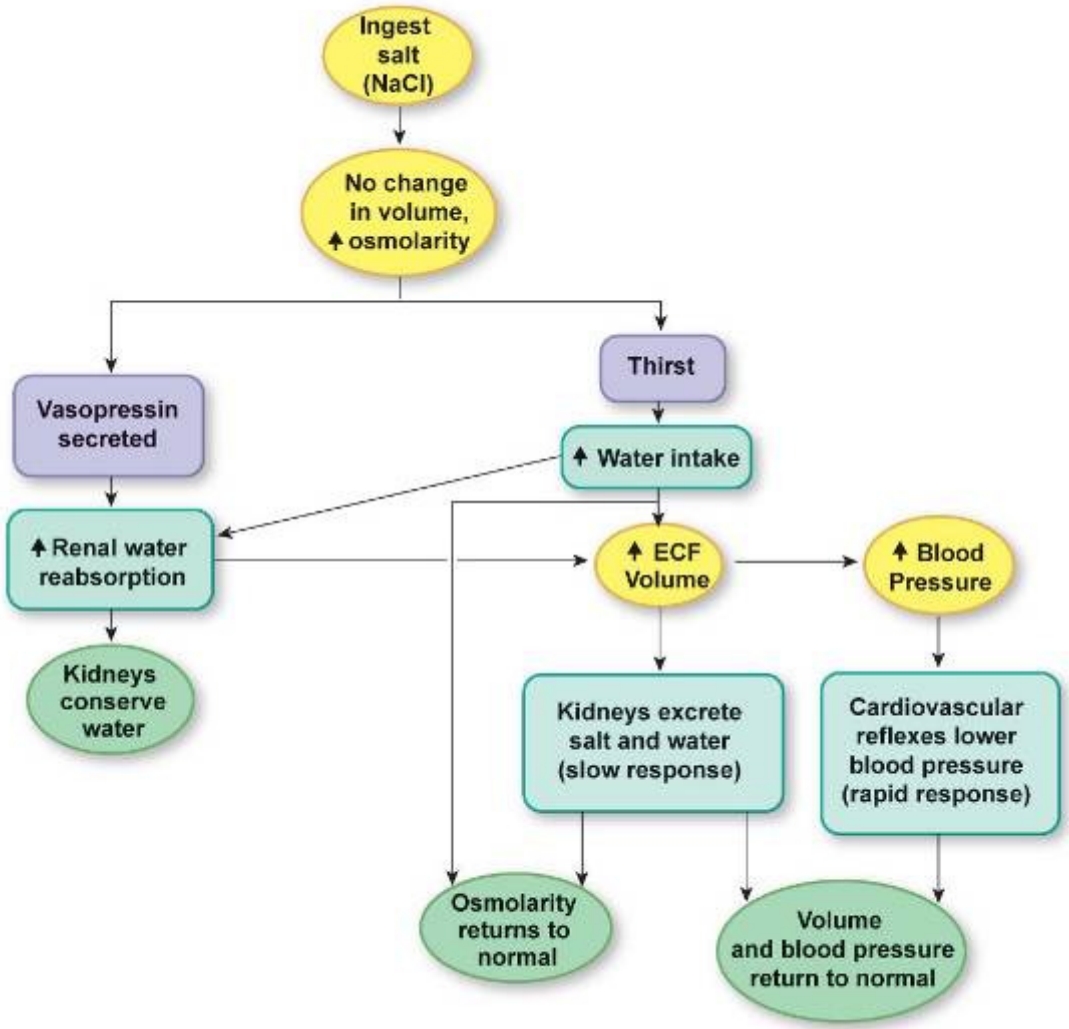
- ADH
    - Stimuli: increase in ECF osmolarity registered in terminal lamina of the HT, decrease in blood volume (atrial receptors), AT II, emotions, nausea
    - Effects: reabsorption of water, increase in ECF volume, decrease in osmolarity
- Thirst
    - Stimuli: increase in ECF osmolarity (receptors in subfornical organ), decrease in ECF volume (atrial receptors) and AT II
    - Effects: fluid intake, increase in ECF volume, decrease in osmolarity
- Atrial natriuretic peptide
    - Stimuli: stretch of cardiac muscle wall
    - Effects: natriuresis & diuresis, reduction in ECF volume and BP
    - NB: antagonist to AT II, aldosterone & sympathetic discharge

Atrial natriuretic peptide



- Prostaglandins
    - Stimuli: vasoconstriction – fall in renal perfusion pressure
    - Effects: vasodilation, natriuresis & diuresis, aim is to protect kidney against ischaemic damage
- Sympathetic discharge
    - Stimuli: decrease in blood volume and pressure and emotions
    - Effects: increase in cardiac output, vasoconstriction, volume conservation by the kidney

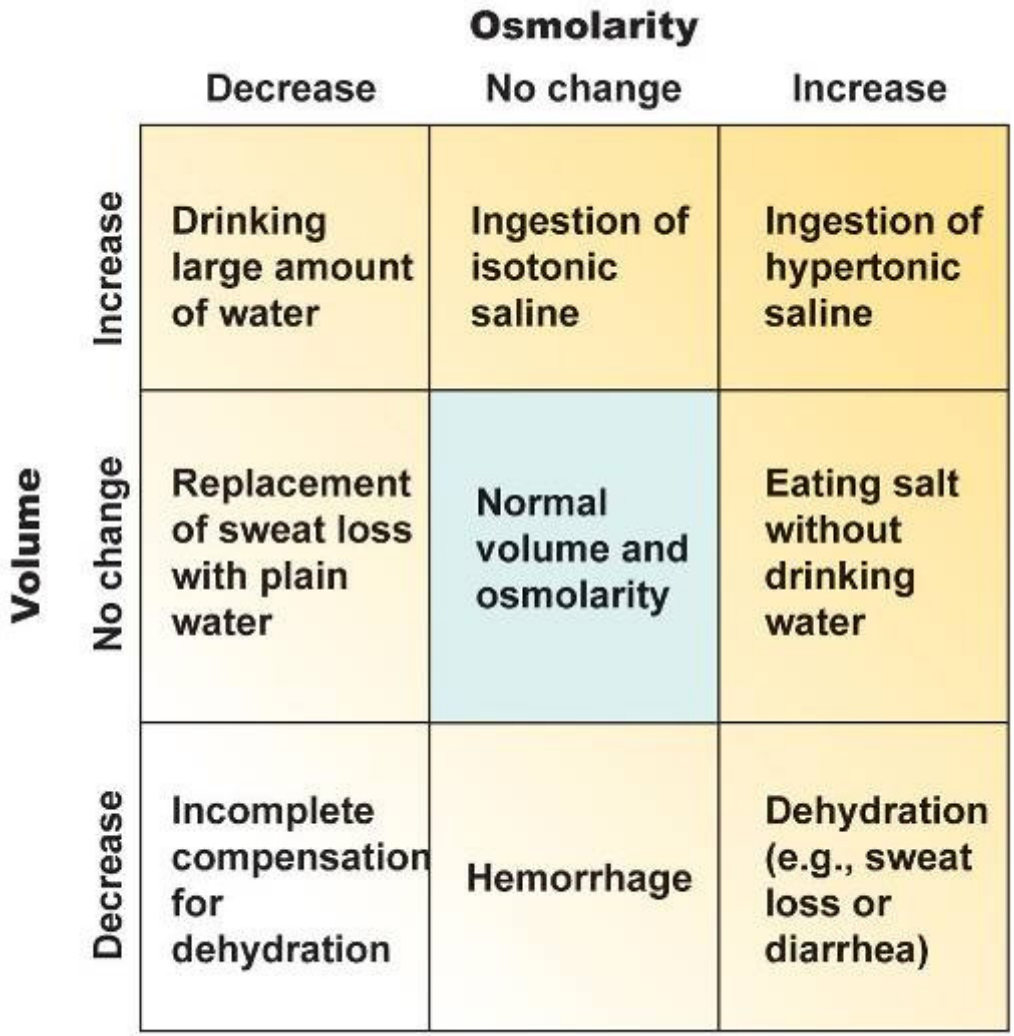
Homeostatic responses to eating salt



Free water clearance

- used to assess ability of kidneys to concentrate or dilute urine
- $C_{water} = V - C_{osm}$ = Free water clearance
  $= V - [U]_{osm} / [P]_{osm} \times V$
- (+) = large volumes hypotonic urine
- (-) = small volumes hypertonic urine

Disturbances of volume and osmolarity



Abnormalities of water balance

- Water diuresis due to:
  - HT/pituitary diabetes insipidus
  - excessive water intake
  - suppression of ADH by alcohol
  - cold diuresis, redistribution of blood increases central BP $\rightarrow$ inhibits ADH
  - defective renal ADH receptors, defective aquaporin insertion/production (nephrogenic diabetes insipidus)

- Osmotic diuresis due to:
  - glucose-induced (diabetes mellitus)
  - diuretic-induced, mediated through NaCl
  - mannitol administration
  - glucose & NaCl, due to decline of ATP in proximal tubule (Fanconi syndrome)
  - NaCl, due to defects in the Na^+-K^+-pump – congenital disorders

Diuretics

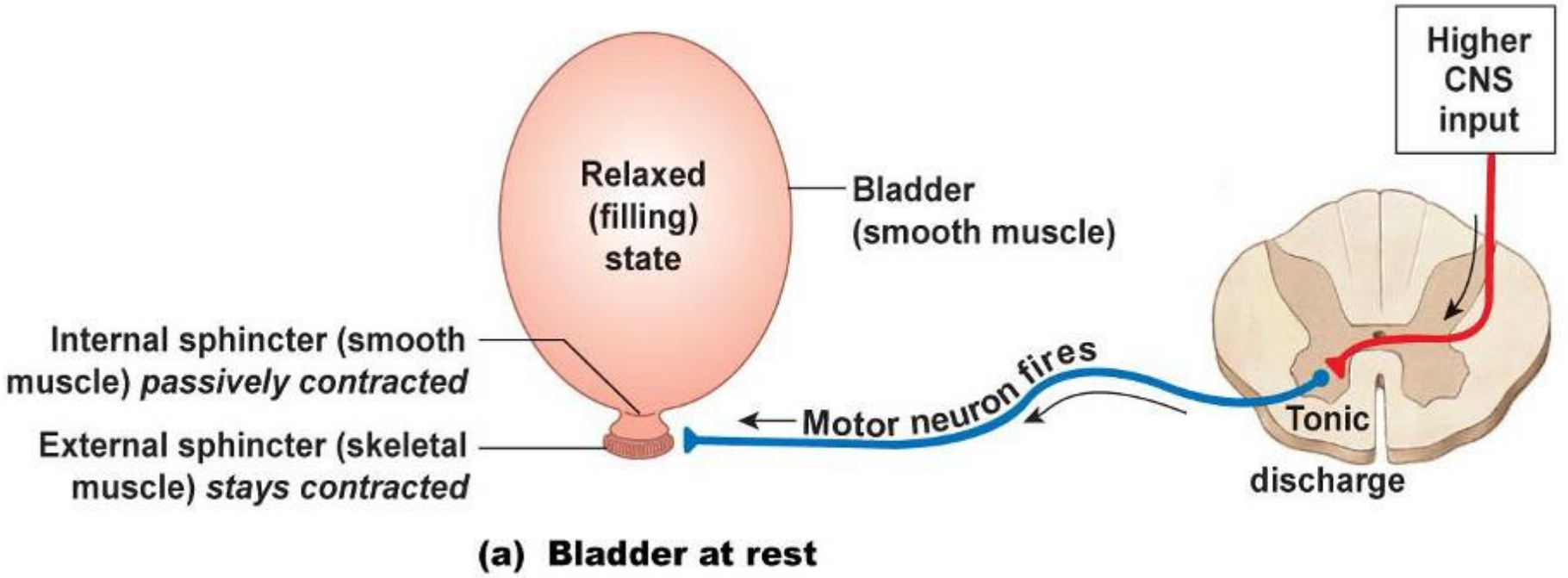
- Water and alcohol – inhibit ADH
- Glucose
    - glucosuria causes osmotic diuresis
- Acetazolamide (Diamox)
    - inhibits carbonic anhydrase
- Thiazides (Dichlortride)
    - inhibits proximal NaCl reabsorption
- Furosemide (Lasix)
    - inhibits NaCl reabsorption in thick ascending loop of Henlé
- Spironolactone (Aldactone)
    - inhibits aldosterone action

Micturition

- renal calyces → renal pelvis → ureters (25-30 cm) → bladder
- ureters enter bladder obliquely – prevents backflow of urine
- urine transported with peristaltic waves
- "Trigone" on internal floor of bladder between openings of ureters and the urethra – position does not change
- bladder wall contains mucosa, submucosa, detrusor muscle (spiral, longitudinal, circularly arranged smooth muscle) and serosa

- internal sphincter – smooth muscle
- external sphincter – voluntary muscle
- detrusor muscle and internal sphincter receive sympathetic innervation from L1-2 and parasympathetic innervation from S2-4
- external sphincter supplied with somatic fibres from N pudendus
- efferent sensory fibres from bladder & post urethra to sacral spinal cord centre – in contact with brain stem and cerebral cortex

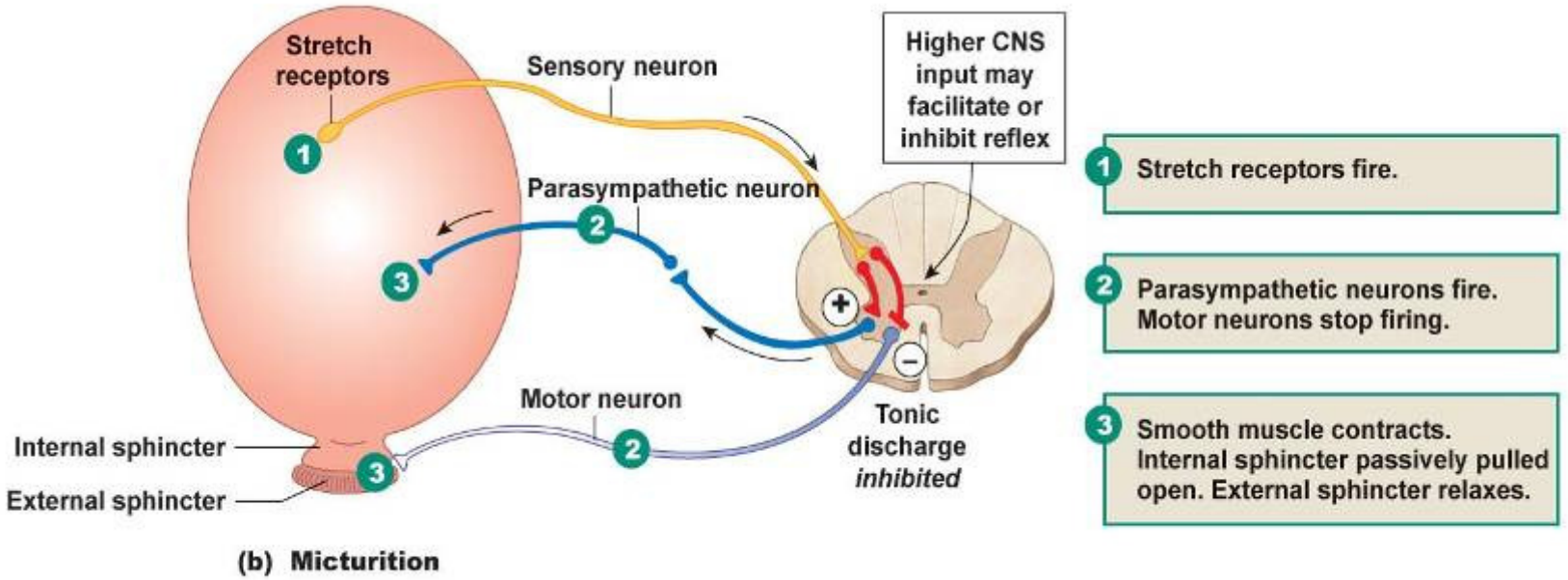
sympathetic L1-3
beta2 – relax detrusor
alpha1 – closure of internal sphincter



1. sensory neurons
stimulated by stretch of detrusor
carried to spinal cord and brain centres, if facilitated;

2. parasympathetic efferents – muscarinic – contraction of detrusor, relaxation of internal sphincter

3. somatic efferents (pudendal) – relaxation/opening of external sphincter → micturition



(b) Micturition

The cystometrogram

Due to plasticity the pressure remains low until urine volume reaches about 400 ml