(Renal Physiology 7)

Renal Regulation of Body Fluid

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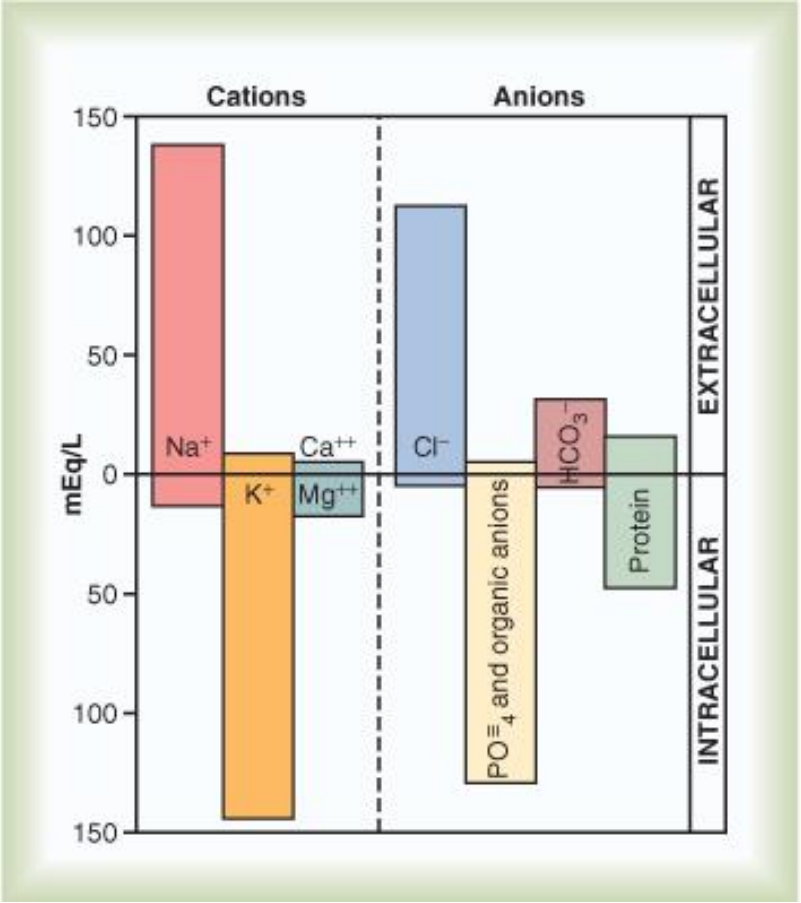
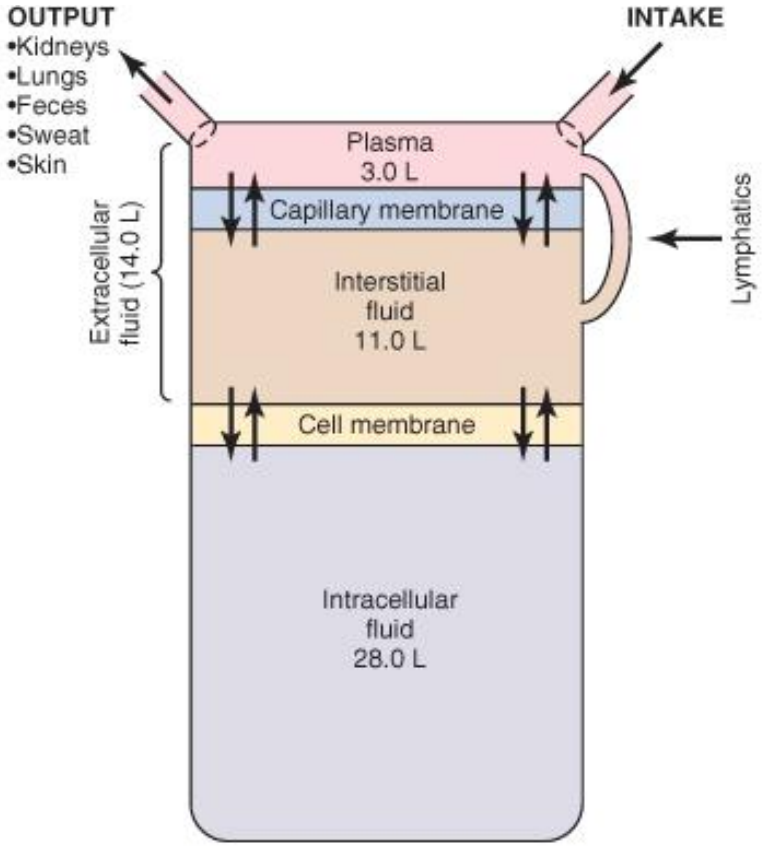
Solute Overview: Intracellular vs. Extracellular

- Ionic composition very different
- Total ionic concentration very similar
- Total osmotic concentrations virtually identical



The major body fluid compartment and membranes separate them

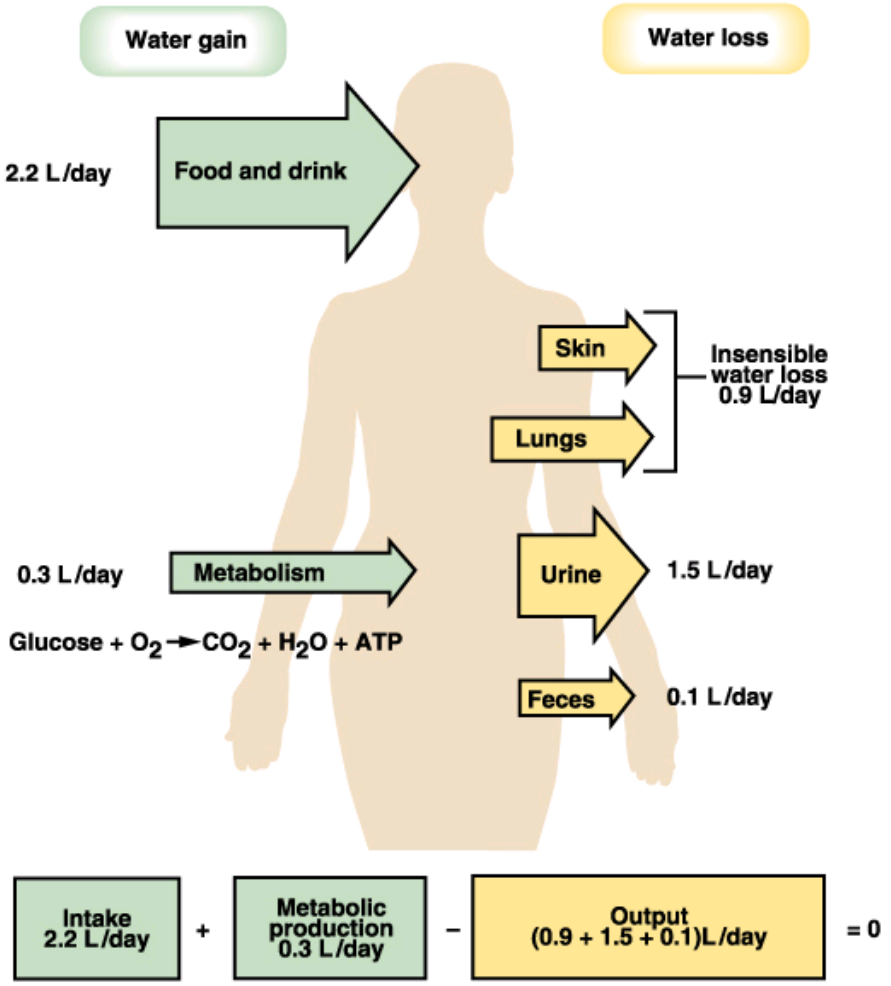


Regulation of volume & osmolality

- Body water balance must be maintained.
- Kidneys concentrate or dilute urine.
- To remain properly hydrated, water intake must equal water output.
- Increases in plasma osmolality trigger thirst and release of antidiuretic hormone (ADH)

Water Steady State:

- Amount ingested = amount eliminated.
- Pathological losses:
  - Vascular bleeding.
  - Vomiting.
  - Diarrhea.



Control of circulating volume

- All down to Na^+ balance i.e. absorption & excretion

Volume sensors: (Effectively pressure receptors)

a) Vascular:
    1. Low pressure sensors: Cardiac atria (ANP), pulmonary vasculature.
    2. High pressure: carotid sinus, aortic arch and juxtaglomerular apparatus of the kidney.

b) Central nervous system.

c) Hepatic.

Control of circulating volume

- Volume sensor signals/Mediators:

A) Neural:

If pressure ↓

Renal sympathetics:

a) afferent & Efferent arterioles constrict

i) GRF ↓

ii) less Na^+ filtred

iii) more Na^+ absorbed by PCT

b) renin released

i) ↑ aldosterone

ii) ↑ angiotensin II

Control of circulating volume

B) Hormonal:

1) Renin-angiotensin-aldosterone system (↓ pressure):

- Renin secreted, by:
  - a) Sympathetic stimulation
  - b) ↓ perfusion pressure
  - c) ↓ Na+ reaching macula densa
- Angiotensin II:
  - i) aldosterone release by adrenal cortex
    - ↑ Na^+ reabsorption in TAL, DT, CD
  - ii) Vasoconstriction
  - iii) ADH release
  - iv) ↑ Na^+ reabsorption in PCT

2) ANP:

From **atrial** myocytes

Released by stretch of atrium

$\Rightarrow \uparrow$ NaCl & water excretion

Antagonist of renin-angiotensin:

i) vasodilation of afferent arteriole, vasoconstriction of efferent

i.e. $\uparrow$ GFR

ii) $\downarrow$ renin release

iii) direct $\downarrow$ aldosterone release

iv) $\downarrow Na^+$ reabsorption in CD

v) $\downarrow$ ADH release

Regulation of volume & osmolality

- If ↑ water intake ⇒ hypoosmotic urine
  - dilute (~ 50 mOsm/kg)
  - large volume (up to 18 L/d!!)
- If ↓ water intake ⇒ hyperosmotic urine
  - concentrated (up to 1200 mOsm/kg)
  - small volume (0.5 L/d)

- Renal water excretion mechanism(s) independent of solute excretion mechanism(s)

∴ allows water balance maintenance without damaging solute homeostasis (e.g. Na+, K+)

Antidiuretic hormone (ADH)/Vasopressin

- It is synthesized in neuroendocrine cells located within the supraoptic and paraventricular nuclei of the hypothalamus
- The synthesized hormone is packaged in granules that are transported down the axon of the cell and stored in nerve terminals located in the neurohypophysis (posterior pituitary).

- prevents water loss
- small protein hormone (only 9 amino acids)
- fast acting, short half life in circulation
- ↑ thirst

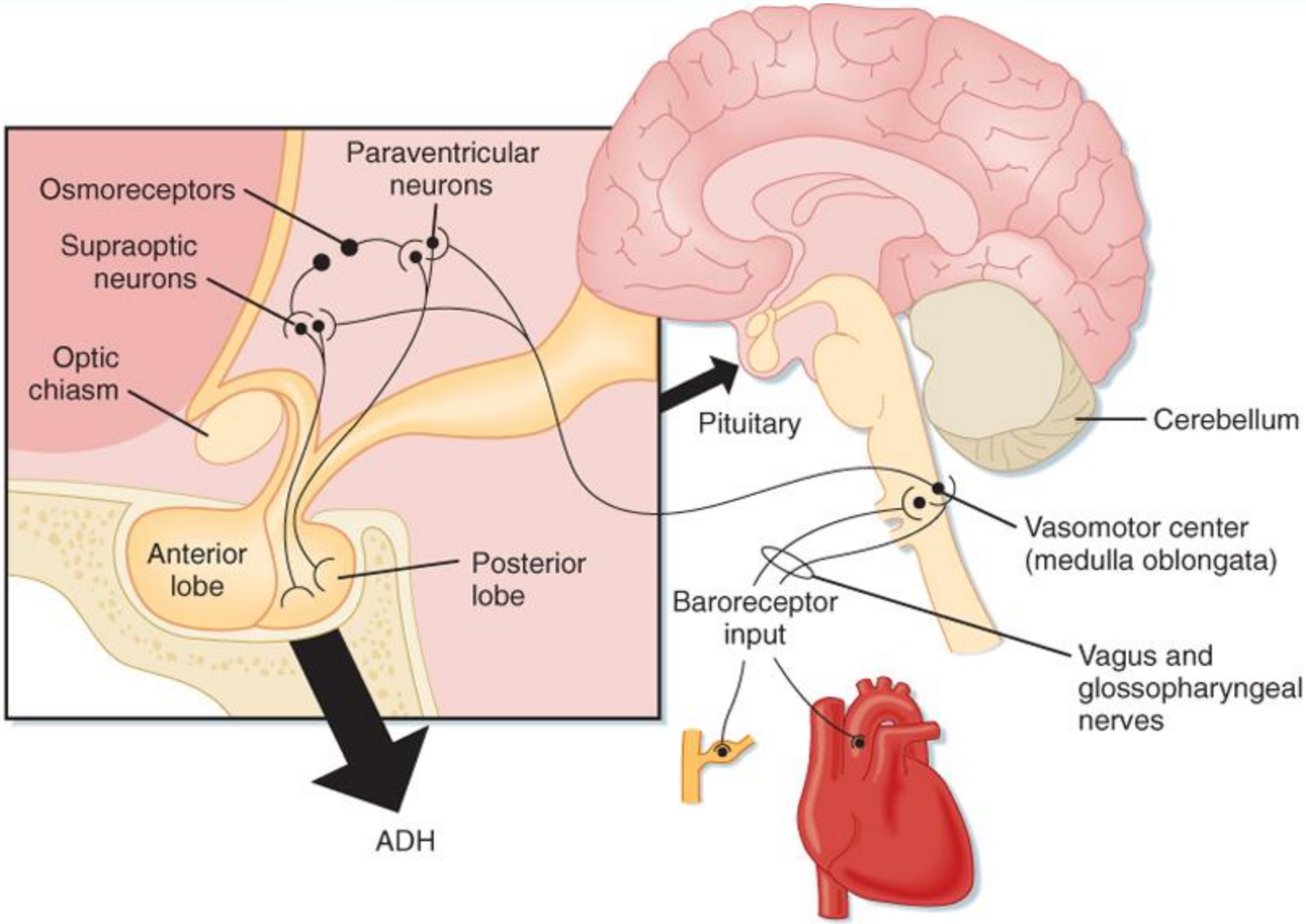
Antidiuretic hormone (ADH)/Vasopressin

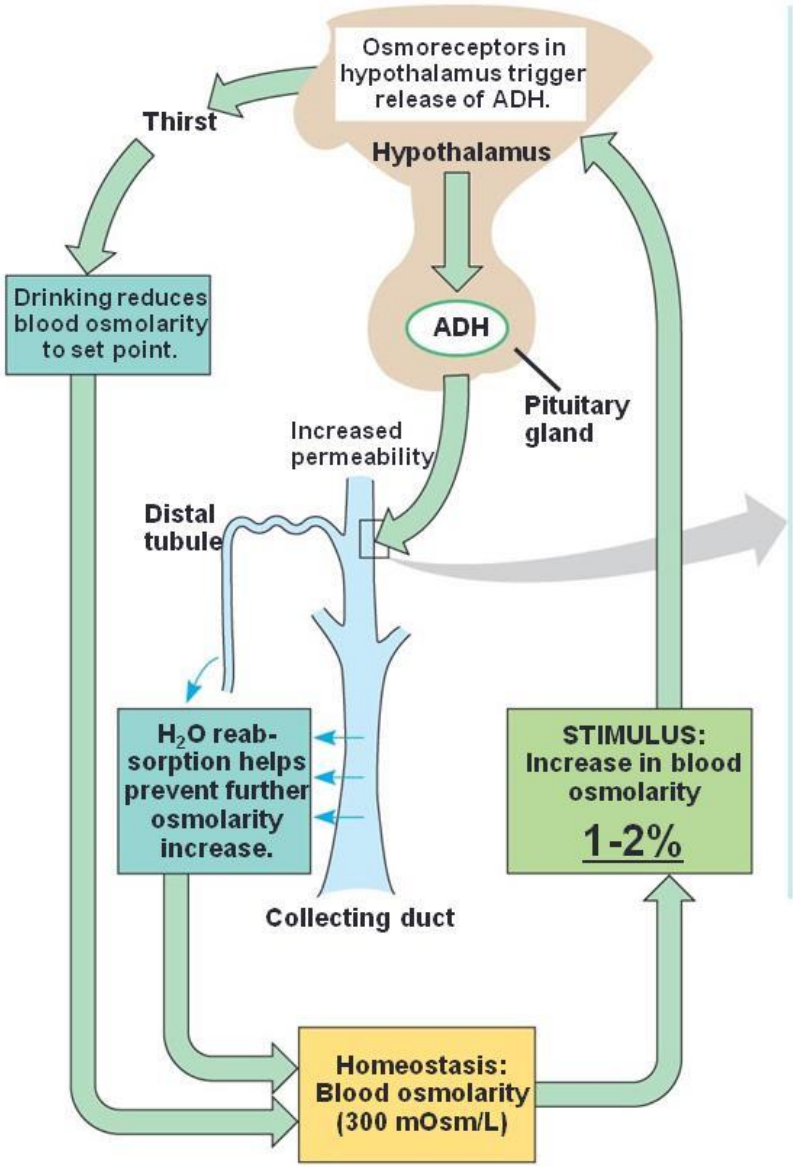
- Factors influencing release:

1) Osmolality
2) Haemodynamic factors

} Main physiological factors

3) Nausea → stimulates
4) Atrial natriuretic peptide (ANP) → inhibits
5) Angiotensin II → stimulates




Osmoreceptors in hypothalamus trigger release of ADH.
Thirst
Hypothalamus
Drinking reduces blood osmolarity to set point.
ADH
Pituitary gland
Increased permeability
Distal tubule
H_2O reab-sorption helps prevent further osmolarity increase.
STIMULUS: Increase in blood osmolarity
1-2%
Collecting duct
Homeostasis: Blood osmolarity (300 mOsm/L)

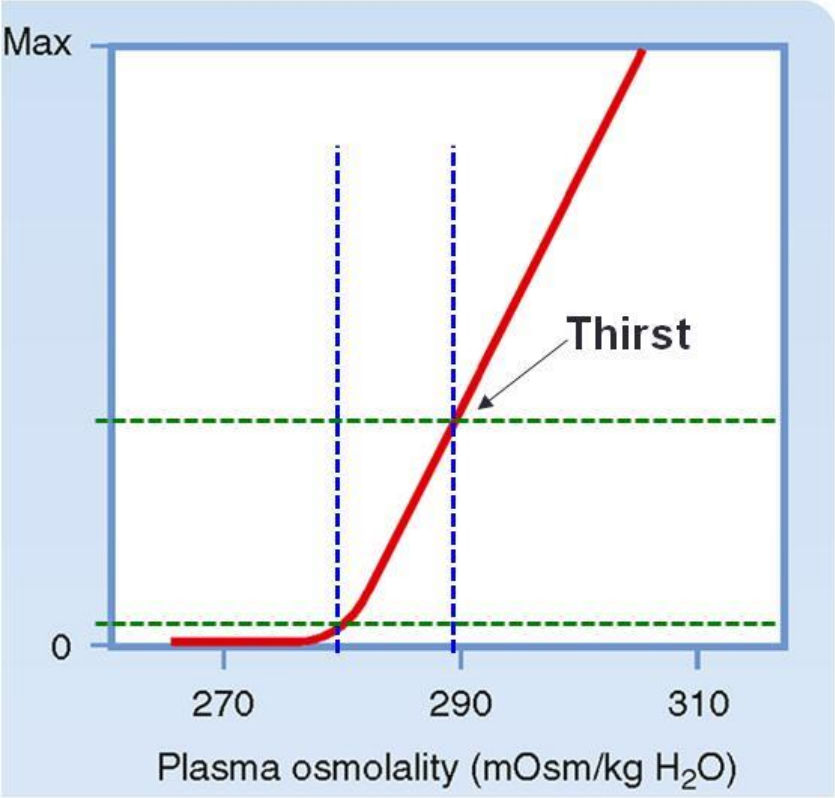
- A rough estimate of ECF osmolality can be obtained by doubling Plasma sodium concentration
- 145mEq/l X 2 = 290 (Normal 285-295 mOsm/kg H2O)

∴ Sodium concentration gives best estimate of effective osmolality of ECF.

- In clinical situations glucose & urea concentrations (mmols) are also taken into account, useful in cases of patients with diabetes mellitus or chronic renal failure.
- (non-absorbed glucose in kidney tubule can however prevent fluid absorption generating an osmotic diuresis).

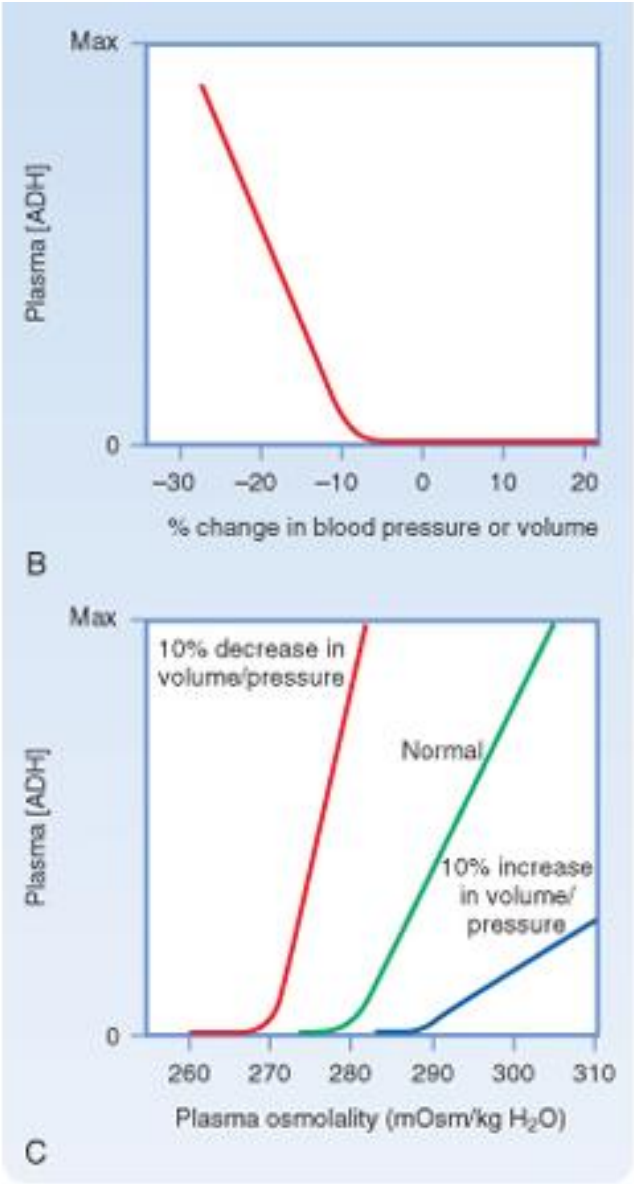
Osmolality

- Osmoreceptors in hypothalamus, outside blood-brain barrier.
- ↑ osmolality ⇒ ADH release
- “set point” ~ 280 – 285 mOsm/kg H2O



Blood volume

- ↓ blood volume ⇒ ADH release
- less sensitive than osmolality
- need 5 – 10% ↓ blood volume
- As would be expected changes in blood volume affect osmolality
- ↓ volume/BP ⇒ ↓ set point steeper curve



ADH renal target

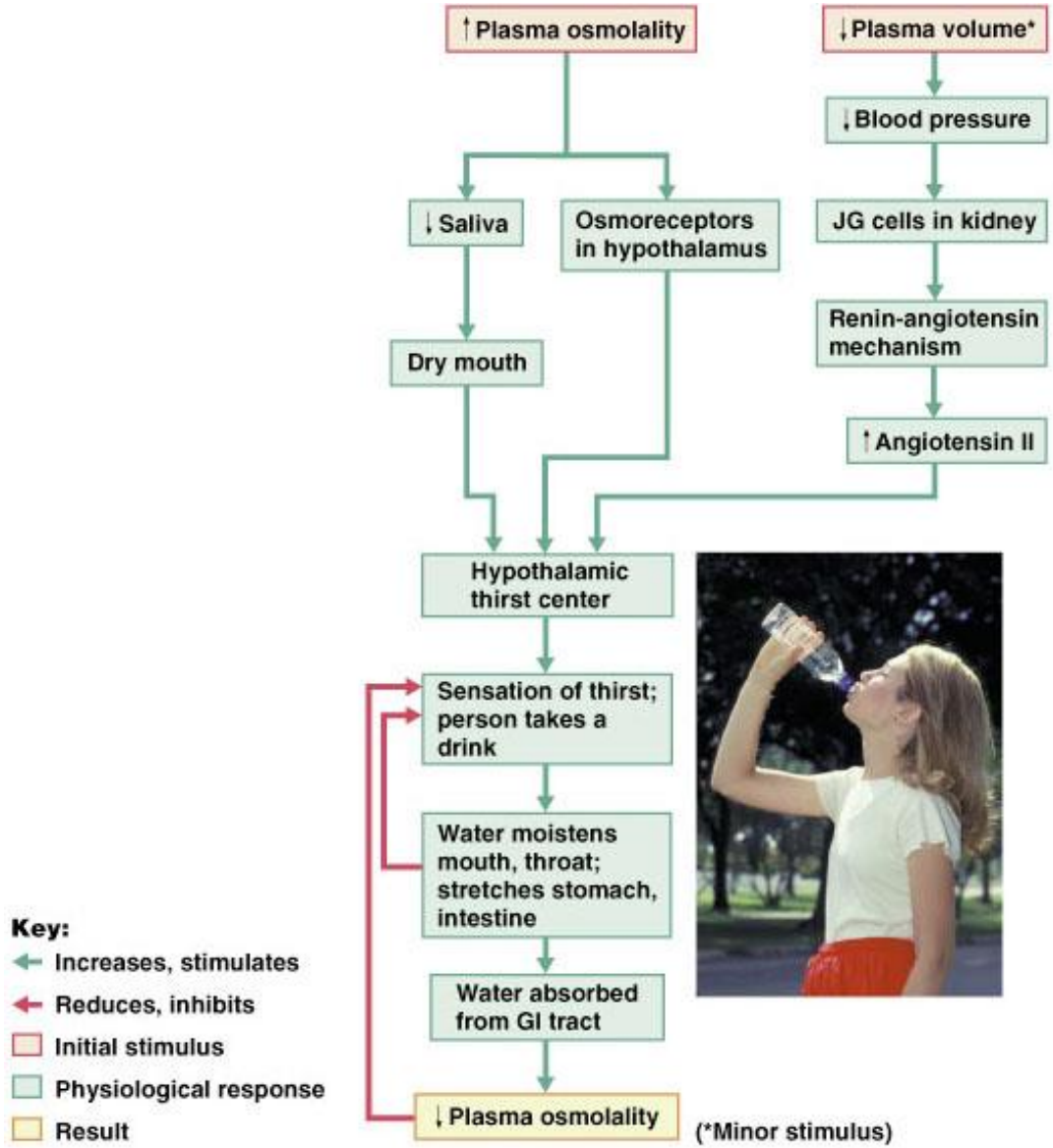
- Collecting duct cells only permeable to water in presence of ADH
- ADH causes ↑ in **urea** permeability in inner medullary CD
- ADH stimulates reabsorption of NaCl by the thick ascending limb of Henle's loop and by the DCT and cortical segment of CD

Regulation of Water Intake

- The hypothalamic thirst center is stimulated:
  - By a decline in plasma volume of 10%–15%
  - By increases in plasma osmolality of 1–2%
  - Via baroreceptor input, angiotensin II, and other stimuli.

Regulation of Water Intake

- Thirst is quenched as soon as we begin to drink water
- Feedback signals that inhibit the thirst centers include:
  - Moistening of the mucosa of the mouth and throat
  - Activation of stomach and intestinal stretch receptors


↑Plasma osmolality
↓Plasma volume*
↓Blood pressure
↓Saliva
Osmoreceptors in hypothalamus
JG cells in kidney
Renin-angiotensin mechanism
Dry mouth
↑Angiotensin II
Hypothalamic thirst center
Sensation of thirst; person takes a drink
Water moistens mouth, throat; stretches stomach, intestine
Water absorbed from GI tract
↓Plasma osmolality
(*Minor stimulus)
Key:
Increases, stimulates
Reduces, inhibits
Initial stimulus
Physiological response
Result

Actions of Angiotensin II

1. Angiotensin II receptors are found on the zona glomerulosa cells of the adrenal cortex.

- Activation of these receptors leads to an immediate and rapid increase in aldosterone secretion.

- Aldosterone acts on the distal tubule and collecting duct to cause *sodium* retention.

- This is likely to be an important mechanism for determining long-term sodium balance.

Actions of Angiotensin II

2. Vascular actions

- Angiotensin II is one of the most potent vasoconstrictors known.

- Constriction of vascular smooth muscle leads to a prompt rise in blood pressure.

- It plays an important role in maintaining vascular tone and blood pressure in volume depleted states, for example haemorrhage and fluid depletion.