

Water Balance: Regulation of Fluid Balance

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Fluid balance is a carefully regulated system with many mechanisms to monitor and modify the absorption and secretion of water. Water is in constant motion between compartments that make up the body. When the body senses a drop in the effective circulating volume it stimulates a response to restore blood pressure and retain fluids. When there is too much fluid the body increases secretion and excretion of the excess.



Body Fluid Distribution

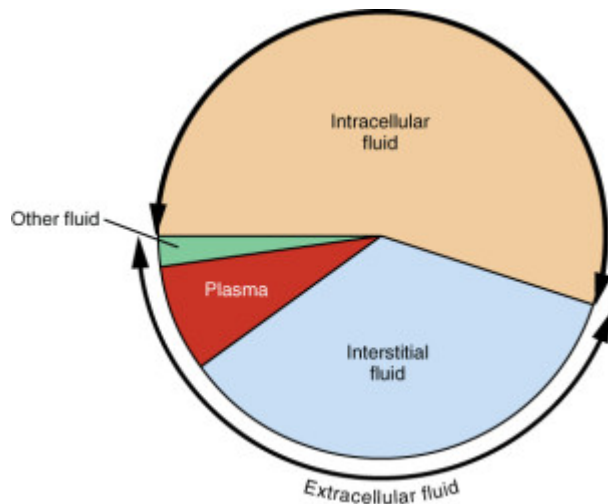


Image: "Distribution of Water in the Human Body" by OpenStax College. License: [CC BY 3.0](https://creativecommons.org/licenses/by/3.0/)

The average human body is composed of 35–40 % **tissue** and **bone** by weight and 60–65 % water. We call this water **total body water** and it is distributed into three compartments throughout the body. **2/3** of the total body water is **intracellular** and found in the cytoplasm and nucleus of all types of **cells**: red blood cells, white blood cells, epithelial cells, fat cells, etc.

The other **1/3** of total body water is in the **extracellular space**. 1/3 of the extracellular water is found **intravascularly**, this is the plasma in the **blood vessels**, and 2/3 in the interstitium, the space between cells that makes up tissue. So all of the plasma that maintains tissue perfusion and blood pressure only equals a paltry **1/9** of the total body water.

| | | |
|--|--|---|
| Intracellular Water 2/3 of total body water or 6/9 of total body water | Interstitial Water 2/3 of extracellular water or 2/9 of total body water | Intravascular Fluid 1/3 of extracellular water or 1/9 of total body water |
| | Extracellular Water 1/3 of total body water | |

Water is constantly moving between compartments via **osmosis** and always down its concentration gradient. Increasing the intracellular solute concentration will result in a fluid shift from the extracellular space (both interstitial water and intravascular fluid).

As total body water is gained or lost it always comes from the intravascular space first. For instance, if a person drinks hypotonic or pure water, it dilutes the intravascular fluid, resulting in a fluid shift to the interstitial space and then the intracellular space. If a person drinks hypertonic salt water, it will increase the solute concentration of the intravascular space and fluid will shift from the interstitial space into the intravascular space followed by a fluid shift from the intracellular space into the interstitial space until the body is once again in equilibrium.

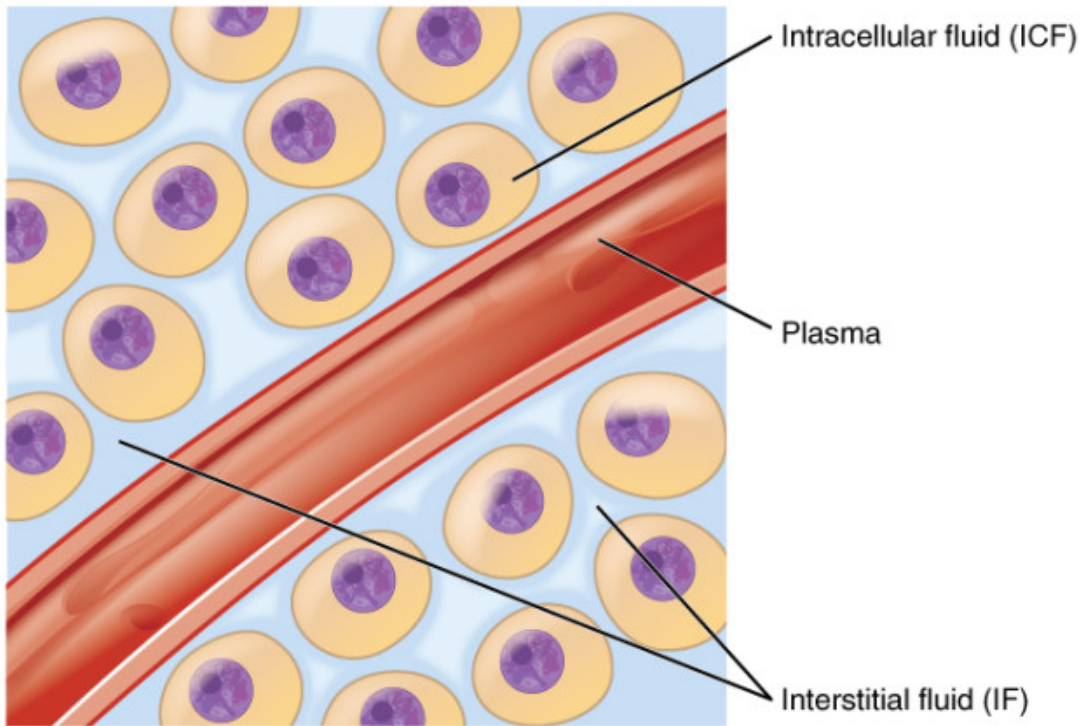


Image: "Fluid Compartments in the Human Body" by PhilSchatz. License: [CC BY 4.0](https://creativecommons.org/licenses/by/4.0/)

Intake and Output

| | Normal | Prolonged, heavy exercise |
|---------------------|--------|---------------------------|
| Intake | | |
| Fluids ingested | 2100 | ? |
| From metabolism | 200 | ? |
| Total intake | 2300 | ? |
| Output | | |
| Insensible: skin | 350 | 350 |
| Insensible: lungs | 350 | 650 |
| Sweat | 100 | 5000 |
| Feces | 100 | 100 |
| Urine | 1400 | 500 |
| Total output | 2300 | 6600 |

Water addition

Water is added to the body in a variety of ways. Under normal conditions, water is **consumed as a free liquid or bound in solid food**. About 22 % of consumed water comes from food consumption in a typical western diet.

Normally, as much as 2 L of dietary fluid can be consumed in any one day. As it passes through the gastrointestinal (GI) system water and food is mixed with 6-7 L of digestive secretions consisting of saliva, [liver](#), [stomach](#), and [pancreatic](#) secretions and bicarbonate solutions. Most of this fluid will be **absorbed by the mucous membranes** in the [small intestine](#) and, to a lesser extent, the [large intestine](#).

80 % of consumed water is absorbed by the small intestine. Water passes through the

membranes of the epithelial cells that line the small intestine by solutes, especially sodium, are absorbed. **Sodium** is absorbed into **enterocytes** through transport proteins found in the luminal side of the cells. These are primarily cotransporters that move sodium and glucose or amino acids into the enterocytes. This forms an **osmotic gradient** that pulls water into the cell. Water continues to follow the sodium as it is pumped into the interstitial space at the basal-luminal side of the cell and then into the capillaries of the portal system. Water continues to be absorbed in the large intestine with other nutrients and vitamins.

Fluids can also be added **intravenously** when in the hospital. It is always preferred to provide nutrients PO (“per os” or “by mouth”) but some procedures, tests, and most surgeries require the patient to be NPO (“nil per os” or “nothing by mouth”). In these cases and when the patient is physically unable to eat due to unconsciousness or aspiration concerns nutrients and fluids are supplied intravenously. The type and rate of fluid provided can be a very powerful medical tool for treating a variety of ailments.

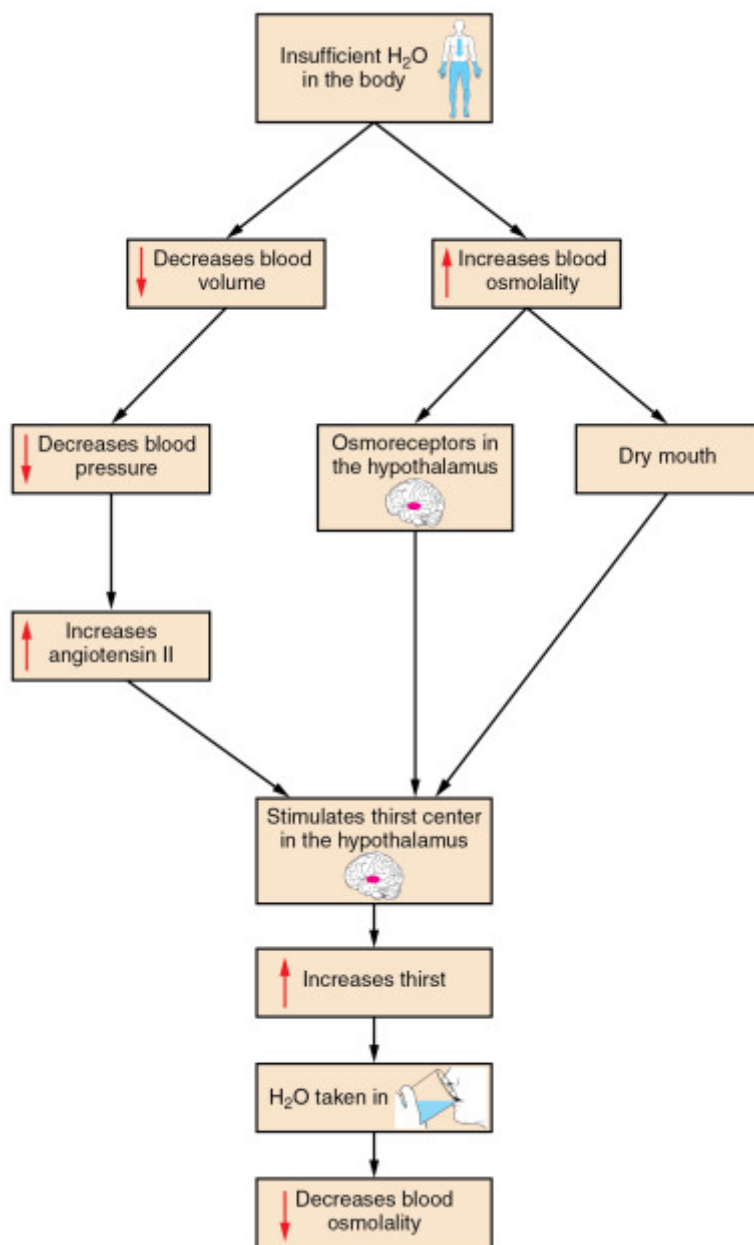


Image: “Flowchart Showing the Thirst Response” by PhilSchatz. License: [CC BY 4.0](https://creativecommons.org/licenses/by/4.0/)

Water removal

Fluids are removed by three different ways: urination, defecation, and intravascular fluid loss.

The process of **urination** starts at the [kidneys](#) where **electrolytes and other small particles are filtered out of the blood and then some material is reabsorbed or secreted into the urine which is then excreted**. This process is very carefully controlled by several modulators including three hormones aldosterone, vasopressin (antidiuretic protein) and natriuretic peptide. These hormones are released in response to the body's physiologic state to regulate plasma volume, plasma osmolality, and certain electrolyte concentrations (mostly sodium).

Water is also lost during **defecation**. Most fluid is reabsorbed from consumed food and drink by the small intestine, but some escapes in feces. This is an osmotic process as the food bolus travels down the gastrointestinal system. If the bolus travels too fast and has spent an insufficient time to allow for sufficient water absorption then the stool is watery, called [diarrhea](#) (a condition where there is too much fluid in the fecal matter). Young and healthy adults may not suffer any consequences from occasional diarrhea but in both the very young and elderly the water loss due to diarrhea could lead to major health concerns including dehydration, malnutrition, metabolic acidosis, and [hypovolemic shock](#).

Uncontrolled intravascular fluid loss, as in **trauma**, can also lead to **hypovolemic shock**. Fluid can also be removed from the intravascular space during the process of **dialysis** in patients with kidney injury.

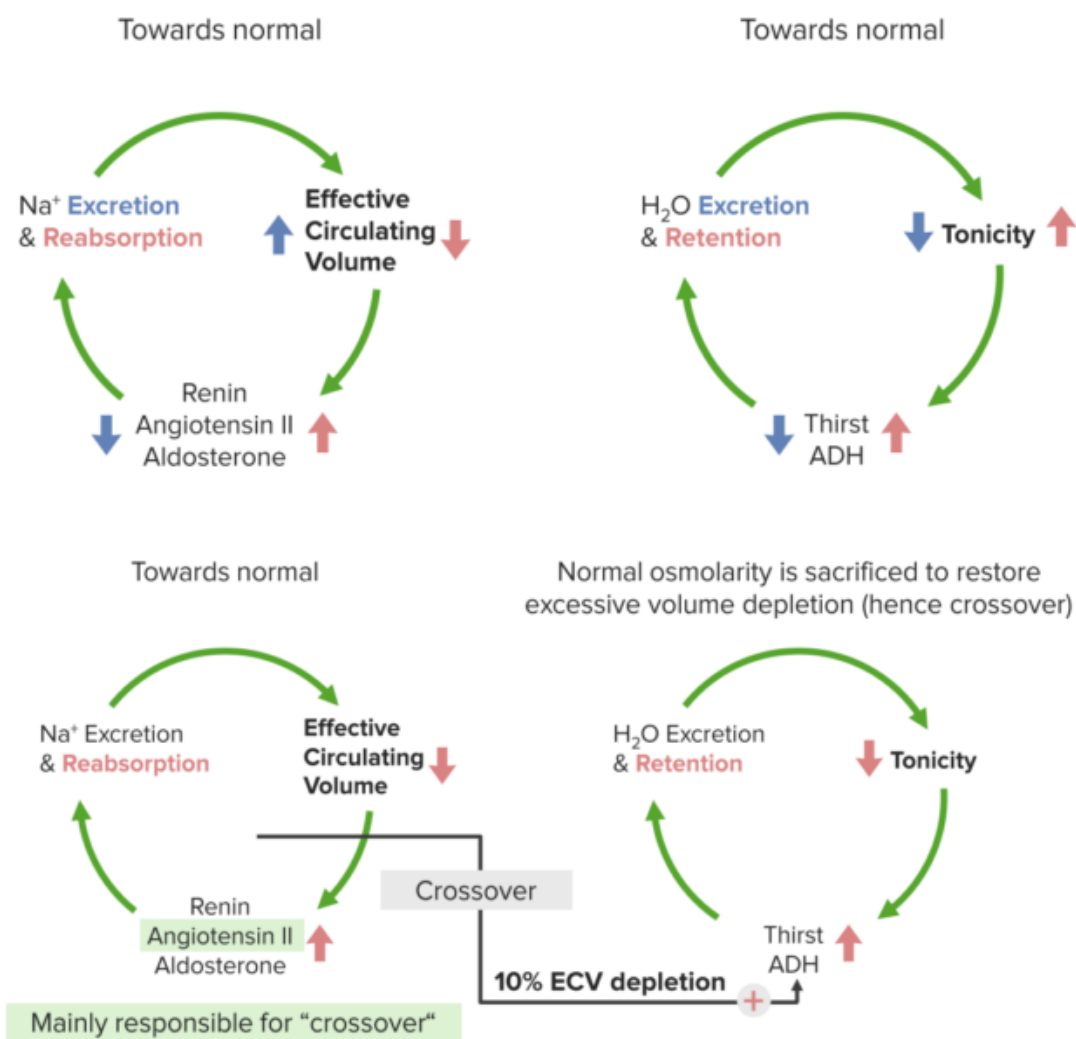
Regulation of water and Na⁺ Balance

Two carefully **regulated** parameters

| | | |
|--|------------------------------------|-------------------------------------|
| Portion of the intravascular volume that is effectively perfusing our organs | Effective circulating volume (ECV) | Tonicity |
| What the body actually senses and regulates: | | Serum osmolality |
| What we most readily detect or measure clinically: | Extracellular fluid volume | Serum Na ⁺ concentration |

Normally, body fluid volumes (ECF) are regulated by changes in Na⁺ balance. Normally, serum osmolality and its primary determinant, Na⁺ concentration, are regulated by changes in H₂O balance.

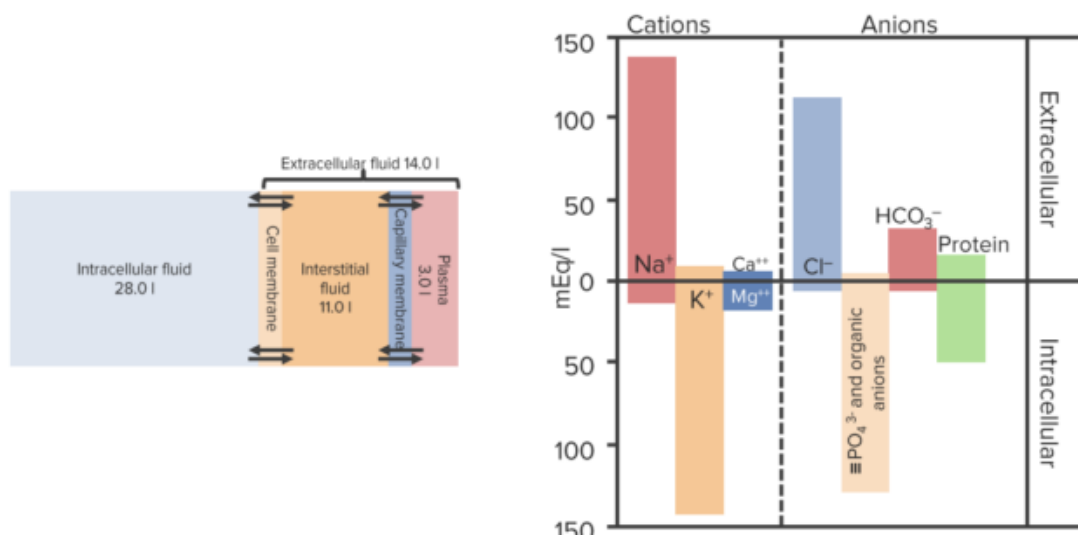
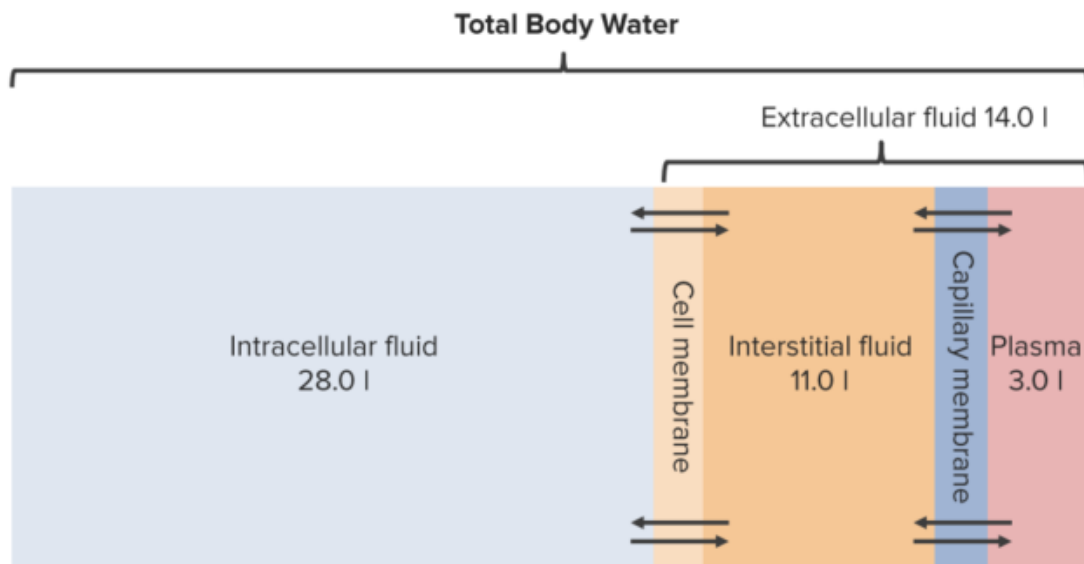
- Changes in Na⁺ balance → changes in volume status
- Changes in H₂O balance → changes in Na⁺ concentration and osmolality
- In certain pathologic states, there can be “crossover” between these two systems



The body has no way of measuring extracellular fluid levels (EFC). However, through various receptors found throughout the body, the **effective circulating volume (ECV)** can be measured. ECV is a measure of the fluid that perfuses tissue.

EFC and ECV are proportional in a healthy adult. However, in a diseased state such as congestive heart failure or cirrhosis, the EFC may appear low resulting in a response by the body to retain fluids even though the EFC appears normal. The result is a hypervolemic state with peripheral edema, pulmonary edema and ascites.

Fluid Distribution Diagrams



Measuring Ions and Fluid Compartments

| Basic metabolic panels | Comprehensive metabolic panels |
|--|--|
| Chem-7 (SMA-7) | |
| • Ions: Na ⁺ , K ⁺ , Cl ⁻ & HCO ₃ ⁻ | • Ions: Na ⁺ , Cl ⁻ , HCO ₃ ⁻ (CO ₂), Ca ₂ ⁺ |
| • Other: Glucose, BUN & Creatinine | • Other: Glucose, BUN, Creatinine, ALP, ALT, AST, Bilirubin, TP, Albumin |
| Plasma, Serum & interstitial osmolality | |
| • Direct measurement: Freeze point depression/ vapor pressure | |
| • Estimated: Posm = (2 x Na) + (glucose/18) + (BUN/2.8) | |

Serum Total Proteins (Oncotic)

- Total
- Albumin
- Globulins: α₁, α₂, β, γ

Changes in Body Fluid Compartment

| | Hypo-osmotic Volume Expansion | Hypo-osmotic Volume Contraction | |
|---|--------------------------------|--|--|
| <p>ECF Measurements ABP = \uparrow \leftrightarrow [Na⁺] = \downarrow TP = \downarrow Hct = \leftrightarrow Endocrine Response Aldo = \downarrow ADH = \downarrow</p> | | <p>ECF Measurements ABP = \downarrow [Na⁺] = \downarrow TP = \uparrow Hct = \uparrow Endocrine Response Aldo = \uparrow ADH = \downarrow \leftrightarrow</p> | |
| | Iso-osmotic Volume Expansion | Iso-osmotic Volume Contraction | |
| <p>ECF Measurements ABP = \uparrow [Na⁺] = \leftrightarrow TP = \downarrow Hct = \downarrow Endocrine Response Aldo = \downarrow ADH = \leftrightarrow \downarrow Example • IV solution</p> | | <p>ECF Measurements ABP = \downarrow [Na⁺] = \leftrightarrow TP = \uparrow Hct = \uparrow Endocrine Response Aldo = \uparrow ADH = \leftrightarrow \uparrow Example • Diarrhea • Vomiting</p> | |
| | Hyper-osmotic volume expansion | Hyper-osmotic Contraction | |
| <p>ECF Measurements ABP = \uparrow [Na⁺] = \uparrow TP = \downarrow Hct = \downarrow Endocrine Response Aldo = \downarrow ADH = \uparrow \leftrightarrow Example • Aldosterone • Tumor</p> | | <p>ECF Measurements ABP = \downarrow [Na⁺] = \uparrow TP = \uparrow Hct = \leftrightarrow Endocrine Response Aldo = \uparrow ADH = \uparrow Example • Lack of water</p> | |

Renin-Angiotensin-Aldosterone System

The renin-angiotensin-aldosterone system (RAAS) involves **several peptide and steroid hormones to regulate fluid balance and blood pressure.**

When activated, RAAS works to increase blood pressure and fluid retention and is the target of many hypertension medications including ACE inhibitors and [aldosterone receptors antagonists](#). This system starts at the afferent arterioles of the kidney. Modified smooth muscle cells called juxtaglomerular cells located in these arterioles detect blood pressure with stretch receptors. When blood pressure drops or when they are signaled by the macula densa sensing low sodium concentration the juxtaglomerular cells release the enzyme renin into circulation.

Renin converts **angiotensinogen**, synthesized by the liver, into angiotensin I. This is then quickly activated by angiotensin-converting enzyme (ACE), synthesized by the [lungs](#), into **angiotensin II**. Angiotensin II is a strong vasoactive peptide consisting of eight residues. It affects multiple systems to increase circulating blood volume and blood pressure. It causes the afferent arterioles to constrict increasing systemic blood

pressure and the sodium, chloride, and water reabsorption in the kidney.

In the brain angiotensin, II stimulates the release of vasopressin (ADH) and the thirst center. It also causes the adrenal glands to release the mineralocorticoid **aldosterone**. Aldosterone then affects the kidney even further to increase reabsorption of sodium, chloride, and water and also secrete potassium.

Renin-angiotensin-aldosterone system

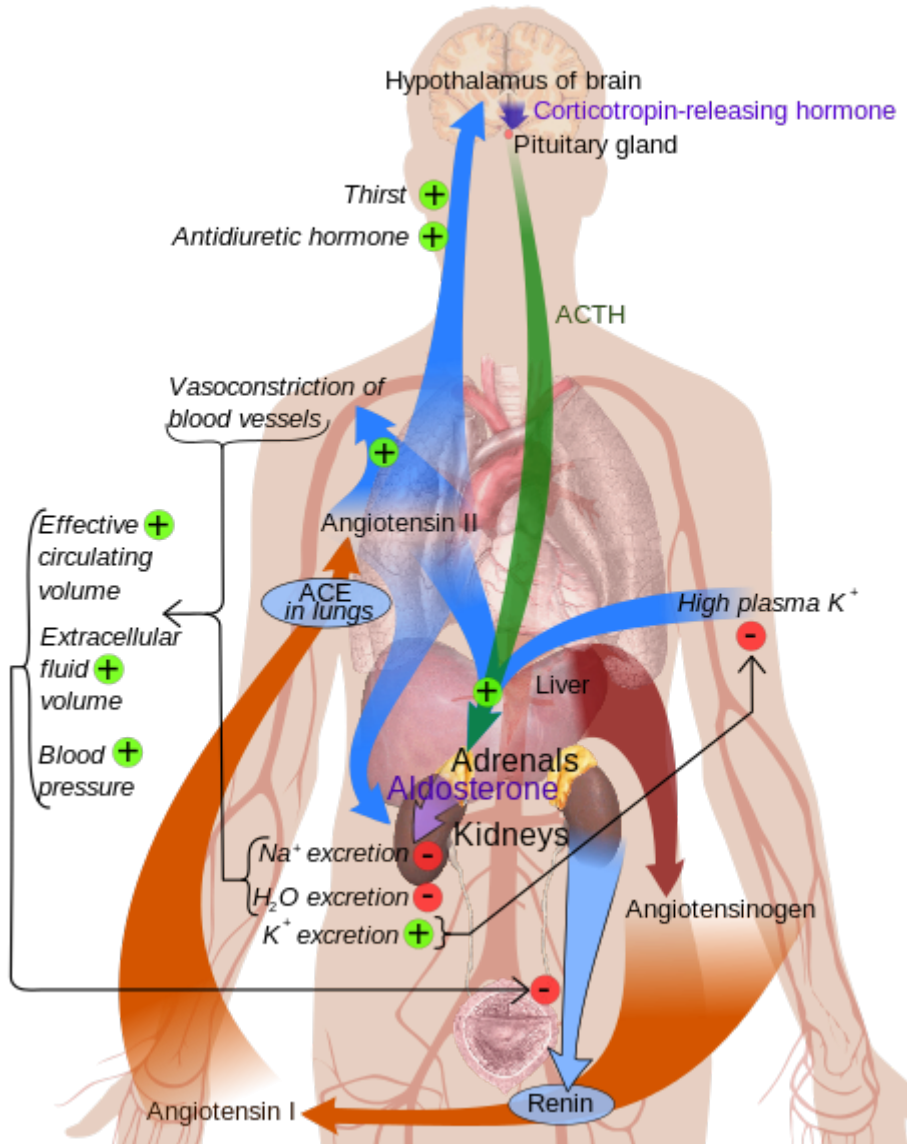


Image: "Overview of the renin-angiotensin system" by Mikael Häggström. License: Public Domain

Atrial Natriuretic Peptide

Atrial natriuretic peptide (ANP) works to **oppose aldosterone**. It is a peptide hormone that is synthesized and released by myocytes found in the atria of the heart in response to stretching (too much blood volume) or angiotensin II. In the kidney, it works to increase glomerular filtration rate and excretion of sodium, chloride and water. It also relaxes systemic afferent arterioles to lower systemic blood pressure.

Antidiuretic Hormone and Osmolality

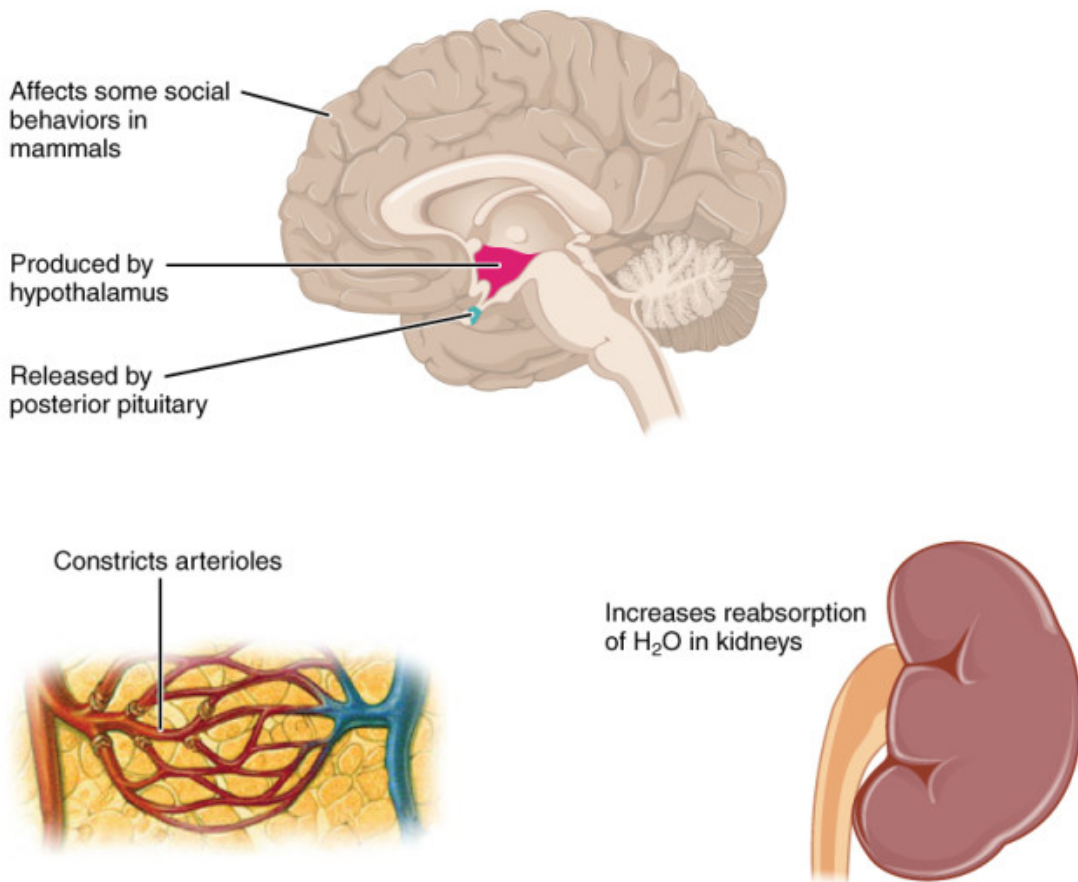


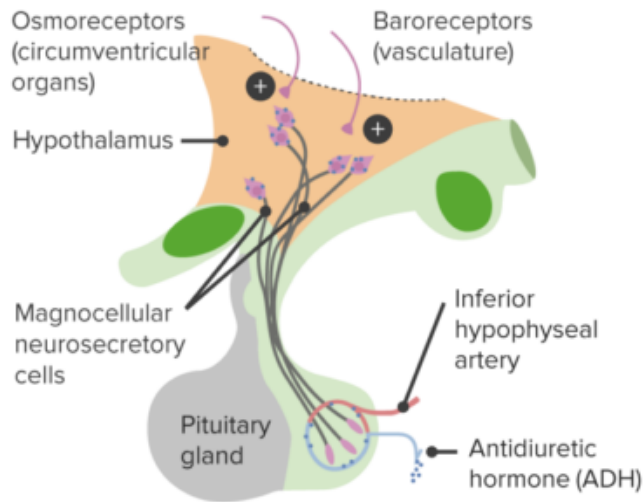
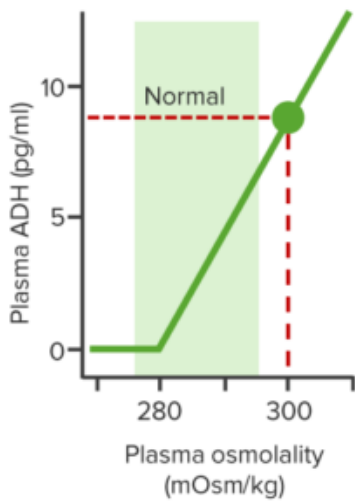
Image: "Antidiuretic Hormone (ADH)" by PhilSchatz. License: [CC BY 4.0](https://creativecommons.org/licenses/by/4.0/)

Antidiuretic hormone (ADH) or **arginine vasopressin** is a short peptide hormone. This hormone works to **increases blood volume**. ADH is released from the posterior pituitary when stimulated by low-pressure baroreceptors found in the vasculature or osmoreceptors found in the hypothalamus.

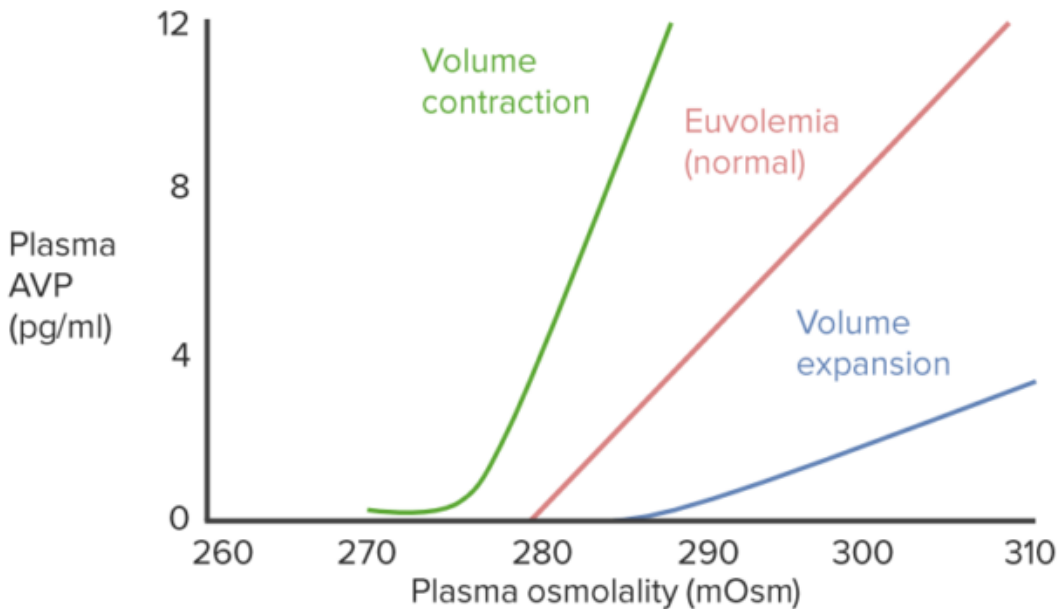
When blood volume is low these receptors send a signal to the **posterior pituitary** to release ADH. Osmoreceptors measure the osmotic pressure of blood. When the blood is too concentrated (too much solvent) they will shrivel as fluid shifts out of the cells by osmosis. This sends a signal to the posterior pituitary to release ADH into circulation.

There are several ADH receptors. **AVPR2 is found in the basolateral side** of the epithelial cells that line the collecting ducts and tubules in the kidney. When AVPR2 is stimulated multiple copies of the water transport protein aquaporin-2 are inserted into the luminal side of the collecting duct cells and water is reabsorbed down its concentration gradient and into the systemic circulation.

ADH/AVP

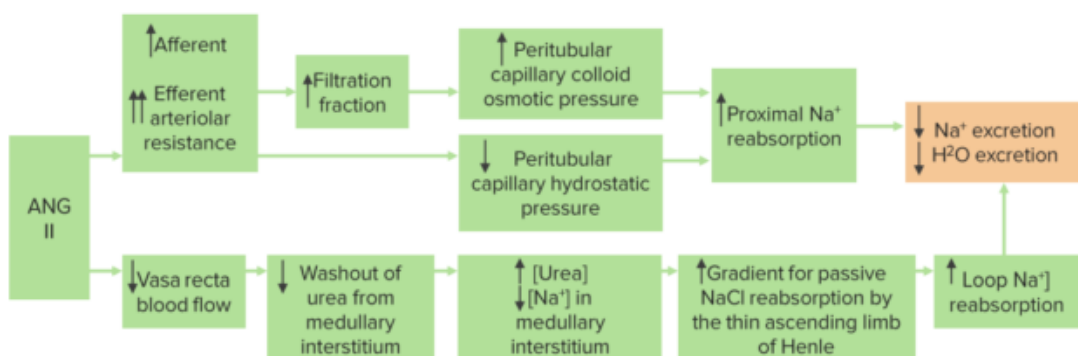


Interaction of plasma osmolality and volume on AVP/ADH secretion

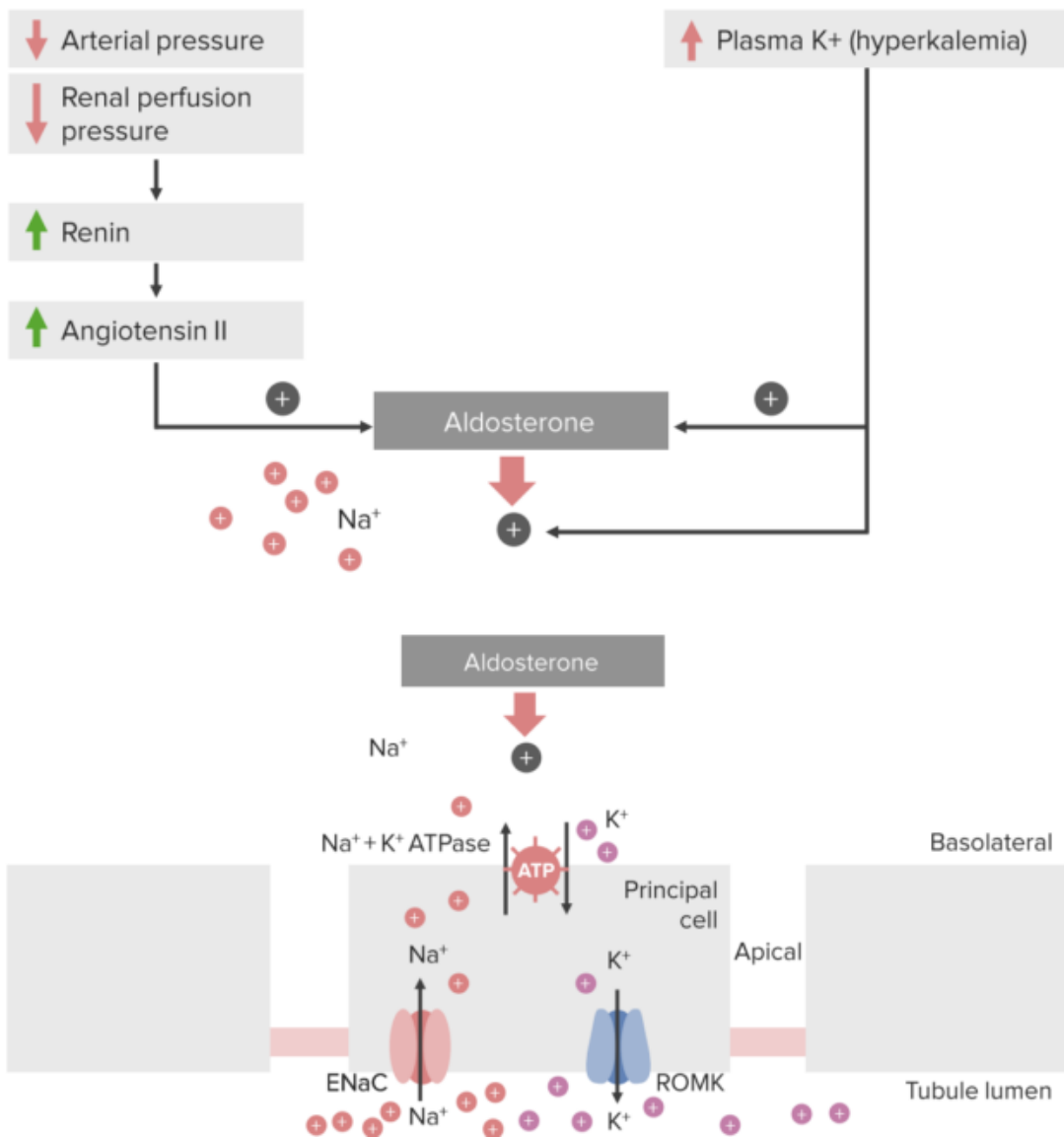


Angiotensin II and Na⁺ excretion

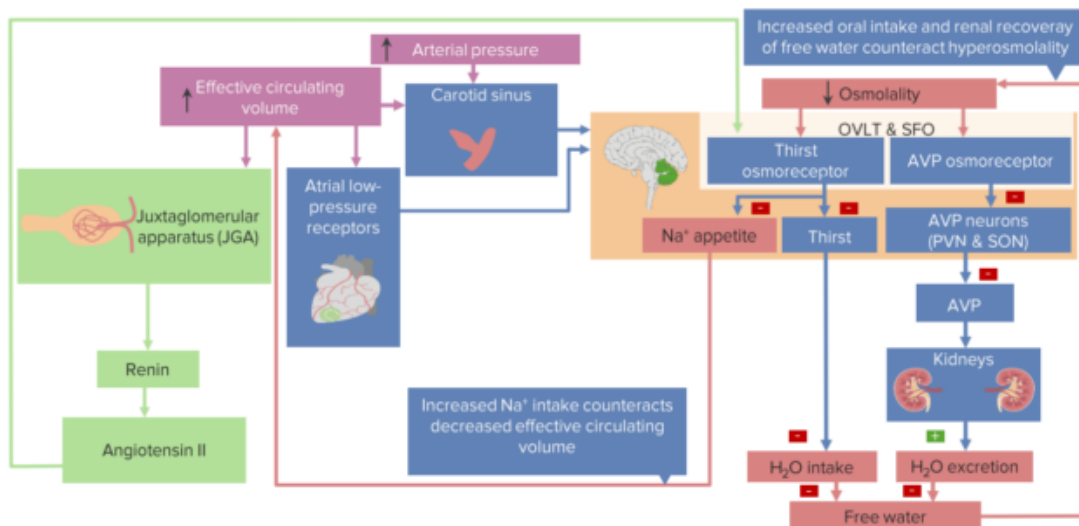
Direct role of a change in blood flow affecting Na⁺ and H₂O excretion (e.g., ANG II and high catecholamines)



Regulation of Aldosterone



Osmolality



Review Questions

The correct answers can be found below the references.

1. The majority of the total body water is found in which compartment?

- A. Extracellular space
- B. Intracellular space
- C. Intravascular space
- D. Interstitial space

2. Which volume does the body measure when assessing fluid state?

- A. Effective circulating volume
- B. Intracellular volume
- C. Intravascular circulating volume
- D. Effective interstitial volume

3. Which two systems oppose each other to balance fluid levels?

- A. Effective circulating volume and intracellular volume
- B. Renin and Aldosterone
- C. Angiotensin II and Aldosterone
- D. RAAS and ANP

References

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Correct answers: 1B, 2A, 3D

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