Osmoregulation

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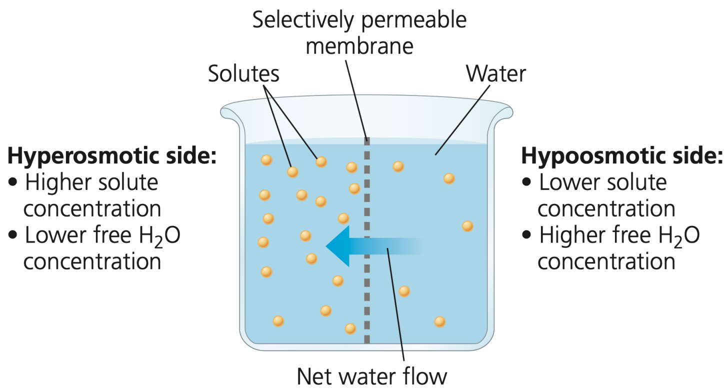
1 Introduction

Welcome to this comprehensive packet on the intricate topic of osmoregulation. In the realm of biology, osmoregulation stands as a fundamental process essential for the survival and proper functioning of a diverse array of organisms. This packet will delve into the mechanisms, significance, and regulatory strategies that living beings employ to maintain optimal internal balance in the face of fluctuating environmental conditions. From unicellular organisms to complex multicellular life forms, the ability to manage water and solute concentrations within their internal environments is crucial.

2 Function of Osmoregulation

2.1 Osmolarity, Osmolality, Tonicity, Osmosis

- **Osmosis** is the movement of solvent molecules (usually water) across a semipermeable membrane.
  - It occurs from a region of lower solute concentration to a region of higher solute concentration.
  - Osmosis aims to equalize solute concentrations on both sides of the membrane.
- **Osmolarity** is the concentration of osmotically active particles in a solution measured in osmoles per liter (osmol/L).
  - Solutions are either hyperosmotic, isoosmotic (equal osmolarity), or hyperosmotic (lower osmolarity) relative to the solution being compared to (usually the inside of the cell).
    * Water will flow from lower osmolarity to higher osmolarity, a key physiological principle in filtration.
- **Osmolality** is the concentration of osmotically active particles in a solution per unit mass of the solvent measured in osmoles per kilogram (osmol/kg).
  - Temperature independent as it is based upon the mass of solvent.
- **Tonicity** refers to the ability of a solution to cause water movement across a semipermeable membrane.
  - Tonicity is based on the concentration of solutes that cannot cross the membrane.
    * This is unique compared to osmolarity/osmolality as non-penetrating solutes results in a difference in water potential across the membrane compared to the penetrating solutes which would just reach an osmotic equilibrium and thus be useless when considering osmosis.



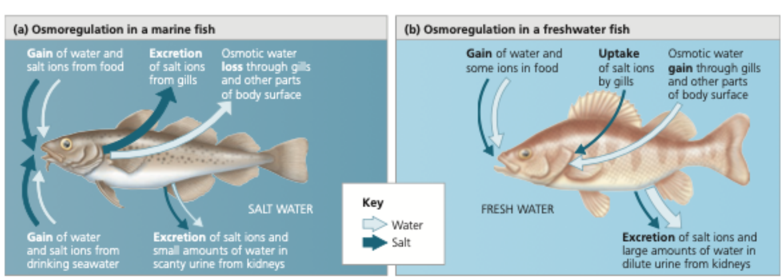
Source: Campbell Biology

2.2 Osmoregulatory Mechanisms

- An **osmoconformer** is an animal that maintains an internal osmolarity which is the same as the environment.
  - Osmoconformers are marine animals that live in a stable environment (with a somewhat constant osmolarity)
- An **osmoregulator** is an animal with an internal osmolarity maintained to be different from the external environment.
  - This regulatory mechanism is common in animals that migrate between locations; this occurs in terrestrial and freshwater animals and animals such as salmon that migrate between freshwater and marine waters.
- **Stenohaline** animals cannot survive large fluctuations in external osmolarity, both, in fact most, osmoregulators and osmoconformers are stenohialine.
- **Euryhaline** animals have to survive large fluctuations in external osmolairty; this group includes osmoconformers such as mussels and clams along with osmoregulators such as striped bass and salmon.
- **Marine Animals**
  - **Marine Invertebrates** are mostly osmoconformers with the same osmolarity as the environment, yet they also actively transport certain solutes out of the hemolyph to maintain **specific** ion concentrations, such as lowered magnesium concentrations. Note that this does not change the fact that they are osmoconformers as they still maintain the same osmolarity as the external environment.
  - **Marine Vertebrates** include the bony fishes and chondrichthyans.
    - Bony fishes lose water by osmosis to the highly salted external environment, they therefore constantly drink water and excrete salt through their gills. They also produce scanty amount of urine to minimize water loss.

    * Sharks and other chondrichthyans contain a large amount of a protein called **TMAO** which prevents denaturation of proteins by urea. This allows them to store large amounts of urea without toxic effects and thus maintain an osmolarity slightly higher than the external environment to allow for water to diffuse into the body allowing sharks to gain water without drinking. Sharks excrete some salts and water diffused into their bodies via urine and feces.

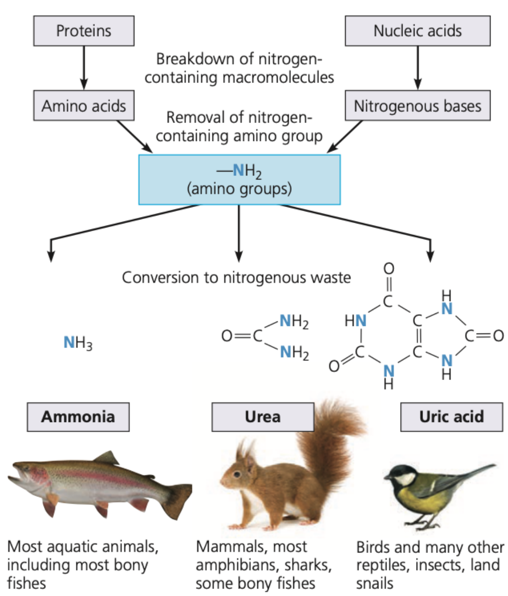
- **Freshwater Animals**
  - Freshwater animals gain large amounts of water from the external environment and thus excrete large amounts of water in dilute urine and across the gills (they also uptake salts via gills and food).
    * Euryhaline fish such as salmon acclimatize to their different migratory environments, changing their volume of urine production and salt uptake depending if the environment is freshwater or saltwater.
      · In salmon, for example, cortisol increases the amount of salt excreting cells when migrating to a saltwater environment.
- **Anhydrobiosis**
  - Some aquatic invertebrates live in temporary water sources such as puddles and must therefore survive such areas, they survive long stretches of time by entering a dormant state known as anhydrobiosis. Animals such as roundworms (during anhydrobiosis) use a sugar called **trehalose** which "replaces" the water in proteins and membranes to allow the membrane to be intact.
- **Land Animals**
  - Terrestrial animals often contain a covering that prevents water loss, the exoskeleton in insects, keratinized epithelium in humans, etc.
    * Desert animals can survive large fluctuations in body water and temperature by modulating water loss (e.g. sweat production lowered as in camels) and they are often nocturnal to prevent excessive water loss.
- Animals are adapted to maintain an internal osmolarity as similar to the environment to prevent excessive energy consumption in osmoregulation. For example, marine molluscs have a much higher solute concentration at which they can survive compared to freshwater molluscs.



Source: Campbell Biology

3 Nitrogenous Wastes

- When animals break down proteins for digestion or energy, ammonia is created. **Ammonia** is toxic as its ion, ammonium, interferes with oxidative phosphorylation; ammonia is therefore dissolved in water and excreted from the body.
  - Animals that excrete ammonia require ammonia to be dissolved in large amounts of water to reduce dangerous concentrations. This mode of excretion is therefore found in aquatic animals with access to plenty of water for which ammonia can dissolve in. Often aquatic invertebrate passively diffuse ammonia across their body membrane rather than through a specialized excretory system (not to say they don't have an excretory system, they simply don't use it to excrete nitrogenous waste).
- **Urea** is found in terrestrial animals to conserve water. Ammonia must be dissolved in large amounts of dilute water while urea, although requiring a higher energetic cost for production, can dissolve in smaller amounts of water and is thus helpful for water conservation.
  - Generated through a reaction between carbon dioxide and ammonia in the liver via an energetic process.
  - Urea has low toxicity.
    - Amphibians switch between urea and ammonia secretion when moving from aquatic to terrestrial environments.
- **Uric Acid** is nontoxic and insoluble and is thus secreted as a paste with minimal water loss. This is the most energetically expensive form of waste secretion yet least toxic.
  - **Gout** involves the build up of uric acid crystals in joints that leads to joint inflammation.
  - In animals that develop from an egg, ammonia and urea cannot diffuse out of the egg (urea in mammals is carried by mothers blood) thus, animals like birds and reptiles store nitrogenous waste as uric acid within the egg.



Source: Campbell Biology

4 Excretory Systems

4.1 Central Theme

- Animals contain a diversity of excretory systems that are variations upon a central theme.
- 1. Body fluid is pumped through a selectively permeable membrane that allows transport of sugars, ion, nitrogenous wastes, etc. but blocks the transport of cells, proteins, and large molecules (the basis of this filtration will be explained later).
- 2. Certain molecules within the filtrate are **reabsorbed** into the bloodstream to prevent excretion of useful molecules such as glucose, vitamins, hormones, etc.
- 3. Some molecules are **secreted** into the lumen of an excretory duct to rid the organism of certain unwanted substances.
- 4. This waste fluid is then **excreted** from the body.

Example 1 (USABO Semifinal Exam 2016) You injected your patient with a chemical known as PZB and collected the following data. Based on this data, calculate the amount of PZB appearing in his urine per minute?
Rate of PZB filtration $\rightarrow$ 10mg/min
Rate of PZB reabsorption $\rightarrow$ 2mg/min
Rate of PZB secretion $\rightarrow$ 4mg/min

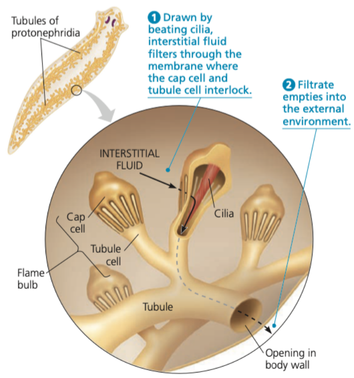
(A) 16mg/min
(B) 4mg/min
(C) 12mg/min
(D) 8mg/min
(E) 0mg/min.

Solution: If the filtration of the substance, or amount initially in the filtrate, is 10mg/min and reabsorption, or amount leaving the filtrate, is 2mg/min and the secretion, or the amount added into the filtrate after filtration, is 4 mg/min: 10 mg/min (filtration) - 2 mg/min (reabsorption) + 4 mg/min (secretion) should be equivalent to the amount of PZB excreted in the urine per minute. This amounts to 12 mg/min or **C**.

4.2 Protonephridia

- Lancelets, flatworms, mollusc larvae, rotifers, and some annelids contain network of tubules that branch to form dead ends capped with **flame bulbs**.

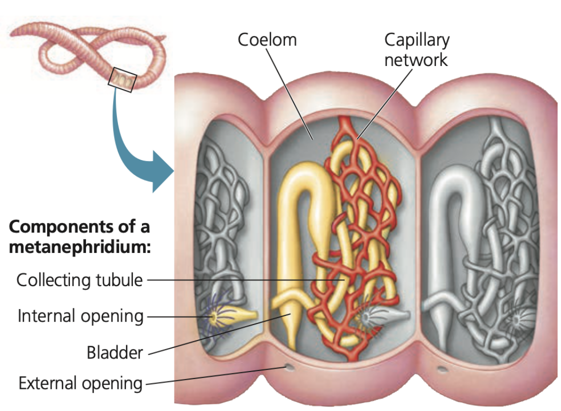
  - Flame bulbs are composed of an upper cap cell and a lower tubule cell. Within the flame bulb a rod of cilia rotates to bring in water through flame bulb which enters the tubule as a filtrate and is then excreted via external openings.
  - In flatworms urine is hypo osmotic as they live in moist areas and thus absorb an excess of water.
    * Nitrogenous waste in this case simply diffuses across the body.
    * However, parastic flatworms in isotonic environments secrete nitrogenous waste in this urine.



Source: Campbell Biology

4.3 Metanephridia

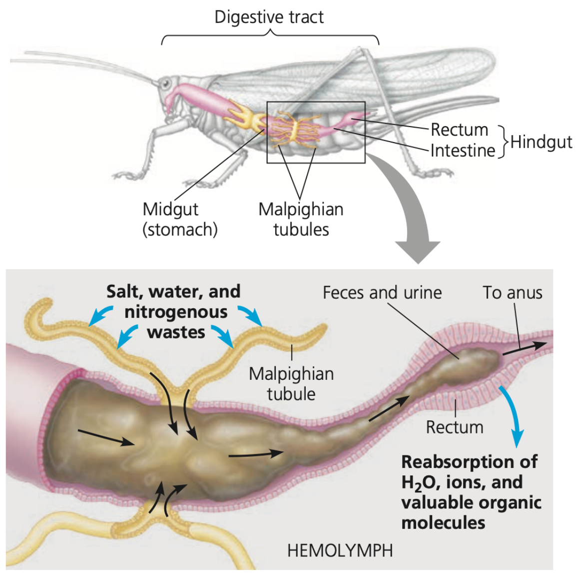
- Annelids, such as earthworms, contain a complex set of tubules which collect hemocoel from the anterior body segment's coelom.
- The opening of the metanphridia is lined with cilium that draws in water to the collecting tubule and then enters a duct and capillary network and finally a storage bladder. Annelids live in mostly moist environments and thereby produce a hypoosmotic urine.
  - Nitrogenous wastes however, are excreted from the body via urine.



Source: Campbell Biology

4.4 Malphigian Tubules

- Malphigian tubules are dead end outgrowths from the insects digestive system, the epithelium of these cells secrete solutes into the lumen of the tubules while water follows by osmosis. Most of the solutes are reabsorbed, leaving a concentrated solution of uric acid secreted as a paste along with the other excretions of the digestive system.
  - There is no separate gland for digestive and excretory secretion.



Source = Campbell Biology

5 Anatomy of the Kidney

There are two kidneys in the human body, each of them are located below the diaphragm and liver and is about the size of a fist. The two sections of the kidney are the outer cortex and the inner medulla. The medulla is composed of multiple renal pyramids inter-spaced by renal columns.

- The filtered urine drains into a minor calyx which then drains into a major calyx which drains into the renal pelvis which drains into the ureter which fills the bladder. The process of micturition (urine being expuled from the bladder will be explained later).
- The ureter undergoes peristaltic contractions to transport urine for excretion.

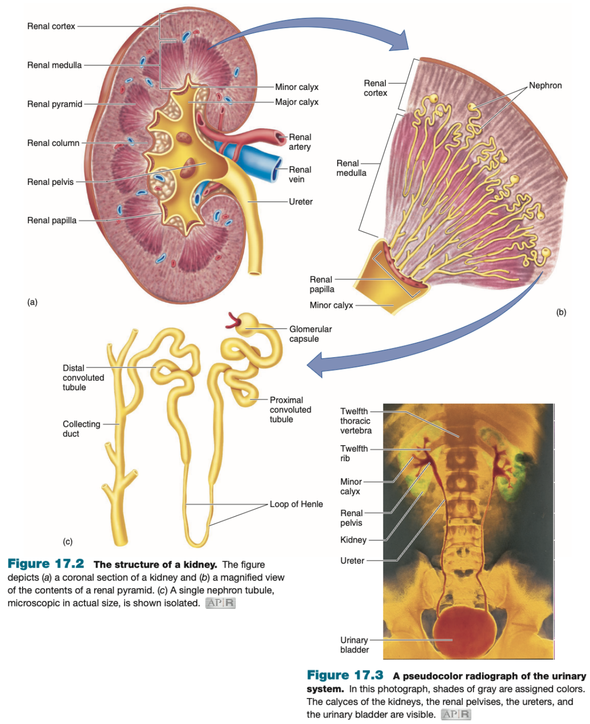


Figure 17.2 **The structure of a kidney.** The figure depicts (a) a coronal section of a kidney and (b) a magnified view of the contents of a renal pyramid. (c) A single nephron tubule, microscopic in actual size, is shown isolated.

Figure 17.3 **A pseudocolor radiograph of the urinary system.** In this photograph, shades of gray are assigned colors. The calyces of the kidneys, the renal pelvises, the ureters, and the urinary bladder are visible.

Source: Fox Human Physiology

5.0.1 The Nephron

- Note that reabsorption of solutes ends up on the blood vessels that surround the tubules of the kidney and are carried back into circulation.

- The nephron is the functional unit of the kidney responsible for filtering blood, reabsorbing essential substances, and excreting waste to regulate body fluid balance and eliminate toxins; it is composed of 5 different sections that will be explained independently.

- **The glomerulus** is surrounded by a capsule known as the **Bowman's capsule**, together the two are known as the **renal corpuscle**.
  - The capsule contains two layers of epithelial tissues, and the space in the middle is continuous with the lumen of the tubule.

- Filtrate from the glomerulus enters the **proximal tubule** in which a layer of ciliated cuboidal epithelial cells function in reabsorption of salt, water, etc.

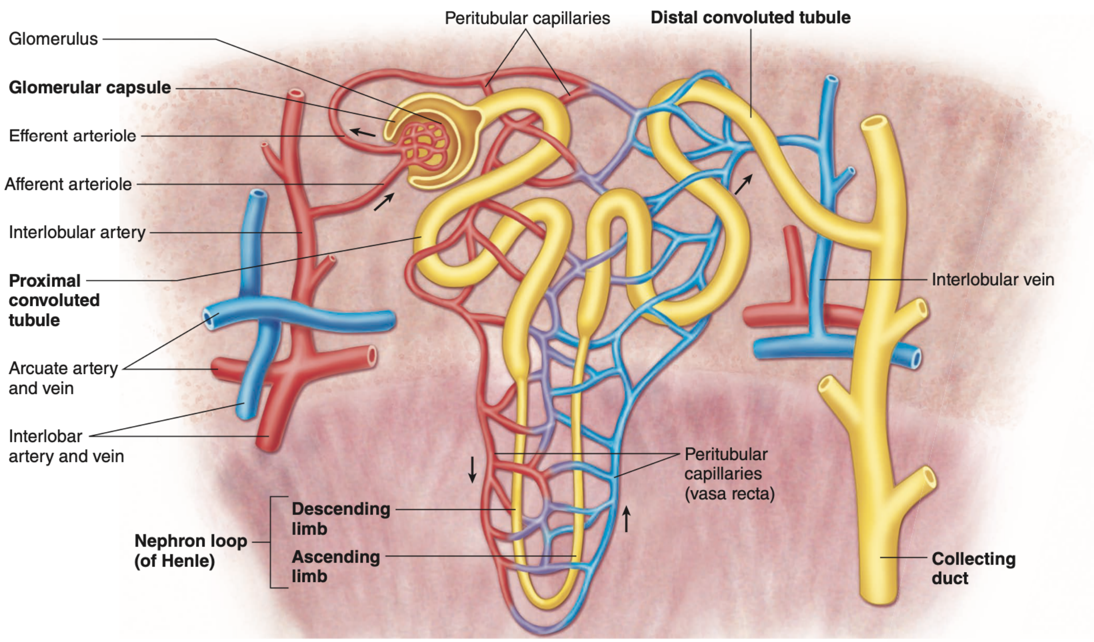
- The next three tubules are the **descending loop of Henle, ascending loop of Henle,** and the **distal convoluted tubule** and as with the rest will be discussed in conjunction of their function.

- **Juxtamedullary Nephrons** originate in the inner third of the cortex and have longer loops of Henles compared to **cortical nephrons** which begin in the outer two thirds of the cortex.

- Fluid from multiple nephrons travel into the collecting ducts which eventually drain into the minor calyx and end up excreted as urine.

5.0.2 Blood Flow

- Blood travels into the kidney via the **renal artery** which divides into the **arcuate artery** at the intersection of the medulla and cortex. The arcuate artery then divides into the **interlobar artery** and **interlobular artery** in the cortex. The **interlobular artery** radiates throughout the cortex to deliver blood to **glomeruli**, a capillary network that produces filtrate. The remaining blood from the **glomeruli** enters the **efferent arteriole** and travels into the **peritubular capillary** system which picks up reabsorbed solutes from the kidney and is involved in secretion of certain substances into the kidney (the peritubular capillary system includes the vasa recta). The peritubular capillary passes blood to the **interlobular veins** which pass blood to the **arcuate vein** to the **interlobar vein**. Finally, all the interlobar veins come together to form the **renal vein** which empties into the **inferior venae cavae**.



Source: Fox Human Physiology

6 Filtration

- The glomerulus is **fenestrated** (contains large pores) and is therefore very permeable to water and solutes, however it prevents the movement of blood cells.

- The basement membrane of the epithelial cells of the glomerulus contain large amounts of collagen and peptidoglycan which blocks movement of proteins and slows movement of fluid.

- **Podocytes** form the third filtration barrier. These are epithelial cells that are composed of a floating cell body, primary processes, and foot processes extending from the primary processes. The foot processes surround the basement membrane and the slits between each foot process provides a passage for solutes but blocks the passage of large negatively charged proteins.

  - **Proteinuria**, protein in the urine, is a disorder that occurs when the **slit diaphragm** (the membrane covering slits between each podocytes) are broken, resulting in faulty filtration.

- Filtration is a result of the hydrostatic pressure of blood and is opposed by hydrostatic pressure in the capsule and the osmotic force of the blood. Together, however, these forces do not match the hydrostatic pressure of blood and thus net filtration occurs.

  - **Glomerular Filtration Rate (GFR)** is the volume of filtrate produced by the kidney per unit of time.

6.1 Regulation of GFR

- Dilation of the afferent arteriole and constriction of the efferent arteriole result in an increase in GFR. Constriction of the afferent arteriole and dilation of the efferent arteriole result in a reduction of GFR.

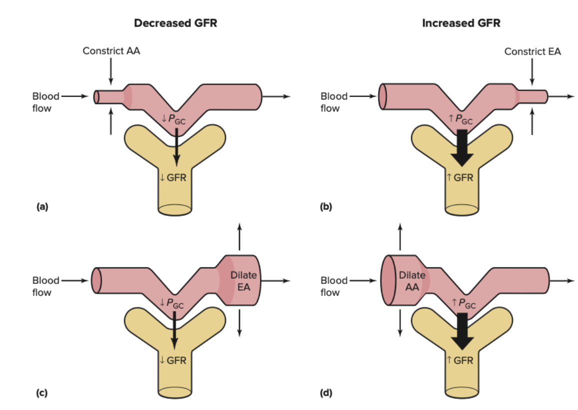
  - Increase in sympathetic activity (as in exercise or loss of blood pressure) results in constriction of afferent arteriole that preserves blood volume by lowering GFR and thus fluid excretion.

- The kidney can maintain a constant GFR during fluctuating arterial pressures and this is called **autoregulation**.

  - When arterial pressure rises or falls, smooth muscles of the afferent arteriole detect and respond to this fluctuation by constricting or dilating to regulate GFR.

  - **Tubuloglomerular feedback** occurs when the **macula densa**, a group of cells found in the ascending limb of Henle, responds to increased sodium and water delivery and secretes ATP that constricts the afferent arteriole.

    * Prevents overloading of the kidney and thus protects the tubules of the kidney.



Source: Vanders Human Physiology

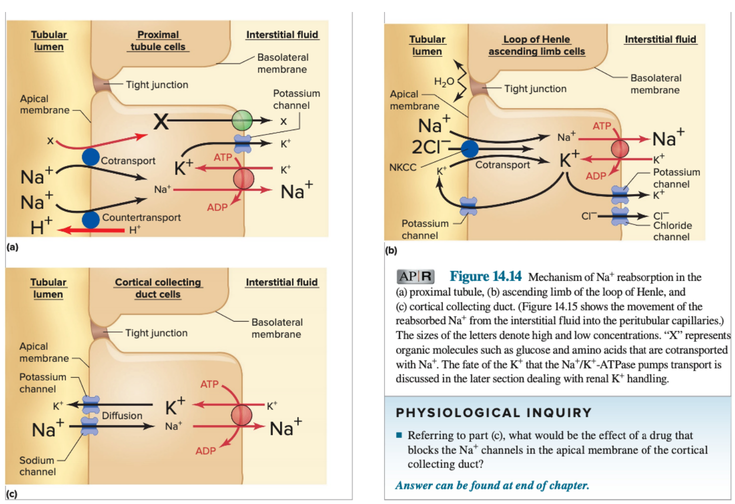
7 Reabsorption of Salt and Water

- Only about 1% of filtrate is secreted as urine, and the minimum amount of urine produced, as would occur during dehydration, is around 400 ml which is known as **obligatory water loss**, the smallest amount of water required to excrete metabolic wastes.
- **Reabsorption** is mainly done in the proximal tubule (85%) and descending loop of Henle under no hormonal regulation.
- Because the renal corpuscle freely filters all solutes, the filtrate is isotonic to the plasma (excluding proteins).
  - However, the epithelial cells lining the proximal tubule have a low sodium concentration and thus sodium passively diffuses into the proximal tubule cells.
  - This low concentration of sodium within the epithelial cells is formed by sodium and potassium antiporter pumps in the basal and lateral sides of the epithelial cells but not the apical side.
  - The low sodium levels within the tubule brought upon by reabsorption favors the passive diffusion of chloride via an electrical gradient (chloride is negative and will thus follow a positive charge).
    - At first chloride diffuses across the proximal tubule cells and later across the permeable tight junctions directly into the blood vessels.
  - This movement of NaCl across the membrane favors the movement of water out of the tubule.
- Although solutes are reabsorbed in the proximal tubule, the osmolarity of the tubule remains isotonic as a cooresponding amount of water is also reabsorbed with a cooresponding amount of solutes. Thus, the osmolarity of the tubule remains the same as the filtrate that entered.

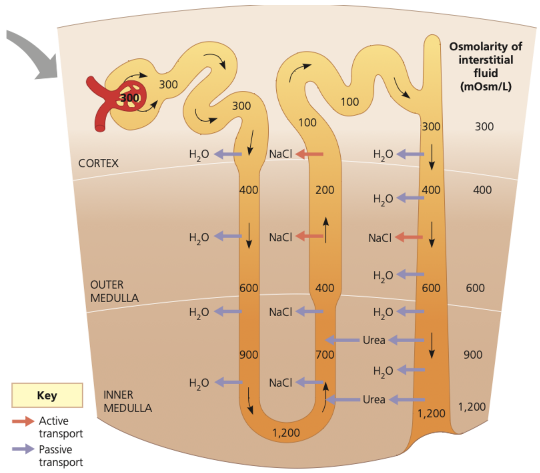
7.1 Countercurrent Multiplier System and Concentration

- The thick ascending limb of Henle contains transporters that transport sodium, potassium and two chlorides via a transporter known as the NKCC.
  - The basal and lateral sides of the epithelium contain potassium and sodium antiporters and thus results in the movement of NaCl out of the cell (potassium diffuses back into the lumen).
  - However, the thick ascending limb of Henle is impermeable to water and thus the fluid becomes hypoosmotic.
  - This movement of sodium out of the ascending limb of Henle creates a hyperosmotic environment in the medulla of the kidney.
- The descending limb of Henle is impermeable to salt, however, it is permeable to water and thus at the bottom of the loop the filtrate becomes concentrated and hyperosmotic.

- This system is known as a countercurrent multiplier system, more water reabsorption in the descending limb of Henle allows for higher salt reabsorption in the ascending limb and thus a higher osmolarity in the medulla of the kidney that then allows for more water reabsorption in the descending limb and the cycle continues.
  - This countercurrent multiplier system allows for a hypertonicity of 1200 mOsm in the renal medulla (compared to 30 mOsm in the renal cortex), which will be the driving force of reabsorption in the collecting tubule.
- This degree of osmolarity must be maintained by the vessels surrounding the loops of Henle known as the **vasa recta**. These capillaries use **countercurrent exchange** (note this is not a multiplier system). The descending vasa recta loses water and gains salts, however the ascending vasa recta gains water and loses salts, as at each point of its system, the ascending vasa recta has a higher osmolarity than the surrounding environment. This process maintains the osmolarity of the renal medulla.
  - During dehydration, the blood flow in the ascending vasa recta slows, allowing for more salt loss and water gain that serves to produce more concentrated urine (a self adjusting system, dehydration cooresponds to less blood volume and this system results in less excretion to prevent a further decrease in blood volume).
- Urea also diffuses out from the collecting tubule and into the loop of henle, forming a cycle that further contributes to renal medulla osmolarity (see image below).



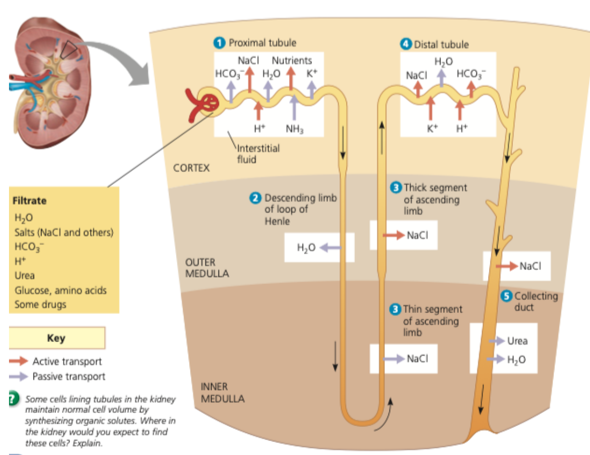
Summary of transport proteins. Source: Vanders Human Physiology



Source: Campbell Biology

7.2 Antidiuretic Hormone (ADH) and the Collecting Duct

- Fluid that reaches the collecting duct is hypoosmotic, due to the active transport of salt from the ascending loop of Henle without cooresponding water reabsorption. However, the surrounding interstitial fluid is hyperosmotic. This higher interstitial fluid osmolarity drives the movement of water out of the collecting duct via osmosis. The volume of water that can move by osmosis is determined by the quantity of **aquaporins**, channels dedicated to water transport that greatly improve the efficiency of osmosis across a membrane.
  - **ADH** is released by the posterior pituitary in response a higher blood osmolarity; via a cAMP second messenger system, ADH results in increased aquaporin concentration within the plasma membrane of the collecting tubule cells.
- **Diabetes Insipidus** is a condition with excessive urine production
  - **Central Diabetes Insipidus** is due to lack of ADH secretion from the posterior pituitary.
  - **Nephrogenic Diabetes Insipidus** is due to either A) inability of the kidney's to respond to ADH or B) a mutation within the aquaporin channel that renders them nonfunctional.



Summary of kidney components Source: Campbell Biology

Example 2 (USABO Semifinal Exam 2012) What are some effects of antidiuretic hormone (ADH)?
I. The distal tubules and collecting ducts of kidney nephrons are targeted.
II. The osmolarity of the blood increases following ADH activity.
III. Urine volume is increased.
IV. The number of aquaporins in the collecting ducts is increased.

(A) I only
(B) III only
(C) I and IV only
(D) II and III only
(E) II, III, and IV only

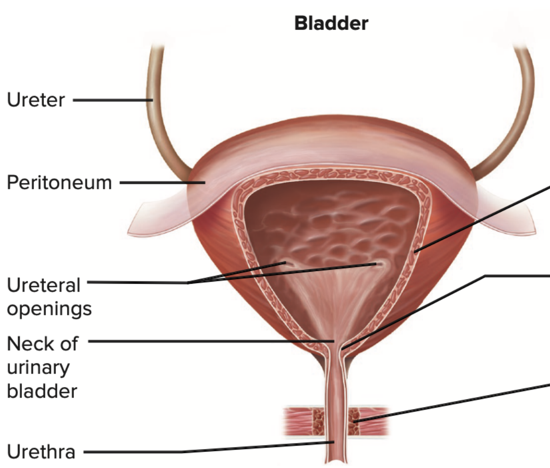
Solution: ADH or antidiuretic hormone increases the aquaporin concetration in the collecting ducts of the kidney, however, late parts of the dital tubule are also targeted making I true. The osmolarity of the blood is proportional to solute concentration, because ADH is secreted in response to higher osmolarity and is involved with reabsorption of water, it would decrease the osmolarity of blood making II incorrect. III is incorrect and is in the name of the hormone (anti diuretic or anti urination), we also know that ADH increases water reabsorption and thus lowers urine volume. IV is correct as aquaporin concentration is directly correlated with ADH function. The answer is thus I and IV or **C**

8 Micturition

Micturition or urination is the process by which individuals release the urine made by their kidney's (note this section is heavy on nervous and muscle, see said handout if confused).

- The detrusor muscle is the muscle which controls the bladder and is stimulated to contract by acetylcholine released by parasympathetic nerves (see nervous handout) binding to muscarinic acetylcholine receptors.
- **Guarding Reflex**
  - Contraction of the bladder is inhibited by a parasympathetic nerve when the external sphincter is contracted
  - This prevents involuntary contraction of the bladder and thus involuntary release of urine.
- **Voiding Reflex**
  - As liquid fills the bladder the detrusor muscle stretches. Sensory information travels to the pons in the brain which activates parasympathetic nerves to contract the detrusor muscle allowing for urination
    * Note that during this time the individual will feel urgency to urinate but will still have control over their external sphincter via somatic motor neurons and thus will not urinate (unless they want to).

- The switch between the guarding and voiding reflexes occur when upper brain regions such as the prefrontal cortex and insula innervates the pons to switch from filling of bladder (guarding reflex) to secretion (voiding reflex).
- **Pudenal Nerve**
  - Innervates the external sphincter of bladder



Muscle	Innervation		
	Type	During filling	During micturition
Detrusor (smooth muscle)	Parasympathetic (causes contraction)	Inhibited	Stimulated
Internal urethral sphincter (smooth muscle)	Sympathetic (causes contraction)	Stimulated	Inhibited
External urethral sphincter (skeletal muscle)	Somatic motor (causes contraction)	Stimulated	Inhibited

Source: Vander's Human Physiology

9 Clearance

- If a substance is not reabsorbed nor secreted it would equal the GFR. One such molecule is known as inulin which is produced in plants and must be injected in the body.
  - Creatinine is produced by muscles from creatine and secreted into the blood where it is filtered and secreted but not reabsorbed by the kidney. Because of the slight amounts of secretion into the kidney the estimated GFR (**eGFR**) can be determined which would result in a slight overestimation due to minimal secretion by the kidney.
- The clearance of a substance is (UV)/P where V = urine volume per minute; U = urine concentration of substance; and P = plasma concentration of substance.
  - The clearance of inulin (refrenced earlier) would be equal to GFR.

9.1 Reabsorption of Glucose

- Glucose and amino acids are present in the initial filtrate but are completely reabsorbed via sodium cotransport.
  - However, these transporters can become saturated and can handle a maximum level of glucose or amino acids before their transport velocity plateau. This is known as the transport maximum and is usually around 375 mg/min for glucose.

        * If levels of glucose reach above the transport maximum glycosuria can develop. Glycosuria is the condition of glucose in the urine. Such a high level of glucose in the blood can be reached through diseases such as diabetes mellitus, for instance, and would also be accompanied by large quantities of urine (glucose would create a hyperosmotic environment in the tubule thus lowering water reabsorption).

10 Renal Control of Electrolyte and Acid Base Balance

10.1 Aldosterone

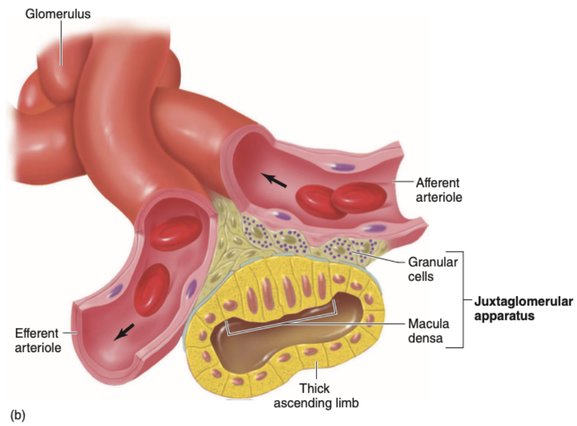
- All but ten percent of sodium and potassium is reabsorbed in the proximal tubule under no regulation via hormonal systems. However, the remaining reabsorption of sodium and secretion of potassium is under regulation of the hormonal system, specifically aldosterone.
- Aldosterone effects the late cortical collecting tubule, but mainly the collecting duct where it stimulates the activation of sodium potassium pumps to create a larger driving force for sodium reabsorption (chloride follows by osmosis).
    - Greater secretion of sodium creates a route for potassium into the tubule (secretion) by following the favorable potential difference
        * Furthermore, increased sodium and water stimulates renin secretion which results in greater amounts of aldosterone which again contributes to more potassium secretion and sodium reabsorption.
- **Hypokalemia** can be caused by the use of certain diuretics which increase sodium sodium reabsorption and can cause hypokalemia by causing potassium secretion (as explained above potassium and sodium have an inverse relationship).

10.2 Juxtaglomerular Apparatus

- The juxtaglomerular apparatus is located where the ascending loop of Henle meets the afferent artery of the kidney. Here, the **granular cells** of the artery interact with the **macula densa** of the loop to form the juxtaglomerular apparatus. The granular cells of the arteriole secrete renin into the bloodstream which converts angiotensinogen (secreted by the kidney) into angiotensin I which is converted by endothelial enzymes in the lungs to angiotensin II. Angiotensin II vasoconstricts blood smooth muscle to raise blood pressure and directly stimulates the release of aldosterone from the adrenal cortex.
    - These effects coorespond to increase in blood volume and pressure.
- Fall in blood pressure stimulates the granular cells which act as baroreceptors to secrete renin; furthermore, when the baroreceptor reflex (occurs when the cardiovascular baroreceptors detect low blood pressure) results in greater sympathetic output, receptors on the granular cells respond to this and secrete more renin.
- **Macula Densa**

  - Increased sodium concentrations stimulates the macula densa to release paracrine factors which reduces renin secretion from the granular cells, resulting in restoration of blood volume homeostasis.

- **ANP**
  - Atrial Natriuretic Peptide is a protein released by the right atrium of the heart in response to stretch during periods of high blood pressure. ANP acts as a diuretic by promoting secretion of sodium and water.
    * BNP (B-type natriuretic peptide) is also released by the heart in repsonse to high blood pressure. High levels of BNP are a marker for congestive heart failure.



10.3 Acid-Base Balance

- **Acidification of Urine**
  - Carbonic acid (H_2CO_3) is formed in the proximal tubule cells from CO_2 and H20 via an enzyme called carbonic anyhydrase. Carbonic acid dissociates into bicarbonate (HCO_3^-) and an H^+ ion. The HCO_3^- is secreted into the plasma while the H^+ travels via sodium antiport channels into the lumen of the proximal tubule where it combines with bicarbonate to make carbonic acid in the lumen.
    * Carbonic acid in the lumen is changed into CO_2 and H20 via the same enzyme catalyzing the reverse reaction in the proximal tubule, carbonic anhydrase.
      · This CO_2 and H_2O diffuses into the proximal tubule cells allowing for reaction explained at the beginning to be continued, thus in total 1 HCO_3^- is reabsorbed and can be considered a different HCO_3^- than was found in the lumen.
      · Thus, when the blood is slightly acidic there is more H^+ to react with HCO_3^- and allow for reabsorption and thus increases HCO_3^- in blood. This is a compensatory mechanism to regulate acidosis.
  - The distal convoluted tubule also actively transports H^+ into the lumen to make it slightly acidic.

  - The proximal tubule cells also metabolize glutamine (an amino acid) into two bicarbonate molecules which is reabsorbed and an ammonia (NH4) which is secreted into the filtrate.
    * The proximal tubule cells are thus also a source of new bicarbonate and provide an invaluable role in regulating acid base disorders.

- **Buffering of Urine**
  - Phosphates previously presented in the tubule and ammonia secreted by the proximal tubule buffer the acidity generated by H+ secretion. This allows the kidney to secrete more valuable acids involved in reabsorbtion of HCO3- without damaging the kidney.

Example 3 (USABO Semifinal Exam 2016) Which of the following statements about kidney function is FALSE?

(A) The kidneys help to regulate overall extracellular fluid volume.
(B) The kidneys help to regulate the overall osmotic concentration of the ECF, but not the concentration of specific solutes.
(C) The kidneys help to eliminate waste products from the ECF.
(D) The kidneys help to regulate the pH of the ECF.
(E)Urine is formed in the kidneys through the process of ultrafiltration.

Solution: We know A is correct as urine is formed from the blood and therefore varying the amount of urine excretion allows for variation in blood volume. C is correct as the kidneys are a route for excretion of drugs or other unwanted substances in the body. D is correct as the reabsorption of bicarbonate allows for an increase in blood pH and thus ECF (extracellular fluid pH). Ultrafiltration was the process talked about earlier in podocytes, therefore E is correct. That leaves us with B which we know is incorrect as the kidney can selectively increase the reabsorption of certain solutes like salt or bicarbonate. Most of this question can be done with intuition knowing that the kidney is the major site of fluid excretion from the body. The answer is **B**

11 Diuretics and Dialysis

Diuretics are enzymes involved in lowering blood pressure and buildup of fluid in the body (edema). They do this by increasing urination and excretion by the kidneys.

- **Loop Diuretics**
  - Inhibit the NKCC channels talked about earlier. These class of diuretics decrease sodium reabsorption in the ascending limb of Henle and therefore lower water reabsorption in the collecting tubule and distal tubule to increase excretion.

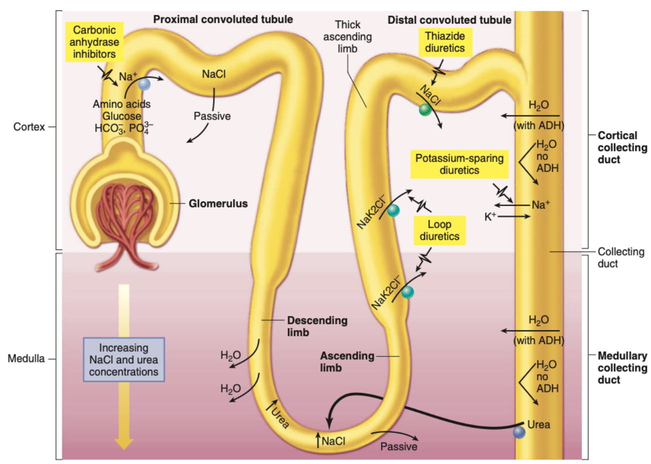
- **Thiazimides** decrease sodium absorption in the beginning of the distal tubules

- **Carbonic Anhydrase Inhibitors**

  - Inhibit the action of carbonic anhydrase, thus prevent the minimal water absorption involved with bicarbonate absorption.

- **Osomotic Diuretics**
  - Sugars like mannose increase the osmotic pressure of the filtrate, lowering reabsorption of water and increasing urine volume.

- **Potassium Sparing Diuretics**
  - The diuretics listed above increase sodium flow to the cortical collecting ducts.
    * This increased sodium flow to the cortical collecting duct results increased sodium reabsorption in the tubule (there is more sodium that **can** be reabsorbed.
    * This results in higher potassium secretion due to sodium reabsorption and thus hypokalcemia.
  - Aldosterone antagonists are an example of such potassium sparing diuretics. Along with inhibiting reuptake of water aldosterone antagonists also inhibit the reuptake of sodium (thus lowering secretion of potassium).



12 Conclusion

In conclusion, the osmoregulatory system is a fundamental and intricate aspect of the body's physiology, playing a crucial role in maintaining the balance of water and solute concentrations within our cells and tissues. This complex system involves a variety of organs, hormones, and intricate feedback mechanisms working together to ensure our body functions optimally despite fluctuations in our external environment. I hope this packet serves you well on your USABO journey. Thanks for reading - Zelmay Jan