

- I. Function of the urinary system
 - a. The organs of the urinary system (**kidneys, ureters, urinary bladder** and **urethra**) all play a role in **urine** formation, storage, or expulsion.
 - b. However the function of the urinary system cannot be simply defined as “urine production” or “waste removal.”
 - c. The primary functions of the urinary system include:
 - i. Regulating blood volume.
 - ii. Regulating the chemical make-up of blood.
 - d. Secondary functions include:
 - i. Metabolism of **vitamin D**
 - ii. Regulation of acid/base balance.
 - iii. Production of **renin**.
 - iv. Production of **EPO**.

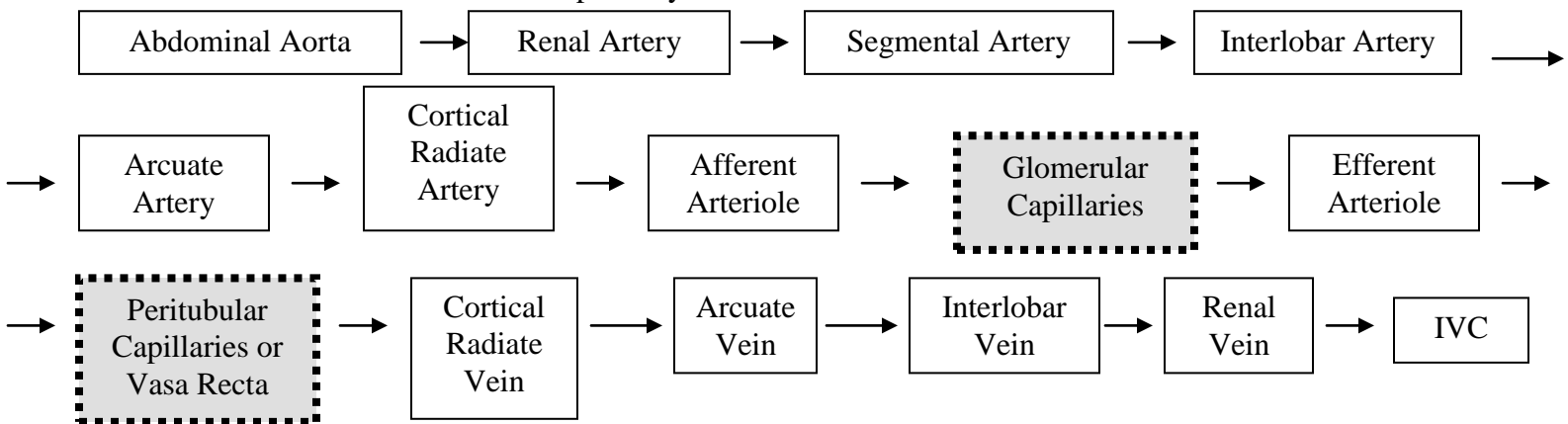
- II. Basic pathway of urine
 - i. Urine is formed in the renal cortex
 - ii. Travels thru collecting ducts in the renal medulla
 - iii. Continuously drips out of the renal papillae into the minor calyces
 - iv. Flows into major calyces
 - v. Flows into the renal pelvis
 - vi. Flows into the ureter
 - vii. Flows into and is stored in the urinary bladder
 - viii. Exits the body via the urethra.

b. The walls of the calyces, pelvises, ureters, bladder, and urethra all contain smooth muscle to propel urine.

III. Basic pathway of renal blood flow

a. Since the kidney’s main function is regulating the volume and composition of the blood, it requires an extensive blood supply ($\approx 25\%$ of cardiac output).

b. This is the basic pathway of renal blood flow:



- c. The **glomerular capillaries** are the sites of **filtration**
- d. The **peritubular capillaries** are the sites of **reabsorption** and **secretion**.

IV. The **Nephron**

- a. The functional unit of the kidney is a set of tubules known as the **nephron**.
- b. Each kidney contains 1 million nephrons.

- c. Each nephron begins with a ball of capillaries known as a **glomerulus**.
 - i. Blood filtration occurs here. The filtered fluid is known as **filtrate**.
- d. The filtrate travels through the **renal tubules** of the nephrons and is modified and turned into urine.
- e. The renal tubules run alongside the peritubular capillaries, so exchange may take place between the two.
- f. Any substance that was filtered but should not be excreted in urine will be reabsorbed – transported from the filtrate within the renal tubules to the blood within the peritubular capillaries.
- g. Any substance that was not filtered but should be excreted in urine will be secreted – transported from the blood within the peritubular capillaries to the filtrate within the renal tubules.
- h. Whatever remains after filtration, reabsorption and secretion are complete is urine.
- i. By regulating how much water is reabsorbed in the nephrons, we can regulate blood volume.
- j. By regulating whether or not, and to what degree, certain chemicals are reabsorbed or secreted allows us to regulate the chemical constituency of blood.
- k. Each nephron delivers its urine into a **collecting duct**. Each kidney contains 1000's of collecting ducts.
- l. Each nephron consists of a **glomerulus** – the ball of capillaries where filtration takes place – associated with a renal tubule.
- m. The renal tubule begins with the **glomerular capsule**, which is a double-layered structure that almost completely surrounds the glomerulus.
- n. The glomerular endothelium is fenestrated. This lets lots of solute-rich, protein-free fluid pass from the lumen of the glomerular capillaries to the lumen of the glomerular capsule.
- o. The parietal layer of the glomerular capsule is composed of simple squamous epithelium. It plays no role in the formation of filtrate.
- p. The visceral layer of the glomerular capsule is composed of branching epithelial cells called **podocytes**. The podocytes wrap around the glomerular capillaries and help filter the blood.
- q. Once in the capsular lumen, the filtrate will pass through a series of tubules. First it enters the **proximal convoluted tubule**. The PCT is composed of simple cuboidal epithelial cells.
 - i. They have multiple mitochondria and luminal microvilli. These structures reflect the large role of the PCT in reabsorption & secretion.
- r. Next the filtrate flows into the **loop of Henle**. The loop of Henle has descending and ascending regions. The descending limb is simple squamous epithelium and is freely permeable to water. The ascending limb is simple cuboidal and is impermeable to water, but actively transports salts from the filtrate into the ISF. These permeability differences will play a role in the loop's primary function – concentrating urine and maximizing water reabsorption.

- s. Next the filtrate passes into the **distal convoluted tubule**. The cells of the DCT are similar to those of the PCT but they have fewer mitochondria and lack microvilli.
 - t. From the distal convoluted tubule, the filtrate will enter the collecting duct. At this point, the filtrate has been modified and is now urine. Several distal convoluted tubules empty into a single collecting duct.
 - u. Collecting ducts run thru the medullary pyramids and fuse to form larger and larger ducts that eventually terminate at the renal papillae and continuously drip urine into the minor calyces.
 - v. The DCT and collecting ducts are where hormones adjust what is reabsorbed and secreted.
- V. Filtration
- a. The glomerular capillaries receive blood from an afferent arteriole and empty into an efferent arteriole.
 - i. They are the sites of filtration.
 - ii. The high glomerular BP facilitates filtration.
 - 1. High glomerular pressure is created b/c the diameter of the afferent arteriole >>> diameter of the efferent arteriole.
 - b. The peritubular capillaries receive blood from the efferent arteriole and empty into the cortical radiate vein.
 - i. They're the sites of reabsorption and secretion.
 - 1. Reabsorption is assisted by the capillaries' low blood pressure and high osmotic pressure. 99% of filtered fluid is reabsorbed at the peritubular capillaries.
 - c. The **filtration membrane** is the structure that separates the lumen of the glomerular capillaries from the lumen of the glomerular capsule.
 - d. It consists of:
 - i. Glomerular endothelium
 - ii. The visceral layer of the glomerular capsule (podocytes)
 - iii. Loose CT btwn the two.
 - e. Just about all solutes are filtered except for formed elements and plasma proteins larger than albumin.
 - f. Every time blood enters the glomerulus, about 20% of the contained fluid, with solutes, is filtered, enters the nephron and becomes filtrate.
 - i. (More than 19% of this fluid will be reabsorbed.)
 - ii. The reason for the large volume of filtrate is the high blood pressure within the glomerular capillaries.
 - iii. The actual pressure forcing fluid into the nephron is known as **net filtration pressure** and consists of glomerular BP minus glomerular osmotic pressure minus capsular fluid pressure.
- VI. Regulating the rate of filtration, i.e., the **glomerular filtration rate (GFR)**
- a. 2 intrinsic mechanisms maintain GFR.
 - b. **Myogenic regulation** helps maintain a constant filtration rate and pressure via adjustment of the diameters of the afferent and efferent arterioles.

- i. If systemic BP drops, the afferent arteriole dilates and the efferent constricts. This \uparrow the volume of blood in the glomerulus and this brings glomerular BP back to normal.
 - ii. If systemic BP rises, the afferent arteriole constricts and the efferent arteriole dilates. This \downarrow the volume within the glomerulus and thus brings glomerular BP back to normal.
 - c. The **tubuloglomerular feedback mechanism** is a bit more involved.
 - i. If GFR is too high, filtrate flows quickly thru the nephron and there is little time for sodium reabsorption.
 - ii. Thus, high $[\text{Na}^+]$ in the DCT indicates a high GFR.
 - iii. The **macula densa cells** of the DCT sense the high $[\text{Na}^+]$ and increase the release of a vasoconstrictor that causes constriction of the afferent arteriole.
 - iv. This reduces GBP and thus GFR.
 - v. If GFR is too slow, filtrate flows slowly and there is a lot of time for sodium reabsorption.
 - vi. Thus, low $[\text{Na}^+]$ in the DCT indicates a low GFR.
 - vii. The macula densa cells will sense the low $[\text{Na}^+]$ and release less of the vasoconstrictor.
 - viii. This causes the afferent arteriole to dilate, which will increase GBP and GFR.
 - d. The **sympathetic neural mechanism** refers to the effect of the fight-or-flight response on GFR.
 - i. When sympathetic nervous activity increases, norepinephrine (from nerve fibers of the renal plexus) and epinephrine (from the adrenal medulla) both act to constrict the afferent arteriole. This reduces GBP and GFR. Reduction of GFR can help maintain BP.
- VII. A related process is the **renin-angiotensin mechanism**.
 - a. **Granular cells** of the afferent arteriole release large amounts of the enzyme **renin** when:
 - i. BP drops (as measured by the stretch of the afferent arteriole)
 - ii. Stimulated by sympathetic nerve fibers (via NE).
 - b. Renin cleaves the plasma protein **angiotensinogen** (made by the liver) into a compound called **angiotensin I**.
 - c. Angiotensin I is converted to **angiotensin II** by the **Angiotensin-Converting-Enzyme (ACE)** (primarily released by pulmonary capillary endothelial cells).
 - d. Ag II is a vasoconstrictor so it increases resistance and thus increases BP.
 - e. AgII will stimulate the release of the hormone **aldosterone** from the adrenal cortex.
 - i. Aldosterone will increase the renal retention of water. This will help maintain blood volume (and thus BP).
 - f. AgII also prompts the pituitary to release **antidiuretic hormone (ADH)**, which will also increase the renal retention of water.
 - g. AgII also promotes thirst which will maintain blood volume (and thus BP).
- VIII. Reabsorption

- a. Assuming that everything is normal, filtrate will be produced at the glomerulus and enter the renal tubules. This filtrate contains both “good” and “bad” substances and the “good” ones must be reabsorbed.
- b. The bulk of reabsorption occurs in the proximal convoluted tubule.
- c. The primary chemical that will drive most reabsorption is **sodium**.
 - i. Sodium is normally high in concentration in the lumen of the PCT and low in concentration inside the cells lining the PCT lumen.
 - ii. B/c of this concentration gradient, sodium will passively diffuse out of the PCT lumen and into the cytoplasm of the PCT cells.
 - iii. Sodium will then be actively pumped out the other side of the PCT cell and diffuse back into the blood of the peritubular capillaries.
 - iv. This movement of sodium has 3 important effects:
 1. It creates an **osmotic gradient** that results in water reabsorption. (**Obligatory water reabsorption**).
 2. It creates an **electrical gradient** that causes **anions** (negatively charged ions) to “follow along” and be reabsorbed.
 3. Diffusion of sodium into the PCT cells releases energy that is harnessed to pump nutrients (glucose, amino acids, etc.) into the PCT cells. This is an example of **secondary active transport**. The nutrients will then diffuse out of the other side of the PCT cells and enter the peritubular capillaries.

IX. **Transport Maximum**

- a. If substance X is filtered at the glomerulus, then as plasma [X] rises, filtrate [X] rises.
- b. Suppose 100% of substance X is normally reabsorbed in the PCT.
- c. If plasma levels of X rise way higher than normal, filtrate X will rise way above normal.
- d. If this occurs it can become physically impossible for all of X to become reabsorbed and X will start to appear in the urine.
- e. There are a finite number of proteins in the PCT that can reabsorb X. If they're **saturated**, all of the X cannot be reabsorbed.
- f. The maximal rate of reabsorption of a substance in the kidney tubules is known as the **transport maximum**.

X. **Tubular Secretion**

- a. Process by which undesirable substances, which were not filtered at the glomerulus, are moved from the peritubular capillaries into the PCT lumen.

XI. **Maintaining the concentration of body fluids**

- a. Concentration is measured in **osmolality** (moles/kg of sltn).
 - i. A concentrated solution will have a high osmolality and a dilute solution will have a low osmolality.
- b. If blood osmolality rises, the response will be for water reabsorption to increase and urine volume to decrease.
- c. If blood osmolality falls, the response will be for water reabsorption to decrease and urine volume to increase.
- d. Blood osmolality is measured by specialized neurons in the **hypothalamus** called **osmoreceptors**.

- e. The level of osmolality measured by the osmoreceptors of the hypothalamus will determine how much **antidiuretic hormone** is secreted by the **posterior pituitary gland**.
 - f. ADH increases the water reabsorption in the collecting duct and decreases urine volume.
 - i. When blood osmolality rises, ADH release increases.
 - ii. When blood osmolality falls, ADH release decreases.
 - g. ADH works by increasing the permeability of the CD to water.
 - i. But, not only must the CD be permeable to water, there must also be a concentration gradient btwn the lumen of the CD and the surrounding ISF.
 - 1. This gradient is established by the **loop of Henle**.
 - h. The water that exits the collecting duct is picked up by the **vasa recta** – a network of blood vessels that run along collecting ducts and loops of Henle in the renal medulla.
 - i. Water reabsorption dependent on ADH is **facultative water reabsorption**.
- XII. **Aldosterone**
- a. Produced by the **adrenal medulla**.
 - b. Acts to increase sodium reabsorption in the DCT and CD. This causes an increase in water reabsorption.
 - c. Also increases the secretion of potassium in the DCT.
 - d. The release of aldosterone is stimulated by:
 - i. Low plasma Na⁺ levels
 - ii. High plasma K⁺ levels
 - iii. Low blood volume and pressure.
- XIII. Diuretics
- a. Chemicals that enhance urine output.
 - b. An **osmotic diuretic** is a substance that is filtered but not reabsorbed. It will increase the osmolality of the filtrate and prevent water from flowing out.
 - c. **Alcohol** is a diuretic b/c it inhibits pituitary ADH release.
 - d. **Caffeine** is a diuretic b/c it inhibits renal sodium reabsorption.
- XIV. Urine
- a. Clear to pale yellow fluid (depending on its concentration).
 - b. Volume varies with fluid intake and with fluid output via other routes.
 - c. pH is usually 6, slightly acidic. Normal range is 4.5 to 8 and varies with diet.
 - d. 95% water.
 - e. Solutes (5%) include: **uric acid** (a metabolite of nucleic acids, **creatinine** (metabolite of creatine, a chemical used by skeletal muscle for energy storage), and **urea** (an end product of protein metabolism), ions such as Na⁺, K⁺, Ca²⁺, Mg⁺ and HCO₃⁻).
- XV. **Ureters**
- a. Slender tubes that convey urine from the kidneys to the bladder.
 - b. Gravity contributes to urine flow but the primary impetus is provided by peristalsis of ureteric smooth muscle.
- XVI. **Urinary Bladder**
- a. Collapsible, muscular sac that temporarily stores urine.

- b. Both ureters connect with the posterior bladder.
- c. The urethra opens inferiorly at the **internal urethral orifice**. In males, it immediately passes through the **prostate gland**.
- d. Mucosa lined by transitional epithelium and exhibiting **rugae**.
- e. Thick smooth muscle muscularis referred to as the **detrusor muscle**.
- f. A moderately full bladder will hold approximately 500mL of urine. The maximum capacity of the bladder is 800-1000mL.
- g. The bladder allows urine release to be discontinuous even though renal formation of urine is continuous.

XVII. Urethra

- a. Thin walled, muscular tube that conveys urine from the bladder to the body exterior.
- b. At the bladder-urethra junction, the detrusor muscle thickens to form the **internal urethral sphincter**. As smooth muscle, it is involuntary.
- c. The **external urethral sphincter** surrounds the urethra where it passes through the skeletal muscle layer, known as the **urogenital diaphragm**.
 - i. The urogenital diaphragm is a small portion of an expanse of skeletal muscle known as the **pelvic diaphragm**. The pelvic diaphragm forms the floor of the pelvic cavity.

XVIII. Micturition

- a. The process of urination – the act of emptying the bladder.
- b. As >200mL of urine accumulates in the bladder, the bladder wall stretches.
- c. Stretch receptors sense the stretch and signal the **micturition center** in the **pons**.
- d. They also initiate a reflex response in the spinal cord resulting in increased parasympathetic outflow to the bladder.
 - i. It causes opening of the internal urethral sphincter and contraction of the detrusor muscle.
- e. At this point, somatic activation of the external urethral sphincter can prevent urination.
- f. If the external urethral sphincter is voluntarily contracted, the reflex contractions of the bladder will subside.
- g. When volume and stretch become too great, signals from the pons inhibit any motor output to the external urethral sphincter and urination ensues.