

# **Title: Physiology of urinary system**

**Teacher: Dorota Nowak M.D., Ph.D.**

**Coll. Anatomicum, Święcicki Street no. 6, Dept. of Physiology**

## **I. Kidney Physiology**

### **A. Organization of the Urinary System**

The urinary system consists of two kidneys, two ureters, the urinary bladder, and the urethra.

### **B. Functions of the Kidneys**

1. The most important function of the kidneys is to rid the body of waste materials that are ingested or produced by metabolism and to control the volume and composition of the body fluids. All of the following processes contribute to this basic purpose.
  - a. The kidneys filter blood plasma, separate wastes, return useful materials to the blood, and eliminate the waste products and foreign chemicals.
  - b. They regulate blood volume and pressure.
  - c. They regulate the osmolarity of the body fluids.
  - d. They secrete renin, a hormone that activates mechanisms that control blood pressure and electrolyte balance.
  - e. They secrete erythropoietin, which controls RBCs production and the oxygen-carrying capacity of the blood.
  - f. They help to regulate acid-base balance of the body fluids.
  - g. They contribute to calcium homeostasis through their role in synthesizing calcitriol.
  - h. They detoxify free radicals and drugs.
  - i. They deaminate amino acids in times of starvation for use in energy (gluconeogenesis, the amino portion is excreted as ammonia).

### **C. Nitrogenous Wastes**

1. A waste is any substance of no use to the body or present in excess of the body's needs.

A metabolic waste is a waste produced by metabolic reactions within cells.

  - a. Metabolism produces a great quantity of wastes that are lethal to cells if allowed to accumulate.
  - b. Two of the most toxic metabolic wastes are carbon dioxide and nitrogenous wastes, most of which is urea (a product of protein metabolism).
  - c. Other nitrogenous wastes in the urine are uric acid (from nucleic acid), creatinine (from muscle creatine), end-products of hemoglobin breakdown (bilirubin) and metabolites of various hormones.
  - d. These waste products must be eliminated from the body as rapidly as they are produced.
2. Renal failure can lead to azotemia, the accumulation of nitrogenous wastes in the blood. This condition may progress further to uremia, a syndrome of diarrhea, vomiting, dyspnea, and cardiac arrhythmia. Convulsions, coma, and death follow within a few days. Renal failure requires hemodialysis or kidney transplant, if available.

### **D. Excretion**

1. Excretion is the process of separating wastes (no longer needed by the body) from the body fluids and eliminating them. It is carried out by the respiratory system, integumentary system, digestive system, and urinary system working together.

## **II. Functional structure of the kidney**

### **A. The Nephron**

1. The kidney contains about 1 million nephrons, the functional units of the kidney. The kidney cannot regenerate new nephrons.

### **B. Blood Supply**

- a. The renal fraction of the cardiac output is 20%. Each kidney is supplied by a renal artery entering the hilum that gives rise to a few interlobar arteries that penetrate the renal columns and travel between the pyramids to the boundary between the cortex and medulla.
- b. At this boundary, interlobar arteries branch to form arcuate arteries from which interlobular arteries arise.
- c. As an interlobular artery ascends through the cortex, a series of afferent arterioles arise from it, each supplying blood to a single nephron. It ends in a rounded cluster of capillaries, called a glomerulus, where urine production begins.
- d. The glomerulus is drained by an efferent arteriole that leads to the peritubular capillaries surrounding the renal tubule.
- e. Blood flows from the peritubular capillaries through the interlobular veins, arcuate veins, and interlobar veins to the renal veins, which drain blood from the kidney and return it to the vena cava.
- f. The renal medulla is supplied by the vasa recta, long straight vessels that arise from the efferent arterioles of the juxtamedullary nephrons.

#### **C. The Renal Corpuscle.**

- a. The renal corpuscle consists of a glomerulus enclosed in a two-layered glomerular (Bowman's) capsule. The visceral layer of the glomerular capsule has special cells called podocytes wrapped around the capillaries.

#### **D. The Renal Tubule**

- a. The renal tubule is a duct that leads away from the glomerular capsule and ends at the tip of a medullary pyramid. It consists of the proximal convoluted tubule /PCT/, nephron loop, distal convoluted tubule /DCT/, and collecting duct.
- b. The DCTs of several nephrons merge to form a collecting duct that passes down into the medulla. Urine in the collecting duct is passed to a papillary duct, then to a minor and major calyx, to the renal pelvis, and out the ureter.

#### **E. Cortical and Juxtamedullary Nephrons**

- a. Cortical nephrons lie just beneath the renal corpuscle and have short nephron loops.
- b. Juxtamedullary nephrons have very long nephron loops and lie close to the medulla.

### **III. Urine Formation I: Glomerular Filtration**

**A.** The kidney converts blood plasma to urine by four processes: glomerular filtration, tubular reabsorption, tubular secretion, and water conservation.

#### **B. The Filtration Membrane**

1. To get from the bloodstream to the capsular space, fluid passes through three barriers that make up the filtration membrane.
  - a. The fenestrated epithelium of the capillary allows these cells to be more permeable than endothelial cells elsewhere.
  - b. The basement membrane is a proteoglycan gel that excludes molecules larger than 8 nm. Some smaller molecules are also prevented from passing by a negative electrical charge on the proteoglycans.
  - c. The armlike podocytes of the glomerular capsule have little extensions called foot processes (pedicels) that, in turn, have negatively charged filtration slits, which are an additional obstacle to large anions.
2. Almost any molecule smaller than 3 nm can pass freely through the filtration membrane into the capsular space. This includes water, electrolytes, glucose, amino acids, nitrogenous wastes, and vitamins.
3. Kidney infections and trauma commonly damage the filtration membrane and allow albumin or blood cells to pass through.

#### **C. Filtration Pressure**

1. Glomerular filtration follows the same principles that govern filtration in other capillaries, but there are significant differences in the magnitude of the forces involved.
  - a. The blood pressure (BP) is higher here than elsewhere. This results from the fact that the afferent arteriole is substantially larger than the efferent arteriole.
  - b. The hydrostatic pressure in the capsular space results from the high rate of filtration occurring and the continual accumulation of fluid in the capsule.
  - c. The colloid osmotic pressure (COP) of the blood is the same here as elsewhere.
  - d. The glomerular filtrate is almost protein-free and has no significant COP.

#### **D. Glomerular Filtration Rate**

1. Glomerular filtration rate (GFR) is the amount of filtrate formed per minute by the two kidneys combined. For every 1 mmHg of net filtration pressure, the kidneys produce about 12.5 mL of filtrate per minute. For the average adult male, this amounts to a rate of 180 L/day. An average of 99% of the filtrate is reabsorbed, so that 1–2 L of urine is excreted per day.
2. Glomerular filtration occurs because the high blood pressure of the glomerular capillaries overrides reabsorption.

#### **E. Regulation of Glomerular Filtration**

1. GFR must be precisely controlled.
  - a. If GFR is too high, urine output rises and creates a threat of dehydration and electrolyte depletion.
  - b. If GFR is too low, fluid flows sluggishly through the tubules, and they reabsorb wastes that should be eliminated in the urine.
  - c. The only way to adjust GFR from moment to moment is to change glomerular blood pressure.

#### **2. Renal Autoregulation**

- a. Renal autoregulation is the ability of the kidneys to maintain a relatively stable GFR in spite of changes in arterial blood pressure.
- b. The nephron has two ways to prevent drastic changes in GFR when blood pressure rises: It can constrict the afferent arteriole and reduce blood flow into the glomerulus, or it can dilate the efferent arteriole and allow the blood to flow out more easily. Conversely if blood pressure falls, the nephron can compensate by either dilating the afferent arteriole or constricting the efferent arteriole.
- c. The juxtaglomerular apparatus that allows the nephron to compensate for pressure differences is made up of these cells: (1) juxtaglomerular (JG) cells, enlarged smooth muscle cells of the afferent arteriole that can dilate or constrict and secrete renin in response to a drop in BP; (2) the macula densa, a patch of slender epithelial cells of the distal tubule that apparently monitor the salinity of the tubular fluid in the DCT; and (3) mesangial cells between the afferent and efferent arterioles, whose role is not yet understood.
- d. Two important points must be noted about renal autoregulation. First, it does not completely prevent changes in the GFR. Second, renal autoregulation cannot compensate for extreme blood pressure variations.

#### **3. Sympathetic Control**

- a. Sympathetic nerve fibers richly innervate the renal blood vessels.
- b. In strenuous exercise or acute conditions (circulatory shock), the sympathetic nervous system and adrenal epinephrine stimulate the afferent arterioles to constrict. This reduces GFR and urine production, while it redirects blood from the kidneys to the heart, brain, and skeletal muscles.

#### **4. The Renin-Angiotensin Mechanism**

- a. When BP drops, the JG cells secrete renin that acts to convert angiotensinogen into angiotensin I. As angiotensin I circulates through the lungs, angiotensin-converting enzyme (ACE) converts it to angiotensin II.
- b. Angiotensin II has multiple effects: It raises blood pressure by widespread vasoconstriction; constricts the efferent arterioles and prevents the glomerular blood pressure from dropping too low; increases tubular reabsorption of water; stimulates the secretion of aldosterone; and stimulates the sense of thirst.

#### **IV. Urine Formation II: Tubular Reabsorption and Secretion**

##### **A. The Proximal Convoluted Tubule**

1. The proximal convoluted tubule (PCT) reabsorbs about 65% of the glomerular filtrate and returns it to the blood. Its cells also contain abundant large mitochondria that provide ATP for active transport.
2. Tubular Reabsorption
  - a. While the glomerular capillaries are filtering the plasma, the peritubular capillaries are engaged in tubular reabsorption. Since fluid has been extracted from the blood at the glomerulus, the blood remaining in the capillary has an unusually high colloid osmotic pressure (COP) downstream from this point. Water is reabsorbed by osmosis and carries other solutes along by solvent drag.
  - b. The PCT reabsorbs a greater variety of chemicals than any other part of the nephron. Some pass through the cytoplasm of the cell via the transcellular route, while others slip between epithelial cells using a paracellular route.
  - c. Sodium is reabsorbed using both routes. There is a steep concentration gradient favoring the diffusion of sodium into the epithelial cell. Some enters the cell by simple diffusion through membrane channels, and some is reabsorbed by facilitated diffusion using transport proteins in the apical plasma membrane.
  - d. Some of the apical sodium carriers bind simultaneously to a sodium ion and a glucose molecule and transport them both into the cell. Such a carrier protein is called the sodium-glucose transport protein (SGLT). Normally all glucose in the tubular fluid is reabsorbed and there is none in the urine.
  - e. Amino acids are reabsorbed in the same way as glucose, using apical sodium carriers.
  - f. Sodium reabsorption makes the ICF and ECF hypertonic to the tubular fluid. Water follows sodium by diffusion through the paracellular route and by osmosis through the transcellular route. In the PCT, water is reabsorbed by a constant rate called obligatory water reabsorption.
  - g. Chloride is reabsorbed along both the paracellular and transcellular routes. Its reabsorption is favored by two factors: (1) Negative chloride ions tend to follow the positive sodium ions by electrostatic attraction, and (2) water reabsorption raises the  $\text{Cl}^-$  concentration in the tubular fluid, creating a gradient favorable to  $\text{Cl}^-$  reabsorption.
  - h. Potassium, magnesium, and variable amounts of calcium pass through the paracellular route by solvent drag.
  - i. The glomerulus filters a small amount of protein from the blood. The PCT reclaims it by pinocytosis, hydrolyzes it to amino acids, and releases these to the ECF by facilitated diffusion.
  - j. Nitrogenous wastes are dealt with in several ways. Urea diffuses through the tubule epithelium with water. The nephron as a whole reabsorbs 40–60% of the urea in the tubular fluid, but since it reabsorbs 99% of the water, urine has a substantially higher urea concentration than blood or glomerular filtrate. The PCT reabsorbs nearly all the uric acid entering it, but parts of the nephron secrete it back to the tubular fluid later. Creatinine is

not reabsorbed at all because there are no transport proteins for it. All creatinine filtered by the glomerulus is excreted in the urine.

### 3. The Transport Maximum

- a. There is a limit to the amount of solute the renal tubule can reabsorb because there are limited numbers of transport proteins in the plasma membranes. If all the transporters are occupied as solute molecules pass through, some solute remains in the tubular fluid and appears in the urine.

### 4. Tubular Secretion

- a. Tubular secretion is a process in which the renal tubule extracts chemicals from the capillary blood and secretes them into the tubular fluid. Tubular secretion serves the purposes of waste removal and maintenance of acid-base balance.

## B. The Nephron Loop

1. The primary purpose of the nephron loop is to enable the collecting duct to concentrate the urine. In addition, it reabsorbs about 25% of the  $\text{Na}^+$ ,  $\text{K}^+$ , and  $\text{Cl}^-$  and 20% of the water in the glomerular filtrate.
2. The thick segment (ascending limb) is impermeable to water; water cannot follow the reabsorbed electrolytes, and the tubular fluid becomes very dilute by the time it passes from the nephron loop into the distal convoluted tubule.

## C. The Distal Convoluted Tubule and Collecting Duct

1. Fluid arriving in the DCT still contains about 20% of the water and 10% of the salts of the glomerular filtrate. A distinguishing feature of these parts of the renal tubule is that they are subject to hormonal control.
2. Aldosterone
  - a. Aldosterone secretion is stimulated by a drop in blood sodium or rise in potassium concentration.
  - b. The general effect of aldosterone is to cause the DCT and cortical portion of the collecting duct to reabsorb more sodium and to secrete more potassium. Thus the urine volume is reduced. Salt and water reabsorption helps to maintain blood volume and pressure.
3. Atrial Natriuretic Factor
  - a. Atrial natriuretic factor (ANF) is secreted by the atrial myocardium of the heart in response to high blood pressure. It inhibits sodium and water reabsorption, increasing the output of both in the urine and thus reducing blood volume and pressure.
4. Antidiuretic Hormone (ADH)
  - a. ADH is secreted by the posterior lobe of the pituitary gland in response to dehydration and rising blood osmolarity. It makes the collecting duct more permeable to water.

## V. Urine Formation III: Water Conservation

### A. The Collecting Duct

1. The collecting duct (CD) begins in the cortex, where it receives tubular fluid from numerous nephrons. As it passes through the medulla, it reabsorbs water.
2. This ability to concentrate wastes and control water loss was crucial to the evolution of terrestrial animals.
3. Two facts enable the collecting duct to produce such hypertonic urine.
  - a. The osmolarity of the cellular fluid is four times as high near the renal papilla as it is in the cortex.
  - b. The medullary portion of the CD is permeable to water but not to  $\text{NaCl}$ . Therefore, as urine passes down the CD through the increasingly salty medulla, water leaves the tubule by osmosis.

### B. Control of Water Loss

1. How concentrated urine becomes depends on the body's state of hydration.

- a. In a state of full hydration, ADH is not secreted and the cortical part of the CD reabsorbs salt without reabsorbing water, leaving the water to be excreted.
- b. In a state of dehydration, ADH is secreted, the medullary portion of the CD reabsorbs water, and the urine is more concentrated.
- C. The Countercurrent Multiplier**
  - 1. The ability of the CD to concentrate urine depends on the salinity gradient of the renal medulla.
  - 2. The nephron loop acts as a countercurrent multiplier that continually returns salt to the deep medullary tissue.
  - 3. The descending limb is very permeable to water but not to NaCl. Therefore, more and more water leaves as the tubular fluid descends into the increasingly salty medulla, while NaCl remains behind in the tubule.
  - 4. The essence of the countercurrent mechanism is that the two limbs of the nephron loop are close enough to influence each other through the positive feedback relationship.
- D. The Countercurrent Exchange System**
  - 1. The vasa recta are arranged as a countercurrent exchange system that enables them to supply blood to the medulla without subtracting from its salinity gradient.

## **VI. Urine and Renal Function Tests**

### **A. Composition and Properties of Urine**

- 1. Urinalysis gives an indication of the physiological state of the tissues.
  - a. Appearance is noted. The yellow color of urine is due to the presence of urochrome. Fresh urine is clear; if cloudy, it could indicate the presence of bacteria, semen, blood, or menstrual fluid.
  - b. Other commonly observed features of urine are odor, specific gravity, osmolarity, pH, and chemical composition.

### **B. Urine Volume**

- 1. An average adult produces 1–2 L of urine per day.
  - a. Excessive urine output is called polyuria.
  - b. Scanty urine output is oliguria. An output of less than 400 mL/day is insufficient and can lead to azotemia.
- 2. Some of the diabetic patients reveal chronic polyuria.
  - a. In most cases, the polyuria results from a high concentration of glucose in the renal tubule.
  - b. In diabetes mellitus, pituitary diabetes, and adrenal diabetes, the high glucose concentration in the tubule is a result of hyperglycemia.
- 3. Diuretics are chemicals that increase urine volume. They are used for treating hypertension and congestive heart failure because they reduce overall fluid volume.
  - a. Diuretics work by either increasing glomerular filtration or reducing tubular reabsorption. Caffeine falls into the former category; alcohol into the latter (alcohol suppresses the release of ADH).
  - b. Many diuretic drugs produce osmotic diuresis by inhibiting sodium reabsorption.

### **C. Renal Function Tests**

#### **1. Renal Clearance**

- a. Renal clearance is the volume of blood plasma from which a particular waste is removed in 1 minute.
- b. Renal clearance can be measured indirectly by collecting samples of blood and urine, measuring the waste concentration in each, and measuring the urine output.

#### **2. Glomerular Filtration Rate**

- a. Measuring GFR requires a substance that is not secreted or reabsorbed at all. Garlic and artichoke produce inulin, a polymer of glucose, that is suitable for GFR measurement.

- b. All inulin filtered by the glomerulus remains in the renal tubule and appears in the urine; none is reabsorbed, and the tubule does not secrete it. For this solute, GFR is equal to the renal clearance.

## **VII. Urine Storage and Elimination**

### **A. The Ureters**

1. The ureters are muscular tubes leading from the renal pelvis to the lower bladder. As pressure builds in the bladder, it compresses the ureters and prevents the backflow of urine into the ureters.
2. The ureter has three layers: an adventitia, a muscularis, and a mucosa. The muscularis consists of two layers of smooth muscle that convey urine by peristaltic contraction to the urinary bladder.

### **B. The Urinary Bladder**

1. The urinary bladder is a muscular sac on the floor of the pelvic cavity. It is covered by parietal peritoneum on its flattened superior surface and by fibrous adventitia elsewhere. The bladder is highly distensible and expands superiorly.
  - a. Its muscularis, called the detrusor muscle, consists of three layers of smooth muscle.
  - b. The mucosa has a transitional epithelium, and in the relaxed bladder it has conspicuous wrinkles called rugae.
  - c. The openings of the two ureters and the urethra mark a triangular area called the trigone on the bladder floor.

### **C. The Urethra**

1. The urethra conveys urine from the urinary bladder to the outside of the body.
  - a. In females, it is 3–4 cm long and its opening, the external urethral orifice, lies between the vaginal orifice and clitoris.
  - b. The male urethra is 18 cm long and has three regions: prostatic urethra, membranous urethra, and penile urethra.
2. In both sexes, the detrusor muscle is thickened near the urethra to form an internal urethral sphincter that is under involuntary control. Where the urethra passes through the pelvic floor, it is encircled by an external urethral sphincter of skeletal muscle that provides voluntary control over the voiding of urine.

### **D. Micturition**

1. Micturition is the process by which the urinary bladder empties when it becomes filled.
2. When the bladder contains about 200 ml of urine, stretch receptors in the wall send impulses to the spinal cord. Parasympathetic signals return to the bladder and stimulate contraction of the detrusor muscle and relaxation of the internal urinary sphincter. This is the micturition reflex that voids the bladder in infants.
3. Once voluntary control has developed, emptying of the bladder is controlled predominantly by a micturition center in the pons. This center receives signals from stretch receptors and integrates this information with cortical input concerning the appropriateness of urinating at the moment. It sends back impulses that excite the detrusor and relax the internal sphincter. Waves of impulses continue until the external sphincter is relaxed and the detrusor muscle expels the urine.

## **VIII. Diuretics and kidney diseases**

1. A diuretic is a substance that increases the rate of urine volume output.
  - a. Osmotic diuretics decrease water reabsorption by increasing osmotic pressure of tubular fluid.
  - b. “Loop diuretics” decrease active  $\text{Na}^+ - \text{Cl}^- - \text{K}^+$  reabsorption in thick ascending loop of Henle
  - c. Thiazide diuretics inhibit  $\text{Na}^+ - \text{Cl}^-$  reabsorption in early distal tubule

- d. Carbonic anhydrase inhibitors
  - e. Competitive inhibitors of aldosterone
  - f. Blockers of sodium channels in the collecting tubule.
2. Severe kidney diseases can be lumped into two major categories
- a. Acute renal failure (prerenal, intrarenal, postrenal)
  - b. Chronic renal failure (e.g. metabolic disorders, renal vascular disorders, immunologic disorders, infections, congenital disorders)