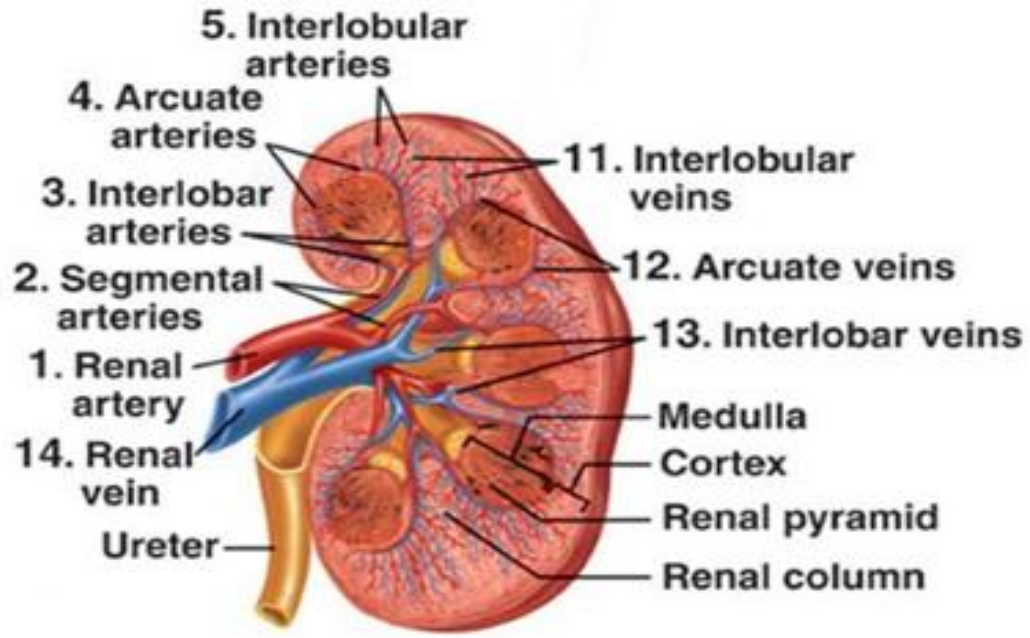
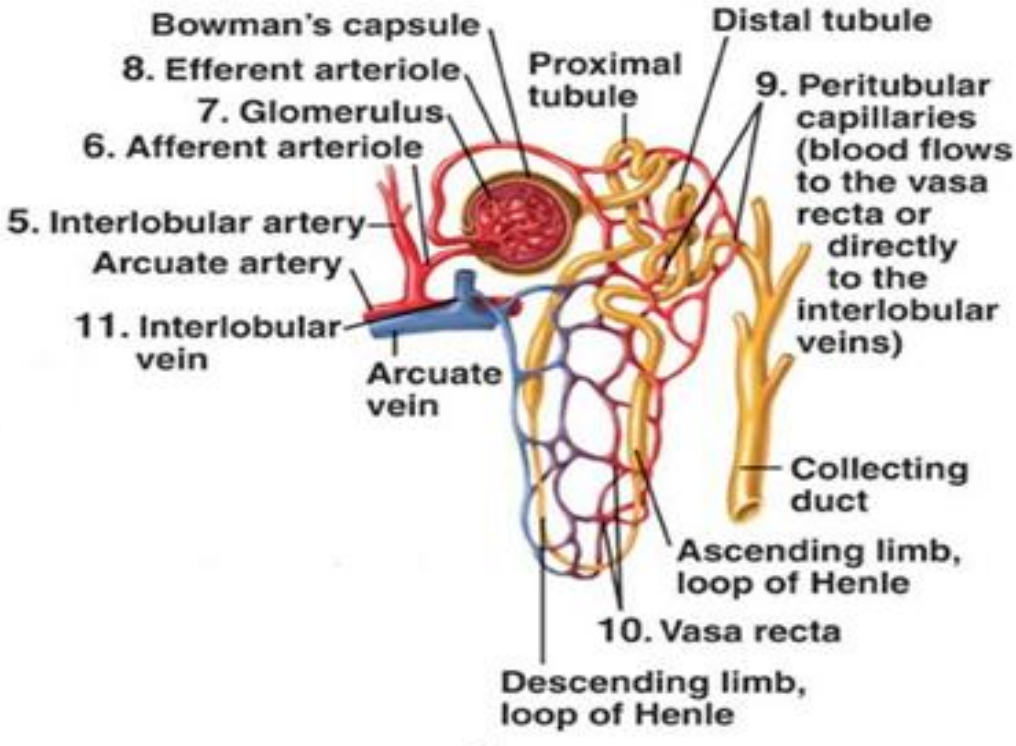
Lecture 6

RENAL PHYSIOLOGY





Each of two kidneys consists of 8-10 conical pyramids. Each pyramid has its base outward and its apex toward the pelvis. Each pyramid consists of outer cortex and inner medulla. Renal blood flow is 1.25 L/min which is about 25% of the resting cardiac output supplies 300 grams of renal tissue with much greater flow to the cortex (97%) than to the medulla (3%). The structural and functional unit of kidney is called nephron. More than one million nephrons are present in each kidney. Renal blood vessels and renal tubules are shown in the next page.

Several collecting ducts unite to form the main duct of pyramid. Each pyramid pours its urine into a minor calyx. Every 2-3 calyces unite to form a major calyx. Major calyces unite to form the renal pelvis. Renal pelvis leads urine through the ureter which emerges through the hilum of kidney. At the hilum also, renal artery enters and renal vein leaves. Two ureters pour into single urinary bladder from which urethra emerges.

Glomerular capillary membrane

Filtration occurs across that membrane which is composed of 3 layers:

1- Single layer of capillary endothelial cells
2- Basement membrane
3- Visceral layer of Bowman's capsule which is called podocytes.

The endothelial layer is fenestrated. All blood components are filtered across fenestrae except some large plasma proteins and cells. The basement membrane is very highly permeable. Filtered materials and ions (but not proteins) can pass easily through the membrane and the slit pores between the feet of podocytes.

Functions of kidney

1- Regulation of extracellular fluid (ECF)volume, osmolarity and composition
2- Regulation of blood pressure
3- Regulation of acid-base balance
4- Regulation of bone metabolism by regulation of excretion of calcium and phosphate ions and formation of active the form of vitamin D(1, 25 dihydroxycholecalcipherol)
5- Production of erythropoietin hormone (production of red blood cells)
6- Excretion of various metabolic waste products, drugs, toxic substances and poisons.

Urine formation

When certain amount of substance (x) is cleared away from plasma and excreted in urine, it is called renal clearance of that substance (C_x). Not all of the substance filtered from glomerular capillaries appears in urine, instead; some of this substance may be reabsorbed back to the blood via peritubular capillaries, while additional amounts of the same substance may be secreted from tubular cells to tubular lumen to appear in urine. So:

$$C_x = GFR - TR + TS$$

GFR is glomerular filtration, TR is tubular reabsorption and TS is tubular secretion.

Hence, about 180 liters of plasma are filtered by renal glomeruli every day. But, about 179 liters are reabsorbed by renal tubules back to the circulation and only about 1 liter is excreted as urine every day.

Glomerular filtration

Glomerular filtration is passive non-selective process. GFR = 125 ml/min. When renal plasma flows from afferent to efferent arterioles, about 20% of its contents is filtered by glomerular filtration from glomerular capillaries to Bowman's capsule. This 20% is called the filtration fraction (FF)

In order to measure GFR, we measure the clearance of creatinine (endogenous substance) or inulin (exogenous substance). Clearance of paraaminohippuric acid (C_{PAH}) is used to measure renal plasma flow.

$RPF = C_{PAH} / 0.9.$

Control of GFR

1- Sympathetic nervous activity (decreases GFR)
2- Hormones and autacoids: *Some chemicals decrease* GFR like adrenaline (also called epinephrine), nor-adrenaline (also called nor-epinephrine), angiotensin II, aspirin and endothelin. Some chemicals increase GFR like nitric oxide, prostaglandin and bradykinin.
3- Autoregulation
4- Plasma levels of amino acids and glucose (increase GFR).

Tubular reabsorption and secretion

Tubular reabsorption is a highly selective process that may be passive or active. [1]Some substances are completely reabsorbed like amino acids and glucose. The actual renal threshold for glucose is about 180 mg/100 ml above which glucose will appear in urine. [2]Some substances are mostly reabsorbed like bicarbonates and some other electrolytes. [3]Some substances are mostly reabsorbed in the presence of specific hormones like water (in the presence of antidiuretic hormone), and Na^+ (in the presence of aldosterone and/or angiotensin-II hormones). [4]Many substances are reabsorbed along with other substances (Cl^- follows Na^+, and NaCl follows H_2O). [5]Some substances are 50% reabsorbed like urea. [6]Some substances are about completely excreted like creatinine and some drugs and poisons.

Control of tubular reabsorption

1-Sympathetic control: (increases tubular reabsorption of sodium ions).
2- Hormonal control:

a- Aldosterone: increases reabsorption of Na^+ and excretion of K^+.

b- Angiotensin-II: acts directly (or indirectly after stimulation of aldosterone) to increase Na^+reabsorption.

c- Antidiuretic hormone (ADH or called vasopressin): increase water reabsorption.

d- Atrial natriuretic peptide (ANP): decreases Na^+ and water reabsorption.

e- Parathyroid hormones: increases Ca^{++} and Mg^{++} reabsorption and decreases phosphate reabsorption.

Water and electrolytes' reabsorption

[1]The major bulk of tubular reabsorption of water and solutes (about 65%) occurs in proximal tubules. [2]About 15% of water reabsorption occurs in thin descending loop

of Henle. [3]Very little amounts of solutes are passively reabsorbed in thin ascending loop of Henle. [4]The major active reabsorption of electrolytes occurs in thick ascending loop of Henle (about 30%). [5]The remaining reabsorption processes of electrolytes (about 5%) occur in distal segments. [6]Further water reabsorption (about 19%) from collecting ducts in the presence of ADH and only about 1% of filtered water is excreted in urine. Without ADH, about 20% of filtered water is excreted.

Acid – base buffer systems and acid – base disturbances

Regulation of [H^+] is by one or more of the following systems: *[1]Chemical acid-base buffer systems, [2]Respiratory regulation and [3]Renal regulation.*

a. Buffer systems are:

1- Bicarbonate buffer system: It is the most important buffer system in ECF.

Clinical considerations

When HCO_3^- decreases; pH is decreased and there will be metabolic acidosis
When CO_2 increases; pH is decreased and there will be respiratory acidosis
When HCO_3^- increases; pH is increased and there will be metabolic alkalosis
When CO_2 decreases; pH is increased and there will be respiratory alkalosis

2- Phosphate buffer system: It is important in ICF and renal tubular fluids.
3- Protein buffer systems: The most available ICF buffer systems but also work in ECF. Hemoglobin in red blood cells is a protein buffer.
4- Ammonium buffer system: It is the last choice buffer system in renal tubules.

b. Respiratory regulation

Increased breathing reduces CO_2 and raises pH from 7.4 to 7.63 and vice versa. Respiratory regulation of acid-base balance is by stimulation or inhibition of the respiratory center in the brain stem. Central chemosensitive areas are sensitive to changes in H^+ and partial pressure of carbon dioxide (P_{CO2}). They stimulate the respiratory center and result in hyperventilation or inhibit or the respiratory center and result in hypoventilation.

c. Renal regulation:

It occurs by excretion of acidic or alkaline urine. Normally, daily renal secretion of H^+ is about 4400 mmol. Bicarbonates system buffers 4320 mmol in renal tubules and the other 80 mmol are buffered by phosphates and then ammonium buffer systems. Most of renal tubular cells utilize secondary active transport to secrete H^+ and reabsorb Na^+ (Na^+- H^+ countertransport). Other distal tubular cells utilize primary active transport called proton pump.