

LECTURE 11

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RENAL PATHOPHYSIOLOGY / REVIEW

Read through the background review material in your textbook (Chapter 32) prior to beginning this lecture material.

Introduction

The kidneys (renal system) in combination with the skin (integumentary system) comprise a complex system for waste removal. Before the mechanisms of waste removal can be understood, an understanding of the term “waste” must be achieved. By definition, a waste material has no further use by the body. We commonly think of the nitrogenous wastes, urea and uric acid, as examples of these materials. Yet, the definition is much broader. Certainly, urea (from the metabolic deamination of amino acids in the liver) and uric acid (nucleotide derivatives from the metabolism of nucleic acids in the liver) qualify as wastes. In reality, any material that occurs in the body in quantities greater than those needed become wastes. Thus, excess water, excess salts, excess hydrogen or bicarbonate ions, or even excess vitamins that exist at levels above those required by the body must be excreted. All these excess materials along with the classic urea and uric acid molecules comprise urine. Consequently, urine composition is constantly changing as different materials occur in excess in the body.

The capacity of the renal system to eliminate wastes is much greater than required in the normal physiology of the human. Each kidney contains about one million functional units, the **nephrons**. This represents about 75% more renal capacity than needed. So, one complete kidney could be removed and still leave about 25% more capacity than required. All this excess renal capacity may seem superficially to be beneficial, but that is not always the case. Because of the excess capacity, renal disease can become quite advanced before it is symptomatic and detectable.

Mechanism of Urine Formation

Familiarize yourself with the basic anatomy and function of the nephron from your textbook (pp. 618-626). Pay particular attention to the two capillary networks associated with each nephron (the glomerulus and the vasa recta/peritubular capillaries) and the various anatomical regions of the nephron tubule.

Since different materials can occur in excess at different times, excretory organs must be able to selectively eliminate these when they occur. Nephron structures and functions make this possible. Specialized regions of the nephron provide for three major processes in urine formation: (1) **glomerular filtration**; (2) **tubular reabsorption**; and (3) **tubular secretion**.

Glomerular Filtration. Like the respiratory membrane of the lungs, the kidney nephrons possess a membrane surface, the **glomerular membrane**, with an extensive surface area. The glomerular membrane consists anatomically of the capillary walls of the glomerulus in close association with the epithelial layer that comprises the wall of the Bowman's capsule. By design, fluids that filter across the glomerular capillary walls from pressure differences will also cross the capsule layer to end up in the lumen of the Bowman's capsule. This filtration process, glomerular filtration, is poorly selective and resembles that which occurs in interstitial fluid formation. Basically, everything except blood cells and high molecular weight proteins will cross the membrane. This filtrate contains both nutrients and wastes. If allowed to remain in the nephron, essential nutrients would be lost with the urine.

Tubular Reabsorption. To prevent this potential loss of essential materials, nephron tubule cells, especially those of the proximal tubule, selectively reabsorb the nutrients back into blood of the peritubular capillaries and vasa recta leaving only the wastes in the lumen of the nephron. The tubular reabsorption of materials occurs by selective membrane transport mechanisms and each material exhibits a maximal threshold of reabsorption (T_{max}). Thus, if the concentration of a material in the filtrate is greater than the maximal threshold, the excess will not be reabsorbed and will appear in the urine. Thus, in normal kidneys only the excesses (wastes) will be excreted.

Tubular Secretion. In order to enhance the kidney's capacity to cleanse the blood of wastes, nephron tubule cells have the added capacity to extract materials from blood of the peritubular capillaries and vasa recta and secrete them directly into urine. A classic example of this process was discussed with pH regulation involving the kidney's capacity to secrete hydrogen ions into the urine during acidosis.

Assessing Kidney Function. Although a number of specialized tests exist to pinpoint disruptions in kidney function, a few generalized screening tests are readily available to detect initial kidney problems. A simple blood test, **Blood Urea Nitrogen (BUN)** reveals increases in blood levels of nitrogenous wastes, which may be indicative of early stage kidney failure. Another blood test, **creatinine** level, screens for accumulation of the muscle waste product creatinine, which is derived from muscle stores of creatine phosphate and is normally excreted by the kidneys.

Regulation of Kidney Function (Extrinsic Mechanisms)

Review the mechanisms of kidney regulation in your textbook (pp. 624-628) before proceeding.

Kidney function is subject to a number of regulatory influences from both extrinsic (outside the kidney) and intrinsic (within the kidney) sources. Those mechanisms acting from outside the kidney include: (1) systemic blood pressure; (2) aldosterone; and (3) Antidiuretic Hormone (ADH).

The role of **systemic blood pressure** in controlling kidney function should be apparent by now. Since the rate of glomerular filtration is directly related to the hydrostatic blood pressure in glomerular capillaries, any increase in blood pressure results in a corresponding increase in filtration and urine output. Since this process ultimately decreases blood volume, the kidneys are a powerful means of controlling long-term blood pressure. Conversely, drops in blood pressure have the opposite effect. This mechanism is important because it illustrates how circulatory and renal systems interact as blood pressure changes affect kidney function and vice versa.

The steroid hormone, **aldosterone**, released from the adrenal cortex in response to elevated levels of potassium, causes nephrons to secrete potassium into the urine. But, since potassium and sodium share the same transport carrier, as potassium is excreted sodium is retained. Chloride ions and water follow the retained sodium to cause an increase in fluid retention and expansion of blood volume with corresponding increases in blood pressure. Recall that fluid retention is a common side effect of steroid hormone activity.

The posterior pituitary hormone, **antidiuretic hormone (ADH)**, is produced by the hypothalamus and released from the posterior pituitary when the osmotic pressure of blood and body fluids increases. Recall that increased osmotic pressure correlates directly with solute concentration, indicating that water retention and/or intake is required to correct the situation. Distal convoluted tubules and the proximal collecting ducts are the targets for ADH action. Membrane pores for water transport increase in these target cells under ADH influence. Because of the high sodium ion concentration in the kidney interstitial fluids, increasing the number of these pores increases the rate of water reabsorption from the urine back into blood in this distal region of the nephron. It is important to notice that only water is reabsorbed under ADH influence allowing this mechanism to “fine tune” the osmolarity of body fluids and blood while concentrating or diluting the urine output.

REVIEW QUESTIONS:

1. Why would people abusing steroids or on steroid therapy appear puffy and edematous?
2. If alcohol and anesthetics block ADH release, what physiological effects might they produce?
3. What effects would you expect on blood composition and pressure from a failure of the kidneys to produce urine?

4. What effect might a weakened left heart have on kidney function?

Regulation of Kidney Function (Intrinsic Mechanisms)

Review the Juxtaglomerular Apparatus structure and function and its related rennin-angiotensin-aldosterone mechanism in your textbook (p. 627) before proceeding.

In addition to the extrinsic mechanisms of kidney regulation, the kidneys also have the intrinsic capacity to control their own function during bouts of hypotension. For such a mechanism to work, the kidney must first detect a drop in blood pressure and then initiate corrective measures. The **Juxtaglomerular (J.G.) Apparatus** serves both these functions. A portion of the distal convoluted tubule, the **macula densa**, detects a reduction in fluid flow through the nephron as would occur if glomerular filtration pressures were to drop. Once detected, cells of the afferent arteriole, the **Juxtaglomerular Cells**, are stimulated to release the enzyme **Renin** into blood entering the glomerulus.

Renin starts a chain of linked biochemical reactions in blood when it catalyzes the conversion of a plasma precursor protein, **angiotensinogen**, into the compound **Angiotensin I**. A second enzyme, **Angiotensin Converting Enzyme (ACE)**, occurs in capillary beds especially in the lungs and kidneys. ACE converts Angiotensin I into **Angiotensin II**, which is a powerful vasoconstrictor. Exiting the glomerulus through the efferent arteriole, angiotensin II constricts the efferent arteriole causing blood to congest backwards into the glomerular capillaries. As glomerular pressures increase, filtration rates increase accordingly. As angiotensin II spills back into systemic circulation, it causes generalized vasoconstriction increasing systemic blood pressure while stimulating aldosterone release to expand blood volume and further increase pressure. Through this mechanism renal function is maintained during low pressure events.

Renal Ischemia. Notice that renin release occurred when glomerular filtration was lower than normal. Renal ischemia, a reduced blood flow to the kidneys, can drop glomerular filtration rate and trigger the juxtaglomerular corrective mechanism. This situation can be particularly problematic if hypertension is the cause of renal ischemia through high pressure damage to the small vessels of the kidney. With impaired blood supply, the affected kidney nephrons release renin which raises the blood pressure still higher and can damage more renal blood vessels. Without intervention, the situation can lead to chronic hypertension and serious kidney damage.

DISCUSSION QUESTIONS: (Post answers to the “Patho Discussion Group”)

1. What clinical use might an “ACE blocker” drug have?
2. Trace step-by-step how renal artery atherosclerosis could lead to left CHF.