

RENAL SYSTEM 1
FLUID & ELECTROLYTE HOMEOSTASIS
Emma Jakoi, Ph.D.

Learning Objectives
1. Describe the structure of the kidney nephron.
2. List the homeostatic functions of the kidney.
3. Explain filtration, reabsorption, secretion, and excretion.
4. Explain how glomerular filtration rate (GFR) is regulated.
5. Define autoregulation and list 3 mechanisms involved in autoregulation.
6. Describe the factors that determine renal blood flow and explain how it is regulated independent of MAP.
7. Define filtration fraction and filtration load.

WHAT DOES THE KIDNEY DO?
The kidney is a filter of the blood that maintains water and electrolyte homeostasis by balancing intake with excretion in the urine. Specifically it regulates:

1. Extracellular fluid volume
2. Osmolarity
3. Specific ion balance (e.g., Na+, K+, Ca++)
4. pH
5. Excretion of waste products
6. Production of hormones [*erythropoietin* needed for production of red blood cells] and enzymes [*renin* needed for blood pressure and volume control]

ANATOMY OF THE URINARY SYSTEM
Each kidney is divided into a cortex and medulla (Fig 1).

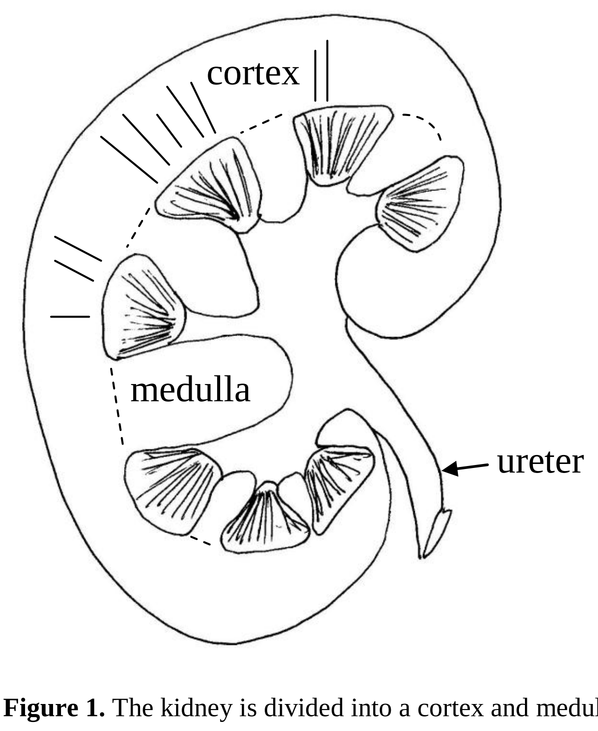

Figure 1. The kidney is divided into a cortex and medulla.

The kidney contains approximately 1 million filtering units called **nephrons**. The nephron begins in the cortex of the kidney with a ball-like structure called the glomerulus. The glomerulus is a capillary bed, fed by an afferent arteriole and drained by an efferent arteriole. Surrounding this capillary bed is a cup-like structure called Bowman's capsule. Bowman's capsule is derived from the closed end of the renal tubule (Fig 2). This is the site where blood is filtered. The filtrate within Bowman's capsule contains molecules and fluid but not cells and large proteins (such as albumen).

The efferent arteriole drains into a second capillary bed that surrounds the renal tubule in the cortex (called peritubular capillary) and follows the tubule as it extends down into the medulla. The renal tubule and this capillary bed form a loop in the medulla and then return to the cortex. The renal tubule from each nephron drains into a collecting duct which in turn empties into the ureter.

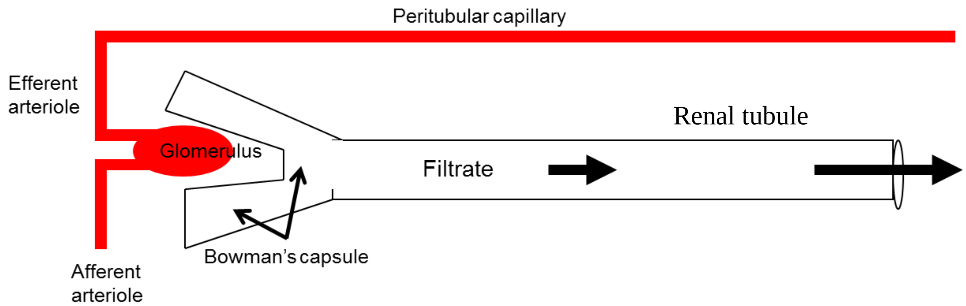

Figure 2. Organization of the nephron and its blood supply.

There are two types of nephrons: cortical and juxtamedullary. The **cortical nephron** has most of its renal tubule located within the cortex. The **juxtamedullary nephron** has a renal tubule that extends deep into the medulla. The juxtamedullary nephrons are responsible for maintaining a hyperosmotic gradient within the medulla that is critical for concentrating urine.

In sequence, the regions of the tubule are: proximal convoluted tubule (PCT), thin loop of Henle, ascending thick loop of Henle (TAL), distal convoluted tubule (DCT).

The renal tubule from several nephrons empties into a collecting duct (CD). Urine exits from the collecting duct to enter the ureter.

HOW DOES THE NEPHRON WORK?

RENAL BLOOD FLOW

In a given day, 180 L of plasma are filtered, but only 1.5 L are excreted as urine. The solute and/or water content of the filtrate are modified within specific regions of the renal tubule (Table 1). The basic processes that occur along the renal tubule include: filtration (F), reabsorption (R), secretion (S) and excretion (E) (Fig 3).

Excretion (E) = Amt Filtered (F) - Amt Reabsorbed (R) + Amt Secreted (S)

TABLE 1. Fluid volume and osmolarity of filtrate in the renal tubule

Location in nephron	Volume	Osmolarity
Bowman's capsule	180 L/day	300 mOsM (isotonic)
End of proximal tubule	54 L/ day	300 mOsM (isotonic)
End of loop of Henle	18 L/ day	100 mOsM (hypotonic)
End of collecting duct	1.5 L/ day	50-1200 mOsM

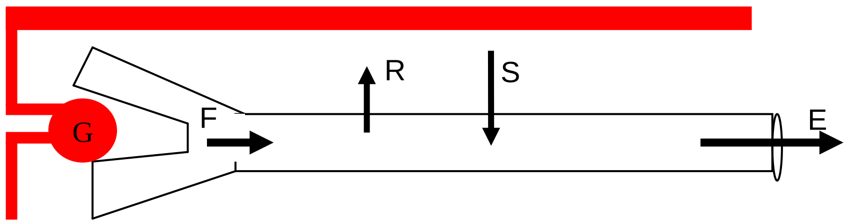

Figure 3. Net handling of a substance by the renal tubule is given by the following equation. Excretion (E) = Filtration (F) – Reabsorption (R) + Secretion (S).

FILTRATION (F) is the movement of material from blood into the tubular lumen. It follows the same principles that govern movement of water across other capillaries.

REABSORPTION (R) is the movement of filtered material from the tubular lumen back to the blood.

SECRETION (S) is the movement of material from the blood directly into the renal tubule.

EXCRETION (E) is the movement of filtrate (urine) from the kidney into the ureter.

Net handling of a substance is described as:

Net reabsorption when filtration rate > excretion rate
No net reabsorption when filtration rate = excretion rate
Net secretion when filtration rate < excretion rate

FILTRATION

GLOMERULAR FILTRATION RATE (GFR) describes the efficiency of filtration. This is the amount of fluid that enters into Bowman's capsule per unit time. **Average GFR is 125 ml/min or 180L/day**.

GFR is influenced by two factors: the net filtration pressure and the filtration coefficient. The filtration pressure is determined by renal blood flow and pressure.

Net filtration = Hydrostatic pressure $_{GC}$ - Oncotic pressure $_{GC}$ - Hydrostatic pressure $_{BC}$

For example, if the hydrostatic pressure in the glomerulus capillary is 55 mm Hg and the oncotic pressure is 30 mmHg, and the minus the fluid pressure in Bowman's capsule is 15 mmHg, then the net filtration pressure is 55 – 30 – 15 = 10 mmHg.

The filtration coefficient is determined by the surface area of the glomerular capillaries available for filtration and the permeability of the capillary-Bowman capsule interface.

If a substance is freely filtered then the **filtration load of any substance can be calculated as follows:**

Filtration Load = [plasma concentration of substance] X (GFR).

For example, the filtration load of glucose = [100 mg glucose/ 100 mL] X [125 mL /min] =125 mg/min

Usually about 1/5 of the plasma that flows through the kidney is filtered with each pass. Why not filter all of the blood at one time? Recall that capillaries in the area are in series. If too much water is removed from the plasma in the glomerulus, then the viscosity of the blood in the efferent arterioles and peritubular capillaries increases. If the viscosity is too high, then the flow will decrease dramatically.

The rate of filtration in each glomerulus is regulated independently. Because each glomerulus (capillary bed) is fed and drained by arterioles, a change in resistance of either arteriole will alter the net filtration pressure (Fig 4).

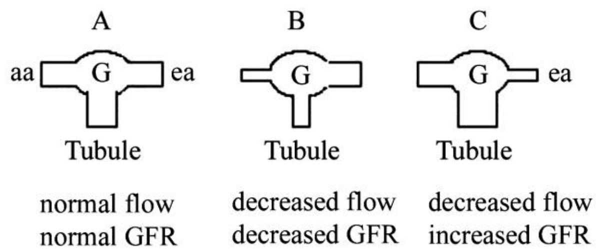

Figure 4. Schematic demonstrates regulation of GFR by (A) normal blood flow, (B) constriction of afferent arteriole (aa) , and (C) constriction of efferent arteriole (ea). G is the glomerulus.

This geometry also enables the kidney to maintain GFR independent of the mean arterial pressure. In fact, **GFR and renal blood flow are maintained nearly constant as the mean arterial pressure varies between 80 and 180 mm Hg.** This is accomplished by **auto-regulation**.

AUTO-REGULATION involves the following two control mechanisms:
1. Myogenic mechanism: refers to the stretch response of smooth muscle cells in the walls of the afferent arteriole. If the renal arterial pressure changes (up or down), then the resistance in the afferent arteriole will change to maintain a constant flow (GFR).

GFR = $\mathbf{F = \triangle P/R}$

2. Tubulo-glomerular feedback: involves two regions of the same nephron, the smooth muscle cells of the afferent arteriole and specialized cells (called the **macula densa**) of the thick ascending loop of Henle (TAL). These two sets of cells form the **juxtaglomerular apparatus (JGA)**. The JGA provides a negative feedback loop mediated by paracrines which change the resistance of the afferent arteriole and hence GFR. For example, when the macula densa detect low filtrate flow in the TAL, it signals the afferent arteriole to dilate thereby increasing GFR. The opposite occurs when increased flow is detected. The activity of the JGA controls volume and Na+ reabsorption because an increase in GFR delivers more solutes to the PCT permitting greater uptake of Na+ by the PCT. Conversely, a decrease in GFR leads to lower reabsorption of Na+.

REGULATION BY REFLEX LOOPS (hormonal or nervous): is mediated by changing the resistance of the afferent and efferent arterioles. Increased sympathetic activity (Norepi) and certain hormones (Epi) cause a decrease in GFR by constricting the afferent arteriole more than the efferent arteriole (Fig 4B). Other hormones (vasopressin) affect the efferent arteriole preferentially and thus partially offset the overall decrease in GFR by modulating the hydrostatic pressure within the glomerulus (Fig 4C).

RENAL BLOOD FLOW & FILTRATION FRACTION

Recall the equation for blood flow through an organ is: $\mathbf{Q = \Delta P/R}$.

For the kidneys, renal blood flow is calculated as follows:

RBF = (aortic pressure – renal venous pressure)/(renal vascular resistance)

The renal arteries, afferent arterioles, and efferent arterioles are the resistance vessels in the kidneys which determine renal vascular resistance. The kidneys receive about **20 to 25 percent of cardiac output**. In normal humans, renal blood flow is approximately **1,000 ml/min**.

Plasma is the fluid phase of blood. It normally accounts for roughly 60% of blood volume; cells account for the remainder 40%. The fraction of blood volume that is cells is called the hematocrit. Therefore renal plasma flow (RPF) is approximately 600 ml/min.

Renal plasma flow = (1-hematocrit) X (renal blood flow)

The **Filtration Fraction** is the fraction of plasma that becomes glomerular filtrate. The filtration fraction is the ratio of GFR to renal plasma flow. Since normal GFR is 120 ml/min, the normal filtration fraction is about 0.2.

Filtration Fraction = GFR/ RPF = (120ml/min)/(600 mml/min) = 0.2.

RBF & GFR RESPOND TO PHYSIOLOGICAL STRESS

Hemorrhagic (hypotensive) shock*:* causes renal vasoconstriction to shunt blood to other tissues (heart and brain) if the MAP is less than 80 mmHg. If prolonged, then the ischemia (lack of blood flow) to the kidney will trigger apoptosis (cell death of the renal tubules) and cause kidney failure.

KEY CONCEPTS

1. The kidneys' primary functions are to maintain fluid volumes of the body by regulating salt balance and to maintain the osmolarity of the body by regulating water balance.
2. GFR is regulated independent of mean arterial pressure (MAP) ranging from 80-180 mmHg because of autoregulation which alters arteriolar resistance.
3. Autoregulation includes the myogenic response and tubular-glomerular feedback.
4. Reflex regulation of GFR involves hormones and sympathetic nervous activity.
5. Filtration fraction is the ratio of GFR to RBF.

PROBLEMS

1. Measurements in a nephron reveal a glomerular hydrostatic pressure of 70 mm Hg and a fluid pressure in Bowman's capsule of 15 mm Hg. Assuming an oncotic pressure of 30 mmHg and essentially no plasma protein are filtered, what is the glomerular filtration pressure in this case?

    A. 40 mmHg
    B. 115 mmHg
    C. 55 mmHg
    D. 25 mmHg

2. In response to a decrease in systemic blood pressure, the afferent arteriole of a nephron dilates. What happens to the afferent arteriole resistance and glomerular filtration rate (GFR) in that nephron?

    A. arteriolar resistance increases/ GFR increases
    B. arteriolar resistance decreases/ GFR increases
    C. arteriolar resistance increases/GFR decreases
    D. arteriolar resistance decreases/ GFR decreases

ANSWERS:

1. D.
2. B.