LECTURE 1
RENAL FUNCTION

Components of the Urinary System
- 2 Kidneys
- 2 Ureters
- Bladder
- Urethra
- Refer to “Renal System Vocabulary” in your notes
  Figure 2-1, page 10

Kidney Composition
- Cortex
  - Outer region
  - Contains portion of convoluted tubules
- Medulla
  - Located deep in the cortex
  - Nephrons are located in both cortex and medulla
  Figure 2-1, page 10
4 Physiological Functions of the Kidney

- Waste elimination
- Regulate acid/base balance
- Regulate volume of body fluids
- Maintain blood pressure and erythropoiesis

Each function is possible due to renal blood flow, filtration, reabsorption, and secretion.

Purpose of Nephron

- Each kidney contains 1 to 1.5 million nephrons
- Nephrons help the kidney to selectively clear waste products from the blood and simultaneously maintain the body's essential water and electrolyte balance
  - The filtration system

Purpose of Nephron

- The nephron consists of a capillary network
  - Glomerulus
  - Long tubule
    - The tubule is divided into three parts
      - Proximal convoluted tubule
      - Loop of Henle
      - Distal convoluted tubule
Components of Nephron
- Glomerulus
- Bowman’s capsule
- Proximal convoluted tubule
- Loop of Henle
- Distal convoluted tubule
- Collecting tubule

Nephron components in the Cortex and Medulla
- Cortex contains
  - Glomerulus
  - Bowman Capsule
  - Tubules
    - Distal
    - Convoluted
- Medulla contains
  - Loop of Henle
  - Collecting tubules

Kidney and Nephron
Renal Blood Flow

- Blood is supplied to the kidney by the renal artery and enters the nephron through the afferent arteriole (approaches)
  - 20-25% of blood that leaves the left ventricle enters the kidney by renal artery
- Blood then flows through the glomerulus and into the efferent arteriole

Variation in size of these arterioles creates the hydrostatic pressure differential for
- Glomerular filtration
- Renal blood flow within the glomerulus

In a normal adult, blood passes through the kidneys at a rate of 1,200 mL/min for both kidneys (total renal blood flow)
- 600 mL/min/kidney
Renal Blood Flow

- Before returning to the renal vein, the blood from the efferent arteriole enters the peritubular capillaries and the vasa recta, where it flows through the cortex and medulla.
- As the blood flows through the cortex and medulla, it is close the tubules.

Peritubular capillaries surround the proximal and distal tubules.

Purpose of this capillary system is:
- Reabsorption of essential substances from the fluid in the proximal convoluted tubule.
- Final adjustment of the urinary composition in the distal convoluted tubule (pH and electrolyte content).
Renal Blood Flow

- The vasa recta is located adjacent to ascending and descending Loop of Henle
  - This is the area of major exchange of water and salts between the blood and medulla interstitium

Glomerular Filtration

- The glomerulus is surrounded by the Bowman's capsule
- The glomerulus serves as a non-selective filter of plasma substance with molecular weights of less than 70,000 Daltons

Several factors influence filtration
- Hydrostatic pressure of vessels
- Cellular structure of capillary walls and Bowman's capsule
- Negative feedback mechanisms of the renin-angiotensin-aldosterone system
  - When blood pressure is low, renin (enzyme) is produced
  - Renin causes secretion of aldosterone and formation of angiotensin
Definitions

- **Aldosterone**: a mineral corticoid steroid hormone produced by the adrenal cortex with action in the renal tubule to regulate sodium and potassium balance in the blood.
- **Renin**: A proteolytic enzyme that affects the blood pressure by catalyzing the change of angiotensinogen to angiotensin, a strong pressor.
- **Angiotensin**: Polypeptide in the blood causing vasoconstriction, increased blood pressure, and the release of aldosterone from the adrenal cortex.

Glomerular Filtration

- The pressure of the blood in the glomerulus forces water and dissolved solutes through the membrane into the Bowman's space.
- Blood cells, plasma proteins, and large molecules leave the glomerulus through the efferent arterioles.
Glomerular Filtration

- About **120 mL/minute** of renal plasma is filtered through the kidneys
  - Referred to as an ultrafiltrate
  - Ultrafiltrate contains water, glucose, electrolytes, amino acids, urea, creatinine, and ammonia
  - Only difference between plasma (blood) and filtrate is the absence of plasma protein, protein-bound substances, and cells

Tubular Reabsorption

- How can the body lose 120 mL/minute of water containing essential substances?
  - Cellular mechanisms of active and passive transport are responsible for tubular reabsorption of essential substances and water
  - 80% of filtrate is reabsorbed in proximal convoluted tubule

Active Transport

- Substance combines with a carrier protein from the membrane of the renal tubular cells
  - Substance is transferred across the membrane back into the blood stream
Location where Active Transport of Substances Occurs

- Proximal convoluted tubule - glucose, amino acids, and salts
  - Glucose absorption is dependent of renal threshold
- Ascending Loop of Henle - chloride
- Distal convoluted tubule - sodium

Table 2-2, page 16

Passive Transport

- Movement of substances across the membrane due to difference in concentration or electrical potential on each side of membrane
  - Gradient difference

Location where Passive Transport of Substances Occurs

- Loop of Henle - water
  - Except ascending loop
  - Walls are impermeable to water
- Proximal tubule and ascending loop of Henle – urea
- Ascending loop of Henle – sodium

Table 2-2, page 16
Renal Threshold

- Some substances, such as glucose are actively transported back into the blood until the blood concentration reaches a certain level
  - Reabsorption will then cease
  - Will be excreted in the urine
- Glucose threshold is **160-180 mg/dL**
  - Uncontrolled diabetics have sugar in urine

Final Urine Concentration through Reabsorption

- The final concentration of the filtrate through the reabsorption of water begins in the late distal convoluted tubule and continues in the collecting duct.
- Reabsorption depends on the osmotic gradient in the medulla and the hormone vasopressin
Final Urine Concentration through Reabsorption

- The main function of the distal tubule and collecting duct is
  - Adjustment of pH
  - Osmolality
  - Electrolyte content of the urine

Role of Vasopressin

- Vasopressin is an antidiuretic hormone
- The amount of vasopressin present in the nephron is dependent upon the body’s state of hydration
- High levels of vasopressin increases permeability
  - Increased reabsorption of water
  - Low-volume, concentrated urine
Role of Vasopressin

- Low or absence of vasopressin (ADH) makes the tubular walls impermeable to the reabsorption of water
  - Increased, dilute urine
- Caffeine inhibits ADH

Tubular Secretion

- Tubular Activities
  - Reabsorption
    - Substances are removed from the glomerular filtrate and returned to the blood
  - Secretion
    - Passage of substances from the blood in the peritubular capillaries to the tubular filtrate

Function of Tubular Secretion

- Two functions of tubular secretion
  - Elimination of waste products not filtered by the glomerulus
    - Substances such as medications that are bound to protein
    - While in the peritubular capillaries, the substance develops an affinity to the tubular cells
      - Will be excreted in the urine
Second Function of Tubular Secretion

- Regulation of the acid-base balance in the body through the secretion of hydrogen ions
  - To maintain the normal blood pH of 7.4, the blood must buffer and eliminate the excess acid formed by dietary intake and body metabolism
  - Bicarbonate ions are filtered but returned to the blood after the secreted hydrogen ion attaches to the bicarbonate
    - Figures 2-7,8,9, page 14

Secretion of Hydrogen Ion

- Almost 100% of filtered bicarbonate is reabsorbed after combining with the hydrogen ion
- Excess hydrogen ions may combine with phosphate or ammonia and be excreted in the urine
- This process determines the acidity of the urine

Renal Function Test

- The two most common tests used to assess renal function are:
  - Glomerular Filtration Test
  - Concentration Tests
    - Tubular Reabsorption
    - Tubular Secretion
Glomerular Filtration Test

- This is a standard test that measures the filtering capacity of the glomeruli.
- Referred to as a **Clearance Test**
  - Measures the rate at which the kidneys are able to remove a filterable substance from the blood.
  - Considered the best screen for glomerular filtration.

What Substance to Measure?

- To ensure glomerular filtration is being accurately measured, the substance that is measured must:
  - Neither be excreted or reabsorbed by the tubules.
  - Be produced at a constant rate and not be influenced by the body state of hydration.

What Substance to Measure?

- **Creatinine** is a waste product of muscle metabolism and is normally found at a constant level in the blood.
- The **Creatinine Clearance Test** is the most common test used to measure glomerular filtration rate.
  - Reported as mL/minute.
Creatinine Clearance Test

- Must use a timed urine sample
  - 2, 4, 12, or 24 hour specimen
    - mL per minute must be determined
- Must know the creatinine level in the blood (plasma)
- Must know the urine creatinine level

Creatinine Clearance Test

- Formula
  - Creatinine Clearance (CC) = \( \frac{\text{U} \times \text{V}}{\text{P}} \)
    - CC = mL of plasma cleared/minute
    - P = mg/dL of plasma creatinine
    - U = mg/dL of urine creatinine
    - V = specimen volume in mL/min

Example

- Calculate the creatinine clearance:
  - Urine creatinine 120 mg/dL; plasma creatinine 1.0 mg/dL; urine volume 60 mL obtained from a 1-hour specimen.
  - Calculate the creatinine clearance.
Step 1

- Calculate the urine for mL/min

\[ V = \frac{60 \text{ mL}}{60 \text{ min}} = 1 \text{ mL/min} \]

(24 hour sample, divide by 1440 minutes)

Step 2

- CC = \( \frac{120 \text{ mg/dL} \times 1 \text{ mL/min}}{1.0 \text{ mg/dL}} \)

\[ CC = 120 \text{ mL/min} \]

(If surface area is given, \( C = \frac{UV}{\text{P} \times \text{A}} \times 1.73 \))

A - Can be obtained from a nomogram

Clinical Significance of Creatinine Clearance

- Creatinine clearance looks at both the number of nephrons as well as the functional capacity of nephrons

- Useful in
  - Determining extent of nephron damage in renal disease
  - Monitor effect of treatment for nephron damage
  - Monitor effect medications have on nephron
Clinical Significance of Creatinine Clearance

- Creatinine clearance will not be elevated until greater than 50% of the nephrons are damaged in both kidneys
- This is why many people can live normal lives with only one kidney
  - Nephrons work twice as hard to provide adequate filtration

Urine Concentration Tests

- Tubular Reabsorption Tests
  - Specific Gravity
    - Hydrometer
    - Refractometer
  - Osmolarity (Osmolality)

Urine Concentration Tests

- The loss of tubular reabsorption ability is often the first function affected in renal disease
- Concentration tests are used in determining the ability of tubules to reabsorb the essential substances and water that have been non-selectively filtered by the glomerulus
Urine Concentration Tests

- The final urine volume is dependent on the body’s state of hydration.
- The ultrafiltrate that enters the tubules has a specific gravity of 1.010.
- The final urine concentration (density) may be greater or less than the 1.010.
  - Dependent on the body’s state of hydration.

Figure 2-14, Page 22

Tubular Secretion and Renal Blood Flow Tests

- Tests to measure tubular secretion of non-filtered substances and renal blood flow are closely related in that total renal blood flow through the nephron must be measured by a substance that is secreted rather than filtered through the glomerulus.
Tubular Secretion and Renal Blood Flow Tests

- The test most commonly associated with tubular secretion and renal blood flow is the para-aminohippuric acid (PAH) test
  - Principle is the same as the creatinine clearance test
- Measurement of hydrogen ions are also used as an indicator
  - Urine pH, titratable acidity, and urine ammonia

Renal Function Tests

![Diagram](image_url)