

Clinical Chemistry of Kidney

Lec.1

Classification of Kidney Function Tests

❖ Classification of Kidney Function Tests:

1. Tests to measure glomerular function rate → glomerular function tests : all Clearance tests (insulin , creatinine , urea), glomerular filtration rate (GFR), glomerular permeability, proteinuria are included in this group.
2. Tests to measure Renal Tubular function → Tubular function tests: include urine concentration or dilution tests, urine acidification test (acid excretion test), measurement of Tubular secretory mass , reabsorption studies
3. Analysis of blood /serum : estimation of blood urea , serum creatinine, serum protein, serum electrolytes , urine protein, urine electrolytes, beta 2-microglobulin (all these tests are often useful to assess renal functions).
4. Urine output/examination: simple routine examination of Urine for volume , pH, specific gravity, osmality and presence of certain abnormal constituents (proteins, blood , ketone bodies , glucose etc.) help to assess kidney functions /diseases to limited extent.
5. Renal blood flow

Clinical applications of Kidney Function Tests

❖ Clinical applications of Kidney Function Tests:

1. Establish presence & absence of renal disease
2. Define the nature of disease
3. Assessment of the extent of renal damage
4. Define the degree of renal dysfunction
5. Monitoring progression of renal disease
6. Monitoring and adjusting the dose of renal toxic drugs which are mainly excreted by the kidney.
7. Monitoring the response of treatment

3-Endocrine function.

4- Urine formation.

Kidneys filter blood in a three-step process. **First**, the nephrons filter blood that runs through the capillary network in the glomerulus. Almost all solutes, except for proteins, are filtered out into the glomerulus by a process called **glomerular filtration**. **Second**, the filtrate is collected in the renal tubules. Most of the solutes get reabsorbed in the PCT by a process called **tubular reabsorption**. In the loop of Henle, the filtrate continues to exchange solutes and water with the renal medulla and the peritubular capillary network. Water is also reabsorbed during this step. Then, additional solutes and wastes are secreted into the kidney tubules during tubular secretion, which is the opposite process to tubular reabsorption. The collecting ducts collect filtrate coming from the nephrons and fuse in the medullary papillae. From here, the papillae deliver the filtrate, now called urine **Nephron structure:**

- 1.This is the functional unit of the kidney.
- 2.Each kidney contains 400,000 to 800,000 nephrons.
- 3.Each nephron consists of the following:
 1. **Glomerulus.**
 2. **Proximal Tubule.**
 3. **The loop of Henle.**
 4. **Distal Tubule.**
 5. **Collecting ducts.**

Each part of the nephron performs a different function in filtering waste and maintaining homeostatic balance.

1.The glomerulus forces small solutes out of the blood by pressure.

2.The proximal convoluted tubule reabsorbs ions, water, and nutrients from the filtrate into the interstitial fluid, and actively transports toxins and drugs from the interstitial fluid into the filtrate. The proximal convoluted tubule also adjusts blood pH by selectively secreting ammonia (NH₃) into the filtrate, where it reacts with H⁺ to form NH₄⁺. The more acidic the filtrate, the more ammonia is secreted.

3.The descending loop of Henle is lined with cells containing aquaporins that allow water to pass from the filtrate into the interstitial fluid. **4-In the thin part of the ascending loop** of Henle, Na⁺ and Cl⁻ ions diffuse into the interstitial fluid. In the thick part, these same ions are actively transported into the interstitial fluid. Because salt but not water is lost, the filtrate becomes more dilute as it travels up the limb.

5-In the distal convoluted tubule, K⁺ and H⁺ ions are selectively secreted into the filtrate, while Na⁺, Cl⁻, and HCO₃⁻ ions are reabsorbed to maintain pH and electrolyte balance in the blood.

6- The collecting duct reabsorbs solutes and water from the filtrate, forming dilute urine. (credit: modification of work by NIDDK)

Nephron Function

Nephrons filter blood and then reabsorb useful materials from the filtrate before eliminating the remainder as urine

This process occurs over three key stages:

1.Ultrafiltration – Blood is filtered out of the glomerulus at the Bowman’s capsule to form filtrate

2.Selective reabsorption – Usable materials are reabsorbed in convoluted tubules (both proximal and distal)

3.Osmoregulation – The loop of Henle establishes a salt gradient, which draws water out of the collecting duct

The proximal tubules:

These are most metabolically active and lead to the reabsorption of :

1.60 to 90% of the glomerular filtrate.

2.70% of the Na and Cl.

3.Other substances are potassium, glucose, bicarbonate, phosphate, and sulfate.

4.90% of H⁺ is excreted.

The Distal tubules are involved in excretion and secretion of :

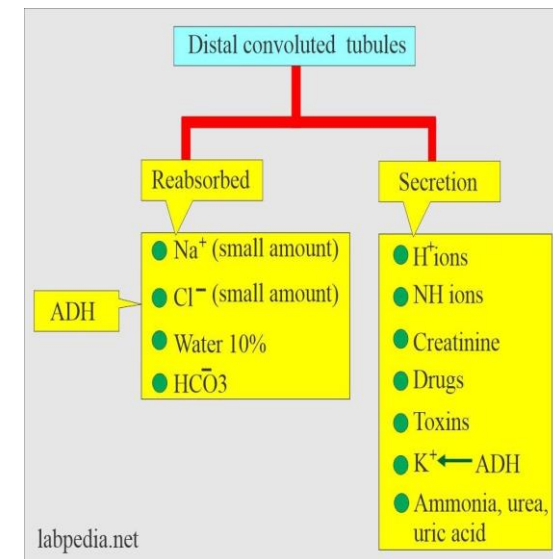
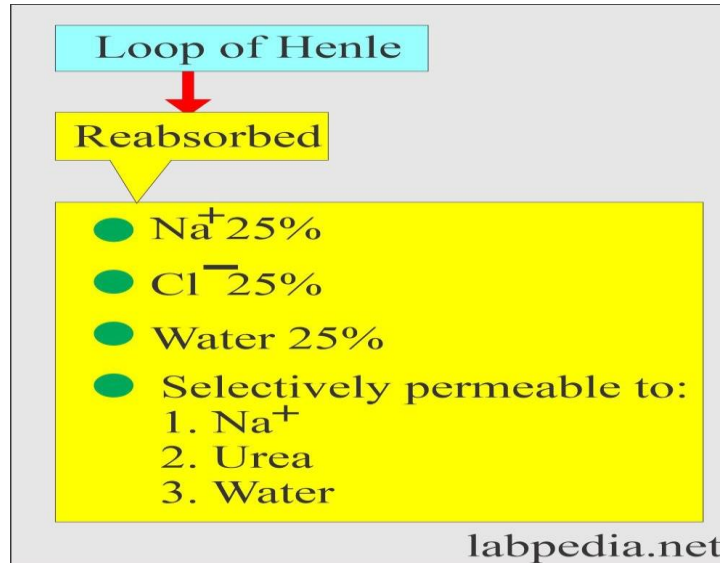
ADH and aldosterone help in reabsorption.

Sodium, Potassium

Chloride and hydrogen H⁺, ammonia, urea, and uric acid secreted and bicarbonate reabsorbed.

The Loop of Henle is:

Selectively permeable to sodium, urea, and water. The descending loop is highly permeable to water but not salt. Urine becomes concentrated. The ascending loop is impermeable to water but actively reabsorbs salts, decreasing the concentration of the urine.



The collecting system is under the control of ADH.

Aldosterone regulates NaCl reabsorption.

K⁺, H⁺, and ammonia are reabsorbed.

Urine formed is carried to the ureter and the urinary bladder.

The fluid filtered from blood, called **filtrate**, passes through the nephron, much of the filtrate and its contents are reabsorbed into the body.

Reabsorption is a finely tuned process that is altered to **maintain homeostasis** of blood volume, blood pressure, plasma osmolarity, and blood pH. Reabsorbed fluids, ions, and molecules are returned to the bloodstream through the peri-tubular capillaries, and are not excreted as urine.

The mechanisms of reabsorption into the peri-tubular capillaries include:

Passive diffusion—passing through plasma membranes of the kidney epithelial cells by concentration gradients.

Active transport—membrane-bound ATPase pumps (such as Na⁺/K⁺ ATPase pumps) with carrier proteins that carry substances across the plasma membranes of the kidney epithelial cells by consuming ATP.

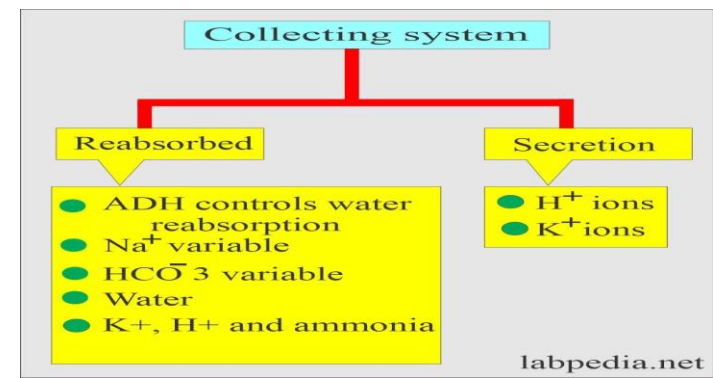
Cotransport—this process is particularly important for the reabsorption of water. Water can follow other molecules that are actively transported, particularly glucose and sodium ions in the nephron. **Tubular Reabsorption and Secretion**

Tubular reabsorption occurs in the PCT part of the renal tubule. Almost all nutrients are reabsorbed, and this occurs either by passive or active transport. Reabsorption of water and some key electrolytes are regulated and can be influenced by hormones. Sodium (Na⁺) is the most abundant ion and most of it is reabsorbed by active transport and then transported to the peritubular capillaries. Because Na⁺ is actively transported out of the tubule, water follows it to even out the osmotic pressure. Water is also independently reabsorbed into the peritubular capillaries due to the presence of aquaporins, or water channels, in the PCT. This occurs due to the low blood pressure and high osmotic pressure in the peritubular capillaries. However, every solute has a **transport maximum** and the excess is not reabsorbed.

In the loop of Henle, the permeability of the membrane changes. The descending limb is permeable to water, not solutes; the opposite is true for the ascending limb. Additionally, the loop of Henle invades the renal medulla, which is naturally high in salt concentration and tends to absorb water from the renal tubule and concentrate the filtrate. The osmotic gradient increases as it moves deeper into the medulla. Because two sides of the loop of Henle perform opposing functions, it acts as a **countercurrent multiplier**. The vasa recta around it acts as the **countercurrent exchanger**.

The loop of Henle (seen in Figure) acts as a countercurrent multiplier that uses energy to create concentration gradients. The descending limb is water permeable.

Water flows from the filtrate to the interstitial fluid, so osmolality inside the limb increases as it descends into the renal medulla. At the bottom, the osmolality is higher inside the loop than in the interstitial fluid. Thus, as filtrate enters the ascending limb, Na⁺ and Cl⁻ ions exit through ion channels present in the cell membrane. Further up, Na⁺ is actively transported out of the filtrate and Cl⁻ follows. Osmolarity is given in units of milliosmoles per liter (mOsm/L)



Osmolality

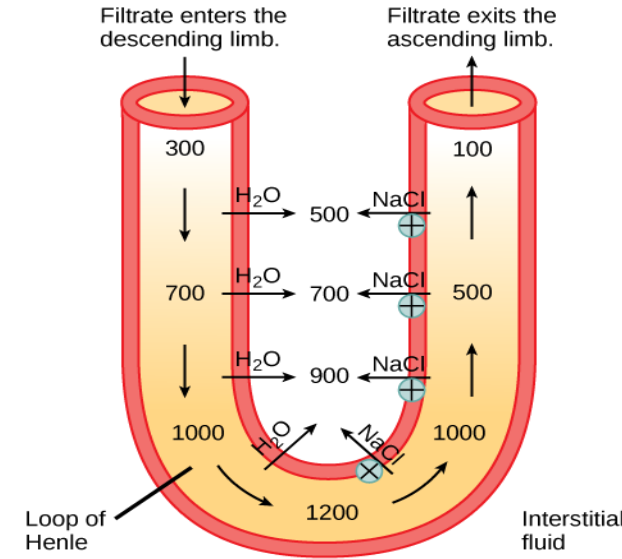
- 1-The number of solute particles dissolved in 1L of water
- 2-Reflects the solution's ability to cause osmosis
- 3-Body fluids are measured in milliosmols (mOsm)
- 4-The kidneys keep the solute load of body fluids constant at about 300 mOsm
- 5-This is accomplished by the counter current mechanism

Countercurrent Mechanism

- 1-Interaction between the flow of filtrate through the loop of Henle (countercurrent multiplier) and the flow of blood through the vasa recta blood vessels (countercurrent exchanger)
- 2-The solute concentration in the loop of Henle ranges from 300 mOsm to 1200 mOsm.
- 3-Vasa Recta prevents loss of medullary osmotic gradient equilibrates with the interstitial fluid.
- 4- Maintains the osmotic gradient.
- 5-Delivers blood to the cells in the area.

Urine formation requires

- Glomerular Filtration The amount of filtrate that flows out of all the renal corpuscles of both kidneys every minute.
- Tubular reabsorption many molecules are reabsorbed from the nephron into the capillary (diffusion, facilitated diffusion, osmosis, and active transport) i.e. Glucose is actively reabsorbed with transport carriers.
- Tubular secretion Substances are actively removed from blood and added to tubular fluid (active transport) i.e. H^+ , creatinine, and some drugs are moved by active transport from the blood into the distal convoluted tubule.



What is Urine Formation?

Urine formation is the physiological process through which the kidneys filter blood to get rid of waste materials, and excess substances, and keep the body's fluid and electrolyte balance.

This procedure involves **filtration**, **reabsorption**, **secretion**, and concentration adjustments inside the nephrons, the functional units of the kidneys, to create urine, which is ultimately excreted from the body.

This vital process is crucial for maintaining blood pressure, pH levels, fluid and electrolyte balance, and the removal of toxic substances from the body.

There are four basic processes in the formation of urine starting with plasma.

Filtration

Filtration is the mass movement of water and solutes from plasma to the renal tubule that occurs in the renal corpuscle.

About 20% of the plasma volume passing through the glomerulus at any given time is filtered.

This means that about **180 liters** of fluid are filtered by the kidneys every day.

Thus, the entire plasma volume (about 3 liters) is filtered 60 times a day! Filtration is primarily driven by hydraulic pressure (blood pressure) in the capillaries of the glomerulus.

The kidneys filter much more fluid than the amount of urine that is actually excreted (about 1.5 liters per day). This is essential for the kidneys to rapidly remove waste and toxins from the plasma efficiently.

Reabsorption

Reabsorption is the **movement of water and solutes from the tubule back into the plasma.**

Reabsorption of water and specific solutes occurs to varying degrees over the entire length of the renal tubule.

Bulk reabsorption, which is not under hormonal control, occurs largely in the proximal tubule.

Over 70% the filtrate is reabsorbed here. In addition, many important solutes (glucose, amino acids, bicarbonate) are actively transported out of the proximal tubule such that their concentrations are normally extremely low in the remaining fluid. Further bulk reabsorption of sodium occurs in the loop of Henle.

Regulated reabsorption, in which hormones control the rate of transport of sodium and water depending on systemic conditions, takes place in the distal tubule and collecting duct.

Secretion

Even after filtration has occurred, the tubules continue to secrete additional substances into the tubular fluid. This enhances the kidney's ability to eliminate certain wastes and toxins. It is also essential to regulation of plasma potassium concentrations and pH.

Excretion

Excretion is **what goes into the urine**, the end result of the above three processes. Although the original concentration of a substance in the tubule fluid may initially be close to that of plasma, subsequent reabsorption and/or secretion can dramatically alter the final concentration in the urine.

The amount of a particular substance that is excreted is determined by the formula:

Amount excreted = Amount filtered - Amount reabsorbed + Amount secreted

Urine Formation Glomerular Filtration

The first step in the production of urine is called glomerular filtration

Glomerular Filtration Rate (GFR) Affected by:

1-Total filtration surface area

2-Membrane permeability

3- Net Filtration Pressure

Filtration: the forcing of fluids and dissolved substances through a membrane by pressure occurs in the renal corpuscle of the kidneys across the endothelial capsular membrane (Bowman's) capsule. - **The resulting fluid is called the filtrate.**

The total filtration rate of the kidneys is mainly determined by the **difference between the blood pressure in the glomerular capillaries and the hydrostatic pressure in the lumen of the nephron**

Glomerular filtration rate (GFR):

This is the quantity of blood cleared of substances like creatinine and urea per unit of time.

The excretion rate of the kidney will reflect the following:

1-Renal plasma flow.

2-Glomerular filtration rate.

This substance used should not be reabsorbed, secreted, synthesized, or degraded in the nephron.

GFR may be measured by giving exogenous substances like Inulin clearance.

Urine composition Organic substances are:

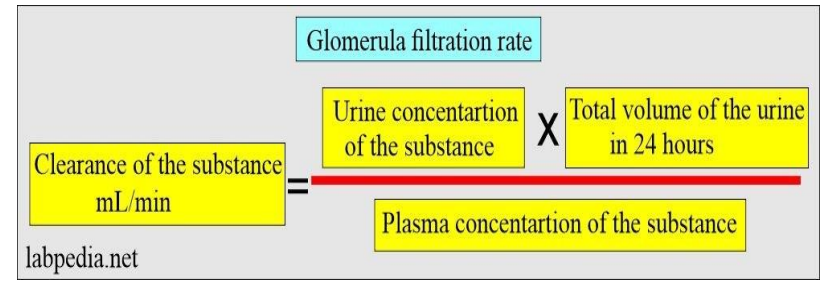
Urea , Creatinine , and Uric acid.

Inorganic substances are:

Chloride , Sodium , Potassium , and Traces of Ammonia.

Other substances are:

Hormone, Vitamins , Medications , Cells , Casts , Crystals , Mucous , and Bacteria.



The Role of ADH

- There is a high osmolarity of the renal medullary interstitial fluid, which provides the osmotic gradient necessary for water reabsorption to occur.
- Whether the water actually leaves the collecting duct (by osmosis) is determined by the hormone ADH (anti-diuretic hormone)
- Osmoreceptors in the hypothalamus detect the low levels of water (high osmolarity), so the hypothalamus sends an impulse to the pituitary gland which releases ADH into the bloodstream.
- ADH makes the wall of the collecting duct more permeable to water.
- Therefore, when ADH is present more water is reabsorbed and less is excreted.

Formation of Concentrated Urine Antidiuretic

hormone (ADH) inhibits diuresis.

This equalizes the osmolality of the filtrate and the interstitial fluid.

In the **presence of ADH, 99%** of the water in filtrate is **reabsorbed**

ADH-dependent water reabsorption is called facultative water reabsorption.

ADH is the signal to produce concentrated urine.

The kidneys' ability to respond depends upon the **high medullary osmotic gradient**.

Formation of Dilute Urine

Filtrate is diluted in the **ascending loop of Henle** if the **antidiuretic hormone (ADH)** or vasopressin is **not secreted**.

Dilute urine is created by allowing this filtrate to continue into the renal pelvis.

Collecting ducts remain impermeable to water; no further water reabsorption occurs.

Sodium and selected ions can be removed by **active and passive** mechanisms.

Urine osmolality can be as low as 50 mOsm (one-sixth that of plasma)

Urinary excretion rate =

(Filtration rate – Reabsorption rate + Secretion rate)

The Urine Flow Rate (or urine excretion rate) is a measurement of the quantity of urine produced in a specified period of time. Urine analyte concentrations from single determinations (spot urines) can vary depending on level of hydration. Due to this variation, the urine flow rate, when used in conjunction with analyte concentration measured on spot urine, can produce a better measure of analyte excretion rate, especially in the context of exposure to environmental chemicals.

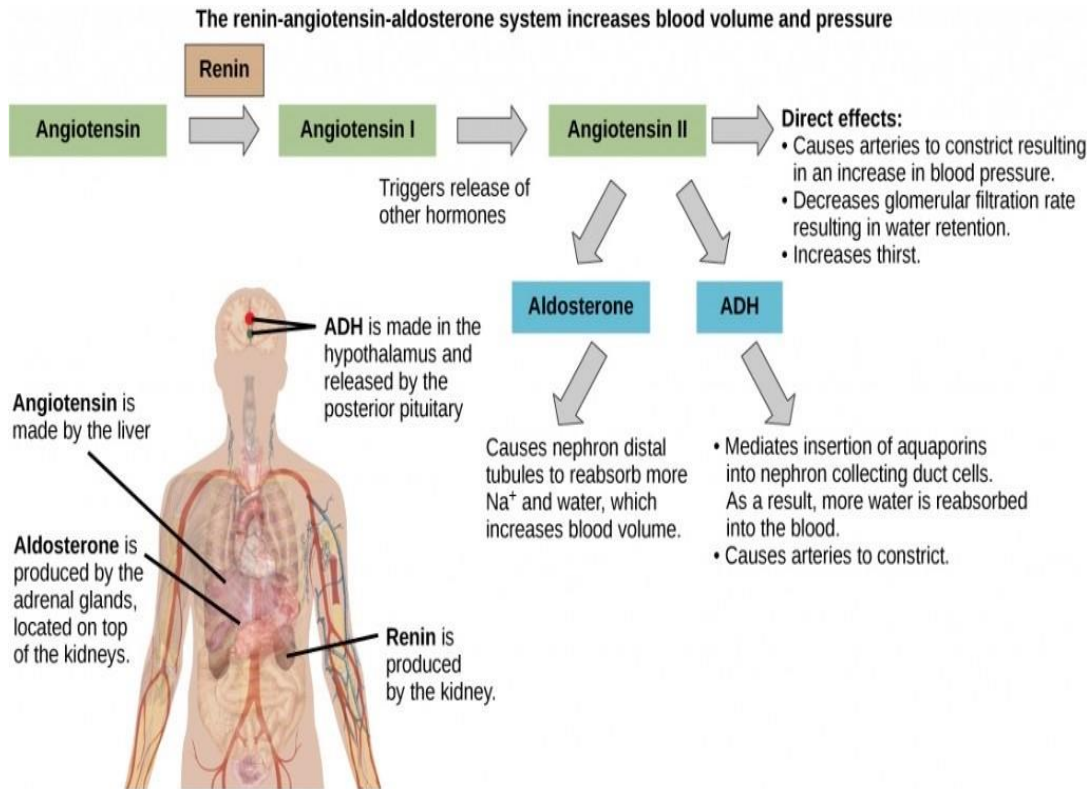
The urine excretion rate (mg/min) is the product of the urine flow rate (mL/min) and the urine analyte concentration (mg/mL).

Some of the hormones signal the tubules to alter the reabsorption or secretion rate, and **maintain homeostasis**.

Endocrine system regulates ion transport in the distal convoluted tubule by :

- 1-In the presence of **parathyroid hormone** ,the distal convoluted tubule reabsorbs more Ca^{+2} and excretes more phosphate.
- 2-When Aldosterone is present ,more Na^{+} is reabsorbed and more K^{+} excreted.
- 3-Atrial Natriuretic peptide causes the distal convoluted tubule to excrete more Na^{+} .
- 4-The tubule also secrete hydrogen and ammonium to regulate **pH**.

ADH and aldosterone increase blood pressure and volume. Angiotensin II stimulates release of these hormones. Angiotensin II, in turn, is formed when renin cleaves angiotensin.



When should we assess renal function?

- 1- Older age
- 2-Family history of Chronic Kidney disease (CKD)

- 3- Decreased renal mass
- 4- Low birth weight
- 5-Diabetes Mellitus (DM)
- 6- Hypertension (HTN)
- 7- Autoimmune disease
- 8-Systemic infections
- 9-Urinary tract infections (UTI)
- 10-Nephrolithiasis
- 11-Obstruction to the lower urinary tract
- 12-Drug toxicity

