Lec.2

Kidney Function Tests

Functions of a healthy kidney include maintaining a person's fluid balance, maintaining an acid-base balance; regulating electrolytes including sodium, potassium, and other electrolytes; clearing toxins; regulating blood pressure; and regulating hormones, such as erythropoietin; and activation of vitamin D.

Part of the assessment of kidney function includes the **measurement of urine and its contents**. Abnormal kidney function may cause too much or too little urine to be produced.

Renal function tests divided into 3 categories

1- Measurement of substances in the blood that are normally excreted by kidney (mainly urea , creatinine & uric acid). **2-** Determination of renal clearance.

3-Chemical & physical analysis of urine

- Biochemical Tests of Renal function tests:
- 1- Measurement of GFR:
- 1- Clearance tests.
- 2-Plasma Creatinine.
- 3- Urea, Uric Acid , and β 2-Microglobulin.
- 2- Renal Tubular function tests:
- 1- Osmolality measurements.
- 2- Specific Proteinurea.
- 3- Glucosuria.
- 4- Aminoaciduria.
- 3- Urinanalysis:
- 1- Appearance. 2- Specific Gravity . 3- pH. 4- Osmolality.
- 5- Glucose. 6- Protein. 7- Urinary sediments.

Symptoms of kidney problems

Symptoms that may indicate a problem with the kidneys include:

1-High blood pressure.

2-Blood in the urine.
3-Frequent urges to urinate.
4-Difficulty beginning urination.
5-Painful urination.
6-Swelling of the hands and feet due to a build up of fluids in the body.

A single symptom may not mean something serious. However, when occurring simultaneously, these symptoms suggest that the kidneys aren't working properly. Kidney function tests can help determine the reason.

Type of kideny function test

1- Urinalysis.
2- Serum creatinine test. 3-
Blood urea nitrogen (BUN).
4- 24h urine sample.
5- Electrolytes.
6- Estimated glomerular filtration rate (GFR).

- **Glomerular Filtration Rate**

Properties of the substances used to measure GFR

❖Properties of the substances used to measure GFR include:

1. Freely filtered by glomerulus.
2. Should not be reabsorbed/ secreted.
3. Should not be metabolized by the kidney.
4. Should not be toxic .
5. Should not be affected by its dietary intake.

❖Endogenous substances used for clearance test : Creatinine and Urea

❖Exogenous substance used for clearance test : Inulin

Calculation of Renal Clearance

❖Renal clearance depends on the **plasma concentration of the substance** ,its **excretory rate** ,which in turn depends on the **GFR** and **renal plasma flow**.

❖GFR can be measured by determining the excretion rate of a substance which is filtered through the glomerulus but neither reabsorbed nor secreted by the renal tubules.

❖ Clearance (C) of a substance(in ml /min) = U X V / P

U= mg/L concentration of a substance in urine

V = volume of urine in ml excreted per min (24hr urine volume/24x60)

P = mg/L concentration of a substance in plasma/serum

Concentration of a substance in urine and plasma /serum should be expressed in same units (mg/dl or mmols /L).

Clearance of a given a substance is determined by mode of excretion .

❖The maximum rate at which the plasma can be cleared of any substance is equal to the GFR.

Glomerular filtration rate (GFR) is the **volume of fluid filtered from the renal (kidney) glomerular capillaries into the Bowman's capsule per unit time.**

Central to the physiologic maintenance of GFR is the differential basal tone of the afferent and efferent arterioles , the **filtration rate** is dependent on the **difference between the higher blood pressure created by vasoconstriction of the input or afferent arteriole versus the lower blood pressure created by lesser vasoconstriction of the output or efferent arteriole**

A GFR test estimates how much blood passes through these filters each minute. The best overall indicator of the glomerular function is the glomerular filtration rate (GFR).

GFR is the rate in millilitres per minutes at which substances in plasma are filtered through the glomerulus, (the clearance of a substance from the blood).

The characteristics of an ideal marker of GFR are as follows:

1-It should **appear endogenously** in the plasma at a **constant rate**.

2-It should be **freely filtered** at the glomerulus.

3-It can be **neither reabsorbed nor secreted** by the renal tubule. 4-It should **not undergo extrarenal** elimination.

Renal Clearance

The volume of plasma that is cleared of a particular substance in a given time:

RC = UV/P

RC = renal clearance rate

U = concentration (mg/ml) of the substance in urine

V = flow rate of urine formation (ml/min)

P = concentration of the same substance in plasma

Renal clearance tests are used to: Determine the GFR

Inulin Clearance tests

❖**Inulin** :

1. a plant carbohydrate(polysaccharide composed of fructose units) .
2. Not metabolized by the human body/renal tubules.
3. Inulin is freely filtered by the glomerulus and is neither reabsorbed neither secreted in the tubules of kidney. Therefore GFR can be calculated by measuring Clearance of Inulin(close to GFR).
4. Inulin Clearance =125 ml/min
5. Inulin is administered intravenously(exogenous) to measure GFR. Therefore Inulin Clearance tests is not preferred but it is the method of choice when accurate determination of GFR is required.

❖^{51}**Cr-EDTA** satisfy similar criteria. The GFR is calculated from the rate of fall of plasma radioactivity as the isotope is cleared .

• **Creatinine and Urea** are employed and preferred for measurement of Clearance as they are present in the blood (endogenous).

Disadvantages of measurement of inulin clearance Test

❖**Disadvantages of measurement of inulin clearance Test :**

1. The need for its intravenous administration.
2. The technical difficulty of its analysis.

Creatinine Clearance

It is a measure of the **glomerular filtration rate.** It is defined as **the quantity of blood cleared of a substance per unit time and depends on the plasma concentration of the substance and excretion rate of the kidney which reflects GFR and renal plasma flow.**

Creatinine clearance is the amount of creatine in the urine, divided by the concentration in the blood plasma, over time. Creatinine is used because it fulfils these requirements (though not perfectly), and it is produced naturally by the body.

The result of this test is an important gauge used in assessing excretory function of the kidneys.

Indications for creatinine clearance

Creatinine clearance reflects the Kidneys ability to excrete creatinine.it is used to measure the glomerular filtration rate (GFR) of the kidney.

This test will give information on the renal functions like:

1-Obstruction of the kidney.

2-Acute or chronic renal failure.

3- Dysfunction due to other causes like heart failure.

Creatinine clearance can be used to diffreneciate between the glomerular disease in comparison to diffuse chronic structural changes.

This is good test to assess the overall renal functional damage.

If one kidney is knocked out then another kidney is normal, can **compensate for the filtration**, and GFR will be in the normal limit.

Creatinine clearance depends upon:

1-With each decade of life, CrC decreases 6.5 mL/min because of a decrease in GFR.

2-Urine collection is for 24 hours, so any error in the collection will give false results.

3-Muscle mass varies among the people will also affect the CrC.

4-Decreasing muscle mass will give decreased values.

5-Ingestion of a large amount of meat for the time will increase the CrC

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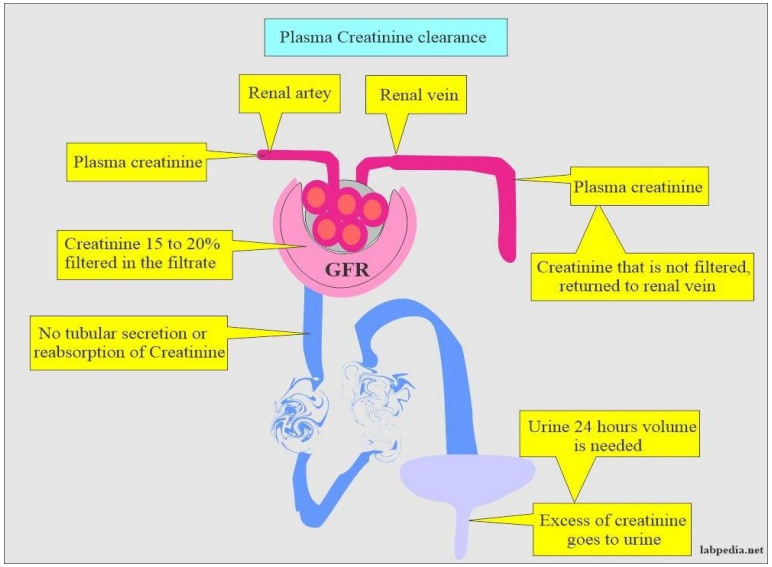
- **Creatinine**

Creatinine is a **metabolic product** of creatine-phosphate dephosphorylation in the muscles , which has an important role in the contraction of muscles.

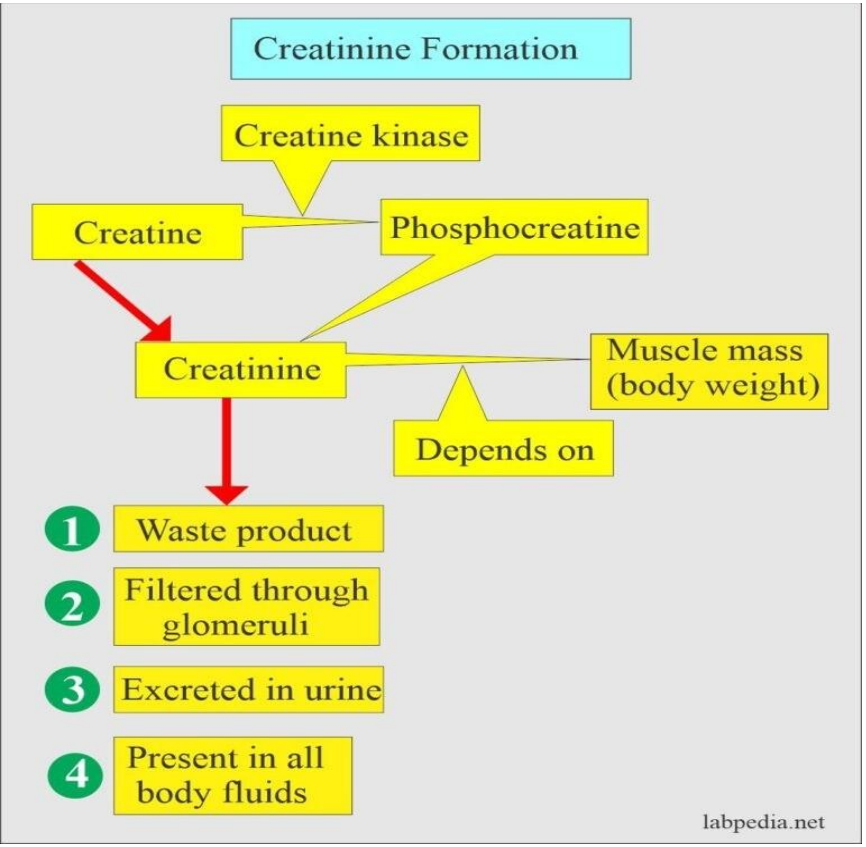


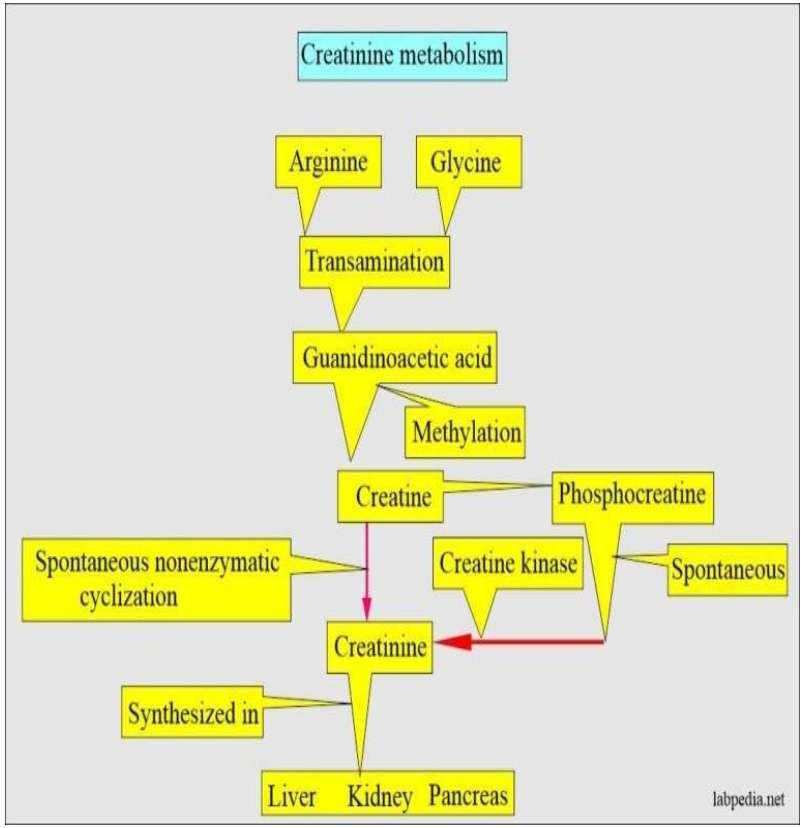
The daily production of creatine and creatinine depends upon the muscle mass, which fluctuates very little. Most of the creatinine production is stable thorough out the day

Normally, creatinine is filtered out of the blood by the kidneys.

The responsible for cleaning blood, the material that's removed from blood leaves the body by urine.

Creatine is present in muscle to mediate **energy transfer during muscle contraction.** Through interconversion of creatine and phosphocreatine about **2%** of muscle creatine is spontaneously converted into creatinine daily which appears in urine as a waste product.





Creatinine is freely and mainly excreted by the kidney so this will reflect the **filtration power** of the kidney.

Women excrete less creatinine than men because of less muscle mass.

The daily excretion of the creatinine is relatively constant and is ±15% for a person per day.
Creatinine excretion is **not affected** by protein metabolism or other external factors.

So serum creatinine is the best measure of glomerular function (filtration).

Creatinine is raised only when the 50% function of the kidney is lost.

There is a minimal amount of creatinine in the urine from tubular secretion.
Creatinine in the urine increases as the creatinine concentration rises in the blood.
The kidneys entirely excrete creatinine, so directly proportional to kidney function.

Creatine Degradation

1. Creatine and creatine phosphate spontaneously form creatinine as an end product.
2. Creatinine is excreted in the urine.
3. Serum creatinine is a sensitive indicator of kidney disease (Kidney function test).
4. Serum creatinine increases with the impairment of kidney function.

The increased creatinine level is seen in:

1-Renal function impairment is both acute and chronic disease.
2-Postrenal obstruction of urine.
3-Decrease in the blood perfusion because of any reason.
4-Gigantism and Acromegaly.
5-Injury to the muscles (Rhabdomyolysis).
6-Myasthenia gravis.
7-Poliomyelitis.

Relationship between glomerular filtration rate (GFR)and Serum creatinine

- It is observed that the **GFR** must fall to about 50% of its normal value before significant increase in **Serum creatinine** occurs .
- Normal **Serum creatinine** level dose not necessarily mean that all is well with the kidney.
- Loss of 50% of the functions of nephrons leads to doubling of Serum creatinine concentration(approximate).

Correction of creatinine clearance for body surface area

- It is useful to correct the clearance value for surface area especially in children ,person with short and tall frame .
- creatinine clearance = U X V X 1.73/ P X A
- After Correction for body surface area, creatinine clearance becomes comparable for male , female and children which is 100 ml/min/1.73 sq. meter.

8-Muscular dystrophy.
9-Dehydration due to loss of body fluids.
10-It may be seen in pregnancy during eclampsia and preeclampsia.

The decreased creatinine level is seen in: 1-Old-age.
2-Decreased muscle mass.
3-Pregnancy, especially in the first and second trimesters.
4-Advanced and severe liver disease.

Factors that affect serum creatinine

5-Inadequate dietary intake.

Increases with:	Decreases with:
• low GFR	• high GFR
• increased muscle mass	• decrease muscle mass
• skeletal muscle damage	• advanced age
• high meat or creatine uptake	
• drugs such as cimetidine, trimethoprim, triamterene, and amiloride	

Increased values of creatinine clearance:

This has no clinical significance, suspect some error in the collection procedure.

Pregnancy
Exercise.

High cardiac output syndrome.

Decreased values:

When done with all precautions then it is a very sensitive indicator of decreased glomerular filtration rate.

Diseases of the kidney with impaired renal function.

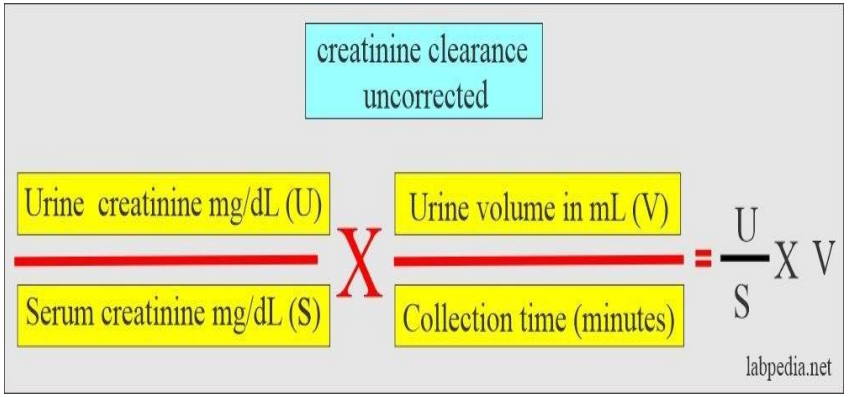
Congestive heart failure.

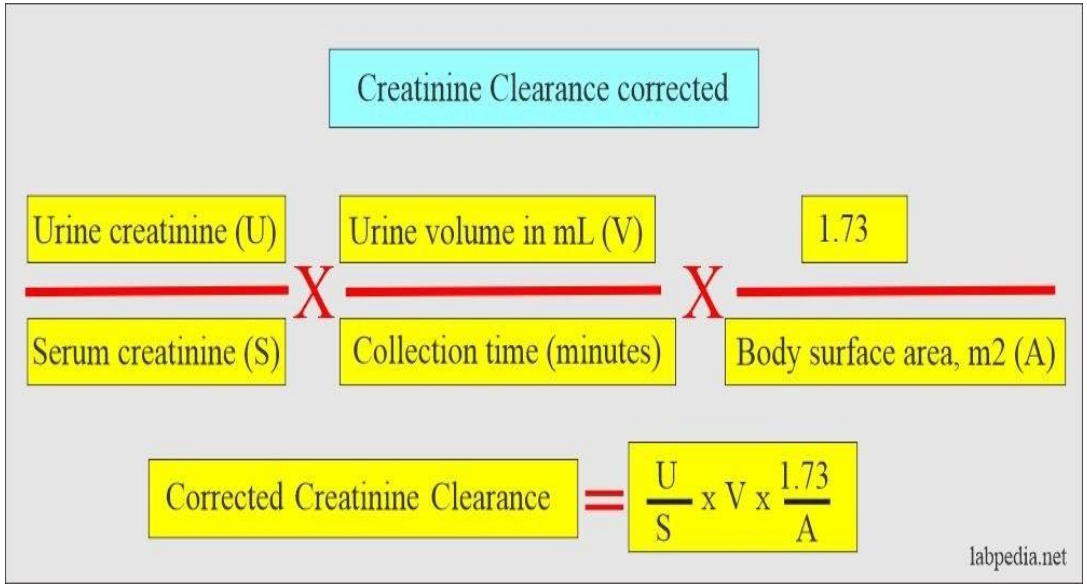
Cirrhosis with ascites.

Shock.

Dehydration (loss of body fluids).

Bladder outlet obstruction.





Advantages of creatinine clearance method:

1- Sensitive indicator for GFR.

2- It is a normal metabolite of the body.

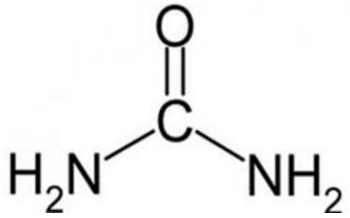
3- It does not require I.V. administration.

4- Estimation of creatinine is simple.

Collecting a 24-Hour Urine Specimen

- This is required for test of renal function and urine composition.
- The entire volume of urine from a 24-hour period is collected.
- If urine is accidentally discarded or contaminated or patient is incontinent, restart time period.
- Pt. must void just before the "start" time – this voiding is discarded

5- In early stages it has got advantages over serum creatinine.



Disadvantage of clearance test:

1- Should measure 2 parameters

2- Need volume of urine /24 hours.

3- Need admission of the patient to the hospital.

4- In established renal disease, clearance test is not helpful because the clearance test fixed at low level.

Blood Urea

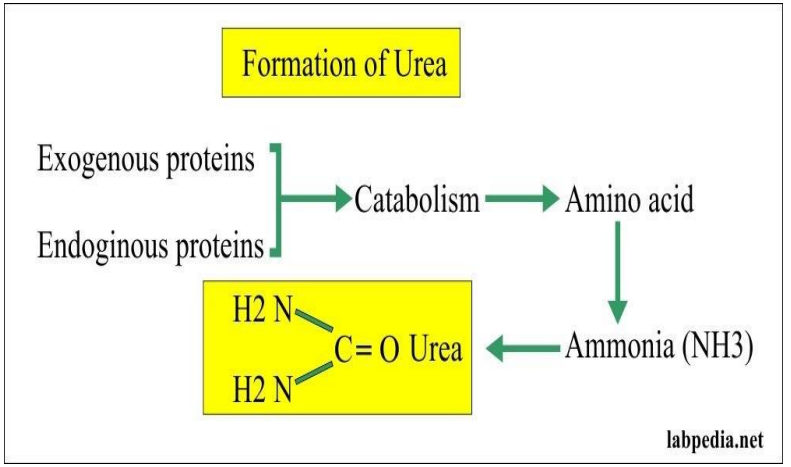
A common blood test urea nitrogen (BUN) test detect important information about how well the kidney and liver are working . (BUN) • measure the amount of urea nitrogen that's in the blood.

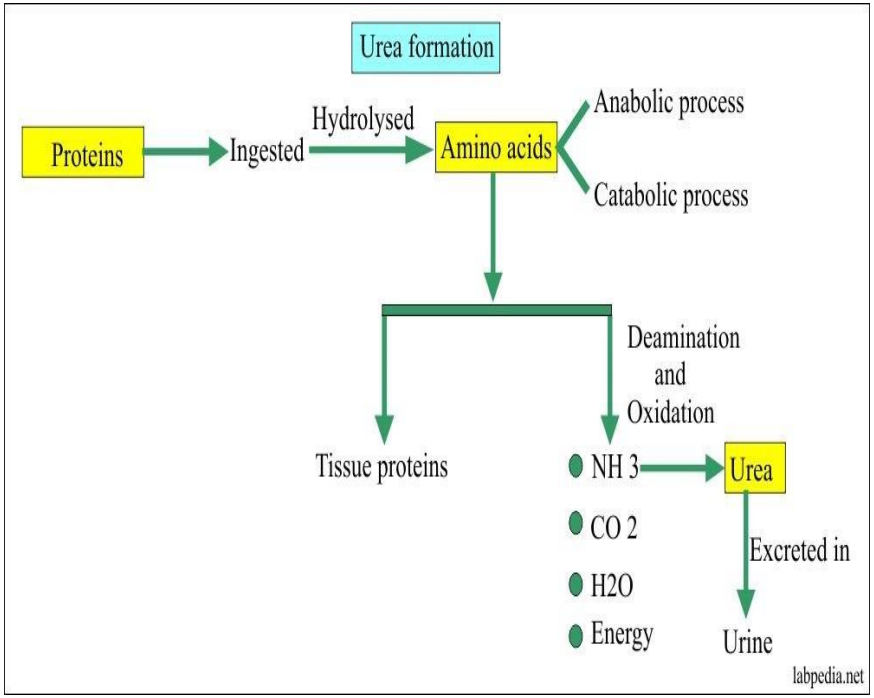
Nitrogen is an essential element of amino acids, which are the building blocks of protein

When we eat protein-rich food, it is broken down by the digestive system into amino acids. These amino acids has 1 of 2 fates: It is either used to make protein for muscle formation or degraded in the liver to form urea

Indications

To assess renal function.
As a routine test in the patient with dialysis.
To assess liver function.
This may be part of the routine test..





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Urea is **freely filtered** and then partially **absorbed** by the nephron. **The BUN** is used as the **index of glomerular function** in the production and its excretion of urea.

Urea reabsorption is **increased in hypovolemia** so BUN will underestimate Glomerular filtration rate (GFR) and more in hypovolemia.

Blood Urea level

- Normal Blood Urea level : 20- 40 mg/dL
- Estimation of Blood Urea level is done by enzymatic method using urease and glutamate dehydrogenase .
- Blood Urea level is expressed in terms of its nitrogen(nitrogenous substances analyzed by kjeldahl method).
- Blood Urea level = Blood Urea nitrogen (BUN) x 2.14♣
- Molecular weight of urea = 60 and each 60 gram of Urea contains 28 gram of nitrogen→ 60/28 ♣

Since route of urea excretion is through kidney ,blood urea level is estimated to assess kidney function.

As urea level is affected by dietary protein and other pre-renal factors ,serum creatinine estimation should also be done simultaneously.

Clearance of the urea:

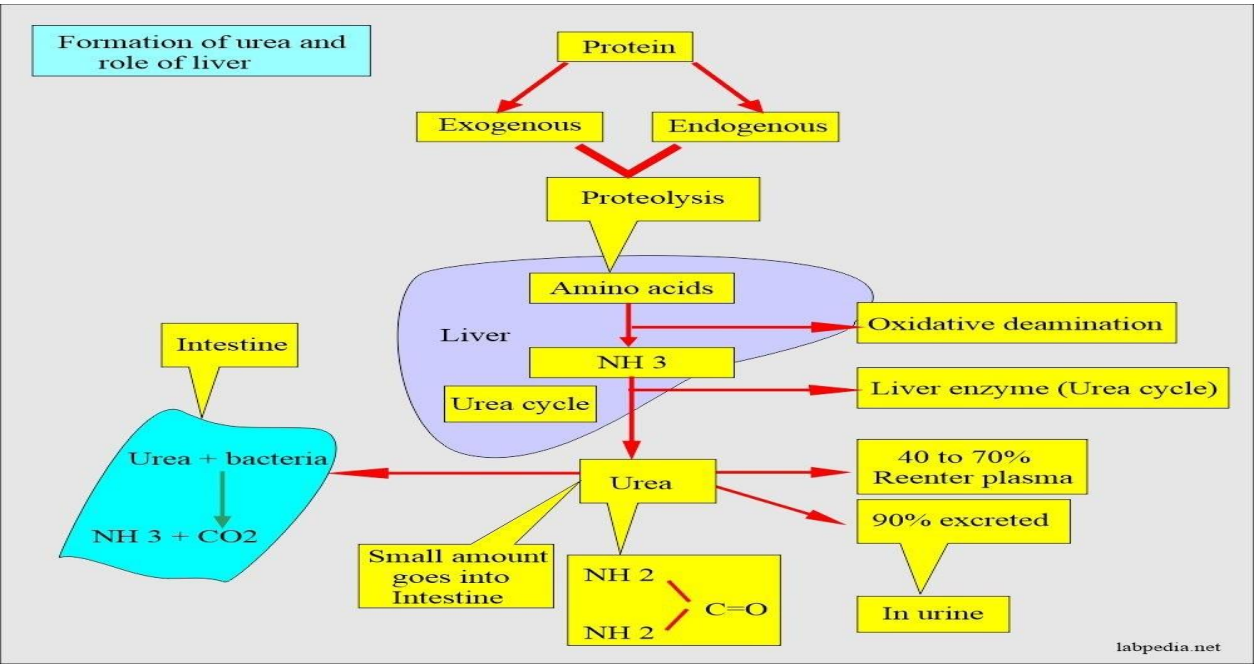
through the kidney in the urine.

excretory function of the kidneys.

BUN measures the nitrogen part of the urea.This BUN or urea excreted

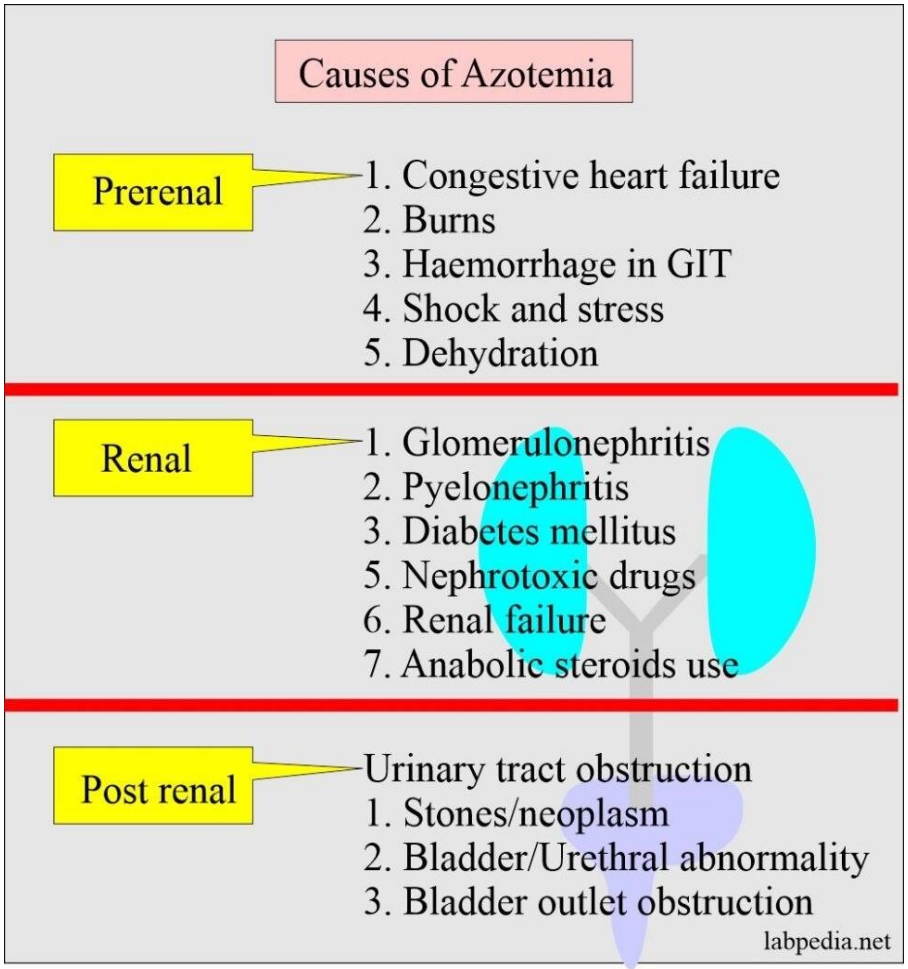
The **measurement of urea** nitrogen gives an idea of the **ratio between excretion and production of urea.** Ammonia molecules combine to form urea.The urea through blood goes to the kidney and excreted in the urine.

So BUN depends upon the metabolic function of the liver and



The BUN is directly related to the metabolic function of the liver and the excretory function of the kidneys.
A high protein diet may increase the BUN, and low protein intake may decrease its level.
In chronic renal diseases, the BUN level correlates better than creatinine with the sign and symptoms of the patient.
As the synthesis of BUN depends upon life, patients with severe primary liver disease will have decreased BUN.

In combined liver and renal disease, as in hepatorenal syndrome, the BUN may be normal because of poor liver function resulting in decreased formation of urea.
The BUN is **less accurate than creatinine** for renal diseases.
In chronic renal diseases, BUN correlates better with the symptoms than the creatinine.



- States associated with elevated levels of urea in blood are referred to as **uremia or azotemia.**
  - **Causes of urea plasma elevations**
- 1- Prerenal: renal hypoperfusion
- 2- Renal: acute tubular necrosis
- 3- Postrenal: obstruction of urinary flow

Decreased Urea (BUN) seen in:

1-Liver failure.

2-Malnutrition and a low protein diet.

3-Impaired absorption of Celiac disease.

4-Syndrome of inappropriate antidiuretic hormone secretion.

5-Pregnancy.

6-Overhydration.

Diagnostic importance of Blood Urea level :2

❖Causes of increased Blood Urea levels :

Prerenal	Renal	Postrenal	Medication
Dehydration	Acute glomerulonephritis *	Stones in urinary tract	ACE inhibitors
Severe vomiting	Nephrosis	Enlarged prostrate	Acetaminophen
Intestinal obstruction	Malignant hypertension	Stricture of the urethra	Aminoglycosides
Diarrhea	Chronic pyelonephritis	Tumors of bladder affecting the ureteric junction	Amphotericin B
Diabetic coma	Renal tuberculosis		Diuretics
Severe burns	Mercurial poisoning		NSAIDs
Fever	Nephritis		
Severe infections	* Values may be as high as 300mg/dl		

Gastrointestinal bleeding.
Trauma.

7-Nephrotic syndrome.

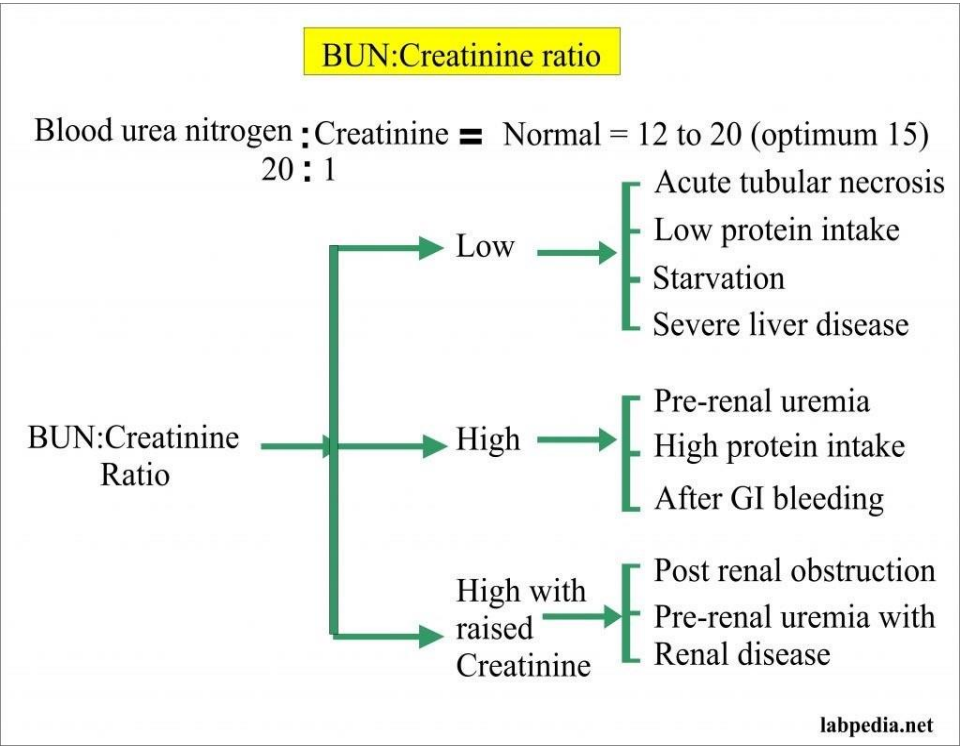
$$\text{BUN/Creatinine Ratio} = \frac{\text{Serum BUN}}{\text{Serum Creatinine}}$$

BUN/Creatinine ratio is raised, this is suggestive of:
Prerenal azotemia:
There is poor renal perfusion like hypovolemia or hypotension.
Postrenal azotemia:
Seen in congestive heart failure.
Urinary tract obstruction.

BUN/Creatinine ratio is decreased suggestive of:

This is rare and seen in: Dietary protein deficiency Severe liver disease

- **Tests of Tubular Function**
- The renal tubules play an important role in **reabsorption of electrolytes, water, and maintaining acid-base balance.**
- These tests are not used so much in the routine clinical works, which include:



- **A-** Concentration – Dilution studies.

B- Acid-base balance studies.

- Electrolytes, sodium, potassium, chloride, magnesium, and phosphate can be measured in urine as well as glucose. Measurement of urine **osmolality** allows for assessment of **concentrating ability of urine tubules**.

Mechanism of Urine Concentration In order for the kidneys to be able to concentrate urine, **two important factors must be present:**

1- Hyperosmolar interstitium in the renal medulla surrounding the collecting duct.

2- The main idea is that if the interstitium surrounding area (the collecting duct) is hyperosmolar and the collecting duct is permeable to water, water will move –by osmosis- into the interstitium leaving the tubular fluid concentrated.

- **Acid-base balance studies**

- Acid-base balance is essential for life.

- The tubules help to maintain the daily hydrogen ion balance by the:
- **1-** Reabsorption of bicarbonate HCO_3^- .
- **2-** Production & excretion of ammonia NH_3.
- **3-** Secretion of hydrogen ion H^+.

Definition of acid-base balance:

This regulation of the extracellular fluid environment involves the ratio of acid to base, measured clinically as pH.

The regulation of intracellular and extracellular electrolytes concentration depends on the following factors:

1. There is a balance between the intake of substances in a diet containing electrolytes and the electrolytes' output in feces, urine, and sweating.
2. It also depends upon the transport of fluids and electrolytes between ECF and ICF. Physiological changes in the concentration of H^+ ions in the blood lead to acid-base balance.

Acid-base balance and electrolytes facts:

1.Electrolytes in different compartments are present in the bodies.

2.There are three compartments in our body, and these communicate with each other.

1. Intracellular fluid.
2. Extracellular fluid (Vascular fluid containing blood and lymph).
3. Interstitial fluid.

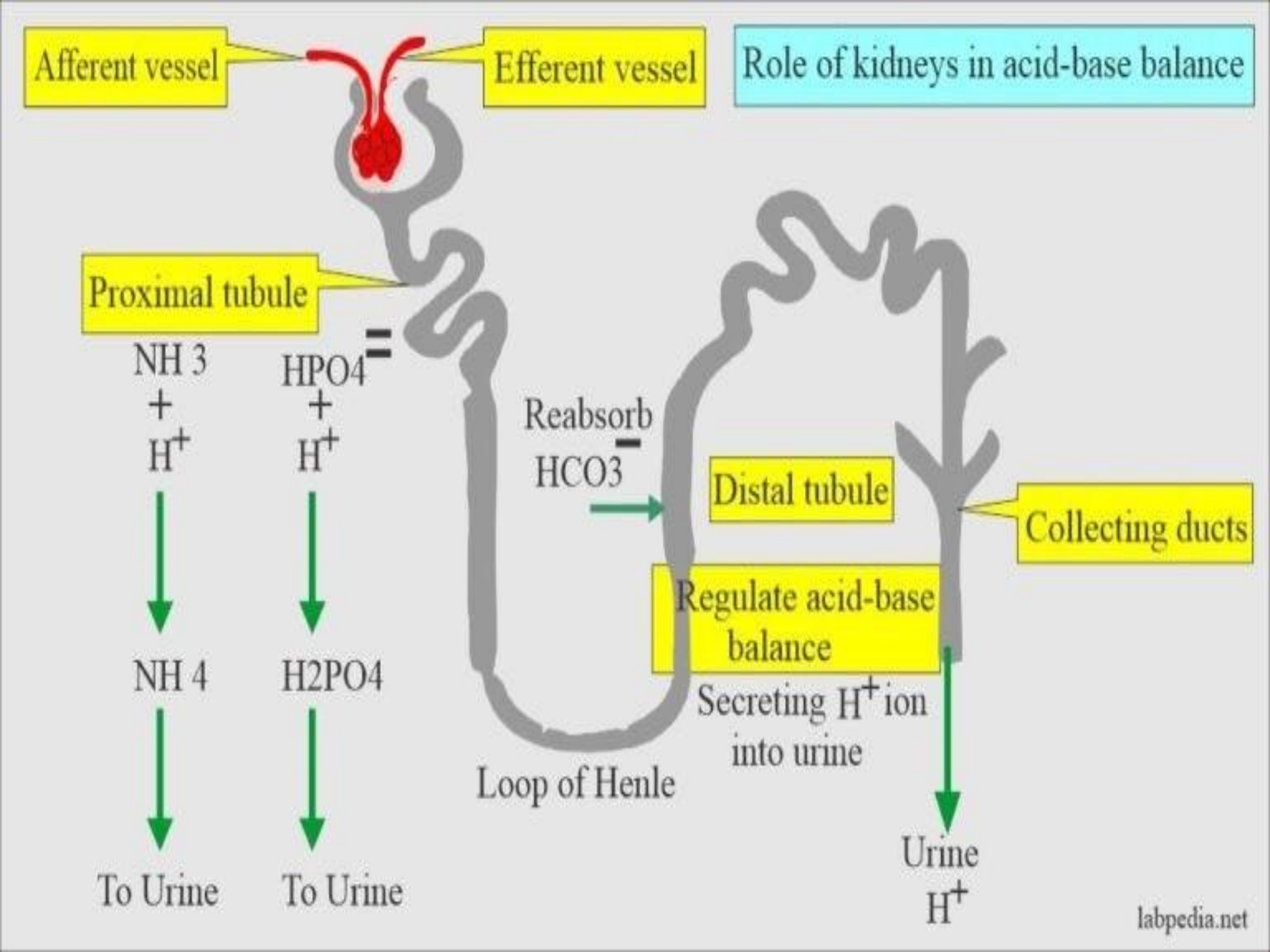
3.There are continuous movements of electrolytes and fluid among these compartments to maintain homeostasis, cell metabolism, and organ functions.

Renal buffering system

The **distal tubule** of the kidneys regulates acid-base balance by **secreting** the **H+** ions in the urine and **reabsorbs** the **HCO3–.** Dibasic phosphate (HPO4—) and ammonia (NH3) are two important renal buffer.

The renal buffering of H+ ions requires **CO2 and water (H2O) to form the H2CO3.**
The enzyme c**arbonic anhydrase** catalyses the reaction.

H+ ions are **secreted** from the tubular cells and buffer in the lumen by PO4— and NH3 = H2PO–3 + NH4+. The rest of HCO3– is reabsorbed.


Afferent vessel
Efferent vessel
Role of kidneys in acid-base balance
Proximal tubule
NH 3
+
H+
HPO4=
+
H+
Reabsorb
HCO3-
Distal tubule
Collecting ducts
Regulate acid-base balance
Secreting H+ ion into urine
NH 4
H2PO4
Loop of Henle
To Urine
To Urine
Urine
H+
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Carbonic acid-bicarbonate buffering system:

This buffer system operates both in the lungs and kidneys,it is the major extracellular buffer system.

Lungs can decrease the **carbonic acid** by blowing out the CO2 and leaving water behind.

Kidneys can reabsorb HCO3- or regenerate new HCO3- from CO 2 and water.

Both the systems are very efficient because:

1-HCO3– is easily reabsorbed or regenerated by the kidneys. **2-**

The lungs adjust acid concentration.

Compensation of the pH is done as:

1-The respiratory system compensates pH by decreasing or increasing CO2 by changing the rate of respiration.

2-The renal system produces more acidic or more alkaline urine.

Excretion of Hydrogen (H+) Ions

There are 2 methods by which this is achieved:

1- Excretion of H+ ions in the form of dihydrogen phosphate (H2PO4–).

2- Excretion of hydrogen ions in the form of ammonium (NH4+).

Bicarbonate (HCO3–) Reabsorption

H+ ions are secreted into the lumen via the sodium-hydrogen (Na+-H+) exchanger to combine with any filtered bicarbonate.

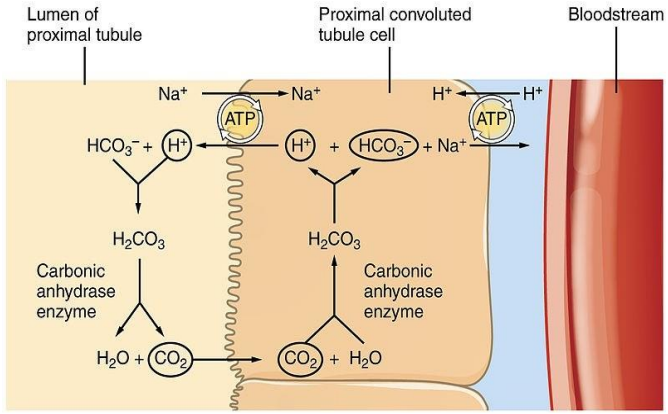
This then forms carbonic acid (H2CO3), catalysed by **carbonic anhydrase** on the luminal side.

Carbonic acid then **dissociates** into carbon dioxide and water, which both can diffuse into the cell.

Here, the reaction is undone, and carbonic anhydrase inside the cell converts carbon dioxide and water to carbonic acid, which then dissociates into H+ and HCO3– ions.

HCO3– can then be transported into the blood whilst the H+ ions can be transported back into the lumen for the cycle to repeat.

Bicarbonate (HCO3–) Production.

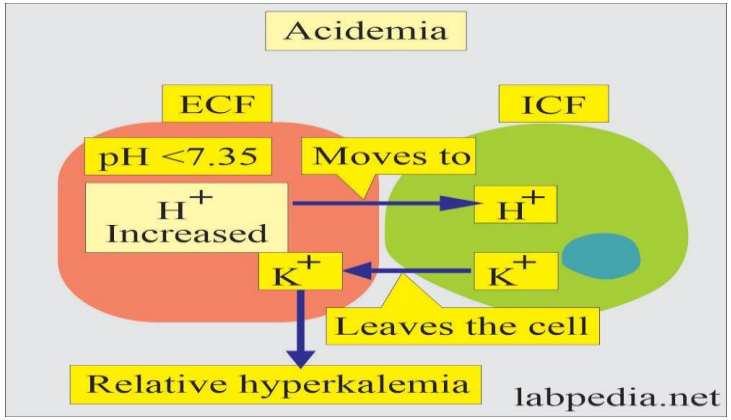


Acidosis (Acidemia) 1-

A systemic increase in the H^+ ions concentration is called **acidosis (academia).**

2.Metabolic acidemia: There is an excess accumulation of acids like lactic acidosis, ketoacidosis, and organic acids due to metabolic disorders.

3.Respiratory academia: It occurs when there is an excess of CO2, leading to carbonic acid. It occurs in chronic obstructive pulmonary disease, pneumonia, and severe asthma.



Alkalosis (Alkalemia)

1.A systemic decrease in the H^+ ions is called **alkalosis (alkalemia).**

2.Metabolic alkalemia: It occurs when there is an excess of $HCO3^/$ or a decrease in non-carbonic acid.

2. It may be seen in severe vomiting.
3. Excessive intake of alkaline substances.
4. In some kidneys disease.

3.Respiratory alkalemia: There is a decrease in the CO2 in the blood, leading to a decrease in carbonic acid.

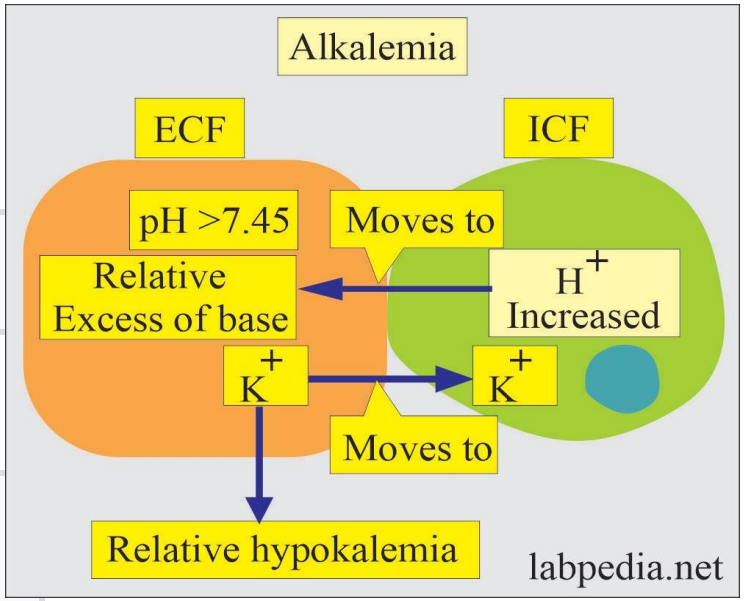
It is seen in hyperventilation leading to excessive elimination of CO2.

Must regulate acid-base balance within a narrow range for the body to function normally.

A very slight change in the pH will affect the body.

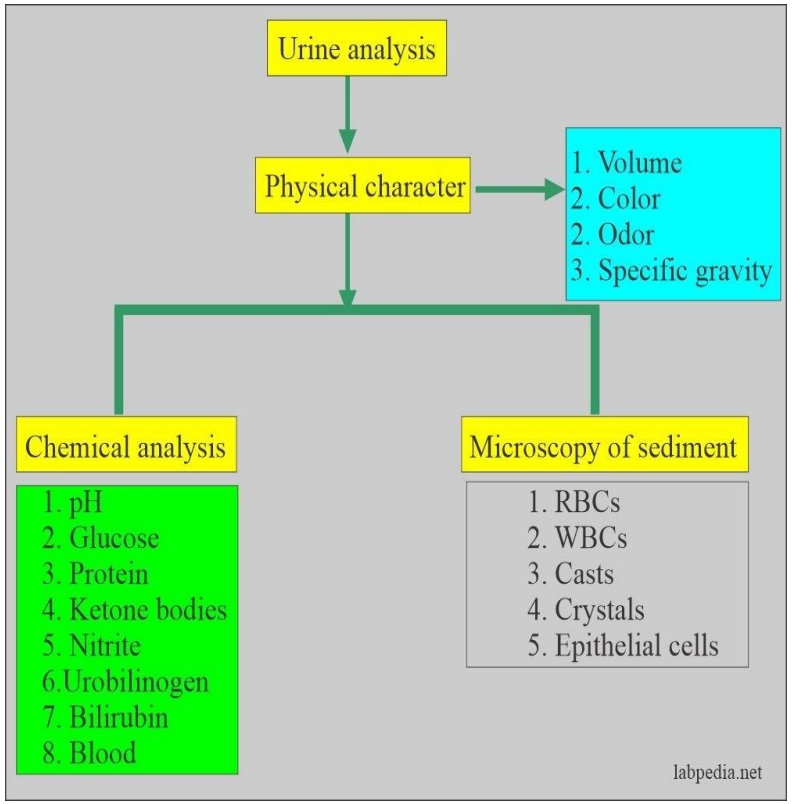
A slight change in the H^+ ions can change the cell and tissue.

•For normal body functions, the pH range is very narrow and needs to be maintained within these limits.



pH value	Effects on the body
<6.8	This is incompatible with life.
<7.2	The cell's functions are seriously impaired.
<7.35	This indicate acidosis
7.37 to 7.43	**This indicates a normal range**
>7.45	This indicates alkalosis
>7.55	The cell functions are seriously affected
>7.8	This is incompatible with the life

pH significance in our life:

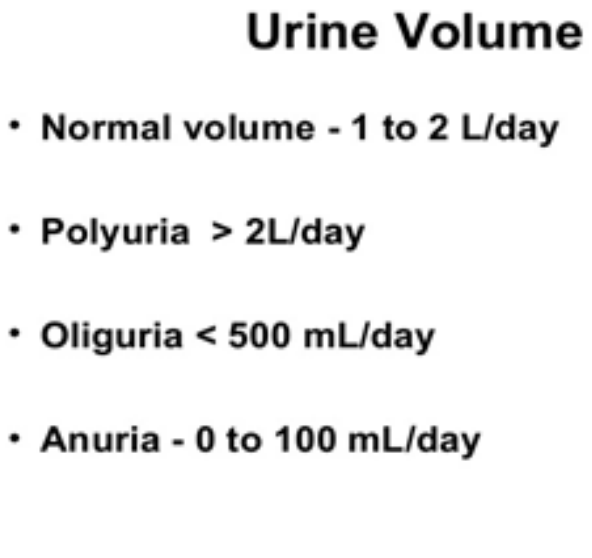


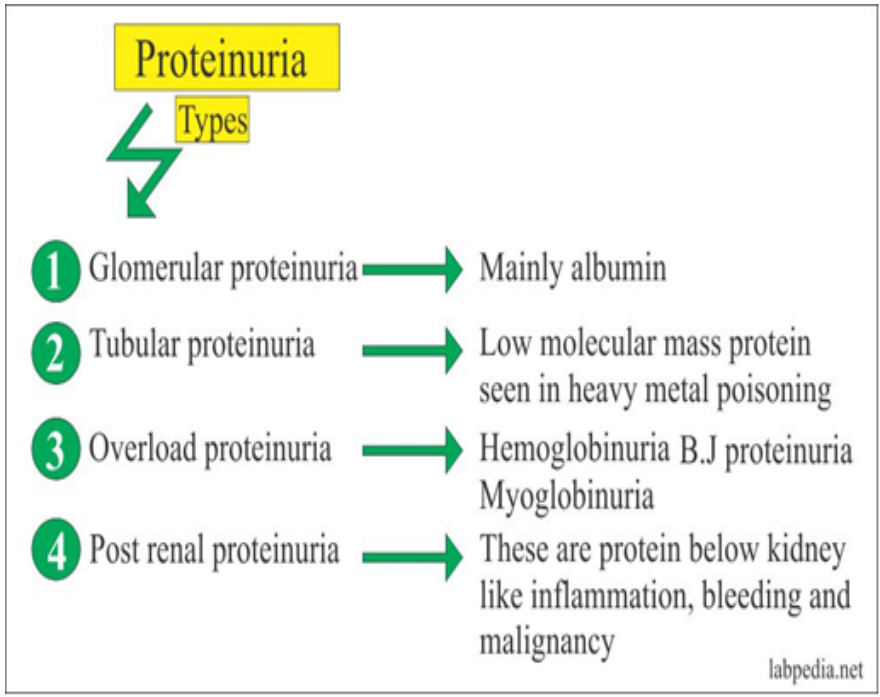
Theoretically, acidification of urine could be brought about **either by the 1- secretion of hydrogen ions into the tubular fluid or 2- by the selective absorption of a buffer base** (a substance capable of accepting hydrogen ions; e.g., filtered bicarbonate).
Both filtration and secretion are essential to hydrogen ion excretion and that **both proximal and distal convoluted tubules** are involved.
The **bulk of the bicarbonate filtered** at the glomerulus is reabsorbed in the **proximal tubule,** from which it passes back into the peritubular capillaries. **This mechanism is designed to keep the normal plasma bicarbonate concentration constant at about 25 millimoles per litre.**

- Colour & appearance
- The normal urine is a yellow coloured due to the presence of small amount of urobilin & hematoporphyrin.
- Red urine: may result from presence of intact R.B.C., free Hb, &myoglobin (which result from crushing large muscle) or it might result from ingestion of large amount of beet root.
- Milky color: is due to pus or fat (leakage of lipoprotein into urine due to defect in tubular reabsorption of lipoprotein as nephrotic syndrome)
- Brown to dark brown (tea colour): is caused by bilirubinaemia.
- Normal urine is clear, turbidity usually due to the presence of pus, protein, fat or salts of uric acid, phosphate & oxalate.

Urine dipstick provides qualitative analysis of different analytes in urine using chemical analysis(dry chemistry) methods to detect for the presence of protein, glucose, blood, ketones, bilirubin, urobilinogen, nitrite, and leukocyte esterase.

Volume of urine

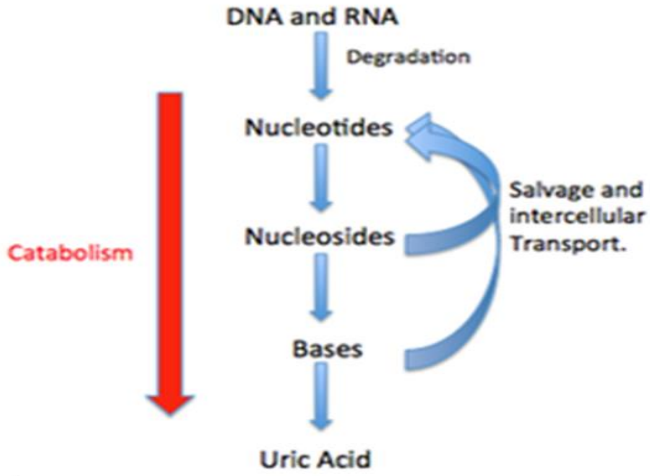




- Uric acid
- Is the major product of the catabolism of the purine nucleosides, (adenosine and guanosine)
- Purines are derived from catabolism of dietary nucleic acid (nucleated cells, like meat) and from degradation of endogenous nucleic acids.

Dietary nucleic acids(foods rich in nucleoproteins such as liver , pancreas and meat are mostly directly converted into uric acid.

Adenine, inosine , hypoxanthine and guanine are catabolised into xanthine. Then it is converted into uric acid by action of the enzyme xanthine oxidase.



Xanthine oxidase is a form of xanthine oxidoreductase, a type of enzyme that generates reactive oxygen species.

These enzymes catalyze the oxidation of hypoxanthine the to xantheine and can further catalyze the oxidation of xanthine to uric acid.

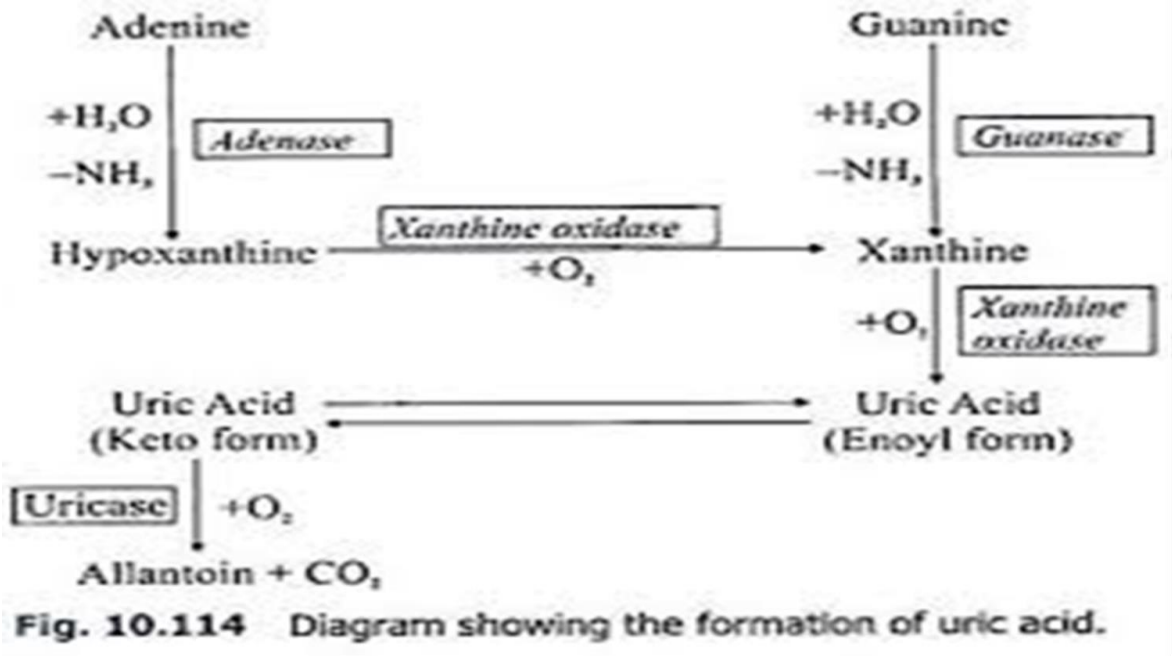
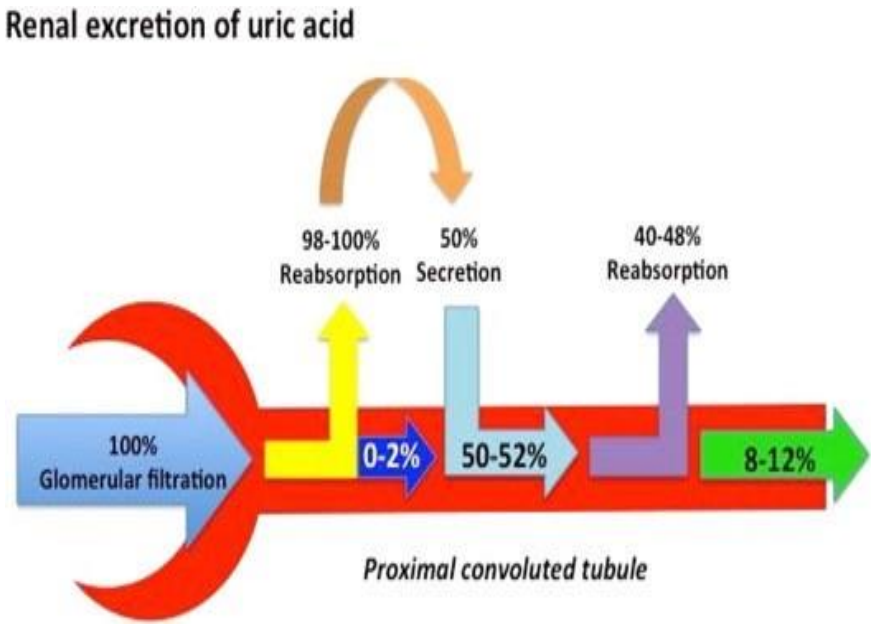
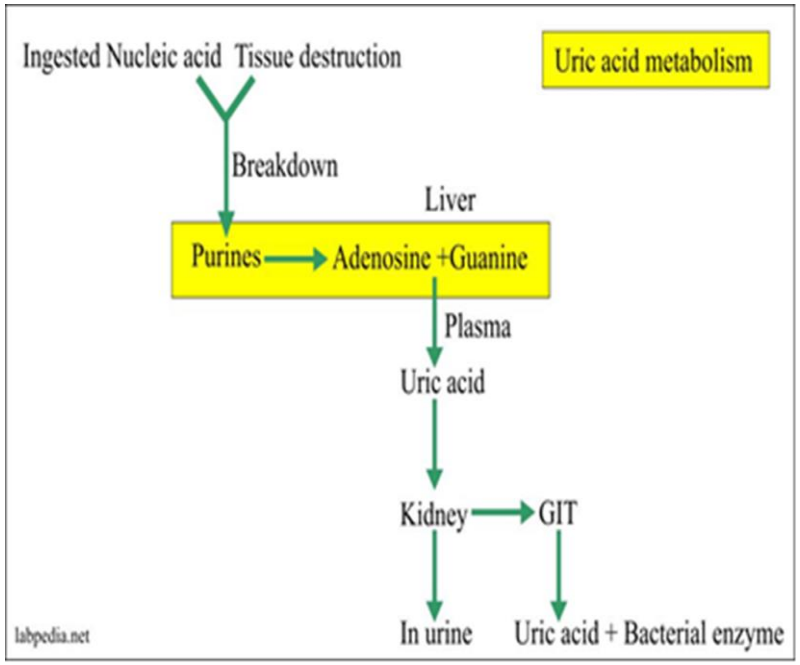


Fig. 10.114 Diagram showing the formation of uric acid.

The majority of uric acid is excreted by the kidney and the rest in feces, although a substantial amount of uric acid is reabsorbed at the proximal tubule of the kidney.





Cystatin C

❖**Cystatin C** is

- produced at constant rate and expressed in all organs of body.
- freely filtered by kidney glomeruli.
- completely reabsorbed but degraded in the tubules.
- Serum **Cystatin C not** affected by age ,sex ,muscle mass or inflammatory processes.
- Sensitive to changes in the creatinine blind area of GFR(40-70 ml/min/1.73 m^2)
- There is no tubular secretion of **Cystatin** C ,it is sensitive to minor changes in GFR in the earliest stages of chronic kidney diseases .

Cystatin C as a glomerular filtration maker

- **Cystatin** C:
- a protein maker of kidney Function and more sensitive than creatinine .
- is non glycosylated protein and has 120 amino acids (13 KD) .It is most abundant extracellular cysteine protease inhibitor.
- High concentration of **Serum Cystatin C** in all fluids e.g. milk, tears , saliva, semen .
- **Serum Cystatin C reference range :** 0.8-1.2 µg/dl (mg/L)
- Even minor changes in GFR in the early stages of chronic kidney diseases are associated with increased Serum **Cystatin** C levels .

Comparing Categories of Acute Renal Failure

Characteristics	Categories		
	Prerenal	Intrarenal	Postrenal
Etiology	Hypoperfusion	Parenchymal damage	Obstruction
BUN value	Increased	Increased	increased
Creatinine	Increased	Increased	Increased
Urine output	Decreased	Varies, often decreased	Varies, may be decreased, or sudden anuria
Urine sodium	Decreased to < 20 mEq/L	Increased to >40mEq/L	Varies, often decreased to 20mEq/L or less
Urinary sediment	Normal, few hyaline casts	Abnormal casts and debris	Usually normal
Urine osmolality	Increased to 500mOsm	About 350 mOsm similar to serum	Varies, increased or equal to serum
Urine specific gravity	Increased	Low normal	Varies