Urine

- **Reference Books:**

- **Urinanalysis and body fluids** (Susan King Strasinger- Marjorie Schaub De Lorenzo) Fifth edition

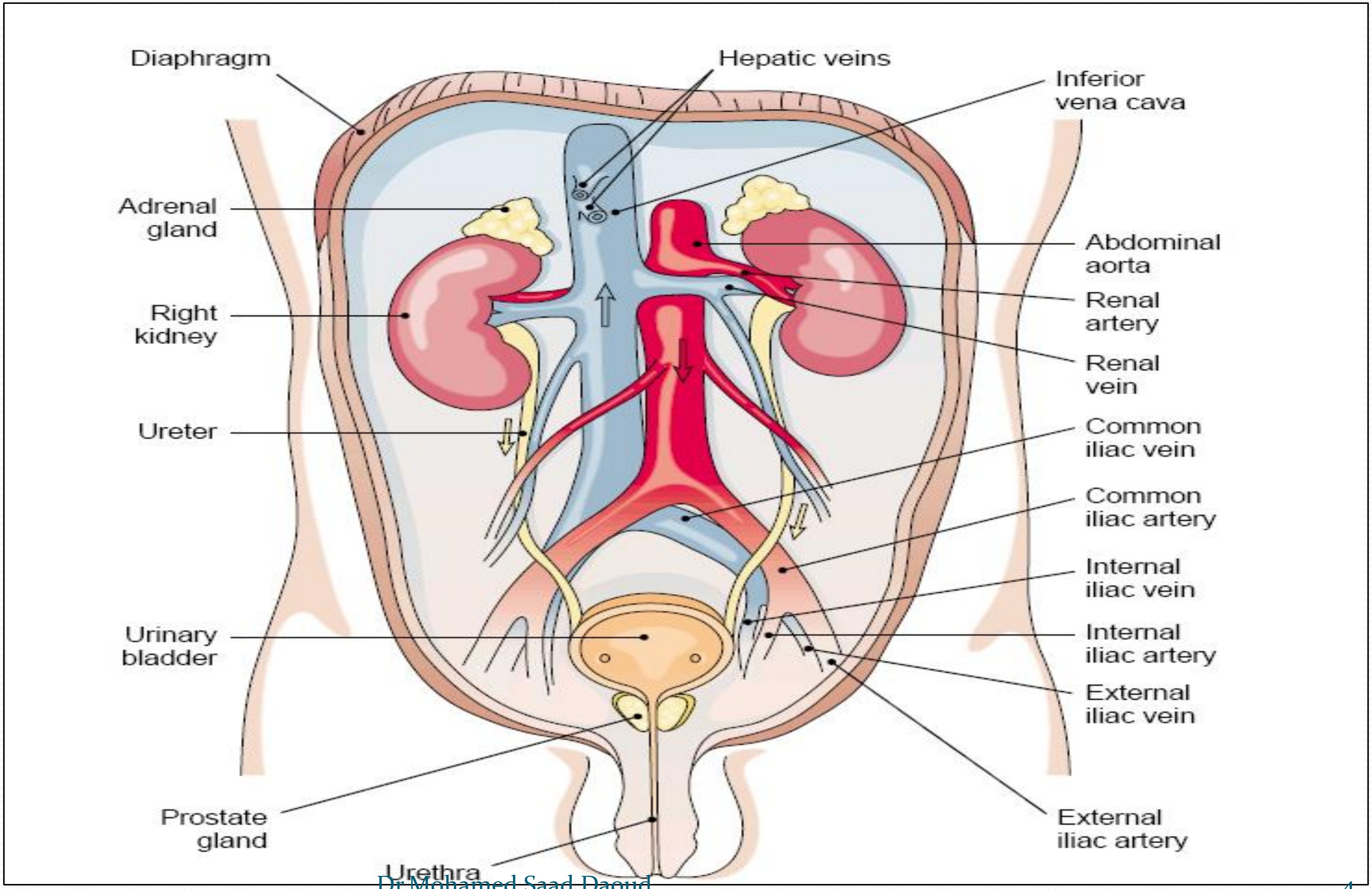
- **Fundamentals of Clinical Chemistry** (Tietz) Sixth edition

Urine:

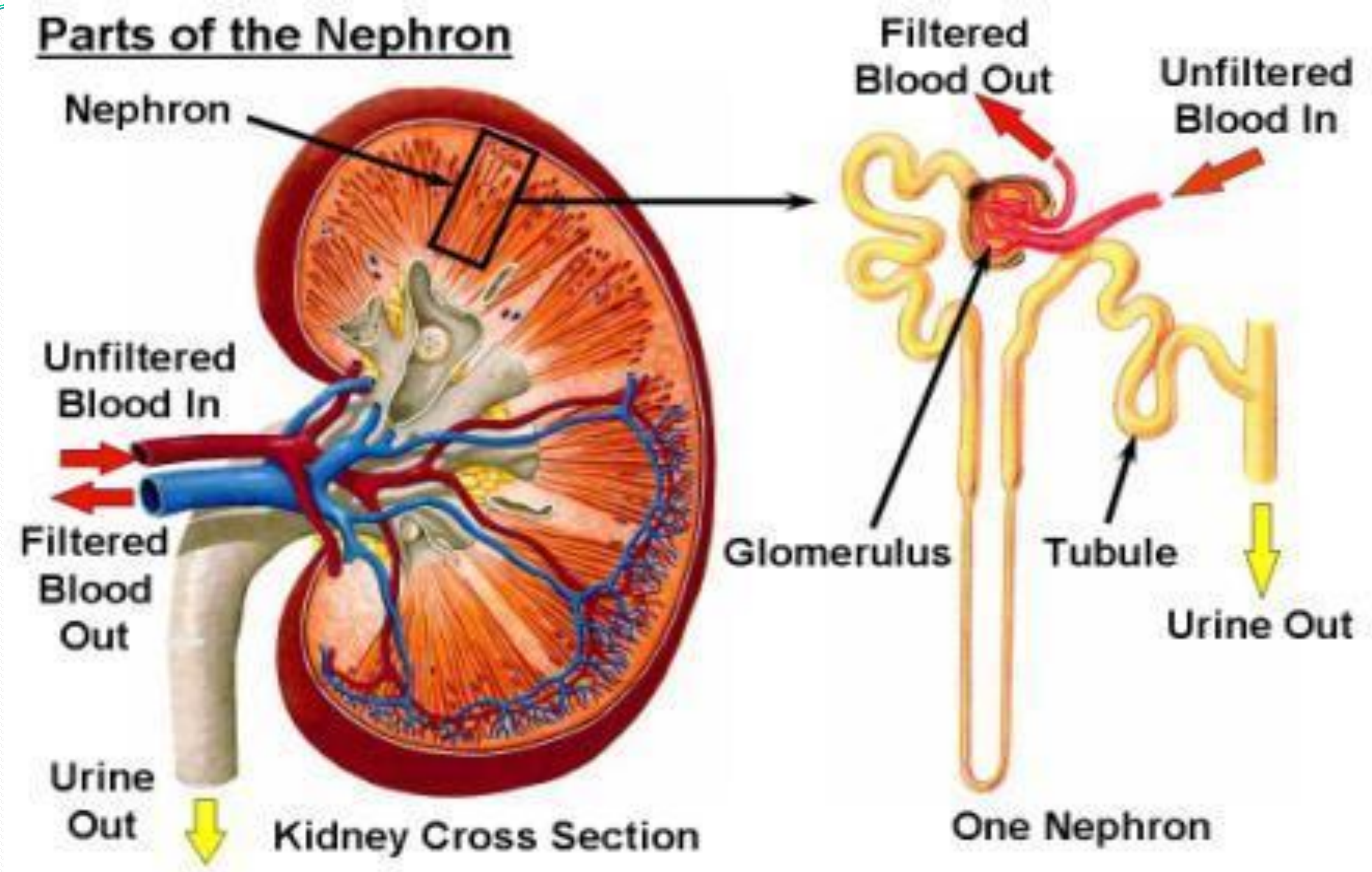
Sterile fluid (in the absence of a disease condition) is secreted by the kidneys through a process called urination and excreted through the urethra.

Urine contains a whole range of substances that the body has no need for. It might contain chemicals that are potentially harmful but the levels are going to be very low when expelled by the body, and even lower when diluted by water.

Urinary system



- Clear waste products from the blood to maintain the body’s essential water and electrolyte balances.
- Renal blood flow, glomerular filtration, tubular reabsorption, and tubular secretion.
- Kidney contains approximately 1 to 1.5 million functional units called nephrons.
- Number of nephrons do not increase after birth. Kidney growth is due to enlargement of existing nephrons.
- Damaged nephrons are not regenerated. About 1/3 of the nephrons in a kidney must be functional to ensure survival of the organ.

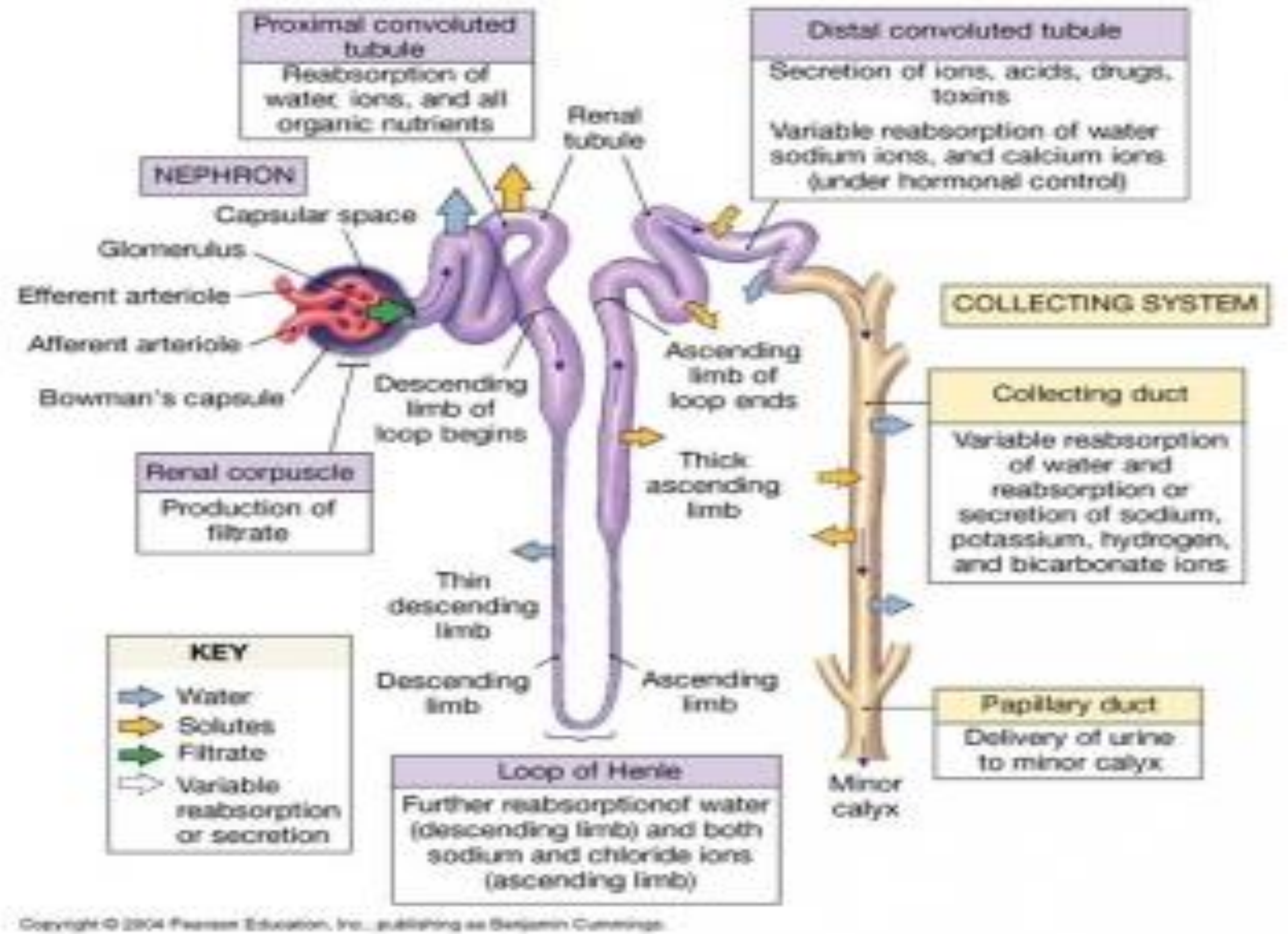

Parts of the Nephron
Nephron
Unfiltered
Blood In
Filtered
Blood
Out
Urine
Out
Kidney Cross Section
Filtered
Blood Out
Unfiltered
Blood In
Glomerulus
Tubule
Urine Out
One Nephron

Urine formation

- The kidneys continuously form urine as an ultra-filtrate of plasma.

- Reabsorption of water and filtered substances essential to body function (170,000 mL of filtered plasma urine give 1200 mL urine per day).

- Tubular secretion serves two major functions: elimination of waste products not filtered by the glomerulus and regulation of the acid-base balance in the body through the secretion of hydrogen ions.


Proximal convoluted tubule
Reabsorption of water, ions, and all organic nutrients
Renal tubule
Distal convoluted tubule
Secretion of ions, acids, drugs, toxins
Variable reabsorption of water sodium ions, and calcium ions (under hormonal control)
NEPHRON
Capsular space
Glomerulus
Efferent arteriole
Afferent arteriole
Bowman's capsule
Descending limb of loop begins
Ascending limb of loop ends
COLLECTING SYSTEM
Collecting duct
Variable reabsorption of water and reabsorption or secretion of sodium, potassium, hydrogen, and bicarbonate ions
Renal corpuscle
Production of filtrate
Thick ascending limb
Thin descending limb
KEY
Water
Solutes
Filtrate
Variable reabsorption or secretion
Descending limb
Ascending limb
Papillary duct
Delivery of urine to minor calyx
Loop of Henle
Further reabsorptionof water (descending limb) and both sodium and chloride ions (ascending limb)
Minor calyx
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- **Glomerular Filtration**

Glomerulus serves as a nonselective filter of plasma substances

Factors affected on filtration:

- The presence of hydrostatic pressure resulting from the smaller size of the efferent arteriole and the glomerular capillaries enhances filtration.

- Hydrostatic pressure opposite pressures from the fluid within Bowman’s capsule and the oncotic pressure of unfiltered plasma proteins in the glomerular capillaries.

- The glomerular apparatus maintains the glomerular blood pressure at a relatively constant rate by increasing or decreasing the size of the afferent arteriole.

Action of the renin-angiotensin-aldosterone system

- Dilation of the afferent arteriole and constriction of the efferent arteriole.
- Stimulation of sodium reabsorption in the proximal convoluted tubule.
- Triggers the adrenal cortex to release the sodium retaining hormone, aldosterone, to cause reabsorption of sodium and excretion of potassium in the distal convoluted tubule

  and collecting duct.
- Triggers release of antidiuretic hormone by the hypothalmus to stimulate water reabsorption in the collecting duct.

Glomerular mechanisms, every minute approximately two to three million glomeruli filter approximately 120 ml of water-containing low-molecular weight substances.

Tubular Reabsorption

- The plasma ultrafiltrate enters the proximal convoluted tubule, the nephrons, through cellular transport mechanisms, begin reabsorbing these essential substances and water.

- The cellular mechanisms involved in tubular reabsorption are termed ***active*** and ***passive transport.***

- For active transport to occur, the substance to be reabsorbed must combine with a carrier protein contained in the membranes of the renal tubular cells.

- Passive transport is the movement of molecules across a membrane as a result of differences in their concentration or electrical potential on opposite sides of the membrane.

	Substance	Location
Active transport	Glucose, amino acids, salts	Proximal convoluted tubule
	Chloride	Ascending loop of Henle
	Sodium	Proximal and distal convoluted tubules
Passive transport	Water	Proximal convoluted tubule, descending loop of Henle, and collecting duct
	Urea	Proximal convoluted Tubule and ascending loop of Henle
	Sodium	Ascending loop of Henle

Renal threshold

When the plasma concentration of a substance that is normally completely reabsorbed reaches an abnormally high level, the filtrate concentration exceeds the **maximal reabsorptive capacity (Tm)** of the tubules, and the substance begins appearing in the urine. The plasma concentration at which active transport stops is termed the **renal threshold.**

- For glucose, the renal threshold is 160 to 180 mg/dL, and glucose appears in the urine when the plasma concentration reaches this level.

Tubular Secretion

- Elimination of waste products not filtered by the glomerulus (foreign substances, such as medications).
- The major site for removal of these nonfiltered substances is the proximal convoluted tubule.
- Regulation of the acid-base balance in the body through the secretion of hydrogen ions.

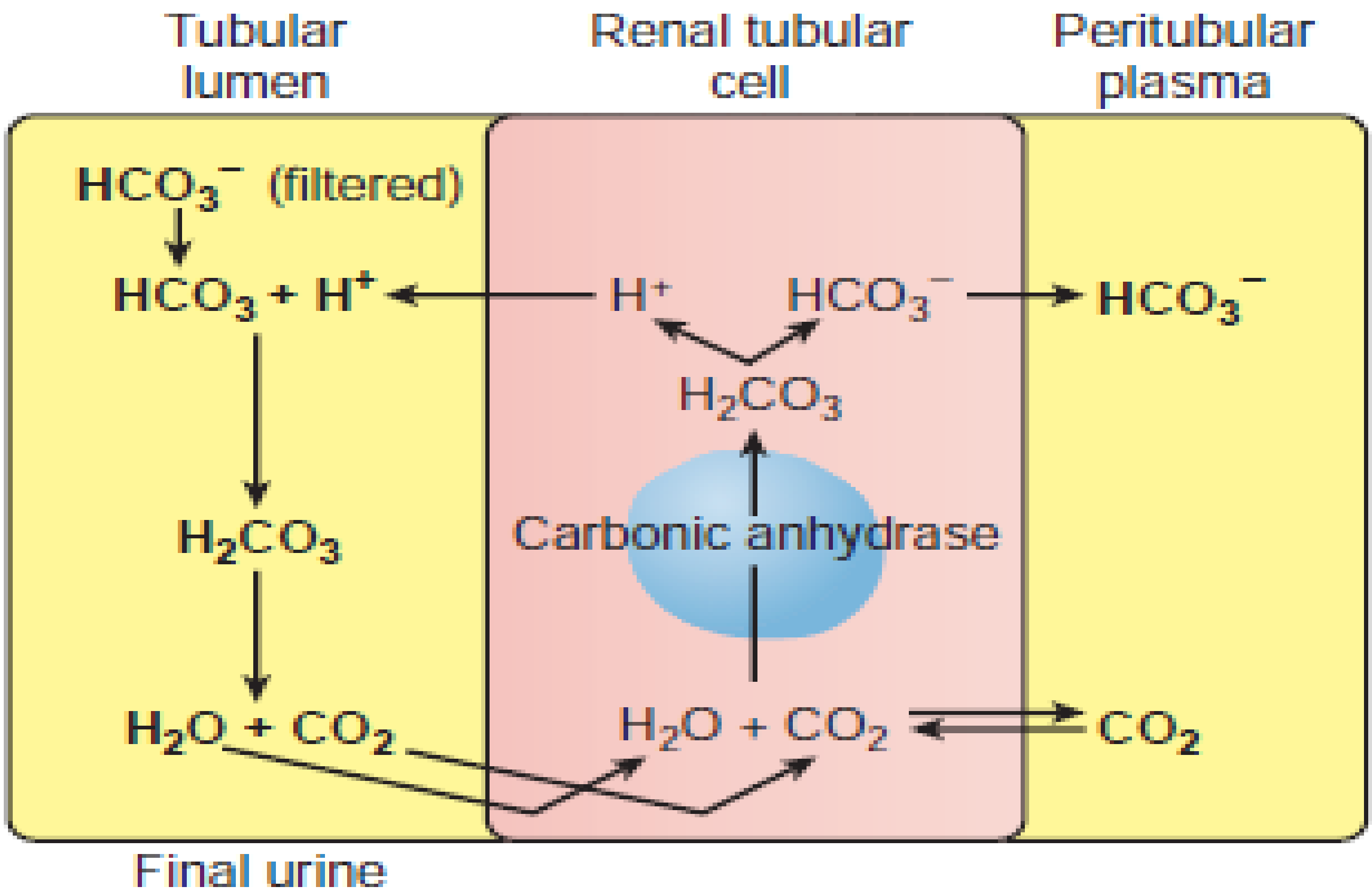
Acid-Base Balance

- The normal blood pH of 7.4, the blood must buffer and eliminate the excess acid formed by dietary intake and body metabolism.

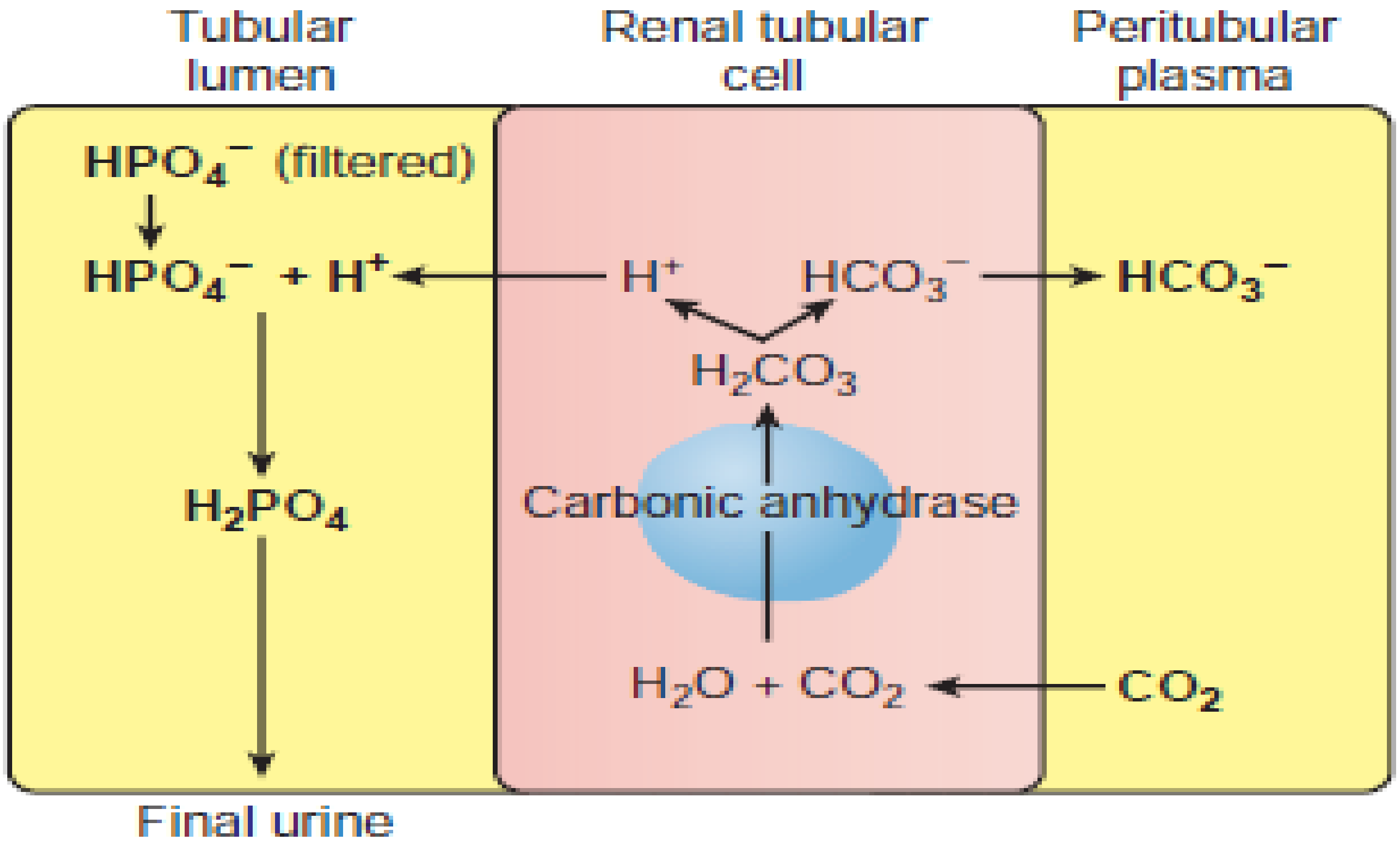
- The buffering capacity of the blood depends on bicarbonate **(HCO_3^-) ions,** which are readily filtered by the glomerulus and must be expediently returned to the blood to maintain the proper pH.

- A disruption in these secretory functions can result in metabolic acidosis or renal tubular acidosis, the inability to produce an acid urine.

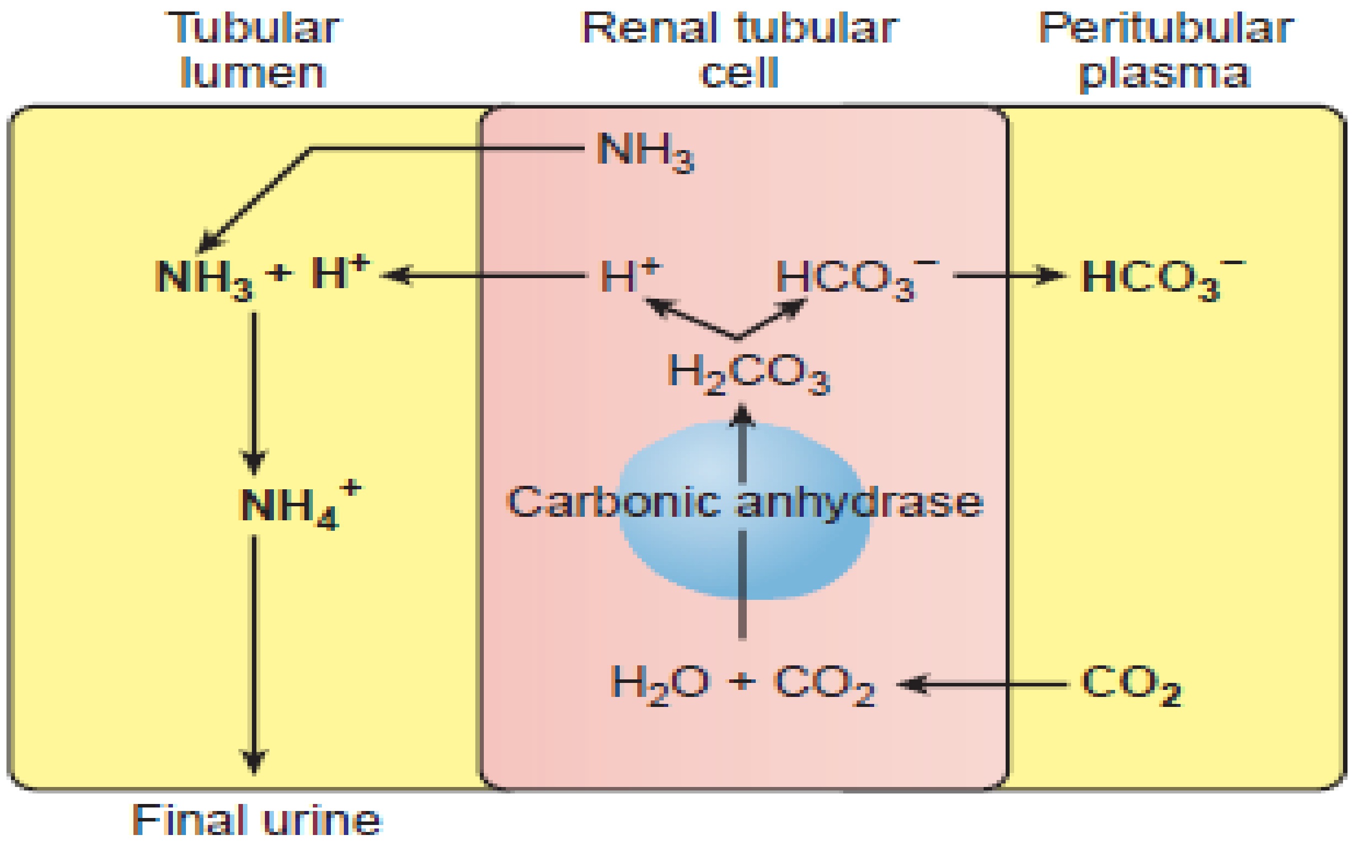
Reabsorption of filtered bicarbonate



Excretion of secreted hydrogen ion combined with phosphate



Excretion of secreted hydrogen ion combined with ammonia produced by the tubules



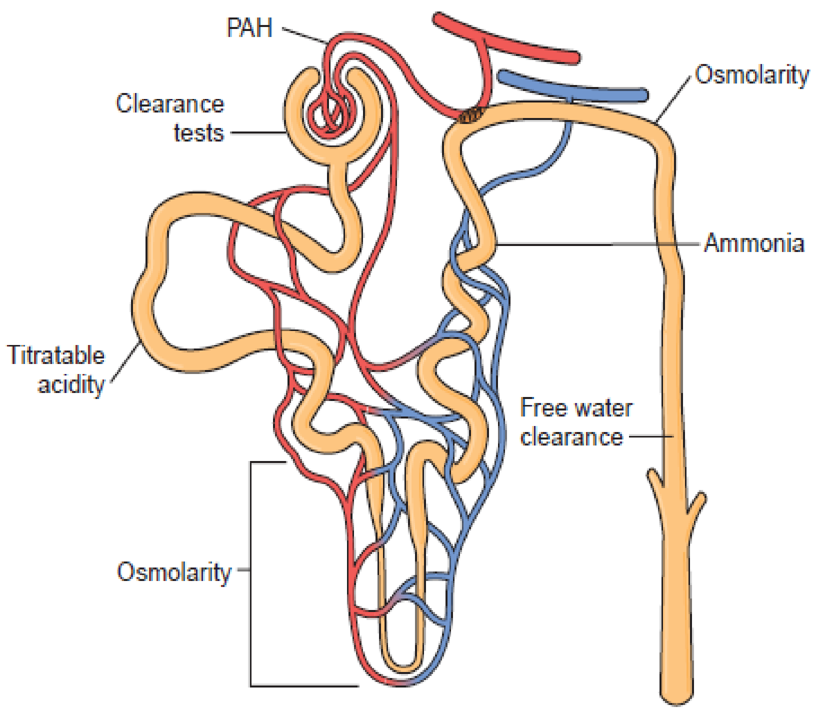
Renal Function Tests

There are metabolic functions and chemical interactions to be evaluated through laboratory tests of renal function.

1- Glomerular filtration tests

2- Tubular reabsorption tests

3-Tubular secretion and renal blood flow tests



Glomerular Filtration Tests

- The standard test used to measure the filtering capacity of the glomeruli is the **clearance test.**
- A clearance test measures the rate at which the kidneys are able to remove substance from the blood.
- the substance analyzed must be one that is neither reabsorbed nor secreted by the tubules.
- the stability of the substance in urine during a possible 24-hour collection period
- the consistency of the plasma level the substance's availability to the body, and the availability of tests for analysis of the substance.

Creatinine Clearance

- Creatinine, a waste product of muscle metabolism that is normally found at a relatively constant level in the blood, provides the laboratory with an endogenous procedure for evaluating glomerular function.
- The GFR is reported in mL/min; therefore, determining the number of milliliters of plasma from which the clearance substance (creatinine) is completely removed during 1 minute is necessary.

Procedure

- Urine volume in mL (V), urine creatinine concentration in mg/dL (U), and plasma creatinine concentration in mg/dL (P).

- The urine volume is calculated by dividing the number of milliliters in the specimen by the number of minutes used to collect the specimen (V mL/min).

- The plasma and urine concentrations are determined by chemical testing.

- The standard formula used to calculate the milliliters of plasma cleared per minute (C) is: $C = UV/P$

- Normal creatinine clearance values 120 mL/min (men 107 to 139 mL/min; women, 87 to 107 mL/min). The normal plasma creatinine is 0.5 to 1.5 mg/dL.
- These normal values take into account variations in size and muscle mass. Values are considerably lower in older people, however, and an adjustment may also have to be made to the calculation when dealing with body sizes that deviate greatly from 1.73 m^2 of surface, such as with children.

- To adjust a clearance for body size, the formula is:

C= UV/P x 1.73/A

- with A being the actual body size in square meters of surface. The actual body size may be calculated as:

log A= (0.425 x log weight)+ (0.725 x log height) -2.144

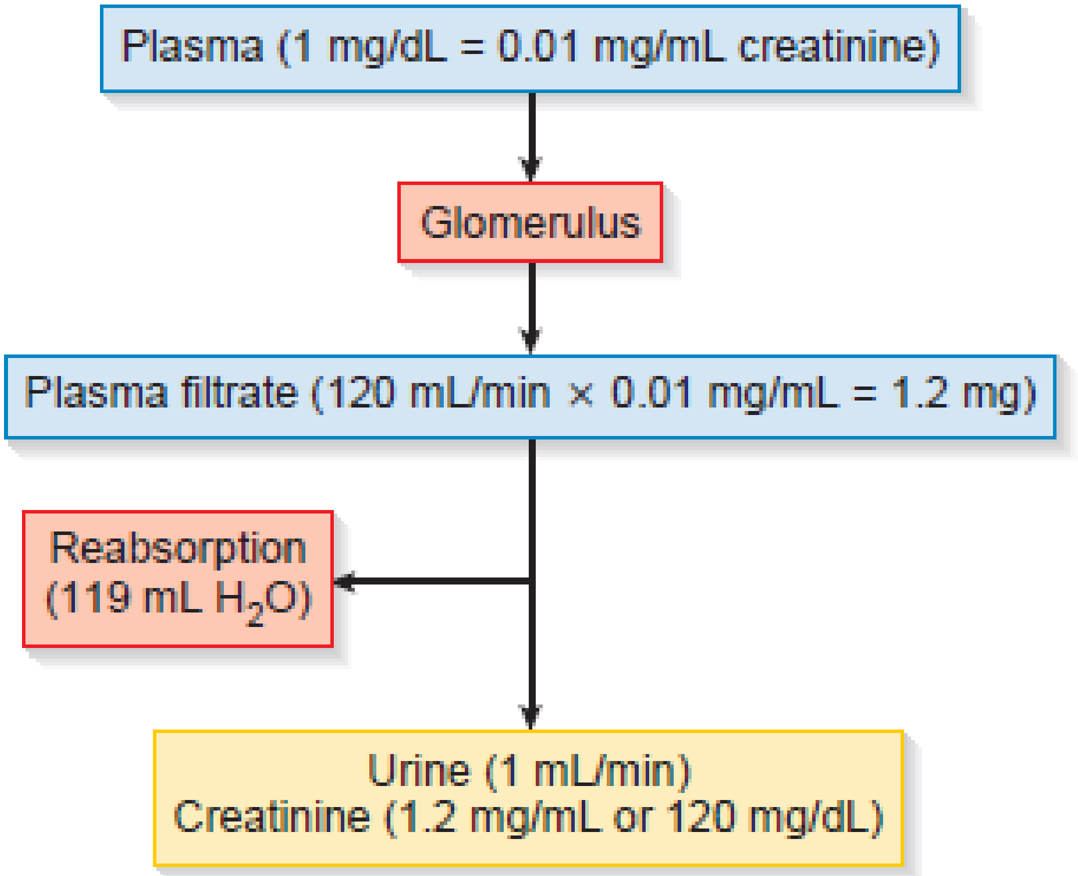
Clinical Significanse

- The GFR is determined by the number of functioning nephrons and also by the functional capacity of these nephrons.

- Determination the extent of nephron damage in known cases of renal disease, to monitor the effectiveness of treatment designed to prevent further nephron damage.

- Determination the feasibility of administering medications, which can build up to dangerous blood levels if the GFR is markedly reduced.

Creatinine filteration and excretion



Tubular Reabsorption Tests

- Tests to determine the ability of the tubules to reabsorb the essential salts and water that have been non selectively filtered by the glomerulus are called concentration tests.
- the ultrafiltrate that enters the tubules has a specific gravity of 1010

Osmolarity

- Specific gravity depends on the number of particles present in a solution and the density of these particles.
- Renal concentrating ability, monitoring the course of renal disease, monitoring fluid and electrolyte therapy.

- Establishing the differential diagnosis of **hypernatremia** and **hyponatremia,** and evaluating the secretion of and renal response to ADH. These evaluations may require determination of serum in addition to urine osmolarity
- Normal serum osmolarity values (275 -300 mOsm).
- Normal values for urine osmolarity are difficult to establish, because factors such as fluid intake and exercise can greatly influence the urine concentration. Values can range from 50 to 1400 mOsm.
- The ratio of urine to serum osmolarity should be at least 1:1; after controlled fluid intake, it should reach 3:1

Tubular Secretion and Renal Blood Flow Tests

- The test most commonly associated with tubular secretion and renal blood flow is the *p*-aminohippuric acid **(PAH)** test.
- Excretion of the dye phenolsulfonphthalein **(PSP)** was used to evaluate these functions.

PAH test

- To measure the exact amount of blood flowing through the kidney, it is necessary to use a substance that is completely removed from the blood (plasma) each time it comes in contact with functional renal tissue.

- C_{PAH} (mL/min)= $$\frac{U\ (\text{mg/dL PAH}) \times V\ (\text{mL/min urine})}{P\ (\text{mg/dL PAH})}$$

- Normal values for the effective renal plasma flow range from 600 to 700 mL/min, making the average renal blood flow about 1200 mL/min.

Urine analysis

Purpose

- General evaluation of health
- Diagnosis of disease or disorders of the kidneys or urinary tract
- Diagnosis of other systemic disease that affect kidney function
- Monitoring of patients with diabetes
- Screening for drug abuse

Urine Composition

urine consists of urea and other organic and inorganic chemicals dissolved in water. Urine is normally 95% water and 5% solutes.

- The concentrations of these solutes can occur owing to the influence of factors such as dietary intake, physical activity, body metabolism, endocrine functions, and even body position.
- Urea, a metabolic waste product produced in the liver from the breakdown of protein and amino acids, accounts for nearly half of the total dissolved solids in urine.

- Organic substances include primarily creatinine and uric acid.
- The major inorganic solid dissolved in urine is chloride, followed by sodium and potassium. Small or trace amounts of many additional inorganic chemicals are also present in urine.
- Other substances found in urine include hormones, vitamins, and medications. Although not a part of the original plasma filtrate, the urine also may contain formed elements, such as cells, casts, crystals, mucus, and bacteria. Increased amounts of these formed elements are often indicative of disease.

Organic components	Amount	Remark
Urea	25.0-35.0 g	60%–90% of nitrogenous material; derived from the metabolism of amino acids into ammonia
Creatinine	1.5 g	Derived from creatine, nitrogenous substance in muscle tissue
Uric acid	0.4-1.0 g	Common component of kidney stones; derived from catabolism of nucleic acid in food and cell destruction
Hippuric acid	0.7 g	Benzoic acid is eliminated from the body in this form; increases with high-vegetable diets
Other substances	2.9 g	Carbohydrates, pigments, fatty acids, mucin, enzymes, hormones; may be present in small amounts depending on diet and health

Inorganic constituent	Amount	Remark
Sodium chloride (NaCl)	15.0 g	Principal salt; varies with intake
Potassium (K)	3.3 g	Occurs as chloride, sulfate, and phosphate salts
Sulfate (SO_4^{2-})	2.5 g	Derived from amino acids
Phosphate (PO_4^{3-})	2.5 g	Occurs primarily as sodium compounds that serve as buffers in the blood
Ammonium (NH_4^+)	0.7 g	Derived from protein metabolism and glutamine in kidneys; amount varies depending on blood and tissue fluid acidity
Magnesium (Mg^{2+})	0.1 g	Occurs as chloride, sulfate, phosphate salts

Urine Volume

Urine volume depends on the amount of water that the kidneys excrete.

- **Factors that influence urine volume** include fluid intake, fluid loss from non renal sources, variations in the secretion of antidiuretic hormone, and need to excrete increased amounts of dissolved solids, such as glucose or salts.
- **Normal daily urine output** is usually 1200 to 1500 ml, a range of 600 to 2000 ml is considered normal.

Oliguria: A decrease in urine output

- Less than 1 ml/kg/hr in infants
- less than 0.5 ml/kg/hr in children
- less than 400 ml/day in adults
- Causes of oliguria: When the body enters a state of dehydration as a result of excessive water loss from vomiting, diarrhea, perspiration, or severe burns
- Oliguria leading to **anuria**

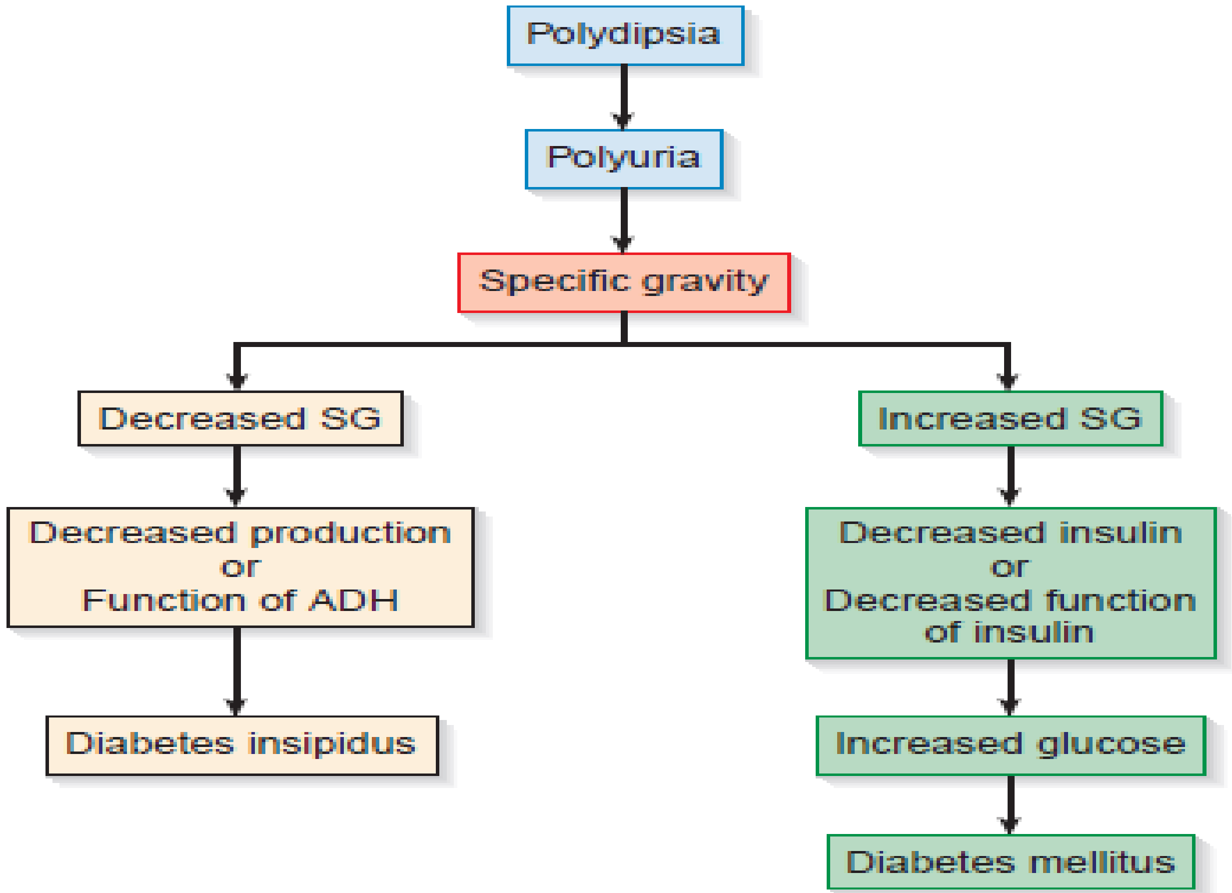
Anuria: Cessation of urine flow, may result from any serious damage to the kidneys or from a decrease in the flow of blood to the kidneys.

Nocturia: An increase in the nocturenal excretion of urine, the kidneys excrete two to three times more urine during the night than during the day.

Polyuria: an increase in daily urine volume

- greater than 2.5 l ml/kg/day in adults
- Greater than 2.5–3 ml/kg/day in children
- Diabetes mellitus and diabetes insipidus
- Induced by diuretics, caffeine, or alcohol, all of which suppress the secretion of antidiuretic hormone.

Differentiation between diabetes mellitus and diabetes insipidus.



Urine Collection

- Specimens must be collected in clean, dry and disposable containers.
- Individually packaged sterile containers with secure closures should be used for microbiologic urine studies. Sterile containers are also suggested if more than 2 hours elapse
- Following collection, specimens should be delivered to the laboratory and tested within 2 hours. A specimen that cannot be delivered and tested within 2 hours should be refrigerated or have an appropriate chemical preservative added.

Table 3–3 Urine Preservatives

Preservatives	Advantages	Disadvantages	Additional Information
Refrigeration	Does not interfere with chemical tests	Raises specific gravity by hydrometer Precipitates amorphous phosphates and urates	Prevents bacterial growth 24 h[3]
Thymol	Preserves glucose and sediments well	Interferes with acid precipitation tests for protein	
Boric acid	Preserves protein and formed elements well Does not interfere with routine analyses other than pH	May precipitate crystals when used in large amounts	Keeps pH at about 6.0 Is bacteriostatic (not bactericidal) at 18 g/L; can use for culture transport[4] Interferes with drug and hormone analyses
Formalin (formaldehyde)	Excellent sediment preservative	Acts as a reducing agent, interfering with chemical tests for glucose, blood, leukocyte esterase, and copper reduction	Rinse specimen container with formalin to preserve cells and casts
Toluene	Does not interfere with routine tests	Floats on surface of specimens and clings to pipettes and testing materials	
Sodium fluoride	Prevents glycolysis Is a good preservative for drug analyses	Inhibits reagent strip tests for glucose, blood, and leukocytes	May use sodium benzoate instead of fluoride for reagent strip testing[5]

Preservatives	Advantages	Disadvantages	Additional Information
Phenol	Does not interfere with routine tests	Causes an odor change	Use 1 drop per ounce of specimen
Commercial preservative tablets	Convenient when refrigeration not possible Have controlled concentration to minimize interference	May contain one or more of the preservatives including sodium fluoride	Check tablet composition to determine possible effects on desired tests
Urine Collection Kits[6] (Becton Dickinson, Rutherford, NJ)	Contains collection cup, C&S preservative tube or UA tube		
Gray C&S tube	Sample stable at room temperature (RT) for 48 hr; preserves bacteria	Decreases pH; do not use if urine is below minimum fill line	Preservative is boric acid and may not be used for UA
Yellow plain UA tube	Use on automated instruments	Must refrigerate within 2 hours	Round or conical bottom
Cherry red/yellow top tube	Stable for 72 hours at RT; instrument-compatible	Bilirubin and urobilinogen may be decreased if specimen is exposed to light and left at RT	Preservative is sodium propionate; conical bottom
Saccomanno Fixative	Preserves cellular elements		Used for cytology studies

Changes in Unpreserved Urine

Analyte	Change	Cause
Color	Modified/darkened	Oxidation or reduction of metabolites
Clarity	Decreased	Bacterial growth and precipitation of amorphous material
Odor	Increased	Bacterial multiplication or breakdown of urea to ammonia
pH	Increased	Breakdown of urea to ammonia by urease-producing bacteria/ loss of CO_2
Glucose	Decreased	Glycolysis and bacterial use
Ketones	Decreased	Volatilization and bacterial metabolism
Bilirubin	Decreased	Exposure to light/photo oxidation to biliverdin
Urobilinogen	Decreased	Oxidation to urobilin
Nitrite	Increased	Multiplication of nitrate-reducing bacteria
Red and white blood cells and casts	Decreased	Disintegration in dilute alkaline urine
Bacteria	Increased	Multiplication

Types of Urine Specimens

Type of Specimen	Purpose
Random	Routine screening
First morning	Routine screening Pregnancy tests Orthostatic protein
Fasting (second morning)	Diabetic screening/monitoring
2-hour postprandial	Diabetic monitoring
Glucose tolerance test	Optional with blood samples in glucose tolerance test
24-h (or timed)	Quantitative chemical tests
Catheterized	Bacterial culture
Midstream clean-catch	Routine screening Bacterial culture
Suprapubic aspiration	Bladder urine for bacterial culture Cytology
Three-glass collection	Prostatic infection

Physical examination

The physical examination of urine includes the determination of the urine color, clarity, and specific gravity

Color:

The color of urine varies from almost colorless to black. These variations may be due to normal metabolic functions, physical activity, ingested materials, or pathologic conditions.

Normal Urine Color

The yellow color of urine is caused by the presence of a pigment named urochrome (product of endogenous metabolism)

Laboratory Correlation of Urine Color

Color	Cause	Clinical/Laboratory Correlations
Colorless	Recent fluid consumption	Commonly observed with random specimens
Pale yellow	Polyuria or diabetes insipidus	Increased 24-hour volume
	Diabetes mellitus	Elevated specific gravity and positive glucose test result
	Dilute random specimen	Recent fluid consumption
Dark yellow	Concentrated specimen	May be normal after strenuous exercise or in first morning specimen
Amber		Deydration from fever or burns
Orange	Bilirubin	Yellow foam when shaken and positive chemical test results for bilirubin
	Acriflavine	Negative bile test results and possible green fluorescence
	Phenazopyridine (Pyridium)	Drug commonly administered for urinary tract infections May have orange foam and thick orange pigment that can obscure or interfere with reagent strip readings
	Nitrofurantoin	Antibiotic administered for urinary tract infections
	Phenindione	Anticoagulant, orange in alkaline urine, colorless in acid urine
Yellow-green Yellow-brown	Bilirubin oxidized to biliverdin	Colored foam in acidic urine and false-negative chemical test results for bilirubin
Green	*Pseudomonas* infection	Positive urine culture
Blue-green	Amitriptyline	Antidepressant
	Methocarbamol (Robaxin)	Muscle relaxant, may be green-brown
	Clorets	None
	Indican	Bacterial infections
	Methylene blue	Fistulas
	Phenol	When oxidized

Color	Cause	Clinical/Laboratory Correlations
Pink Red	RBCs	Cloudy urine with positive chemical test results for blood and RBCs visible microscopically
	Hemoglobin	Clear urine with positive chemical test results for blood; intravascular hemolysis
	Myoglobin	Clear urine with positive chemical test results for blood; muscle damage
	Porphyrins	Negative chemical test results for blood Detect with Watson-Schwartz screening test or fluorescence under ultra-violet light
	Beets	Alkaline urine of genetically susceptible persons
	Rifampin	Tuberculosis medication
	Menstrual contamination	Cloudy specimen with RBCs, mucus, and clots
Brown Black	RBCs oxidized to methemo-globin	Seen in acidic urine after standing; positive chemical test result for blood
	Methemoglobin	Denatured hemoglobin
	Homogentisic acid (alkap-tonuria)	Seen in alkaline urine after standing; specific tests are available
	Melanin or melanogen	Urine darkens on standing and reacts with nitroprusside and ferric chloride
	Phenol derivatives	Interfere with copper reduction tests
	Argyrol (antiseptic)	Color disappears with ferric chloride
	Methyldopa or levodopa	Antihypertensive
	Metronidazole (Flagyl)	Darkens on standing

Clarity:

General term that refers to the transparency /turbidity of a urine specimen.

- Freshly voided normal urine is usually clear, particularly if it is a midstream clean-catch specimen. Precipitation of amorphous phosphates and carbonates may cause a white cloudiness.

- The presence of squamous epithelial cells and mucus, particularly in specimens from women, can result in a hazy but normal urine.

Urine clarity

Clarity	Term
Clear	No visible particulates, transparent.
Hazy	Few particulates, print easily seen through urine.
Cloudy	Many particulates, print blurred through urine.
Turbid	Print cannot be seen through urine.
Milky	May precipitate or be clotted.

Pathologic and non pathologic causes of urine turbidity

Non pathologic Causes of Urine Turbidity	Pathologic Causes of Urine Turbidity
Squamous epithelial cells	RBCs
Mucus	WBCs
Amorphous phosphates, carbonates, urates	Bacteria
Semen, spermatozoa	Yeast
Fecal contamination	Nonsquamous epithelial cells
Radiographic contrast media	Abnormal crystals
Talcum powder	Lymph fluid
Vaginal creams	Lipids

Laboratory Correlations in Urine Turbidity

Acidic Urine

Amorphous urates
Radiographic contrast media

Alkaline Urine

Amorphous phosphates, carbonates

Soluble With Heat

Amorphous urates, uric acid crystals

Soluble in Dilute Acetic Acid

RBCs
Amorphous phosphates, carbonates

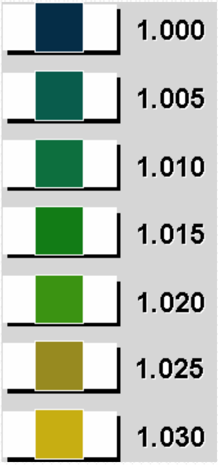
Insoluble in Dilute Acetic Acid

WBCs
Bacteria, yeast
Spermatozoa

Soluble in Ether

Lipids
Lymphatic fluid, chyle

Specific Gravity



- Chemicals and water reabsorption is often the first renal function to become impaired; therefore, an assessment of the kidney's ability to reabsorb is performed by measuring the specific gravity of the specimen.
- Specific gravity detects possible dehydration or abnormalities in antidiuretic hormone and can be used to determine whether specimen concentration is adequate to ensure the accuracy of chemical tests.

Specific gravity is defined as the density of a solution compared with the density of a similar volume of distilled water at a similar temperature.

the specific gravity of urine is a measure of the density of the dissolved chemicals in the specimen.

Urine Specific Gravity Measurements

Method	Principle
Urinometry	Density
Refractometry	Refractive index
Harmonic oscillation densitometry	Density
Reagent strip	pK_a changes of a polyelectrolyte

Odor

- Freshly voided urine has a faint aromatic odor
- The breakdown of urea is responsible for the characteristic ammonia odor
- Causes of unusual odors include bacterial infections, diabetic ketones and some metabolic disorders

Odor	Cause
Aromatic	Normal
Foul, ammonia-like	Bacterial decomposition, urinary tract infection
Fruity, sweet	Ketones (diabetes mellitus, starvation, vomiting)
Maple syrup	Maple syrup urine disease
Mousy	Phenylketonuria
Rancid	Tyrosinemia
Sweaty feet	Isovaleric acidemia
Cabbage	Methionine malabsorption
Bleach	Contamination

Chemical Examination of Urine

Reagent Strips:

Care of Reagent Strips

1. Store with desiccant in an opaque, tightly closed container.

2. Store below 30°C; do not freeze.

3. Do not expose to volatile fumes.

4. Do not use past the expiration date.

5. Do not use if chemical pads become discolored.

6. Remove strips immediately prior to use.

Reagent strips technique

- Dip the reagent strip briefly into a well-mixed uncentrifuged urine specimen at room temperature.
- Remove excess urine by touching the edge of the strip to the container as the strip is withdrawn.
- Blot the edge of the strip on a disposable absorbent pad.
- Wait the specified amount of time for the reaction to occur.
- Compare the color reaction of the strip pads to the manufacturer’s color chart in good lighting.

Quality Control

1. Test open bottles of reagent strips with known positive and negative controls every 24 hr.

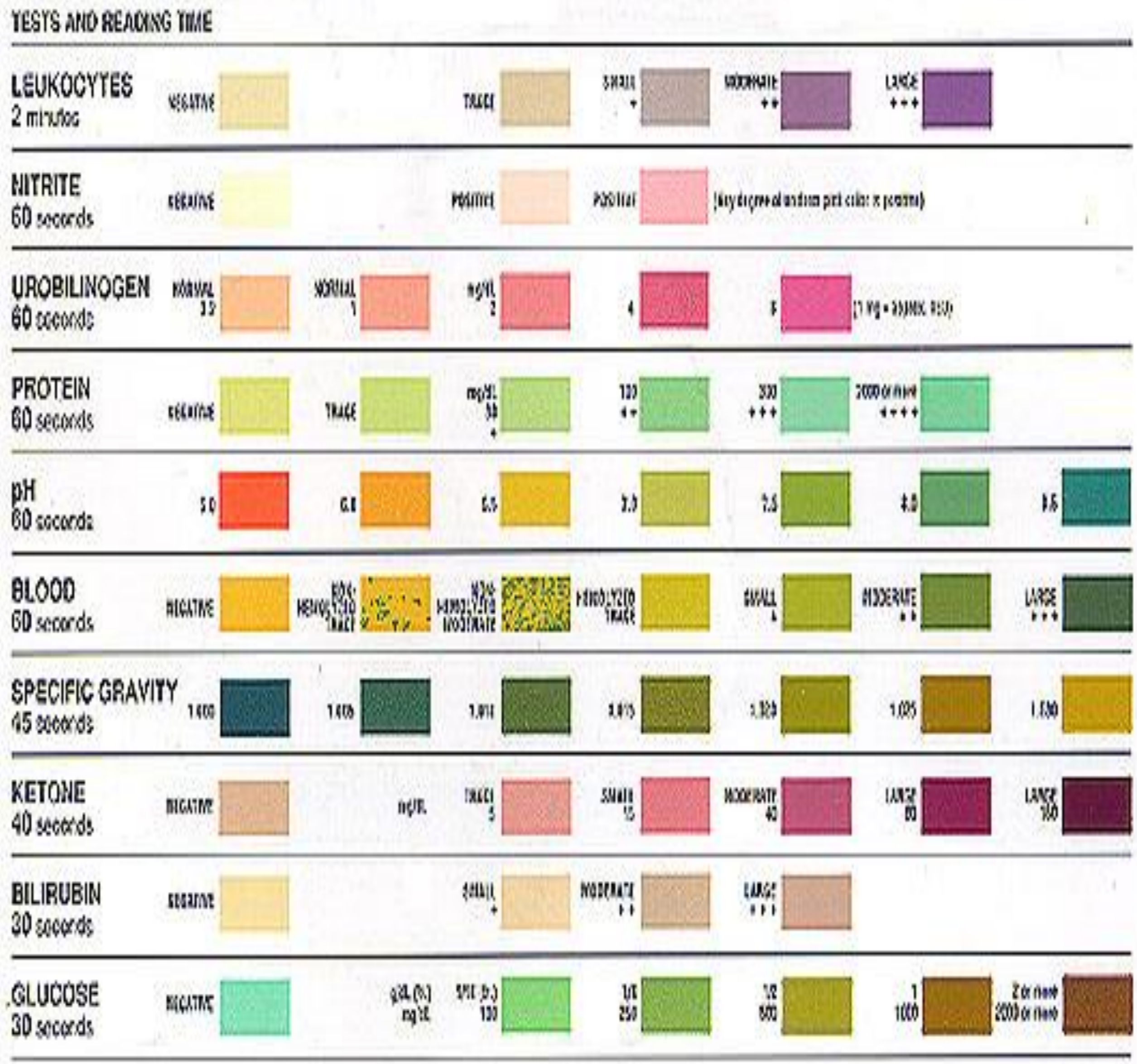
2. Resolve control results that are out of range by further testing.

3. Test reagents used in backup tests with positive and negative controls.

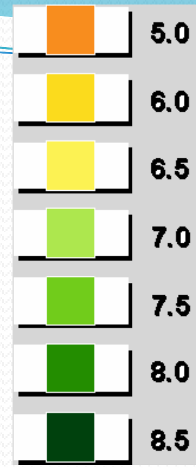
4. Perform positive and negative controls on new reagents and newly opened bottles of reagent strips.

5. Record all control results and reagent lot numbers.


Multistix 10 SG
Reagent Strips for Urinalysis


TESTS AND READING TIME
LEUKOCYTES
2 minutes
NEGATIVE
TRACE
SMALL +
MODERATE ++
LARGE +++
NITRITE
60 seconds
NEGATIVE
POSITIVE
POSITIVE
UROBILINOGEN
60 seconds
NORMAL 0.2
NORMAL 1
mg/dL 2
4
8
PROTEIN
60 seconds
NEGATIVE
TRACE
mg/dL 30 +
100 ++
300 +++
2000 or more ++++
pH
60 seconds
5.0
6.0
6.5
7.0
7.5
8.0
8.5
BLOOD
60 seconds
NEGATIVE
NON-HEMOLYZED TRACE
NON-HEMOLYZED MODERATE
HEMOLYZED TRACE
SMALL +
MODERATE ++
LARGE +++
SPECIFIC GRAVITY
45 seconds
1.000
1.005
1.010
1.015
1.020
1.025
1.030
KETONE
40 seconds
NEGATIVE
mg/dL
TRACE 5
SMALL 15
MODERATE 40
LARGE 80
LARGE 160
BILIRUBIN
30 seconds
NEGATIVE
SMALL +
MODERATE ++
LARGE +++
GLUCOSE
30 seconds
NEGATIVE
g/dL (%)
mg/dL
1/10 (tr.) 100
1/4 250
1/2 500
1 1000
2 or more 2000 or more

pH



- kidneys are the major regulators of the acid-base content in the body.
- First morning specimen with a slightly acidic pH (5.0 to 6.0).
- Alkaline pH is found following meals.
- The pH of normal random samples can range from 4.5 to 8.0

Causes of Acid and Alkaline Urine

Acid Urine	Alkaline Urine
Emphysema	Hyperventilation
Diabetes mellitus	Vomiting
Starvation	Renal tubular acidosis
Dehydration	Presence of urease-producing bacteria
Diarrhea	Vegetarian diet
Presence of acid-producing bacteria (*Escherichia coli*)	Old specimens
High-protein diet	
Cranberry juice	
Medications (methenamine mandelate [Mandelamine], fosfomycin tromethamine)	

Protein

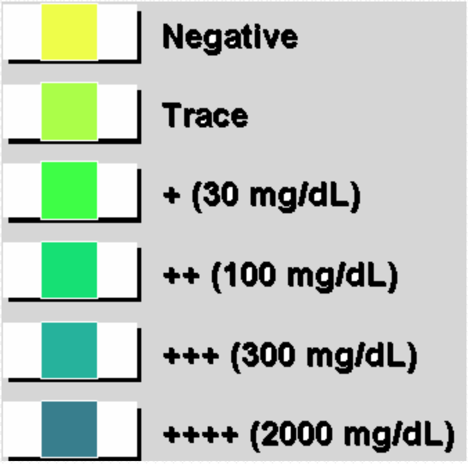
- The presence of proteinuria is often associated with early renal disease

- Normal urine contains less than 10 mg/dL or 100 mg per 24 hours is excreted (low molecular weight protein, Albumin).

- Clinical proteinuria is indicated at ≥30 mg/dL (300 mg/L).

- The causes of proteinuria are varied and can be grouped into three major categories: ***prerenal, renal,*** and ***postrenal,*** based on the origin of the protein.

- At a pH level of 3, both indicators appear yellow in the absence of protein; however, as the protein concentration increases, the color progresses through various shades of green and finally to blue. Readings are reported in terms of negative, trace, 1, 2, 3, and 4; or the semiquantitative values of 30, 100, 300, or 2000 mg/dL corresponding to each color change. Trace values are considered to be less than 30 mg/dL.



Clinical Significance of Urine Protein:

Prerenal Proteinuria

- caused by conditions affecting the plasma prior to its reaching the kidney and, therefore, is not indicative of actual renal disease.
- Increased levels of low molecular-weight plasma proteins such as hemoglobin, myoglobin, and the ***acute phase reactants*** associated with infection and inflammation.
- Intravascular hemolysis
- Muscle injury
- Acute phase reactants
- Multiple myeloma (Bence Jones protein)

Renal Proteinuria

- Proteinuria associated with true renal disease may be the result of either glomerular or tubular damage.

Glomerular disorders

- the glomerular membrane is damaged, selective filtration is impaired, and increased amounts of serum protein and eventually red and white blood cells pass through the membrane and are excreted in the urine
- e.g., ***amyloid material,*** toxic substances, and the immune complexes found in lupus erythematosus and streptococcal glomerulonephritis
- The amount of protein that appears in the urine ranges from slightly above normal to 4 g/day

Tubular Proteinuria

- Increased albumin is also present in disorders affecting tubular reabsorption because the normally filtered albumin can no longer be reabsorbed.
- Causes of tubular dysfunction include exposure to toxic substances and heavy metals, severe viral infections.

- Benign proteinuria is usually transient and can be produced by conditions such as strenuous exercise, high fever, dehydration, and exposure to cold.

Postrenal Proteinuria

- Protein can be added to a urine specimen as it passes through the structures of the lower urinary tract (ureters, bladder, urethra, prostate, and vagina).

- Bacterial and fungal infections and inflammations produce exudates containing protein from the interstitial fluid.

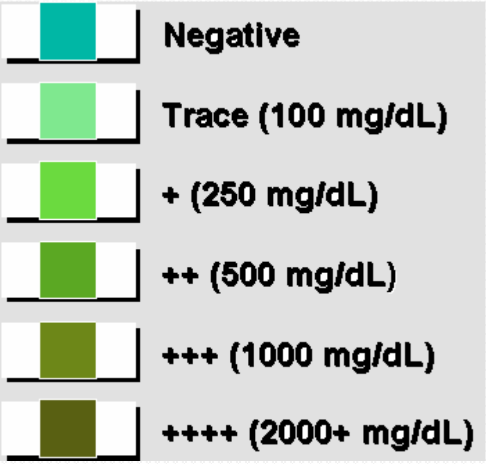
- The presence of blood as the result of injury or menstrual contamination contributes protein, as does the presence of prostatic fluid and large amounts of spermatozoa.

Glucose

- The glucose filtered by the glomerulus is reabsorbed in the proximal convoluted tubule; therefore, urine contains only minute amounts of glucose. Tubular reabsorption of glucose is by active transport in response to the body’s need to maintain an adequate concentration of glucose.
- The blood level of glucose become elevated (hyperglycemia), as occurs in diabetes mellitus, the tubular transport of glucose ceases, and glucose appears in the urine. The blood level at which tubular reabsorption stops (renal threshold) for glucose is approximately 160 to 180 mg/dL.

- Hyperglycemia that occurs during pregnancy and disappears after delivery is called gestational diabetes.
- Hyperglycemia of nondiabetic origin is seen in a variety of disorders and also produces glycosuria. (pancreatitis, pancreatic cancer, acromegaly, Cushing syndrome and hyperthyroidism and The hormones (glucagon, epinephrine, cortisol, thyroxine, and growth hormone, which are increased in these disorders, work in opposition to insulin, thereby producing hyperglycemia and glucosuria.
- Glycosuria occurs in the absence of hyperglycemia when the reabsorption of glucose by the renal tubules is compromised. "renal glycosuria" is seen in end-stage renal disease.

- Reagent strip manufacturers use several different chromogens, including potassium iodide (green to brown) and tetramethylbenzidine (yellow to green). Urine glucose may be reported in terms of negative, trace, 1+, 2+, 3+, and 4+.



Ketones

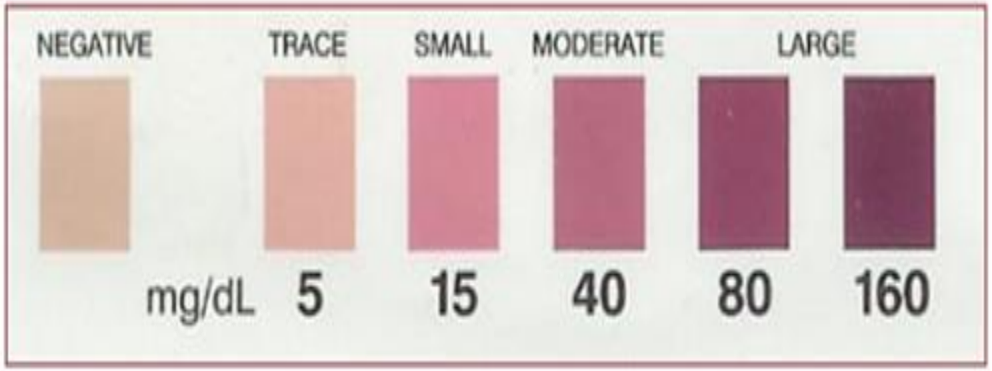
- Including three ketone bodies: The products of fat metabolism

acetoacetic acid	20%
acetone	2%
β-hydroxybutyric acid	78%

Clinical Significance of Urine Ketones

1. Diabetic acidosis
2. Insulin dosage monitoring
3. Starvation
4. Malabsorption/pancreatic disorders
5. Strenuous exercise
6. Vomiting
7. Inborn errors of amino acid metabolism

- Results are reported qualitatively as negative, trace, small (1+), moderate (2+), or large (3+), or semiquantitatively as negative, trace (5 mg/dL), small (15 mg/dL), moderate (40 mg/dL), or large (80 to 160 mg/dL).



Blood

- Blood may be present in the urine either in the form of intact red blood cells (hematuria) or as the product of red blood cell destruction, hemoglobin (hemoglobinuria) and myoglobin (myoglobinuria).
- blood present in large quantities can be detected visually; hematuria produces a cloudy red urine, and hemoglobinuria appears as a clear red specimen.
- Any amount of blood greater than five cells per microliter of urine is considered clinically significant,

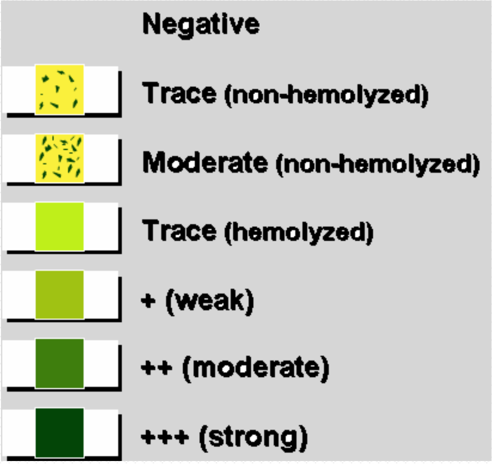
Hematuria (Renal calculi, Glomerulonephritis, Pyelonephritis, Tumors, Trauma, Exposure to toxic, chemicals, Anticoagulants and Strenuous exercise).

Hemoglobinuria (Transfusion reactions, Hemolytic anemias, Severe burns, Infections/malaria, Strenuous exercise/red blood cell trauma and Brown recluse spider bites).

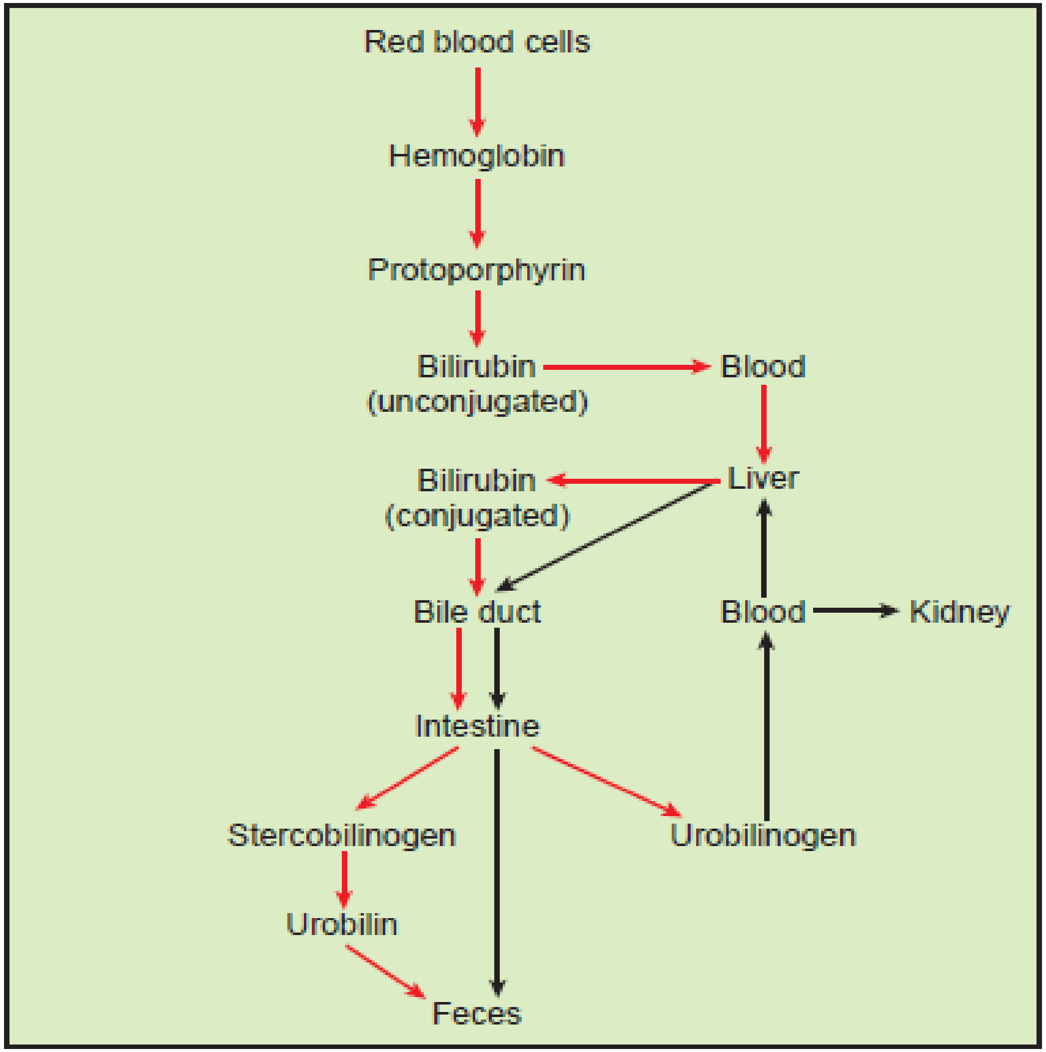
Myoglobinuria (Muscular trauma/crush syndromes, Prolonged coma, Convulsions, Muscle-wasting diseases, Alcoholism/overdose, Drug abuse, Extensive exertion and Cholesterol-lowering statin medications

- In the presence of free hemoglobin/myoglobin, uniform color ranging from a negative yellow through green to a strongly positive green-blue

- The terms trace, small, moderate, and large or trace, 1+, 2+ and 3+ are used for reporting



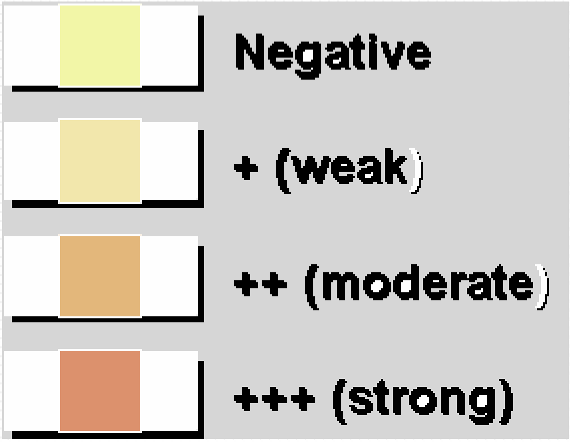
Hemoglobin Degradation



Bilirubin

- The appearance of bilirubin in the urine can provide an early indication of liver disease.
- Highly pigmented yellow compound.
- Degradation product of hemoglobin.
- Conjugated bilirubin appears in the urine when the normal degradation cycle is disrupted by obstruction of the bile duct (e.g., gallstones or cancer) or when the integrity of the liver is damaged, allowing leakage of conjugated bilirubin into the circulation. Hepatitis and cirrhosis are common examples of conditions that produce liver damage, resulting in bilirubinuria.

- Routine testing for urinary bilirubin by reagent strip uses the diazo reaction. Colors ranging from increasing degrees of tan or pink to violet, respectively. Qualitative results are reported as negative, small, moderate, or large, or as negative, 1+, 2+, or 3+.



Urobilinogen

- Urobilinogen appears in the urine because, as it circulates in the blood en route to the liver, it passes through the kidney and is filtered by the glomerulus. Therefore, a small amount of urobilinogen (less than 1 mg/dL) is normally found in the urine.
- Increased urine urobilinogen (greater than 1 mg/dL) is seen in liver disease and hemolytic disorders. Measurement of urine urobilinogen
- Clinical Significance of Urine Urobilinogen:

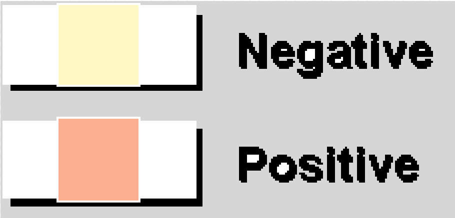
1. Early detection of liver disease
2. Liver disorders, hepatitis, cirrhosis, carcinoma
3. Hemolytic disorders

- **Urine Bilirubin and Urobilinogen in Jaundice**

	Urine Bilirubin	Urine Urobilinogen
Bile duct obstruction	+ + +	Normal
Liver damage	+ or −	+ +
Hemolytic disease	Negative	+ + +

Nitrite

- The reagent strip test for nitrite provides a rapid screening test for the presence of urinary tract infection **(UTI).**
- Based on the ability of certain bacteria to reduce nitrate, a normal constituent of urine, to nitrite.



- Clinical Significance of Urine Nitrite:

1. Cystitis
2. Pyelonephritis
3. Evaluation of antibiotic therapy
4. Monitoring of patients at high risk for urinary tract infection
5. Screening of urine culture specimens

Leukocyte Esterase

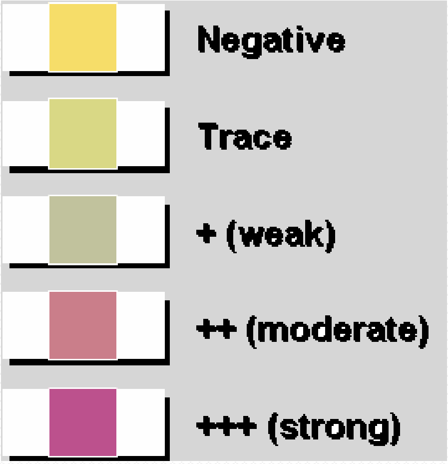
- Leukocyte estrase test detects the presence of leukocytes that have been lysed, particularly in dilute alkaline urine, and would not appear in the microscopic examination.

- Normal values for leukocytes are based on the microscopic sediment examination and vary from 0 to 2 to 0 to 5 per high power field.

- Increased urinary leukocytes are indicators of UTI.

- The LE test detects the presence of esterase in the granulocytic white blood cells (neutrophils, eosinophils, and basophils) and monocytes. Neutrophils are the leukocytes most frequently associated with bacterial infections

- Reactions are reported as trace, small, moderate, and strong or trace, 1+, 2+, and 3+.



Renal calculi

- Renal calculi (kidney stones) may form in the calyces and pelvis of the kidney, ureters, and bladder.
- the calculi vary in size from barely visible to large, staghorn calculi resembling the shape of the renal pelvis and smooth, round bladder stones with diameters of 2 or more inches. Small calculi may be passed in the urine, subjecting the patient to severe pain radiating from the lower back to the legs. Larger stones cannot be passed and may not be detected until patients develop symptoms of urinary obstruction.

- Conditions favoring the formation of renal calculi are similar to those favoring formation of urinary crystals, including pH, chemical concentration, and urinary stasis.

- The finding of clumps of crystals in freshly voided urine suggests that conditions may be right for calculus formation.

- Analysis of the chemical composition of renal calculi plays an important role in patient management.

- Approximately 75% of the renal calculi are composed of calcium oxalate or phosphate. Magnesium ammonium phosphate, uric acid, and cystine are the other primary calculi constituents.

- Calcium calculi are frequently associated with metabolic calcium and phosphate disorders and occasionally diet. Magnesium ammonium phosphate calculi are frequently accompanied by urinary infections involving urea-splitting bacteria. The urine pH is often higher than 7.0. Uric acid calculi may be associated with increased intake of foods with high purine content. The urine pH is acidic. Most cystine calculi are seen in conjunction with hereditary disorders of cystine metabolism