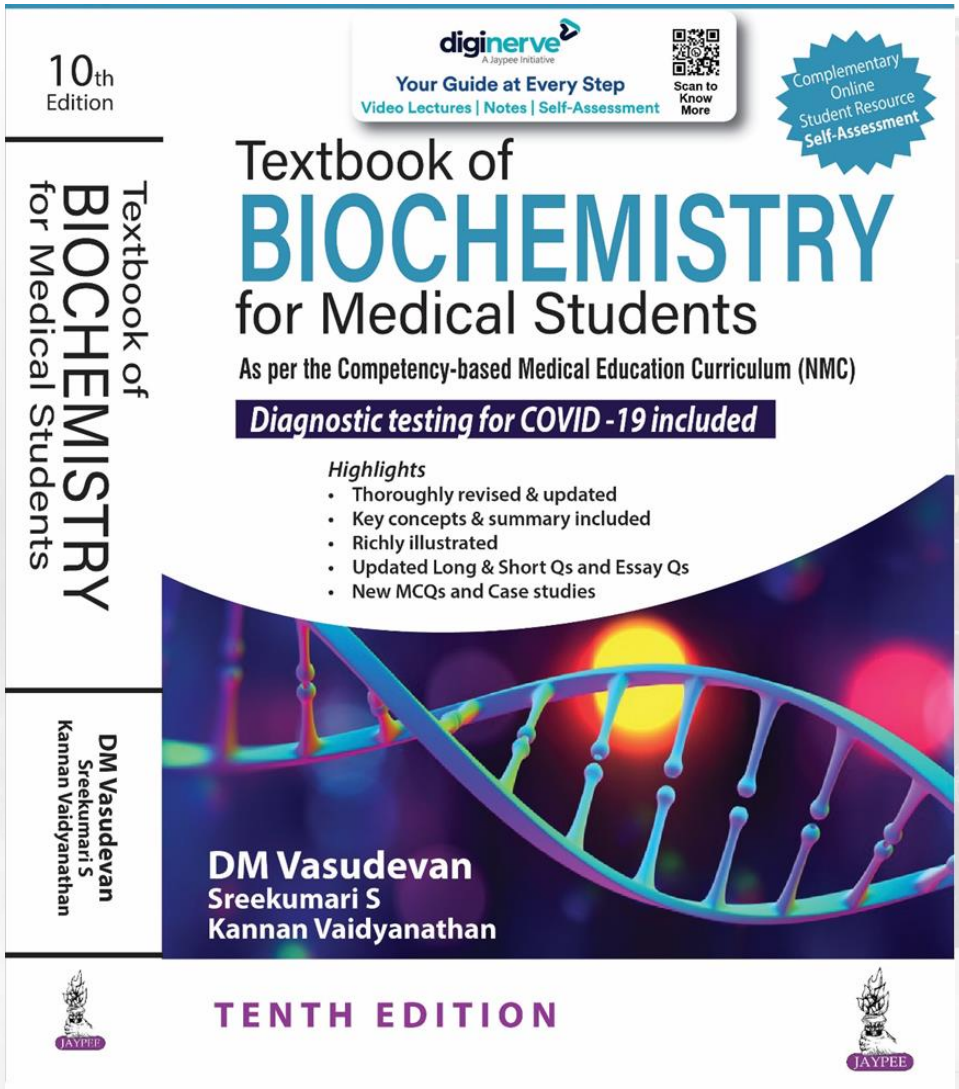


Chapter 25:

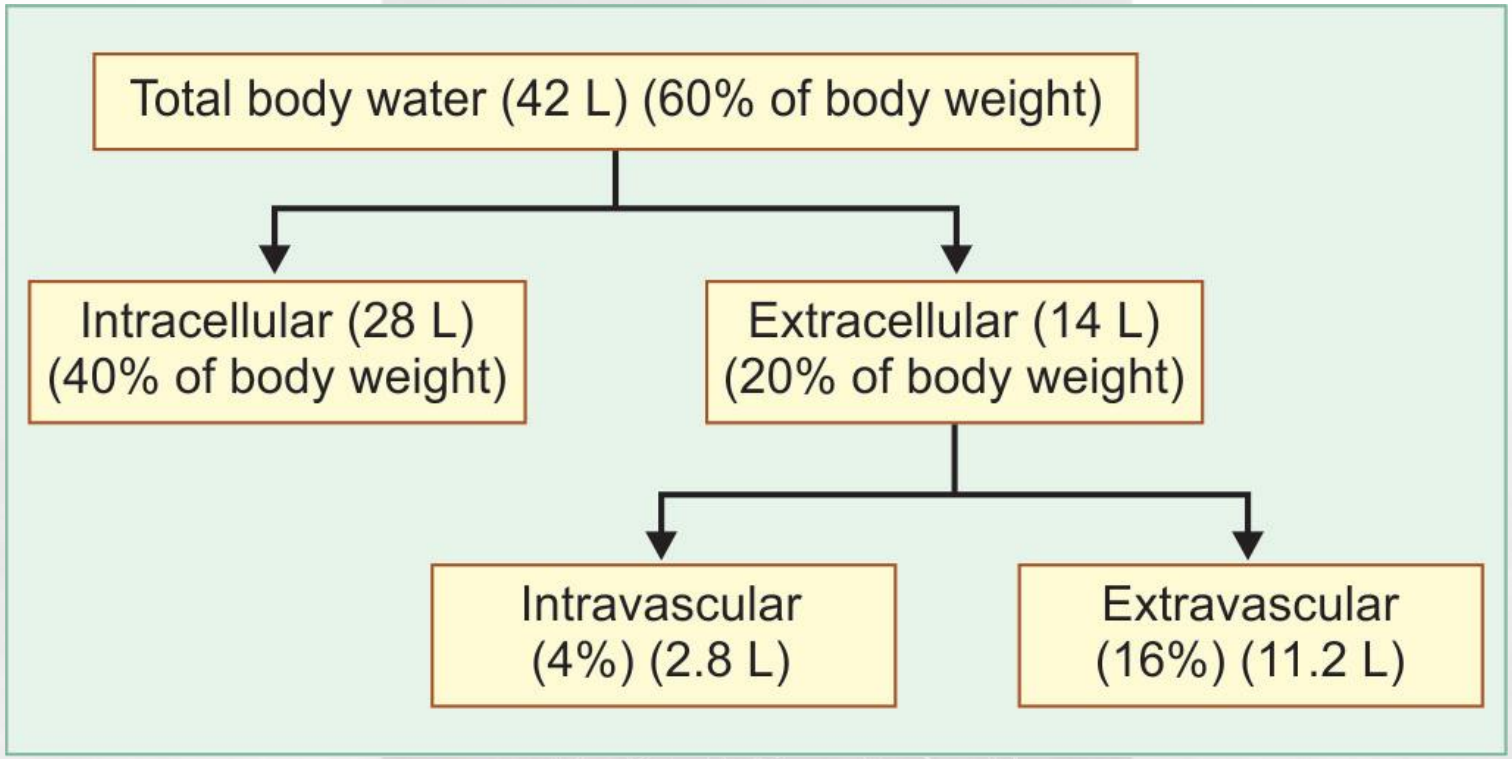
Water Balance, Electrolyte Balance (Sodium, Potassium, Magnesium, Chloride), Milk, CSF, Amniotic fluid

Textbook of
BIOCHEMISTRY
for Medical Students

By DM Vasudevan, *et al.*

TENTH EDITION

Water Balance

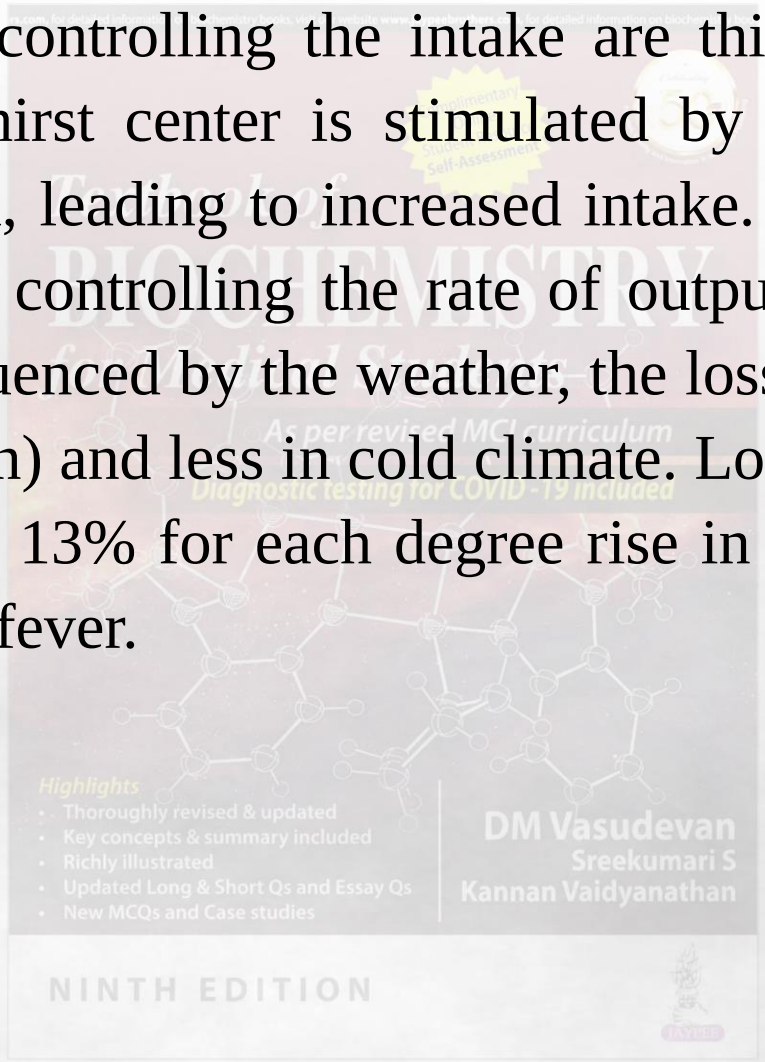


The body water compartments.

Water Balance in the Body

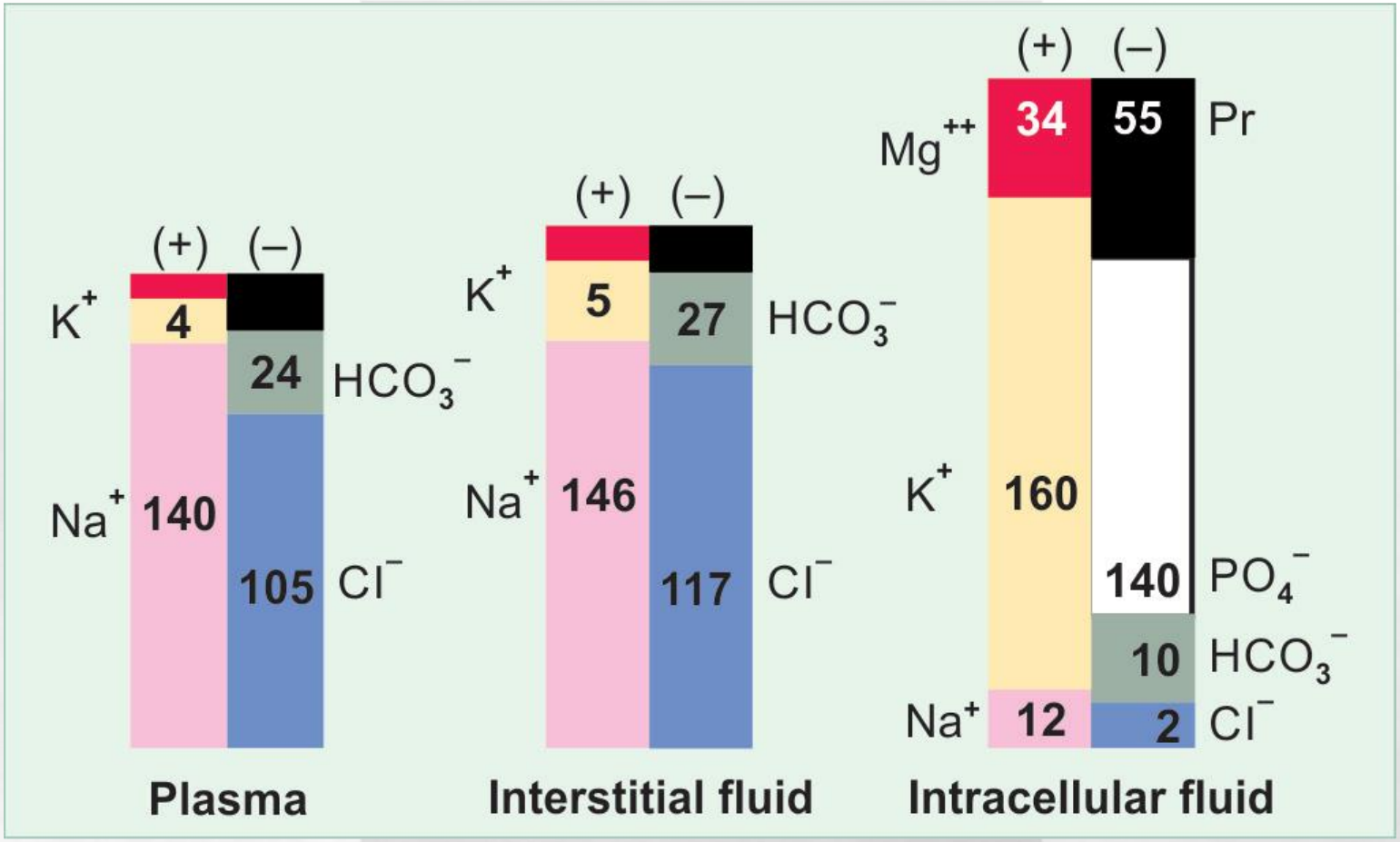
Intake per day		Output per day	
Water in food	1250 ml	Urine	1500 ml
Oxidation of food	300 ml	Skin	500 ml
Drinking water	1200 ml	Lungs	700 ml
		Feces	50 ml
Total	2750 ml		2750 ml

The major factors controlling the intake are thirst and the rate of metabolism. The thirst center is stimulated by an increase in the osmolality of blood, leading to increased intake. The renal function is the major factor controlling the rate of output. The rate of loss through skin is influenced by the weather, the loss being more in hot climate (perspiration) and less in cold climate. Loss of water through skin is increased to 13% for each degree rise in centigrade in body temperature during fever.



Gastrointestinal Secretions and their Electrolyte Composition

GI secretion	*Volume in L*	*Sodium mmol/L*	*Potas-sium mmol/L*	*Chloride or bicarbonate mmol/L*
Saliva	1.5	40	20	Chloride 40
Gastric juice	1.5	70–120	10	Chloride 100
Bile	1	140	5	Chloride 100
Pancreatic juice	1.5–2	140	5	Bicarbonate 75–90
Intestinal secretion	12	100-120	5-10	Bicarbonate 105



Gamblegrams Showing Composition of Fluid Compartments

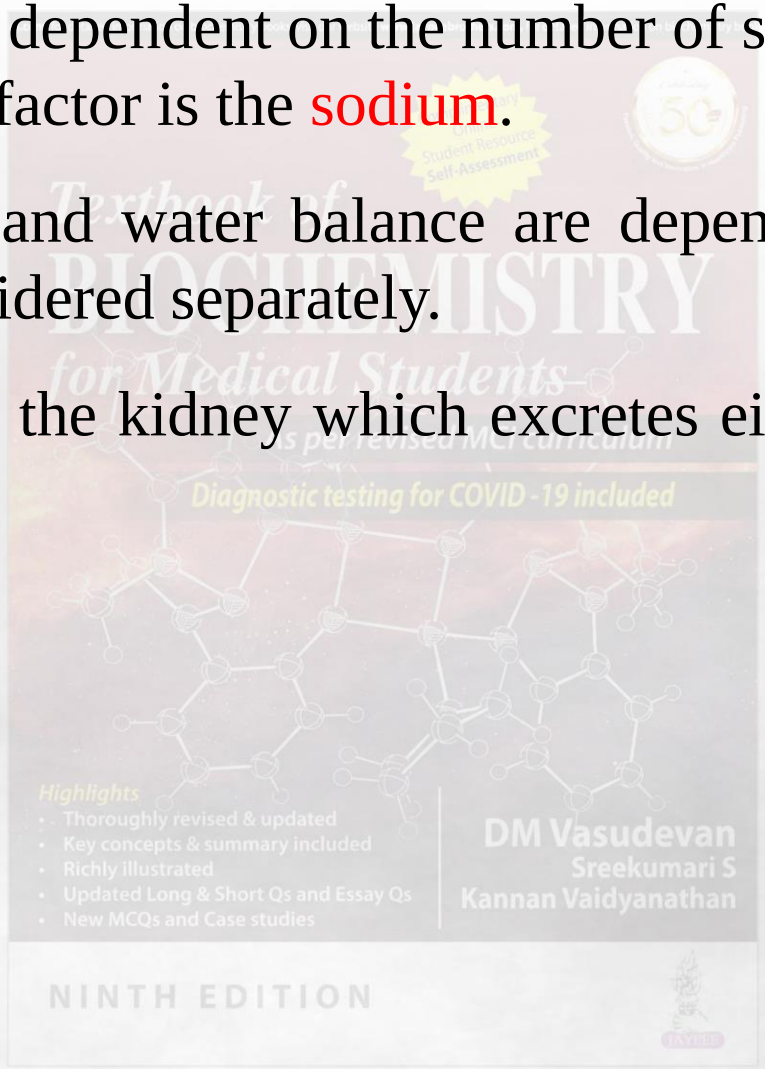
Electrolyte Concentration of body Fluid Compartments

Solutes	Plasma mEq/L	Interstitial fluid (mEq/L)	Intracellular fluid (mEq/L)
Cations:		146	12
Sodium	140	5	160
Potassium	4	3	-
Calcium	5	1	34
Magnesium	1.5		
Anions:			
Chloride	105	117	2
Bicarbonate	24	27	10
Sulphate	1	1	-
Phosphate	2	2	140
Protein	15	7	54
Other anions	13	1	-

Since osmolality is dependent on the number of solute particles, the major determinant factor is the sodium.

Therefore sodium and water balance are dependent on each other and cannot be considered separately.

It is maintained by the kidney which excretes either water or solute as the case may be.



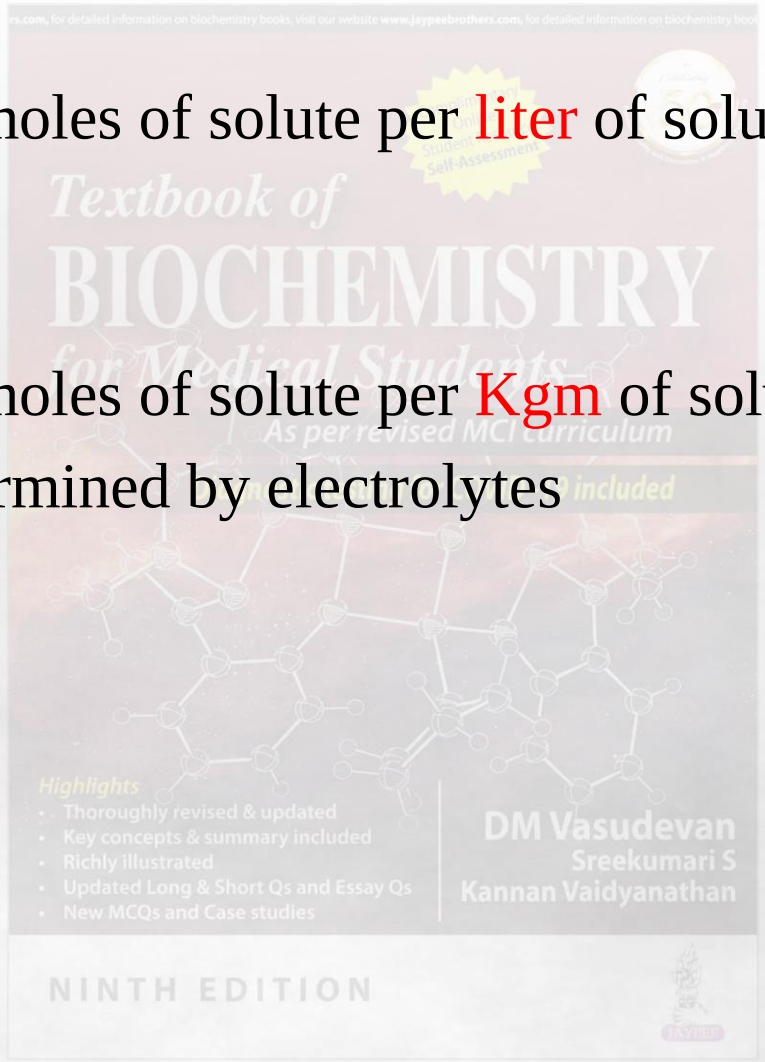
- ***Osmolarity***

  No. of moles/ mmoles of solute per liter of solution

- ***Osmolality***

  No. of moles/ mmoles of solute per Kgm of solvent

  Mainly determined by electrolytes



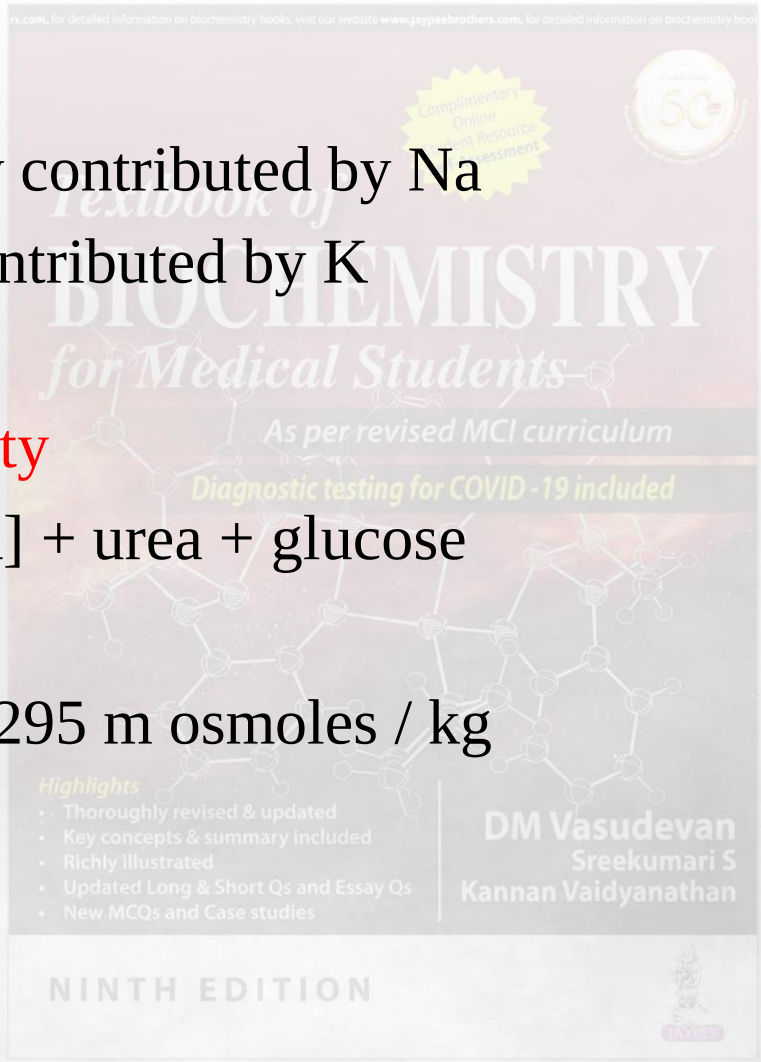
Osmolality

- Plasma – mainly contributed by Na
- ICF – mainly contributed by K

- Plasma osmolality

= 2 x [Na] + 2 x [K] + urea + glucose

- N value = 285 –295 m osmoles / kg

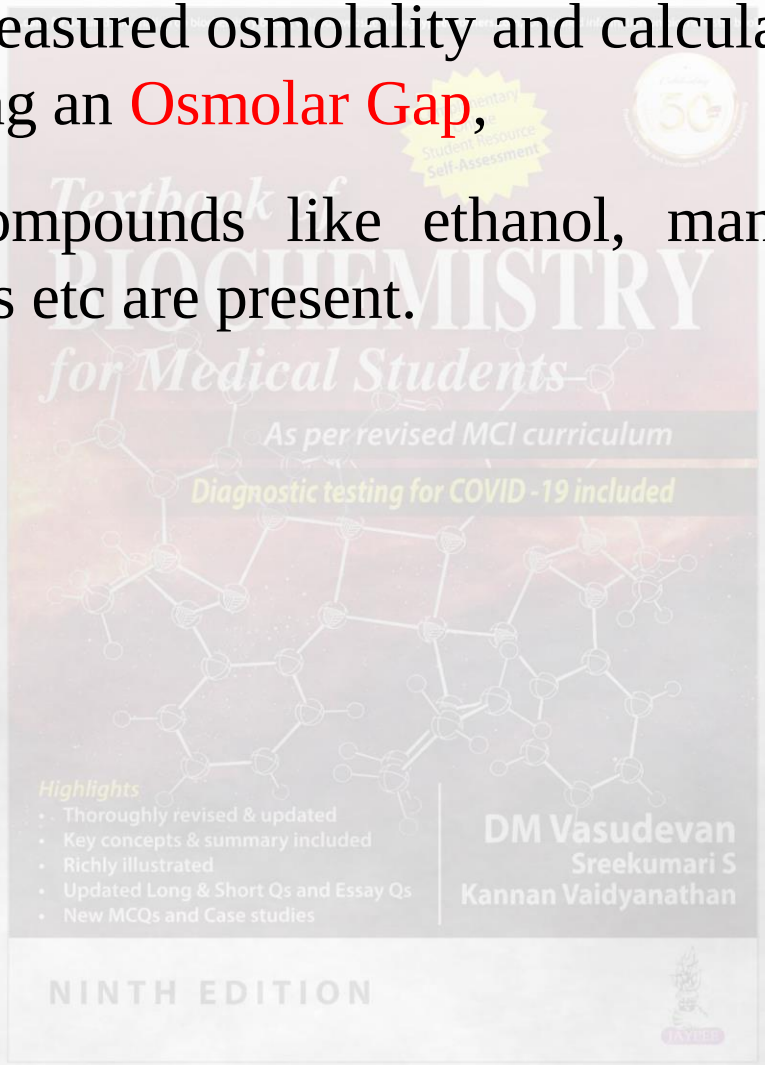


Osmolality of Plasma

Solute	Osmolality in mmol/kg	
Sodium with anions	270	92%
Potassium with anions	7	
Calcium with anions	3	
Magnesium with anions	1	
Urea	5	
Glucose	5	
Proteins	1	8%
	292	

The difference in measured osmolality and calculated osmolality may increase causing an Osmolar Gap,

when abnormal compounds like ethanol, mannitol, neutral and cationic amino acids etc are present.



Effective Osmolality

It is the term used for those extracellular solutes that determine water movement across the cell membrane.
Permeable solutes such as urea and alcohol enter into the cell and achieve osmotic equilibrium. Although there is increase in osmolality, there is no shift in water.

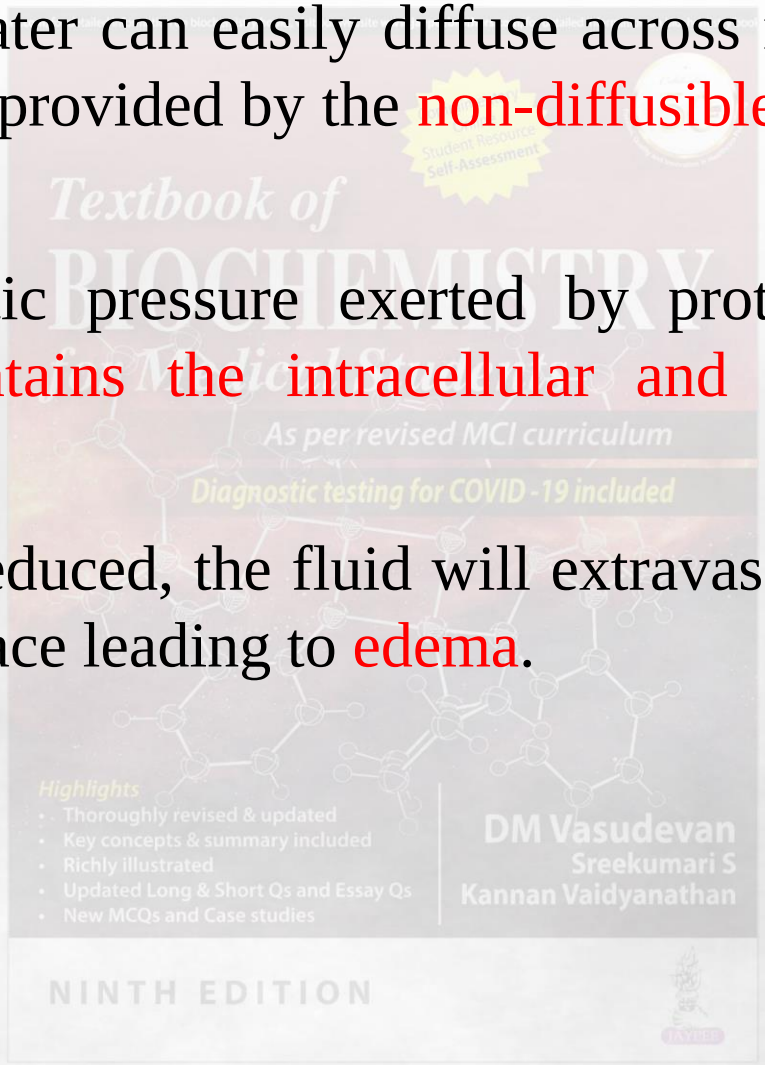
On the other hand, if impermeable solutes like glucose, mannitol, etc. are present in ECF, water shifts from ICF to ECF and extracellular osmolality is increased.

So, for every 100 mg/dl increase in glucose, 1.5 mmol/L of sodium is reduced (dilutional hyponatremia). Hence, the plasma sodium is a reliable index of total and effective osmolality in the normal and clinical situations.

Crystalloids and water can easily diffuse across membranes, but an osmotic gradient is provided by the non-diffusible colloidal (protein) particles.

The colloid osmotic pressure exerted by proteins is the major factor which maintains the intracellular and intravascular fluid compartments.

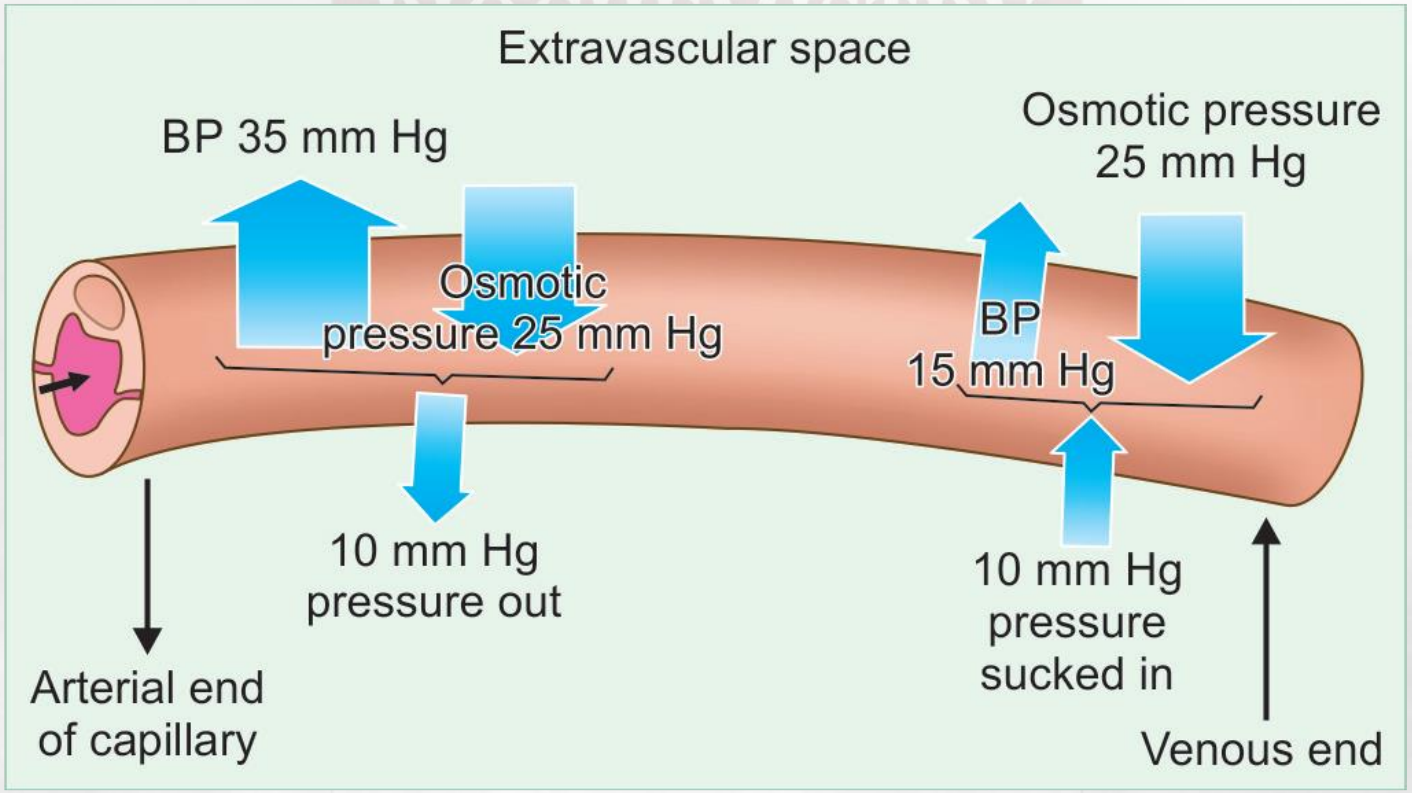
If this gradient is reduced, the fluid will extravasate and accumulate in the interstitial space leading to edema.



Total Osmotic Pressure : 5000 mm Hg

Effective Osmotic pressure: 25 mmHg

80% by albumin; 20% globulins

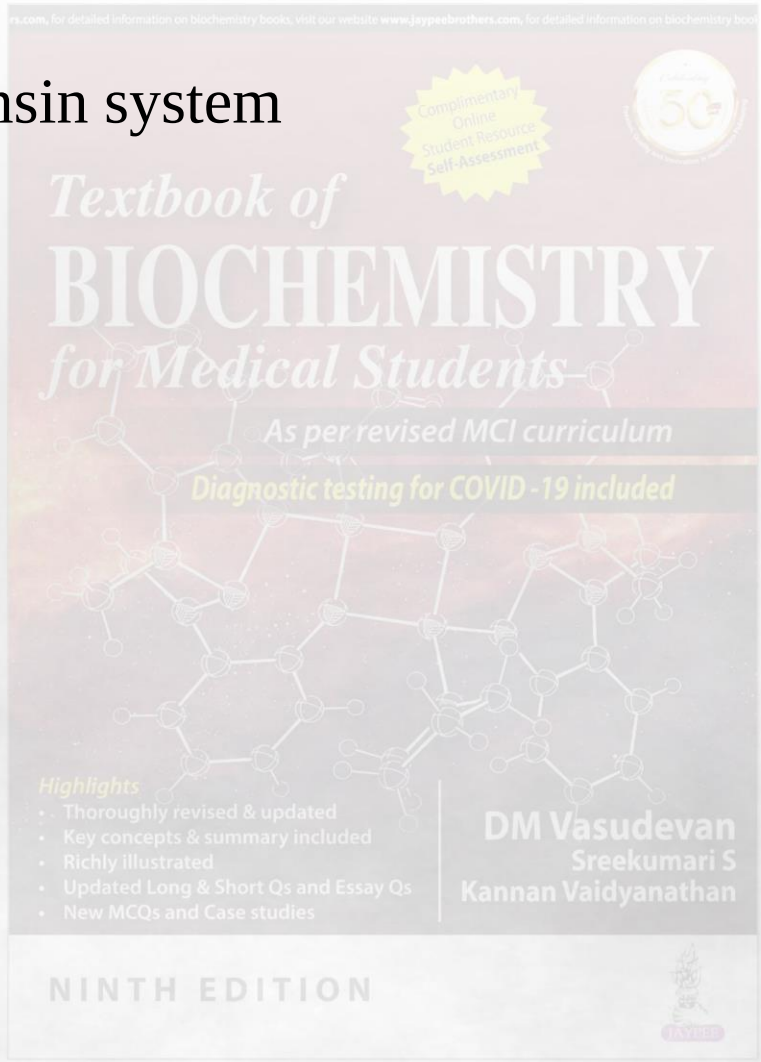


Summary of ECF and ICF

1. At equilibrium, the osmolality of extracellular fluid (ECF) and intracellular fluid (ICF) are identical.
2. Solute content of ICF is constant.
3. Sodium is retained only in the ECF.
4. Total body solute divided by total body water gives the body fluid osmolality.
5. Total intracellular solute divided by plasma osmolality will be equal to the intracellular volume.

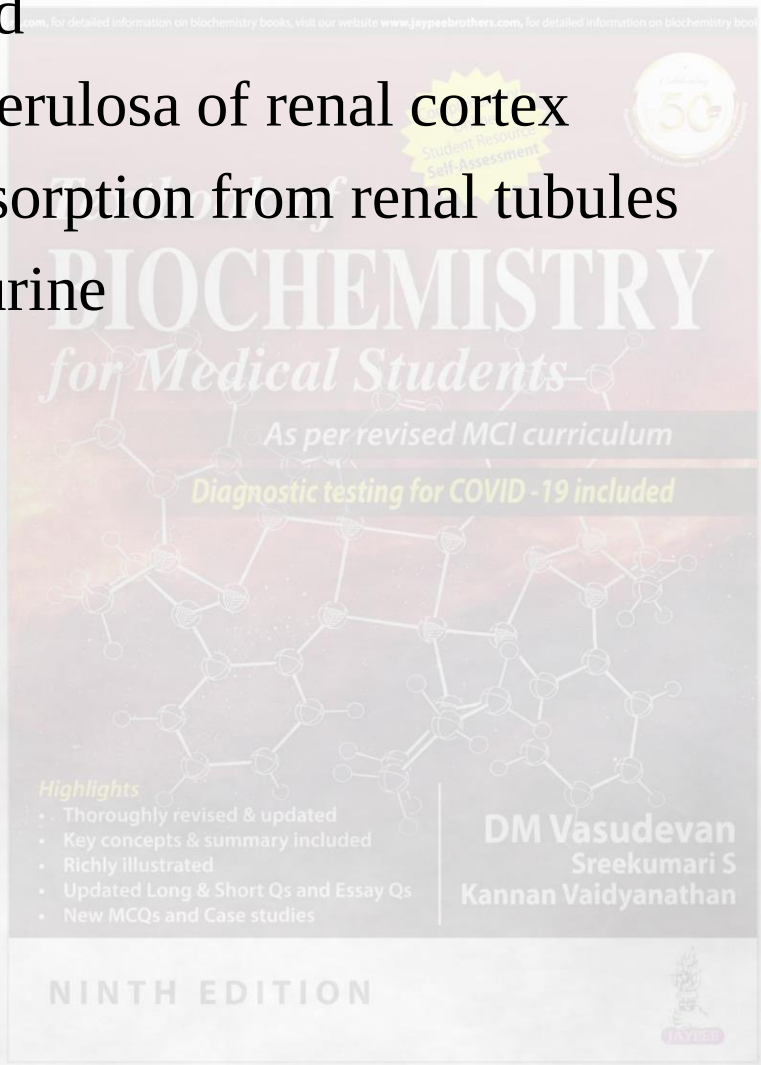
Hormones Regulating Water Balance

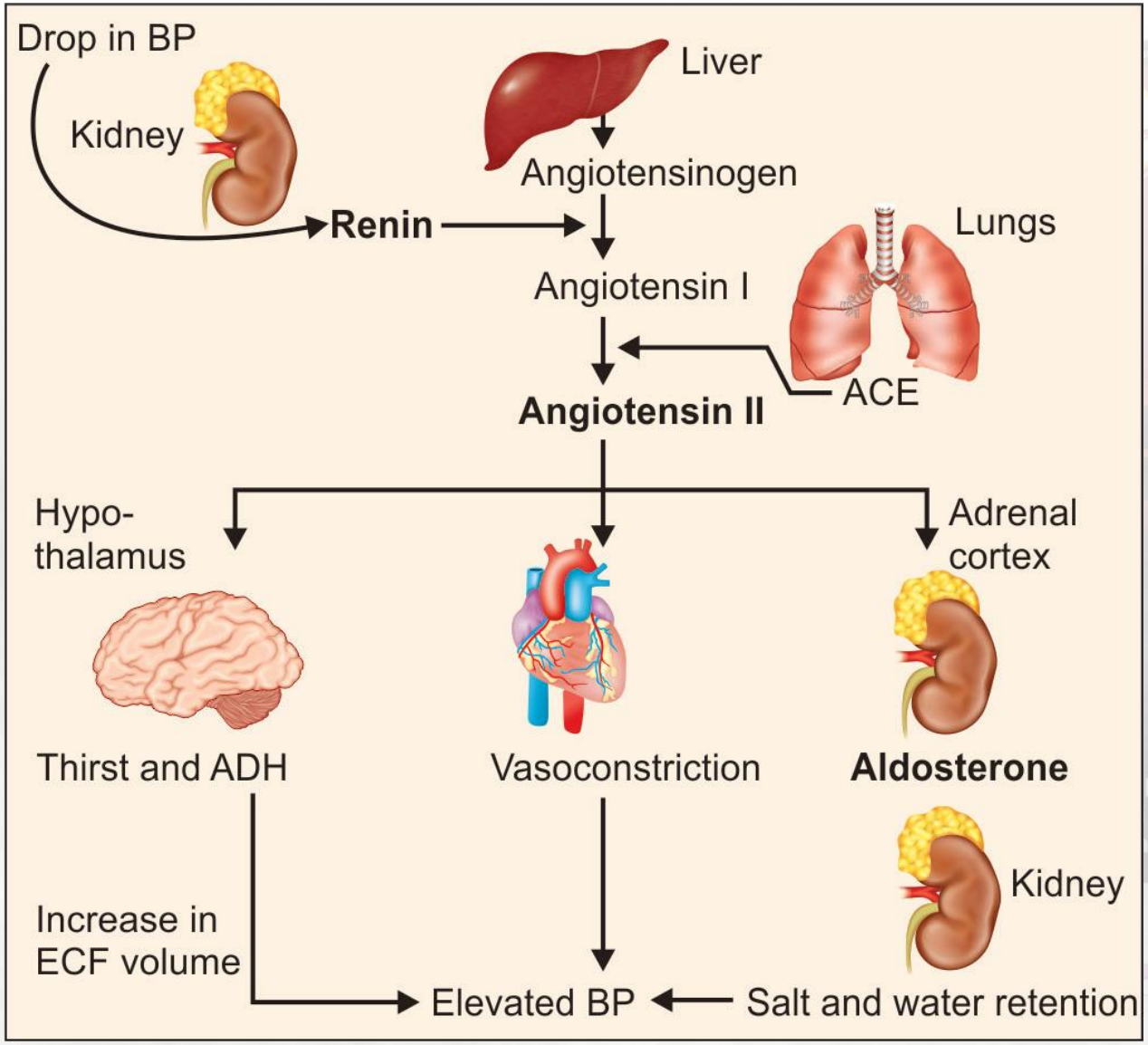
- Aldosterone
- Renin – Angiotensin system
- ADH
- ANP



Aldosterone

- Mineralocorticoid
- From Zona glomerulosa of renal cortex
- Causes Na^+ reabsorption from renal tubules
- K^+ & H^+ lost in urine

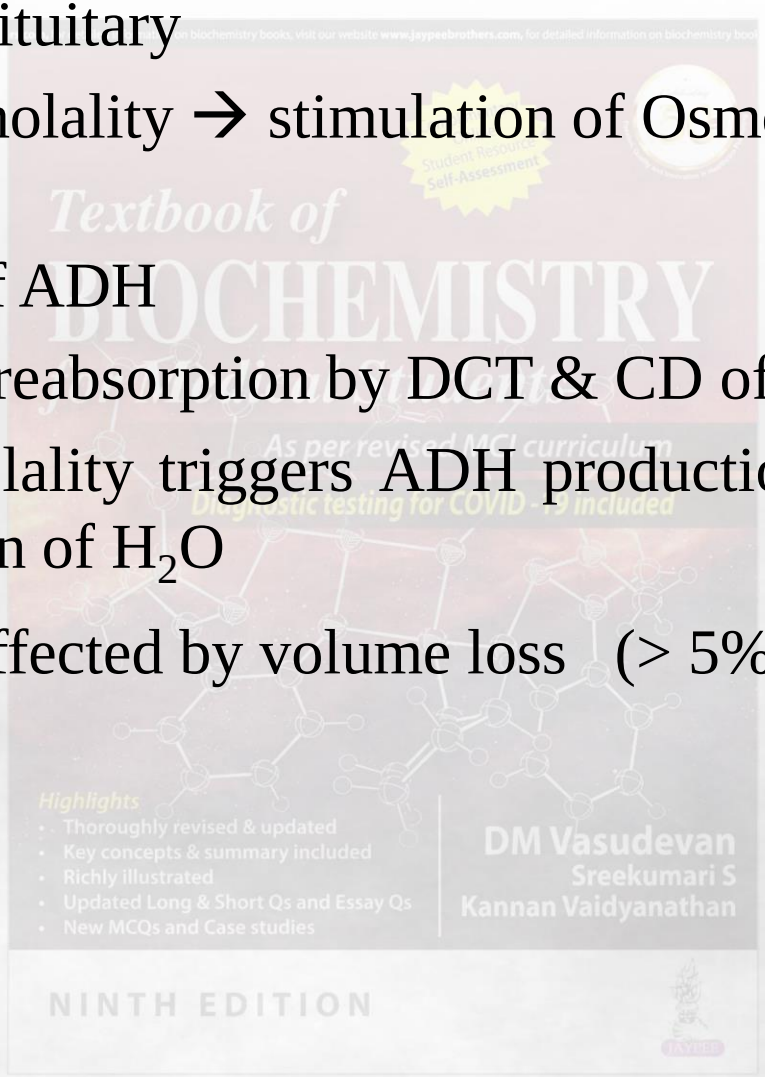




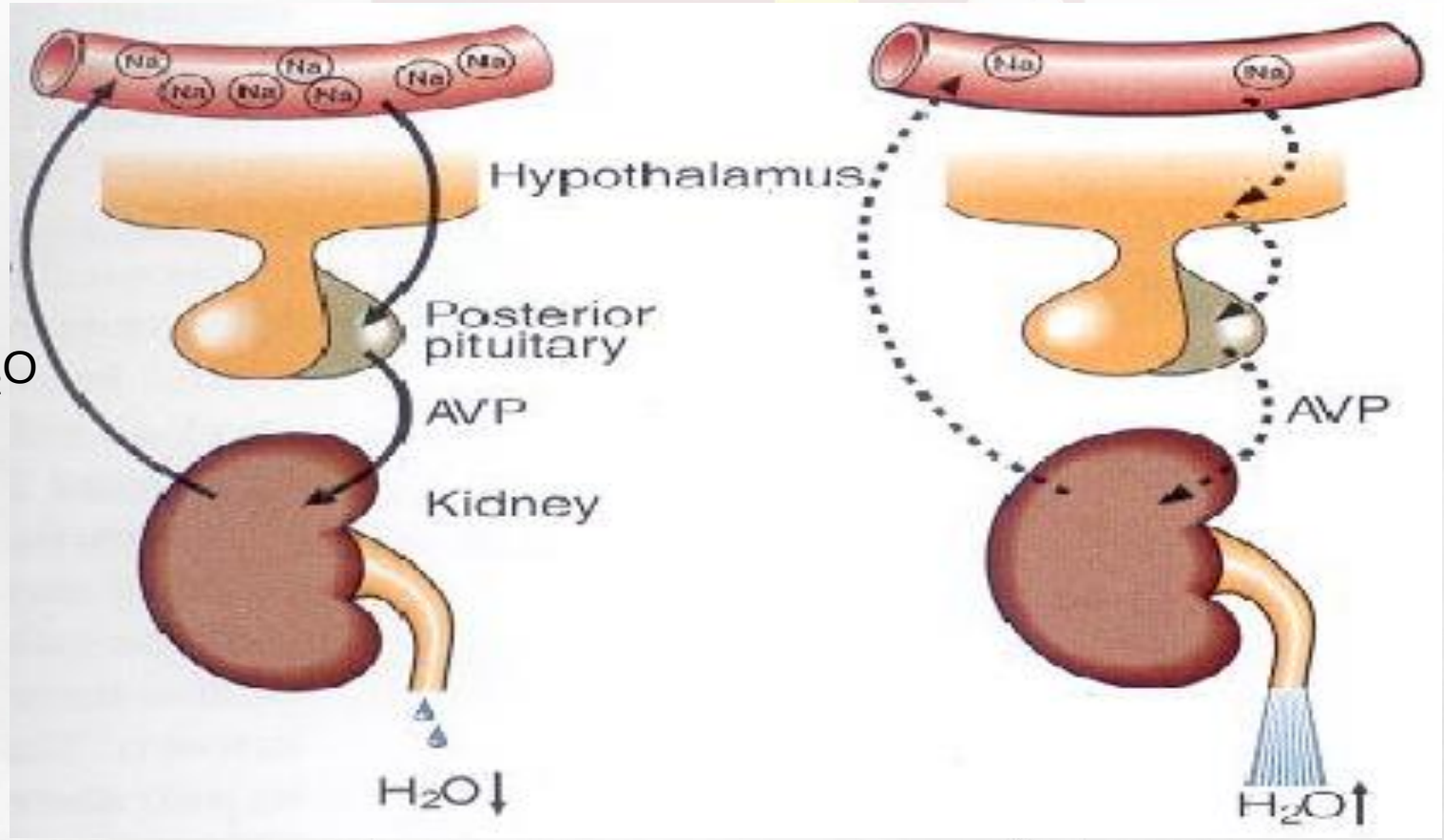
Mechanism of action of renin-angiotensin and aldosterone.

ADH (Vasopressin)

- From posterior Pituitary
- High plasma osmolality → stimulation of Osmoreceptors of hypothalamus
- Causes release of ADH
- Increases water reabsorption by DCT & CD of kidneys
- 1% rise in osmolality triggers ADH production, which increases renal reabsorption of H_2O
- Response also affected by volume loss (> 5%)



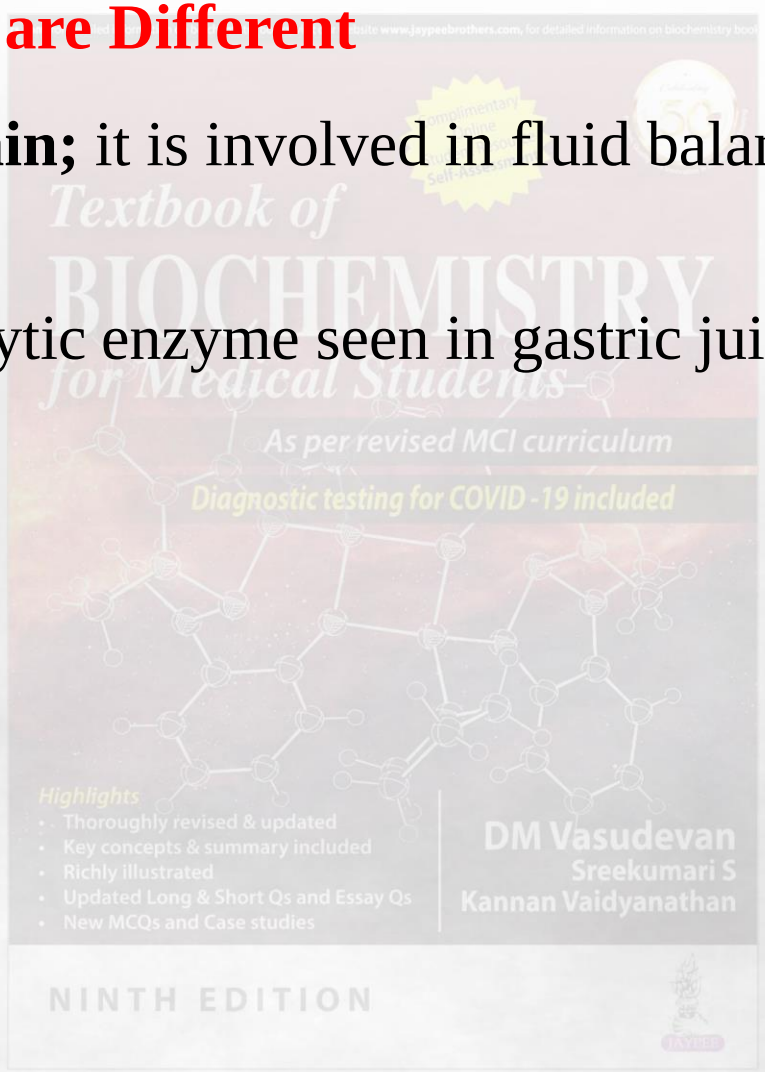
Fluid Regulation by ADH

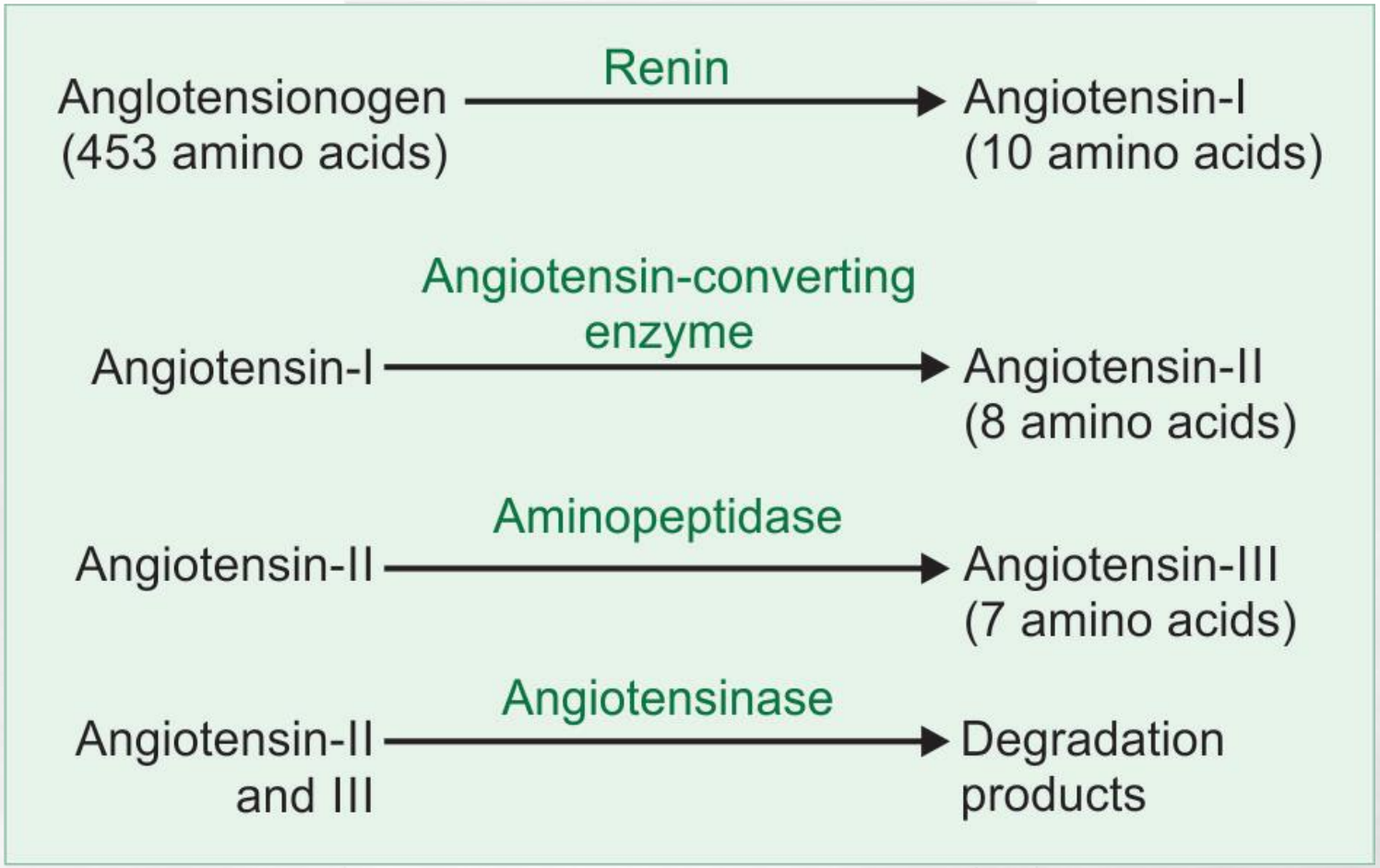


Renin and Rennin are Different

Kidney secretes **renin;** it is involved in fluid balance and hypertension.

Rennin is a proteolytic enzyme seen in gastric juice, especially in children.





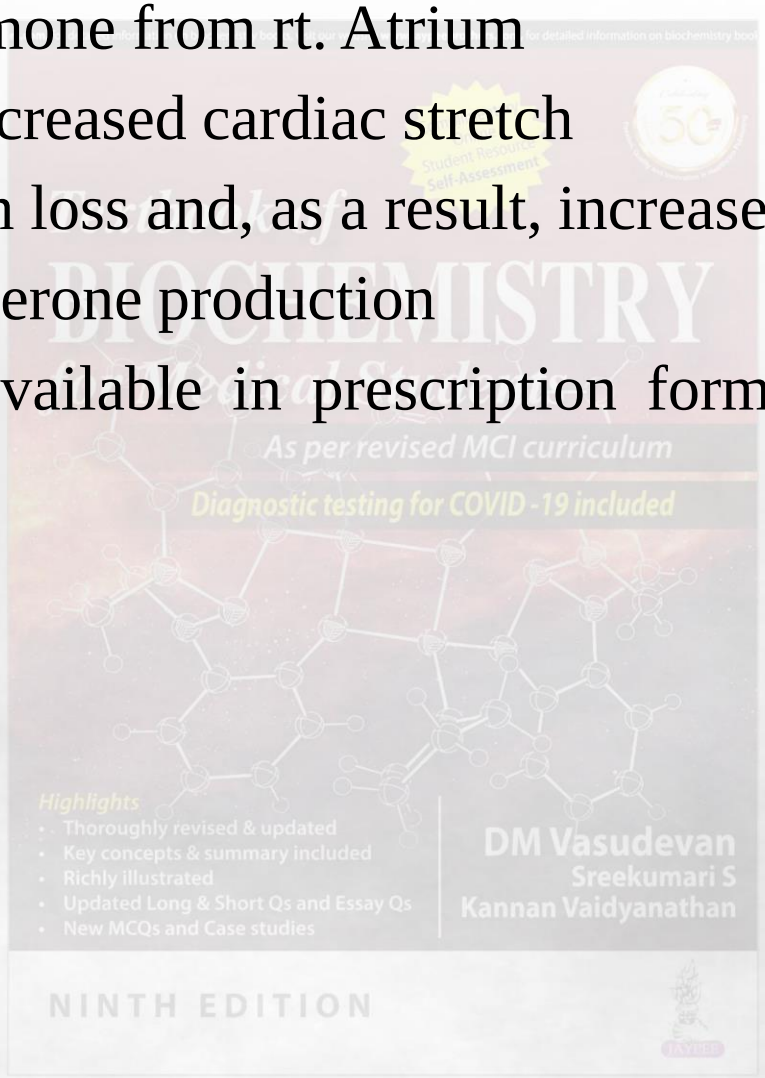
Pathway of Angiotensin Production.

Clinical significance of angiotensin converting enzyme (ACE) inhibitors and its antagonists

Angiotensin converting enzyme (ACE) is a glycoprotein present in the lung. ACE-inhibitors are useful in treating edema and chronic congestive cardiac failure. Various peptide analogues of angiotensin II (saralasin) and antagonists of the converting enzyme (captopril) are useful to treat renin-dependent hypertension. Angiotensin I is inactive; II and III are active.

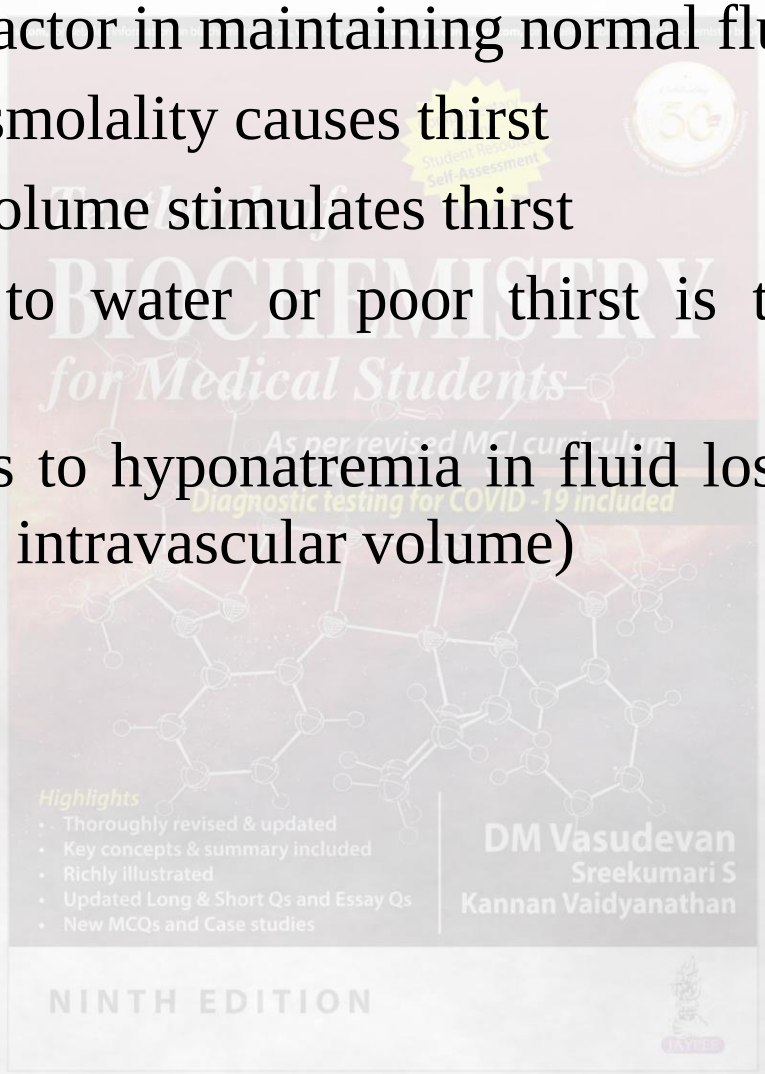
Natriuretic Peptides

- Polypeptide hormone from rt. Atrium
- Stimulated by increased cardiac stretch
- Increases sodium loss and, as a result, increases water excretion
- Decreases aldosterone production
- B-type (BNP) available in prescription form to treat congestive heart failure



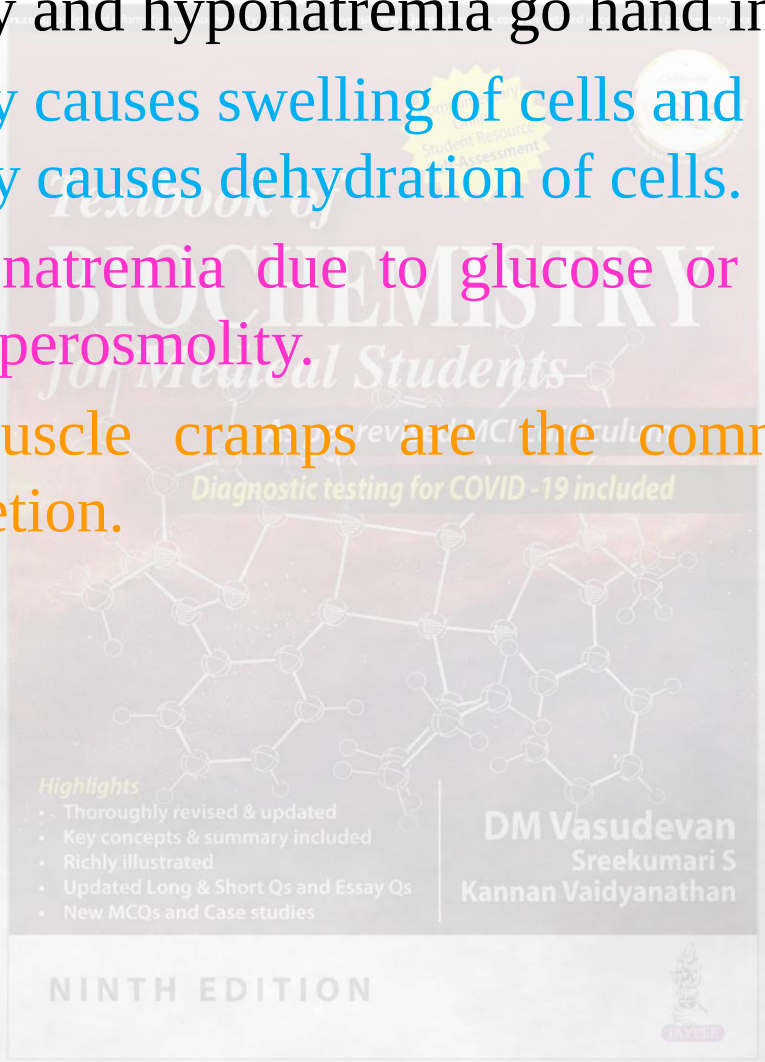
Thirst

- Most important factor in maintaining normal fluid balance
- 1% increase in osmolality causes thirst
- 5% decrease in volume stimulates thirst
- Lack of access to water or poor thirst is the major cause of hypernatremia
- Thirst contributes to hyponatremia in fluid loss, edematous states (triggered by low intravascular volume)



Salient Features of Electrolyte Imbalance

1. Hypo-osmolatiy and hyponatremia go hand in hand.
2. Hypo-osmolality causes swelling of cells and hyper-osmolality causes dehydration of cells.
3. Dilutional hyponatremia due to glucose or mannitol increases the effects of hyperosmolity.
4. Fatigue and muscle cramps are the common symptoms of electrolyte depletion.



Salient Features of Electrolyte Imbalance, Especially in Cases of Patients on Fluids

1. Hypo-osmolality and hyponatremia go hand in hand.
2. Hypo-osmolality causes swelling of cells and hyper-osmolality causes cell dehydration.
3. Hyponatremia of extracellular fluid causes symptoms when associated with hyperkalemia.
4. Dilutional hyponatremia due to glucose or mannitol increases the effects of hyperosmolality.
5. Fatigue and muscle cramps are the common symptoms of electrolyte depletion.
6. Hypo-osmolality of gastrointestinal cells cause nausea, vomiting and paralytic ileus.

Control of Sodium and Water

Factor	Acting through	Effect
Extracellular Osmolality	Thirst and ADH	Increases water intake and reabsorption of water from kidney
Hypovolemia	Stimulation of thirst and ADH	Increases retention of water
-do-	Stimulates Aldosterone	Increases retention of sodium
Expansion of ECF	Inhibits Aldosterone	Decreases reabsorption of sodium
Hypo-osmolality	Inhibits ADH Secretion	Decreases reabsorption of water

Assessment of Sodium and Water Balance

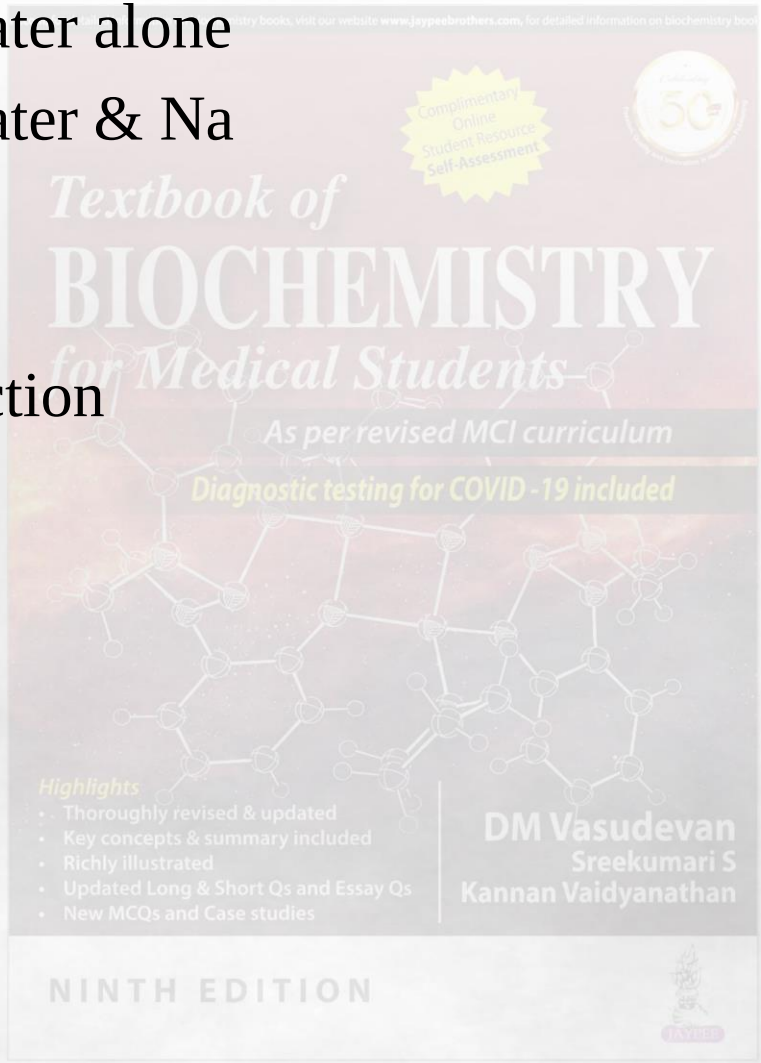
1. Maintenance of intake-output chart, in cases of patients on IV fluids. The insensible loss of water is high in febrile patients.
2. Measurement of serum electrolytes (sodium, potassium, chloride and bicarbonate). This will give an idea of the excess, depletion or redistribution.
3. Measurement of hematocrit value to see if there is hemoconcentration or dilution.
4. Measurement of urinary excretion of electrolytes, especially sodium and chloride.

Dehydration

- Due to loss of water alone
- Due to loss of water & Na

3 types

- Isotonic contraction
- Hypotonic
- Hypertonic

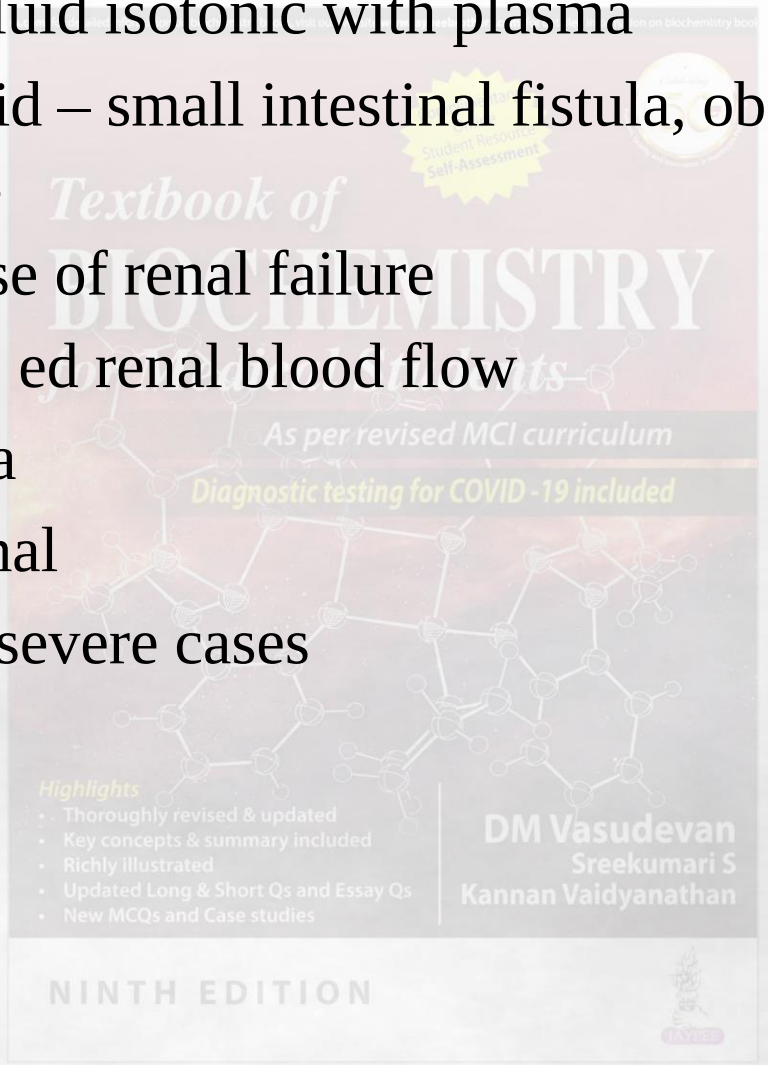


Isotonic Contraction

- Cause – loss of fluid isotonic with plasma
  - Loss of GI fluid – small intestinal fistula, obstruction, paralytic ileus
  - Recovery phase of renal failure
- Hypovolemia - ↓ ed renal blood flow
  - uremia, oliguria

  Plasma Na normal

  Hypotension in severe cases



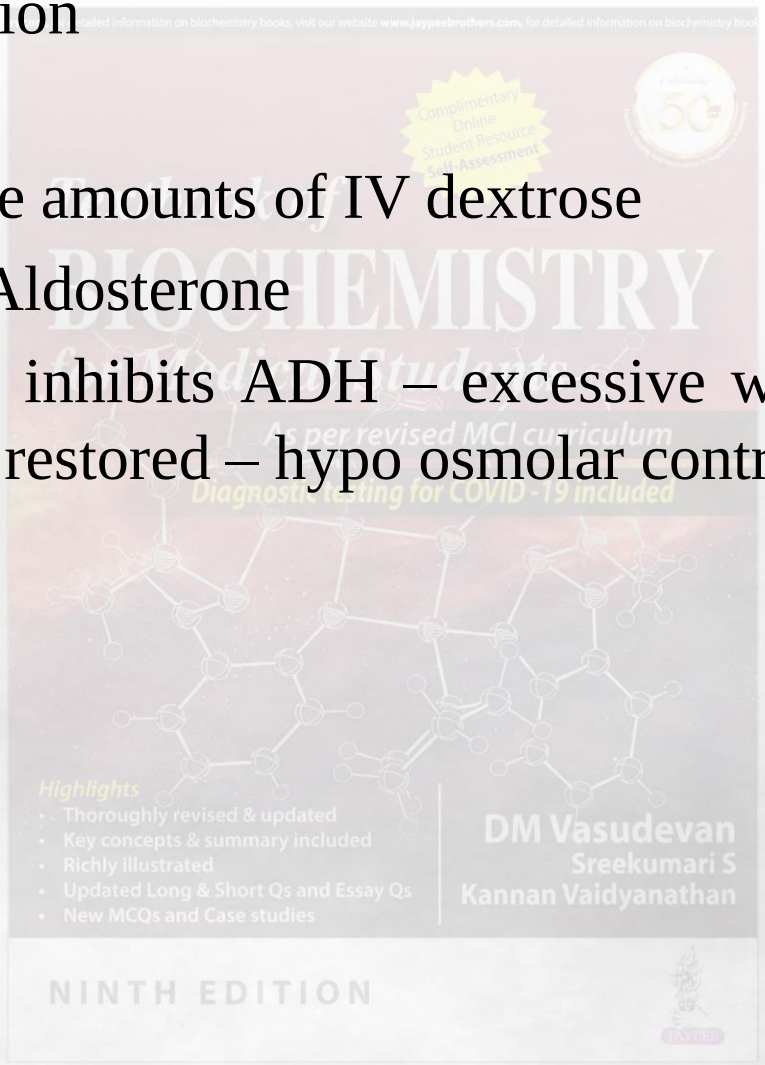
Hypotonic Contraction

- Due to Na depletion
- Causes

  - Infusion of large amounts of IV dextrose

  - Deficiency of Aldosterone

- Hypo osmolality inhibits ADH – excessive water loss – plasma Na & osmolality restored – hypo osmolar contraction



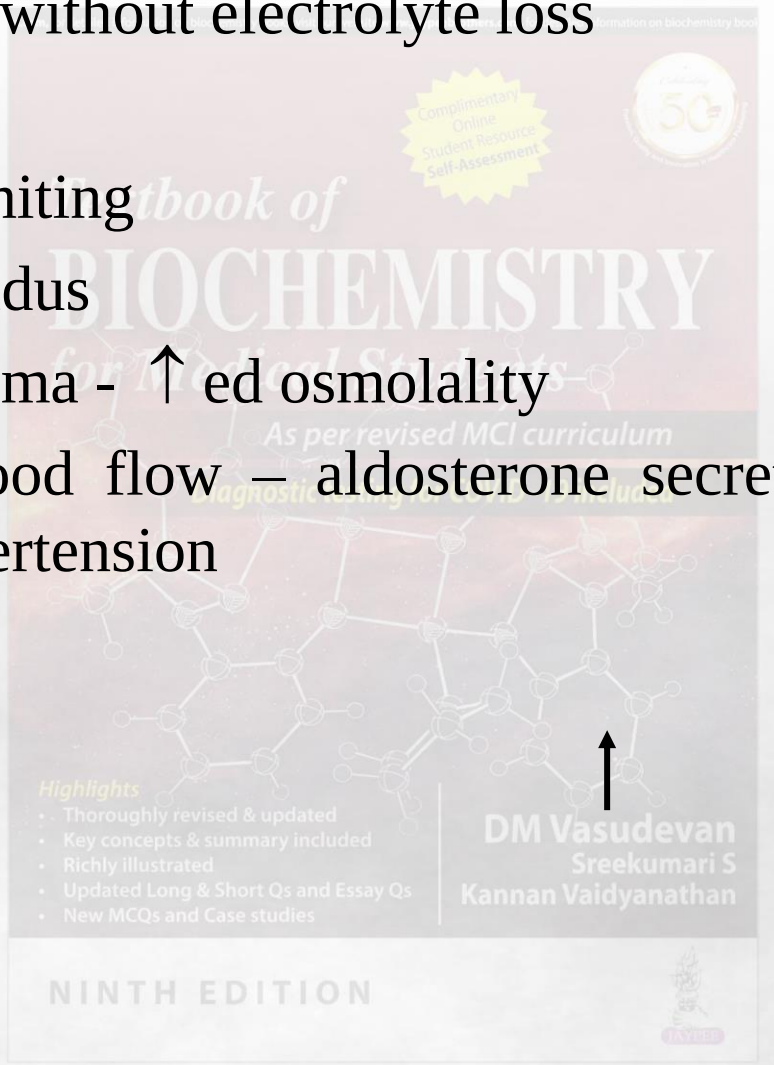
Hypotonic Contraction

- Water depletion without electrolyte loss
- Causes –

  - Diarrhoea, vomiting

  - Diabetes Insipidus

- ↑ ed Na in plasma - ↑ ed osmolality
- ↓ ed renal blood flow – aldosterone secretion – further Na retention & hypertension



Disturbances of fluid volume

Abnormality	Biochemical features	Osmolality	Hematocrit	Plasma sodium
Expansion of ECF				
Isotonic	Retention of Na^+, water	Normal	Low	Normal
Hypotonic	Relative water excess	Decreased	Low	Low
Hypertonic	Relative sodium excess	Increased	Low	High
Contraction of ECF				
Isotonic	Loss of Na+ and water	Normal	High	Normal
Hypotonic	Relative loss of Na+	Decreased	High	Low
Hypertonic	Relative loss of water	Increased	High	High

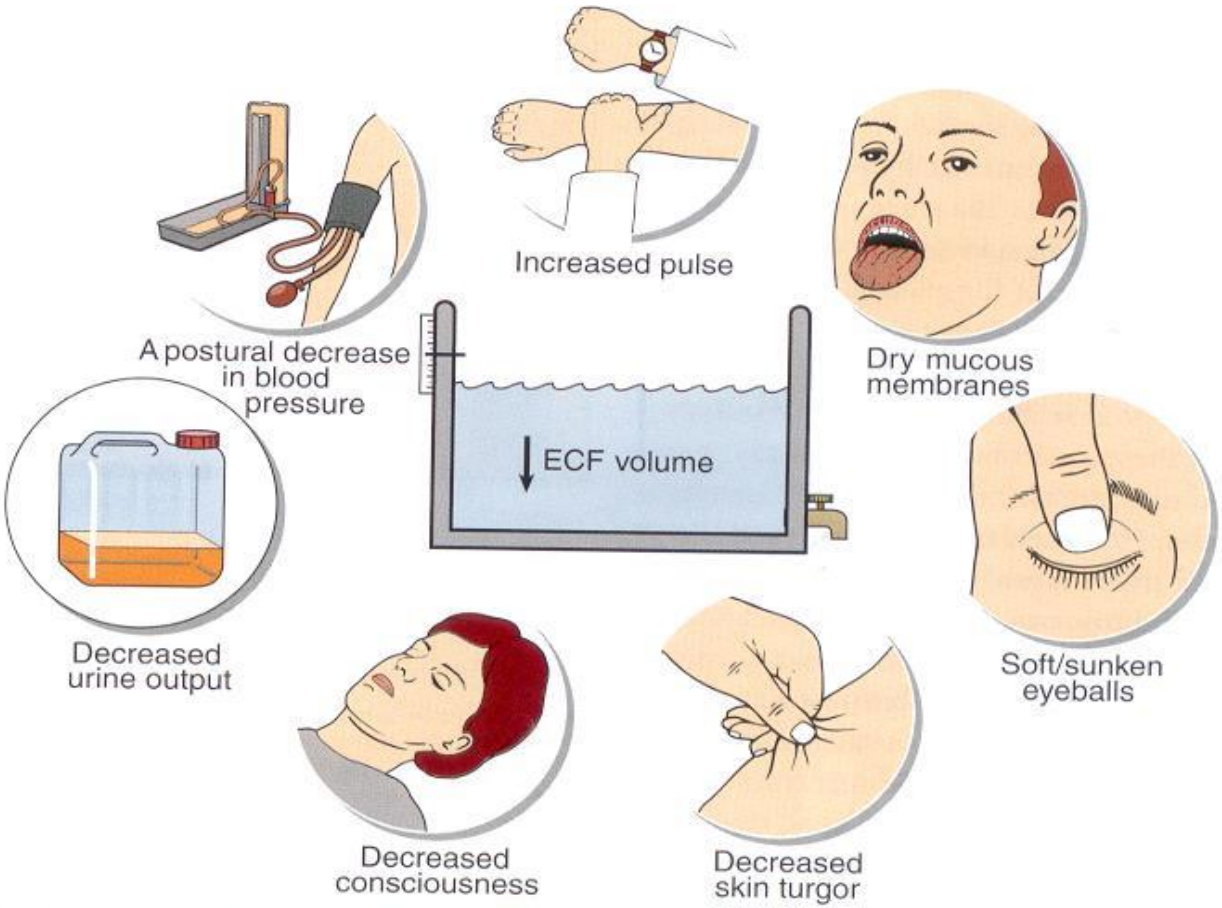
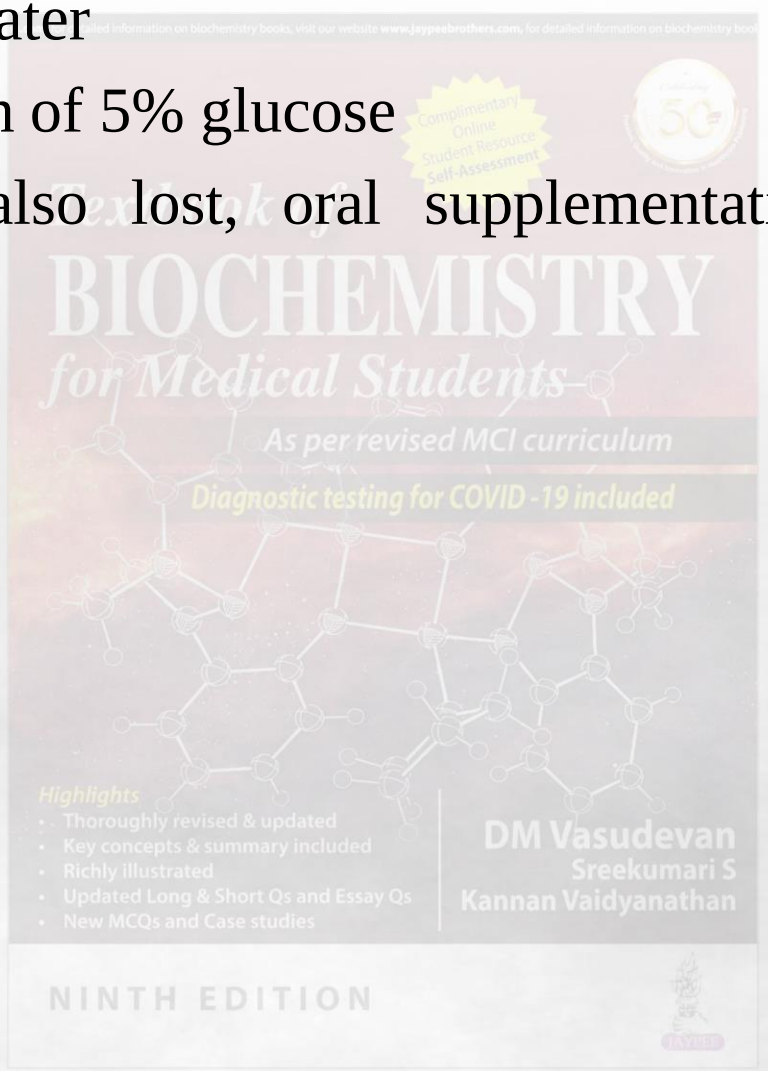


Fig. 1 **The clinical features of ECF compartment depletion.**

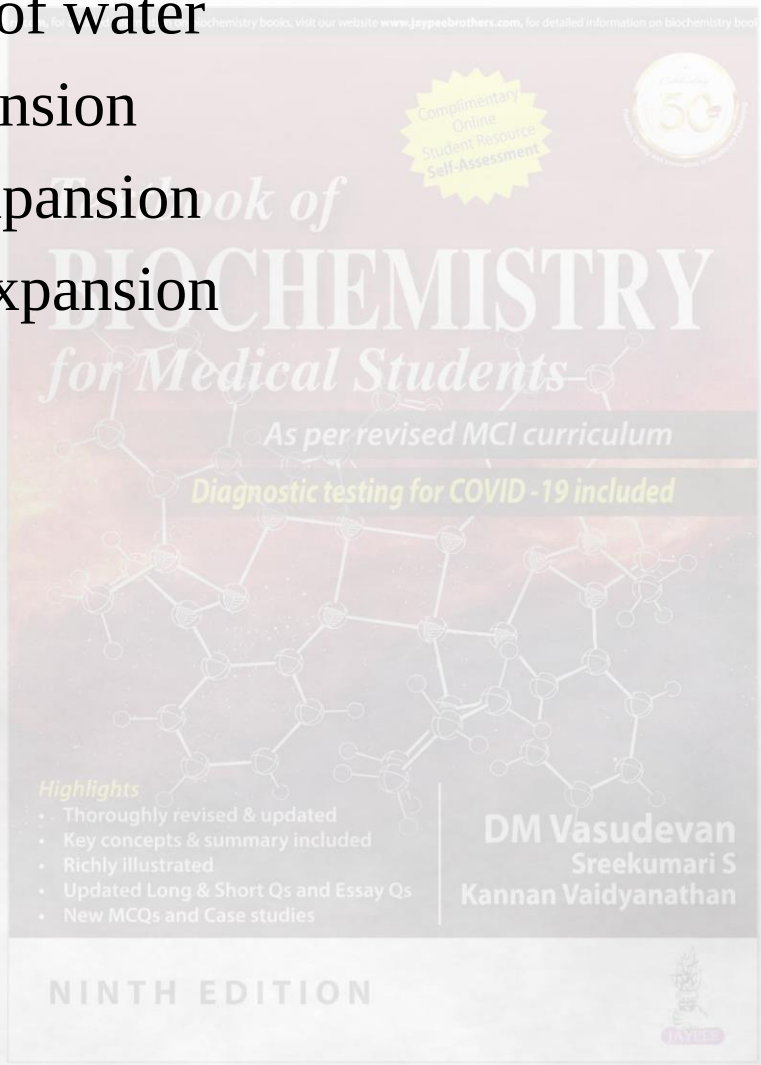
Treatment

- Oral supply of water
- IV administration of 5% glucose
- If electrolytes also lost, oral supplementation or IV saline infusion



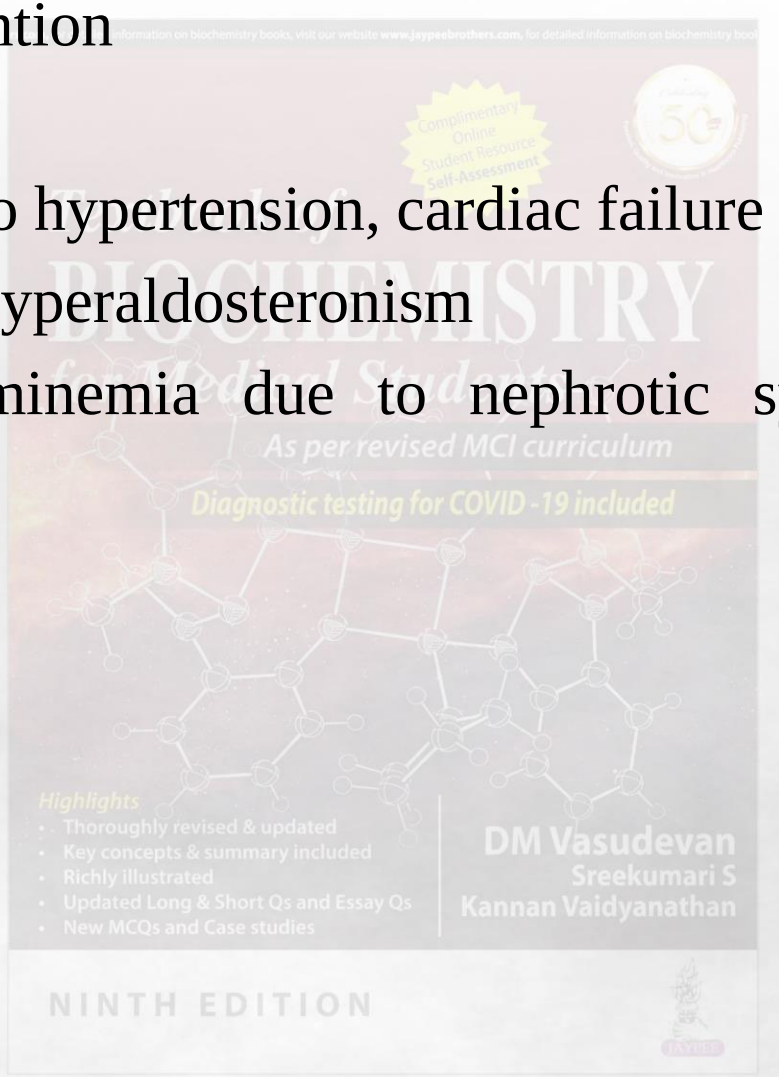
Overhydration (Water Intoxication)

- Due to retention of water
  - Isotonic expansion
  - Hypotonic expansion
  - Hypertonic expansion



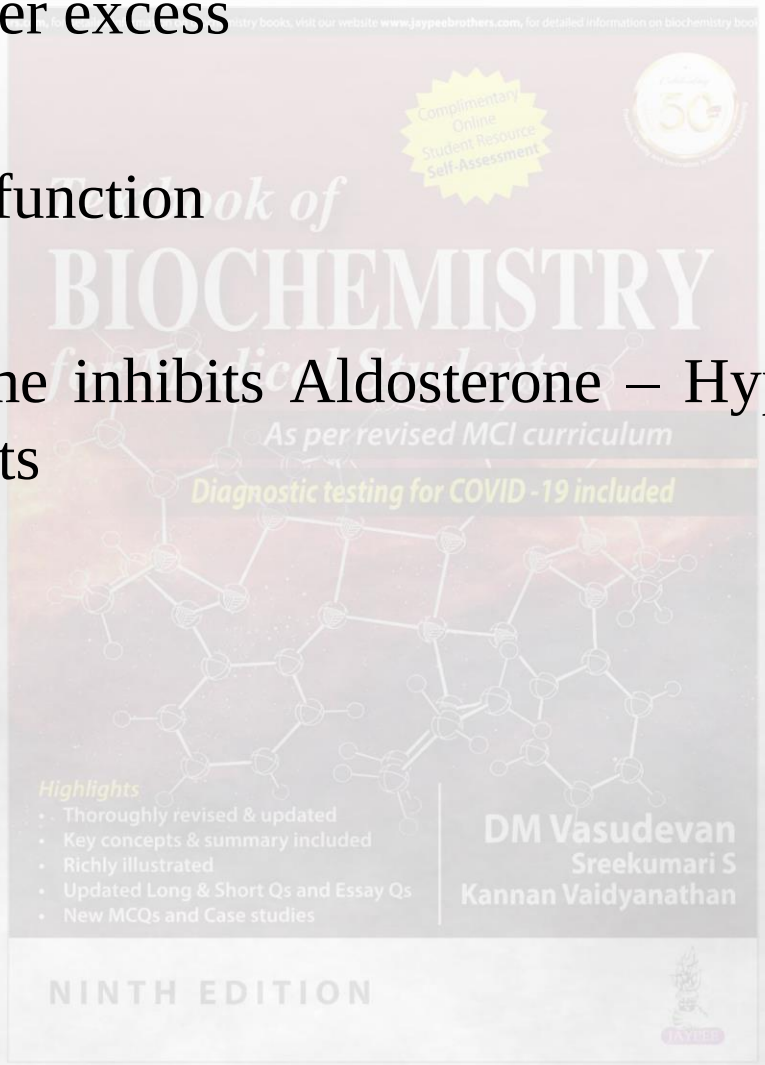
Isotonic Expansion

- Water & Na retention
- Causes
  - Secondary to hypertension, cardiac failure
  - Secondary hyperaldosteronism
  - Hypo albuminemia due to nephrotic syndrome, protein malnutrition



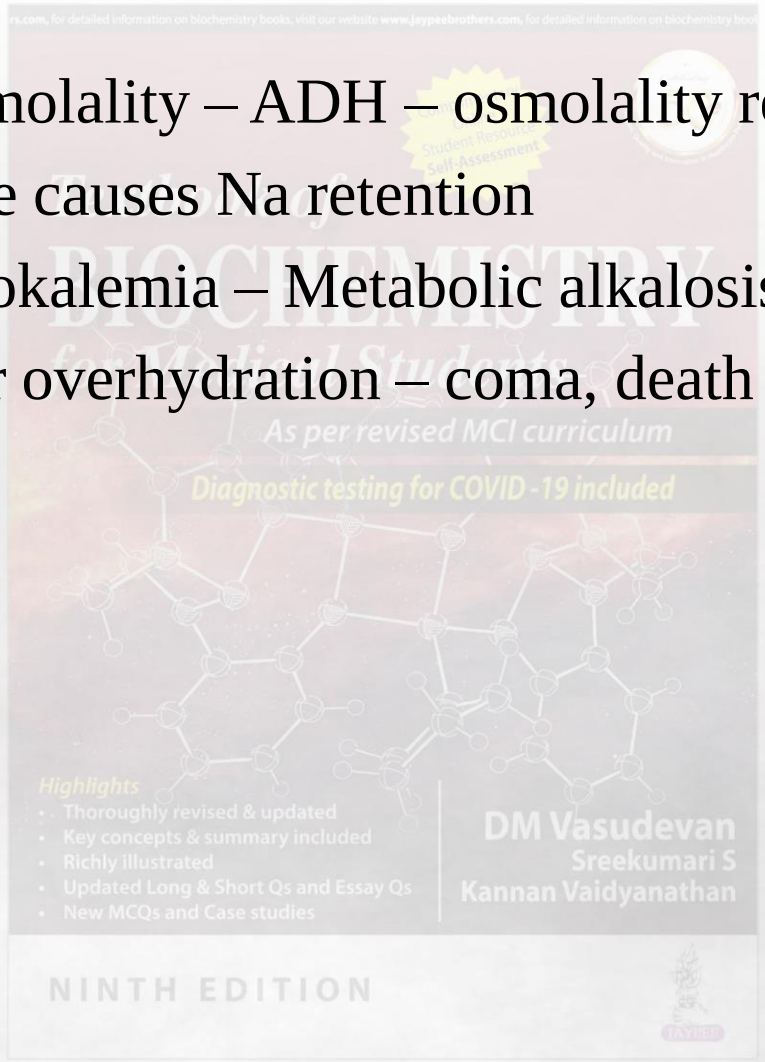
Hypotonic Expansion

- Predominant water excess
- Causes –
  - Glomerular dysfunction
  - Increased ADH
- High ECF volume inhibits Aldosterone – Hyponatremia & low osmolality persists



Hypertonic Expansion

- Retention of Na
- High plasma osmolality – ADH – osmolality restored
- High aldosterone causes Na retention
- Associated Hypokalemia – Metabolic alkalosis
- Cerebral cellular overhydration – coma, death



Disturbances of Fluid Volume

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Hypotonic	Relative water excess	Decreased	Low	**High**
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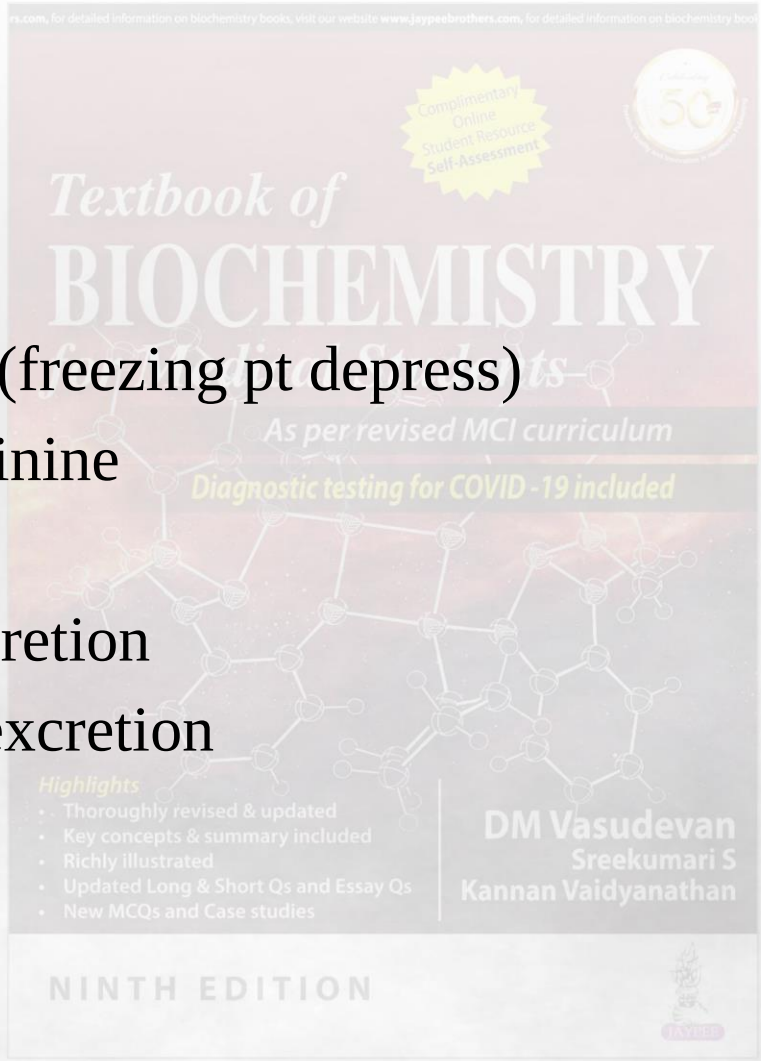
Contraction of ECF				
Isotonic	Loss of Na+ and water	Normal	High	**Normal**
Hypotonic	Relative loss of Na+	Decreased	High	**Low**
Hypertonic	**Relative loss of water**	**Increased**	**High**	**High**

Control of Sodium and Water

Factor	Acting through	Effect
Extracellular Osmolality	Thirst and ADH	water intake; reabsorption of water from kidney
Hypovolemia	Stimulation of thirst and ADH	retention of Water
-do-	Stimulates Aldosterone	retention of Sodium
Expansion of ECF	Inhibits Aldosterone	¯ reabsorption of sodium
Hypo-osmolality	Inhibits ADH Secretion	¯ reabsorption of water

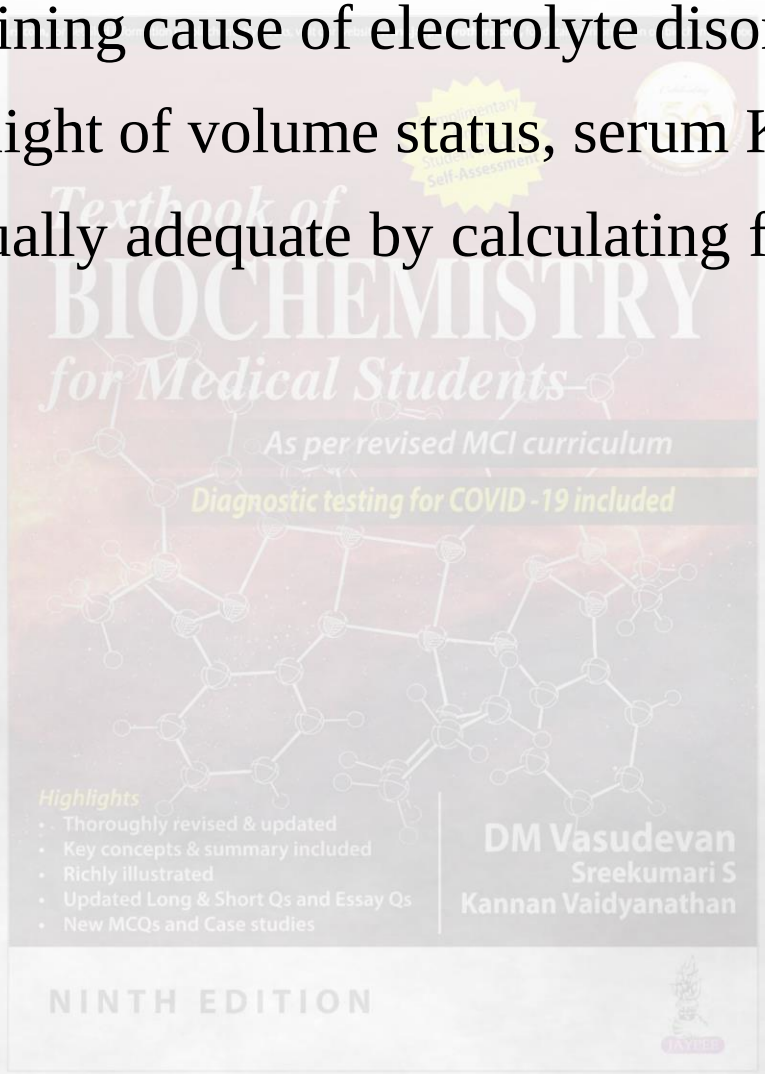
Laboratory Tests of Fluid and Electrolyte Status

- Serum
  - Sodium
  - Potassium
  - Chloride
  - Osmolality (freezing pt depress)
  - Urea, Creatinine
- Urine electrolytes
  - Sodium excretion
  - Potassium excretion
- Hematocrit



Urine Electrolytes

- Useful for determining cause of electrolyte disorder
- Must interpret in light of volume status, serum K^+ of patient
- Random urine usually adequate by calculating fractional excretion or TTKG

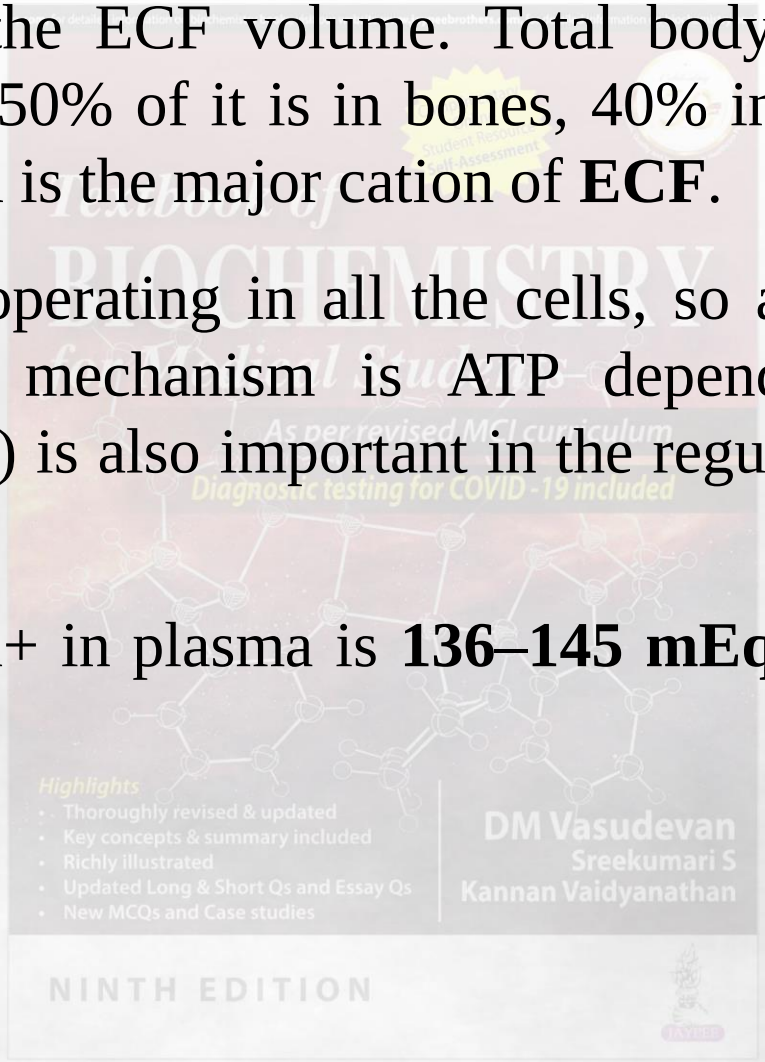


Sodium

Sodium regulates the ECF volume. Total body sodium is about 4,000 mEq. About 50% of it is in bones, 40% in ECF and 10% in soft tissues. Sodium is the major cation of **ECF**.

Sodium pump is operating in all the cells, so as to keep sodium extracellular. This mechanism is ATP dependent. Sodium (as sodium bicarbonate) is also important in the regulation of acid-base balance.

Normal level of Na+ in plasma is **136–145 mEq/L** and in cells 12 mEq/L.



Causes of Hypernatremia

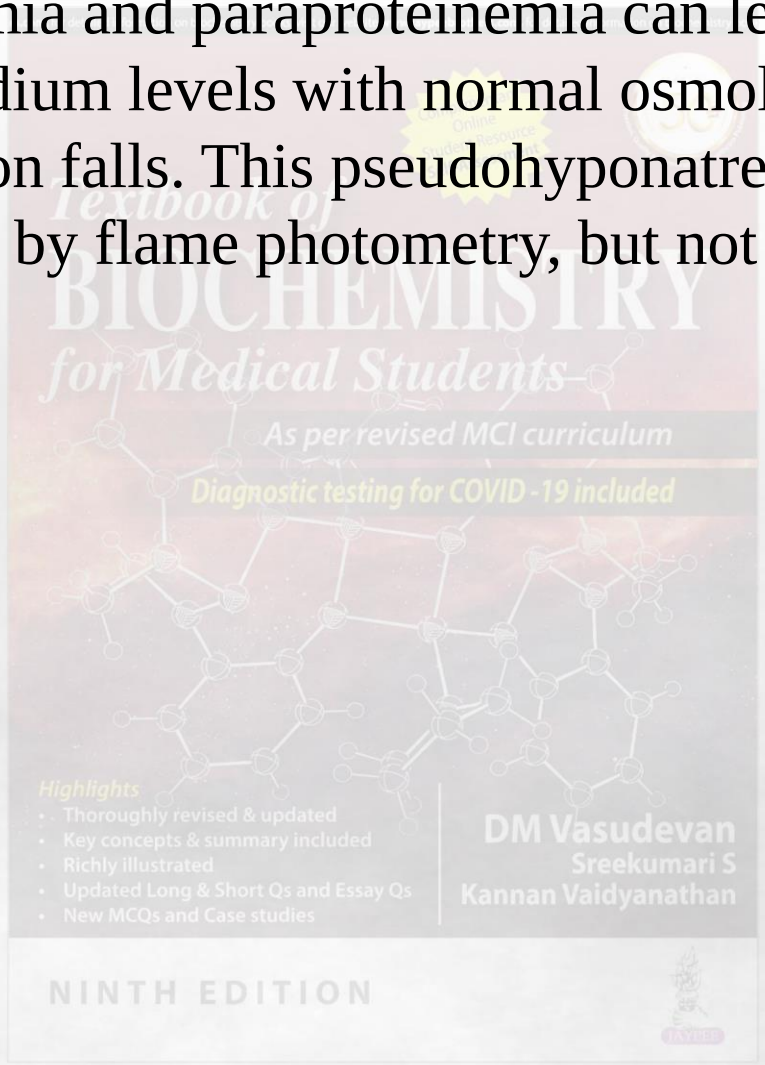
1. Cushing's disease
2. Prolonged cortisone therapy
3. In pregnancy, steroid hormones cause sodium retention
4. In dehydration, when water is predominantly lost, blood volume is decreased with apparent increased concentration of sodium
5. Exchange transfusion with stored blood
6. Primary hyperaldosteronism
7. Elderly patients with poor water intake, and inability to express thirst
8. Excessive intake of salt
9. Drugs:
    - Ampicillin
    - Tetracycline
    - Anabolic steroids
    - Oral contraceptives
    - Loop diuretics
    - Osmotic diuretics

Causes of Hyponatremia

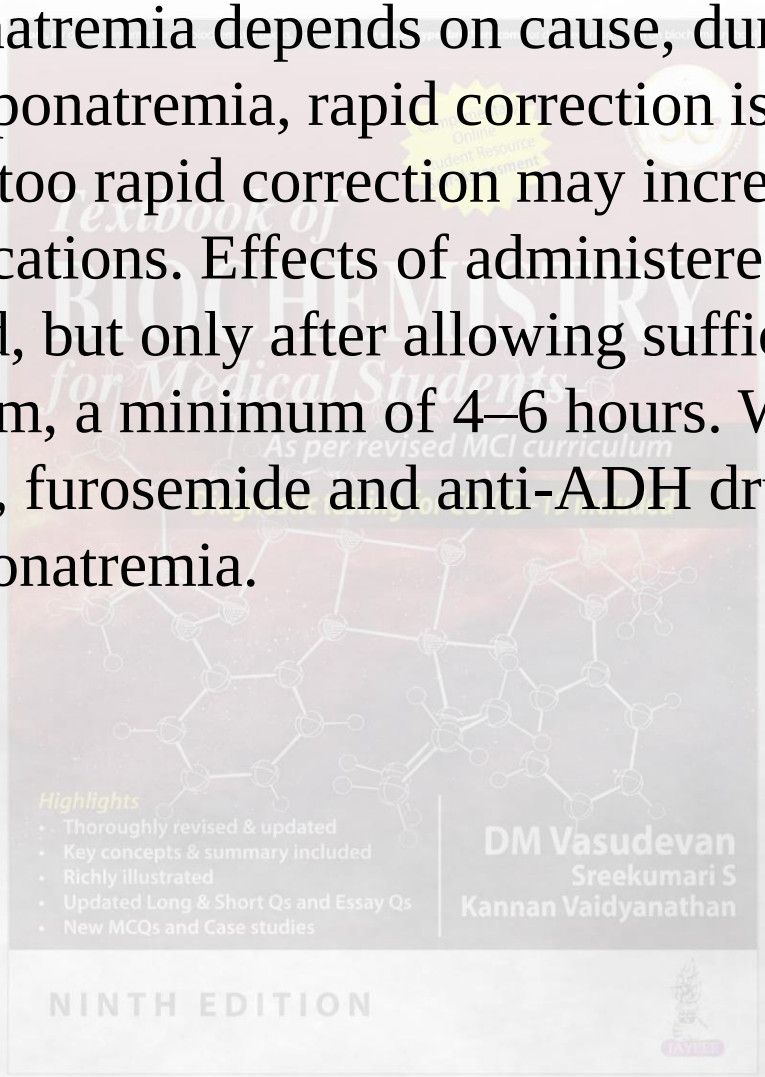
1. Vomiting
2. Diarrhea
3. Burns
4. Addison's disease (adrenalin sufficiency)
5. Renal tubular acidosis, reabsorption of sodium defective.
6. Chronic renal failure, nephritic syndrome
7. Congestive cardiac failure
8. Hyperglycemia and ketoacidosis
9. Excess non-electrolyte (glucose) IV infusion
10. Syndrome of inappropriate antidiuretic hormone and defective antidiuretic hormone secretion
11. Pseudo- or dilutional hyponatremia, hyperproteinemia
12. Drugs:
    Angiotensin converting enzyme inhibitors
    Nonsteroidal anti-inflammatory drugs
    Vasopressin and oxytocin
    Chlorpropamide

Normotonic Hyponatremia:

Severe hyperlipidemia and paraproteinemia can lead to low measured serum sodium levels with normal osmolality since plasma water fraction falls. This pseudohyponatremia is seen when sodium is measured by flame photometry, but not with ion selective electrode.

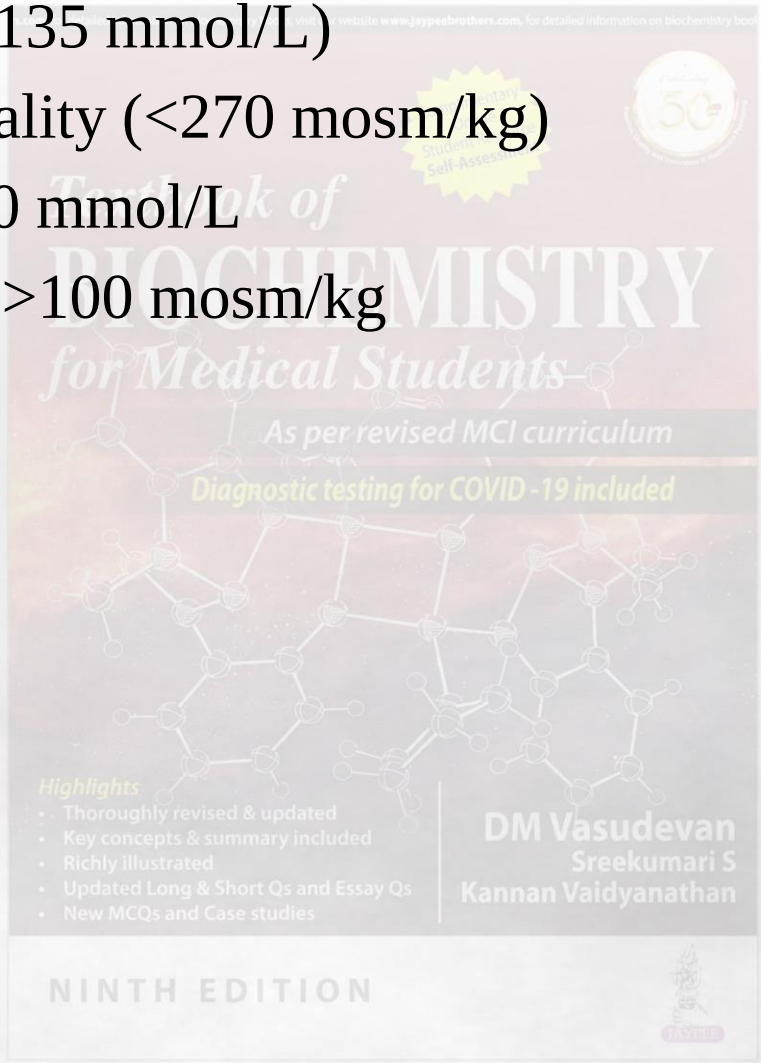


Treatment of hyponatremia depends on cause, duration and severity. In acute hyponatremia, rapid correction is possible; but in chronic cases too rapid correction may increase mortality by neurological complications. Effects of administered sodium should be closely monitored, but only after allowing sufficient time for distribution of sodium, a minimum of 4–6 hours. Water restriction, increased salt intake, furosemide and anti-ADH drugs are the basis of treatment for hyponatremia.



Diagnostic Criteria for Syndrome of Inappropriate Antidiuretic Hormone Secretion

1. Hyponatremia (<135 mmol/L)
2. Decreased osmolality (<270 mosm/kg)
3. Urine sodium >20 mmol/L
4. Urine osmolality >100 mosm/kg



Potassium

Total body potassium(K+) is about 3500 mEq, out of which 75% is in skeletal muscle. Potassium is the major **intracellular** cation, and maintains intracellular osmotic pressure.

The depolarization and contraction of heart require potassium. During transmission of nerve impulses, there is sodium influx and potassium efflux; with depolarization.

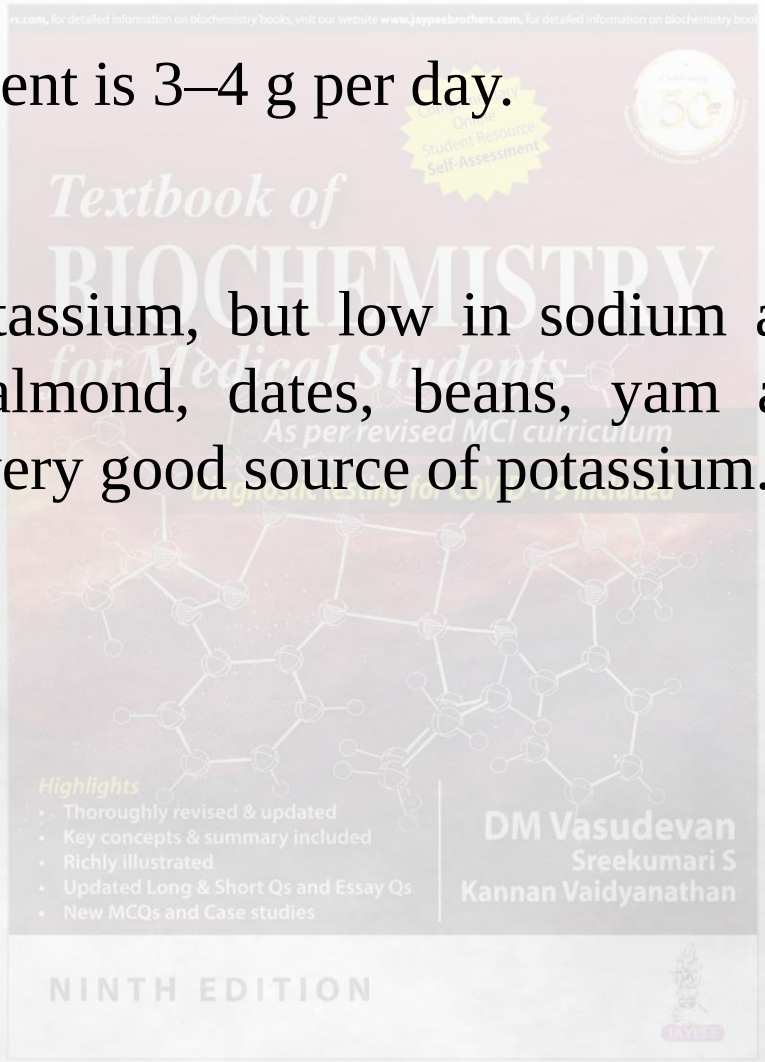
After the nerve transmission, these changes are reversed. The intracellular concentration gradient is maintained by the Na+- K+ ATPase pump.

Requirement

Potassium requirement is 3–4 g per day.

Sources

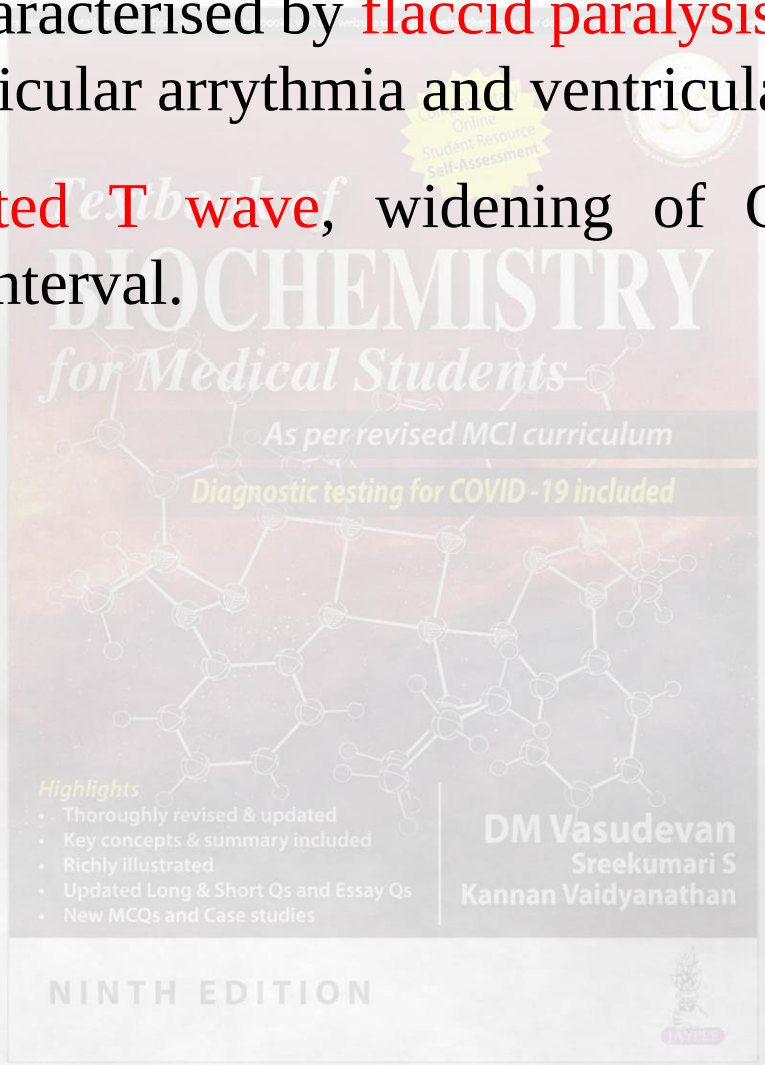
Sources rich in potassium, but low in sodium are banana, orange, apple, pineapple, almond, dates, beans, yam and potato. Tender coconut water is a very good source of potassium.



Hyperkalemia

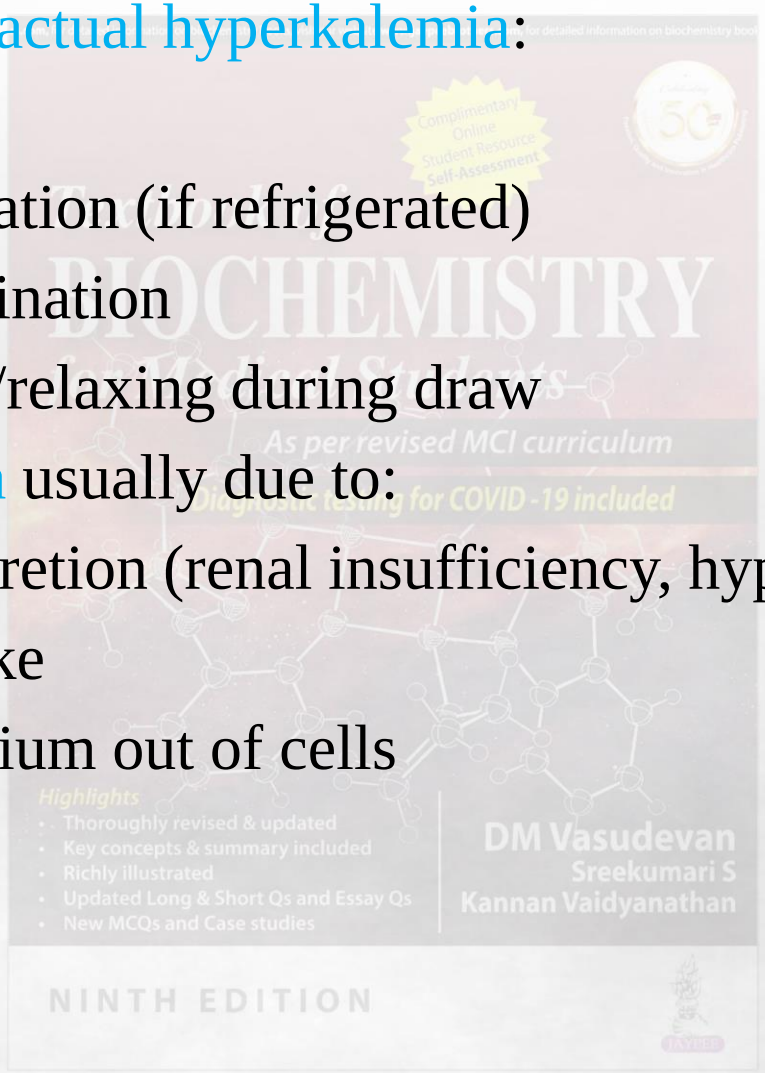
Hyperkalemia is characterised by flaccid paralysis, bradycardia and cardiac arrest, ventricular arrythmia and ventricular fibrillation..

ECG shows elevated T wave, widening of QRS complex and lengthening of PR interval.



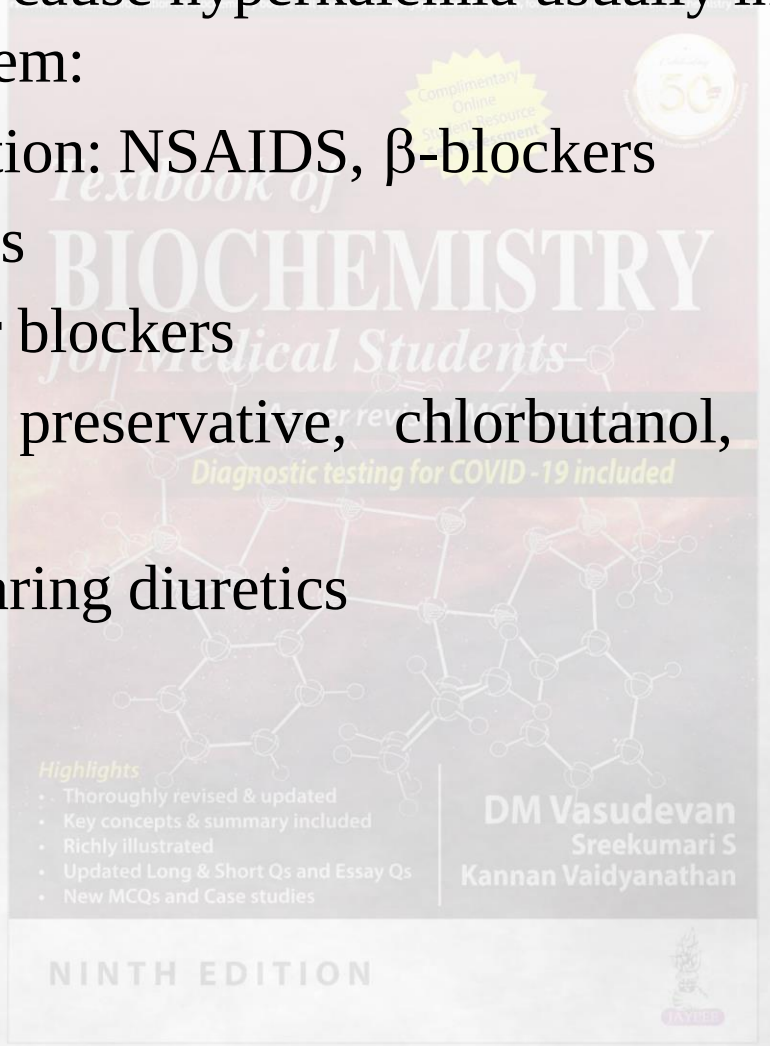
Hyperkalemia

- First exclude artifactual hyperkalemia:
  - Hemolysis
  - Delayed separation (if refrigerated)
  - EDTA contamination
  - Fist clenching/relaxing during draw
- True hyperkalemia usually due to:
  - Decreased excretion (renal insufficiency, hypoaldosteronism)
  - Increased intake
  - Shift of potassium out of cells



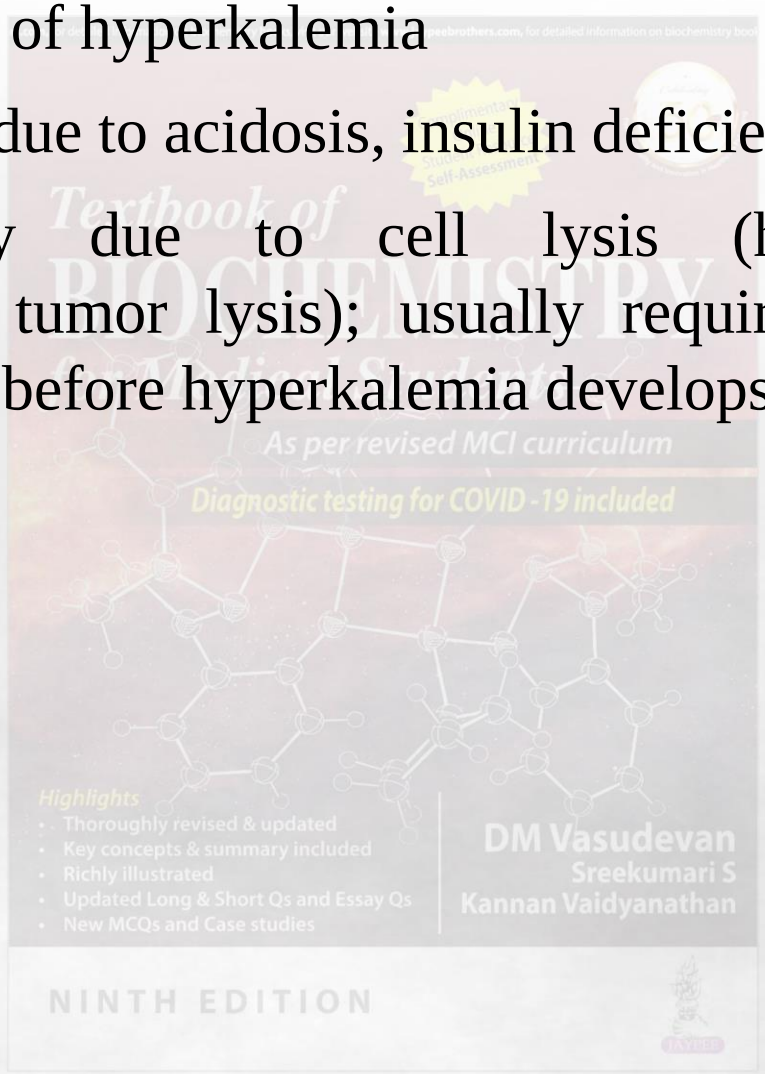
Hyperkalemia

- Medications that cause hyperkalemia usually inhibit renin/ aldosterone system:
  - Renin production: NSAIDS, β-blockers
  - ACE inhibitors
  - AGII-receptor blockers
  - Heparin (its preservative, chlorbutanol, inhibits aldosterone production)
  - Potassium-sparing diuretics



Release From Cells

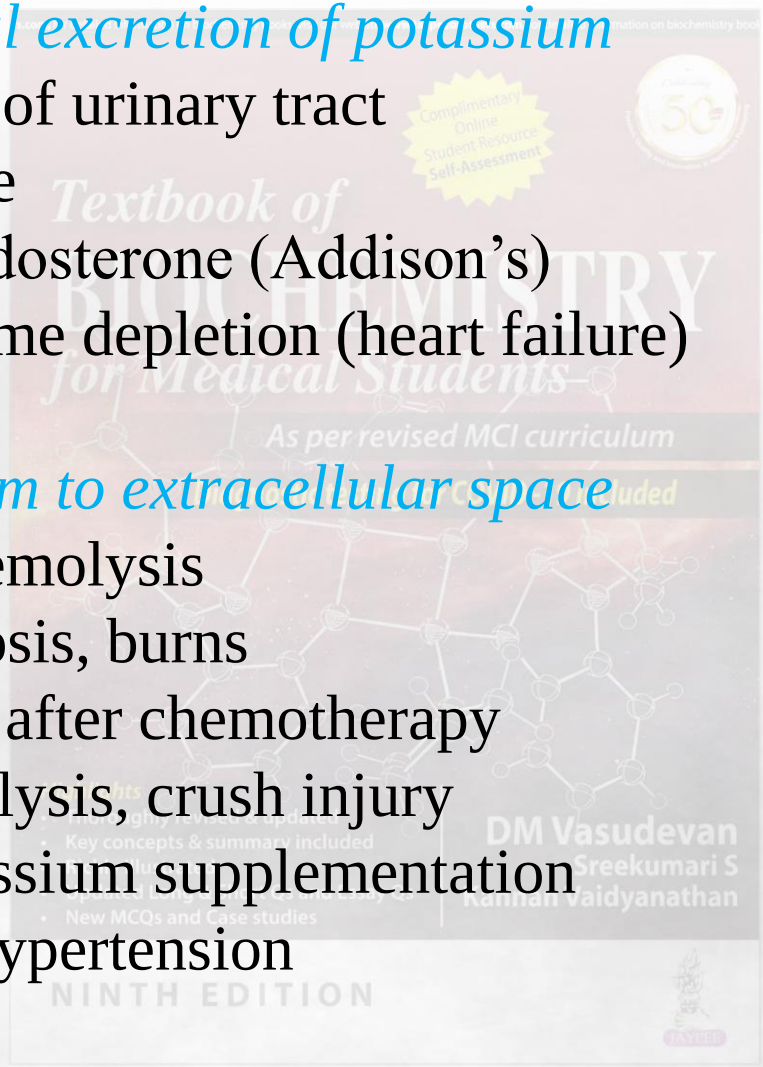
- Occasional cause of hyperkalemia
- Most commonly due to acidosis, insulin deficiency
- Less commonly due to cell lysis (hemolytic anemia, rhabdomyolysis, tumor lysis); usually requires decreased renal excretion as well before hyperkalemia develops



Causes of Hyperkalemia

1. *Decreased renal excretion of potassium*
   - Obstruction of urinary tract
   - Renal failure
   - Deficient aldosterone (Addison's)
   - Severe volume depletion (heart failure)

2. *Entry of potassium to extracellular space*
   - Increased hemolysis
   - Tissue necrosis, burns
   - Tumor lysis after chemotherapy
   - Rhabdomyolysis, crush injury
   - Excess potassium supplementation
   - Malignant hypertension



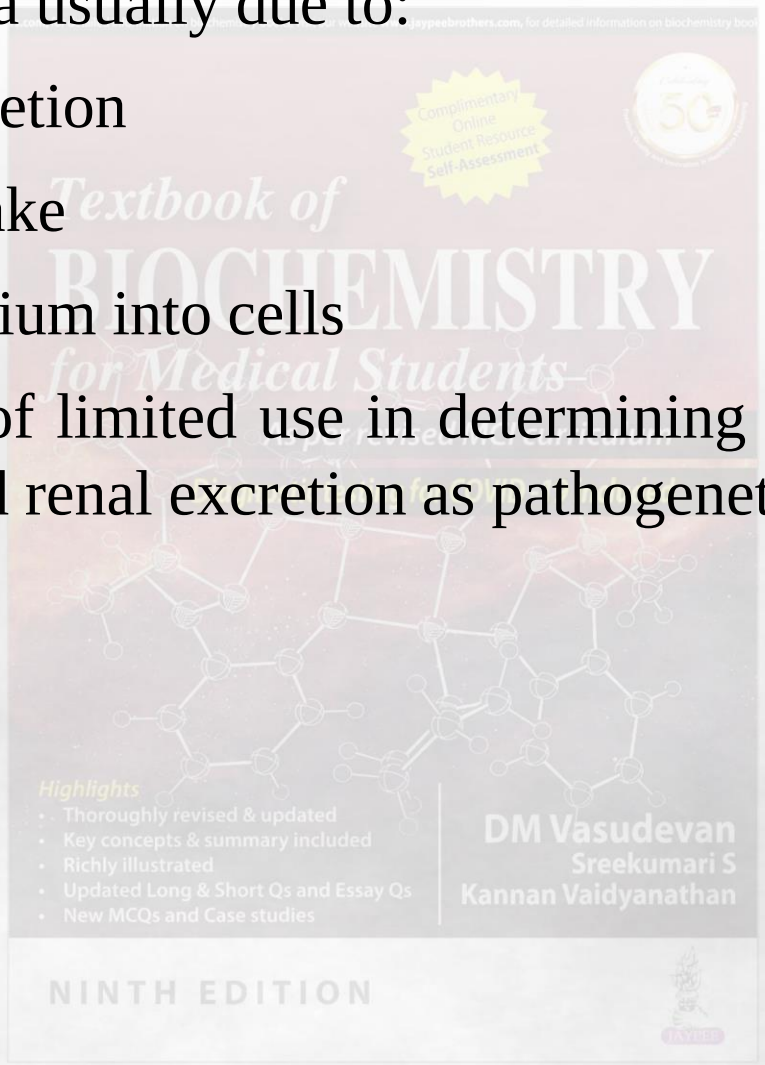
Causes of Hyperkalemia

3. *Redistribution of potassium to extracellular*
    - Metabolic acidosis
    - Insulin deficiency (diabetes mellitus)
    - Tissue hypoxia
4. *Transmembrane shift*
5. *Pseudohyperkalemia*
    - Factitious (K+ leaches out)
    - Improper blood collection (hemolysis)
    - Thrombocytosis (>400 million/mL)
    - Leukocytosis (>11 million/mL)
6. *Hyperkalemic periodic paralysis*
7. *Drugs*

Spiranolactone, ACE inhibitors, Beta blockers Cyclosporine, Digoxin

Hypokalemia

- True hypokalemia usually due to:
  - Increased excretion
  - Decreased intake
  - Shift of potassium into cells
- Laboratory tests of limited use in determining cause; TTKG > 10 confirms increased renal excretion as pathogenetic



Hypokalemia

Plasma potassium level is below 3 mmol/L. A value less than 3.5 mmol/L is to be viewed with caution. Mortality and morbidity are high.

Signs and symptoms: muscular weakness, fatigue, muscle cramps, hypotension, decreased reflexes, palpitation, cardiac arrythmias and cardiac arrest.

ECG waves are flattened, T wave is inverted, ST segment is lowered with AV block.

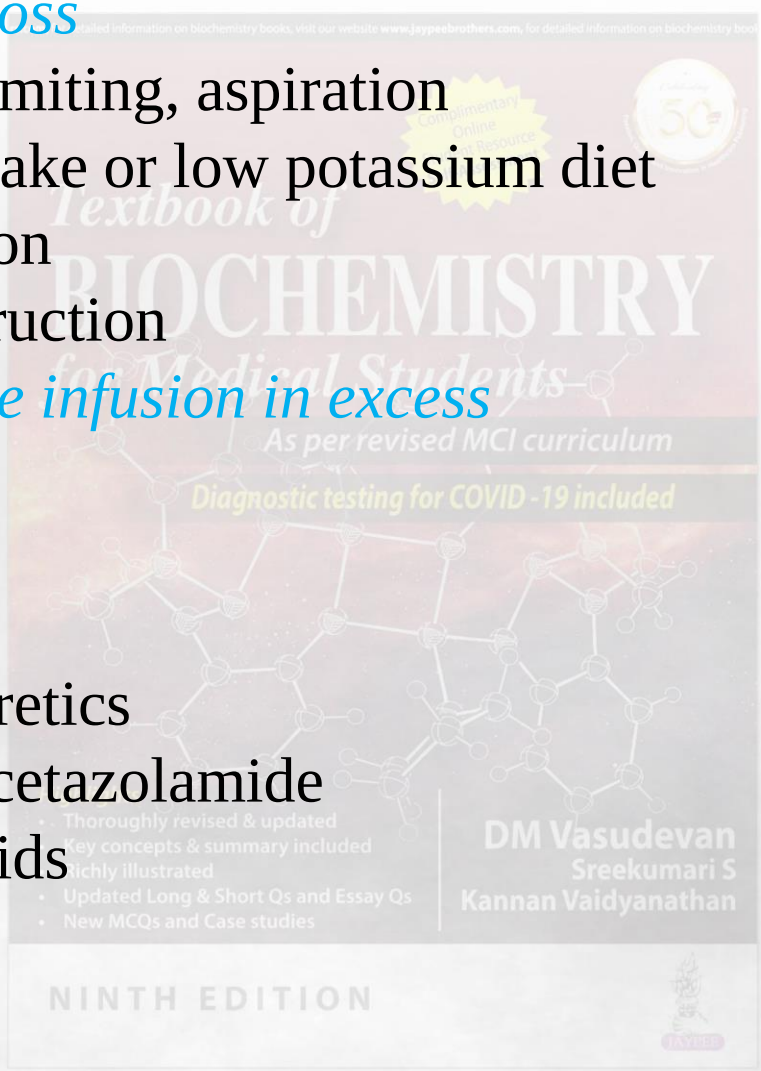
This may be corrected by oral feeding of orange juice.

Causes of Hypokalemia

1. *Increased renal excretion*
   - Cushing's syndrome
   - Hyperaldosteronism
   - Hyper reninism, renal artery stenosis
   - Hypomagnesemia
   - Renal tubular acidosis
   - Adrenogenital syndrome
   - 17 alpha hydroxylase deficiency
   - 11 beta hydroxylase deficiency
2. *Shift or redistribution of potassium*
   - Alkalosis
   - Insulin therapy
   - Thyrotoxic periodic paralysis
   - Hypokalemic periodic paralysis

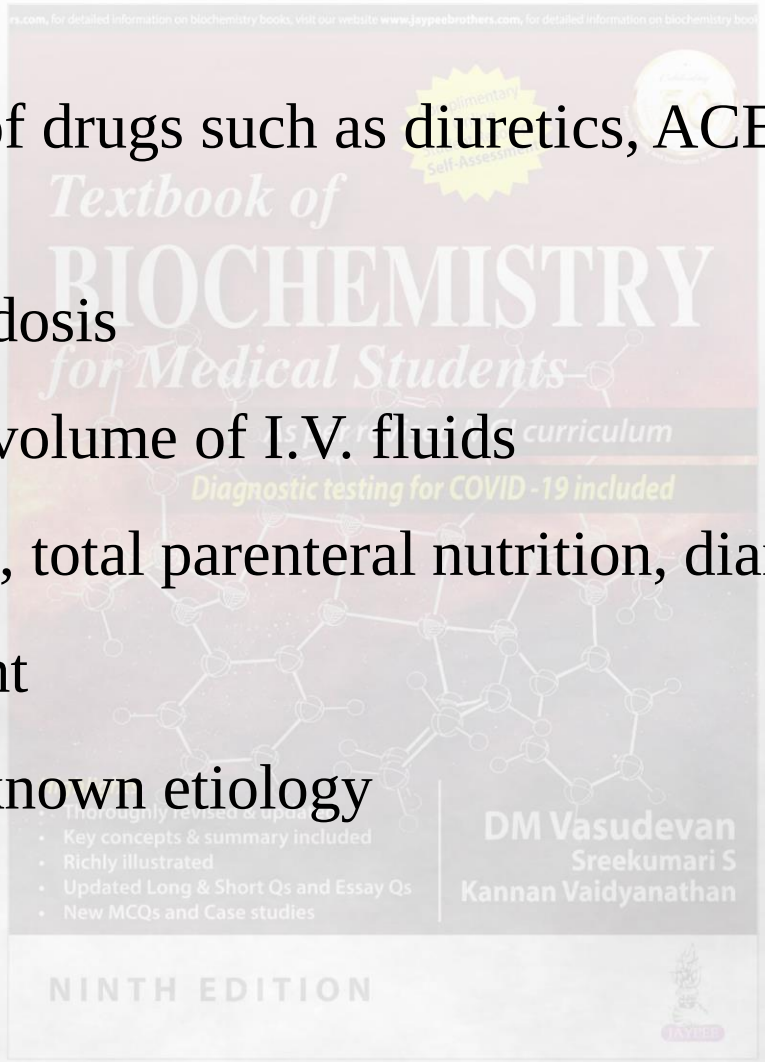
Causes of Hypokalemia

3. *Gastrointestinal loss*
   - Diarrhea, vomiting, aspiration
   - Deficient intake or low potassium diet
   - Malabsorption
   - Pyloric obstruction
4. *Intravenous saline infusion in excess*
5. *Drugs:*
   - Insulin
   - Salbutamide
   - Osmotic diuretics
   - Thiazides, acetazolamide
   - Corticosteroids



When Potassium level should be checked?

1. Cardiac diseases
2. Administration of drugs such as diuretics, ACE inhibitors, NSAIDs
3. Diabetic ketoacidosis
4. Receiving large volume of I.V. fluids
5. Fluid loss (burns, total parenteral nutrition, diarrhea)
6. Renal impairment
7. Weakness of unknown etiology



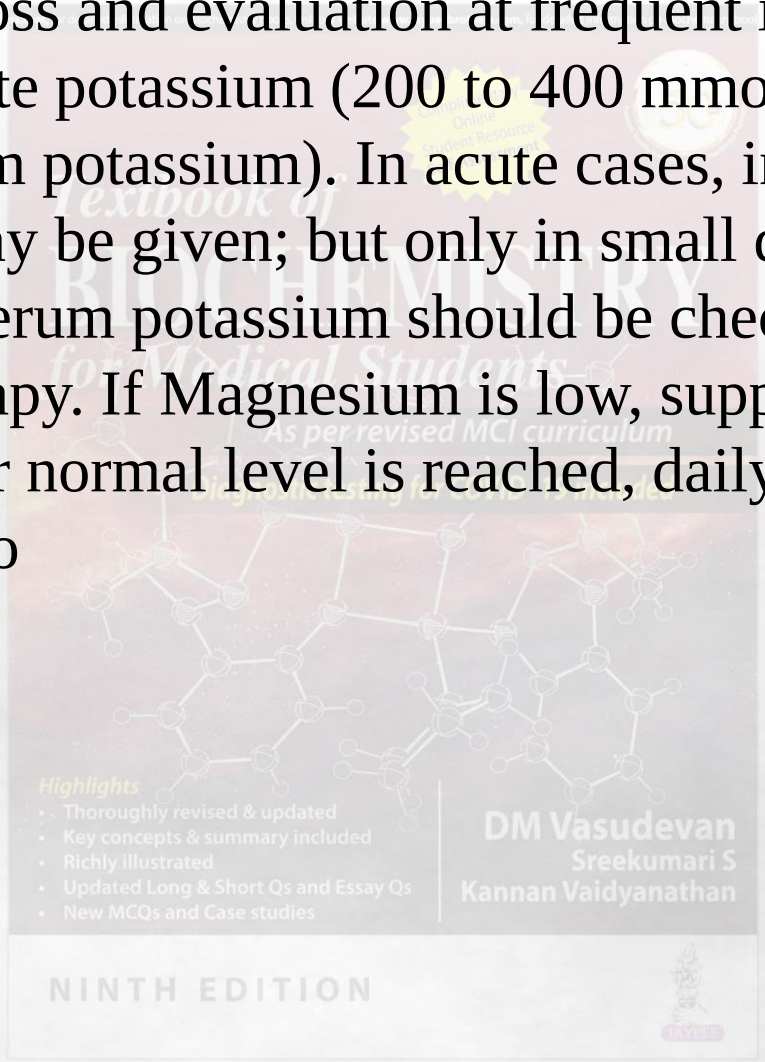
Laboratory Evaluations for Potassium Abnormalities

1. **Serum potassium estimation**
2. **Urine potassium:** Low value (<20 mmol/L) is seen in poor intake, GIT loss or transmembrane shift. High (>40 mol/L) is seen in renal diseases.
3. **Sodium and osmolality** of spot urine: Low sodium (<20 mmol/L) and high potassium indicate secondary hyperaldosteronism. If urine osmolality is low (30–600) and a value of urinary potassium of 60 mmol/L indicate renal loss. On the other hand if urine osmolality is high (1,200), the same value of potassium excreted in urine indicates low renal excretion around 15 mmol/L.
4. **ECG in all cases**
5. **Special tests:** Aldosterone, plasma renin, cortisol and 17 hydroxyprogesterone.

Treatment of Hypokalemia

Aim is to stop the loss and evaluation at frequent intervals. Supplement adequate potassium (200 to 400 mmol for every 1 mmol fall in serum potassium). In acute cases, intravenous supplementation may be given; but only in small doses (not more than 10 mmol/h). Serum potassium should be checked every hour throughout the therapy. If Magnesium is low, supplement it. Correct alkalosis. Even after normal level is reached, daily potassium assay for several days is to

be continued.



Redistribution of serum potassium

Causes of increased K^+ entry into cells leading to hypokalemia	Causes of impaired K^+ entry into cells or exit of K^+ from cells, leading to hyperkalemia
Insulin Beta-adrenergic stimuli Alkalosis	Glucagon Alpha-adrenergic stimuli Acidosis Increased osmolality

Chloride

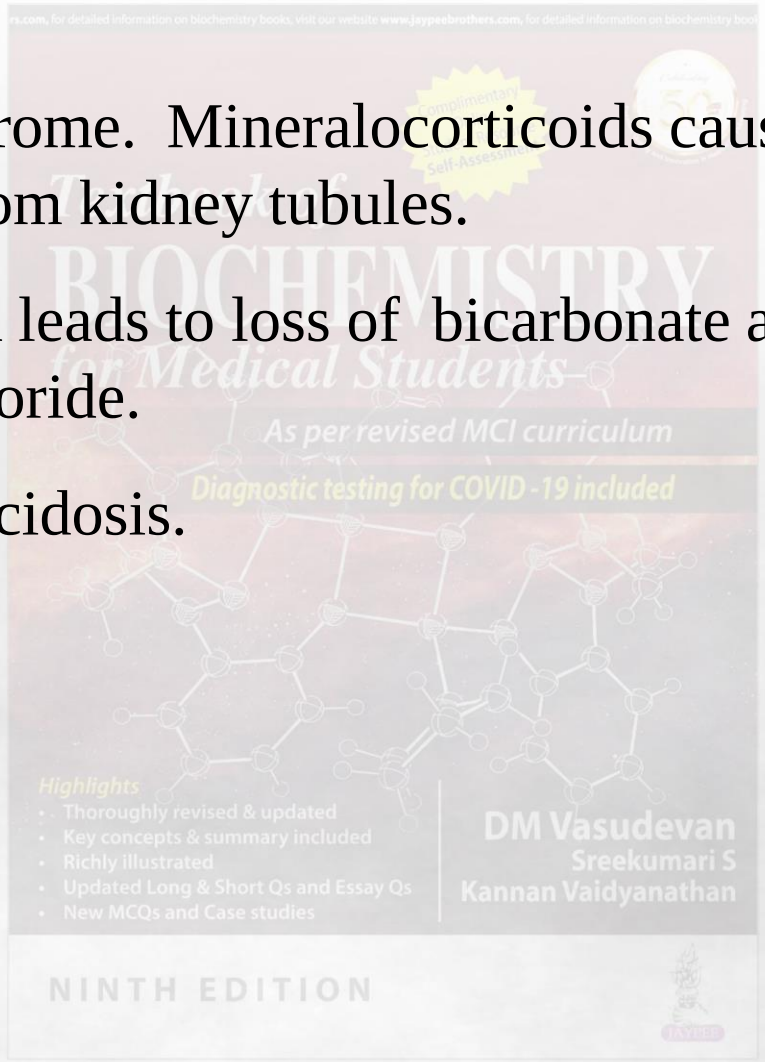
Intake, output and metabolism of sodium and chloride (Cl–) run in parallel. The homeostasis of Na+, K+ and Cl– are inter-related. Chloride is important in the formation of hydrochloric acid in gastric juice.

Chloride ions are also involved in chloride shift.

Chloride concentration in plasma is **96–106 mEq/L**. Chloride concentration in CSF is higher than any other body fluids. Since CSF protein content is low, Cl– is increased to maintain Donnan membrane equilibrium. Excretion of Cl– is through urine, and is parallel to Na+. Renal threshold for Cl– is about 110 mEq/L. Daily excretion of Cl– is about 5–8 g/day.

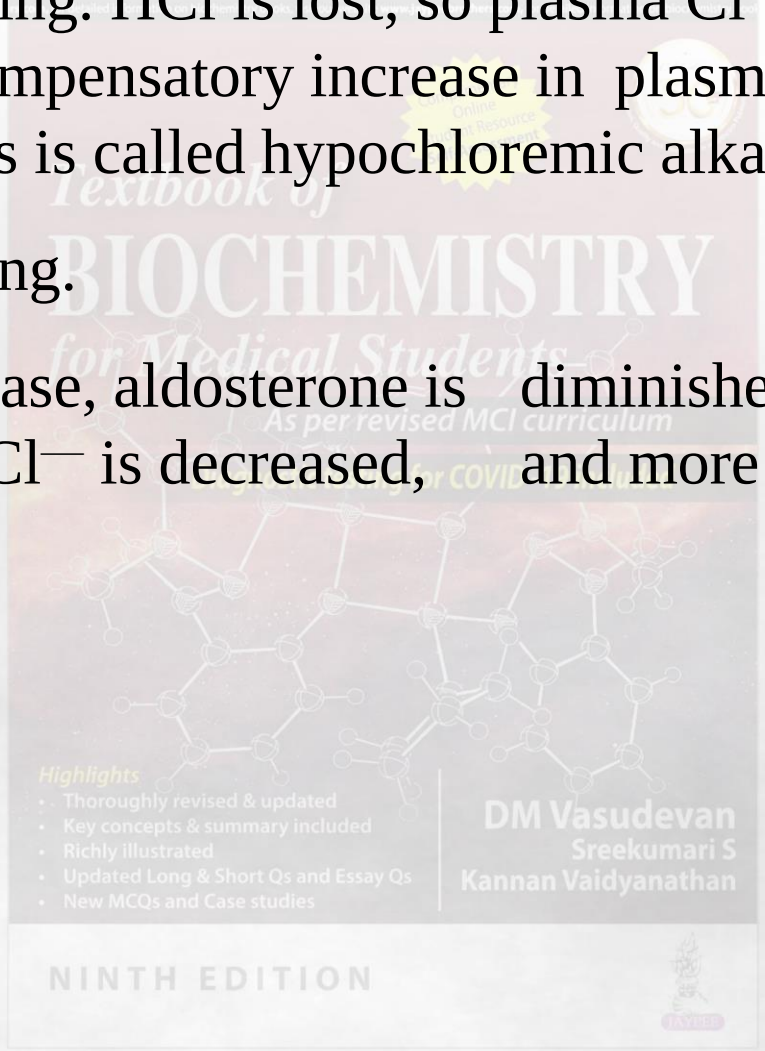
Hyperchloremia is seen in

1. Dehydration
2. Cushing's syndrome. Mineralocorticoids cause increased reabsorption from kidney tubules.
3. Severe diarrhea leads to loss of bicarbonate and compensatory retention of chloride.
4. Renal tubular acidosis.



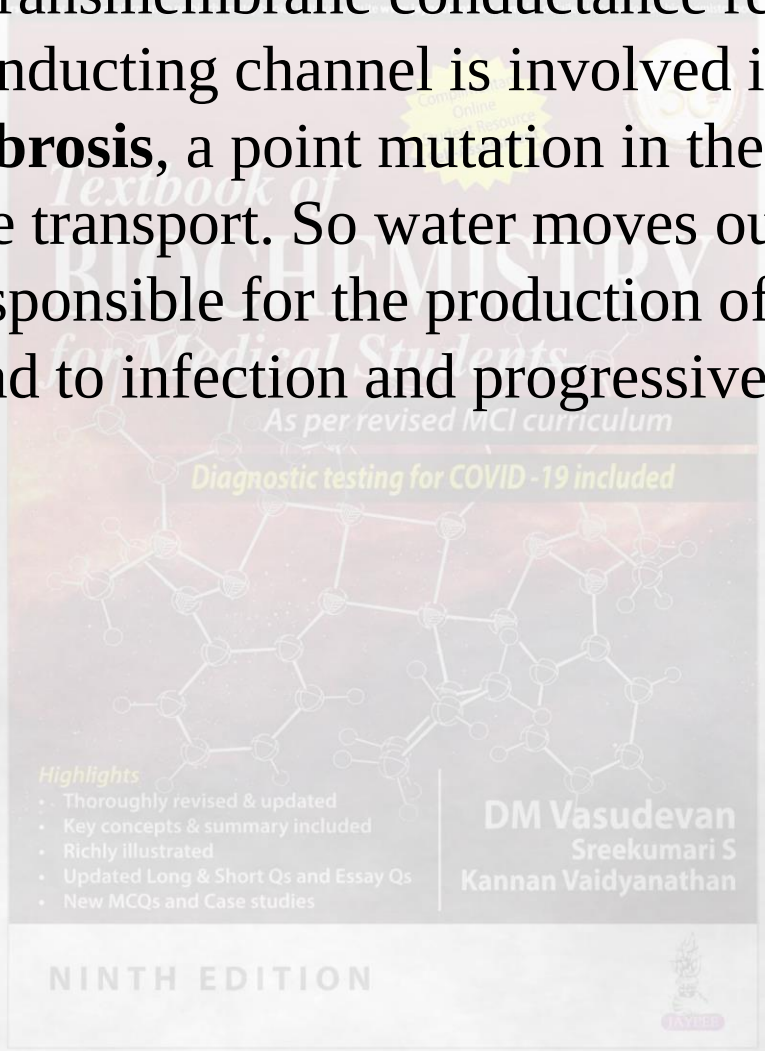
Causes for Hypochloremia

1. Excessive vomiting. HCl is lost, so plasma Cl^- is lowered. There will be compensatory increase in plasma bicarbonate. This is called hypochloremic alkalosis.
2. Excessive sweating.
3. In Addison's disease, aldosterone is diminished, renal tubular reabsorption of Cl^- is decreased, and more Cl^- is excreted.



Chloride Channels

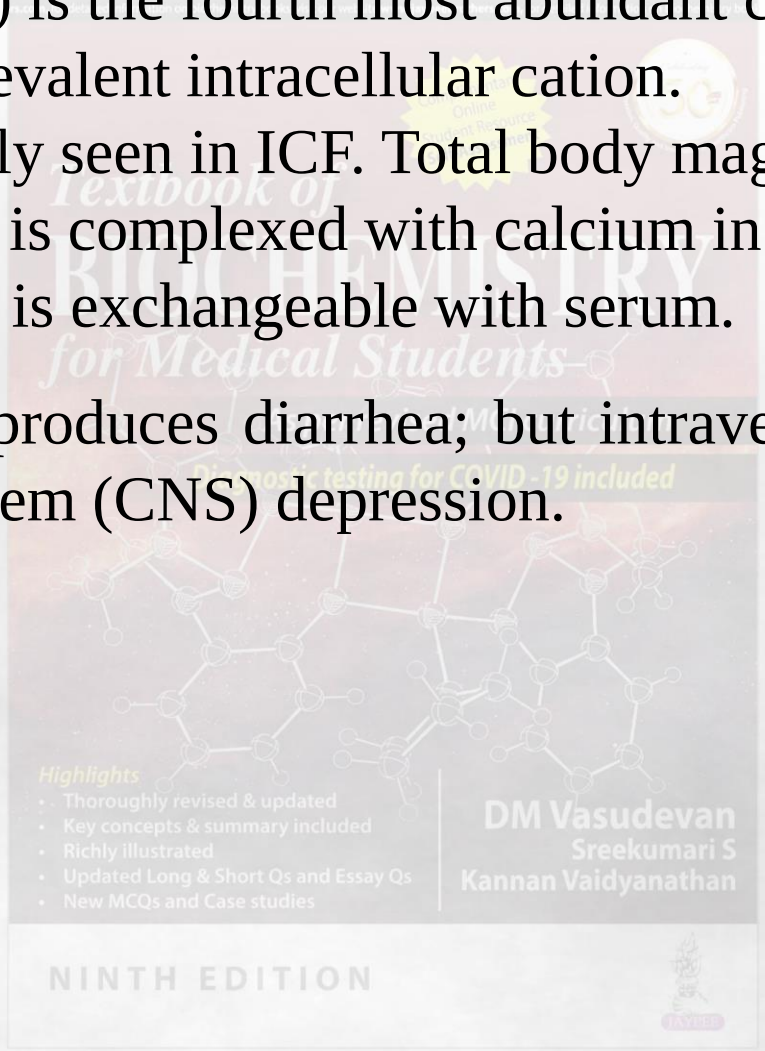
The cystic fibrosis transmembrane conductance receptor (CFTR) chloride conducting channel is involved in cystic fibrosis. In **cystic fibrosis**, a point mutation in the ***CFTR* gene** results in defective chloride transport. So water moves out from lungs and pancreas. This is responsible for the production of abnormally thick mucus. This will lead to infection and progressive damage and death at a young age.



Magnesium

Magnesium (Mg++) is the fourth most abundant cation in the body and second most prevalent intracellular cation.
Magnesium is mainly seen in ICF. Total body magnesium is about 25 g, 60% of which is complexed with calcium in bone. One-third of skeletal magnesium is exchangeable with serum.

Magnesium orally produces diarrhea; but intravenously it produces central nervous system (CNS) depression.

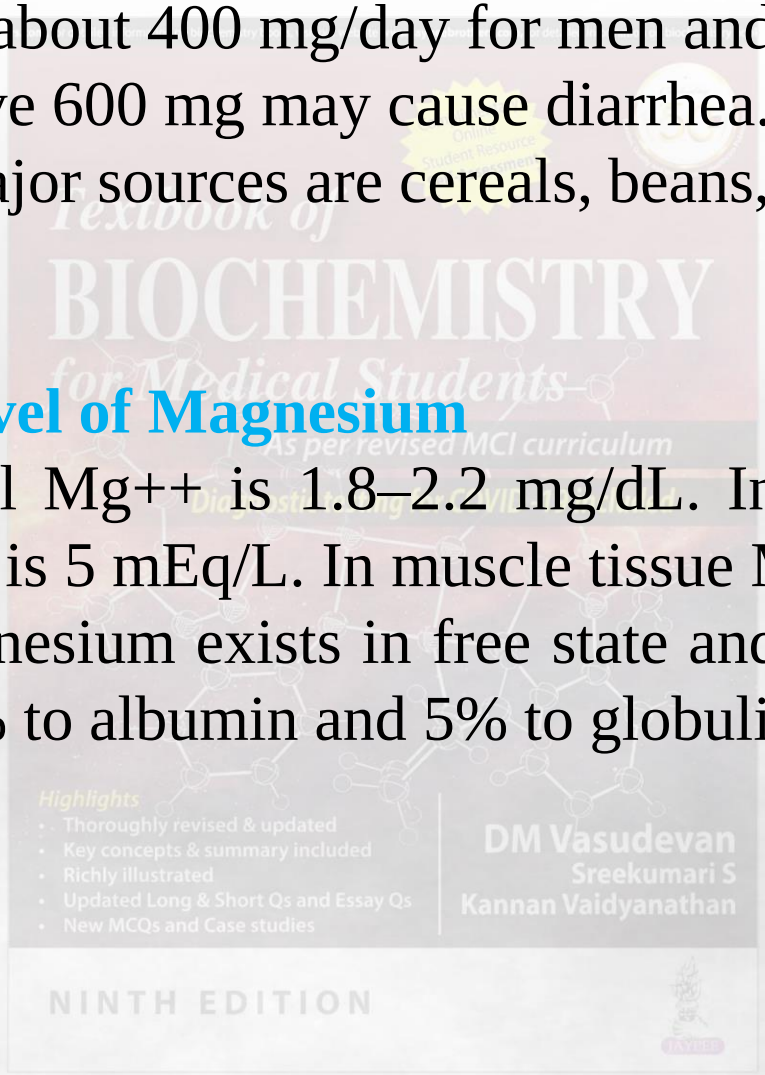


Requirement of Magnesium

The requirement is about 400 mg/day for men and 300 mg/day for women. Doses above 600 mg may cause diarrhea. More is required during lactation. Major sources are cereals, beans, leafy vegetables and fish.

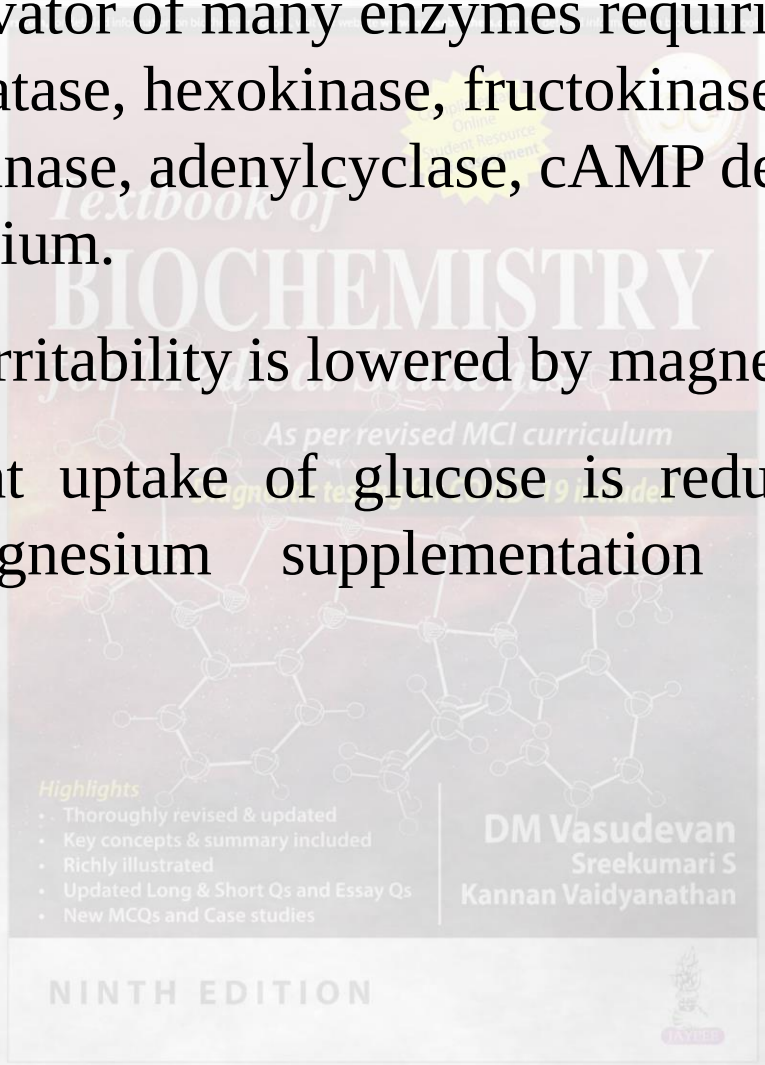
Normal Serum Level of Magnesium

Normal serum level Mg++ is 1.8–2.2 mg/dL. Inside the RBC, the magnesium content is 5 mEq/L. In muscle tissue Mg++ is 20 mEq/L. About 70% of magnesium exists in free state and remaining 30% is protein-bound (25% to albumin and 5% to globulin).



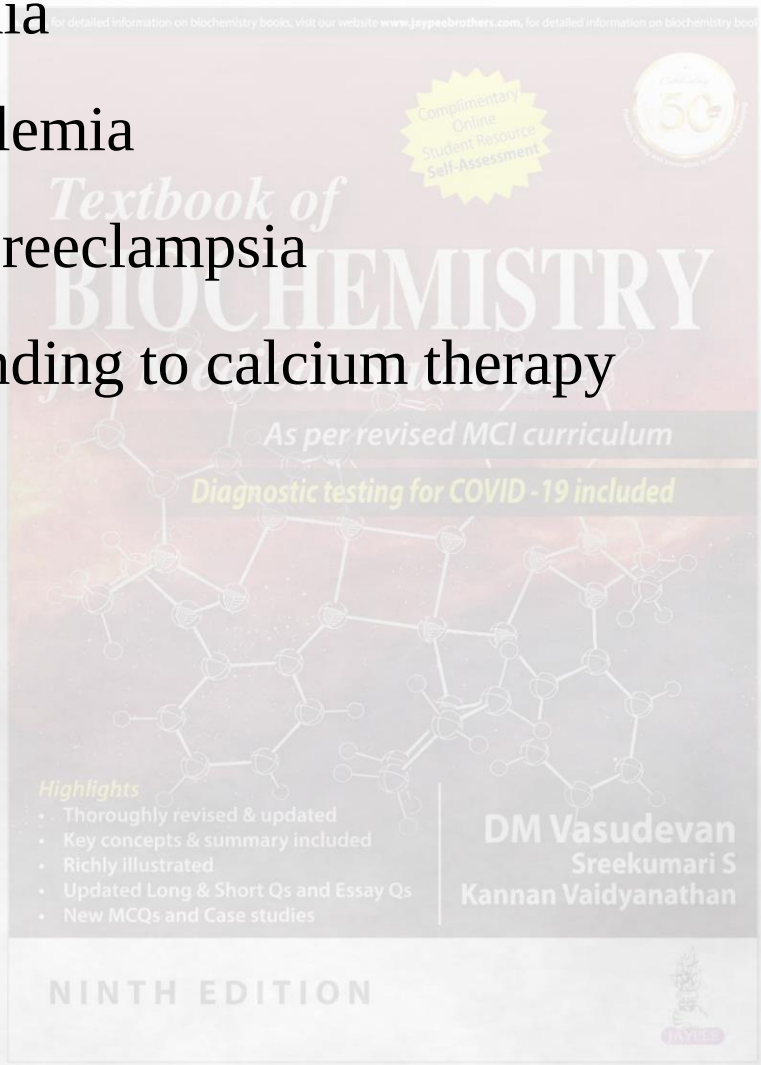
Functions of Magnesium

- Mg++ is the activator of many enzymes requiring ATP. Alkaline phosphatase, hexokinase, fructokinase, phosphofructo-kinase, adenylcyclase, cAMP dependent kinases, etc. need magnesium.
- Neuromuscular irritability is lowered by magnesium.
- Insulin-dependent uptake of glucose is reduced in magnesium deficiency. Magnesium supplementation improves glucose tolerance.



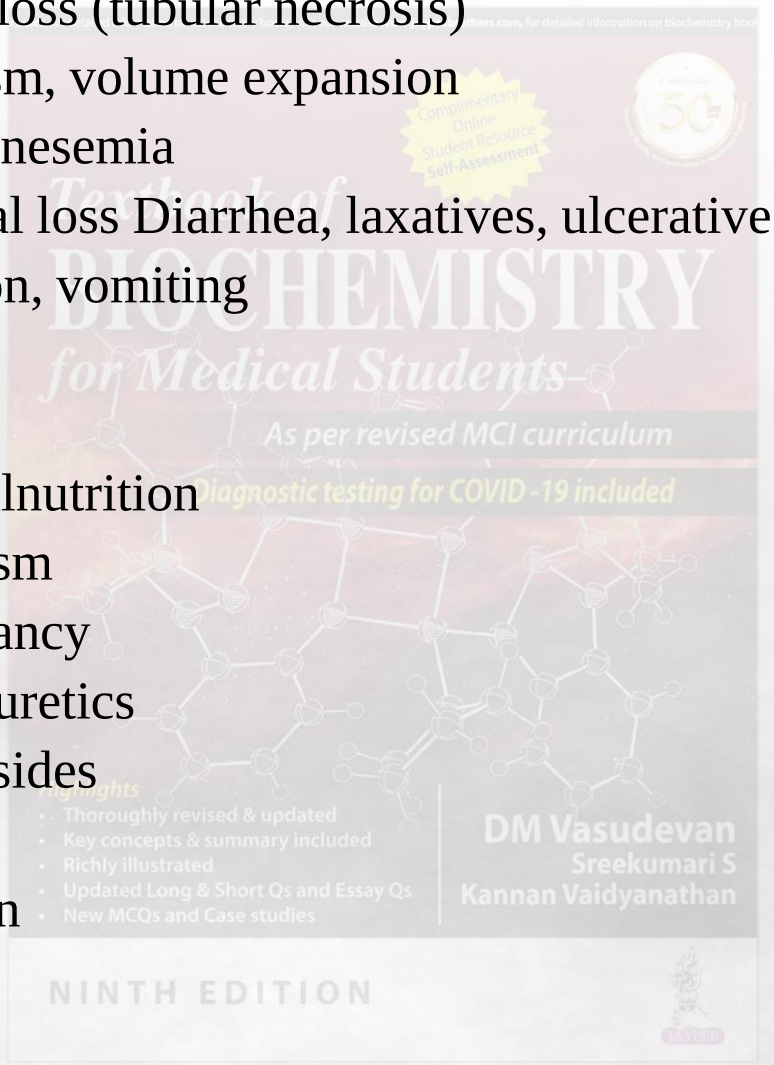
When to Test for Serum Level of Magnesium?

1. Cardiac arrhythmia
2. Resistant hypokalemia
3. Pregnancy with preeclampsia
4. Tetany not responding to calcium therapy



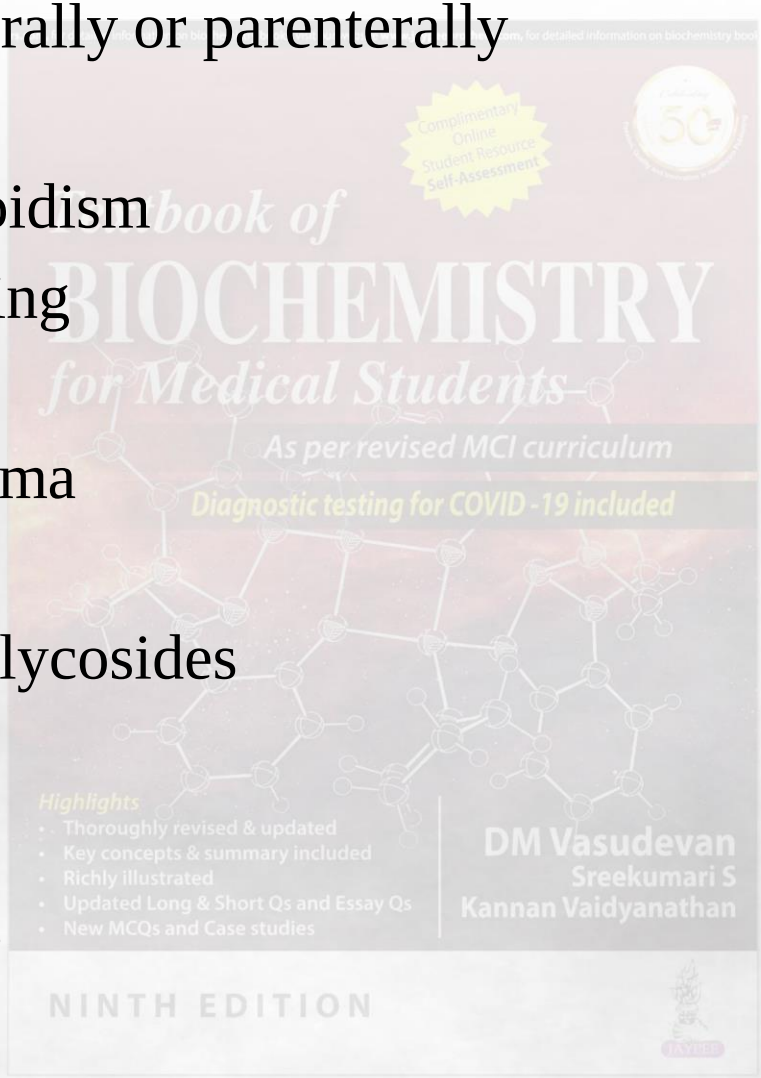
Causes of Hypomagnesemia

1. Increased urinary loss (tubular necrosis)
2. Hyperaldosteronism, volume expansion
3. Familial hypomagnesemia
4. Increased intestinal loss Diarrhea, laxatives, ulcerative colitis
   Nasogastric suction, vomiting
5. Liver cirrhosis
6. Malabsorption
7. Protein calorie malnutrition
8. Hypoparathyroidism
9. Toxemia of pregnancy
10. Drugs: thiazide diuretics
    - Aminoglycosides
    - Cisplatin
    - Amphotericin
    - Cyclosporin
    - Haloperidol



Causes of Hypermagnesemia

1. Excess intake orally or parenterally
2. Renal failure
3. Hyperparathyroidism
4. Oxalate poisoning
5. Rickets
6. Multiple myeloma
7. Dehydration
8. Drugs: Aminoglycosides
   - Antacids
   - Calcitriol
   - Tacrolimus

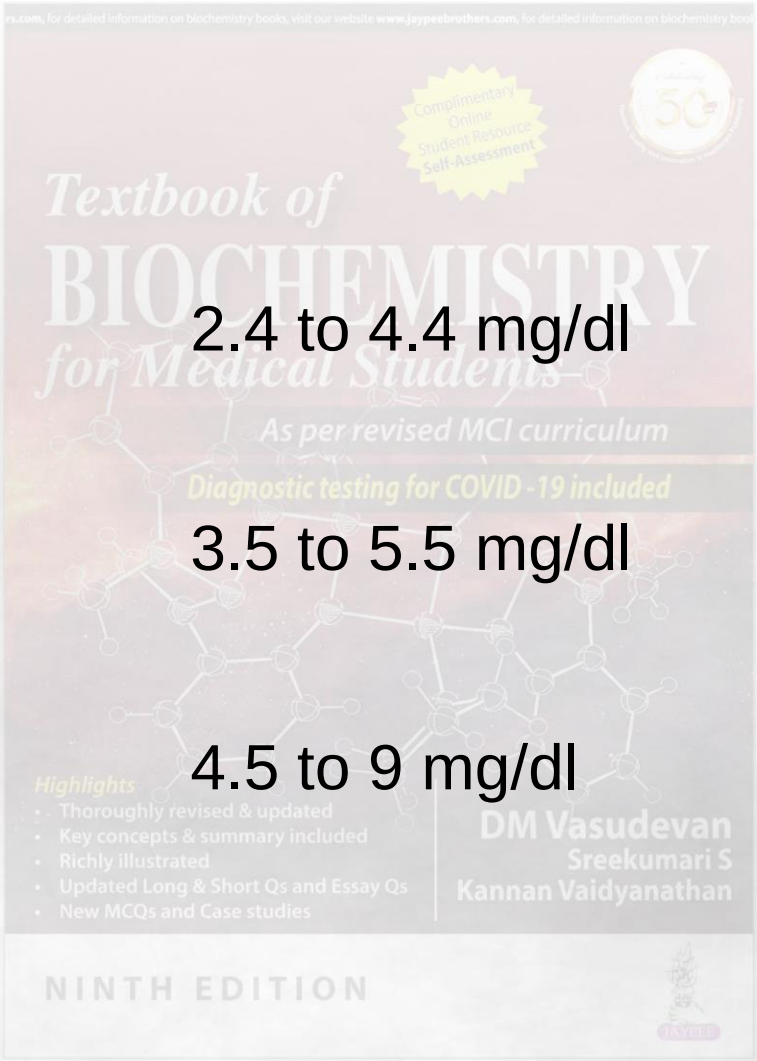


Phosphate

Phosphate ions are the most abundant of intracellular anions. It is present in all tissues and organic phosphates are metabolic intermediates, energy currency and components of nucleic acids. Phosphate ions in turn play an important role in anion cation balance between water components and acid base balance.

Phosphate reference values in blood

Adult	2.4 to 4.4 mg/dl
Children	3.5 to 5.5 mg/dl
Neonates	4.5 to 9 mg/dl



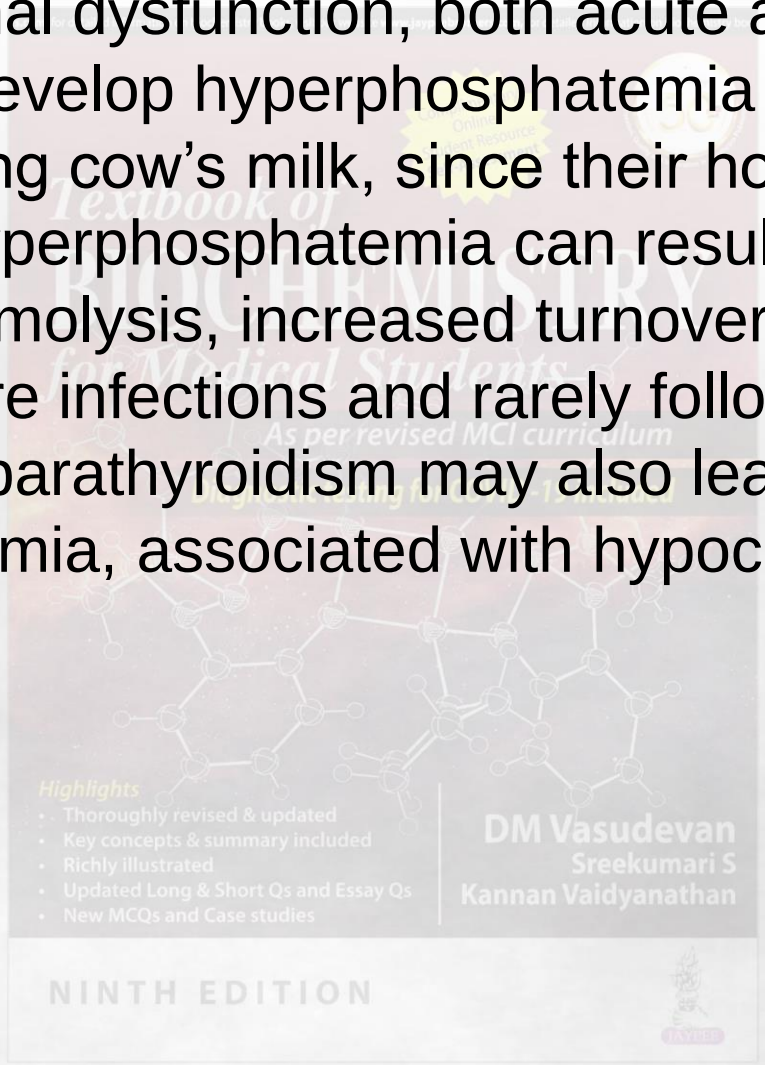
Hypophosphatemia

Low phosphate levels are seen in

- Diabetic ketoacidosis,
- Malignancy,
- COPD,
- Alcoholism,
- Inflammatory bowel disease
- Long term TPN (total parenteral nutrition).
- Hyperparathyroidism
- Vitamin D deficiency
- Prolonged antacid use

Hyperphosphatemia

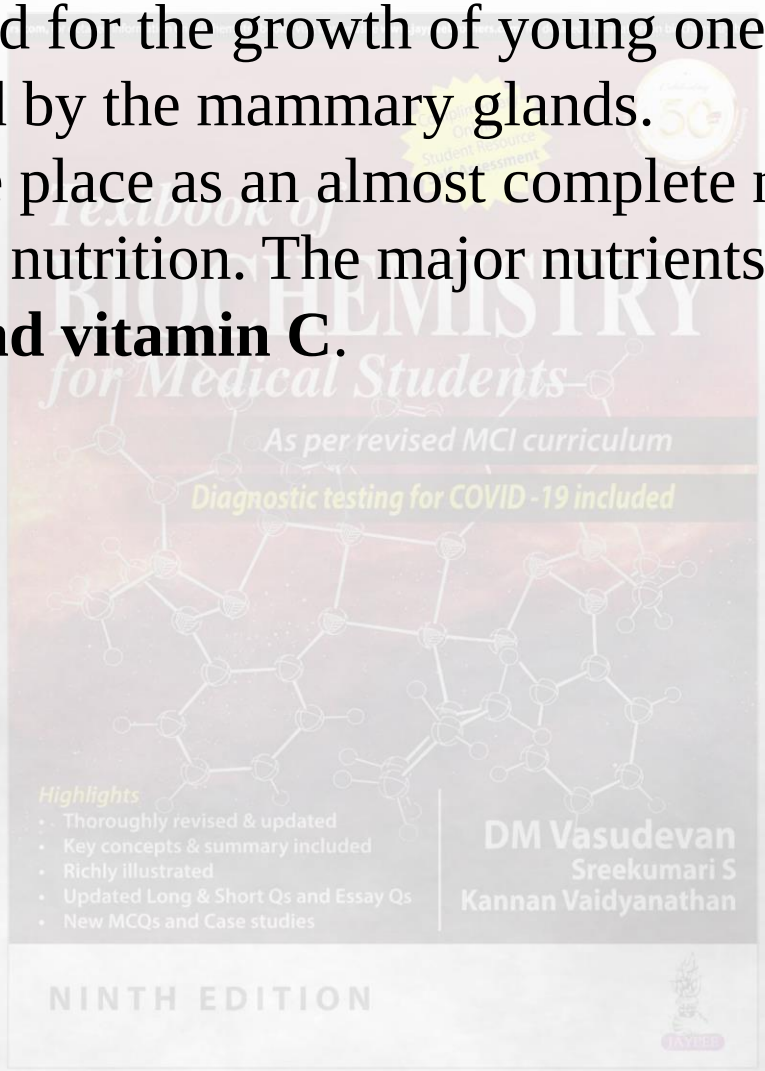
patients with renal dysfunction, both acute and chronic. Neonates can develop hyperphosphatemia due to increased intake like feeding cow's milk, since their hormonal balance is immature. Hyperphosphatemia can result from intravascular hemolysis, increased turnover of cells as in neoplasia, severe infections and rarely following intense exercise. Hypoparathyroidism may also lead to hyperphosphatemia, associated with hypocalcemia



Milk

Milk is the only food for the growth of young ones of all mammals. The milk is secreted by the mammary glands.

Milk holds a unique place as an almost complete natural food from the point of view of nutrition. The major nutrients **lacking in milk are iron, copper and vitamin C**.

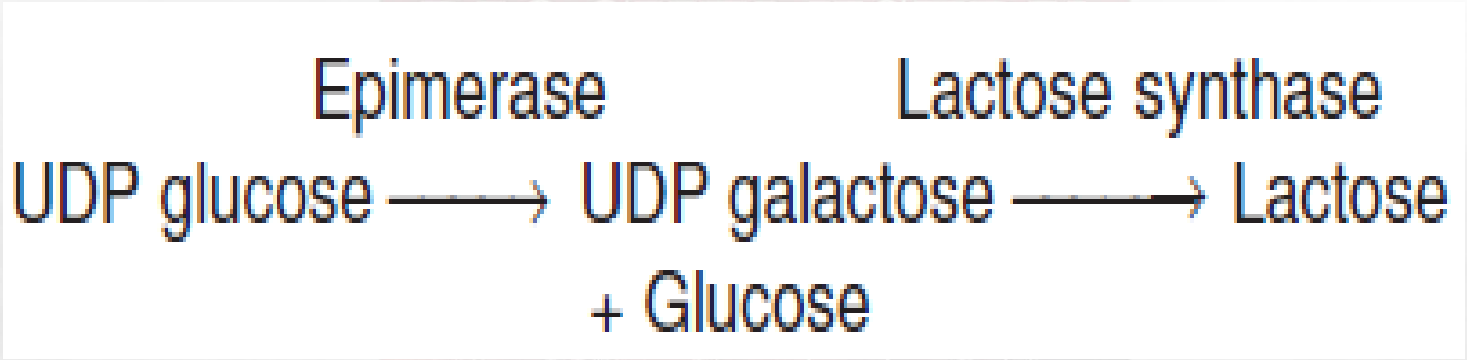


Composition of Milk

Constituent	Human	Cow	Buffalo	Goat
Water (%)	87.5	87.2	83.6	87.5
Total solids (%)	12.5	12.8	16.4	12.5
Proteins (g/dl)	1.1	3.3	4.3	3.7
Lipids (g/dl)	3.8	3.8	6.0	3.5
Carbohydrate(g/dl)	7.5	4.4	5.3	4.7
Calcium (mg/dl)	34	150	160	170

Lactose Synthesis

Synthesis of lactose in mammary gland is catalyzed by lactose synthase. A galactose unit is transferred from UD Pgalactose to glucose.



Lactase deficiency leads to lactose intolerance

Many infants develop diarrhea and skin manifesta-tions due to lactose intolerance. (It may also be due to allergy to milk proteins). These children are to be fed with lactose-free formulae or soybean proteins.

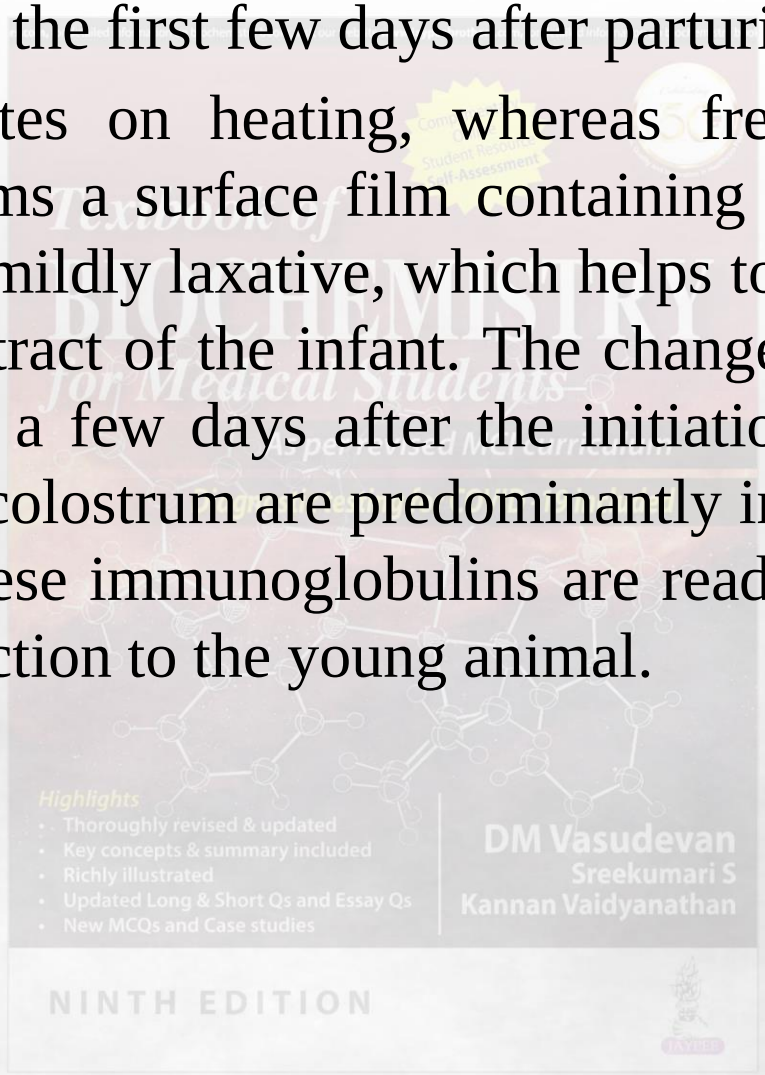
Mineral content of Milk

Mineral	Human milk (mg/100 ml)	Cow's milk (mg/100 ml)	Buffalo's Milk (mg/100 ml)
Magnesium	2.2	13	10
Phosphorus	16	100	100
Sodium	15	58	58
Potassium	55	138	130
Chloride	43	100	60
Iron	Negligible	Negligible	Negligible

Colostrum (Colostral Milk)

It is secreted during the first few days after parturition.

Colostrum coagulates on heating, whereas fresh milk does not. This coagulum forms a surface film containing casein and calcium salts. Colostrum is mildly laxative, which helps to remove meconium from the intestinal tract of the infant. The change from colostrum to milk occurs within a few days after the initiation of lactation. The proteins present in colostrum are predominantly immunoglobulins. In the case of cow, these immunoglobulins are readily absorbed by the calf, and give protection to the young animal.



Cerebrospinal Fluid

The cerebrospinal fluid (CSF) is found within the subarachnoid space and ventricles of the brain, as well as around the spinal cord. The fluid originates in the choroid plexus and returns to the blood in the vessels of the lumbar region.

The total volume of fluid is about 125 mL. It is a transudate or ultra filtrate of plasma. The composition of the fluid is given in Table 25.10. CSF has the chloride concentration higher than the plasma. This is in accordance with the Gibbs-Donnan equilibrium.

Biochemical Analysis of Cerebrospinal Fluid

The protein concentration is usually 10–30 mg/dL, out of which about 20 mg/dL is albumin, and globulin is about 5–10 mg/dL. In **bacterial infections** of the meninges, the protein concentration is increased. But in such cases, the neutrophil cell count is also increased.

In **viral infections,** the protein concentration is not significantly increased, but mononuclear cells are abundant.

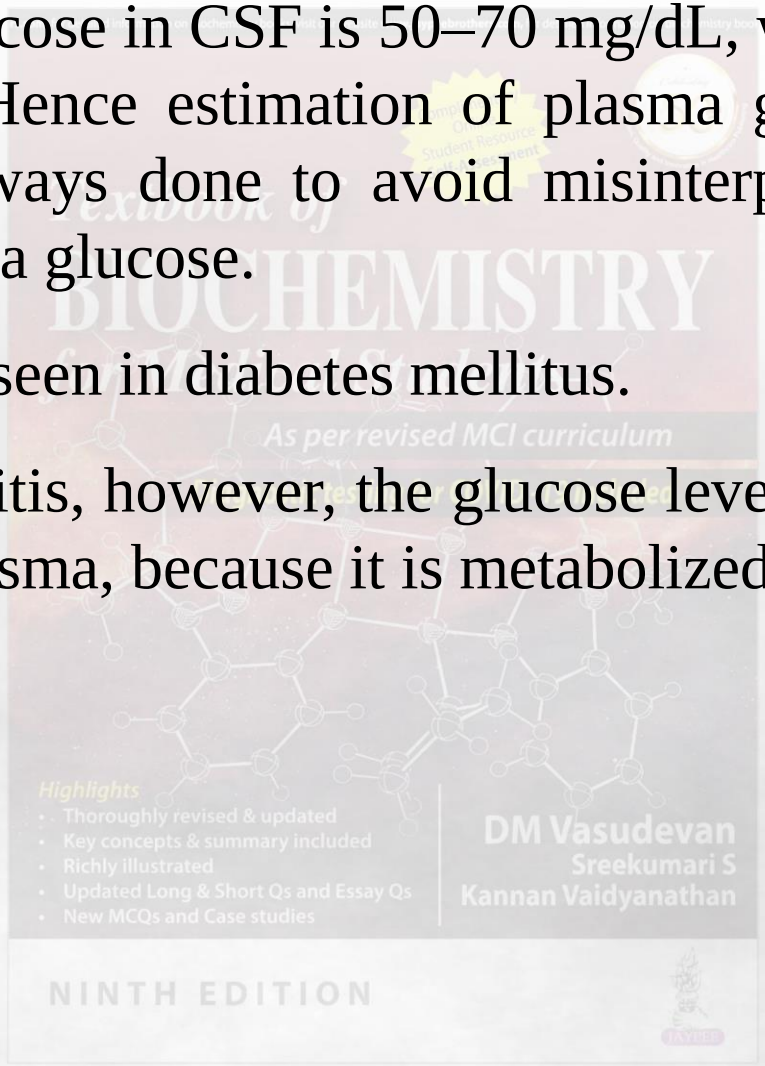
In **brain tumors**, albumin level is raised, but cell count is normal; this is called albumin cytological dissociation.

Glucose Level in Cerebrospinal Fluid

Normal level of glucose in CSF is 50–70 mg/dL, which is lower than the plasma level. Hence estimation of plasma glucose along with CSF glucose is always done to avoid misinterpre-tation due to a change in the plasma glucose.

Elevated levels are seen in diabetes mellitus.

In bacterial meningitis, however, the glucose level is far lower when compared to the plasma, because it is metabolized by bacteria.



Composition of the Cerebrospinal Fluid in Health and Diseases

Disease	Color and appearance	Cell count	Protein	Sugar	Coagulation
Normal	Clear and colorless	0-4 ´ 106/L	10-30 mg/dl	50-70 mg/dl	Not seen
Bacterial meningitis (purulent meningitis)	Opalescent or turbid due to high cell content	Markedly increased polymorphs	Marked increase	Marked decrease	May clot on standing
Tuberculous meningitis	May be opalescent	Lymphocytes and mononuclear cells	Increased	Low but not very much decreased	Cobweb type coagulation
Viral infection	Clear and colorless	Increased	Increased	Normal	Nil
Brain tumor	Clear and colorless	Within normal range	Increased	Low	Solidifies
Sub-arachnoid hemorrhage	Blood stained in fresh hemorrhage	RBCs and WBCs	Increased	Not significant	Nil

Amniotic Fluid

Amniocentesis is the process by which amniotic fluid is collected for analysis. Examination of amniotic fluid is of importance in prenatal diagnosis

Normal Composition of Amniotic Fluid

	Early gestation	Preterm
Volume	450-1200 ml	**500-1400 ml**
Bilirubin	<0.075 mg/dl	**<0.025 mg/dl**
Creatinine	0.8-1.1 mg/dl	**1.8-4.0 mg/dl**
Estriol	10 mg/dl	**>60 mg/dl**
L/S ratio	<1:1	**>2:1**
Protein	0.6-0.24 g/dl	**0.26-0.19 g/dl**
Urea	18 6 mg/dl	**30 11 mg/dl**
Uric acid	**3.71 mg/dl**	**9.92.2 mg/dl**

Lung Maturity

The lung maturity is assessed by measuring the lecithin/sphingomyelin (L/S) ratio, which is an index of the **surfactant** (surface tension lowering complex) concentration in amniotic fluid. In late pregnancy, the cells lining the fetal alveoli start synthesizing dipalmitoyl-lecithin so that the concentration of lecithin increases, whereas that of sphingomyelin remains constant. As a result, as the fetal lung matures, the lecithin sphingomyelin (L/S) ratio rises. An L/S ratio of 2 is taken usually as a critical value.