

# BIOCHEMISTRY

## BIOPHYSICS

### pH

**Q. pH is negative logarithm of hydrogen ion concentration expressed in (BSMMU –Residency - Dentistry – March '19)**

- a) mole/ L
- b) g/ L
- c) mg/ L
- d) nmol/L
- e) g/dL

Ans. a) T   b) F   c) F   d) F   e) F

(Ref. ABC-5<sup>th</sup>, P-31+ Satyanarayana 5<sup>th</sup>)

#### HELP LINK:

■ **Definition:** pH is the negative logarithm of hydrogen ion concentration of a solution to the base 10 where H<sup>+</sup> conc. is expressed as mole/L.

$$\text{pH} = -\log[\text{H}^+] = \log 1/[\text{H}^+]$$

So, there is an inverse relationship between the pH & H<sup>+</sup> concentration. If the H<sup>+</sup> conc. increases, pH decreases and vice versa.

■ **Example:** In case of pure water, [H<sup>+</sup>] = 10<sup>-7</sup> gmEq/L. So, pH = -log(10<sup>-7</sup>) = -(7) = 7.

#### ■ Biomedical importance:

1. Maintenance of appropriate pH is necessary for homeostasis.
2. Maintenance of ECF between pH 7.35 and 7.45 is essential for health.
3. pH controls the biochemical reactions.
4. pH controls the enzymatic activity.
5. pH maintains the cellular viability.
6. pH maintains the structure of the biomolecules.
7. pH maintains activities of the vital organs such as heart, brain.
8. Disturbances of acid-base balance are diagnosed by measuring the pH of arterial blood and the CO<sub>2</sub> content of venous blood.
9. Blood pH < 7.35 causes acidosis which occurs in diabetic ketoacidosis and lactic acidosis.
10. Blood pH > 7.45 causes alkalosis which occurs in vomiting of acidic gastric contents or treatment of certain diuretics.

(Ref: Harper-30<sup>th</sup>, P-6)

#### Methods of determination of pH:

1. Non specific (colorimetric) methods	2. Specific(electrometric) methods
◆ Buffers	◆ pH meter
◆ Indicators	◆ Gas electrode
◆ pH paper	◆ Calomel electrode
◆ Litmus paper	◆ Hydrogen electrode

(Ref: West & Todd-4<sup>th</sup>)

■ **pH scale:** It is the range of pH that covers the practical range of acidity and alkalinity in commonly available solution. It is a logarithmic scale extend from 0-14.

pH scale shows relationship between H<sup>+</sup>, OH<sup>-</sup> and pH in aqueous solution at 25°C when Kw = 10<sup>-14</sup>.

■ **Construction:** pH scale is constructed on the basis of ion product of water (Kw). Kw = 10<sup>-14</sup>. So, the product of H<sup>+</sup> & OH<sup>-</sup> must not exceed 10<sup>-14</sup> in any solution. pH is considered between 0 to 14.

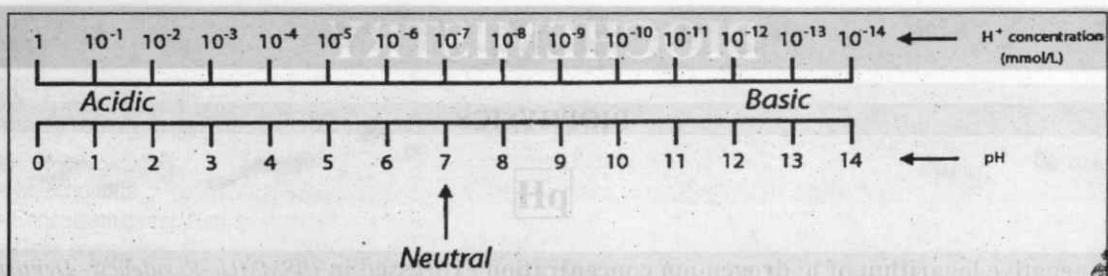


Fig: pH scale

**■ Its salient features/ Properties:**

- pH 0 indicates pure acidic solution and there is no hydroxyl ion. But, practically it is not feasible.
- pH 14 indicates pure alkaline solution and there is no  $\text{H}^+$  ion. But, practically it is not feasible.
- pH 7 indicates neutral pH
- pH below 7 indicates acidic solution
- pH above 7 indicates alkaline solution.
- $[\text{H}^+]$  cannot be zero.
- $[\text{H}^+]$  is inversely proportional to that of pH.
- 1 unit variation in pH 10 times variation in  $[\text{H}^+]$ . e.g. when pH decreases 1 unit  $[\text{H}^+]$  will increase 10 times and vice versa.
- For 1 unit change of pH,  $[\text{OH}^-]$  will change directly 10 times.
- $[\text{H}^+]$  and  $[\text{OH}^-]$  depends on each other.

(Ref: Ganong-25<sup>th</sup>, P-6; West & Todd-4<sup>th</sup>, P-2; Lecture of DMC & SSMC)**Some information:**

- At neutrality  $[\text{H}^+]$  is equal to  $10^{-7}$  moles / L and neutral pH will be 7.
- At  $25^\circ\text{C}$   $K_w = 10^{-14}$  and so  $\text{pH} + \text{pOH} = 14$ .
- Acidity means  $[\text{H}^+]$  more than  $[\text{OH}^-]$  and alkalinity means  $[\text{OH}^-]$  more than  $[\text{H}^+]$ .
- pH 7 = Neutral, pH<7 = Acidic & pH>7 = Alkaline.**
- Even an extreme acidic solution contain some amount of  $\text{OH}^-$  ions and even an extreme alkaline solution contain some amount of  $\text{H}^+$  ions.

	Range of pH	Average pH
<b>Blood</b>	7.35 - 7.45	7.4
<b>Urine</b>	4.5-8.0	6.0
<b>Saliva</b>	6.0 - 7.0	
<b>Milk</b>	6.6-6.9	
<b>Tear</b>	6 - 8	7.2

(Ref: Guyton-13<sup>th</sup>, Orten-10<sup>th</sup>, P-881, West & Todd-4<sup>th</sup>, P-30)**Q. pH is:** (MD/MS (DMC)-04Ja)

- The negative logarithm of  $\text{H}^+$  conc.
- An increase in  $\text{H}^+$  conc. increases pH.
- $\text{H}^+$  conc. is expressed in m.mol/ L.
- Blood pH is about 7.4.
- Normal body fluid pH is maintained only by buffer system.

- T      T  
F      F  
F (gmEq/ L)      F  
T      T

**Q. pH of blood is regulated by-** (BIRDEM-04)

- Hormones
- Urinary system
- Respiratory system
- Blood buffer system
- Food

- F  
T  
T  
T  
T

**Q. pH is** (M. phil, Diploma – 03Ju)

- a) the negative logarithm of  $[H^+]$
- b) the logarithm of  $[I/H^+]$
- c) increased with rise in  $[H^+]$
- d) maintained by liver along with other system
- e) 7 in case of water

T  
F  
F  
F  
T

**Q. The pH of the following -** (BSMMU – MD - 03Ja)

- a) Gastric juice 4 – 4.5.
- b) Urine 6 - 6.5
- c) Blood – 6
- d) Bile - 8
- e) Pancreatic juice 8.2.

F (1 – 3.5)  
F (4.5 – 6)  
F  
T  
T

**Q. The pH of blood is 7.4 when the ratio between  $(NaHCO_3)$  and  $H_2CO_3$  is:** (MD/MS (DMC)-01Ja)

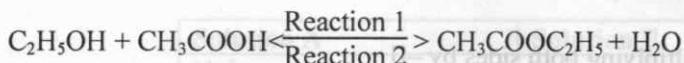
- A. 10:1.
- B. 20:1
- C. 25:1.
- D. 30:1
- E. 5:1.

F  
T  
F  
F  
F

## LAW OF MASS ACTION

■ **Law of mass action:** This law states that the velocity of a reversible reaction, at constant temperature at equilibrium, is directly proportional to the product of concentrations of the reacting substances.

■ **Analysis:** The reaction between ethyl alcohol and acetic acid to form ethyl acetate and water is a reversible reaction:



According to the law of mass action, the velocity ( $V_1$ ) of reaction 1 depends on the product of the conc. of ethyl alcohol and acetic acid:

$$V_1 \propto [C_2H_5OH] \times [CH_3COOH]$$

Or,  $V_1 = K_1 [C_2H_5OH] \times [CH_3COOH]$  [Here  $K_1$  is a constant]

Similarly, the velocity ( $V_2$ ) of reaction 2 depends on the product of the conc. of ethyl acetate and water:

$$V_2 \propto [CH_3COOC_2H_5] \times [H_2O]$$

Or,  $V_2 = K_2 [CH_3COOC_2H_5] \times [H_2O]$  [Here  $K_2$  is another constant]

Now, at equilibrium, the velocity of reactions 1 and 2 are equal:

$$V_1 = V_2$$

Or,  $K_1 [C_2H_5OH] \times [CH_3COOH] = K_2 [CH_3COOC_2H_5] \times [H_2O]$

Or,  $\frac{[CH_3COOC_2H_5] \times [H_2O]}{[C_2H_5OH] \times [CH_3COOH]} = \frac{K_1}{K_2} = K$ .

The new constant  $K$ , is the ‘equilibrium constant’ of the reaction.

■ **Importance:** The law of mass action is used in:

1. Determination of pH of a solution.
2. Determination of  $H^+$  conc. of solution.
3. Determination of the dissociation constant (pK value).
4. Predicting the rate of reaction between known substances.
5. Comparing unknown substances on the basis of constant.
6. Henderson Hasselbalch reaction.

5. Helps in maintenance of different electrolytes concentration. (Ref: West & Todd-4<sup>th</sup>, P-16, Orten-10<sup>th</sup>, P-876)

**Nice to know:****Criteria of equilibrium constant (K):**

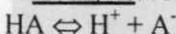
- If "K" is large, A and B will show more tendency to produce C and D compared to the tendency of C and D to produce A and B.
- For highly dissociable (ionizable) substance "K" value is high and for less dissociable substance "K" value is low.
- "K" value of a particular reaction changes with temperature and it is definite for a given reaction at a given temperature.

## Henderson Hasselbalch Equation

■ **Henderson-Hasselbalch equation:** The relationship between pH, pK and the concentration of an acid and its conjugate base can be stated by a convenient equation:  $\text{pH} = \text{pK} + \log \frac{[\text{Conjugate base}]}{[\text{Acid}]}$

This equation is called as Henderson Hasselbalch equation.

■ **Analysis:** A weak acid HA ionizes as follows:



According to the law of mass action

$$\frac{[\text{H}^+] \times [\text{A}^-]}{[\text{HA}]} = K \quad [\text{K} = \text{equilibrium constant}]$$

Or,  $[\text{H}^+] \times [\text{A}^-] = K \times [\text{HA}]$  [Cross multiplication]

$$\text{Or, } \frac{[\text{H}^+]}{[\text{A}^-]} = K \frac{[\text{HA}]}{[\text{A}]} \quad [\text{Dividing each side by A}^-]$$

Or,  $\log [\text{H}^+] = \log(K \times [\text{HA}])$  [Taking the log on both side]

$$\text{Or, } \log [\text{H}^+] = \log K + \log \frac{[\text{HA}]}{[\text{A}]} \quad [\text{A}^- \text{ and alkalinity means } [\text{OH}^-] \text{ more than } [\text{H}^+]]$$

$$\text{Or, } -\log [\text{H}^+] = -\log K - \log \frac{[\text{HA}]}{[\text{A}]} \quad [\text{Multiplying both sides by } -1]$$

$$\text{Or, } \text{pH} = \text{pK} - \log \frac{[\text{HA}]}{[\text{A}]} \quad [\text{Substituting pH and pK for } -\log [\text{H}^+] \text{ and } -\log \frac{[\text{HA}]}{[\text{A}]}]$$

$$\text{Or, } \text{pH} = \text{pK} + \log \frac{[\text{A}^-]}{[\text{HA}]} \quad [\text{Removing minus sign}]$$

$$\text{So, } \text{pH} = \text{pK} + \log \frac{[\text{Conjugate base}]}{[\text{Acid}]}$$

It is Henderson-Hasselbalch equation. From this equation we can say that the pH of a buffer solution can be determined by the logarithm of the ratio of salt and acid and by pK (the negative logarithm of dissociation constant).

**■ Importance:**

- It is used to determine pH of weak acid solution.
- It is used to determine pH of a buffer solution.
- Preparation of a buffer solution of a definite pH.
- Determination and evaluation of acid-base status of the body.
- Assessment of internal consistency of acid-base parameter.
- It is useful in determining how much drug is found on either side of a membrane that separates two compartments that differ in pH, for example stomach and blood plasma.

(Ref: A. C. Deb-8<sup>th</sup>, P-12; Lecture of DMC)

## Gibbs Donnan Membrane Equilibrium

**Q. On both sides of a selectively permeable membrane, Gibbs-Donnan effect leads to (BSMMU – Residency – MD, MS, Basic science – March '16)**

- equal concentration of non diffusible ions
- equal concentration ratio of diffusible ion
- equal concentration of diffusible ions
- electrical potential difference
- osmotic gradient

**Help link:**

**Gibbs-Donnan effect/ G-D effect:** It is the effect on the distribution of diffusible ions between two sides of a semi-permeable membrane due to the presence of non-diffusible ions on one side of membrane. On the side containing non-diffusible ion, diffusible counter ion will be more concentrated and on opposite side same charged diffusible ions will be more concentrated.

■ **Gibbs Donnan membrane equilibrium:** This law states that the unequal distribution of diffusible ions occurs across the semi-permeable membrane when a non-diffusible anion is present on one side of the membrane.

As a result of this type of equilibrium, following things happen:

- Both compartments will be electrically neutral.
- The product of conc. of the diffusible ions on one side of the membrane will be equal to the product of the conc. of the same ions on the opposite side.
- Side containing non-diffusible anion will have more negativity.
- Cation conc. on the side containing non-diffusible anion will be greater than that on the opposite side.
- Diffusible anion conc. will be more on the side without non-diffusible anion.

■ **Example:** Consider that sodium chloride ( $\text{Na}^+\text{Cl}^-$ ) is present in solution A and B, but only A contains a salt ( $\text{Na}^+\text{R}^-$ ); where  $\text{R}^-$  is an non-diffusible anion, unable to cross the membrane. thus-

Solution A	Solution B
$\text{Na}^+$	$\text{Na}^+$
$\text{Cl}^-$	$\text{Cl}^-$
$\text{R}^-$	

The penetrating ions ( $\text{Na}^+$  &  $\text{Cl}^-$ ) diffuse until the equilibrium is attained.

$$\begin{array}{l|l} [\text{Na}^+]_{\text{A}} = [\text{Cl}^-]_{\text{A}} + [\text{R}^-] & \text{Electrically neutral.} \\ [\text{Na}^+]_{\text{B}} = [\text{Cl}^-]_{\text{B}} & \end{array}$$

And  $[\text{Na}^+]_{\text{A}} \times [\text{Cl}^-]_{\text{A}} = [\text{Na}^+]_{\text{B}} \times [\text{Cl}^-]_{\text{B}}$   
Or,  $\frac{[\text{Na}^+]_{\text{A}}}{[\text{Na}^+]_{\text{B}}} = \frac{[\text{Cl}^-]_{\text{B}}}{[\text{Cl}^-]_{\text{A}}}$

Products and ratio of diffusible ions are equal.

From these relationships it follows that

$$\text{Or, } [\text{Na}^+]_{\text{A}} > [\text{Cl}^-]_{\text{A}}$$

And therefore

$$[\text{Na}^+]_{\text{A}} > [\text{Na}^+]_{\text{B}}$$

So,  $[\text{Cl}^-]_{\text{A}} < [\text{Cl}^-]_{\text{B}}$

$$\text{And } [\text{Na}^+]_{\text{A}} + [\text{Cl}^-]_{\text{A}} + [\text{R}^-]_{\text{A}} > [\text{Na}^+]_{\text{B}} + [\text{Cl}^-]_{\text{B}}$$

(Ref: Samson Wright's-13<sup>th</sup>, P-16, 17)

■ **Importance:**

- Unequal distribution of diffusible ions on the cell membrane.
- Generation and maintenance of resting membrane potential.
- It provides the mechanism of absorption
- It provides the mechanism of secretion.
- Helps in maintenance of different electrolytes conc. in various body fluid compartments.

6. Phenomenon of chloride shift can also be explained from this standpoint.  
 7. The Donnan effect is greatly influenced by the metabolic activity.

### Solution

**Q. A solution (BSMMU – Diploma – Dentistry-July '16)**

- a) is a homogenous mixture
- b) has a single phase
- c) has solvent and solute atoms
- d) can be formed if the solute exists as small molecule
- e) can be easily distinguishable

Ans. a) T b) T c) T d) T e) F

(Ref: Sattanarayon-4<sup>th</sup>, P-711)

**Help link:**

■ **Definition:** A solution may be defined as a homogenous mixture of two or more substances which has no definite chemical composition in definite temperature & pressure.

(Ref: Lecture of DMC)

**Or,**

A solution may be defined as a **homogenous mixture** of two or more substances distributed uniformly among each other to form a **single phase**.

(Ref: Lecture of SSMC)

■ **Example:** Solution of sugar, salt in water (saline).

**Colligative properties:**

These are called colligative properties of solution because each of them depends only on the total number of particles per unit volume & not on its chemical nature.

**Colligative properties of solution:**

- Osmotic pressure
- Lowering of vapour pressure
- Elevation of boiling point &
- Depression of freezing point.

**Types:**

■ **Aqueous solution:** It is a solution in which water is used as solvent.

■ **Non-aqueous solution:** It is a solution having vehicle other than water as solvent.

■ **Concept of homogenous:**

1. Uniform distribution of solute & solvent.
2. Same composition & concentration.

■ **Components of a solution:** two in number.

1. Solvent
2. Solute

1. **Solvent:** It is the larger part of solution which has the same physiological state as that of the solution. In solution, it is only one in number.

2. **Solute:** It is the minor part of solution which dissolves in the solvent and loses its physical state. In solution, it may be more than one.

## Colloid & Crystalloid

■ **Colloid:** Colloid may be defined as a substance in which solute particles are larger than solvent and is slowly diffusible and is incapable to pass through a semi-permeable membrane. Or,  
*Colloids are the substances which by virtue of their molecular size are slow diffusible rather than soluble in water and are incapable of passing through a semi-permeable membrane.*

**Example:** Proteins (plasma proteins), polysaccharides (starch, gelatin, glycogen), lipid, DNA & RNA etc.  
 This type of solution is most heterogeneous and the mixture is not uniform.

■ **Crystalloid:** A crystalloid may be defined as a substance which can pass through a semi-permeable membrane & cannot be separated by ultracentrifugation.

**Example:** Electrolytes ( $\text{Na}^+$ ,  $\text{K}^+$ ,  $\text{Ca}^{++}$ ), minerals, monosaccharides, amino acids, short chain fatty acids, vitamin, creatinine, uric acid etc.

### PROPERTIES OF COLLOIDS:

#### ■ General properties:

1. Variable colour. Ex: Gold solution – red, Silver solution – grey, Sulphate solution – colourless.
2. Variable shape (usually spherical)
3. Size: 1 – 100  $\mu\text{m}$ . (upto 500  $\mu\text{m}$ )
4. Low osmotic pressure. Ex: Plasma colloidal osmotic pressure: 28 – 32 mmHg.
5. Imbibition of water. Ex: 1 gm. of albumin (colloid) can hold 17 ml of  $\text{H}_2\text{O}$ .
6. Colloids are non-dialysable.
7. Solution can be converted into sol or gel state.(thixotropy)

#### ■ Optical properties:

1. **Brownian movement:** The continuous, hapazard, irregular, zigzag movement of colloidal particles is known as 'Brownian movement'. That can be seen under the ultramicroscope.
  - **Reason of motion:** The pushing effect of solvent molecule.
  - **Rate of motion:** Depends on the size of colloid molecules. The smaller the molecule, the greater the movement.
2. **Tyndall phenomenon:** When a beam of light is passed through a colloidal solution & is observed from right angle, the colloidal particles become visible due to the dispersion of light by the colloid particles. This is known as 'Tyndall phenomenon'.

#### ■ Electrical properties:

1. **Electrophoresis:** Colloidal particles carry electrical charges on surface. When an electric current is passed through the colloidal solution, positively & negatively charged particles move to the opposite poles. This is known as electrophoresis.

Rate of electrophoresis depends upon-• size • amount of charge.

2. **Isoelectric pH:** It is the pH at which the colloids exist in solution as 'Zwitter ion' containing equal number of positive & negative charges on their surface. So the net charge is zero. At pH above the isoelectric pH, they will exist as anion and at pH below their isoelectric pH, they will exist as cation.

#### ■ Other properties:

1. Interfacial tension: Colloid particles exert great interfacial tension which results in imbibition of water and adsorption of many substances by them.
2. Donnan membrane equilibrium.
3. Sol  $\leftrightarrow$  Gel formation
4. Coagulation & salting out.

(Ref: Orten-10<sup>th</sup>, P-884-887, Satyanarayana-4<sup>th</sup>)

### ■ Important colloids in plasma:

1. Plasma proteins:

- Albumin
- Globulin
- Fibrinogen
- Prothrombin

2. Lipids: • Natural fat

- Lipoproteins: Chylomicron, VLDL, LDL & HDL
- Phospholipid
- Cholesterol esters

3. Antibody: IgG, IgA, IgM, IgE, IgD

4. Various enzymes

5. Blood clotting factors.

### ■ Crystallloid in plasma:

1. Ions:  $\text{Na}^+$ ,  $\text{K}^+$ ,  $\text{Cl}^-$ ,  $\text{Ca}^{++}$ ,  $\text{Mg}^{++}$  etc.
2. Amino acid
3. Fatty acid
4. Monosaccharides
5. Urea
6. Uric acid

### Parts of colloidal solution:

1. **Dispersed phase:** The solute part of the colloidal solution is called dispersed phase. It is discontinuous phase.
2. **Dispersion media:** The solvent part of the colloidal solution is called dispersion phase. It is continuous phase.

### ■ Classification of colloids:

1. Lyophilic colloid (Emulsoid)
2. Lyophobic colloid (Suspensoid): Lyophobic means solvent hating. They don't mix with water. e.g, gold, silver.

**Lyophilic colloid (Emulsoid):** Lyophilic means solvent loving. They can mix with water. e.g, starch, blood proteins

#### Properties:

1. The particles in lyophilic colloid system appear to be more or less liquid.
2. Lyophilic colloids exist as emulsoids.
3. Practically all colloids of living cells are emulsoids.
4. They easily form water-shell around them which repel each other and provides stability to colloid solution.
5. They can be adsorbed on lyophobic colloid and thereby can stabilize the solution of lyophobic colloid by preventing their precipitation. Therefore lyophilic colloids are also called protective colloids.

**Lyophobic colloid (Suspensoid):** Lyophobic means solvent hating. They don't mix with water. e.g, gold, silver.

#### Properties:

1. The particles in lyophobic colloid system are generally solid.
2. They exist as suspensoid.
3. They are kept in solution by lyophilic colloid adsorbed around them. (Ref: Orten-10<sup>th</sup>, P-885)

### ■ Biomedical importance of colloids:

1. Essential constituents of all cell cytoplasm.
2. Exert colloidal osmotic pressure required for the fluid exchange in the capillary.
3. Tissue fluid is imbibed by colloids in glandular cells.
4. Colloidal state is responsible for the selective membrane permeability of the certain ions.

### ■ Functions of colloids in our body:

1. Some of the biological fluids are colloidal solution. e.g. blood, milk, CSF.
  2. Biological compounds as colloidal particles- protein, lipid, polysaccharides.
  3. Blood coagulation- when blood is clotted, it forms a gelly like substance.
  4. Fat digestion and absorption - bile in intestine emulcifies fat.
  5. Formation of urine.

(Ref: Satyanarayana-4<sup>th</sup>, Orten-10<sup>th</sup>, P-885)

### **■ Differences between colloid and crystalloid:**

Traits	Colloid	Crystalloid
<b>1. Size</b>	1 - 100 m $\mu$ .	Less than 1 m $\mu$ .
<b>2. Solute particles</b>	are larger than the solvent particles.	are smaller than the solvent particles.
<b>3. Permeability</b>	Cannot pass through the semi-permeable membrane.	Can pass.
<b>4. Physical form</b>	Amorphous and has no definite shape.	Crystaltic and can be crystallised from solution.
<b>5. Visibility</b>	Colloid particles can be seen under ultramicroscope.	Cannot be seen.
<b>6. Dialysability</b>	Non dialysable	Dialysable
<b>7. Osmotic pressure</b>	Low	High
<b>8. Optical activity</b>	Exhibit.	Don't exhibit
<b>9. Movement</b>	Brownian	Molecular
<b>10. Conversion</b>	Solution can be converted into sol. gel state.	Cannot be converted.
<b>11. Separation</b>	Can be separated by ultrafiltration & ultracentrifugation	Can not be separated.
<b>12. Nature of solution</b>	Heterogenous	Homogenous
<b>13. Example</b>	Plasma protein, starch glycogen, lipid, DNA and RNA.	Electrolytes (mainly K $^{+}$ ), minerals, vitamins, glucose, amino acid, fatty acid

(Ref: Lecture of DMC)

**The advantages of crystalloid solutions in clinical practice are:**

- 1) Inexpensive.
  - 2) Easy to store with long shelf life.
  - 3) Readily available.
  - 4) Very low incidence of adverse reactions.
  - 5) A variety of formulations are available.
  - 6) Effective for use as replacement fluids or maintenance fluids.
  - 7) No special compatibility testing is required.
  - 8) No religious objections to their use.

In essence they are cheap and effective and don't cause adverse reactions

## Question Bank

Question Bank

- a) ringers lactate solution      b) hydroxyl ethyl starch
  - c) albumin                          d) one fifth normal saline
  - e) gelatin derivatives

Ans. a) F b) T c) T d) F e) T

(Ref: ABC Biochemistry-6<sup>th</sup>, P-14)

**Q. The colloid solutions are (BSMMU – Residency – MS, Basic Science, Dentistry – March' 16)**

- a) albumin T
- b) 5% dextrose in normal saline F
- c) gelatin derivatives T
- d) hydroxy ethyl starch T
- e) ringer's lactate solution F

**Help link:**

Colloidal solution	Crystalloidal solution
• Plasma	• Normal saline
• Milk	• 5 % DA (Dextrose in aqua)
• CSF	• Cholera saline

**Q. Colloid particles (BSMMU – Residency – MD, MS, Basic Science – March' 15)**

- a) are about 600-1000 nm in sizes
  - b) form homogenous solution in water
  - c) can be seen under ultra-microscope
  - d) are non-dialyzable
  - e) can pass through semi-permeable membrane
- Ans. a) F b) F c) T d) T e) F

## Isotopes

**Q. Isotopes- (BSMMU – MD - 02Ja)**

- a) Are the atoms of same element T
- b) Are compound having same number of proton. T
- c) Atomic weights are different T
- d) All have definite stable state. F
- e) Radioactivity of isotopes can be used as a therapeutic tool. T

**HELP LINK:**

**Isotopes:** The species of same element having the same atomic number but different atomic weight are called isotopes of that element.

**Example:**  ${}^1\text{H}^{16}$ ,  ${}^1\text{H}^{17}$ ,  ${}^1\text{O}^{18}$  are the isotopes of oxygen.

**Classification:** Isotopes are two types-

1. **Stable isotopes:** The isotopes with atomic number less than 20 and  $\frac{\text{neutron}}{\text{proton}}$  ratio is 1 or near about 1 are usually known as stable isotopes (natural isotopes).

They are naturally occurring and do not emit radiation. They can be identified by mass of spectrometry or NMR (Nuclear Magnetic Resonance)

**Example:**  ${}^1\text{H}^1$ ,  ${}^2\text{He}^3$ ,  ${}^4\text{He}^4$ ,  ${}^{12}\text{C}^{12}$ ,  ${}^{13}\text{C}^{13}$  etc.

**Exception-**  ${}^{14}\text{C}^{14}$  and  ${}^2\text{He}^5$

2. **Unstable (Radioactive) isotopes:** The isotopes with atomic number more than 20 and  $\frac{\text{neutron}}{\text{proton}}$  ratio is more than 1 are usually known as unstable isotopes. These isotopes fail to show structural constancy and when break down into more stable atoms, they always gives off radiation that may be  $\alpha$ ,  $\beta$  &  $\gamma$  rays. They can be prepared artificially by cyclotron.

**Example:** Ra, U etc.

**Exception-**  ${}_{53}^{131}\text{I}^{131}$

(Ref: Satyanarayana-4<sup>th</sup>)

**Clinical importance of isotopes:****■ Diagnostic use:**

1. Thyroid diseases by iodine ( $\text{I}^{131}$ ) uptake test.
2. Measurement of hormone in blood by a technique known as RIA (radioimmunoassay).
3. Organ scanning-brain, liver, kidney, thyroid, bone.

4. Tracing of malignant tissue in the body by uptaking  $P^{32}$ .
5. Diagnosis of brain tumours by radio-active di-iodofluorescein.
6. Diagnosis of arterial diseases by  $Na^{24}$ .

■ Therapeutic use:

1. Treatment of hyperthyroidism and thyroid cancer by  $I^{131}$ .
2. Treatment of leukaemia and polycythaemia by  $P^{32}$ .
3. Radiotherapy in malignancy.

■ Measurement of volume & spaces:

1. Measurement of total body fluid by  $D_2O$ .
2. Measurement of ECF volume by radio-active Na.
3. Measurement of plasma volume with  $I^{125}$  – albumin (*Radio-Iodinated serum albumin*).
4. Measurement of RBC volume by  $Cr^{51}$ .

■ Absorbtic & Metabolic study:

1. Absorption studies of iron by  $Fe^{59}$ .
2. Absorption studies of vit-B<sub>12</sub> by  $Co^{60}$ .
3. Absorption studies of fat by  $I^{131}$  – oleic acid.
4. Study of the metabolism of CHO, protein, fat by  $C^{14}, H^2, H^3$  etc and of minerals by  $Na^{24}, K^{42}, Ca^{45}$ .

■ Others:

1. Circulatory studies.
2. Study of antibody formation in R.E system by  $P^{32}$ .
3. Sterilization of medical instruments.
4. Radioactive isotopes are used for scanning of the different organ of the body to locate the malignant cells.

(Ref: A.C.Deb + Lecture of SSMC)

## Serum amylase

Q. Serum amylase raised in (BSMMU – Non-Residency - MD/MS, Basic science – 13Ju)

- |                                 |   |
|---------------------------------|---|
| a) acute pancreatitis           | T |
| b) alcoholic cholecystitis      | T |
| c) severe diabetic ketoacidosis | T |
| d) myeloid leukaemia            | T |
| e) morphine or opioids therapy  | T |

Help link:

(Ref: ABC Biochemistry, S. Chakraborty)

**TABLE 306-2 CAUSES OF HYPERAMYLASEMIA AND HYPERAMYLASURIA****Pancreatic Disease**

- I. Pancreatitis
  - A. Acute
  - B. Chronic: ductal obstruction
  - C. Complications of pancreatitis
    - 1. Pancreatic pseudocyst
    - 2. Pancreatogenous ascites
    - 3. Pancreatic abscess
    - 4. Pancreatic necrosis

- II. Pancreatic trauma
- III. Pancreatic carcinoma

**Nonpancreatic Disorders**

- I. Renal insufficiency
- II. Salivary gland lesions
  - A. Mumps
  - B. Calculus
  - C. Irradiation sialadenitis
  - D. Maxillofacial surgery
- III. "Tumor" hyperamylasemia
  - A. Carcinoma of the lung
  - B. Carcinoma of the esophagus
  - C. Breast carcinoma, ovarian carcinoma

- IV. Macroamylasemia
- V. Burns
- VI. Diabetic ketoacidosis
- VII. Pregnancy
- VIII. Renal transplantation
- IX. Cerebral trauma
- X. Drugs: morphine

**Other Abdominal Disorders**

- I. Biliary tract disease: cholecystitis, choledocholithiasis
- II. Intraabdominal disease
  - A. Perforated or penetrating peptic ulcer
  - B. Intestinal obstruction or infarction
  - C. Ruptured ectopic pregnancy
  - D. Peritonitis
  - E. Aortic aneurysm
  - F. Chronic liver disease
  - G. Postoperative hyperamylasemia

**Cause of increased amylase:**

- Acute and chronic pancreatitis, pancreatic pseudocyst and ascites
- Choledocholithiasis
- Acute parotitis (mumps)
- Renal failure, hepatitis, cirrhosis
- Rupture ectopic pregnancy, Mesenteric infarction,
- intestinal obstruction, Pheochromocytoma, thymoma;
- multiple myeloma, breast cancer, Ketoacidosis, leukaemia, morphine therapy

1. Thyroid disease by iodine ( $I^{131}$ ) uptake test.

2. Measurement of hormone in blood by a technique known as RIA (radioimmunoassay).

3. Organ function tests: brain, liver, kidney, thyroid, bone.

## BIOMOLECULES

### CARBOHYDRATE

■ **Definition:** Carbohydrates may be defined chemically as aldehyde or ketone derivatives of polyhydric alcohol or as compounds that yield these derivatives on hydrolysis. (Ref: Harper-30<sup>th</sup>, P-152)

■ **Classification:**

Carbohydrates			
Monosaccharides	Disaccharides	Oligosaccharides	Polysaccharides
(Cannot be hydrolyzed into simple form) ↓	(Composed of 2 mono saccharides e.g. Sucrose, maltose, lactose)	(yield 3-10 monosaccharides on hydrolysis e.g. Maltotriose, rabinose, raffinose, rhamninose etc.)	(yield more than 10 monosaccharides on hydrolysis)
On the basis of no. of carbon atom			
On the basis of presence of functional group			
Trioses ( $C_3H_6O_3$ ) Tetroses ( $C_4H_8O_4$ ) Pentoses ( $C_5H_{10}O_5$ ) Hexoses ( $C_6H_{12}O_6$ )			<b>Homopolysaccharides</b> (Starch, dextrin, cellulose, glycogen)
Aldoses (-CHO present) Glycerose Erythrose Ribose Glucose			<b>Heteropolysaccharides</b> (Heparin, hyaluronic acid, Chondroitin sulphate)
Ketoses (>C=O present) Dihydroxyacetone Erythrulose Ribulose Fructose			

### Question Bank

**Q. Lactose (BSMMU –Residency - Dentistry – March' 19)**

- a) is present in milk
- b) is a reducing sugar
- c) is a monosaccharide
- d) is a product of hydrolysis of starch
- e) intolerance develops due to excess lactose intake

Ans. a) T   b) T   c) F   d) F   e) F

(Ref. ABC-5<sup>th</sup>, P-49 + Lippincott-7<sup>th</sup>)

Lactose	Sucrose
Known as milk sugar	Known as cane sugar (table sugar)
Composed of D- glucose and D- galactose	Composed of D- glucose and D- fructose
Not invert sugar	Invert sugar
Reducing sugar	Non reducing sugar
Form osazone crystal with phenyl hydrazine	Do not form osazone crystal with phenyl hydrazine
Can be synthesized in lactating breast	Can not be synthesized in human
Hydrolyzed by lactase	Hydrolyzed by sucrase

(Ref. ABC Biochemistry-5<sup>th</sup>, P-49)

**Q. Following compounds are disaccharides:** (BSMMU – M. Phil, Diploma (Non-Residency)–March-2012, DMC & others – MD/MS – March-2012)

- |               |   |
|---------------|---|
| a) laclose    | T |
| b) isomaltose | T |
| c) galactose  | F |
| d) maltose    | T |
| e) fructose   | F |

**Help link:**

**Classification of disaccharides:**

They yield two monosaccharides on hydrolysis. They are further classified into two groups-

- |                     |                         |
|---------------------|-------------------------|
| <b>a) Reducing:</b> | <b>b) Non-reducing:</b> |
| • Maltose           | • Sucrose.              |
| • Lactose           | • Trehalose.            |

**Disaccharides:**

Sugar	Source	Clinical significance
<b>Sucrose</b>	Cane and beet sugar, sorghum and some fruits and vegetables	Rare genetic lack of sucrase leads to sucrose intolerance—diarrhea and flatulence
<b>Lactose</b>	Milk (and many pharmaceutical preparations as a filler)	Lack of lactase (alactasia) leads to <b>lactose intolerance</b> —diarrhea and flatulence; may be excreted in the urine in pregnancy
<b>Maltose</b>	Enzymic hydrolysis of starch (amylase); germinating cereals and malt	
<b>Isomaltose</b>	Enzymic hydrolysis of starch (the branch points in amylopectin)	
<b>Lactulose</b>	Heated milk (small amounts), mainly synthetic	Not hydrolyzed by intestinal enzymes, but fermented by intestinal bacteria; used as a mild osmotic laxative.
<b>Trehalose</b>	Yeasts and fungi; the main sugar of insect hemolymph	

(Ref: Harper-30<sup>th</sup>)

Disaccharides	Another name	Constituent monosaccharide units
<b>Maltose</b>	Malt sugar	Glucose + Glucose
<b>Lactose</b>	Milk sugar	Glucose + Galactose
<b>Sucrose</b>	Cane sugar, table sugar	Glucose + Fructose

**Q. The reducing substances are:** (M. Phil, Diploma-07July)

- |                 |   |
|-----------------|---|
| a) sucrose      | F |
| b) glucose      | T |
| c) triglyceride | F |
| d) lactose      | T |
| e) maltose      | T |

**HELP LINK:**

**Reducing sugars.**

■ The sugar which possess free aldehyde or ketone group in their structure, having free anomeric carbon atom is called reducing sugar. e. g.

- Monosaccharides (simple sugars) - glucose, fructose, galactose.

- Disaccharides (except sucrose & trehalose)

■ Glucose is a reducing sugar because it has a free functional aldehyde group which has reducing property.

**Examples:**

- ✓ Sugars:
  - Glucose, Fructose, Pentose, Lactose, galactose, L-xylose
- ✓ Non sugars:
  - Uric acid, urates, creatinine, glucoronides, salicylates,
  - phenol, PAS, ascorbic acid, levodopa, Nalidixic acid,
  - Tetracycline, Cysteine, Tyrosine, homogentisic acid ketone body

**Q. Why sucrose is not reducing sugar?**

Ans.

**Sucrose = glucose + fructose**

Sucrose consists of glucose and fructose which are linked together by their functional group.

Aldehyde group of glucose are linked to keto group of fructose and make glycosidic bond. As a result both the reducing groups are blocked and so there is no free functional group. That is why the sucrose is not reducing sugar.

(Ref: Satyanarayana-4<sup>th</sup>)**■ Non-reducing sugar:**

- Disaccharides: only sucrose & trehalose
- Oligosaccharides
- Polysaccharides

**Q. The followings are monosaccharides: (BSMMU - M. Phil, Diploma, July-07)**

- |                     |   |
|---------------------|---|
| a) cerebrosides     | F |
| b) dextrose         | F |
| c) inulin           | F |
| d) dextran          | F |
| e) dihydroxyacetone | T |

**Q. The common monosaccharides: (BSMMU – M. Phil, Diploma July, 2004)**

- |  |   |
|--|---|
| A. Contain asymmetric centres.                     | T |
| B. Are of two types aldoses and ketoses            | T |
| C. Exist as ring structure in solution             | T |
| D. Include glucose, galactose and raffinose        | F |
| E. Are readily formed from glucose by living cells | F |

**Q. Carbohydrate is stored as: (BSMMU – M. Phil, Diploma July, 2004)**

- |   |   |
|---|---|
| A. Polyglucans in most living organisms | T |
| B. Cellulose in green plants            | T |
| C. Lactose in mammary gland             | T |
| D. Glycogen in muscle                   | T |
| E. Glycoproteins                        | T |

**Q. Polysaccharides consisting of only glucose (MD/MS (DMC)-03Ja)**

- |                |   |
|----------------|---|
| a) Starch      | T |
| b) Maltotriose | F |
| c) Inulin      | T |
| d) Cellulose   | T |
| e) Glycogen    | T |

**HELP LINK:**

**■ Definition:** Polysaccharides are those carbohydrates that yield more than 10 molecules of monosaccharides on hydrolysis.

**■ Classification:** Polysaccharides can be divided into two groups:

**1. Homopolysaccharides:** are those containing only one type of monosaccharides as the repeating unit and on hydrolysis gives only one type of sugar.

**Examples:** starch, cellulose, glycogen, dextrins etc.

**2. Heteropolysaccharides:** are those made up of mixed disaccharides as repeating units and on hydrolysis gives a mixture of more than one product of monosaccharides and their derivatives of amino sugars and sugar acids.

**Examples:** heparin, hyaluronic acid, chondroitin sulphate.

### ■ Importance of polysaccharides:

1. Starch is the major source of energy in the diet.
2. Glycogen is the storage form of energy.
3. Cellulose increases the bulk of intestinal contents which stimulates peristalsis and helps in defecation. Thus it prevents constipation.
4. Inulin is used in the GFR measurement.
5. Heparin acts as anticoagulants.
6. Hyaluronic acid serves as a lubricant and shock absorber in joints.
7. Some glycosides are used as drugs. E.g. cardiac glycosides.
8. Diseases associated with polysaccharides are glycogen storage disease etc.

**Q. Most calorogenic carbohydrate-(BSMMU-Med/Sur-01Ja)**

- |             |   |
|-------------|---|
| a) Starch   | F |
| b) Sucrose  | F |
| c) Glucose  | F |
| d) Glycogen | T |
| e) Maltose. | F |

## PROTEIN

### Classification:

#### ■ Based on chemical nature & solubility:

**1. Simple protein:** Contains only amino acid.

a. **Globular protein:** spherical or oval in shape. It is soluble in water and other solvents and are digestible. e.g. Albumin, globulin, protamines, histones, globins, insulin and many enzymes.

b. **Fibrous or Sclero-protein:** They are fibre like, insoluble in water and resistant to digestion. e.g., Collagen, elastin, keratin.

**2. Conjugated protein:** Contains amino acid with non-protein substances. This non-aminoacid portion is called prosthetic group. (e.g. Hb which contains haem, the prosthetic group and globin, the protein part)

Examples are-

- Nucleoprotein
- Glycoprotein
- Lipoprotein
- Phospho-protein
- Chromoprotein
- Metaloprotein

**3. Derived protein:** The derivatives produced from protein on hydrolysis.

<b>a. Primary</b>	<ul style="list-style-type: none"> <li>• Coagulated proteins</li> <li>• Proteans</li> <li>• Metaprotein</li> </ul>
<b>b. Secondary</b>	<ul style="list-style-type: none"> <li>• Proteoses</li> <li>• Peptones</li> <li>• Polypeptide</li> <li>• Peptides</li> </ul>

**■ On the basis of biological function:**

1. **Structural protein:** Collagen, elastin.
2. **Enzymes/ Catalytic protein:** pepsin, hexokinase.
3. **Transport protein:** Albumin, Hb, lipoproteins, transferrin.
4. **Hormonal protein:** Insulin.
5. **Contractile protein:** Actin, myosin.
6. **Storage protein:** ova albumin of egg white, casein of milk.
7. **Protective protein:** Snake venom, immunoglobulin
8. **Receptor protein:** receptor for hormones and viruses.
9. **Genetic protein:** Nucleoproteins.

(Ref: Harper-30<sup>th</sup>)**■ On the basis of source:**

1. **First class protein:** Proteins of high biological value which contain all the essential amino acids.  
**Sources:** Animal sources such as meat, fish, egg, milk.
2. **Second class protein:** Proteins of low biological value which are poor in essential amino acids.  
**Sources:** Vegetables such as pulses, cereals, lean, nuts, oil seed etc.

(Ref: Satyanarayana-3<sup>rd</sup>, P-64, 65)**Nice to know:**

- Albumin—soluble in water & salty solutions.
- Globulin --- less soluble in water but soluble in salt.
- Protamine—insoluble in water but soluble in salt.
- Histone--- soluble in salt solutions.
- Scleroprotein—insoluble in water or salt solutions.

**Q. Transport proteins include (BSMMU – Non-Residency – MD, MS, Basic science & Dentistry – July' 18)**

- a) albumin
- b) heptoglobin
- c) transcobalamin
- d)  $\alpha$ -feto protein
- e)  $\beta$ -2 microglobulin

Ans. a) T b) T c) F d) F e) F

**Help Link:****Transport protein:**

- ✓ hemoglobin, myoglobin,
- ✓ albumin, transferrin, ceruloplasmin,
- ✓ Pre-albumin or Transthyretin
- ✓ Retinol binding protein (RBP)
- ✓ Transcortin, Haptoglobin:
- ✓ Hemopexin (for heme)

(Ref: DM Vasudevan-7<sup>th</sup>, P-383)**Q. In cysteinuria reabsorption of following amino acids are defective: (BSMMU - MD/MS (Residency) - January - 11)**

- |               |   |
|---------------|---|
| a) ornithine  | T |
| b) arginine   | T |
| c) lysine     | T |
| d) alanine    | F |
| e) methionine | F |

**HELP LINK:****Cystinuria (Cystine-lysinuria):**

Cystinuria is one of the most common inherited diseases with a frequency of 1 in 7,000. It is primarily characterized by increased excretion of cystine (25-40 times normal). Elevation in the urinary output of lysine,

arginine and ornithine is also observed. A specific carrier system exists in kidney tubules for the reabsorption of amino acids, namely cysteine, ornithine, arginine and lysine (remember COAL to recall). In cystinuria, this carrier system becomes defective leading to the excretion of all these four amino acids in urine.

**Example:** Cystine is relatively insoluble and its increased concentration leads to its precipitation and formation of cystine stones in kidney and urinary tract. Cystinuria is usually identified in the laboratory by cyanide nitroprusside test. The treatment includes restricted ingestion of dietary cystine and high intake of fluids.

#### Regarding cystinuria:

- It is an inherited metabolic disease in which lysine, arginine, ornithine and cystine are excreted in the urine in large amounts.
- Cystinuria is due to renal transport defect.
- Cystinuria is a misnomer, so that cystinlysuria may be preferred as the descriptive term for this disease.
- Cystine is an insoluble amino acid which may precipitate in the kidney tubules to form cystine calculi in cystinuric patients. This is a major complication of this disease.
- The mixed disulfide of L-cysteine and Lhomocysteine present in the urine of cystinuric patients is more soluble than cysteine and hence reduces formation of cystine crystals and calculi.

**Q. The followings are the essential amino acid:** (BSMMU - M. Phil, Diploma - July '10)

- |                   |   |
|-------------------|---|
| a) phenyl alanine | T |
| b) histidine      | T |
| c) Threonine      | T |
| d) valine         | T |
| e) arginine       | T |

#### HELP LINK:

■ **Essential amino acid:** The amino acids which can not be synthesized in the body but essential for the growth and maintenance of the body and hence they have to be supplied in the diet.

There are eight essential amino acids:

1. Isoleucine
2. Tryptophan
3. Methionine
4. Valine
5. Leucine
6. Lysine
7. Threonine
8. Phenylalanine

■ **Non essential amino acids:** They are the amino acids which can be synthesized in the body. Besides above eight, all others are non essential amino acids except Histidine & Arginine. e.g. Glycine, Alanine, Aspartate, Glutamate etc.

■ **Semi essential amino acids:** These are the amino acids which can be synthesized partially in the body but not at a rate to meet the requirement of the body. These are –

- Histidine      • Arginine

(Ref: Harper-30<sup>th</sup>, Satyanarayana-4<sup>th</sup>)

■ There are more than 200 amino acids. But 20 amino acids are clinically important.

■ Essential amino acids in adults – 8

■ Essential amino acids in infants – 10 (8 + Histidine, Arginine)

**Q. The followings are the essential amino acids:** (M. Phil, Diploma-06July)

- |              |   |
|--------------|---|
| a) arginine  | T |
| b) glutamine | F |
| c) leucine   | T |
| d) alanine   | F |
| e) threonine | T |

**Help link: Table: Amino acids:**

<b>Essential amino acids</b>	<ul style="list-style-type: none"> <li>• Tryptophan</li> <li>• Histidine</li> <li>• Methionine</li> <li>• Threonine</li> <li>• Isoleucine</li> <li>• Valine</li> <li>• Phenylalanine</li> <li>• Lysine</li> <li>• Leucine</li> </ul>
<b>Conditionally essential amino acids and their precursors</b>	<ul style="list-style-type: none"> <li>• Cysteine: methionine, serine</li> <li>• Tyrosine: phenylalanine</li> <li>• Arginine: glutamine/ glutamate, aspartate</li> <li>• Praline: glutamate</li> <li>• Glycine: serine, choline</li> </ul>

(Ref: Davidson-23<sup>rd</sup>)**Q. Simple proteins are- (MD/MS (DMC)-05Ja)**

- |                |   |
|----------------|---|
| a) Albumin     | T |
| b) Haemoglobin | F |
| c) Globulin    | T |
| d) Lipoprotein | F |
| e) Histone     | T |

**HELP LINK:**

- **Definition:** Proteins are nitrogenous macromolecules high molecular weight polypeptides made up of  $\alpha$ -amino acids linked together by peptide bond (-CONH-). Proteins contain C, H, O, N, P, S and Fe in varying amounts.
- Proteins are polymers of amino acids. The molecular wt. of protein more than 5,000 and amino acid more than 50.
- Molecular weight of protein ranging from 5500-220000.
- Average molecular weight of an amino acid is 110. So, when 50 amino acid are linked together by peptide bond forming a protein and its molecular weight is  $110 \times 50 = 5500$ .

**Classification:****■ Based on chemical nature & solubility:**

1. **Simple protein:** Contains only amino acid.
  - a. **Globular protein:** spherical or oval in shape. It is soluble in water and other solvents and are digestible. e.g. Albumin, globulin, protamines, histones, globins, insulin and many enzymes.
  - b. **Fibrous or Sclero-protein:** They are fibre like, insoluble in water and resistant to digestion. e.g, Collagen, elastin, keratin.

2. **Conjugated protein:** Contains amino acid with non-protein substances. This non-aminoacid portion is called prosthetic group. (e.g. Hb which contains haem, the prosthetic group and globin, the protein part)

Examples are- • Nucleoprotein      • Glycoprotein      • Lipoprotein      • Phospho-protein  
                                         • Chromoprotein      • Metaloprotein

3. **Derived protein:** The derivatives produced from protein on hydrolysis.

<b>a. Primary</b>	<ul style="list-style-type: none"> <li>• Coagulated proteins</li> <li>• Proteans</li> <li>• Metaprotein</li> </ul>
<b>b. Secondary</b>	<ul style="list-style-type: none"> <li>• Proteoses</li> <li>• Peptones</li> <li>• Polypeptide</li> <li>• Peptides</li> </ul>

**■ On the basis of biological function:**

1. Structural: Collagen, elastin.
2. Enzymes/ Catalytic: pepsin, hexokinase.
3. Transport: Albumin, Hb, lipoproteins, transferrin.
4. Hormonal: Insulin.
5. Contractile: Actin, myosin.
6. Storage: ova albumin of egg white, casein of milk.
7. Protective protein: Snake venom, immunoglobulin
8. Receptor protein: receptor for hormones and viruses.
9. Genetic protein: Nucleoproteins.

(Ref: Harper-30<sup>th</sup>)

**■ On the basis of source:**

1. **First class protein:** Proteins of high biological value which contain all the essential amino acids.

**Sources:** Animal sources such as meat, fish, egg, milk.

2. **Second class protein:** Proteins of low biological value which are poor in essential amino acids.

**Sources:** Vegetables such as pulses, cereals, lean, nuts, oil seed etc.

(Ref: Satyanarayana-4<sup>th</sup>)

- Albumin—soluble in water & salty solutions.
- Globulin --- less soluble in water but soluble in salt.
- Protamine—insoluble in water but soluble in salt.
- Histone--- soluble in salt solutions.
- Scleroprotein—insoluble in water or salt solutions.

**Q. DNA is :** (MD/MS (DMC)-04Ja)

- |                                     |   |
|-------------------------------------|---|
| a) Component of chromosome          | T |
| b) Is found in the eukaryotic cells | T |
| c) Contains the bases uracil        | F |
| d) Contains the sugar moiety ribose | F |
| e) Is present in bacteria           | T |

**HELP LINK:**

**■ Definition:** DNA is a nucleic acid of high molecular weight consisting of deoxyribose, phosphoric acid and 4 bases (Adenine, guanine, thymine & cytosine)

**■ Site:** DNA is present mainly in the chromosomes of the nucleus.

**■ Structure:**

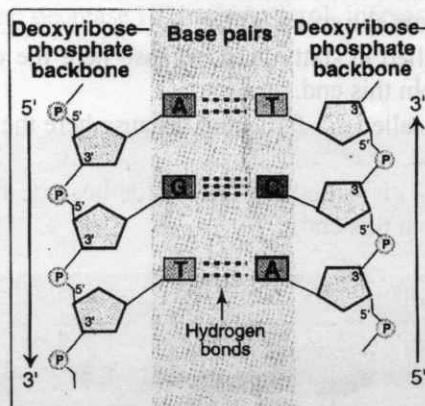
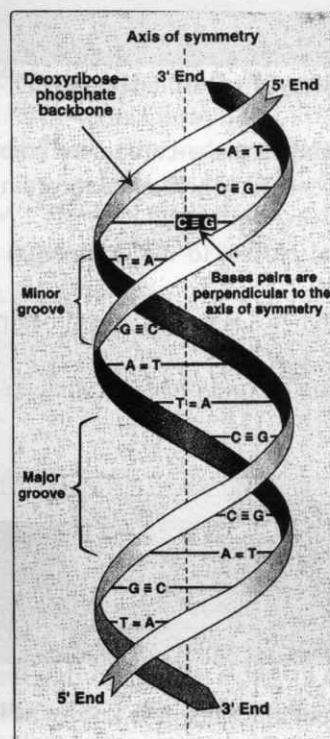
1. DNA consists of two antiparallel polynucleotide chains coiled around a common axis called **axis of symmetry**.
2. The two strands of the double-helical molecule are **antiparallel**, ie, one strand runs in the 5' to 3' direction and the other in the 3' to 5' direction.
3. In the chains, the monodeoxyribonucleotides are covalently linked by 3'-5'-phosphodiester bonds.
4. The adenine (A) of one chain is always paired with the thymine (T) of the opposite chain by two hydrogen bonds.
5. The guanine (G) of one chain is always paired with cytosine (C) of the opposite chain by three hydrogen bonds.
6. Per turn of DNA contains 10 nucleotide molecules having a length of 3.4 nm.
7. The hydrogen bonds and the hydrophobic interactions between the bases stabilize the structure of double- helix.
8. The strands are of two types:
  - **Template strand:** The genetic information resides in the sequence of nucleotides on this strand. This is the strand of DNA that is copied during nucleic acid synthesis. It is sometimes referred to as the **noncoding strand**.
  - **Coding strand:** The opposite strand is considered the coding strand because it matches the RNA transcript that encodes the protein.

9. The spatial relationship between the two strands in the helix creates a major groove and a minor groove. These grooves provide access for the binding of regulatory proteins to their specific recognition sequences along the DNA chain.

(Ref Lippincott-7<sup>th</sup>; Harper-30<sup>th</sup>)

■ **Function:**

1. They are chemical vehicle of heredity.
2. They store & express the genetic information.



**Figure 29.4**  
Two complementary DNA sequences.

**Q. Deoxyribonucleic acid (DNA)- (BIRDEM-04)**

- a) Contains genetic information in its hexose sugar moiety
- b) Controls the formation of RNA
- c) Is composed of pentose sugar and nitrogenous bases
- d) Exists in relaxed and supercoiled forms
- e) Is organized in two strands by the pairing of bases adenine to guanine only

**HELP LINK:**

■ **Location:**

1. Mitochondria
2. Chromosome

■ **Function:**

1. In purine & pyrimidine base
2. Protein synthesis
3. Cell division

**Q. The following statements regarding DNA: (MD/MS (DMC)-01Ja)**

- A. It is found mainly in chromosomes.
- B. Genetic information is stored in it.
- C. The arrangement of the bases in DNA molecule is random.
- D. It contains adenine, guanine, cytosine & thymine
- E. Genetic mutation is mostly due to DNA replication & repair rather than exposure to mutagenic agents

**Help link:** DNA is found in nucleus and mitochondria. RNA is found in nucleolus, ribosome and cytoplasm.

## LIPID

**Q. Omega 6 fatty acids are (BSMMU –Residency - MD/MS, Basic science, Paediatrics – March' 19; Residency –MD, MS, Basic science, Dentistry – March' 16; M. Phil. Diploma– 11Ju. MD/MS (Residency) – January - 11)**

- a) linoleic acid
- b) linolenic acid
- c) oleic acid
- d) arachidonic acid
- e) palmitic acid

Ans. a) T b) F c) F d) T e) F

(Ref. ABC of Biochemistry-2<sup>nd</sup>, P-61 + Harper-30<sup>th</sup>)

**HELP LINK:**

**Omega ( $\omega$ ) numbering system:** Here carbon atoms of UFA are numbered beginning at the  $\omega$ -carbon end (methyl terminal) of the chain. In this norms PUFA are often classified as  $\omega$ -3 fatty acid,  $\omega$ -6 fatty acid. etc. according to the position of first double bond from the co-carbon, e.g.

- Linoleic acid (18:2; 9,12) is called  $\omega$ -6-fatty acid because here the double bond closest to the  $\omega$  (omega) end begins at 6th carbon counted from this end.
- Linolenic acid (18:3;9,12,15) is called  $\omega$ -3-fatty acid because here the double bond closest to the  $\omega$ -end begins at 3rd carbon counted from this end.
- Arachidonic acid (20:4;5,8,11,14) is called  $\omega$ -6-fatty acid because here the double bond closest to the  $\omega$ -end begins at 6th carbon counted from this end.

**Q. Components of serum lipid profile are (BSMMU – Non-Residency – MD, MS, Basic science – July' 18)**

- a) chylomircron
- b) phospholipid
- c) serum triglyceride
- d) serum total cholesterol
- e) serum fatty acid

Ans. a) F b) F c) T d) T e) F

**Help link:**

**■ Lipid profile:** Different types of lipids are present in plasma of blood in different amounts. It is known as lipid profile.

- Plasma triglyceride: 60 - 160 mg/ dl
- Plasma total cholesterol: 150 – 220 mg/ dl
- Plasma LDL cholesterol: < 150 mg/ dl
- Plasma HDL cholesterol: 35 - 60mg/ dl

**Q. An increase in body fat content increases the (BSMMU – Residency - MD, MS, Basic Science, Dentistry - March' 17)**

- a) percentage of water in the body
- b) survival time during fasting
- c) survival time in cold water
- d) specific gravity of the body
- e) probability of mortality

**Ans.**

- A. **False** The reverse is true, since fat tissue contains little water
- B. **True** Fat is the main energy store of the body.
- C. **True** It favours survival by increasing skin insulation.
- D. **False** Fat has a lower specific gravity than the lean body mass.
- E. **True** Actuarial tables show this to be true.

(Ref: Roddy-6<sup>th</sup>)

**Q. Transfatty acids (BSMMU –Residency – MD, MS, Basic – March' 15)**

- a) are unsaturated fatty acids
- b) are found in plants
- c) increase plasma LDL-cholesterol level
- d) are formed during hydrogenation of vegetable oils.
- e) are source of arachidonic acids in the body

Ans. a) F b) F c) T d) T e) F

(Ref: DM Vasudevan-7<sup>th</sup>, P-188)

**Help Link:**

**Saturated and Trans Fatty Acids**

- ✓ Hydrogenation of vegetable oil produces saturation of the double bonds; the product is called Margarine or Vanaspathy.
- ✓ During the hydrogenation process, some cis double bonds are made into trans configuration. Fatty acids with trans double bonds (Trans fatty acids) are injurious to health.
- ✓ They decrease fluidity of membranes; decrease HDL-cholesterol, increase LDL-cholesterol and may cause atherosclerosis.

(Ref: DM Vasudevan-7<sup>th</sup>, P-188)

**Q. Polyunsaturated fatty acids are (BSMMU –Residency - MD/MS, Basic science – March' 14)**

- |                     |   |
|---------------------|---|
| a) arachidonic acid | T |
| b) butyric acid     | F |
| c) palmitic acid    | F |
| d) stearic acid     | F |
| e) linoleic acid    | T |

**Help link:**

Fatty acids are aliphatic monocarboxylic acids with the chain length of 4-24 atoms, mostly are obtained by the hydrolysis of natural fats containing an even number of C atoms.

**Classification of fatty acids on the basis of saturation:**

1. **Saturated** - Fatty acids containing no double bonds. The general formula is  $C_nH_{2n+1}COOH$ .

Examples:

- Acetic acid
- Butyric acid
- Palmitic acid
- Stearic acid etc.

2. **Unsaturated** - Fatty acids containing one or more double bonds. The general formula is  $C_nH_{2n-1}COOH$ .

These may be further subdivided according to the degree of unsaturation.

i) **Monounsaturated/ monoenoic acids** -- containing one double bond. Ex. Oleic acid.

ii) **Polyunsaturated** -- containing more than one double bonds:

- Dienoic acid (2 double bonds): Linoleic acid
- Trienoic acid (3 double bonds): Linolenic acid
- Tetraenoic acid (4 double bonds): Arachidonic acid.
- Pentaenoic acid (5 double bonds): Timnodonic acid.
- Hexaenoic acid (6 double bonds): Cervonic acid

**B. On the basis of number of C atom:**

1. **Odd chain fatty acid**: Propionic acid (3 C), Valenic (5 C)

2. **Even chain fatty acid**: Palmitic acid (16 C), Stearic acid (18 C)

**C. On the basis of carbon atom:**

1. **Long chain fatty acids** -- containing more than 10 carbon atoms.

2. **Short chain fatty acids** -- containing less than 10 carbon atoms.

**■ Differences between saturated fatty acid & unsaturated fatty acid:**

Traits	Saturated fatty acid	Unsaturated fatty acid
<b>1. Definition</b>	Fatty acids containing no double bonds.	Fatty acids containing one or more double bonds.
<b>2. General formula</b>	$C_nH_{2n+1}COOH$	$C_nH_{2n-1}COOH$
<b>3. Subdivision</b>	No	Two subdivisions- Monounsaturated & polyunsaturated fatty acid.
<b>4. Distribution</b>	Mainly in animal fat	Mainly in plant oil
<b>5. Example</b>	Palmitic acid Stearic acid	Linoleic acid Lenolenic acid

**POLYUNSATURATED FATTY ACIDS (PUFA)**

The important poly unsaturated fatty acids are:

1. Linoleic acid (18 C, 2 double bonds)
2. Linolenic acid (18 C, 3 double bonds)
3. Arachidonic acid (20 C, 4 double bonds)
- ✓ They are present in good quantities in **vegetable oils** such as sunflower oil.
- ✓ They are used to esterify cholesterol, whereby the latter can be excreted.
- ✓ So, PUFA in general are **anti-atherogenic**.
- ✓ Other PUFAs belonging to very long chain fatty acids (VLCFA) are timnodonic acid (20C, 5 double bonds); clupanodonic acid (22 C, 5 double bonds) and cervonic acid (22 C, 6 double bonds).
- ✓ They are present in **fish oils**.
- ✓ They are important for development of human brain.

**Significance of PUFA:**

- 1) PUFAs are seen in vegetable oils.
- 2) Linoleic and linolenic acids are nutritionally essential; and are called Essential Fatty Acids.
- 3) Prostaglandins, thromboxanes and leukotrienes are produced from arachidonic acid.
- 4) PUFAs form integral part of mitochondrial membranes. In deficiency of PUFA, the efficiency of biological oxidation is reduced.
- 5) They are components of membranes. Arachidonic acid is 10–15% of the fatty acids of membranes.
- 6) As double bonds are in cis configuration; the PUFA molecules cannot be closely packed. So PUFAs will increase the fluidity of the membrane.
- 7) As PUFAs are easily liable to undergo peroxidation, the membranes containing PUFAs are more prone for damage by free radicals.
- 8) The production of DHA (docosahexaenoic acid) is synthesized to a limited extent from alpha linolenic acid. DHA is present in fish oils. DHA is present in high concentrations in retina, cerebral cortex and sperms.

(Ref: DM Vasudevan-7<sup>th</sup>, P-186)

**Q. The substances derived from Poly Unsaturated Fatty Acid (PUFA) are - (DMC – MD/ MS - 10Ja)**

- a. mucopolysaccharide F
- b. prostaglandins T
- c. pyrimidine F
- d. thromboxanes T
- e. glycoprotein F

**Q. Following fatty acids always require to supply in the diet: (BSMMU – MD – January, 2010)**

- a) Linoleic acid T
- b) Phytic acid F
- c) Arachidonic acid T
- d) Linolenic acid T
- e) Palmitic acid F

**Q. Essential fatty acids are:** (BSMMU – MD - January, 2009)

- |  |   |
|--|---|
| a) precursor of prostaglandins                 | T |
| b) structural component of biological membrane | T |
| c) precursor of leukotriens                    | T |
| d) monounsaturated fatty acid                  | F |
| e) saturated fatty acid                        | F |

**HELP LINK:**

Essential fatty acids are those polyunsaturated fatty acids which are not synthesized in the body but are supplied in the diet from natural sources.

**■ Name, structure & sources:**

Name	Structure	Number of C atoms	Number & position of double bonds	Series	Sources
1. Linoleic		18	2; 9,12	ω <sup>6</sup>	Corn, peanut, cotton seed, soyabean & many plant oils.
2. Linolenic		18	3; 9,12,15	ω <sup>3</sup>	Some plants e.g. oil of evening primrose, borage oil; minor fatty acid in animals.
3. Arachidonic		20	4; 5,8,11,14	ω <sup>6</sup>	Frequently found with linoleic acid but particularly in linseed oil.

**■ Properties:**

- EFA of vegetable oils have low melting point & iodine number.
- They become saturated fatty acids on hydrogenation & the oils becomes solid fats.

**■ Importance:**

- Precursor of eicosanoids (prostaglandin, thromboxane, leukotrienes)
- Synthesis of structural lipid
- It decreases the plasma cholesterol conc. and thus it can reduce coronary artery diseases.
- Concerned with optimum gonadal activity and it is directly related to sterility.
- It causes prolongation of clotting time & ↑ the fibrinolytic activity.
- They cure skin lesions.
- The deficiency of EFA in the diet of baby cause eczema.

(Ref: Harper-30<sup>th</sup> + Lecture of SSMC)

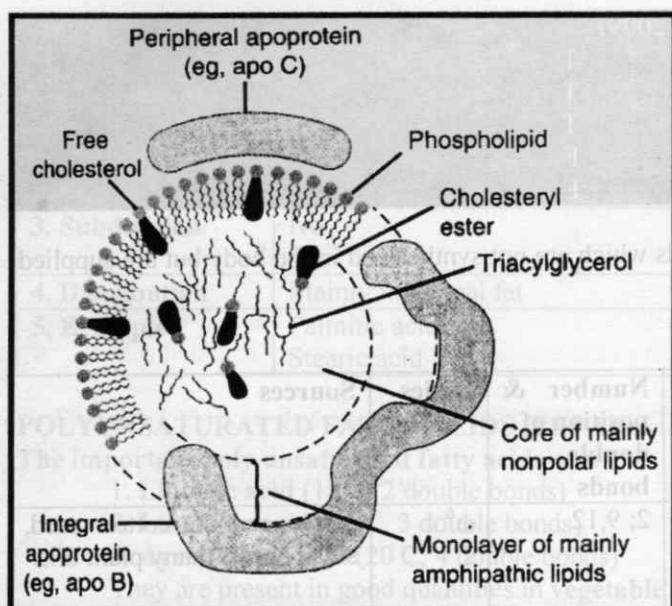
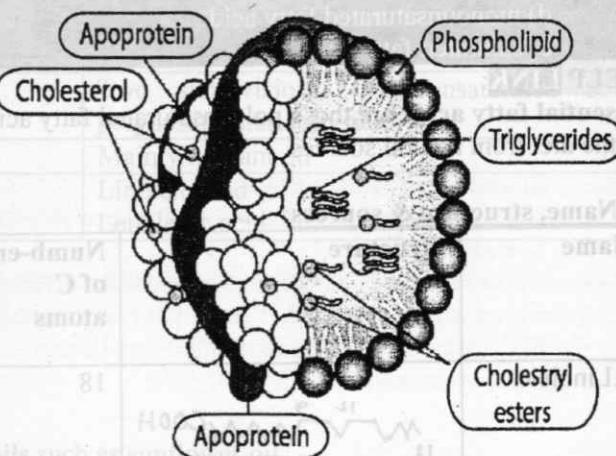
## Lipoprotein

**■ Definition:** Lipoproteins are conjugated proteins consisting of simple proteins combined with lipid components: triglyceride(TG), cholesterol and phospholipid.

**■ Structure:** A typical lipoprotein consists of two parts:

- Lipid core (TG and cholesterol ester)
- Polar part (Free cholesterol, phospholipid & apoproteins): A single surface layer of phospholipid, free cholesterol and apoproteins. Phospholipid and cholesterol are so oriented that their polar groups face outward to the aqueous medium, making the particle water soluble.

High density lipoprotein (HDL) is a major component of HDL-rich lipoproteins.

**Fig: Structure of Lipoprotein****Fig: Structure of Lipoprotein**

### ■ Methods of separation:

1. Ultracentrifugation
2. Electrophoresis

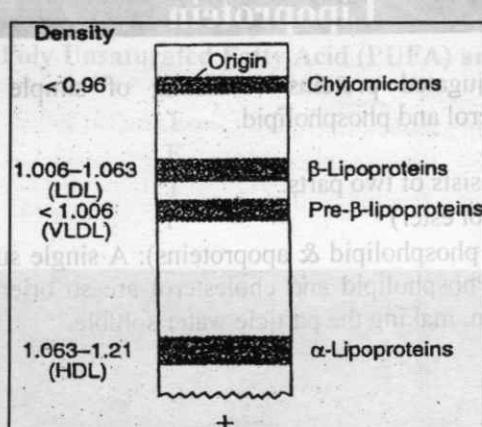
### ■ Classification:

#### A. According to ultracentrifugation:

1. **Chylomicrons** – Transport exogenous TG from intestine to blood.
2. **Very low density lipoproteins (VLDL)**- Transport exogenous TG from liver to peripheral tissue for energy.
3. **Low density lipoproteins (LDL)**- Transport cholesterol from liver to peripheral tissue. It is responsible for atherosclerosis. So LDL is dangerous.
4. **High density lipoproteins (HDL)**- Transport cholesterol from peripheral tissue to liver i.e acts as scavenger. So, it is known as the protector of coronary heart disease.

#### B. According to electrophoresis:

1. Chylomicron.
2.  $\beta$ -lipoprotein
3. Pre  $\beta$ -lipoprotein.
4.  $\alpha$ -lipoprotein.

**Figure: Separation of plasma lipoproteins by electrophoresis on agarose gel.**

**■ Blood values:**

Lipoprotein	mg/dl
VLDL	20-40
LDL	<150
HDL	35-60

**■ Clinical importance:**

1. LDL conc. is increased in diabetes mellitus, atherosclerosis etc.
2. The conc. of chylomicron & VLDL is increased in atherosclerosis and coronary thrombosis.

	Chylomicron	VLDL	LDL	HDL
<b>TG</b>	90%	60%	8%	5%
<b>Cholesterol</b>	5%	20%	50%	25%
<b>Phospholipid</b>	3%	15%	22%	30%
<b>Protein</b>	2%	5%	5%	40%

**Q. Triacylglycerol rich lipoproteins are (BSMMU – Non-Residency – **MD, MS, Basic science – July' 15;** MD/MS (Residency) - January - 11)**

- |                                 |   |
|---------------------------------|---|
| a) low density lipoprotein      | F |
| b) chylomicron                  | T |
| c) high density lipoprotein     | F |
| d) apolipoprotein               | F |
| e) very low density lipoprotein | T |

**HELP LINK:**

Lipoprotein	Size (nm)	Composition					Origin
		Protein	Free cholesterol	Cholesterol esters	Triglyceride	Phospholipid	
<b>Chylomicrons</b>	75-1000	2	2	3	90	3	Intestine
<b>Chylomicron remnants</b>	30-80						Capillaries
<b>VLDL</b>	30-80	8	4	16	55	17	Liver & intestine
<b>IDL</b>	25-40	10	5	25	40	20	VLDL
<b>LDL</b>	20	20	7	46	6	21	IDL
<b>HDL</b>	7.5-10	50	4	16	5	25	Liver & intestine

(Ref: Ganong-25<sup>th</sup>)

N.B.: VLDL = very low density lipoproteins; IDL = intermediate-density lipoproteins; LDL = low-density lipoproteins; HDL = high-density lipoproteins.

**Functions:**

1. Serves as a circulatory reservoir of apoI II, apo – E.
2. Removes free cholesterol from extrahepatic tissues and esterifying it using the plasma enzyme — lecithin-cholesterol acyl transferase (LCAT). It transports cholesterol centripetally for hepatic excretion (reverse cholesterol transport). This process is thought to be anti-atherogenic consistent with the observation that raised level of circulating HDL reduces the risk of coronary heart diseases.
3. Transfers cholesteryl esters to VLDL, and LDL in the exchange for triacylglycerol.
4. Carries cholesteryl esters to the liver.

**N.B. TAG rich lipoproteins are chylomicrons & VLDL, but highest TAG containing lipoprotein is chylomicrons.**

**Structure and functions of the four main lipoproteins**

Lipo-proteins	Main apolipoproteins	Functions
<b>Chylomicrons</b>	B <sub>48</sub> , AI, CII, E	Main transporter of dietary triglyceride, synthesized in the gut after a meal; not present in normal fasting plasma.
<b>VLDL</b>	B <sub>100</sub> , CII, E	Main carrier of endogenous triglyceride synthesized in liver, precursor of LDL
<b>LDL</b>	B <sub>100</sub>	Main cholesterol-carrier in blood, generated from VLDL in the blood stream.
<b>HDL</b>	AI, AII	Smallest but most abundant lipoprotein; transports cholesterol from peripheral tissue to liver for excretion; cardioprotective.

**Q. Atherogenic lipoprotein are:** (BSMMU – MS (Residency)-10Ja)

- a) Chylomicron T
- b) IDL T
- c) LDL T
- d) HDL F
- e) VLDL T

**HELP LINK:****Atherogenic lipoprotein are**

- Chylomicron  
LDL, IDL  
VLDL, Lipoprotein A, CMR

**Q. Antilipolytic agents are:** (BSMMU – MS (Residency)-10Ja)

- a) insulin T
- b) thyroxine F
- c) nicotinic acid F
- d) rennin F
- e) PGE1 F

**Q. Triacylglycerol (TAG) rich lipoproteins are:** (BSMMU - M. Phil, Diploma, July-08)

- a) chylomicron T
- b) VLDL T
- c) LDL F
- d) HDL F
- e) IDL F

**Q. Following lipoproteins are cholesterol rich:** (BSMMU – MD - January, 2008)

- a) LDL T
- b) HDL T
- c) IDL T
- d) LP (a) T
- e) Chylomicron F

**Q. Components of lipoproteins are:** (BSMMU - Basic Science; M. Phil, Diploma, July-07)

- a) Phospholipid T
- b) Dextrin F
- c) Apolipoprotein T
- d) Cholesterol T
- e) Cellulose F

**Q. Cholesterol rich lipoproteins are -** (BSMMU – MD - January, 2007)

- a) Chylomicron F
- b) VLDL F
- c) LDL T
- d) VLDL remnant F
- e) Chylomicron remnant F

**Q. Atherogenic lipoproteins are - (BSMMU – M. Phil, Diploma July, 2005)**

- |                        |   |
|------------------------|---|
| A. triacyl glycerol    | T |
| B. chylomicron remnant | T |
| C. HDL                 | F |
| D. VLDL remnant        | T |
| E. LDL                 | T |

**Q. The beta lipoprotein fraction increases in severe: (MD/MS (DMC)-01Ja)**

- |                        |   |
|------------------------|---|
| A. Diabetes mellitus.  | T |
| B. Uremia.             | T |
| C. Nephritis.          | F |
| D. Heart disease.      | T |
| E. Muscular dystrophy. | F |

**Q. HDL is synthesized and secreted from (BSMMU – Residency - MD/MS, Basic science, Paediatrics – March' 19)**

- a) endothelium of blood vessel
- b) adipose tissue
- c) liver
- d) intestine
- e) kidney

Ans. a) F b) F c) T d) T e) F

(Ref. ABC of Biochemistry-5<sup>th</sup>, P-207 + Lippincott-7<sup>th</sup>)

**Q. Followings are true for HDL: (BSMMU – Residency – MD/MS – March'13)**

- a) synthesized only in liver.
- b) A reservoir of apolipoproteins.
- c) Is a bad lipoprotein.
- d) plays important role in reverse cholesterol transport.
- e) Uptake free cholesterol

Ans. a) F b) T c) F d) T e) T

#### HELP LINK:

**HDL:** It is the smallest & most abundant lipoprotein which transports cholesterol from peripheral tissues to the liver for excretion. It is cardioprotective.

**Site of synthesis: Liver**

**Q. HDL is synthesized and secreted from (BSMMU - MD/MS (Residency) - January - 11)**

- |                                |   |
|--------------------------------|---|
| a) endothelium of blood vessel | F |
| b) adipose tissue              | F |
| c) liver                       | T |
| d) intestine                   | T |
| e) kidney                      | F |

#### HELP LINK:

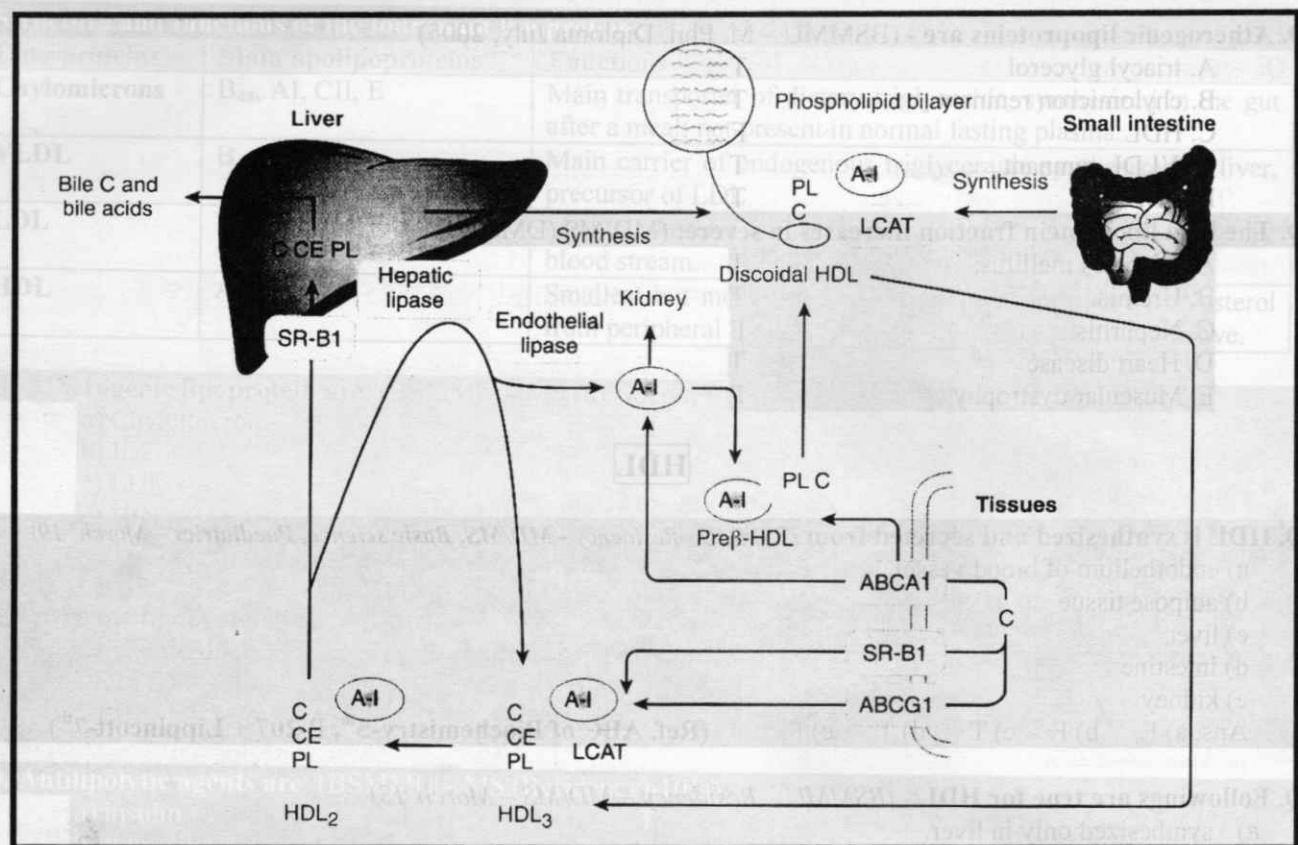
#### METABOLISM OF HDL

■ HDLs are synthesized in the liver and intestine as nascent HDL. They contain free cholesterol and phospholipids and apoproteins (A, C, E).

■ A plasma enzyme LCAT catalyses the esterification of free cholesterol (by transferring a fatty acid from lecithin to cholesterol) to form cholesterol esters & lysolecithin.

■ HDL cholesterol esters enter the liver, the final site of their degradation.

The cholesterol esters are degraded to cholesterol, which is utilized for synthesis of bile acids and lipoproteins or excreted into bile (as cholesterol).



**FIGURE: Metabolism of high-density lipoprotein (HDL) in reverse cholesterol transport. (LCAT, lecithin:cholesterol acyltransferase; C, cholesterol; CE, cholesteryl ester; PL, phospholipid; A-I, apolipoprotein A-I; SR-B1, scavenger receptor B1; ABCA 1, ATP-binding cassette transporter A1; ABCG1, ATP-binding cassette transporter G 1.) Preβ-HDL, HDL<sub>2</sub>, HDL<sub>3</sub>. Surplus surface constituents from the action of lipoprotein lipase on chylomicrons and VLDL are another source of preβ-HDL. Hepatic lipase activity is increased by androgens and decreased by estrogens, which may account for higher concentrations of plasma HDL<sub>2</sub> in women.**

(Ref: Harper-30<sup>th</sup>, P-217)

**Q. HDL is synthesized and secreted from:** (BSMMU - M. Phil, Diploma – July '10)

- |                                |   |
|--------------------------------|---|
| a) endothelium of blood vessel | F |
| b) adipose tissue              | F |
| c) Liver                       | T |
| d) Intestine                   | T |
| e) Kidney                      | F |

### VLDL

**Q. Apoprotein associated with VLDL are:** (BSMMU – MS (Residency)-10Ja)

- |              |   |
|--------------|---|
| a) apo B-100 | T |
| b) apo A-I   | F |
| c) apo C-II  | T |
| d) apo B-48  | F |
| e) apo E     | T |

## Apolipoprotein

**Q. Apolipoprotein (BSMMU –Residency - MD/MS, Basic science – March '14)**

- a) A-I activates LCAT
- b) C-II activates hormone-sensitive lipase
- c) B-100 binds LDL receptor
- d) E mediates remnant up take
- e) B-48 mediates VLDL secretion

**Ans.** a) T b) F c) T d) T e) F

**Help link:**

**Functions of apolipoproteins in lipoprotein:**

1. Provide hydrophilic character to the lipoprotein particles to facilitate their transport in aqueous plasma.

2. Act as a structural component of lipoprotein to maintain their structural stability.

3. Determine the metabolic fate of lipoprotein and facilitate the exchange of lipids between lipoproteins.

- Apo C-II is a cofactor for lipoprotein lipase (LPL)
- Apo A-I is a cofactor for LCAT (lecithin cholesterol acyl transferase.)
- Apo A-II is a cofactor for hepatic lipase (HL), and LCAT.
- 5. Act as inhibitor of enzymes of lipoprotein metabolism. e.g. Apo C-III and Apo A-II inhibit LPL.
- 6. Act as ligand to recognize lipoprotein receptors on cell surface. e.g.

  - Apo B-100 and Apo E together act as ligand for LDL receptor.
  - Apo A is a ligand for HDL receptor.
  - Apo E mediates remnant uptake.

## Phospholipid

**■ Definition:** Phospholipids are composed of fatty acids, glycerol, phosphoric acid and in most cases a nitrogenous base.

**■ Types:**

1. **Glycerophospholipid:** Alcohol is glycerol. e.g. myelin sheath of nerve fibres, major phospholipid in biological membrane.
2. **Sphingo phospholipid:** Alcohol is sphingosine. e.g. brain myelin sheath of nerve fibres.

The glycerophospholipids include the following:

1. Phosphatidic acid (*glycerol + F.A + phosphate*)
2. Phosphatidyl ethanolamine (cephalin)
3. Phosphatidyl choline (lecithine)
4. Phosphatidyl serine.
5. Phosphatidyl inositol.
6. Plasmalogens
7. Cardiolipin

**■ Distribution:** They are widely present in the nervous tissue, brain, liver, kidney, pancreas & heart.

**■ Biomedical importance:**

1. Synthesis of membrane i.e. biological membrane.
2. In bile, it keeps the cholesterol in solution.
3. In the form of surfactant, it can help in expansion of lung.
4. Helps in blood coagulation.
5. Can act as a second messenger of different hormones.
6. Phospholipid of myelin sheath provides insulation.

**■ Definition:** Phospholipids are complex or compound lipids containing phosphoric acid, in addition to fatty acids, nitrogenous base and alcohol.

### ■ Types:

There are two classes of phospholipids.

1. Glycerophospholipids (or phosphoglycerides): contain glycerol as the alcohol.
2. Sphingophospholipids (or sphingomyelins): contain sphingosine as the alcohol.

### Glycerophospholipids:

Glycerophospholipids are the major lipids that occur in biological membranes. They consist of glycerol 3-phosphate esterified at its C1 and C2 with fatty acids. Usually, C1 contains a saturated fatty acid while C2 contains an unsaturated fatty acid.

1. **Phosphatidic acid:** This is the simplest phospholipid. It does not occur in good concentration in the tissues. Basically, phosphatidic acid is an intermediate in the synthesis of triacylglycerols and phospholipids. The other glycerophospholipids containing different nitrogenous bases or other groups may be regarded as the derivatives of phosphatidic acid.

2. **Lecithin (phosphatidylcholine):** These are the most abundant group of phospholipids in the cell membranes. Chemically, lecithin (Greek: lecithos - egg yolk) is a phosphatidic acid with choline as the base. Phosphatidylcholines represent the **storage form of body's choline**. Choline, containing labile methyl groups involved in methylation reactions, besides nerve transmission.

a) **Dipalmitoyl lecithin** is an important phosphatidylcholine found in lungs. It is a surface active agent and prevents the adherence of inner surface of the lungs due to surface tension. Respiratory distress syndrome in infants is a disorder characterized by the absence of dipalmitoyl lecithin.

b) **Lyssolecithin** is formed by removal of the fatty acid either at C1 or C2 of lecithin.

3. **Cephalins (phosphatidylethanolamine):** Ethanolamine is the nitrogenous base present in cephalins. Thus, lecithin and cephalin differ with regard to the base.

4. **Phosphatidylinositol:** The stereoisomer myo-inositol is attached to phosphatidic acid to give phosphatidylinositol (PI). This is an important component of cell membranes. The action of certain hormones (e.g. oxytocin, vasopressin) is mediated through PI. In response to hormonal action, PI is cleaved to diacylglycerol and inositol triphosphate. Both these compounds act as second messengers for hormonal action.

5. **Phosphatidylserine:** The amino acid serine is present in this group of glycerophospholipids. Phosphatidylthreonine is also found in certain tissues.

6. **Plasmalogens:** When a fatty acid is attached by an ether linkage at C1 of glycerol in the glycerophospholipids, the resultant compound is plasmalogen. Phosphatidylethanolamine is the most important which is similar in structure to phosphatidylethanolamine but for the ether linkage (in place of ester). An unsaturated fatty acid occurs at C1. Choline, inositol and serine may substitute ethanolamine to give other plasmalogens. Brain and muscle contain a good concentration (about 10% of phospholipids) of plasmalogens.

7. **Cardiolipin:** It is so named as it was first isolated from heart muscle. Structurally, a cardiolipin consists of two molecules of phosphatidic acid held by an additional glycerol through phosphate groups. It is an important component of inner mitochondrial membrane. Cardiolipin is the only phosphoglyceride that possesses antigenic properties.

### **Sphingomyelins:**

Sphingosine is an amino alcohol present in sphingomyelins (sphingo-phospholipids). They do not contain glycerol at all. Sphingosine is attached by an amide linkage to a fatty acid to produce **ceramide**. Sphingomyelins are important constituents of myelin and are found in good quantity in brain and nervous tissue.

**■ Action of phospholipases:**

Phospholipases are a group of enzymes that hydrolyse phospholipids. There are four distinct phospholipases (A1, A2, C and D), each one of them specifically acts on a particular bond.

**■ Functions of phospholipids:**

Phospholipids constitute an important group of compound lipids that perform a wide variety of functions.

1. In association with proteins, phospholipids form the structural **components of membranes** and regulate membrane permeability.
2. Phospholipids (lecithin, cephalin and cardiolipin) in the mitochondria are responsible for maintaining the conformation of electron transport chain components and thus cellular respiration.
3. Due to their amphipathic nature, phospholipids can combine with polar and non-polar compounds in the cell.
4. Phospholipids participate in the absorption of fat from the intestine.
5. Phospholipids are essential for the synthesis of different lipoproteins and thus participate in the transport of lipids.
6. Accumulation of fat in liver (fatty liver) can be prevented by phospholipids, hence they are regarded as lipotropic factors.
7. Arachidonic acid, an unsaturated fatty acid liberated from phospholipids serves as a precursor for the synthesis of eicosanoids (prostaglandins, prostacyclins, thromboxanes etc.).
8. Phospholipids participate in the reverse cholesterol transport and thus help in the removal of cholesterol from the body.
9. Phospholipids act as surfactants (agents lowering surface tension). For instance, dipalmitoyl phosphatidylcholine is an important lung surfactant. Respiratory distress syndrome in infants is associated with insufficient production of this surfactant.
10. Cephalins, an, important phospholipids participate in blood clotting.
11. Phospholipids (phosphatidylinositol) are involved in signal transmission across membranes.
12. Phospholipids are essential components of bile where they act as detergents and help in the solubilization of cholesterol.

(Ref: Satyanarayana's Biochemistry)

**Q. Substances that are phospholipid in nature include (BSMMU – Residency – MD, MS, Basic Science – March '18)**

- a) sphingomyelin
- b) cerebroside
- c) ganglioside
- d) lecithin
- e) cephalin

Ans. a) T b) F c) F d) T e) T

(Ref: ABC Biochemistry-6<sup>th</sup>, P-68)

**Q. Following substances are phospholipids in nature: (BSMMU – MD - January, 2008)**

- a) lecithin
- b) cardiolipin
- c) sphingomyelin
- d) cerebrosides
- e) lipoproteins

Ans.

a) T (*It is a phosphatidic acid with choline as the base*)

b) T (*It is an important component of inner mitochondrial membrane*)

c) T

d) F (*lipids present in nervous system*)

e) F (*these are compound lipids*)

**Help Link:**

**Phospholipids:**

- Composed of fatty acid+alcohol+phosphoric acid with or without nitrogen bases.

- Glycerophospholipids:**

- Essential fatty acids
- Monounsaturated fatty acids: oleic acid, palmitoleic acid
- Saturated fatty acid: palmitic acid, stearic acid.
- Common glycerophospholipid:
  - Phosphatidic acid, Lecithin, cephalin, Cardiolipin
  - Phosphatidylserine, Phosphatidylinositol, Phosphatidylglycerol,

- Sphingophospholipids(sphingomyelin):** Ceramide,

**Glycolipid/Glycophospholipid:**

- Lipid containing CHO
- Types:
  - Cerebrosides:
    - Glucocerebrosides, Galactocerebrosides
  - Gangliosides:

(Ref: ABC Biochemistry-6<sup>th</sup>, P-68)**Q. Following substances are phospholipid in nature:** (BSMMU - M. Phil, Diploma, July-08)

- |                  |   |
|------------------|---|
| a) sphingomyelin | T |
| b) lecithins     | T |
| c) cephaline     | T |
| d) cerebrosides  | F |
| e) gangliosides  | F |

**Q. The following are anti-lipolytic:** (BSMMU - M. Phil, Diploma, July-08)

- |                    |   |
|--------------------|---|
| a) insulin         | T |
| b) thyroxine       | F |
| c) nicotinic acid  | F |
| d) renin           | F |
| e) prostaglandin-E | F |

**Q. Prostaglandins are synthesized from:** (MD/MS (DMC)-04Ja)

- |                     |   |
|---------------------|---|
| a) Oleic acid       | F |
| b) Linoleic acid    | F |
| c) Arachidonic acid | T |
| d) Acetic acid      | F |
| e) Palmitic acid    | F |

**Q. Prostaglandins-** (MD/MS (DMC)-03Ja)

- |   |   |
|---|---|
| a) are derived from essential fatty acids | T |
| b) are derived from steroid hormones      | F |
| c) exhibits hormones like activity        | T |
| d) Increase HCl secretion in the stomach  | F |
| e) Lower cAMP in adipose tissues          | F |

**ENZYMES**

**■ Definition:** Enzyme may be defined as a soluble colloidal organic catalyst which is produced by living cells, protein in nature, specific in action, capable of catalyzing a chemical reaction without being altered or destroyed at the end of the process. or,

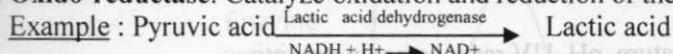
Enzyme may be defined as a reaction specific, thermo-labile, non-dialyzable protein catalyst, produced by the living cells, capable of catalyzing a bio-chemical reaction and reverts to its original state when the reaction is over. (Ref: Lecture of DMC, West & Todd-4<sup>th</sup>, P-419, Satyanarayana-4<sup>th</sup>, P-85)

**Example:** Choline Acetyltransferase

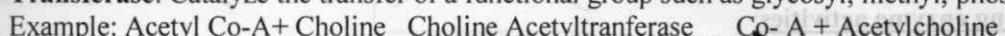
**■ I.U.B.M.B. Classification:**

Enzymes are classified into six major classes. These are-

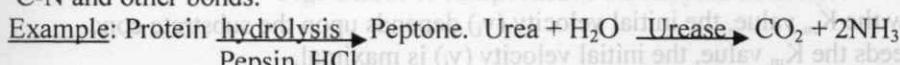
- Oxido-reductase:** Catalyze oxidation and reduction of their substrates.



- Transferase:** Catalyze the transfer of a functional group such as glycosyl, methyl, phosphoryl groups.

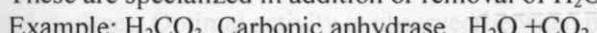


- Hydrolase:** Catalyze the breakdown of their substrates by hydrolysis. i.e. hydrolytic cleavage of C-C, C-O, C-N and other bonds.

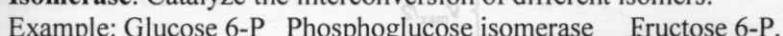


- Lyases:** They catalyze cleavage of C-C, C-O, C-N and other bonds by *atom elimination*, leaving double bonds.

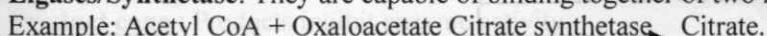
These are specialized in addition or removal of H<sub>2</sub>O, CO<sub>2</sub>, NH<sub>3</sub> sometimes leaving a double bond.



- Isomerase:** Catalyze the interconversion of different isomers.



- Ligases/Synthetase:** They are capable of binding together of two molecules.



(Ref: Harper-30<sup>th</sup>, P-61, Lippincott-7<sup>th</sup>, P-53, Satyanarayana-4<sup>th</sup>, P-86)

**Nice to know:**

I.U.B. = International Union of Biochemists

I.U.B.M.B. = International Union of Biochemistry and Molecular Biology

**Classification of enzymes at a glance:**

Class	Reaction	Enzymes
1) Oxidoreductases	A <sub>red</sub> + B <sub>ox</sub> $\rightarrow$ A <sub>ox</sub> + B <sub>red</sub>	Dehydrogenase, peroxidase
2) Transferases	A-B + C $\rightarrow$ A + B-C	Hexokinase, transminase
3) Hydrolases	A - B + H <sub>2</sub> O $\rightarrow$ A - H + B-OH	Alkaline phosphatase, trypsin
4) Lyases (synthases)	A(XH)-B $\rightarrow$ A-X + B-H	Carbonic anhydrase, dehydratases
5) Isomerases	A Iso-A	Triose phosphate isomerase, phosphoglucomutase
6) Ligases (synthetases)	A + B + ATP $\rightarrow$ A-B + ADP + Pi	Pyruvate carboxylase, DNA ligase

**■ Properties of enzyme:**

- Active site:** Enzyme possesses an active site containing amino acid side chains- interaction with substrate.

- Catalytic efficiency:** Highly efficient, can increase the rate of reaction upto 10<sup>3</sup> - 10<sup>8</sup> times. One enzyme molecule can react with 100 to 1000 molecules of substrate. The number of substrate molecules converted to product per enzyme per second is called turnover number.

- Specificity:** Highly reaction specific.

- Cofactors:** Some enzymes associate with a non-protein cofactor (known as coenzyme) that is needed for enzyme activity.

- Regulation:** Enzymes can be inhibited or activated in their function.

- When the product amount is low  $\rightarrow$  enzymes work more
- When the product amount is high  $\rightarrow$  enzymes work less

- Location within the cell:** Some are in the cytosol so they can only perform reaction in cytosol not in mitochondria or anywhere else.

(Ref: Lippincott-7<sup>th</sup>, P-54)

**Other properties:**

- Protein in nature.

- Heat labile.

- Non-dialyzable.

- Water soluble

5. Lowers the activation energy.
6. Don't initiate the reaction.
7. Effective in very small amount.
8. Neither altered / destroyed in the reaction.
9. Can be activated or inhibited by high temperature, pH, UV rays, heavy metals etc.

(Ref: Lecture of DMC)

### Important factors affecting enzyme activities:

1. **Substrate concentration:** The substrate conc. that produces half-maximal velocity, is termed as  $K_m$  value or Michaelis constant.

- When the substrate conc. is below the  $K_m$  value, the initial velocity ( $v_i$ ) depends upon the substrate conc.
- When the substrate conc. far exceeds the  $K_m$  value, the initial velocity ( $v_i$ ) is maximal.
- When the substrate conc. is equal to  $K_m$  value, the initial velocity ( $v_i$ ) is half-maximal.

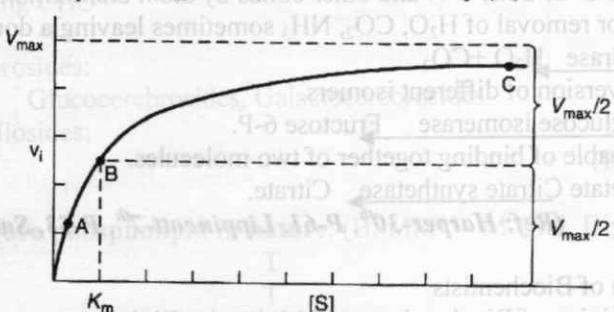


Fig: Effect of substrate conc. on enzyme activity

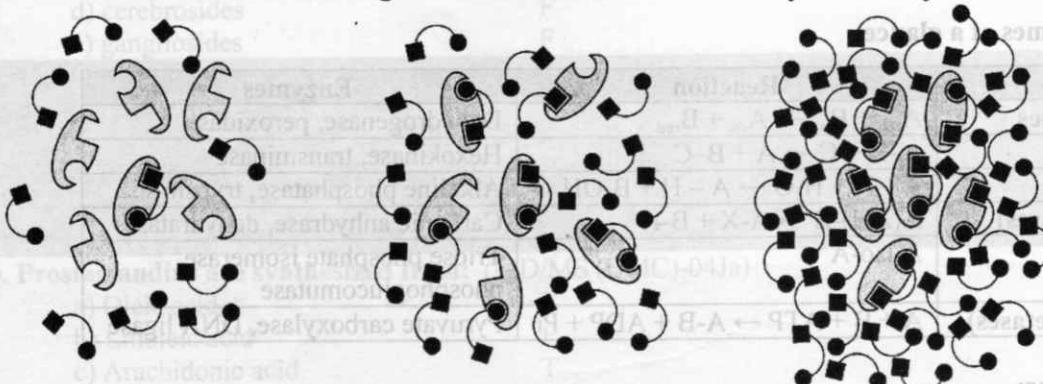


Fig: Representation of an enzyme in the presence of a concentration of substrate that is below  $K_m$  (A), at a concentration equal to  $K_m$  (B), and at a concentration well above  $K_m$  (C).

2. **Enzyme concentration:** The rate of reaction is directly proportional to enzyme concentration at all substrate conc.

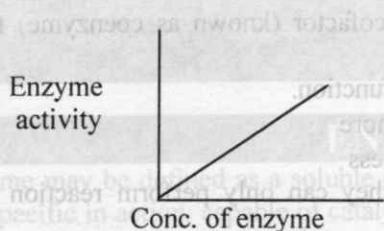
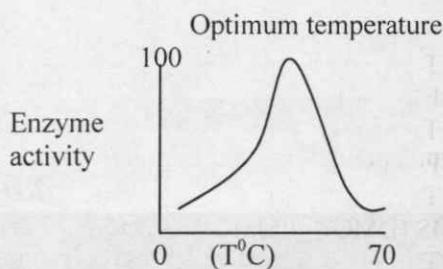


Fig: Effect of enzyme conc. on enzyme activity.

3. **Temperature effect:** The velocity of reaction increases with a rise of temperature upto a maximum level. Then it declines due to denaturation of protein. Each enzyme has an optimum temperature. **Temperature co-efficient,  $Q_{10}$**  - the increase in enzyme activity when the temp. is raised by  $10^\circ\text{C}$ . For majority of enzymes,  $Q_{10} = 2$  between  $0^\circ\text{C}$  -  $40^\circ\text{C}$ . The optimum temp. is  $40^\circ\text{C}$ - $50^\circ\text{C}$  for animal enzymes and  $50$ - $60^\circ\text{C}$  for plant enzymes. Optimum temperature means the level at which enzymes have maximum activity.



**Fig: Effect of temperature on enzyme activity.**

4. **Effect of pH:** Increase in pH increases enzyme activity upto maximum level. Extremes of pH can also denatures protein, so after a certain time, level declines. Optimal activity is observed between pH values of 5 and 9. A few enzymes (eg, pepsin) are active at pH value 2.

**Fig: Effect of pH on enzyme activity.**

5. **Product conc.:** Products inhibit enzyme activity.

Product + active sites of enzymes → product-enzyme complex → this inhibits enzymes.

6. **Activators:** Non-protein substances, known as cofactors :

- Metallic ions (cations, anions)
- Coenzymes (water soluble vitamin B derivatives)

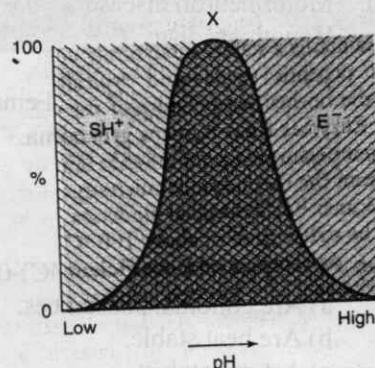
Usually cations act as activators. e.g.  $\text{Ca}^{++}$ ,  $\text{Mg}^{++}$ ,  $\text{Zn}^{++}$  etc. But anion  $\text{Cl}^-$  is needed for amylase.

7. **Effect of time:** Under ideal conditions, enzymes require less time but under non-optimal conditions, enzymes will need more time.

8. **Light & radiation :** Exposure to UV ray,  $\gamma$ -ray → activity is lost.

9. **Anti-enzymes:** Repeated injection of certain enzymes due to enzyme deficiency may produce anti-enzymes in the body which can prevent the normal action of enzymes injected. e.g. anti-pepsin, anti-trypsin, anti-renin etc.

10. **Hormones:** Many hormones can influence the enzyme activity. e.g. Epinephrine and glucagon.



(Ref: Harper-30<sup>th</sup>, P-78-79 + Lippincott + Lecture of DMC)

### Question Bank

**Q. Disorders associated with enzyme defects are (BSMMU –Residency - MD/MS, Basic science, Paediatrics – March '19)**

- a) phenylketonuria
- b) familial hypercholesterolemia
- c) Tay-Sachs disease
- d) vitamin D-resistant rickets
- e) albinism

'Ans. a) T b) F c) T d) F e) T

(Ref. Lippincott-7<sup>th</sup>, P-269 + ABC of Biochemistry + Davidson-23<sup>th</sup>)

**Q. Enzymes are - (BSMMU – M. Phil, Diploma July, 2006)**

- |  |   |
|--|---|
| a) Organic catalysts                     | T |
| b) Protein in nature                     | T |
| c) Not affected by the change in pH      | F |
| d) Not affected by change in temperature | F |
| e) Usually co-factor dependent           | T |

**Q. Enzymes are: (MD/MS (DMC)-05Ja)**

- a) Are colloidal substances.
- b) Are heat stable.
- c) Act as catalyst.
- d) Always require co-factor for action.
- e) Act as 1<sup>st</sup> messenger.

Optimum temperature



(Ref. Lecture of DMC)

T	100
F	0
T	100
F	0
T	100

**Q. Causes of elevated serum creatinine kinase: (MD/MS (DMC) – 05Ja)**

- a. Muscular dystrophy
- b. Acute pancreatitis
- c. MI
- d. Motor neuron disease
- e. Hypothyroidism

T	100
F	0
T	100
F	0
T	100

**HELP LINK:**

Normal: Male: 30 – 200 U/ L.; Female : 30 – 150 U/ L

CK1 ↑ → severe shock, carcinoma

CK2 ↑ → MI

CK3 ↑ → Muscle dystrophy

**Q. Enzymes are: (MD/MS (DMC)-04Ja)**

- a) Are colloidal substances.
- b) Are heat stable.
- c) Act as catalyst.
- d) Always require co-factor for action.
- e) Act as 1<sup>st</sup> messenger.

T	100
F	0
T	100
F	0
T	100

**Q. Non-functional plasma enzymes are (BSMMU – Residency – MD, MS, Basic Science, Dentistry – March' 18)**

- a) lactate dehydrogenase
- b) alkaline phosphatase
- c) prostate specific antigen
- d) creatine kinase
- e) troponin

Ans. a) T b) T c) F d) T e) F

**Help link:**

	Functional plasma enzymes	Non-functional plasma enzymes
<b>Concentration in plasma</b>	Present in plasma in higher concentrations in comparison to tissues	Normally, present in plasma in very low concentrations in comparison to tissues
<b>Function</b>	Have known functions	No known functions
<b>The substrates</b>	Their substrates are always present in the blood	Their substrates are absent from the blood
<b>Site of synthesis</b>	Liver	Different organs e.g. liver, heart, brain and skeletal muscles
<b>Effect of diseases</b>	Decrease in liver diseases	Different enzymes increase in different organ diseases
<b>Examples</b>	Clotting factors e.g. prothrombin, Lipoprotein lipase and pseudo-choline esterase	ALT, AST, CK, LDH, alkaline phosphatase, acid phosphatase and amylase,

temperature means the level at which enzymes have maximum activity.

## Clinically important enzymes

Enzymes	Normal value (IU/L)	Increased in
i. Alanine transaminase (ALT)/SGPT	10-40	1. Liver damage (markedly ↑) 2. MI (slightly ↑) 3. Muscular dystrophy 4. Severe muscle injury 5. Dermatomyositis
ii. Aspartate transaminase (AST)/SGOT	10-35	1. MI (markedly↑) 2. Non-viral hepatitis 3. Cirrhosis 4. Neoplastic disease of liver
iii. Lactate dehydrogenase (LDH)	230-460	1. MI 2. Viral hepatitis 3. Megaloblastic anaemia 4. Pernicious anaemia 5. Haemolytic anaemia 6. Leukaemia 7. Malignancy 8. Muscular dystrophy 9. Hodgkin's disease 10. Renal disease 11. Infectious mononucleosis.
iv. Acid phosphatase	0.5-4	1. CA of prostate 2. Paget's disease 3. Hyperparathyroidism 4. Metastatic CA of bone
v. Alkaline phosphatase	40-125	1. Physiological: Children, Late pregnancy 2. Obstructive jaundice 3. Hepatocellular jaundice 4. Cirrhosis of liver.  <b>Also ↑ in:</b> 1. Osteomalacia & rickets 2. Paget's disease 3. Hyperparathyroidism 4. Metastatic CA of bone
vi. Creatinine phosphokinase	Male: 30-200 Female: 30-150	1. MI (markedly ↑) 2. After exercise 3. Muscle injury 4. Muscular atrophy
vii. $\gamma$ - glutamyl transferase	Male: 10-55 Female: 5-35	Diseases of hepatobilary system.
viii. $\alpha$ -amylase	50-300	1. Acute pancreatitis 2. Salivary gland inflammation  <b>Decreased in:</b> 1. Pancreaticinsufficiency. 2. Liver disease

**Q. Serum creatine phosphokinase is increased in (BSMMU-Residency - MD - March' 19)**

- a) muscular dystrophy
- b) Paget's disease
- c) myositis
- d) trauma
- e) spinal muscular atrophy

Ans. a) T   b) F   c) T   d) T   e) F

(Ref. Davidson-23<sup>th</sup>, P-991)

## Isoenzyme

■ **Definition:** Isoenzymes are enzyme variants i.e. they are the enzymes which perform the same catalytic action but are present in multiple molecular forms within the same animal species.

**Properties:** Isoenzymes differ from each other with respect to-

1. Structure and electrophoretic property
2. Immunological property
3. Optimum pH and Km value
4. Relative susceptibility to inhibitors
5. Degree of denaturation
6. Rate of reaction catalyzed.

■ **Examples:**

a) **Creatine kinase:** (formerly called creatine phosphokinase)

Type	Composition	Location
CK <sub>1</sub>	BB	Brain
CK <sub>2</sub>	MB	Myocardium
CK <sub>3</sub>	MM	Skeletal muscle

b) **Lactate dehydrogenase (LDH):**

Lactate dehydrogenase isozymes	Composition	Location
I <sub>1</sub>	HHHH	Myocardium & RBC
I <sub>2</sub>	HHHM	Myocardium & RBC
I <sub>3</sub>	HHMM	Brain & kidney
I <sub>4</sub>	HMMM	Liver & skeletal muscle
I <sub>5</sub>	MMMM	Liver & skeletal muscle

c) **Alkaline phosphatase**

- α<sub>1</sub>-ALP
- α<sub>2</sub>-heat labile ALP
- α<sub>2</sub>-heat stable ALP
- Pre-β-ALP
- β-ALP

■ **Sources:** Isozymes are present in the serum and tissues of mammals, amphibians, birds, plants and unicellular organisms.

■ **Clinical importance:**

1. CK<sub>1</sub> is increased in severe shock, carcinoma.
2. CK<sub>2</sub> is specific for the diagnosis of myocardial infarction (MI). It rises in 4 to 8 hours following onset of chest pain & reaches a peak in activity at about 24 hours.

3. CK<sub>3</sub> is increased in muscle dystrophies.
4. LDH is also increased in plasma in 12 hours following a MI & reaches a peak in activity 3 to 6 days after onset of symptoms.
5. LDH may be high in leukaemias, haemolytic & megaloblastic anaemias, malignancy & renal diseases.
6. LDH<sub>4</sub> & LDH<sub>5</sub> is increased in:
  - Acute hepatitis
  - Acute muscle injury
  - Muscular dystrophies.

(Ref: Lippincott-7<sup>th</sup>, P-65 + Khaleq's pathology + Satyanarayana-4<sup>th</sup>, P-108-111)  
**Question Bank**

**Q. Enzymes indicating necrosis in muscle tissues include (BSMMU – Non-Residency – MD, MS, Basic Science & Dentistry – July '17)**

- a) lactate dehydrogenase
- b) alanine aminotransferase
- c) creatinine phosphokinase
- d) alkaline phosphatase
- e) acid phosphatase

Ans. a) T b) F c)T d) F e) F

(Ref: Sattanarayon biochemistry 4<sup>th</sup> edition page 113)

**Q. Followings are cardiospecific isoenzymes (BSMMU – Non-Residency - MD/MS, Basic science – 13Ju)**

- |                               |                      |
|-------------------------------|----------------------|
| a) c- reactive protein        | F                    |
| b) aspartate aminotransferase | T                    |
| c) creatine kinase MB         | T                    |
| d) lactate dehydrogenase      | T                    |
| e) cardiac troponin-I         | F (it is not enzyme) |

Note: cardiac troponin-I is not enzyme.

Diagnostic marker used for the evaluation of acute MI:

- Myoglobin: not specific to cardiac disease but early marker for MI
- Brain natriuretic peptide: is a marker of CCF
- Troponin I: peak 12-24 hours and return to normal 5-9 days.
- Troponin T
- CPK(MB)
- LDH
- AST/SGOT

(Ref: Sattanarayon-4<sup>th</sup>, P-112)

### CREATINE KINASE (CK)

**Q. Causes of an elevated serum creatinine kinase includes (BSMMU – Non-Residency – MD – July '18)**

- a) inflammatory myositis
- b) strenuous exercise
- c) motor neuron disease
- d) hyperthyroidism
- e) hypertrophic cardiomyopathy

Ans. a) T b) T c) T d) F e) F

Help link:

**25.8 Causes of an elevated serum creatine kinase**

- Inflammatory myositis ± vasculitis
- Muscular dystrophy
- Motor neuron disease
- Alcohol, drugs (N.B. statins)
- Trauma, strenuous exercise, long lie after a fall
- Myocardial infarction\*
- Hypothyroidism, metabolic myopathy
- Viral myositis

\*The CK-MB cardiac-specific isoform is disproportionately elevated compared with total CK.

(Ref: Davidson-23<sup>rd</sup>, P-991)

**Q. Increased CK-MB relative to total creatine kinase is seen in (BSMMU – Non-Residency – MD – July' 17)**

- a) rhabdomyolysis
- b) muscle necrosis
- c) polymyositis
- d) acute myocardial infarction
- e) statin therapy

Ans. a) T b) F c) T d) T e) F

**Q. Creatinine phosphokinase is high in: (BSMMU – M. Phil, Diploma – IJu, DMC & others – MD – IJu)**

- |                              |   |
|------------------------------|---|
| a) chronic alcoholism.       | T |
| b) rhabdomyolysis.           | T |
| c) polymyositis              | T |
| d) tabes dorsalis            | F |
| e) chronic myeloid leukemia. | F |

**HELP LINK:**

**CREATINE KINASE (CK)**

CK is most abundant in cells of cardiac and skeletal muscle and in brain, but also occurs in other tissues such as smooth muscle.

**Causes of raised plasma CK activities:**

**Artefactual:** Due to in vitro haemolysis, Using most methods.

**Physiological:** neonatal period (slightly raised above the adult reference range); during and for a few days parturition!

**Marked increase:**

- ‘Shock’ and circulatory failure; myocardial infarction
- Muscular dystrophies
- Rhabdomyolysis (breakdown of skeletal muscle).

**Moderate increase:**

- Muscle injury
- After surgery (for about a week)
- Physical exertion There may be a significant rise in plasma activity after only moderate exercise, muscle cramp or following an epileptic fit.
- After an intramuscular injection; hypothyroidism (thyroxin may influence the catabolism of the enzyme)
- Alcoholism (possibly partly due to alcoholic myositis)
- Some cases of cerebrovascular accident and head injury
- Some patients predispose to malignant hyperprexia.

Plasma CK activity is raised in all types of muscular dystrophy, but not usually in neurogenic muscle diseases such as poliomyelitis, myasthenia gravis, multiple sclerosis or Parkinson’s disease.

**Isoenzymes of CK:** CK consists of two protein subunits, M and B, which combine to form three isoenzymes, BB (CK-1), MB (CK-2) and MM (CK-3). CK-MM is the predominant isoenzyme in skeletal and cardiac muscle and is detectable in the plasma of normal subjects.

CK-MB accounts for about 35 percent of the total CK activity in cardiac muscle and less than five percent in skeletal muscle; its plasma activity is always high after myocardial infarction. It may be detectable in the plasma of patients with a variety of other disorders in whom the total CK activity is raised, but this accounts for less than six percent of the total.

CK-BB is present in high concentrations in the brain and in the muscle of the gastrointestinal and genital tracts. Raised plasma activities may occur during parturition. Although they have also been reported after brain damage and in association with malignant tumours of the bronchus, prostate and breast, measurement is not of proven value for diagnosing these conditions. In malignant disease plasma total CK activity is usually normal.

**Q. Increased CK-MB relative to total creatinine kinase (CK) is seen in:** (BSMMU – MD – 10Ja)

- |  |   |
|--|---|
| a) rhabdomyolysis                        | F |
| b) extensive muscle trauma               | F |
| c) polymyositis                          | F |
| d) acute myocardial infarction           | T |
| e) vigorous exercise in marathon runners | F |

(Ref: Sattanarayon-4<sup>th</sup>, P-112)

**Q. Causes of elevated serum creatinine kinase are:** (MD/MS (DMC) – 08Ja)

- |                          |   |
|--------------------------|---|
| a) motor neuron disease  | T |
| b) myocardial infarction | T |
| c) hypothyroidism        | T |
| d) acute pancreatitis    | F |
| e) renal failure         | F |

#### **HELP LINK:**

#### **Creatinine kinase (CK):**

1. CK<sub>1</sub> is increased in severe shock, carcinoma.
2. CK<sub>2</sub> is specific for the diagnosis of myocardial infarction (MI). It rises in 4 to 8 hours following onset of chest pain & reaches a peak in activity at about 24 hours.
3. CK<sub>3</sub> is increased in muscle dystrophies.

**Q. Serum creatinine kinase is increase in:** (M. Phil, Diploma-07July)

- |                         |   |
|-------------------------|---|
| a) motor neuron disease | T |
| b) hypothyroidism       | T |
| c) polymyositis         | T |
| d) polio                | F |
| e) renal failure        | F |

## **Lactate dehydrogenase**

**Q. Lactate dehydrogenase is increased in –** (MD/MS (DMC) – January, 2008)

- a) myocardial infarction
- b) chronic renal failure
- c) leukaemia
- d) iron deficiency anaemia
- e) malignancy

Ans. a) T

b) F (increased blood loss due to capillary fragility & poor platelet function → increased LD)

c) T d) F (hemolytic anaemia) e) T

#### **HELP LINK:**

**Causes of increased Lactate dehydrogenase**

<b>Marked increase</b>	<b>Moderate increase</b>	<b>Mild increase</b>
<ul style="list-style-type: none"> <li>• Circulatory failure with shock and hypoxia</li> <li>• Myocardial infarction</li> <li>• Renal infarction</li> <li>• Rejection of renal transplant</li> </ul>	<ul style="list-style-type: none"> <li>• Malignancy</li> <li>• Viral hepatitis</li> <li>• Pulmonary embolism</li> <li>• Skeletal muscle disease</li> <li>• Infectious mononucleosis</li> </ul>	<ul style="list-style-type: none"> <li>• Haemolytic anaemia</li> <li>• Thalassaemia</li> <li>• Myelofibrosis</li> </ul>

**Alkaline phosphatase**

**Q. Serum alkaline phosphatase is increased in:** (BSMMU – MD - January, 2008)

- |                            |   |
|----------------------------|---|
| a) haemolytic jaundice     | F |
| b) obstructive jaundice    | T |
| c) viral hepatitis         | T |
| d) Paget's disease of bone | T |
| e) osteomalacia            | T |

**HELP LINK:****About Alkaline phosphatase (ALP)**

- These are a group of enzymes that hydrolyse organic phosphates at high pH.
- They are present in most tissues but are in particularly high conc. in –
  - the osteoblasts of bone
  - the cells of the hepatobiliary tract, intestinal wall, renal tubules and placenta.
- ALP is probably important for calcification of bone.
- In adults, plasma ALP is derived mainly from bone and liver. (when bone fraction is increased, there is increased osteoblastic activity → ↑ ALP)

**■ Causes of raised plasma ALP:****A. Physiological cause:**

1. During the last trimester of pregnancy, the plasma total ALP activity rises due to the contribution of the placental isoenzyme.
2. In preterm infants plasma total ALP activity is upto five times the upper reference limit in adults, and consists predominantly of the bone isoenzyme.
3. In children the total activity is about 2.5 times, and increases to up to five times, this upper limit during the pubertal bone growth spurt.
4. There is a gradual increase in the proportion of liver ALP with age. In the elderly the plasma bone isoenzyme activity may increase slightly.

**B. Pathological cause:****1. Bone diseases:**

- Rickets and osteomalacia
- Paget's disease of bone (may be very high)
- Secondary malignant deposits in bone
- Osteogenic sarcoma, only if very extensive.
- Primary hyperparathyroidism with extensive bone disease (usually normal but may be slightly elevated)
- Secondary hyperparathyroidism.

**2. Liver disease:**

- Intra-or extrahepatic cholestasis
- Space-occupying lesions, tumours, granulomas
- Other causes of hepatic infiltration.

**3. Malignancy:**

- Bone or liver involvement or direct tumour production.

- A placental-like, so-called 'Regan', isoenzyme may occasionally be identified in plasma in patients with malignant disease, especially carcinoma of the bronchus.
- Transient very high levels of ALP have been recorded in children under three years, but the clinical significance of this finding is unknown.
- In myelomatosis, plasma ALP activity is not usually increased. But there is X-ray appearance of multiple 'punched-out' osteolytic lesions. The lesions are in the marrow cavity, not the bone substance, and osteoblastic activity is not stimulated.
- However, ALP activity may be raised if there is liver involvement, or, more rarely, if there is healing of very extensive pathological fractures.

**Causes of low plasma ALP activity:**

1. Arrested bone growth:
  - Achondroplasia
  - Cretinism
  - Severe ascorbate deficiency.
2. Hypophosphatasia, an autosomal recessive disorder, associated with rickets or osteomalacia.

**■ Isoenzymes of ALP:**

These may be separated by electrophoresis. The placental and 'Regan' isoenzymes are more stable at 65°C than the bone, liver and intestinal isoenzymes, and heat inactivation may help to differentiate the heat-stable from the heat-labile fraction.

The placental isoenzyme does not cross the placenta and is therefore not detectable in the plasma of the newborn.

**Q. Serum alkaline phosphatase is - (BSMMU – M. Phil, Diploma July, 2006)**

- |   |   |
|---|---|
| A. derived from liver, bone, small bowel and placenta               | T |
| B. typically increased more than six times in viral hepatitis       | F |
| C. derived mainly from hepatic sinusoidal and canalicular membranes | T |
| D. of particular prognostic value in chronic liver disease          | T |
| E. increased more in extrahepatic than in intrahepatic cholestasis  | T |

**HELP LINK:**

**Serum alkaline phosphatase is increased in -**

1. Physiological: Children, Late pregnancy
2. Obstructive jaundice
3. Hepatocellular jaundice
4. Cirrhosis of liver.

Also ↑ in:

1. Osteomalacia & rickets
2. Paget's disease
3. Hyperparathyroidism
4. Metastatic CA of bone

**Serum acid phosphatase**

**Acid phosphatase (ACP)**

- Acid phosphatase is found in cells of the prostate, liver, erythrocytes, platelets and bone.
- The estimation is gradually being replaced by the measurement of plasma prostate specific antigen (PSA), a protein derived from the prostate. This test is more specific and sensitive for diagnosis and monitoring treatment. However, it may be raised in, similar circumstances to those affecting prostatic ACP and is more expensive to estimate.

Normally acid phosphatase drains from the prostate, through the prostatic ducts, into the urethra and very little can be detected in plasma. In extensive prostatic carcinoma, particularly if it has spread extensively or has metastasized, plasma acid phosphatase activity rises, probably because of the increased number of prostatic acid

phosphatase containing cells. If the tumour is small, or is too undifferentiated to synthesize the enzyme, plasma activities may be normal. For this reason the assay of a known case of disseminated prostatic carcinoma than for making the diagnosis.

**■ Causes of raised serum acid phosphatase activity:**

**1. Tartrate-labile:**

- Artefactually following acute retention of urine
- Passage of a catheter, prostatic cells
- Disseminated carcinoma of the prostate.

**2. Total:**

- Artefactually in a haemolysed specimen, or following rectal examination
- Acute retention of urine or passage of a catheter
- Disseminated carcinoma of the prostate
- Paget's disease of bone
- Some cases of metastatic bone disease, especially with osteosclerotic lesions;
- Gaucher's disease (probably from Gaucher cells)
- Occasionally in thrombocythaemia.

**α-AMYLASE**

**α-AMYLASE**

Amylase breaks down starch and glycogen to maltose. It is present at a high concentration in pancreatic juice and in saliva and may be extracted from such other tissues as the gonads, Fallopian tubes, skeletal muscle and adipose tissue. In normal subjects most plasma amylase is derived from the pancreas and salivary glands. Being of relatively low molecular weight, it is excreted in the urine.

Estimation of plasma amylase activity is mainly requested to help in the diagnosis of acute pancreatitis, in which the plasma activity may be very high. However, it may also be raised in association with other intra-and extra-abdominal conditions that cause similar acute abdominal pain; a high result is not a specific diagnostic marker for acute pancreatitis.

**Causes of raised plasma amylase activity:**

**Marked increase** (five to 10 times the upper reference limit):

- Acute pancreatitis
- Severe glomerular impairment
- Severe diabetic ketoacidosis
- Perforated peptic ulcer especially if there is perforation into the lesser sac.

**Moderate increase** (upto five times the upper reference limit):

- Perforated peptic ulcer
- Acute cholecystitis
- Intestinal obstruction
- Abdominal trauma
- Ruptured ectopic pregnancy
- Salivary gland disorders: mumps; salivary calculi; Sjogren's syndrome
- After injection of contrast medium into salivary ducts for sialography
- Morphine administration (spasm of the sphincter of Oddi)
- Severe glomerular dysfunction (may be markedly raised)
- Myocardial infarction (occasionally)
- Acute alcoholic intoxication; diabetic ketoacidosis (may be markedly raised)
- Macroamylasaemia.

**Macroamylasaeemia:**

In some patients a high plasma amylase activity is due to low renal excretion of the enzyme, despite normal glomerular function. The condition is symptomless; it is thought that the either the enzyme is bound to a high molecular weight plasma component such as protein, or that the amylase molecules form large polymers that

cannot pass through the glomerular membrane. This harmless condition may be confused with other causes of hyperamylasaemia.

#### Pancreatic pseudocyst:

If the plasma amylase activity fails to fall after an attack of acute pancreatitis there may be leakage of pancreatic fluid into the lesser sac (a pancreatic pseudocyst). Urinary amylase levels are high, differentiating it from macroamylasaemia. This is one of the few indications for estimating urinary amylase activity, which is inappropriately low relative to the plasma activity if there is glomerular impairment or macroamylasaemia.

#### Isoenzymes of Amylase

Plasma amylase is derived from the pancreas and salivary glands. It is rarely necessary to identify the isoenzyme components in plasma, but they can be distinguished by electrophoresis, or by using an inhibitor derived from wheat germ. Possible indications for isoenzyme determination include:

- The coexistence of mumps or renal failure, which complicate the interpretation of high activities due to acute pancreatitis;
- The possibility of chronic pancreatic disease, in which low activities may be found.

Some laboratories now measure the plasma 'pancreatic' amylase activity using a method that incorporates wheat germ rather than starch. The different substrates affect the results and it is important to interpret the result against the reference range from the same laboratory.

## Coenzyme

**Q. Vitamins acting as co-enzymes in different biochemical reactions are (BSMMU – Non-Residency – MD, MS, Basic science & Dentistry – July '18)**

- a) vitamin C
- b) vitamin D
- c) vitamin A
- d) riboflavin
- e) cyanocobalamin

Ans. a) T b) F c) F d) T e) T

**Help Link:** All water soluble vitamin including vitamin K has a specific coenzyme function.

(Ref: Sattanarayon-4<sup>th</sup>, P-118)

**Q. Thiamine pyrophosphate is an essential coenzyme for: (BSMMU – M. Phil. Diploma (Non-Residency) – March-2012, DMC & others – MD/ms – March-2012, BSMMU – M. Phil. Diploma July, 2007)**

- |  |   |
|--|---|
| a) conversion of pyruvate to acetyl CoA  | T |
| b) transamination reaction               | F |
| c) conversion of $\alpha$ -ketoglutarate | T |
| d) haem synthesis                        | F |
| e) transketolase in HMP shunt            | T |

#### HELP LINK:

Thiamine (anti-beri beri or anti-neuritic vitamin) is water soluble. It has a specific coenzyme, **thiamine pyrophosphate (TPP)** which is mostly associated with carbohydrate metabolism.

The coenzyme, thiamine pyrophosphate or cocarboxylase is intimately connected with the energy releasing reactions in the carbohydrate metabolism.

1. The enzyme **pyruvate dehydrogenase** catalyses (oxidative decarboxylation) the irreversible conversion of pyruvate to acetyl CoA. This reaction is dependent on TPP, besides the other coenzymes.
2.  **$\alpha$ -Ketoglutarate dehydrogenase:** It is an enzyme of the citric acid cycle. This enzyme is comparable with pyruvate dehydrogenase and requires TPP.

3. **Transketolase:** Is dependent on TPP. This is an enzyme of the hexose monophosphate shunt (HMP shunt). This pathway is concerned with the production of ribose and NADPH, respectively required for nucleic acid and lipid synthesis.
4. The **branched chain  $\alpha$ -keto acid dehydrogenase (decarboxylase):** Catalyses the oxidative decarboxylation of branched chain amino acids (valine, leucine and isoleucine) to the respective keto acids. This enzyme also requires TPP.
5. TPP plays an important role in the transmission of nerve impulse. It is believed that TPP is required for acetylcholine synthesis and the ion translocation of neural tissue.

(Ref: ABC Biochemistry-6<sup>th</sup>, P-212)

**Q. Coenzyme of B complex vitamin are:** (BSMMU – MD – January, 2010)

- |                                |   |
|--------------------------------|---|
| a) Thiamin pyrophosphate       | T |
| b) Tetrahydrofolate            | T |
| c) Cystidine diphosphate       | F |
| d) Flavin adenine dinucleotide | T |
| e) Adenosine triphosphate      | F |

**HELP LINK:**

■ **Coenzymes formed by vitamin B-complex:**

Vitamins	Co-enzymes
Thiamin(B <sub>1</sub> )	Thiamin pyrophosphate
Riboflavin(B <sub>2</sub> )	FMN, FAD
Niacin(B <sub>3</sub> )	NAD <sup>+</sup> , NADP <sup>+</sup>
Pantothenic acid(B <sub>5</sub> )	CO-enzyme A
Pyridoxin(B <sub>6</sub> )	Pyridoxal phosphate
Cyanocobalamin(B <sub>12</sub> )	Methylcobalamin, Deoxyadenosylcobalamin
Biotin	Pyruvate carboxylase, Acetyl-CoA carboxylase
Folic acid	Tetrahydrofolic acid

**Q. Co-enzymes are:** (M. Phil. Diploma-07July)

- |   |   |
|---|---|
| a) heat labile                              | F |
| b) inorganic substance                      | F |
| c) nonprotein in nature                     | T |
| d) vitamin derivatives                      | T |
| e) not required in energy releasing pathway | F |

**HELP LINK:**

■ **Definition:** Co-enzymes are specific heat stable, dialyzable low molecular weight organic non-protein compound which in combination with enzyme helps in enzyme activity.

It constitutes the prosthetic group of compound protein enzyme.

(Ref: Satyanarayan-4<sup>th</sup>, Orten-10<sup>th</sup>, P-99)

■ **Characteristics:**

1. They are heat stable, dialyzable and non-protein organic molecules
2. Low molecular weight
2. Generally derived from water soluble vitamins.
3. They may be regarded as second substrate or co-substrate.

■ **Classification:** Coenzymes can be classified according to the group whose transfer they facilitate as follows:

A. **For transfer of H<sup>+</sup>:**

- NAD<sup>+</sup>, NADP<sup>+</sup>
- FMN, FAD
- Lipoic acid
- Co-enzyme Q.

**B. For transfer of groups other than H<sup>+</sup>:**

- Sugar phosphate
- CoA-SH
- Thiamin pyrophosphate
- Pyridoxal phosphate
- Folate coenzymes
- Biotin
- Cobamide (B<sub>12</sub>) coenzymes
- Lipoic acid

**■ Function:**

1. They accept atoms or groups from a substrate and transfer them to another.
2. The same co-enzyme can act in a number of different reactions.
3. They participate in hydride(H) and electron transfer reactions. e.g. NAD, NADH, FADH, FMN, FAD.
4. They participate in group transfer reactions e.g. Co-A, TPP etc.

**■ Differences:**

Enzyme	Coenzyme
1. Organic catalyst	1. Accessory substance
2. Protein in nature	2. Non-protein in nature
3. High molecular weight	3. Low molecular weight
4. Non-dialyzable	4. Dialyzable
5. Heat labile	5. Heat stable
6. Capable of catalyzing a biochemical reaction	6. In combination with enzyme helps in enzyme activity.

**METABOLISM****Metabolic pathways in mitochondria****Metabolic pathways that occurs inside the mitochondria:**

- Oxidative phosphorylation/ /respiratory chain
- TCA cycle
- Reduction and oxydation of pyruvate
- β-oxidation of fatty acids
- Ketone body formation.

**■ In mitochondria& cytosol: Urea cycle****■ In cytosol:**

- Glycolysis, glycogenesis, glycogenolysis, gluconeogenesis
- HMP shunt
- Uronic acid pathway
- Fatty acid synthesis
- Cholesterol synthesis

**Q. Reactions occurring in mitochondria are (BSMMU – Residency - MD/MS, Basic science, Paediatrics – March' 19)**

- a) pentose phosphate pathway
- b) ketogenesis
- c) reduction of pyruvate
- d) fatty acid synthesis
- e) oxidation of fatty acids

Ans. a) F b) T c) T d) F e) T

(Ref. ABC of Biochemistry, Chapter 10)

**Q. Reactions occur in mitochondria are (BSMMU – Residency – MD, MS, Basic Science – March' 18)**

- a) pentose phosphate pathway
- b) ketogenesis
- c) reduction of pyruvate
- d) synthesis of fatty acids
- e)  $\beta$ -oxidation of fatty acids

Ans. a) F b) T c) T d) F e) T

(Ref. ABC Biochemistry Chapter 10)

**Q. Metabolic pathways that occur in mitochondria are (BSMMU – Residency - MD, MS, Basic Science, Dentistry - March' 17)**

- a) TCA cycle
- b) glycolysis
- c)  $\beta$ - oxidation of fatty acid
- d) HMP—shunt pathway
- e) glycogenolysis

Ans. a) T b) F(cytoplasm) c)T d) F(cytoplasm) e)F(cytoplasm)

**Q. Metabolic pathway occurs in mitochondria (BSMMU – Residency - MD/MS, Basic science – March' 14)**

- |                          |   |
|--------------------------|---|
| a) HMP shunt pathway     | F |
| b) fatty acid synthesis  | F |
| c) oxidation of pyruvate | T |
| d) glycolysis            | F |
| e) TCA cycle             | T |

**Q. Following metabolic pathways are found in mitochondria: (BSMMU - M. Phil, Diploma, July-08)**

- |                                |   |
|--------------------------------|---|
| a) glycolysis                  | F |
| b) TCA cycle                   | T |
| c) respiratory chain           | T |
| d) beta oxidation              | T |
| e) Hexose Mono Phosphate shunt | F |

**Q. Metabolic pathways occurring within the mitochondria: - (MD/MS (DMC)-03Ja)**

- |                                 |   |
|---------------------------------|---|
| a) Glycolysis                   | F |
| b) Beta-oxidation of fatty acid | T |
| c) Fatty acid synthesis         | F |
| d) Oxidative phosphorylation    | T |
| e) Citric acid cycle            | T |

### Higher energy compound

**Q. High energy phosphate compounds are (BSMMU –Residency - MD/MS, Basic science, Paediatrics – March' 19)**

- a) glucose 6-phosphate
- b) phosphoenol pyruvate
- c) GTP
- d) AMP
- e) creatine phosphate

Ans. a) F b) T c) T d) F e) T

(Ref. ABC of Biochemistry-2<sup>nd</sup>, P-141)

**Help Link:**

**Phosphorylated compounds produced by phosphorylation may be of two types:**

**High energy phosphate compounds:**

- ✓ energy contents >6 kcal/mol
- ✓ Eg: ADP, ATP, GDP, GTP, Creatinin phosphate, carbamoyl phosphate, phosphoenolpyruvate, cyclic AMP, pyrophosphate

**Low energy phosphate compound:**

- ✓ <5kcal/mol
- ✓ eg: AMP, glucose 1-phosphate, glucose 6 phosphate, fructose 6 phosphate

**Q. Following are the high energy phosphate compounds: - (MD/MS (DMC)-03Ja)**

- |                        |   |
|------------------------|---|
| a) ATP                 | T |
| b) Phosphoenolpyruvate | T |
| c) AMP                 | F |
| d) Glucose 6-phosphate | F |
| e) Creatine phosphate  | T |

**HELP LINK:**

■ **Higher energy compound:** Certain compounds are entercounted in biological system which on hydrolysis, yield energy.

- High energy compound or energy rich compound are usually applied to substance which possesses sufficient free energy to liberate, at least 7 cal/ mol at pH 7.0.
- Certain other compounds which liberate less than 7.0 cal/ mol are referred to as low energy compounds.

1. **Very high energy phosphate compounds:** Compounds that contain phosphate with an energy higher than that of ATP. e.g. Phosphoenol pyruvate, 1,3-Bisphosphoglycerate. These have a standard free energy of hydrolysis of greater than – 10 cal/ mol.

- Phosphoenol pyruvate → 14.8 Kcal/ mol
- 1,3-Bisphosphoglycerate → 11.8 Kcal/ mol
- Phosphocreatine → 10.3 Kcal/ mol

2. **High energy compounds:** e.g. ATP.

Standard free energy of hydrolysis of ATP approximately –7.3 cal/ mol for each of the two terminal phosphate group.

- ATP → 7.3 Kcal/ mol
- ADP → 6.6 Kcal/ mol

3. **Low energy compounds:** Standard free energy of hydrolysis is less than 7.0 cal/ mol.

- Glucose 1 phosphate → 5.0 Kcal/ mol
- Glucose 6 phosphate → 3.0 Kcal/ mol
- Glucose 3 phosphate → 2.2 Kcal/ mol

## Respiratory chain

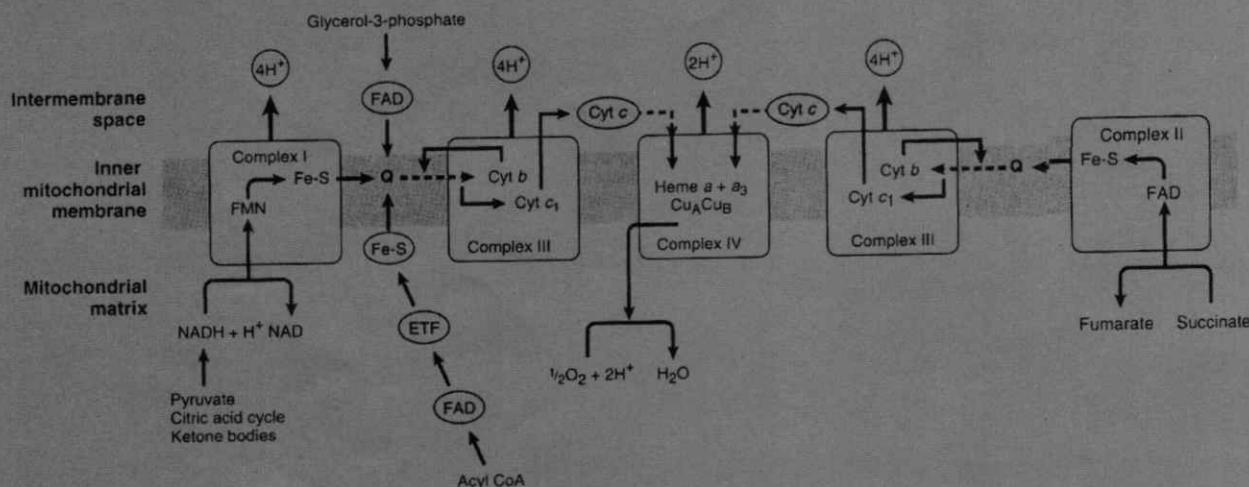
■ **Respiratory chain (Electron transport chain):** It is the sequence of enzymes & carriers in the inner mitochondrial membrane that are responsible for the transport of reducing equivalents ( $H^+$ ) or electron from the substrate to molecular oxygen to form water with the generation of ATP.

■ **Site:** Inner mitochondrial membrane.

■ **Components:**

1. Enzymes: Oxygenase, dehydrogenase, oxydases.
2. Co-enzymes: NAD, FAD (FMN), coenzyme Q [*coenzyme Q is formed by Quinone + 10 isoprenoid (Ubiquinone)*]
3. Cytochromes: cytochrome b, c, a, a<sub>3</sub>.

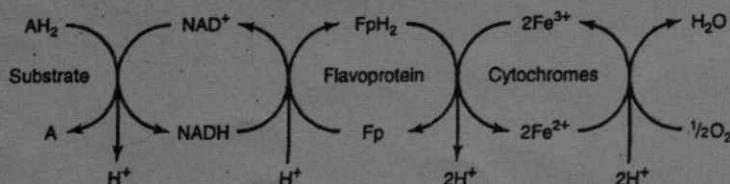
Phosphorylating units are present in the inner membrane of mitochondria. They are the centers for ATP formation.



**FIGURE: Flow of electrons through the respiratory chain complexes**, showing the entry points for reducing equivalents from important substrates. Q and cyt care mobile components of the system as indicated by the dotted arrows. (Fe-S, iron-sulfur protein; ETF, electron transferring flavoprotein; Q, coenzyme Q or ubiquinone; cyt, cytochrome.)

(Ref: Harper-30<sup>th</sup>, P-129)

■ **Transport of electron:** The electron is transported in different forms, for example, as hydride ions ( $H^-$ ) to  $NAD^+$ , as hydrogen atom (H) to FMN, Coenzyme Q and FAD or as free electrons (e) to cytochromes.



**Figure: Transport of electron (or reducing equivalents) in ETC.**

(Ref: Harper-30<sup>th</sup>)

■ **Release of free energy:** As electron passes though respiratory chain, free energy is released. This is utilized to produce ATP by oxidative phosphorylation.

■ **Sites of ATP production:**

- 1) Complex I:  $FMN \rightarrow Coenzyme\ Q$  (or  $NAD^+ \rightarrow Coenzyme\ Q$ )
- 2) Complex III:  $Cyt\ b \rightarrow Cyt\ C_1$ .
- 3) Complex IV:  $Cyt\ a \rightarrow Cyt\ a_3$ .

(Ref: Harper-30<sup>th</sup>, P-125)

$\text{NAD}^+$ , FMN, cytochromes are the carriers for transporting electrons.

When electrons are transferred from one level to another (carriers), free energy is formed which is represented by  $\Delta G$ .

■ **Inhibitors of respiratory chain:**

1. Amytal, Rotenone
2. Antimycin A
3. Cyanide ( $\text{CN}^-$ )
4. CO
5. Sodium azide
6. Dimercaprol
7.  $\text{H}_2\text{S}$

(Ref: Lippincot-6<sup>th</sup> + Harper-30<sup>th</sup>)

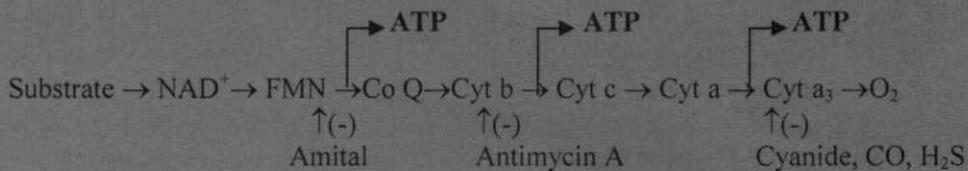


Fig: Inhibitors of ETC & site of ATP formation

■ **Importance:** The carriers in the respiratory chain are arranged so that spontaneous flow of electrons to oxygen is ensured. This is important to release energy by electron flow through respiratory chain. Electron transport from NADH to oxygen produce 3 moles of ATP.

Q. Enzymes of respiratory chain are (BSMMU – Non-Residency – MD, MS, Basic science – July ' 15)

- |                                      |   |
|--------------------------------------|---|
| a) glucose 6-phosphate dehydrogenase | F |
| b) succinate dehydrogenase           | T |
| c) NADH dehydrogenase                | T |
| d) lactate dehydrogenase             | F |
| e) cytochrome oxidase                | T |

Help Link:

Enzymes of respiratory chain are

- Four membrane-bound complexes have been identified in mitochondria.
- Each is an extremely complex transmembrane structure that is embedded in the inner membrane. Three of them are proton pumps.
- **Complex 1:**
  - NADH:ubiquinone oxidoreductase, NADH-CoQ reductase, or NADH dehydrogenase;
- **Complex 2:**
  - succinate dehydrogenase or succinate-CoQ reductase;
- **Complex 3**
  - cytochrome bc<sub>1</sub> complex or CoQH<sub>2</sub>:cytochrome c reductase;
- **Complex 4**
  - cytochrome c oxidase

(Ref: Sattanarayon-4<sup>th</sup>, P-227 + Wikipedia)

Q. Electron transport chain (BSMMU – Residency - MD/MS, Basic science – March ' 14)

- a) is present in inner mitochondrial membrane
- b) is present in nuclear membrane
- c) electron combine with oxygen and proton
- d) has three separate protein complexes
- e) flow of election to oxygen directly synthesis ATP

Ans. a) T b) F c) T

d) F (has four separate protein complexes)

e) F

(Ref: Sattanarayon-4<sup>th</sup>, P-227)

**Q. Respiratory chain impairment is associated with: (BSMMU – MD/MS (Residency) – 10Ja)**

- |                           |   |
|---------------------------|---|
| a) Hypoxic cell injury    | T |
| b) Lactic acidosis        | T |
| c) Mitochondrial myopathy | T |
| d) Phenyl ketonuria       | F |
| e) Essential fructosuria  | F |

**HELP LINK:**

**Clinical disorder related to resp chain dysfunction:**

- Hypoxic cell injury
- Mitochondrial myopathy, neuropathy
- MELAS(mitochondrial encephalopathy, lactic acidosis and stroke)
- Stroke, renal dysfunction
- Epilepsy, Alzheimer disease, DM

(Ref: ABC Biochemistry-6<sup>th</sup>, P-142)

**CLINICAL ASPECTS OF RESPIRATORY CHAIN:** The condition known as **fatal infantile mitochondrial myopathy and renal dysfunction** involves severe diminution or absence of most oxidoreductases of the respiratory chain. **MELAS** (mitochondrial encephalopathy, lactic acidosis, and stroke) is an inherited condition due to NADH-Q oxidoreductase (Complex I) or cytochrome oxidase (Complex IV) deficiency. It is caused by a mutation in mitochondrial DNA and may be involved in **Alzheimer's disease and diabetes mellitus**. A number of drugs and poisons act by inhibition of oxidative phosphorylation.

(Ref: Harper-30<sup>th</sup>, P-112)

**Others**

**Q. Coenzymes required for the conversion of pyruvate to acetyl CoA are - (BSMMU – M. Phil,**

*Diploma – 11Ju, DMC & others – MD – 11Ju)*

- |                           |   |
|---------------------------|---|
| a) thiamine pyrophosphate | T |
| b) biotin                 | F |
| c) pyridoxal phosphate    | F |
| d) CoA                    | T |
| e) FAD                    | T |

**Help Link:**

**Oxidation of pyruvate to Acetyl CoA**

• **Salient features:**

- Substrate: Pyruvate
- Products: Acetyl CoA
- Site: All cells and tissues
- Compartment: Mitochondria
- Nature: Cataolic
- Coenzyme needed: TPP, NAD, FAD, CoA, Lipoic acid
- ATP production: 06
- Significance: Central step for linking glycolysis with TCA cycle
- Due to complete oxidation of pyruvate in TCA cycle it moves from cytoplasm to mitochondria and converted to acetyl CoA by oxidative decarboxylation catalyzed by the enzyme pyruvate dehydrogenase

(Ref: ABC Biochemistry-6<sup>th</sup>, P-152)

**Q. Glucose 6 phosphatase enzyme is found in: (BSMMU – M. Phil, Diploma (Non-Residency) – 11Ju, DMC & others – MD/MS – 11Ju, BSMMU –MD(Residency) – 11Ja)**

- |                    |   |
|--------------------|---|
| a) liver           | T |
| b) kidney          | T |
| c) skeletal muscle | F |
| d) adipose tissue  | F |
| e) brain           | F |

**HELP LINK:**

**Glucose 6-phosphatase:** Catalyses the conversion of glucose 6-phosphate to glucose. The presence or absence of this enzyme in a tissue determines whether the tissue is capable of contributing glucose to the blood or not. It is mostly present in liver and kidney but absent in muscle, brain and adipose tissue.

## Carbohydrate metabolism

**Q. Excess fructose in the diet can promote (BSMMU – Residency – MD, MS, Basic Science – March' 18)**

- a) diabetic cataract formation
- b) VLDL secretion from the liver
- c) insulin secretion
- d) hypercholesterolemia
- e) hyperuricemia

Ans. a) T b) F (LDL) c) F d) T e) T

**Q. Agents causes lactic acidosis (BSMMU – Residency – MD – March' 16)**

- |                |   |
|----------------|---|
| a) salicylates | T |
| b) methanol    | T |
| c) iron        | F |
| d) metformin   | T |
| e) cyanide     | T |

**Help Link:**

**Causes of Lactic acidosis:**

- **Genetic conditions**

- Diabetes mellitus and deafness
- Fructose 1,6-bisphosphatase deficiency
- Glucose-6-phosphatase deficiency
- Mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes
- Pyruvate dehydrogenase deficiency
- Pyruvate carboxylase deficiency

- **Drugs**

- Salicylate toxicity, Methanol, Linezolid, Phenformin, Metformin
- Isoniazid toxicity, Propofol, Epinephrine
- Propylene glycol (D-lactic acidosis), Nucleoside reverse-transcriptase inhibitors
- Abacavir/dolutegravir/lamivudine, Emtricitabine/tenofovir<sup>[7]</sup>
- Potassium cyanide (cyanide poisoning)

- **Other**

- Thiamine deficiency (especially during TPN)
- Polymyositis, Ethanol toxicity, Sepsis, Shock
- Advanced liver disease, Diabetic ketoacidosis
- Excessive exercise (overtraining)
- Cancers such as Non-Hodgkin's and Burkitt lymphomas
- Pheochromocytoma, Tumor lysis syndrome

**Q. Enzymes of carbohydrate metabolism are: (BSMMU – M. Phil, Diploma (Non-Residency)–March-2012, DMC & others – MD/MS – March-2012)**

- |                          |   |
|--------------------------|---|
| a) aldolase              | T |
| b) aminotransferase      | F |
| c) HMG CoA reductase     | F |
| d) ribose 5-P- isomerase | F |
| e) triose-P- isomerase   | T |

**Q. Under basal conditions the following tissues produce lactate: (BSMMU - M. Phil, Diploma – July '10)**

- |                 |   |
|-----------------|---|
| a) Erythrocyte  | T |
| b) Renal cortex | F |
| c) Skin         | T |
| d) Liver        | F |
| e) Intestine    | F |

**HELP LINK:**

**Structure involved in lactic acid production: due to poorly vascularized or lack of mitochondria**

- ✓ RBC (without mitochondria)
- ✓ WBC, renal medulla, retina(few mitochondria)
- ✓ Lens, cornea(avascular tissue)
- ✓ Skeletal muscle
- ✓ Testis
- ✓ Skin

**Q. Following tissues produce lactate under basal conditions- (BSMMU – MD - 06Ja)**

- |                  |   |
|------------------|---|
| A. Erythrocytes  | T |
| B. Thyroid gland | F |
| C. Muscle        | T |
| D. Skin          | T |
| E. Brain         | T |

### Pentose Phosphate Pathway

**Hexose monophosphate shunt:** It is an alternative pathway to glycolysis and TCA cycle for the oxidation of glucose to  $\text{CO}_2$  &  $\text{H}_2\text{O}$  without generating ATP.

■ **Others name:** 1. Pentose phosphate pathway 2. Phosphogluconate pathway

■ **Nature:** Catabolic

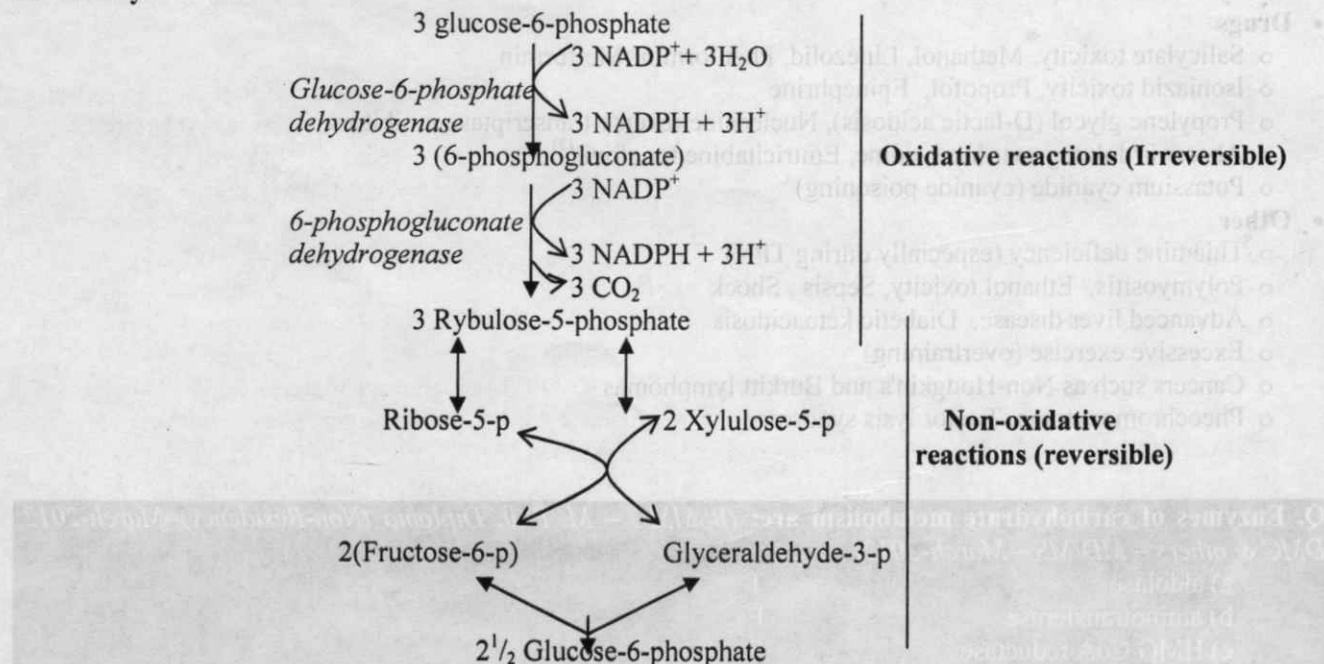
■ **Substrate:** Glucose-6-phosphate

■ **Product:** Ribose sugar (5 C), NADPH, Glucos-6-phosphate

■ **Possible sites:** Liver, RBC, adipose tissue, adrenal cortex, testes/ovary, lactating gland.

■ **Compartment:** Cytoplasm

■ **Pathway:**



**Fig: Pentose phosphate pathway**  
No ATP is directly consumed or synthesized.

(Ref: Harper-30<sup>th</sup>)

**Question Bank**

**Q. Hexose monophosphate shunt generates (BSMMU – Residency – MD, MS, Basic Science – March' 18)**

- a) NADPH
- b) FADH
- c) NADH
- d) GTP
- e) pentose sugar

Ans. a) T b) F c) F d) F e) T

(Ref. ABC Biochemistry-6<sup>th</sup>, P-163)

**Q. NADPH is required for (BSMMU – Residency - MD, MS, Basic Science - March' 17)**

- a) ATP production
- b) oxidation of glutathion
- c) drug metabolism
- d) generation of superoxide in phagocytes
- e) fatty acid synthesis

Ans. a) F b) F c) T d) T e) T

**Help Link:**

**Provides NADP2H:**

- Reductive synthesis of fatty acid, steroid, cholesterol
- Supports detoxifying functions of liver
- Prevent hemolysis by antioxidant activity.
- Facilitate superoxide and free radical production in phagocytes through oxygen dependent myeloperoxidase system to kill microbes
- Helps in reduction of H<sub>2</sub>O<sub>2</sub>
- Helps in synthesis of NO and EDRF(endothelial derived relaxing factor)

(Ref. ABC Biochemistry-6<sup>th</sup>, P-163)

**Q. Pentose phosphate pathway is active in (BSMMU – Residency – MD, MS, Basic science – March' 16)**

- |                   |   |
|-------------------|---|
| a) liver          | T |
| b) spleen         | F |
| c) adrenal cortex | T |
| d) erythrocytes   | T |
| e) brain          | F |

**Help Link:**

**Site:** Liver, RBC, Adipose tissue, Adrenal cortex, testis/ovary, macrophage, lactating gland

**Q. Pentose phosphate pathway (BSMMU – Residency – MD, MS, Basic – March' 15)**

- a) produces NADH
- b) does not produce ATP
- c) occurs in the cytosol
- d) requires mitochondrial enzymes
- e) is not important for erythrocytes

Ans. a) F b) T c) T d) F e) F

(Ref: ABC Biochemistry-6<sup>th</sup>, P-163)

**Q. NADPH is (BSMMU – Residency – MD, MS, Basic Science – March' 15)**

- a) required in fatty acid synthesis
- b) derived mainly from Hexose Monophosphate Shunt (HMS)
- c) used for synthesis of ketone bodies
- d) required for bile acid synthesis
- e) taken up by respiratory chain for ATP production

Ans. a) T b) T c) F d) T e) F

**Q.** Under basal conditions the following tissues produce lactate: (BSMMU – M. Phil, Diploma (Non-Residency) – March-2012, DMC & others – MD/MS – March-2012)

- |                                   |   |
|-----------------------------------|---|
| a) reductive biosynthesis         | T |
| b) synthesis of nitric oxide      | T |
| c) glycolysis                     | F |
| d) TCA cycle                      | F |
| e) reduction of hydrogen peroxide | T |

(Ref: ABC Biochemistry-6<sup>th</sup>, P-163)

**Q. NADPH is required for:** (BSMMU – M. Phil, Diploma (Non-Residency) – March-2012, DMC & others – MD/MS – March-2012)

- a) reductive biosynthesis
- b) synthesis of nitric oxide
- c) glycolysis
- d) TCA cycle
- e) reduction of hydrogen peroxide

**Help link:**

**Provides NADPH to:**

- Help in reductive synthesis of fatty acid, steroid, cholesterol etc.
- Support detoxifying functions of liver by hydroxylation of toxic water insoluble aromatic/ aliphatic substances (e.g. drugs) into water soluble, less toxic or nontoxic forms. Prevent hemolysis by facilitating anti-oxidant activity (neutralization of superoxides and free radicals) in RBC. Facilitate superoxide and free radical production in phagocytes through oxygen dependant myeloperoxidase system to kill bacteria and other pathogens.
- Help in reduction of  $H_2O_2$ .
- Help in synthesis of nitric oxide (NO) or endothelial derived relaxing factor (EDRF).

**Q. Major products of pentose phosphate pathway are:** (BSMMU – MD/MS (Residency) – January, 2010)

- |                        |   |
|------------------------|---|
| a) NADPH               | T |
| b) Six carbon sugar    | F |
| c) Five carbon sugar   | T |
| d) NADH                | F |
| e) Glucose-6-phosphate | T |

(Ref: ABC Biochemistry-6<sup>th</sup>, P-163)

**Q. Impairment of HMP shunt leads to:** (BSMMU – MD/MS (Residency) – January, 2010)

- |                             |   |
|-----------------------------|---|
| a) Hemolytic anaemia        | T |
| b) Chronic granulomatosis   | T |
| c) Ribose sugar deficit     | F |
| d) Wernick's encephalopathy | T |
| e) Mucopolysaccharidosis    | F |

**HELP LINK:**

**■ Importance of HMP shunt:**

1. It provides pentose sugar ribose for the nucleotide & nucleic acid biosynthesis.
  2. It generates NADPH for
    - i. Reductive synthetic process in our body. (*Reductive synthetic process = Reduction + synthesis*)
- Example:**
- Fatty acid synthesis
  - Synthesis of cholesterol
  - Synthesis of steroids
  - Synthesis of sphingolipid
- ii. Reduction of methemoglobin.
  - iii. Antioxidant activity in RBC
  - iv. Support generation of superoxide & free radicals in the phagocytes to kill bacteria by supporting  $O_2$  dependant myeloperoxidase system
  - v. It supports detoxifying function of liver.
  3. Provides arabinose for glycoprotein synthesis.
  4. Alternate pathway for glucose oxidation.
  5. Reduction of  $H_2O_2$ .
  6. Helps in synthesis of NO or EDRF.

(Ref: Lecture of DMC)

■ **Importance of HMP shunt in RBC:** In RBC there is a production of superoxide or free radicals ( $O_2^-$ ). It is a normal happening but it is very dangerous as it can destroy the RBC membrane completely. So this  $O_2^-$  is neutralized by antioxidant activity that needs NADPH which comes from HMP shunt. This NADPH reduces the oxidized glutathione to reduced glutathione catalyzed by glutathione reductase (a Fp containing FAD). In turn, reduced glutathione removes  $H_2O_2$  from RBC in a reaction catalyzed by glutathione peroxidase (an enzyme containing selenium). This reaction is important, since accumulation of  $H_2O_2$  may decrease the life span of RBC by increasing the oxidation rate of Hb to methaemoglobin.

Thus HMP shunt helps in protecting RBC against haemolysis. Otherwise there may happen haemolytic anaemia because of break down of membrane.

2. the availability of ADP  
3. the rate of utilization of ATP in chemical & physical work  
■ **Impairment of the Pentose Phosphate Pathway leads to red cell hemolysis:**

A mutation present in some populations causes a deficiency in glucose 6-phosphate dehydrogenase, with consequent impairment of the generation of NADPH. This impairment is manifested as red cell hemolysis when the susceptible individuals are subjected to oxidants or have eaten fava beans.

### What is Glucose 6-P dehydrogenase deficiency?

Glucose 6-phosphate dehydrogenase deficiency is an inherited disease characterized by hemolytic anaemia caused by the inability to detoxify oxidizing agents. It is the most common disease-producing enzyme abnormality in humans, affecting more than 200 million individuals worldwide.

■ **Advantage of Glucose 6-P dehydrogenase deficiency:** Falciparum malaria does not occur.

### Precipitating factors in Glucose 6-P dehydrogenase deficiency?

#### 1. Oxidant drugs:

- Antibiotics- Sulfamethoxazole
- Antimalarial- Primaquine
- Antipyretics- Acetanilid.

2. **Favism:** Some G6PD deficiency (Mediterranean variant) are susceptible to the hemolytic effect of the fava bean. All patients with favism have G6PD deficiency.

#### 3. Infection

#### 4. Neonatal jaundice.

### Wernicke-Korsakoff syndrome:

This is a genetic disorder associated with HMP shunt. An alteration in Transketolase activity that reduces its affinity (by ten fold or so) with thiamine pyrophosphate is the biochemical lesion. The symptoms of **Wernicke-Korsakoff syndrome** include mental disorder, loss of memory and partial paralysis. The symptoms are manifested in alcoholics whose diets are vitamin deficient.

In pernicious anaemia, erythrocyte transketolase activity is found to increase. (Ref: Satyanarayana-4<sup>th</sup>)

**Q. Pentose phosphate pathway is important in – (MD/MS (DMC) – January, 2008)**

- |                    |   |
|--------------------|---|
| a) kidney          | F |
| b) adrenal gland   | T |
| c) erythrocytes    | T |
| d) skeletal muscle | F |
| e) mammary gland   | T |

### HELP LINK:

■ **Possible sites:** Liver, RBC, adipose tissue, adrenal cortex, testes/ovary, lactating mammary gland.

The diagram illustrates the Pentose Phosphate Pathway (PPP) showing its role in various tissues. It highlights the conversion of glucose-6-phosphate (G6P) to ribulose-5-phosphate (R5P) via the action of Glucose-6-phosphate dehydrogenase (G6PDH), which is inhibited by primaquine. The pathway branches into the reduction of NADP+ to NADPH and the generation of ribose-5-phosphate (R5P) for nucleotide synthesis. Other enzymes shown include 6-phosphogluconate dehydrogenase (6PGD), transketolase (TKT), and transaldolase (TA).

## TCA cycle

■ **Citric acid cycle/Krebs cycle/TCA cycle:** It is a series of reactions in mitochondria that bring about the catabolism of acetyl residues, liberating hydrogen equivalents, which, upon oxidation, lead to the release and capture as ATP of most of the available energy of tissue fuels.

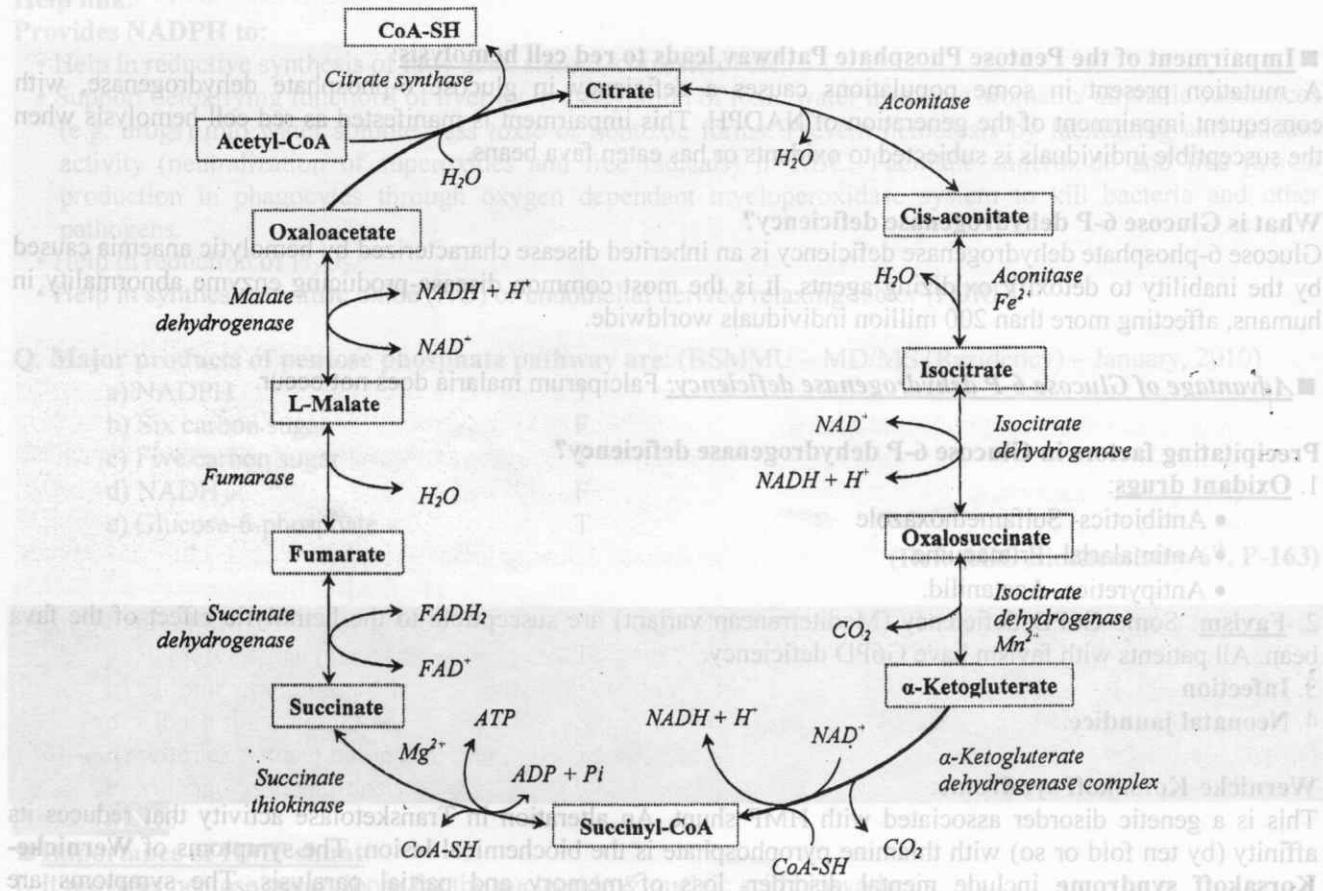
■ **Substrate:** Acetyl-CoA

■ **Product:** CO<sub>2</sub>, H<sub>2</sub>O, energy.

■ **Site:** Almost all cells & tissues.

■ **Compartment:** Mitochondrial matrix.

■ **Steps of citric acid cycle:**



**Fig: The citric acid cycle.**

(Ref: Harper-30<sup>th</sup>, P-163)

### Importance / Functions of TCA cycle:

1. It is the final pathway where the oxidative metabolism of carbohydrates, amino acids, and fatty acids converge, their carbon skeletons being converted to CO<sub>2</sub>. This oxidation provides energy for the production of the majority of ATP in most animals, including humans.
2. Most of the body's catabolic pathways converge on the TCA cycle.
3. TCA cycle also participates in a number of important synthetic reactions. For example,
  - a. Gluconeogenesis
  - b. Synthesis of some amino acids and heme.
  - c. Transamination
  - d. Deamination
  - e. Lipogenesis.
4. Therefore, this cycle should not be viewed as a closed circle, but instead as a traffic circle with compounds entering and leaving as required.
4. It utilizes (indirectly) about 2/3rd of total oxygen consumed by the body and generates about 2/3rd of total energy (ATP).

(Ref: Lippincott-7<sup>th</sup>, P-109; Harper-30<sup>th</sup>)

**Nice to know:**

**Regulation of TCA cycle:** TCA cycle is regulated at the nonequilibrium/ irreversible reactions catalyzed by

1. Pyruvate dehydrogenase
2. Citrate synthase
3. Isocitrate dehydrogenase
4.  $\alpha$ -ketoglutarate dehydrogenase

**Activation of these enzymes depends on**

1. the supply of the NAD
2. the availability of ADP
3. the rate of utilization of ATP in chemical & physical work

- a) cholesterol      b) oxaloacetate  
c) pyruvate        d) fatty acid

**Vitamins in TCA cycle:** 4 vitamins are essential in the TCA cycle and therefore in energy-yielding metabolism.

1. Riboflavin (in the form of FAD)
2. Niacin (in the form of NAD)
3. Thiamin (as thiamin diphosphate)
4. Pantothenic acid (as a part of coenzyme A).

(Ref: Harper-30<sup>th</sup>)

(Ref: Harper-30<sup>th</sup>)

**Q. Rate limiting enzymes for TCA cycle are (BSMMU – Residency - MD/MS, Basic science, Paediatrics – March' 19)**

- a) citrate synthase
- b) succinate dehydrogenase
- c) malate dehydrogenase
- d)  $\alpha$ -ketoglutarate dehydrogenase
- e) isocitrate dehydrogenase

Ans. a) T    b) F    c) F    d) T    e) T

**Help Link:****Rate limiting enzymes for TCA cycle:**

1. Citrate synthase
2. Isocitrate dehydrogenase
3. Alpha ketoglutarate dehydrogenase

(Ref. ABC of Biochemistry-6<sup>th</sup>, P-152 + Harper-30<sup>th</sup>)

**Sources of pyruvic acid:**

1. From glucose (by glycolysis)
2. From amino acid (by transamination)

**Q. Following vitamins have important role in TCA cycle: (BSMMU – MD/MS (Residency) – January, 2010)**

- a) Riboflavin
- b) Pyridoxine
- c) Niacin
- d) Biotin
- e) Thiamine

T

F

T

F

T

**HELP LINK:****Following vitamins have important role in TCA cycle:**

- Thiamin (as thiamine diphosphate)
- Riboflavin (in the form of FAD)
- Niacin (in the form of NAD)
- Pantothenic acid (as a part of coenzyme A)

(Ref: Lippincott-7<sup>th</sup>)

## Acetyl CoA

**Q. Sources of acetyl CoA are (BSMMU – Non-Residency – MD, MS, Basic science – July' 18)**

- a)  $\beta$ -oxidation of fatty acids
- b) glycolysis
- c) Krebs's cycle
- d) breakdown of cholesterol
- e) breakdown of ketone bodies

Ans. a) T b) T c) F d) F e) T

**Help Link:**

**Sources of Acetyl CoA:**

1. Oxidation of glucose via glycolysis
2. Oxidation of fatty acid by beta oxidation
3. Oxidation of amino acid
4. Degradation of ketone body
5. Oxidation of ethanol

**Q. Substances synthesized from acetyl CoA include (BSMMU – Non-Residency – MD, MS, Basic science – July' 16)**

- |                        |   |
|------------------------|---|
| a) ketone body         | T |
| b) pentose sugar       | F |
| c) cholesterol         | T |
| d) phosphatidylcholine | F |
| e) fatty acid          | T |

**HELP LINK:**

**Acetyl co-A:** Acetyl-CoA is the C<sub>2</sub> compound active acetate. When CoA reacts with acetic acid, acetyl-CoA is formed which is rich in energy.

**■ Sources of Acetyl- CoA:**

1. Carbohydrate metabolism (glycolysis)
2. Fat metabolism ( $\beta$ -oxidation)
3. Protein metabolism (transamination)
4. Ketone bodies (acetoacetate)

**■ Fate of Acetyl - CoA:**

1. Oxidation in TCA cycle
2. Synthesis of fatty acids
3. Synthesis of cholesterol
4. Synthesis of ketone bodies
5. Synthesis of steroids
6. Acetylation reactions (detoxication)

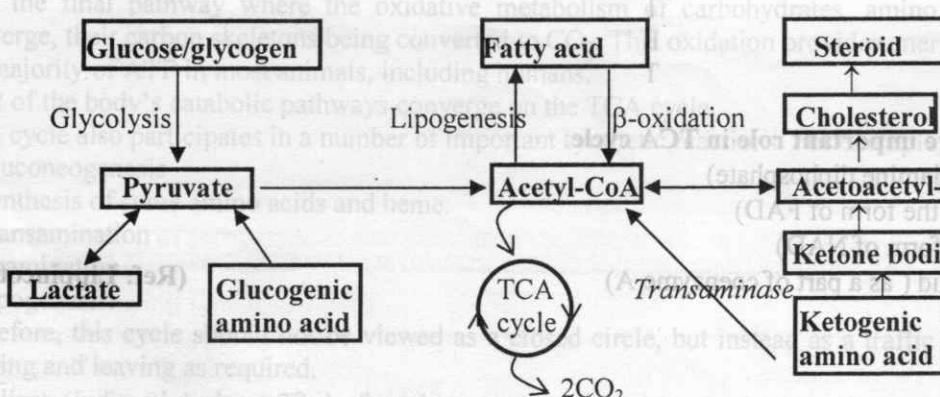


Fig: Sources & fate of acetyl-CoA

■ **Biosynthesis & catabolism of Ach:**

Choline + Acetyl Co-A  
 $\downarrow$  Choline acetyltransferase  
 Acetylcholine  
 $\downarrow$  Acetylcholinesterase  
 Choline + Acetate

■ **Release of Ach:** Impulse  $\rightarrow$  entrance of  $\text{Ca}^{++}$  within the nerve terminal  $\rightarrow$  release of Ach by exocytosis.

**Q. Fates of acetyl CoA are (BSMMU – Non-Residency – MD/MS, Basic science – July '14)**

- a) cholesterol      b) oxaloacetate
- c) pyruvate          d) fatty acid
- e) acetoacetate

Ans. a) T   b) F   c) F   d) T   e) T

**Q. Acetyl Co-A is involved with synthesis of - (MD/MS (DMC)-09Ja)**

- a. cholesterol      T
- b. ketone body      T
- c. glucose            F
- d. acetyl choline      T
- e. fatty acid          T

### Sources & fates of pyruvate

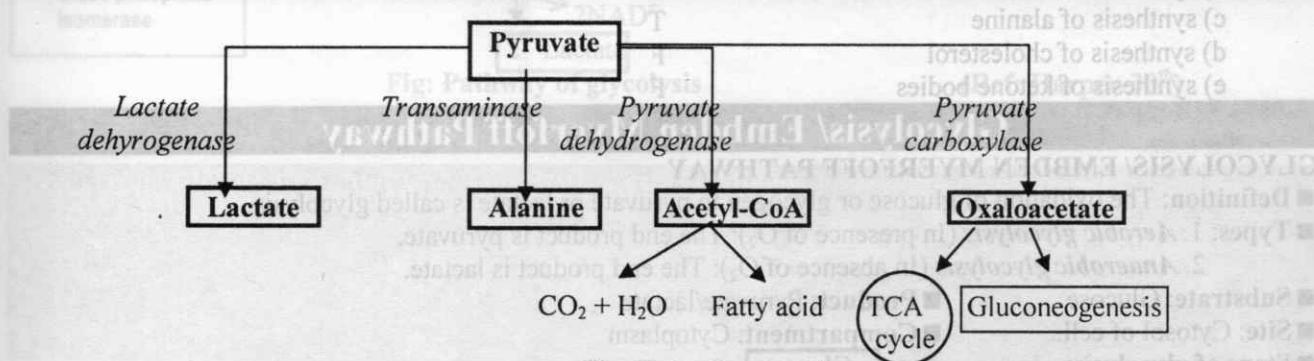


Fig: Fate of pyruvate

■ **Sources of pyruvic acid:**

1. From glucose (by glycolysis)
2. From amino acid (by transamination)
3. From fatty acid (by  $\beta$ -oxidation)
4. Lactic acid oxygenation

■ **Fates of pyruvic acid:**

1. Lactic acid under anaerobic condition.
2. Alanine by transamination
3. Acetyl CoA by oxidative decarboxylation
4. Oxaloacetic acid by carboxylation
5. Glucose by gluconeogenesis

**Q. Pyruvates are produced from (BSMMU – Non-Residency – MD, MS, Paediatrics, Basic Science – July '19)**

- a) lactate
- b) palmitate
- c) alanine
- d) glucose
- e) acetyl COA

Ans. a) T   b)   c) T   d) T   e) F

(Ref: ABC Biochemistry-6<sup>th</sup>, P-157)

- Q. Substrate for pyruvate production are (BSMMU –Residency – MD, MS, Basic Science – March' 18)**
- a) acetyl CoA      b) glucose  
c) cholesterol      d) alanine  
e) lactate

Ans. a) F b) T c) F d) T e) T (Ref. ABC Biochemistry Page-149)

- Q. Fates of pyruvate in the body are (BSMMU – Residency – MD, MS, Basic science – March' 16)**

- |                       |   |
|-----------------------|---|
| a) alanine            | T |
| b) glycerol           | F |
| c) oxaloacetate       | T |
| d) ketoacid formation | F |
| e) acetyl CoA         | T |

- Q. Metabolic fates of pyruvate are (BSMMU – Residency - MD/MS, Basic science – March' 14)**

- |                                  |   |
|----------------------------------|---|
| a) conversion to fatty acid      | F |
| b) conversion to acetyl CoA      | T |
| c) carboxylation to oxaloacetate | T |
| d) reduction to lactate          | T |
| e) oxidation to citrate          | F |

- Q. Metabolic fates of pyruvate are: (BSMMU - M. Phil, Diploma, July-08)**

- |                               |   |
|-------------------------------|---|
| a) synthesis of acetyl-CoA    | T |
| b) synthesis of lactic acid   | T |
| c) synthesis of alanine       | T |
| d) synthesis of cholesterol   | F |
| e) synthesis of ketone bodies | F |

## Glycolysis/ Embden Myerhoff Pathway

### GLYCOLYSIS/ EMBDEN MYERFOFF PATHWAY

■ **Definition:** The oxidation of glucose or glycogen to pyruvate or lactate is called glycolysis.

■ **Types:** 1. **Aerobic glycolysis** (In presence of O<sub>2</sub>): The end product is pyruvate.

2. **Anaerobic glycolysis** (In absence of O<sub>2</sub>): The end product is lactate.

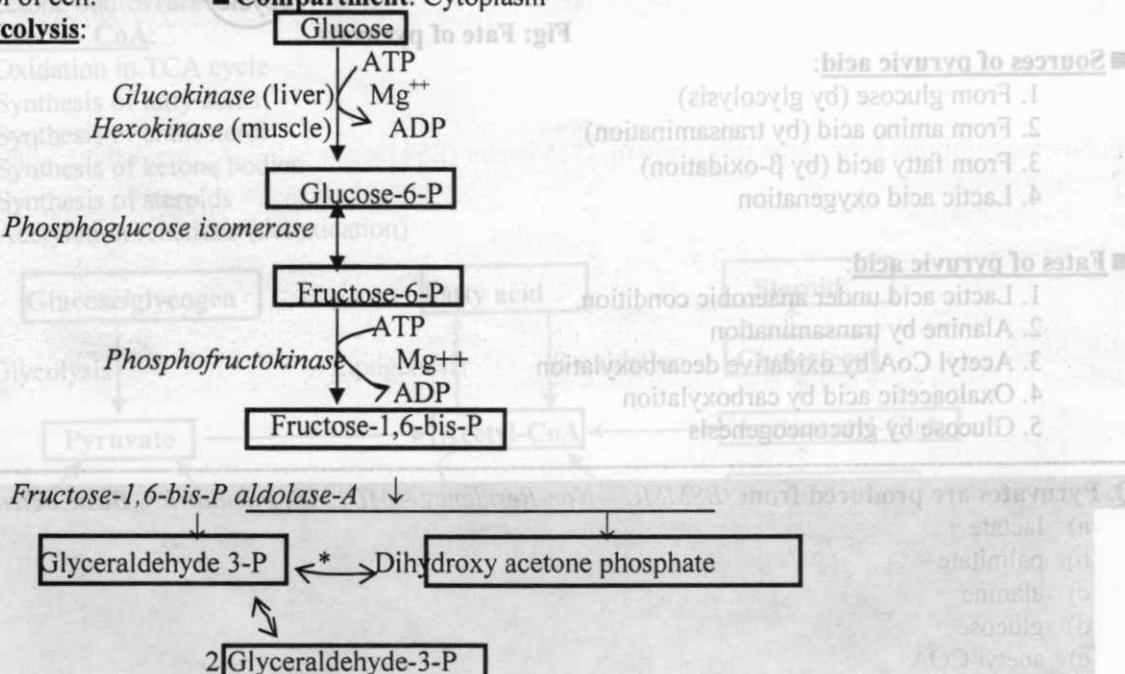
■ **Substrate:** Glucose

■ **Product:** Pyruvate/lactate

■ **Site:** Cytosol of cell.

■ **Compartment:** Cytoplasm

■ **Steps of glycolysis:**



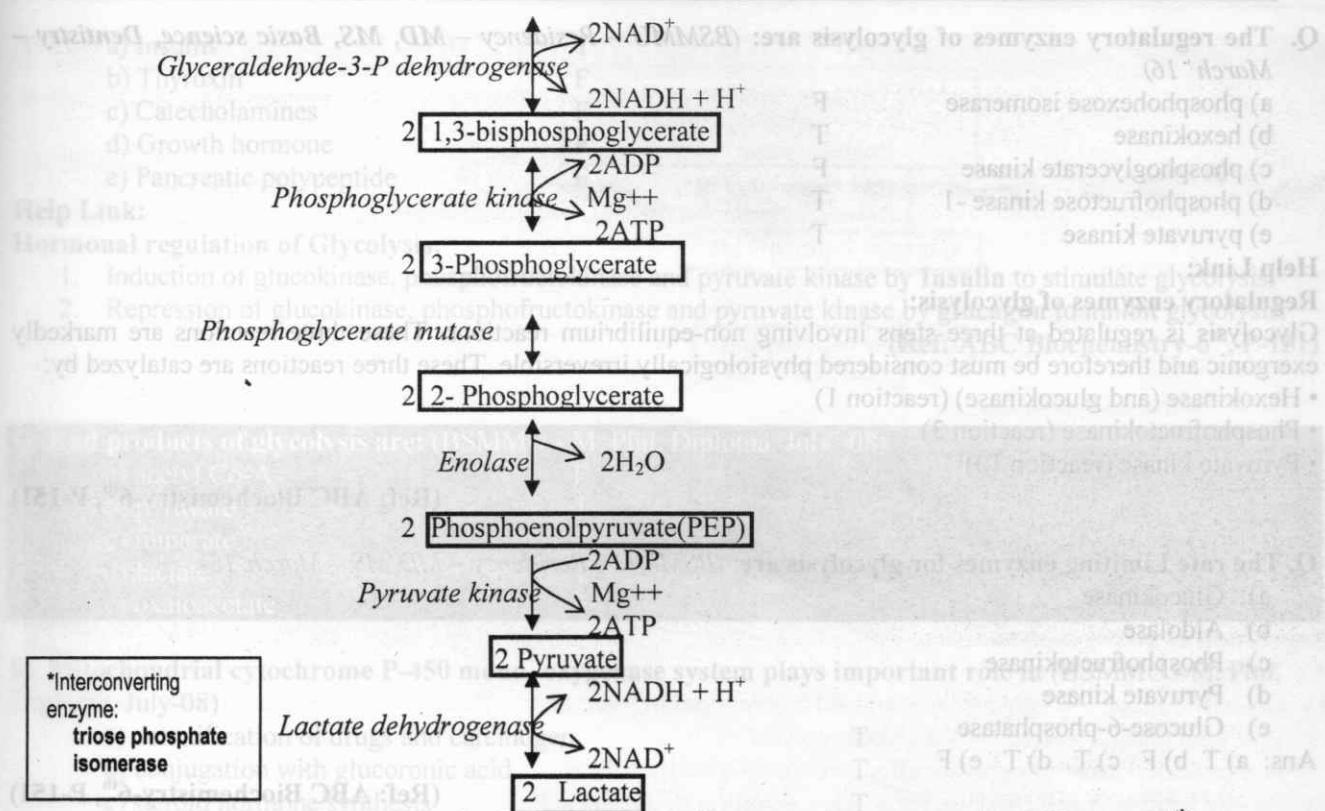


Fig: Pathway of glycolysis

(Ref: Harper-30<sup>th</sup>)**Q. Anaerobic glycolysis produces (BSMMU – Residency - Dentistry – March '19)**

- a) ATP
- b) lactate
- c) lactose
- d) acetyl CoA
- e) NAD

Ans. a) T b) T c) F d) F e) F

(Ref. Lippincott 7<sup>th</sup> + Harper 31<sup>st</sup> + ABC-5<sup>th</sup>, P-150-154)**Q. Anaerobic glycolysis is a valuable source of energy for (BSMMU – Residency - MD, MS, Basic Science, Dentistry - March '17)**

- a) cardiac muscle
- b) skeletal muscle during exercise
- c) RBC
- d) smooth muscle
- e) leucocytes

Ans. a) F b) T c) T d) F e) F

**Help Link:****Importance of anaerobic glycolysis**

- To generate small amount of ATP for basic activity of Na-K<sup>+</sup> pump in RBC
- Skeletal muscle can survive anoxic episodes
- Cardiac muscle use fatty acid as a metabolic fuel and can not sustain anoxic episodes.
- Neonate during delivery prevent hypoxic injury to muscle and other organ to escape cong. Defects.

(Ref: ABC Biochemistry-6<sup>th</sup>, P-150)

**Q. The regulatory enzymes of glycolysis are:** (BSMMU – Residency – MD, MS, Basic science, Dentistry – March '16)

- a) phosphohexose isomerase
- b) hexokinase
- c) phosphoglycerate kinase
- d) phosphofructose kinase -1
- e) pyruvate kinase

F  
T  
F  
T  
T

Ans: e) T (Ref: ABC Biochemistry-6<sup>th</sup>, P-151)

**Help Link:** Regulatory enzymes of glycolysis

Glycolysis is regulated at three steps involving non-equilibrium reactions. These three reactions are markedly exergonic and therefore must be considered physiologically irreversible. These three reactions are catalyzed by:

- Hexokinase (and glucokinase) (reaction 1)
- Phosphofructokinase (reaction 3)
- Pyruvate kinase (reaction 10)

(Ref: ABC Biochemistry-6<sup>th</sup>, P-151)

**Q. The rate Limiting enzymes for glycolysis are:** (BSMMU – Residency – MD/MS – March '13)

- a) Glucokinase
- b) Aldolase
- c) Phosphofructokinase
- d) Pyruvate kinase
- e) Glucose-6-phosphatase

Ans: a) T b) F c) T d) T e) F

(Ref: ABC Biochemistry-6<sup>th</sup>, P-151)

**Q. Anaerobic glycolysis occurs in:** (BSMMU-M. Phil, Diploma(Non-Residency)-IIJu, DMC & others-MD-IIJu)

- a) occurs in cells without mitochondria
- b) is not important for RBC
- c) produces ATP
- d) produces lactate
- e) produces NADPH

T  
F  
T  
T  
F

**HELP LINK:**

**■ Anaerobic glycolysis:** Oxidation of glucose in absence of oxygen is called anaerobic glycolysis.

**■ Sites:**

- Mature RBC
- Leukocytes
- Lens & cornea of the eyes
- Renal medulla
- Testes

These tissues contain a few or no mitochondria. As the enzymes of the respiratory chain oxidation are located in the mitochondria, therefore no respiratory chain oxidation occurs in these tissues.

Products of Anaerobic glycolysis (from 1 mole of glucose) are:

- 2 moles of lactate
- 2 ATP in substrate level oxidation

**Q. Anaerobic glycolysis occurs in:** (BSMMU – MD/MS (Residency) - January, 2011, 08)

- a) testes
- b) kidney medulla
- c) brain
- d) liver
- e) red blood cells

T  
T  
T  
F  
T

**Q. Hormones causing glycolysis:** (BSMMU – MD – January, 2010)

- a) Insulin  
 b) Thyroxin  
 c) Catecholamines  
 d) Growth hormone  
 e) Pancreatic polypeptide

T	
F	
F	
F	
F	

**Help Link:****Hormonal regulation of Glycolysis:**

1. Induction of glucokinase, phosphofructokinase and pyruvate kinase by **Insulin** to stimulate glycolysis.
  2. Repression of glucokinase, phosphofructokinase and pyruvate kinase by **glucagon** to inhibit glycolysis.
- (Ref: ABC Biochemistry-6<sup>th</sup>, P-151)

**Q. End products of glycolysis are:** (BSMMU - M. Phil, Diploma, July' 08)

- |                 |   |
|-----------------|---|
| a) acetyl-Co-A  | F |
| b) pyruvate     | T |
| c) fumarate     | F |
| d) lactate      | T |
| e) oxaloacetate | F |

**Q. Mitochondrial cytochrome P-450 mono-oxygenase system plays important role in** (BSMMU - M. Phil, Diploma, July-08)

- |   |   |
|---|---|
| a) detoxification of drugs and carcinogen   | T |
| b) conjugation with glucuronic acid         | T |
| c) steroid hormone synthesis                | T |
| d) 1,25 dihydroxychole calciferol synthesis | T |
| e) bile acid synthesis                      | F |

**Q. Anaerobic oxidation of glucose leads to -** (BSMMU – MD - January, 2007)

- |                               |   |
|-------------------------------|---|
| a) Lactic acid overproduction | T |
| b) Metabolic acidosis         | T |
| c) Raised plasma anion gap    | T |
| d) Hypokalemia                | F |
| e) Hypouricemia               | F |

## GLYCOGENOLYSIS

■ **Definition:** Breakdown of glycogen to glucose (in liver) or glucose-6-phosphate (in muscle) is called glycogenolysis.

■ **Substrate:** Glycogen

■ **Product:** 1. Glucose (in liver) 2. Glucose-1-phosphate (in muscle)

■ **Site:** Liver & skeletal muscle

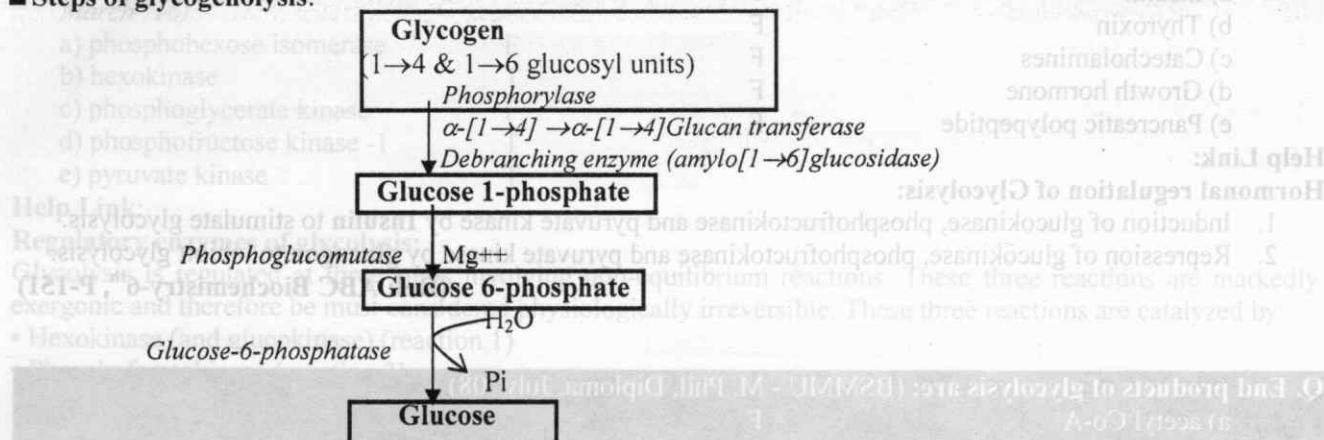
■ **Compartment:** Cytoplasm      ■ **Nature:** Catabolic      ■ **Rate limiting enzyme:** Glycogen phosphorylase

■ **Coenzyme needed:** Pyridoxal phosphate

■ **ATP involvement:** No ATP is used or produced.

■ **Regulation:** Stimulated by glucagon, catecholamine, AMP & inhibited by insulin, ATP, Glucose 6-P.

■ Steps of glycogenolysis:



These steps occur in hepatic glycogenolysis. But in muscle, as the enzyme glucose-6-phosphatase is absent, glucose 6-phosphate can not be converted into glucose.

(Ref: Harper-30<sup>th</sup>, P-178)

**Regulation of glycogenolysis:**

**A) Allosteric regulation:**

- In well-fed state → ↑ glucose 6-P and ATP level (and in liver, also ↑ free glucose) → allosterically inhibit glycogen phosphorylase → No glycogenolysis.  
But in fasting state → opposite effects occur → glycogenolysis.
- During muscle contraction → ↑ Ca<sup>2+</sup> concentration in muscle cell → Ca<sup>2+</sup> binds with calmodulin → (+) glycogen phosphorylase → ↑ glycogenolysis in muscle.
- ↑AMP in muscle → (+) glycogen phosphorylase → ↑ glycogenolysis in muscle.

**B) Hormonal regulation:**

- Epinephrine, Norepinephrine, glucagon → ↑cAMP → inhibition of glycogen synthase and activation of phosphorylase → ↑ glycogenolysis.
- Insulin → ↓cAMP → Activation of glycogen synthase and inhibition of phosphorylase → No glycogenolysis.

(Ref: Lippincott-7<sup>th</sup>, P-131-134)

**Question Bank**

**Q. Glycogen phosphorylase is activated by (BSMMU – Non-Residency – MD, MS, Basic Science & Dentistry – July' 17)**

- a) glucagon
- b) epinephrine
- c) ATP
- d) insulin
- e) AMP

Ans. a) T b) T c) F d) F e) F

**Help link:** Stimulated by glucagon, catecholamine, AMP & inhibited by insulin, ATP, Glucose 6-P.

(Ref: ABC biochemistry-4<sup>th</sup>, P-169)

**Q. Hormones causing glycolysis: (BSMMU – MD – January, 2010)**

## GLUCONEOGENESIS

■ **Definition:** Synthesis of glucose from non-carbohydrate sources is called gluconeogenesis.

■ **Substrate:**

1. Glycerol (derived from triglyceride hydrolysis)
2. Intermediate products of glycolysis (e.g. dihydroxy acetone phosphate)
3. Lactate
4. Glucogenic amino acid
5.  $\alpha$  - ketoacids: • Pyruvate • Oxaloacetate •  $\alpha$ -ketoglutarate • Propionate
6. Krebs cycle intermediates via oxaloacetate

■ **Product:** Glucose

■ **Sites:** 1. Liver- normally 90% of total gluconeogenesis.

2. Kidney- 10% or less 10%.

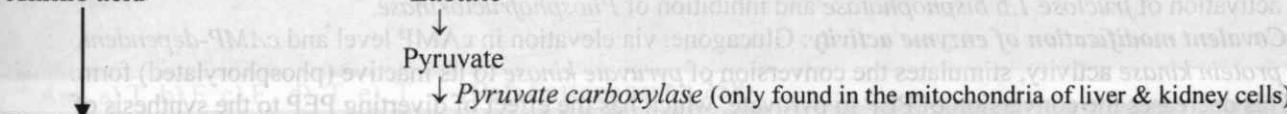
[N.B. Intestinal epithelium-not more than 5%, if it precipitates vigorously. But normally it does not contribute at all]

**ATP requirement:** 6 ATP is needed to make one glucose from two pyruvate or two lactate.

■ **Compartment:** Cytoplasm (mainly), but partly mitochondria

■ **Steps of gluconeogenesis:**

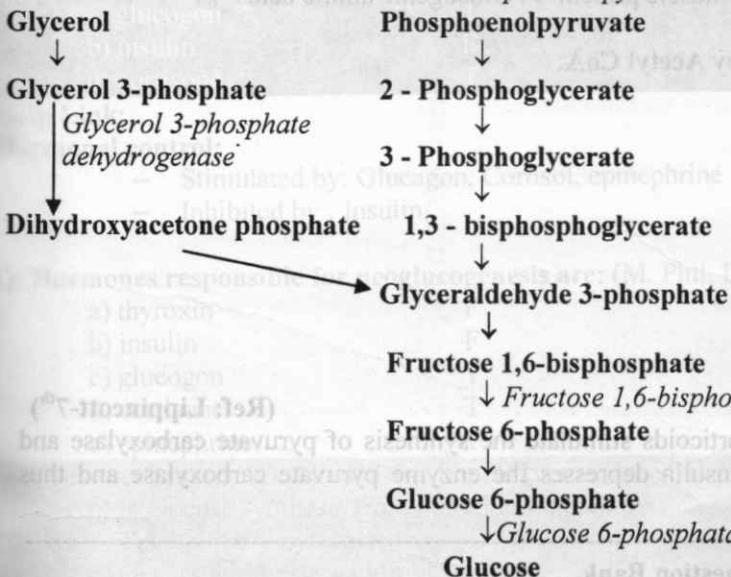
Amino acid



Krebs cycle intermediates → Oxaloacetate (→ converted into malate → comes to

cytosol → reoxidized into oxaloacetate)

↓ Phosphoenol pyruvate carboxykinase



For every mole of glucose synthesized from pyruvate, 6 ATP are required and from glycerol, 2 ATP is produced.

(Ref: Harper-30<sup>th</sup>)

■ **Biomedical importance:**

1. Meets the needs of the body for glucose when carbohydrate is not available in sufficient amount from diet or from glycogen reserves.
2. Failure of gluconeogenesis is usually fatal. Hypoglycaemia causes brain dysfunction which can lead to coma & death.
3. Maintains the level of intermediates of the TCA cycle.

4. Clears lactate produced by muscle & RBC and glycerol produced by adipose tissue. If not, then  $\downarrow$  pH & causes acidosis  
 5. Maintains blood glucose conc. during fasting and starvation & in between meals.

#### Important information:

- The amino acids which participate in the formation of glucose - the glucogenic amino acids. These amino acids are first converted to  $\alpha$ -keto acids.
- **Glucogenic amino acids:** Amino acids whose catabolism yields  $\alpha$ -keto acids, one of the intermediates of TCA cycle.
  1. **Essential A.A:** Tryptophane, Methionine, Valine, Threonine, Phenyl alanine, Iso-leucine, Arginine, Histidine
  2. **Non-essential:** Serine, proline, cysteine, Asparagine, Aspartate, Glutamate, Glutamine, Tyrosine.
- **Bisphosphate** = attached by one bond.
- **Biphosphate** = attached by two bonds.
- Hypoglycemia is more dangerous than hyperglycaemia.

#### ■ Regulation of Gluconeogenesis:

- A. **Glucagon:** It stimulates gluconeogenesis by 2 mechanisms-
  1. **Changes in allosteric effectors:** Glucagon lowers the level of fructose 2,6-bisphosphate, resulting in activation of fructose 1,6 bisphosphatase and inhibition of Phosphofructokinase.
  2. **Covalent modification of enzyme activity:** Glucagone, via elevation in cAMP level and *cAMP-dependent protein kinase* activity, stimulates the conversion of *pyruvate kinase* to its inactive (phosphorylated) form. This decreases the conversion of PEP to pyruvate, which has the effect of diverting PEP to the synthesis of glucose.

#### B. Availability of substrate:

- $\downarrow$  Insulin  $\rightarrow$  Mobilization of amino acid from muscle protein  $\rightarrow$   $\uparrow$  Glucogenic amino acids  $\rightarrow$   $\uparrow$  Gluconeogenesis

#### C. Allosteric activation of pyruvate carboxylase by Acetyl CoA:

During starvation,

$\uparrow$  Lipolysis

$\downarrow$

$\uparrow$  Fatty acid

$\downarrow$   $\beta$  oxidation

$\uparrow$  Acetyl CoA

$\downarrow$  Activates

Pyruvate carboxylase

$\downarrow$

Pyruvate  $\rightarrow$  Oxaloacetate

(Ref: Lippincott-7<sup>th</sup>)

The hormones glucagon, epinephrine, and glucocorticoids stimulate the synthesis of pyruvate carboxylase and thus enhance gluconeogenesis. But the hormone insulin depresses the enzyme pyruvate carboxylase and thus reduces gluconeogenesis.

#### Question Bank

Q. Glucogenic amino acids are (BSMMU – Non-Residency – MD, MS, Paediatrics, Basic Science – July '19)

- a) lysine
- b) leucine
- c) alanine
- d) glycine
- e) serine

Ans. a) F (Absolute ketogenic) b) F (Absolute ketogenic) c) T d) T e) T

(Ref: ABC Biochemistry-6<sup>th</sup>, P-55)

**Help link:**

- **Absolute Glucogenic amino acid**
  - **Essential AA:**
    - methionine, valine, threonine, , arginine, Histidine
  - **Non essential AA:**
    - Alanine, Aspartic acid, Glutamic acid, Serine, Glycine, proline, cysteine, asparagine, glutamine,
- **Absolute ketogenic:**
  - **Essential AA:**
    - Leucine, Lysine
- **Both glucogenic and ketogenic:**
  - **Essential:**
    - Phenylalanine, Tryptophan, Isoleucine,
  - **Non essential AA:**
    - Tyrosine

(Ref: ABC Biochemistry-6<sup>th</sup>, P-55)**Q. Precursors of gluconeogenesis are (BSMMU – Non-Residency – MD, MS, Basic Science & Dentistry – July' 17)**

- a) lactate  
b) leucine  
c) lysine  
d) glycerol  
e) pyruvate

Ans. a) T b) F c) F d) T e) T (Ref: Sattanarayon 258)

**Q. Hormones responsible for neoglucogenesis are: (BSMMU – MD/MS (Residency) – 11Ja)**

- |                |   |
|----------------|---|
| a) thyroxin    | F |
| e) epinephrine | T |
| c) glucagon    | T |
| b) insulin     | F |
| d) cortisone   | T |

**Help Link:****Hormonal control:**

- Stimulated by: Glucagon, Cortisol, epinephrine
- Inhibited by : Insulin

**Q. Hormones responsible for neoglucogenesis are: (M. Phil, Diploma-07July)**

- |                |   |
|----------------|---|
| a) thyroxin    | F |
| b) insulin     | F |
| c) glucagon    | T |
| d) cortisone   | T |
| e) epinephrine | T |

**Q. Gluconeogenesis: (BSMMU – M. Phil, Diploma, July-06)**

- |  |   |
|--|---|
| a) Is glucose synthesis from non-glucose precursor | T |
| b) Take place in cytosol                           | T |
| c) Occurs during starvation                        | T |
| d) Enzyme has no role in their process             | F |
| e) Insulin has got no role over it                 | F |

**Q. Substrate for gluconeogenesis in starvation are - (BSMMU – M. Phil, Diploma July, 2006)**

- |                  |   |
|------------------|---|
| a) Amino acids   | T |
| b) Glycerol      | T |
| c) Fatty acids   | F |
| d) Acetyl- CoA   | T |
| e) Ketone bodies | T |

**Q. Hormones associated with glucose metabolism are:** (BSMMU – M. Phil, Diploma July, 2004)

- |                   |   |
|-------------------|---|
| A. Glucagon       | T |
| B. ADH            | F |
| C. Growth hormone | T |
| D. Parathormone   | F |
| E. Insulin        | T |

**HELP LINK:**

**Hormones involved in glucose metabolism:**

Hormone	Main actions	Main effect
<b>1. Insulin</b>	↑Glucose uptake from blood to all cells of body ↑Glycolysis ↑Glycogenesis ↓Glycogenolysis ↓Gluconeogenesis	↓ Blood glucose
<b>2. Glucagon</b>	↑Glycogenolysis ↑Gluconeogenesis	↑ Blood glucose
<b>6. Thyroid hormones</b>	↑Glycogenolysis ↑Gluconeogenesis	
<b>3. Glucocorticoids</b>	↑Glycogenolysis ↓Glucose uptake	
<b>4. Growth hormone</b>	↓Glucose uptake & utilization	↑ Blood glucose
<b>5. Epinephrine</b>	↑Glycogenolysis	
<b>7. ACTH</b>	↑Gluconeogenesis	

**Q. Entry of glucose into muscle is** (BSMMU - M. Phil, Diploma, July-04)

- A. Increased by epinephrine
- B. Inversely proportional to plasma glucose concentration
- C. Increased by insulin
- D. Increased by the transport of free fatty acids into muscle
- E. Increased by exercise

**Q. End Products of glycolysis may be : -** (MD/MS (DMC)-03Ja)

- a) Pyruvate
- b) Acetyl COA
- c) Lactate
- d) Oxaloacetate
- e) Phosphoenolpyruvate

**Storage disease**

**Q. Abnormal storage of glycogen results from deficiency of** (BSMMU – Residency - MD, MS, Basic Science - March' 17/ March' 16)

- a) phosphorylase
- b) lactate dehydrogenase
- c) phosphofructokinase
- d) amylo-1,6 glucosidase
- e) glycogen synthetase

**Ans.** a) T b) F c) T d) T e) T

**Help link:**

**■ Glycogen storage diseases:** Genetic diseases that result from a defect in an enzyme required for either glycogen synthesis or degradation.

(Ref: Harper-30<sup>th</sup>, P-179)

## ■ Various types of glycogen storage diseases:

	Name of disease	Enzyme deficient	Characteristics
<b>0</b>	-	Glycogen synthase	Hypoglycemia, hyperketonemia, early death
<b>Ia</b>	Von Gierk's disease	Glucose 6-phosphatase	Glycogen accumulation in liver and renal tubule cells. Hypoglycemia, lactic acidosis, ketosis, hyperlipidemia
<b>Ib</b>	-	Endoplasmic reticulum glucose 6-phosphate transporter	As type Ia; neutropenia and impaired neutrophil function leading to recurrent infections.
<b>II</b>	Pompe's disease	Lysosomal $\alpha$ 1 $\rightarrow$ 4 and $\alpha$ 1 $\rightarrow$ 6 glucosidase (acid maltase)	Accumulation of glycogen in lysosomes; juvenile onset variant, muscle hypotonia, death from heart failure by age 2; adult onset variant, muscle dystrophy.
<b>IIIa</b>	Limit dextrinosis, Forbes or Cori's disease	Liver and muscle debranching enzyme	Fasting hypoglycaemia, hepatomegaly in infancy, accumulation of characteristic branched polysaccharide (limit dextrin), muscle weakness
<b>IIIb</b>	Limit dextrinosis	Liver debranching enzyme	As type IIIa, but no muscle weakness
<b>IV</b>	Amylopectinosis, Andersens' disease	Branching enzyme	Hepatosplenomegaly, accumulation of polysaccharide having few branch points. Death from heart or liver failure before age 5.
<b>V</b>	Myophosphorylase deficiency McArdles' syndrome	Muscle phosphorylase	Poor exercise tolerance; muscles glycogen abnormally high (2.5 - 4%). Blood lactate very low after exercise.
<b>VI</b>	Hers' disease	Liver phosphorylase	Hepatomegaly, accumulation of glycogen in liver, mild hypoglycaemia, generally good prognosis.
<b>VII</b>	Tarui's disease	Phosphofructokinase in muscles & RBC.	As for type V, and also hemolytic anaemia
<b>VII</b> <b>I</b>	-	Liver phosphorylase kinase	As for type VI
<b>IX</b>	-	Liver and muscle phosphorylase kinase	As for type VI
<b>X</b>	-	cAMP-dependant protein kinase A	Hepatomegaly, accumulation of glycogen in liver

(Ref: Harper-30<sup>th</sup>, P-179)**Protein metabolism****Q. In oxidative deamination (BSMMU – Non-Residency – MD/MS, Basic science – July '14)**

- a) pyruvate is substrate
  - b) mitochondria is involved
  - c) NH<sub>3</sub> is removed from amino acid
  - d) nature of the pathway is amphibolic
  - e) carbon skeleton of amino acid is generated
- Ans. a) F b) T c) T d) F e) T

**Help link:**

■ **Definition:** Oxidative deamination is the liberation of free ammonia from the amino group of amino acids coupled with oxidation. The purpose of oxidative deamination is to provide ammonia and  $\alpha$ -ketoacid.

Or,

The process in which  $\alpha$ -amino group from an amino acid is cleaved as ammonia and the amino acid is transformed into the corresponding  $\alpha$ -ketoacid is called oxidative deamination.

■ **Site:** Liver, kidney, heart, skeletal muscle.

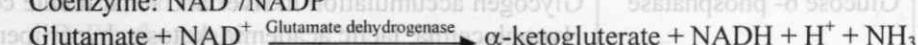
■ **Substrate:** Amino acid (glutamate, alanine)

■ **Product:** NH<sub>3</sub> and a keto acid ( $\alpha$  ketoglutarate)

■ **Enzyme:**

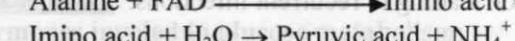
1. Glutamate dehydrogenase

Coenzyme: NAD<sup>+</sup>/NADP<sup>+</sup>



2. Amino acid oxidase

Alanine + FAD  $\xrightarrow{\text{Amino acid oxidase}}$



■ **Importance:**

- Formation of NH<sub>3</sub> which serves as a source of nitrogen in urea synthesis.
- Formation of  $\alpha$ -ketoacid which can enter into the central pathway of energy metabolism.
- Generate carbon skeleton of amino acid for catabolic purpose.

**Q. Catabolism of ketogenic amino acid produce:** (BSMMU – M. Phil, Diploma (Non-Residency)–March-2012, DMC & others – MD/MS – March-2012)

a) acetyl CoA

T

b)  $\beta$ -hydroxybutyryl CoA

F

c) acetone

T

d) acetoacetyl CoA

T

e) Serine

F

#### HELP LINK:

**Metabolic classification of amino acid (based on their catabolic fate):**

1. **Absolute glucogenic (glycogenic) amino acid:**

- These are the amino acids having carbon skeleton that possesses metabolic potential to produce glucose.
- In fact they initially produce pyruvate or intermediates of TCA cycle from which later on, glucose is produced. e.g.- Gly, Ala, Ser, Cys, Pro, Glu, Gln, Asp, Asn, Arg, His, Met, Thr, Val.

2. **Absolute ketogenic amino acid:**

- These are the amino acids having carbon skeleton that possesses metabolic potential to produce ketone body.
- In fact they initially produce acetyl CoA or aceto acetyl CoA from which later on, ketone body is produced. e.g.- Leu (Leucine), Lys (Lysine).

3. **Both glucogenic and ketogenic amino acid:**

- These are the amino acids having carbon skeleton that possesses metabolic potential to produce both glucose and ketone body.
  - In fact they initially produce acetyl CoA or aceto acetyl CoA along with pyruvate to TCA cycle intermediates and then produce ketone body and glucose.
- e.g.- The (Phenyl alanine), Tyr (Tyrosine), Trp (Tryptophan), Ile (Isoleucine)

All ketogenic amino acids are essential amino acid except the Try (tyrosine).

## Ammonia

**Q. Sources of ammonia are** (BSMMU –Residency - MD/MS, Basic science, Paediatrics – March' 19)

- purines
- phosphatidic acid
- glutamine
- amines
- glycosaminoglycans

Ans. a)T b) F c) T d) T e) F

(Ref. Lippincott-7<sup>th</sup>, P-256-257)

**Q. Following are the sources of ammonia:** (BSMMU – M. Phil, Diploma (Non-Residency)–March-2012, DMC & others – MD/MS – March-2012)

- |                       |   |
|-----------------------|---|
| a) purines            | T |
| b) phospholipids      | F |
| c) glycosaminoglycans | F |
| d) glutamine          | T |
| e) amines             | T |

**HELP LINK:**

■ **Sources of Ammonia:**

1. Amino acid
2. From glutamine: In mucosal cells of kidney and intestine, glutamine comes from blood and dietary protein. By renal & intestinal  $\text{NH}_3$  is liberated.  
Glutamine *Glutaminase*:  $\text{Glutamate} + \text{NH}_4^+$
3. From bacterial action in the intestine: Urea formed in the liver, through blood goes to intestine where by bacterial urease, it is degraded to  $\text{NH}_3$ .
4. Venous nitrogen containing amines: Amines are obtained from diet & monoamine such as hormones & neurotransmitters gives amines by amine oxidase.
5. From purines & pyrimidines: Catabolism of purines & pyrimidines releases ammonia.

(Ref: Lippincott-7<sup>th</sup>, P-256)

**Q. Sources of ammonia are:** (BSMMU – MD – January, 2010)

- |                                     |   |
|-------------------------------------|---|
| a) purine and pyrimidine catabolism | T |
| b) glycerol                         | F |
| c) amino acid                       | T |
| d) succinyl CoA                     | F |
| e) fumarate                         | F |

**Q. The major mechanism for ammonia removal is:** (MD/MS (DMC)-06Ja)

- |                                      |   |
|--------------------------------------|---|
| a. By glutamine formation in brain   | T |
| b. Urea formation in liver           | T |
| c. By creatinine formation in muscle | F |
| d. By oxalate formation ubiquitously | F |
| e. By uric acid formation in kidney  | F |

**Urea cycle**

**Q. Regarding Urea cycle (BSMMU – MD - 02Ja)**

- |  |   |
|--|---|
| a) It is a synthetic process                   | T |
| b) It is a catabolic process                   | F |
| c) Two ATPs are required                       | F |
| d) One molecule of $\text{CO}_2$ is required.  | T |
| e) Whole reactions take place in liver cytosol | T |

**HELP LINK:**

The deamination of amino acids produces ammonia which is toxic. By the urea cycle, it is converted into urea, a non-toxic compound which is transported via blood to the kidneys and excreted in the urine.

■ **Site:** Liver

■ **Steps of urea cycle:**

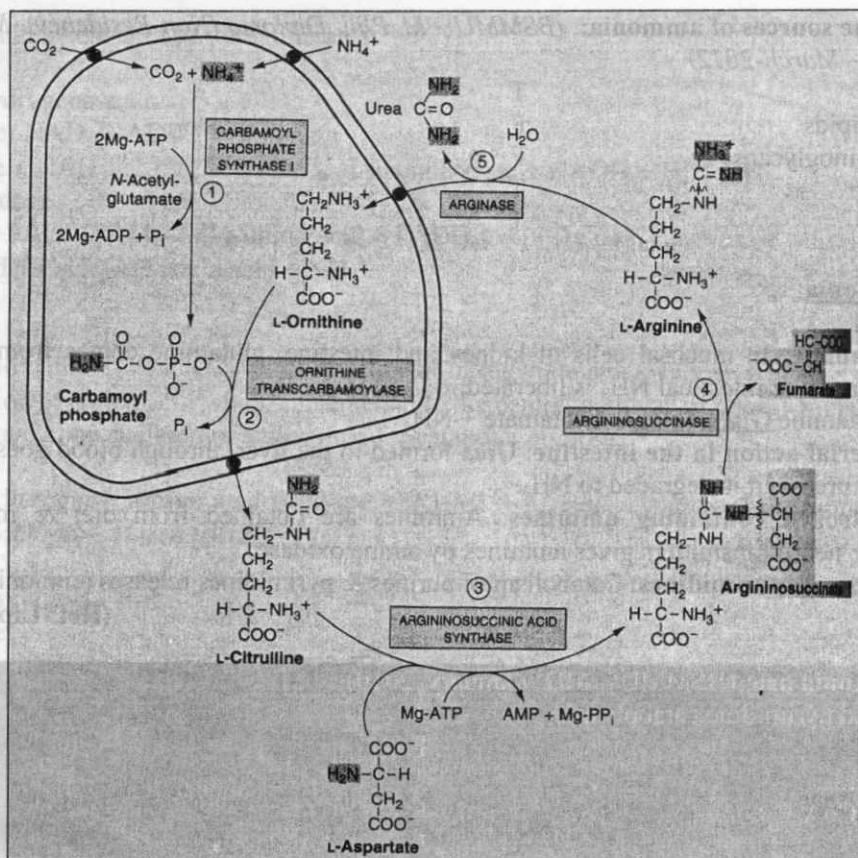


Fig: The urea cycle

(Ref: Harper-30<sup>th</sup>)

Synthesis of 1 mol of urea requires 3 mol of ATP.

**■ Importance:**

1. Detoxification of ammonia.
2. Formation of arginine which is used in protein synthesis.
3. Formation of fumarate is used in TCA cycle & gluconeogenesis.

## Lipid metabolism

Q. Fatty acid synthesis occurs primarily in (BSMMU –Residency - MD/MS, Basic science, Paediatrics – March '19)

- a) liver
- b) lactating mammary gland
- c) brain
- d) intestine
- e) kidney

Ans. a) T    b) T    c) T    d) F    e) T

(Ref. ABC of Biochemistry-5<sup>th</sup> + Satyanarayana-4<sup>th</sup>, P-302)**Help Link:****Lipogenesis/ Synthesis of Fatty acid:**

- ✓ **Substrate:** Acetyl CoA (2 carbon compound)
- ✓ **Product:** Palmitic acid(16 carbon compound)
- ✓ **Site:** Liver, Adipose tissue, Kidney, Brain, Lactating breast,
- ✓ **Compartment:** Cytoplasm
- ✓ **Nature:** Anabolic
- ✓ **Rate limiting enzymes:** Acetyl CoA Carboxylase
- ✓ **Co-enzyme needed:** NADPH provided by HMP shunt

✓ **ATP requirement:** 7 ATP needed to make one molecule palmitic acid

✓ **Speciality:** Reductive synthesis process

✓ **Hormonal control:** Insulin promotes acetyl CoA carboxylase to stimulate lipogenesis

✓ **Glucagon and Cathecholamine** inhibit acetyl CoA carboxylase to inhibit lipogenesis

(Ref. ABC of Biochemistry-6<sup>th</sup>, P-189)

**Q. Hormone-sensitive lipase is activated by (BSMMU-Residency – MD, MS, Basic Science – March' 18)**

- a) TSH
- b) ACTH
- c) nicotinic acid
- d) prostaglandin E<sub>1</sub>
- e) vasopressin

Ans. a) T b) T c) F d) F e) F

**Help Link:**

**Regulation of Hormone sensitive lipase(HSL):**

- Name is justified due to mostly controlled by hormone
- Lipase is present in an inactive form “b” and is activated by a cAMP dependent protein kinase to lipase “a”
- **Enhance the activity by**
  - Epinephrine (most effective)
  - Norepinephrine
  - Glucagon
  - Growth hormone
  - Cortisol
  - Thyroxine, TSH
  - ACTH
  - Caffeine
  - Also in fasting and stress
- **Inactivates lipase:**
  - Insulin, ADH, Oxytocin

(Ref: DM Vasudevan-7<sup>th</sup>, P-159)

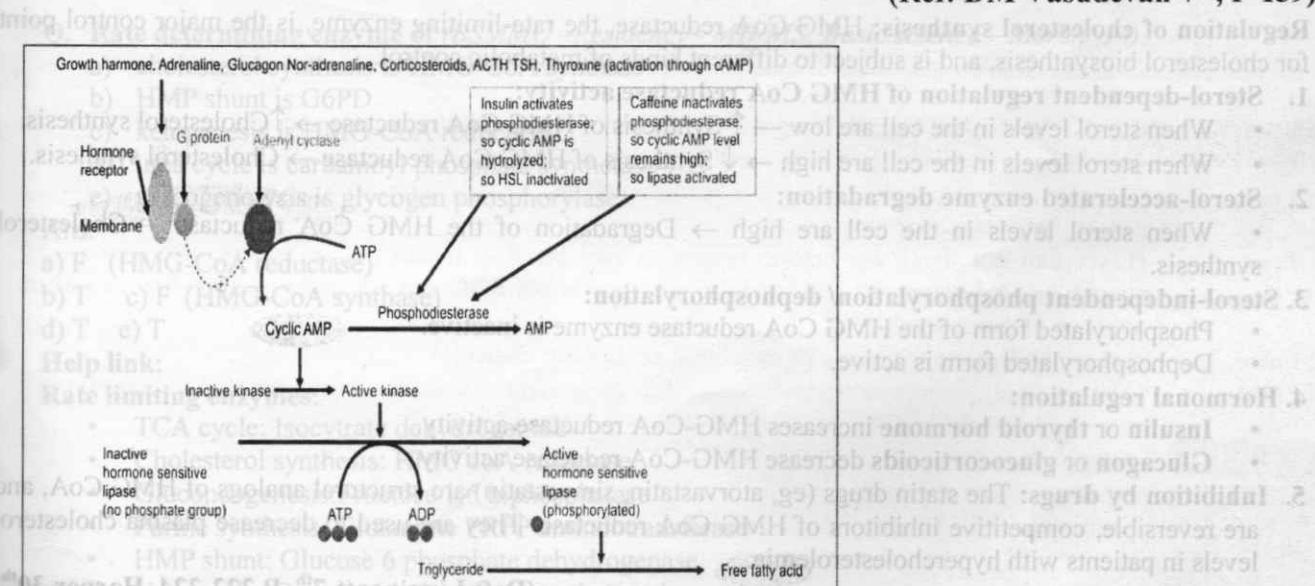


Fig. 12.16: Cascade activation of hormone sensitive lipase

(Ref: DM Vasudevan-7<sup>th</sup>, P-159)

Glycolysis: Phosphofructokinase

Fatty acid oxidation: Carnitine acyl transferase I

Glycogen synthesis: Glycogen synthetase

**Q. Hormone sensitive — lipase is activated by (BSMMU – Residency - MD, MS, Basic Science - March' 17)**

- a) ACTH
- b) nicotinic acid
- c) vasopressin
- d) TSH
- e) prostaglandin E<sub>1</sub>

**Ans.** a) T b) F c) F d) T e) F

**Helplink:** Epinephrine (most effective), nor-epinephrine, Glucagon, thyroxine, caffeine, ACTH enhance the activity of HSL.  
**(Ref: Sattanarayan-287)**

**Q. Hormone sensitive lipase is activated by (BSMMU – Residency – MD, MS, Basic science – March' 16)**

- |                     |   |
|---------------------|---|
| a) ACTH             | T |
| b) TSH              | T |
| c) Prostaglandia E1 | F |
| d) nicotinic acid   | F |
| e) vasopressin      | F |

**Help link:**

**Hormone sensitive lipase (HSL)** is the key enzyme in the regulation of lipid stores. It is the rate limiting enzyme in the degradation of triacylglycerol (TAG) to diacylglycerol (DAG) and free fatty acids (FFA). In addition, it has hydrolyzing activity against cholesterol esters.

**Q. Hormone sensitive lipase: (BSMMU - M. Phil, Diploma – July '10)**

- |  |   |
|--|---|
| a) is present in cell membrane                 | F |
| b) is activated by cAMP                        | T |
| c) activity is increased by prostaglandin E    | F |
| d) activity is decreased by insulin            | T |
| e) activity is increased by fasting and stress | T |

## Cholesterol metabolism

**Regulation of cholesterol synthesis:** HMG CoA reductase, the rate-limiting enzyme, is the major control point for cholesterol biosynthesis, and is subject to different kinds of metabolic control.

**1. Sterol-dependent regulation of HMG CoA reductase activity:**

- When sterol levels in the cell are low → ↑ Synthesis of HMG CoA reductase → ↑ Cholesterol synthesis.
- When sterol levels in the cell are high → ↓ Synthesis of HMG CoA reductase → Cholesterol synthesis.

**2. Sterol-accelerated enzyme degradation:**

- When sterol levels in the cell are high → Degradation of the HMG CoA reductase → Cholesterol synthesis.

**3. Sterol-independent phosphorylation/ dephosphorylation:**

- Phosphorylated form of the HMG CoA reductase enzyme is inactive.
- Dephosphorylated form is active.

**4. Hormonal regulation:**

- **Insulin or thyroid hormone** increases HMG-CoA reductase activity.
- **Glucagon or glucocorticoids** decrease HMG-CoA reductase activity.

**5. Inhibition by drugs:** The statin drugs (eg, atorvastatin, simvastatin) are structural analogs of HMG CoA, and are reversible, competitive inhibitors of HMG CoA reductase. They are used to decrease plasma cholesterol levels in patients with hypercholesterolemia.

**(Ref: Lippincott-7<sup>th</sup>, P-222-224, Harper-30<sup>th</sup>)**

Site: Liver, Adipose tissue, Kidney, Brain, Lactating breast

Initial enzyme involved to convert cholesterol to bile salt

Role: DMV and energy

✓ Nature: Anabolic

Initial enzyme involved to convert cholesterol to bile salt

✓ Rate limiting enzymes: Acetyl CoA Carboxylase

✓ Co-enzyme needed: NADPH provided by HMP shunt

**Q. Substances synthesized from cholesterol are (BSMMU – Residency – MD, MS, Basic Science – March' 18)**

- a) ketone bodies
- b) vitamin D
- c) cortisol
- d) prostaglandins
- e) bile acids

Ans. a) F b) T c) T d) F e) T

**Help Link:**

**Metabolic fates of cholesterol:**

- Synthesis of biological membrane
- Synthesis of steroid hormone
- Synthesis of 7-dehydrocholesterol and cholecalciferol (Vitamin D)
- Conversion to bile acid
- Conversion to neutral sterols (eg: coprostanol) by intestinal bacterial flora

(Ref: ABC Biochemistry-6<sup>th</sup>, P-78)

**Q. HMG - CoA reductase activity is inhibited by (BSMMU – Residency - MD, MS, Basic Science - March' 17)**

- a) insulin
- b) thyroid hormone
- c) glucagon
- d) glucocorticoids
- e) mevalonate

Ans. a) F b) F c) T d) T e) F

(Ref: Sattanarayan 4<sup>th</sup> page 313)

**Help link:**

**Hormonal control of HMG CoA**

- Inactivate HMG-CoA/ inhibited by
  - Glucagon
  - Glucocorticoids
- Potentiate cholesterol synthesis by enhancing HMG-CoA
  - Insulin
  - Thyroxine

**Q. Rate determining enzyme of (BSMMU – Residency - MD/MS, Basic science – March' 14)**

- a) cholesterol synthesis is HMG-CoA synthase
- b) HMP shunt is G6PD
- c) ketogenesis is HMG-CoA reductase
- d) urea cycle is carbamoyl phosphate synthetase-I
- e) glycogenolysis is glycogen phosphorylase

Ans.

- a) F (HMG-CoA reductase)
- b) T c) F (HMG-CoA synthase)
- d) T e) T

**Help link:**

**Rate limiting enzymes:**

- TCA cycle: Isocitrate dehydrogenase
- Cholesterol synthesis: HMG coA reductase
- Gluconeogenesis: Fructose 1,6 biphasphatase
- Purine synthesis: Glutamine PRPP amidotransferase
- HMP shunt: Glucose 6 phosphate dehydrogenase
- Urea cycle: Carbamoyl phosphate synthetase I
- Glycogenolysis: Glycogen phosphorylase
- Glycolysis: Phosphofructokinase 1
- Fatty acid oxydation: Carnitine acyltransferase 1
- Glycogen synthesis: Glycogen synthetase

- Ketogenesis: HMG CoA synthetase
- Fatty acid synthesis: Acetyl CoA carboxylase

**Q. Cholesterol is used in body for- (BSMMU – MD - 06Ja)**

- |  |                                     |
|--|-------------------------------------|
| A. Energy production                     | F                                   |
| B. Bile acid synthesis                   | T (And also synthesis of vitamin D) |
| C. Steroid hormone synthesis             | T                                   |
| D. Biological membrane synthesis         | T                                   |
| E. Intracellular 2nd messenger synthesis | F                                   |

**Q. Cholesterol is the precursor of – (MD/MS (DMC) – January, 2008)**

- |               |   |
|---------------|---|
| a) calcitriol | T |
| b) retinol    | F |
| c) cortisol   | T |
| d) tocopherol | F |
| e) bile acids | T |

**HELP LINK:**

**Cholesterol derivatives**

1. Steroid:
  - Glucocorticoids & mineralocorticoids
  - Androgens
  - Estrogens
  - Progesterone
2. Bile acids: • Cholic acid • Chenodeoxycholic acid
3. Neutral sterols:
  - 7-dehydrocholesterol → Vitamin D3
  - Coprosterol (Coprostanol)

**Q. Ketone bodies are - (BSMMU – M. Phil, Diploma July, 2006)**

- a) The source of energy for muscle
- b) Source of energy for brain in starvation
- c) Produced when acyl-CoA exceeds oxidizing capacity of liver
- d) The cause of metabolic alkalosis in diabetes
- e) Insoluble in aqueous solution

Ans.

- a) **True** (Ketone bodies are the preferred energy substrate of the extrahepatic tissues like heart, skeletal muscle, kidney and brain during starvation)
- b) **True** (Brain can use ketone bodies as fuel because they can cross the blood brain barrier. Fatty acids can not cross the blood brain barrier)
- c) **True** (Liver can not itself use ketone bodies as fuel because it can not reconvert acetoacetate to succinyl coA by enzyme acetoacetyl CoA transferase. RBC can not utilize ketone bodies due to absence of mitochondria)
- d) **False** (ketone bodies are the cause of metabolic acidosis in diabetes)
- e) **False** (They are soluble in aqueous solution and therefore do not need to be incorporated in lipoproteins or carried by albumin as do the other lipids)

**HELP LINK:** Ketone bodies are:

- Acetoacetate (Acetoacetic acid)
- $\beta$ -hydroxybutyrate ( $\beta$ -hydroxy butyric acid) and
- Acetone

**■ Most stable ketone bodies:**

- Acetoacetate (Acetoacetic acid) •  $\beta$ -hydroxybutyrate ( $\beta$ -hydroxy butyric acid) and

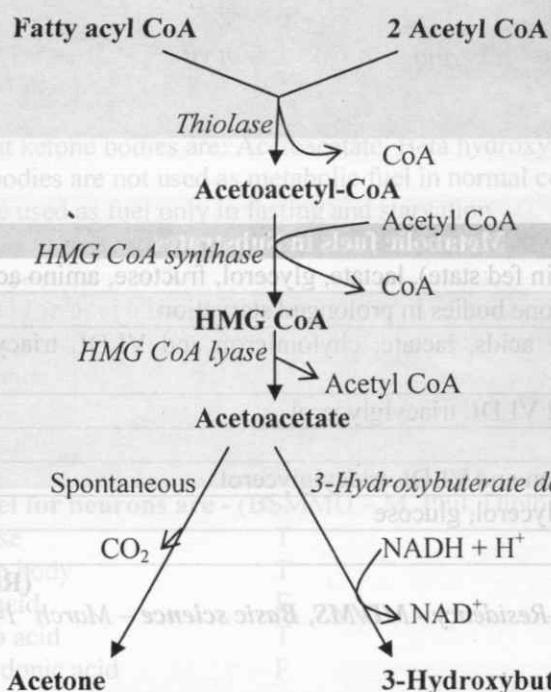
Acetone is volatile, so it is not stable. It is the most unstable form of ketone bodies. When it is heated, it becomes abolished.

**■ Ketone bodies are continuously produced in our body to produce energy.**

■ **Ketogenesis:** Formation of ketone bodies in the body is called ketogenesis.

■ **Site:** Liver (only). ■ **Compartment:** Mitochondria.

■ **Steps of ketogenesis:**



**Fig: Pathway of ketogenesis**

(Ref: Lippincott-7<sup>th</sup>)

■ **Sources of ketone bodies:** Acetyl CoA which is formed from

- Fatty acids
- Ketogenic amino acids i.e. leucine, lysine etc.

## Metabolic fuel

Q. Ketone bodies are metabolic fuels for (BSMMU-Residency – MD, MS, Basic Science – March '18)

- skeletal muscle
- cardiac muscle
- red blood cells
- brain
- liver

Ans. a) T b) T c) F d) T e) F

(Ref. ABC Biochemistry Page-228)

Help Link:

Useable fuel profile of major tissues in different metabolic states

Tissue	Well fed state	Fasting	Short starvation	Prolonged starvation
Brain	Glucose	Glucose,	Glucose,	Ketone body
Heart	Fatty acid	Fatty acid	Fatty acid,	Ketone body Fatty acid,
Skeletal muscle	Glucose	Fatty acid	Fatty acid, Ketone body	Fatty acid,
Liver	Fatty acid, Glucose, Lactate	Fatty acid	Fatty acid	Fatty acid,

(Ref. ABC Biochemistry-6<sup>th</sup>, P-231)

**Q. Energy source of cardiac muscle in the fasting state are (BSMMU – Non-Residency – MD, MS, Basic Science & Dentistry – July '17)**

- a) glucose
- b) amino acid
- c) fatty acid
- d) glycerol
- e) ketone bodies

Ans. a) F b) F c) T d) F e) F

**HELP LINK:**

Organ	Metabolic fuels in Substrates
Liver	Free fatty acids, glucose (in fed state), lactate, glycerol, fructose, amino acids, alcohol
Brain	Glucose, amino acids, ketone bodies in prolonged starvation.
Heart	Ketone bodies, free fatty acids, lactate, chylomicron and VLDL triacylglycerol, some glucose.
Adipose tissue	Glucose, chylomicron and VLDL triacylglycerol
Fast twitch muscle	Glucose, glycogen
Slow twitch muscle	Ketone bodies, chylomicron and VLDL triacylglycerol
Kidney	Free fatty acids, lactate, glycerol, glucose
Erythrocytes	Glucose

(Ref: Harper-30<sup>th</sup>)

**Q. During fasting preferred fuel of (BSMMU – Residency - MD/MS, Basic science – March '14)**

- a) brain is glucose
- b) adipose tissue is ketones
- c) cardiac muscle is fatty acids and ketones
- d) liver is glucose and amino acids
- e) red blood cells is glucose

Ans. a) T b) F c) F (only fatty acid, fatty acid and ketone are used for short and prolonged starvation) d) F (fasting in fatty acid) e) T

(Ref. ABC Biochemistry-6<sup>th</sup>, P-231)

**Q. Following tissues use ketone bodies for energy: (BSMMU – Residency – MD/MS – March '13)**

- a) Brain
- b) Red blood cells
- c) Skeletal muscles
- d) Liver
- e) cardiac muscle

Ans: a) T b) F c) T d) F e) T

(Ref. ABC Biochemistry-6<sup>th</sup>, P-231)

**Q. The following tissue utilize fatty acid as a source of energy: (BSMMU – MD/MS (Residency) - 11Ja)**

- |                    |   |
|--------------------|---|
| a) heart           | T |
| b) adrenal medulla | F |
| c) RBC             | F |
| d) skeletal muscle | T |
| e) brain           | F |

**HELP LINK:**

Brain and other nervous tissue, erythrocytes, and adrenal medulla cannot use plasma free fatty acids as fuel, regardless of the blood levels of fatty acid (fatty acids cannot cross the blood brain barrier, and RBC contains no mitochondria)

**Q. Metabolic fuel for neuron are:** (BSMMU – MD/MS (Residency) – January, 2010)

- |                              |   |
|------------------------------|---|
| a) Glucose                   | T |
| b) Acetoacetate              | T |
| c) $\beta$ -hydroxy butyrate | T |
| d) Acetone                   | F |
| e) fatty acid                | F |

**Help Link:**

- ✓ Important ketone bodies are: Acetoacetate, Beta hydroxybutyrate and Acetone.
- ✓ Ketone bodies are not used as metabolic fuel in normal condition.
- ✓ These are used as fuel only in fasting and starvation.
- ✓ Out of three ketone bodies only acetoacetate and Beta hydroxybutyrate work as metabolic fuel.

(Ref. ABC Biochemistry-6<sup>th</sup>, P-135)

**Q. Metabolic fuel for neurons are:** (BSMMU – MD - January, 2008)

- |                  |   |
|------------------|---|
| a) glucose       | T |
| b) fatty acid    | F |
| c) ketone bodies | T |
| d) amino acid    | T |
| e) acetone       | F |

**Q. Metabolic fuel for neurons are -** (BSMMU – M. Phil, Diploma July, 2005)

- |                     |   |
|---------------------|---|
| A. glucose          | T |
| B. ketone body      | T |
| C. fatty acid       | F |
| D. amino acid       | T |
| E. arachidonic acid | F |

**HELP LINK:**

**■ Metabolic fuels for brain:**

1. Glucose
2. Ketone bodies

**■ Metabolic fuels for heart:**

1. Glucose
2. FFA
3. Ketone bodies

**■ Metabolic fuels for skeletal muscle:**

1. Fatty acids
2. Ketone bodies

**Q. Metabolic fuel for neuron are-** (BSMMU – MD - January, 2007)

- |                |   |
|----------------|---|
| a) Glucose     | T |
| b) Ketone body | T |
| c) Fatty acid  | F |
| d) Amino acid  | T |
| e) Methionine  | F |

**Q. Metabolic fuel for neurons are-** (BSMMU – MD - 06Ja)

- |                  |   |
|------------------|---|
| A. Glucose       | T |
| B. Ketone bodies | T |
| C. Acetone       | F |
| D. Fatty acid    | F |
| E. Amino acid    | T |

**Q. Metabolic pathways found in RBC are-** (BSMMU – MD - 06Ja)

- |                    |   |
|--------------------|---|
| A. Glycolysis      | T |
| B. HMP shunt       | T |
| C. Ketogenesis     | F |
| D. Gluconeogenesis | F |

E. Fatty acid synthesis

F (There is another metabolic pathway present in R.B.C. called 'Rapport-Luebering shunt' which provides 2,3 DPG)

**Q. Which of the following can play a role in energy generation? (BSMMU – MD - 00Ja)**

- |                         |   |
|-------------------------|---|
| A. Glucose              | T |
| B. Amino acids.         | T |
| C. Fatty acids.         | T |
| D. Lactate and ketones. | T |
| E. Vit. C               | F |

## Genetics

**Q. Post translational modifications are (BSMMU – Residency - MD/MS, Basic science, Paediatrics – March' 19; Non-Residency – MD, MS, Basic Science & Dentistry – July' 17)**

- a) limited proteolysis
- b) hydroxylation
- c) splicing
- d) glycosylation
- e) excision of 3' polyA tail

Ans. a) T b) T c) F (Post transcriptional modification) d) T e) F (Post transcriptional modification)

**Help link:**

### Post translational modifications

It is the chemical modification of protein synthesized through translation to make the protein functionally active.

**Types:**

- **Trimming (removal of part of translated sequence):** Removal of N-terminal methionine
- **Covalent modification:**
  - Limited proteolysis (eg: pepsinogen to pepsin)
  - Hydroxylation (eg: Lysine and proline of collagen are hydroxylated after synthesis of collagen)
  - Gamma carboxylation, eg: clotting factor
  - Glycosylation, eg: addition of carbohydrate
  - Phosphorylation: addition of phosphate
- **Ubiquitination:** degradation of protein by addition of one or more ubiquitin molecule to a target protein.

(Ref: ABC biochemistry-6<sup>th</sup>, P-420)

**Q. Following are examples of post-translational modification (BSMMU – Residency - MD/MS, Basic science – March' 14)**

- |                            |   |
|----------------------------|---|
| a) removal of introns      | F |
| b) hydroxylation           | T |
| c) addition of poly-A tail | F |
| d) glycosylation           | T |
| e) trimming                | T |

**Help link:**

### Post-translational modification:

**A. Trimming:** Many proteins destined for secretion from the cell are initially made as large, precursor molecules that are not functionally active. Portions of the protein chain must be removed by specialized endoproteases, resulting in the release of an active molecule. The cellular site of the cleavage reaction depends on the protein to be modified.

For example,

- Some precursor proteins are cleaved in the ER or the Golgi apparatus, others in developing secretory vesicles (for example, insulin), and still others are cleaved after secretion.
- Zymogens are inactive precursors of secreted enzymes (including the digestive proteases). They become activated through cleavage once they have reached their proper sites of action; for example, the pancreatic

zymogen, trypsinogen, becomes activated to trypsin in the small intestine. The synthesis of enzymes such as zymogens protects the cell from being digested by its own products.

**B. Covalent modifications:** Proteins, both enzymatic & structural, may be activated or inactivated by the covalent attachment of a variety of chemical groups. e.g,

1. **Phosphorylation:** It is catalyzed by protein kinases and may be reversed by cellular protein phosphatases. The phosphorylation may increase or decrease the functional activity of the protein.
2. **Glycosylation:** Many of the proteins that are destined to become part of a plasma membrane or lysosome or to be secreted from the cell are glycosylated.
3. **Hydroxylation:** Proline and lysine residues of  $\alpha$ -chains of collagen are extensively hydroxylated in the endoplasmic reticulum.

4. **Other covalent modifications:** These may be required for the functional activity of a protein. e.g,

- Additional carboxyl groups can be added to glutamate by vitamin K dependant carboxylation. The resulting  $\gamma$ -carboxylation is essential for the activity of several blood clotting factors.
- Attachment of lipids, such as, farnesyl groups, can help anchor proteins in membranes.
- Acetylation.

**C. Protein degradation:** Proteins that are defective or destined for rapid turnover are often marked for destruction by the attachment of a small, highly conserved protein, called **ubiquitin**. Proteins marked in this way are rapidly degraded by a cellular component known as the “**proteosome**”.

(Ref: Lippincott-7<sup>th</sup>)

## Clinical Biochemistry

**Q. Synthetic function of the liver is assessed by estimation of serum (BSMMU – Non-Residency – MD, MS, Basic science & Dentistry – July' 18)**

- a) alkaline phosphatase
- b) aspartate aminotransferase
- c) albumin level
- d) prothrombin time
- e)  $\gamma$ -glutamyl transferase

Ans. a) F b) F c) T d) T e) F

**Help Link:**

**Liver Function Tests:**

1. **Tests for synthetic function:**

- Total plasma protein conc. (Normal: 6 – 8 gm/ dl)
- Serum albumin (Normal 4.7 – 5.7 mg/ dl)
- Albumin /globulin ratio (Normal - 1.5 : 1)
- Prothrombin time (Normal: 12-16 sec): It assess the liver function test for production of factor II, VII, IX, X.

2. **Tests for excretory function:**

- a. Test for bile pigment -
  - In blood - Serum bilirubin conc. (*Hyperbilirubinaemia causes jaundice*)
    - Vanden Berg's test
  - In urine – Urine bilirubin, urobilinogen
  - In stool – Stercobilinogen

b. Bromsulphthaline test (*Bromsulphthaline clearance test*) - very rarely done.

3. **Test for enzymatic function:**

- Alanine aminotransferase (ALT)/ Serum glutamate pyruvate test (SGPT)(10-40 U/L) ( $\uparrow$  in hepatocellular damage)
- Aspartate aminotransferase (AST)/ Serum glutamate oxaloacetate test (SGOT) (10 - 35 U/L)

(↑ in hepatocellular damage)

- Alkaline phosphatase (50 - 150 U/L) (↑ in biliary obstruction, cirrhosis of liver, hepatic tumors)
- γ-glutamyl transferase (↑ in alcoholic liver diseases)
- Isocitrate dehydrogenase

#### **4. Tests for metabolic function:**

- CHO metabolism:
  - Glucose tolerance test.
  - Galactose tolerance test.
- Fat metabolism:
  - Serum cholesterol level
  - Faecal fat analysis
- Protein metabolism:
  - Total protein
  - Serum Albumin & globulin and their ratio.

#### **5. Test for detoxification function:**

- Hippuric acid test
- NH<sub>3</sub> conc. in blood

#### **6. Other determinations:**

- Serum ferritin (↑ in liver disease)
- Iron binding capacity saturation
- α<sub>1</sub>-antitrypsin
- α-fetoprotein (Normally it is present in fetus. If it is found in adult, it indicates hepatocellular carcinoma)
- Ceruloplasmin (↑ in Wilson's disease)
- Copper

**Q. Local metabolic activity is the chief factor for determination of the rate of blood flow to (BSMMU – Residency - MD, MS, Basic Science - March' 18/ March' 17)**

- a) heart
- b) skin
- c) skeletal muscle
- d) lung
- e) kidney

**Ans.**

- A. True** There is a close relationship between the work of the heart and coronary flow.
- B. False** Skin blood flow is geared mainly to thermoregulation and normally exceeds that needed for skin's modest metabolic requirements.
- C. True** Local blood flow is largely determined by the vasoactive metabolites such as rising PCO<sub>2</sub>, H<sub>+</sub> concentration and falling PO<sub>2</sub>. The changes produced by vasomotor nerves are small compared with those produced by metabolites.
- D. False** The entire cardiac output must pass through the lungs regardless of the local metabolic needs of the pulmonary tissues. It is greatly in excess of the lungs' metabolic needs.
- E. False** As in skin, renal blood flow (about one quarter of total cardiac output) greatly exceeds local metabolic needs. The blood is sent to the kidneys for processing.

**(Ref. Roddie MCQ 69)**

**Q. In diabetic ketosis, there is decreased breakdown of (BSMMU – Residency - MD, MS, Basic Science - March' 17)**

- a) ketones
- b) glycogen
- c) glucose
- d) fat
- e) amino acid

**Ans. a) T b) F c)T d) F e)F**

**Q. Severe uncontrolled diabetes mellitus leads to a raised (BSMMU – Residency - MD, MS, Basic Science, Dentistry - March '17)**

- a) H<sup>+</sup> ion concentration in body fluid
- b) plasma K<sup>+</sup> ion concentration
- c) urinary specific gravity and osmolality
- d) blood volume
- e) arterial PCO<sub>2</sub>

Ans.

- A. True This is a prime feature of ketoacidosis.
- B. True The excess H<sup>+</sup> ions compete with K<sup>+</sup> ions for excretion in the distal tubules.
- C. True Due to the dissolved glucose.
- D. False This falls due to osmotic diuresis and vomiting.
- E. False Hyperventilation reduces PCO<sub>2</sub> to compensate the metabolic acidosis.

(Ref: Roddy)

**Q.  $\alpha$ 1-antitrypsin (BSMMU – Residency - MD, MS, Basic Science - March '17)**

- a) deficiency leads to cystic fibrosis
- b) deficiency can be treated with vitamin C
- c) inhibits neutrophil elastase
- d) is produced by the liver
- e) is produced by the alveolar macrophage

Ans. a) F b) F c) T d) T e) F

**Help Link:**  $\alpha$ 1 antitrypsin deficiency leads to not inactivation of neutrophil elastase in the lung and unchecked activity of protease that lead to destruction of elastin in the wall of lung and develops pulmonary emphysema.

**Q. Hepatocellular damage is assessed by estimation of serum (BSMMU – Non-Residency – MD, MS, Basic science – July' 16)**

- a) aspartate aminotransferase (AST)
- b) alkaline phosphatase (ALP)
- c) 5'-nucleotidase (5'-NT)
- d) alanine aminotransferase (ALT)
- e) total protein (TP)

T  
F  
F  
T  
F

**HELP LINK:**

**Test for Hepatocellular damage:**

- a) ALT(Alanine transaminase)
- b) AST(Aspartate transaminase)
- c) Gamma glutamyl transferase

**Test for cholestasis(biliary tract obstruction):**

- a) Alkaline phosphatase
- b) Gamma glutamyl transferase
- c) 5- Nucleotidase(5-NT)

**Test for synthetic function:**

- a) Serum total protein
- b) Serum albumin concentration
- c) Serum albumin to globulin ratio
- d) Prothrombin time

(Ref: ABC Biochemistry-6<sup>th</sup>, P-537)

**Q. Liver function tests are (BSMMU – Non-Residency – MS, Basic science, Dentistry – July' 16)**

- a) bleeding time
- b) gamma-glutamyl transpeptidase
- c) serum alanine transaminase
- d) serum aspartate transaminase
- e) serum globulin

F  
T  
T  
T  
F

**Note:** gamma-glutamyl transpeptidase is increased markedly in alcoholic liver disease

**Q. Adenosine deaminase (BSMMU – Residency – MD, MS, Basic science, Dentistry – March '16) (Ref: ABC Biochemistry-6<sup>th</sup>, P-537)**

- a) is found in lymphocyte
- b) converts adenosine to inosine
- c) deficiency cause hyperuricemia
- d) deficiency causes hemolytic anaemia
- e) deficiency causes immunodeficiency diseases

Ans. a) T b) T c) F d) F e) T

**Help link:**

**Adenosine deaminase** (also known as adenosine aminohydrolase; or **ADA**) is an enzyme (EC 3.5.4.4) involved in purine metabolism. It is needed for the breakdown of adenosine from food and for the turnover of nucleic acids in tissues.

Present in virtually all mammalian cells, its primary function in humans is the development and maintenance of the immune system.<sup>[1]</sup> However, the full physiological role of ADA is not yet completely understood.

**Hypouricemia :Adenosine Deaminase (ADA) Deficiency:**

- ✓ It is associated with severe immunodeficiency where both T and B cells are deficient.
- ✓ It is an inherited autosomal recessive disease.
- ✓ ADA deficiency leads to accumulation of adenosine and dATP;
- ✓ this would inhibit further production of precursors for DNA synthesis especially dCTP.
- ✓ Lymphocytes usually contain high levels of ADA.
- ✓ manifested as reduced lymphocytes.
- ✓ leads to impaired cellular and humoral immunity.
- ✓ Hypouricemia is due to defective breakdown of purine nucleotides.
- ✓ Antibiotics and periodic injections of immunoglobulin will be life-saving.
- ✓ Weekly intramuscular injections of bovine ADA were found to be beneficial.
- ✓ Bone marrow stem cells will increase both T and B cells in the patients.
- ✓ The first successful gene replacement therapy has been tried in ADA deficiency.
- ✓ ADA is sometimes used for the rapid diagnosis of tuberculosis.
- ✓ ADA estimation in CSF is used for the diagnosis of tuberculous meningitis.
- ✓ ADA levels can be estimated in various body fluids like blood, CSF, pleural fluid, pericardial fluid, ascitic fluid, etc.
- ✓ The usual cut-off value for CSF is 10.0 U/L and for other fluids is 60.0 U/L.
- ✓ It has very good sensitivity and specificity for the diagnosis of pulmonary as well as extrapulmonary tuberculosis.
- ✓ Adenosine deaminase (ADA) level in pleural or ascites fluid may be used for diagnosis for extra-pulmonary tuberculosis.
- ✓ A negative test cannot rule out a diagnosis of TB.

(Ref: DM Vasudevan-7<sup>th</sup>, P-368-369)

**Q. Reducing sugars in urine include: (BSMMU – MD/MS (Residency) – January, 2011)**

- |              |   |
|--------------|---|
| a) glucose   | T |
| b) fructose  | T |
| c) sucrose   | F |
| d) galactose | T |
| e) lactose   | T |

**Q. Starvation is associated with a reduction in size of the: (BSMMU - M. Phil, Diploma – July '10)**

- |               |   |
|---------------|---|
| a) Fat depots | T |
| b) Heart      | T |
| c) CNS        | F |
| d) Liver      | T |
| e) Bones      | F |

**HELP LINK:**

In the first phase of starvation, the fat depots disappear and this is later followed by a gradual reduction in the size of organs such as the gastrointestinal tract, liver and heart while the central nervous system and skeleton remain unaffected.

An exception to this general pattern occurs in kwashiorkor. In this condition which affects infants and young children in many parts of Southern and Central Africa and the Far East, the diet is deficient in high grade protein but moderately adequate in total calories due to a high carbohydrate intake. Growth is impaired. The liver is enlarged because of fatty infiltration but depleted of RNA and protein.

(Ref: Smiddy)

**Q. Reducing substances found in urine are - (BSMMU – M. Phil, Diploma July, 2004)**

- |                  |   |
|------------------|---|
| A. Glucose       | T |
| B. Bile salt     | F |
| C. L-xylulose    | T |
| D. Urobilinogen  | F |
| E. Ascorbic acid | T |

## TEMPERATURE

**Q. The aerobic exercise: (BSMMU - M. Phil, Diploma - July '10)**

- |  |   |
|--|---|
| a) Require energy supply from break down of ATP                    | T |
| b) Causes increase in muscle bulk                                  | F |
| c) Helps in development of endurance                               | F |
| d) Causes increase in cardiac reserve during exercise by many fold | T |
| e) Helps in development of muscle strength.                        | F |

**Q. Body heat is produced by: (BSMMU - M. Phil, Diploma, July-09)**

- |                              |   |
|------------------------------|---|
| a) Respiration               | F |
| b) Urination                 | F |
| c) Basic metabolic processes | T |
| d) Muscular activity         | T |
| e) Food intake               | T |

**HELP LINK:** We gain heat by two ways:

**A. Heat production within the body:**

1. **Metabolism:** Oxidation of food materials produces large amount of heat in the body.
2. **Food intake:** Ingestion of food increases heat production because of specific dynamic action (SDA) of food.
3. **Muscular activity:** By skeletal muscle contraction during working, exercise, shivering, heat is produced.
4. **Endocrine mechanism:**
  - Epinephrine & norepinephrine produce a rapid but short-lived increase in heat production.
  - Thyroid hormones produce a slowly developing but prolonged increase in heat production.
  - Growth hormone, testosterone also produce heat to a lesser extent.
5. **Sympathetic stimulation** causes ↑ metabolism → ↑heat production
6. A source of considerable heat, particularly in the infants, is **brown fat**. This fat has a high rate of metabolism and its thermogenic function has been linked that of an electric blanket.

**B. Heat gain from environment:**

1. By directly from sun & heated substances.
2. Ingestion of hot foods & drinks.

(Ref: Gyton-13<sup>th</sup> + Ganong-25<sup>th</sup> + Wright's-13<sup>th</sup>, P-347)

**Q. A patient with fever: (DMC - MD/MS - 02Ja)**

- |  |   |
|--|---|
| A. Has warm hands as the central temperature rises.      | T |
| B. Has raised basal metabolic rate.                      | T |
| C. Shows evidence of altered hypothalamic function.      | F |
| D. Loses the capacity for reflex thermoregulation.       | T |
| E. Sweats only while central body emperature is failing. | T |

**Q. Heat production in the body is decreased by:** (BSMMU – MD - 00Ja)

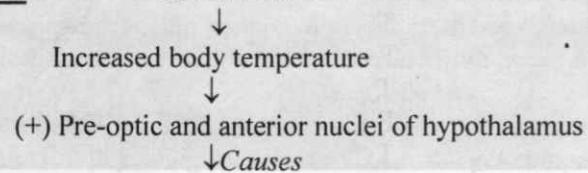
- |                               |   |
|-------------------------------|---|
| A. Shivering.                 | F |
| B. Brown fat.                 | F |
| C. Activity.                  | F |
| D. Circulating norepinephrine | F |
| E. Neuromuscular disease.     | T |

**HELP LINK:**

**Mechanism of temperature regulation:** Heat production must be equal to heat loss.

■ Mechanism activated by heat:

**Excess heat**



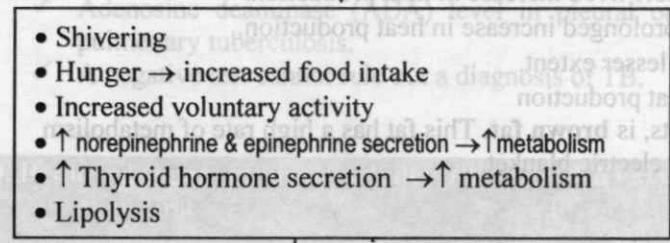
■ Temperature regulation by hypothalamus: Mechanism activated by cold:

**Excess cold**

Decreased body temperature

(+) Posterior hypothalamus

↓Causes



**Q. Local application of heat produces -** (BSMMU – M. Phil, Diploma July, 2005)

- |                                    |   |
|------------------------------------|---|
| A. increased blood flow            | T |
| B. increased muscular stiffness    | F |
| C. increased pain threshold        | T |
| D. increased membrane permeability | T |
| E. decreased metabolism            | F |

# CLINICAL NUTRITION

## Food & Nutrition

Q. Food intake is regulated by (BSMMU – Residency – MD, MS, Basic science – March' 16)

- a) thermostatic F
- b) circulating level of leptin T
- c) specific dynamic action of food F
- d) basal metabolic rate F
- e) ghrelin concentration T

Help link:

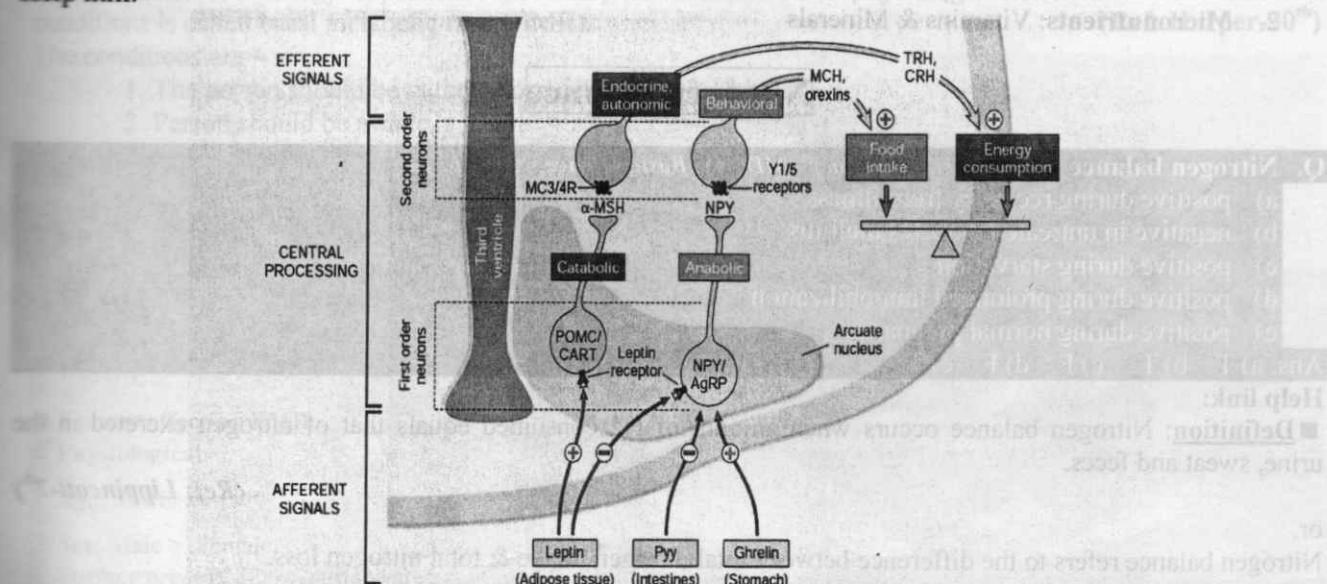


Figure 9-31 Neurohumoral circuits in the hypothalamus that regulate energy balance. Shown are POMC/CART anorexigenic neurons and NPY/AgRP orexigenic neurons in the arcuate nucleus of the hypothalamus, and their pathways. See text for details.

(Ref: Robbins-9<sup>th</sup>, P-446)

## Nutrients

Q. Trace elements are (BSMMU – Residency – MD, MS, Basic science, Dentistry – March' 16)

- a) sodium F
- b) magnesium F
- c) iron T
- d) selenium T
- e) phosphorus F

Help link:

Minerals

■ Classification: 2 types.

1. **Principal/Major elements (macrominerals):** These are the minerals required in large amounts in the body (greater than 100 mg/day). They are 7 in number –

Sodium, Potassium, Calcium, Magnesium, Phosphorus, Sulphur and Chlorine.

2. **Trace elements (microminerals):** These are the minerals required in small amount in the body (less than 100 mg/day).

These are – Iron, Iodine, Copper, Cobalt, Zinc, Manganese, Molybdenum, Selenium, Chromium, Fluorine, Nickel, Vanadium and Silicon.

(Ref: Harper-30<sup>th</sup> + Ganon-25<sup>th</sup>)

**Q. Macronutrient are - (DMC – MD/MS - 09Ja)**

- |                 |   |
|-----------------|---|
| a. carbohydrate | T |
| b. protein      | T |
| c. lipid        | T |
| d. iron         | F |
| e. zinc         | F |

**HELP LINK:**

■ **Nutrient:** Chemical ingredients present in food which produce energy to maintain the normal functions of the body is called nutrient.

**Classification:**

1. **Macronutrients:** CHO, protein & fat.
2. **Micronutrients:** Vitamins & Minerals

### Nitrogen balance

**Q. Nitrogen balance is (BSMMU – Residency - MD/MS, Basic science – March' 14)**

- a) positive during recovery from illness
- b) negative in untreated diabetes mellitus
- c) positive during starvation
- d) positive during prolonged immobilization
- e) positive during normal pregnancy

Ans. a) T b) T c) F d) F e) T

**Help link:**

■ **Definition:** Nitrogen balance occurs when amount of N<sub>2</sub> consumed equals that of nitrogen excreted in the urine, sweat and feces.

(Ref: Lippincott-7<sup>th</sup>)

or,

Nitrogen balance refers to the difference between total nitrogen intake & total nitrogen loss.

■ **Types:** It is two types:

1. **Positive nitrogen balance:** When N<sub>2</sub> intake exceeds N<sub>2</sub> output then it is called positive nitrogen balance.

**Causes:**

- Growing infant
- Pregnant women
- Athletes.
- During recovery from emaciating illness.

2. **Negative nitrogen balance:** When N<sub>2</sub> output exceeds N<sub>2</sub> input then it is called negative nitrogen balance.

**Causes:**

- Postsurgical patient
- Patient with advanced cancer
- Kwashiorkor
- Wasting disease
- Cushing's syndrome
- During physiological stress, trauma, burns.

**Q. Positive nitrogen balance is found (DMC – MD/ MS - January, 2010)**

- a. during ebb phase after stress response F
- b. in uncontrolled diabetes mellitus F
- c. growth of children T
- d. during recovery from illness T
- e. in kwashiorkor F

(Ref: Halsner-30<sup>th</sup> + Chou-32<sup>nd</sup>)

## Basal metabolic rate (BMR)

**Q. The metabolic rate:** (BSMMU – Residency – MD/MS – March '13)

- a) Increases slightly when walking slowly compared to sitting
- b) Is depressed after a meal
- c) Increased during starvation
- d) Is increased following a protein rich meal
- e) Is reduced in acidosis

**Ans:** a) T    b) F    c) F    d) T    e) F

**Help link:**

**Basal metabolic rate (BMR):**

■ **Definition:** The energy expenditure necessary to maintain basic physiologic functions under standardized conditions is called basal metabolic rate (BMR).  
**(Ref: Harper-30<sup>th</sup>)**

The conditions are –

1. The person should be without food for about 12-14 hours.
2. Person should be awake.
3. Complete mental & physical rest.
4. No exercise.
5. Comfortable temperature ( $20 - 25^{\circ}\text{C}$ )

■ **Normal value:**

- ♦ Male:  $35 - 38 \text{ Kcal} / \text{m}^2$  of body surface area /hour. ( $1800 \text{ kcal/day}$ )
- ♦ Female:  $32 - 35 \text{ Kcal} / \text{m}^2$  of body surface area/hour. ( $1300 \text{ kcal/day}$ )

■ **Factors affecting BMR:**

□ **Physiological:**

1. **Age:**  $\text{BMR} \propto \frac{1}{\text{Age}}$

2. **Sex:** Male > Female

3. **Surface area:**  $\text{BMR} \propto \text{surface area}$

4. **Climate:** In cold climate, BMR increases. In warm climate, BMR decreases.

5. **Occupation:** Heavy workers > sedentary workers.

6. **Hormones:**

- Less thyroid hormone :  $\text{BMR} \downarrow$
- Excess thyroid hormone:  $\text{BMR} \uparrow$
- Catecholamines :  $\text{BMR} \uparrow$
- Male sex hormones :  $\text{BMR} \uparrow$
- Growth hormone :  $\text{BMR} \uparrow$

7. **Pregnancy:**  $\uparrow \text{BMR}$

8. **Emotional state:**  $\uparrow \text{BMR}$

9. **Body temperature:**  $\uparrow \text{BMR}$  (about 14% for  $1^{\circ}\text{C}$ )

10. **Malnutrition, starvation:**  $\downarrow \text{BMR}$

11. **Habitary diet:** Meat eaters > strict vegetarians (11%)

12. **Barometric pressure:**  $\text{BMR} \downarrow$  by 5 – 25% when B.P falls to half an atmosphere.

13. **Drugs:**

- Caffeine, benzedine etc.  $\uparrow \text{BMR}$ .
- Anesthetics  $\downarrow \text{BMR}$

□ **Pathological:**

A.  **$\uparrow \text{BMR}$  under the following conditions:**

1. Hyperthyroidism.
2. Fever
3. Leukaemia
4. Polycythaemia
5. Congestive cardiac failure, hypertension

- 6. Renal failure
  - 7. Diabetes insipidus

B. ↓BMR under the following conditions:

1. Hypothyroidism – myxoedema & critinism.
  2. Addison's disease
  3. Nephrotic syndrome

### ■ Importance of BMR:

1. For prescribing a diet of adequate calorie value.
  2. For diagnosis of various pathological conditions e.g. hypothyroidism etc.
  3. To note the effect of different foods and drugs on BMR.

## Dietary fibre

O. Dietary fibres: (BSMMU – MD – January, 2010)

- a) Are monosaccharides F
  - b) Are not absorbed from the gut T
  - c) Increase incidence of colon cancer F
  - d) Lower the blood cholesterol level T
  - e) Prevent constipation T

#### **HELP LINK:**

- **Definition:** The natural packing of plant foods which cannot be digested by human enzymes are called dietary fibres.
  - **Example:** Cellulose, hemicellulose, lignin, pectins, gums and pentosans.
  - **Sources:** Whole grains, legume, wheat, leafy vegetables, root vegetables, fruits (apple, orange), potatoes, yushi of esogbul.
  - **Daily requirement:** 25-40 gm / day.

#### ■ Importance/ advantages of fibre:

- It increases the motility of the bowel. ( $\uparrow$  water retaining capacity of colonic contents and thus  $\uparrow$  bulk of faeces)
  - It causes softening of the stool. Thus relieve constipation.
  - It decreases the risk of development of various diseases:
    - Hemorrhoides (piles)
    - Diverticulosis
    - Colon cancer
    - Some cardiovascular diseases
    - Diabetes mellitus
  - It decreases the absorption of fat soluble vitamins.
  - It decreases the blood cholesterol level.
  - They are very important for slimming.

There are two types of high-fiber diets:

- Water soluble- Beans, guar gum, oat bran and pectin. These swell up and give a sense of fullness in stomach and thus induce early satiety. There is no desire to eat more. Glycemic index is low (glucose tolerance curve is flat.)
  - Water insoluble- Wheat bran (hemi-cellulose of wheat) increases the volume of stools, which is evacuated with ease.

#### **Advantages**

- Advantages**

  - Prevent constipation and colon cancer
  - Useful in the management of diverticular disease and functional bowel disorders
  - Lower cholesterol

**Table: Dietary carbohydrates:**

Class	Components	Examples	Source
Free sugars	Monosaccharides Disaccharides	Glucose, fructose Sucrose, lactose, maltose	Intrinsic: fruits, milks, vegetables Extrinsic (extracted, refined): beet or cane sucrose
Short-chain carbohydrates	Oligosaccharides	Maltodextrins, fructo-oligosaccharides	
Starch polysaccharides	Rapidly digestible Slowly digestible Resistant		Cereals (wheat, rice), root vegetables (potato), legumes (lentils, beans, peas)
Non-starch polysaccharides (NSP, dietary fibre)	Fibrous viscous	Cellulose Hemicellulose Pectins Gums	Plants
Sugar alcohols		Sorbitol, xylitol	Sorbitol: stone fruits (apples, peaches, prunes) Xylitol: maize, berry fruits Both used as low-calorie sugar alternatives

(Ref: Davidson-23<sup>rd</sup>, P-696)

## Hyperlipidaemia & Obesity

**Q. Secondary hypercholesterolaemia occurs in (BSMMU – Non-Residency – MD, MS, Basic science – July 18)**

- a) hyperthyroidism
- b) abdominal obesity
- c) excess alcohol intake
- d) pregnancy
- e) diuretic therapy

Ans. a) F b) F c) F d) T e) T

### HELP LINK:

**Dyslipidemia:** Abnormalities in lipid profile is known as dyslipidemia.

**Hyperlipidaemia:** Excess lipid in blood is called hyperlipidaemia.

### ■ Causes of hyperlipidaemia:

#### A. Primary hyperlipidaemia:

##### 1. Predominant hypercholesterolaemia:

- Polygenic (majority)
- Familial hypercholesterolaemia
- Hyperalphalipoproteinaemia

##### 2. Predominant hypertriglyceridaemia:

- Polygenic (majority)
- Lipoprotein lipase deficiency
- Familial hypertriglyceridaemia

##### 3. Mixed hyperlipidaemia:

- Polygenic (majority)
- Familial combined hyperlipidaemia
- Dysbetalipoproteinaemia

#### B. Secondary hyperlipidaemia:

#### C. Rare dyslipidaemia:

- Tangier disease
- Apo A1 deficiency
- Apo A1 Milano

16.25 Causes of secondary hyperlipidaemia	
<b>Secondary hypercholesterolaemia</b>	
Moderately common	
<ul style="list-style-type: none"> <li>• Hypothyroidism</li> <li>• Pregnancy</li> <li>• Cholestatic liver disease</li> </ul>	<ul style="list-style-type: none"> <li>• Drugs (diuretics, ciclosporin, corticosteroids, androgens, antiretroviral agents)</li> </ul>
Less common	
<ul style="list-style-type: none"> <li>• Nephrotic syndrome</li> <li>• Anorexia nervosa</li> </ul>	<ul style="list-style-type: none"> <li>• Porphyria</li> <li>• Hyperparathyroidism</li> </ul>
<b>Secondary hypertriglyceridaemia</b>	
Common	
<ul style="list-style-type: none"> <li>• Diabetes mellitus (type 2)</li> <li>• Chronic renal disease</li> <li>• Abdominal obesity</li> <li>• Excess alcohol</li> </ul>	<ul style="list-style-type: none"> <li>• Hepatocellular disease</li> <li>• Drugs (<math>\beta</math>-blockers, retinoids, corticosteroids, anti-retroviral agents)</li> </ul>

- Fish eye disease
- LCAT deficiency
- Sitosterolaemia
- Cerebrotendinous xanthomatosis

(Ref: Davidson-23<sup>rd</sup>)

**Q. Secondary hypercholesterolaemia occurs in:** (BSMMU – Non-Residency - MD/MS, Basic science – 13Ju, M. Phil, Diploma (Non-Residency)–March-2012, DMC & others – MD/MS – March-2012, (BSMMU - MD/MS (Residency) - January - II)

- |                          |   |
|--------------------------|---|
| a) Hypothyroidism        | T |
| b) Abdominal obesity     | F |
| c) Pregnancy             | T |
| d) Diuretics therapy     | T |
| e) Excess alcohol intake | F |

**Q. Secondary hypercholesterolaemia occurs in:** (BSMMU - M. Phil, Diploma – July '10)

- |                          |   |
|--------------------------|---|
| a) Hypothyroidism        | T |
| b) Abdominal obesity     | F |
| c) Pregnancy             | T |
| d) Diuretics             | T |
| e) Excess alcohol intake | F |

**Q. Obesity may be associated with:** (BSMMU – MD – January, 2010)

- |                             |                      |
|-----------------------------|----------------------|
| a) Prader – Willi syndrome  | T (also hyperphagia) |
| b) Addison's disease        | F                    |
| c) Stein-Leventhal syndrome | T                    |
| d) Turner's syndrome        | F                    |
| e) Hypothalamic damage      | T                    |

#### HELP LINK:

Causes of obesity:

##### 1. Non-pathological causes:

<b>Genetic</b>	<ul style="list-style-type: none"> <li>• Obesity in either or both parents</li> <li>• Early adiposity rebound</li> </ul>
----------------	--

##### 2. Pathological causes:

- Laurence-Moon-Biedi syndrome
- Down's syndrome
- Prader-Willi syndrome

<b>Environmental</b>	<ul style="list-style-type: none"> <li>• Socioeconomic deprivation</li> <li>• Single child</li> <li>• Single parent</li> </ul>
----------------------	--

<b>Diet-related</b>	<ul style="list-style-type: none"> <li>• Bottle-fed in infancy</li> <li>• High fat diet</li> <li>• Disorganized eating patterns</li> </ul>
---------------------	--

<b>Active-related</b>	<ul style="list-style-type: none"> <li>• Physical inactivity</li> <li>• Increased television watching</li> <li>• Short sleep duration</li> </ul>
-----------------------	--

	<ul style="list-style-type: none"> <li>• Lower cholesterol</li> <li>• Lower triglycerides</li> <li>• Lower blood glucose</li> <li>• Lower blood pressure</li> <li>• Lower body mass index</li> <li>• Lower waist circumference</li> <li>• Lower risk of heart disease</li> <li>• Lower risk of stroke</li> <li>• Lower risk of type 2 diabetes</li> <li>• Lower risk of gallbladder disease</li> <li>• Lower risk of diverticular disease</li> </ul>
--	--

##### Syndromes

##### Hypothalamic damage

##### Endocrine abnormalities

##### Immobility

##### Impaired skeletal growth drugs

- Laurence-Moon-Biedi syndrome
- Down's syndrome
- Prader-Willi syndrome

- Trauma
- Tumours, eg craniopharyngioma
- Post encephalitis

- Growth hormone deficiency
- Hypothyroidism
- Cushings syndrome
- Hyperinsulinism
- Pseudohypoparathyroidism

- Spina bifida
- Cerebral palsy

- Achondroplasia
- Insulin
- Steroids
- Antithyroid drugs
- Sodium valproate

Both Prader Willi and Angelman syndrome are example of genomic imprinting.

## COMPLICATIONS OF OBESITY:

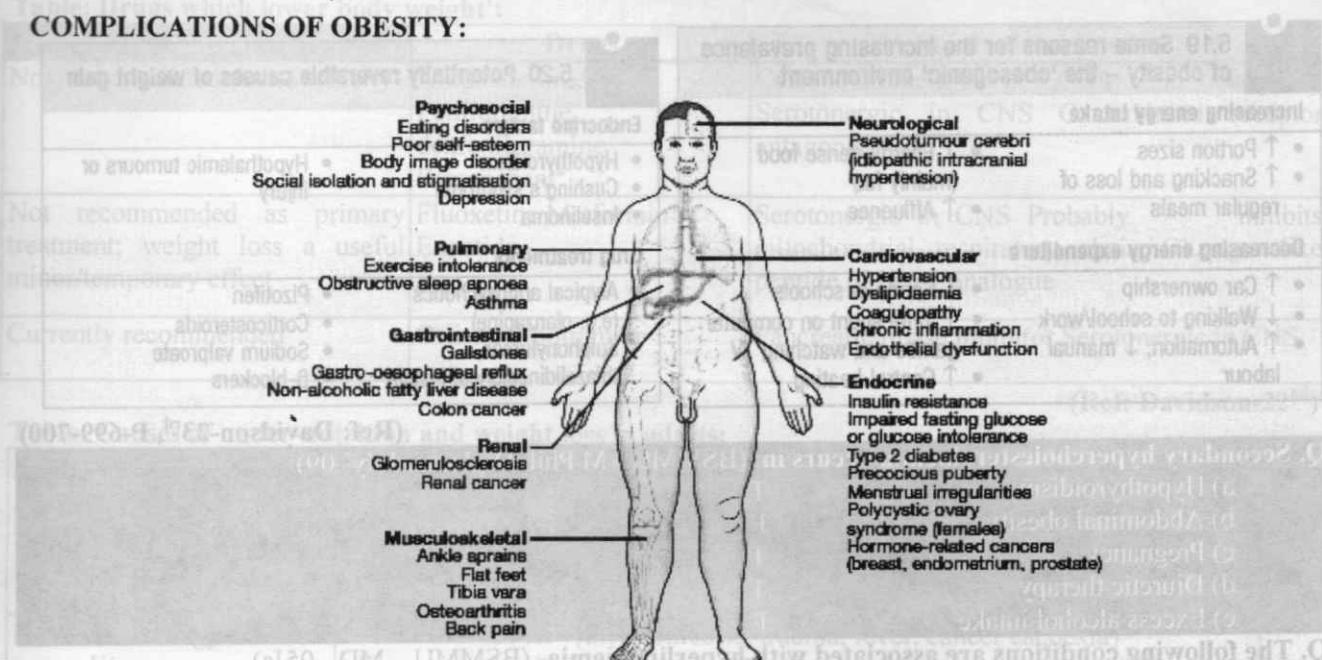


Fig: Complications of obesity

(Ref: Davidson-23<sup>rd</sup>, P-699)

### 5.18 Complications of obesity

Risk factors	Outcomes
'Metabolic syndrome'	
Type 2 diabetes	Coronary heart disease
Hypertension	Stroke
Hyperlipidaemia	Diabetes complications
Liver fat accumulation	Non-alcoholic steatohepatitis Cirrhosis
Restricted ventilation	Exertional dyspnoea Obstructive sleep apnoea Obesity hypoventilation syndrome (Pickwickian syndrome)
Mechanical effects of weight	Urinary incontinence Osteoarthritis Varicose veins
Increased peripheral steroid interconversion in adipose tissue	Hormone-dependent cancers (breast, uterus) Polycystic ovarian syndrome (infertility, hirsutism; p. 764)
Others	Psychological morbidity (low self-esteem, depression) Socioeconomic disadvantage (lower income, less likely to be promoted) Gallstones Colorectal cancer Skin infections (groin and submammary candidiasis; hidradenitis)

(Ref: Davidson-22<sup>nd</sup>, P-115)

### 5.19 Some reasons for the increasing prevalence of obesity – the 'obesogenic' environment

#### Increasing energy intake

- ↑ Portion sizes
- ↑ Snacking and loss of regular meals
- ↑ Energy-dense food (mainly fat)
- ↑ Affluence

#### Decreasing energy expenditure

- ↑ Car ownership
- ↓ Walking to school/work
- ↑ Automation; ↓ manual labour
- ↓ Sports in schools
- ↑ Time spent on computer games and watching TV
- ↑ Central heating

### 5.20 Potentially reversible causes of weight gain

#### Endocrine factors

- Hypothyroidism
- Cushing's syndrome
- Insulinoma
- Hypothalamic tumours or injury

#### Drug treatments

- Atypical antipsychotics (e.g. olanzapine)
- Sulphonylureas, thiazolidinediones, insulin
- Pizotifen
- Corticosteroids
- Sodium valproate
- β-blockers

(Ref: Davidson-23<sup>rd</sup>, P-699-700)

**Q.** Secondary hypercholesterolaemia occurs in: (BSMMU - M Phil, Diploma, July' 09)

- |                          |   |
|--------------------------|---|
| a) Hypothyroidism        | T |
| b) Abdominal obesity     | F |
| c) Pregnancy             | T |
| d) Diuretic therapy      | T |
| e) Excess alcohol intake | F |

**Q.** The following conditions are associated with hyperlipidaemia- (BSMMU – MD - 05Ja)

- |                                   |   |
|-----------------------------------|---|
| A. Thyrotoxicosis                 | F |
| B. Cushing's syndrome             | F |
| C. Hyperaldosteronism             | F |
| D. Nephrotic syndrome             | T |
| E. Familial hypercholesterolaemia | T |

**Q.** Health penalties for obesity includes: (BSMMU-MD-02J)

- |                             |   |
|-----------------------------|---|
| A. Diabetes mellitus        | T |
| B. Ischaemic heart disease  | T |
| C. Improved quality of life | F |
| D. Reduced operative risk   | F |
| E. Osteoarthritis           | T |

### Nice to know

#### 19.7 Quantifying obesity with BMI and waist circumference for risk of type 2 diabetes and cardiovascular disease

BMI (weight in kg/height in m <sup>2</sup> )	Classification <sup>1</sup>	Waist circumference <sup>2</sup>		
		Men <94 cm Women <80 cm	Men 94–102 cm Women 80–88 cm	Men >102 cm Women >88 cm
18.5–24.9	Reference range	Negligible	Mildly increased	Moderate
25.0–29.9	Overweight	Negligible	Moderate	Severe
>30.0	Obese			
30.0–34.9	Class I	Moderate	Severe	Very severe
35.0–39.9	Class II	–	Very severe	Very severe
>40.0	Class III	–	Very severe	Very severe

<sup>1</sup>Classification of the World Health Organisation (WHO) and International Obesity Task Force. The Western Pacific Region Office of WHO recommends that, among Asians, BMI >23.0 is overweight and >25.0 is obese. Lower cut-offs for waist circumference have also been proposed for Asians but have not been validated. <sup>2</sup>When BMI is >35 kg/m<sup>2</sup>, waist circumference does not add to the increased risk.

(Ref: Davidson-23<sup>rd</sup>, P-700)

Both Prader Willi and Angelman syndrome are example of genomic imprinting.

**Table: Drugs which lower body weight<sup>1</sup>:**

Status	Drugs	Mechanism of action
Not recommended due to toxicity	Amphetamines Fenfluramine, dexfenfluramine Rimonabant <sup>2</sup>	Catecholaminergic in CNS and periphery Serotonergic in CNS Cannabinoid receptor antagonist
Not recommended as primary treatment; weight loss a useful minor/temporary effect	Fluoxetine Metformin Exenatide	Serotonergic in CNS Probably inhibits mitochondrial respiratory chain Glucagon-like peptide (GLP)-1 analogue
Currently recommended	Orlistat Sibutramine	Pancreatic lipase inhibitor Serotonergic in CNS

(Ref: Davidson-22<sup>nd</sup>)**Table: Causes of under-nutrition and weight loss in adults:**

<b>Decreased energy intake</b>	<ul style="list-style-type: none"> <li>Famine</li> <li>Persistent regurgitation or vomiting</li> <li>Anorexia, including anorexia nervosa</li> <li>Malabsorption (e.g. small intestinal disease)</li> <li>Maldigestion (e.g. pancreatic exocrine insufficiency)</li> </ul>
<b>Increased energy expenditure</b>	<ul style="list-style-type: none"> <li>Increased BMR (thyrotoxicosis, trauma, fever, cancer cachexia)</li> <li>Excessive physical activity (e.g. marathon runners)</li> <li>Energy loss (e.g. glycosuria in diabetes)</li> <li>Impaired energy storage (e.g. Addison's disease, phaeochromocytoma)</li> </ul>

(Ref: Davidson-23<sup>rd</sup>, P-704)**Table: infections associated with starvation:**

- Gastroenteritis and Gram-negative septicaemia
- Respiratory infections, especially bronchopneumonia
- Certain viral diseases, especially measles and herpes simplex
- Tuberculosis
- Streptococcal and staphylococcal skin infections
- Helminthic infestations

(Ref: Davidson-23<sup>rd</sup>, P-705)**Lipoprotein patterns:**

*Phenotype	Lipoprotein (elevated)	Lipids (elevated)
I	Chylomicrons	Triglycerides
IIa	LDL	Cholesterol
IIb	LDL + VLDL	Cholesterol + triglycerides
III	VLDL + chylomicron remnants	Triglycerides, cholesterol
IV	VLDL	Triglycerides
V	Chylomicron + VLDL	Cholesterol + triglycerides

\* Fredrickson phenotype

**Lipid-lowering drugs:**

Class	Effects
1. Statins-Atorvastatin, ruzavastatin	↓ LDL, ↑ HDL, ↓ TGs
2. Nicotinic acid	↑ HDL, ↓ TGs (in lower doses) ↑ HDL, ↓ TGs (in higher doses) ↓ LDL (in higher doses) ↓ LP (a)
3. Bile acid sequestrants	↓ LDL, ↑ HDL, ↑ TGs(±)
4. Fibrates	↓ TGs, ↑ HDL, ↑ LDL (±)
5. Ezetimide	↓ LDL, ↓ TGs, ↑ HDL

## VITAMINS

**Q. Water soluble vitamins are (BSMMU –Residency - Dentistry – March '19)**

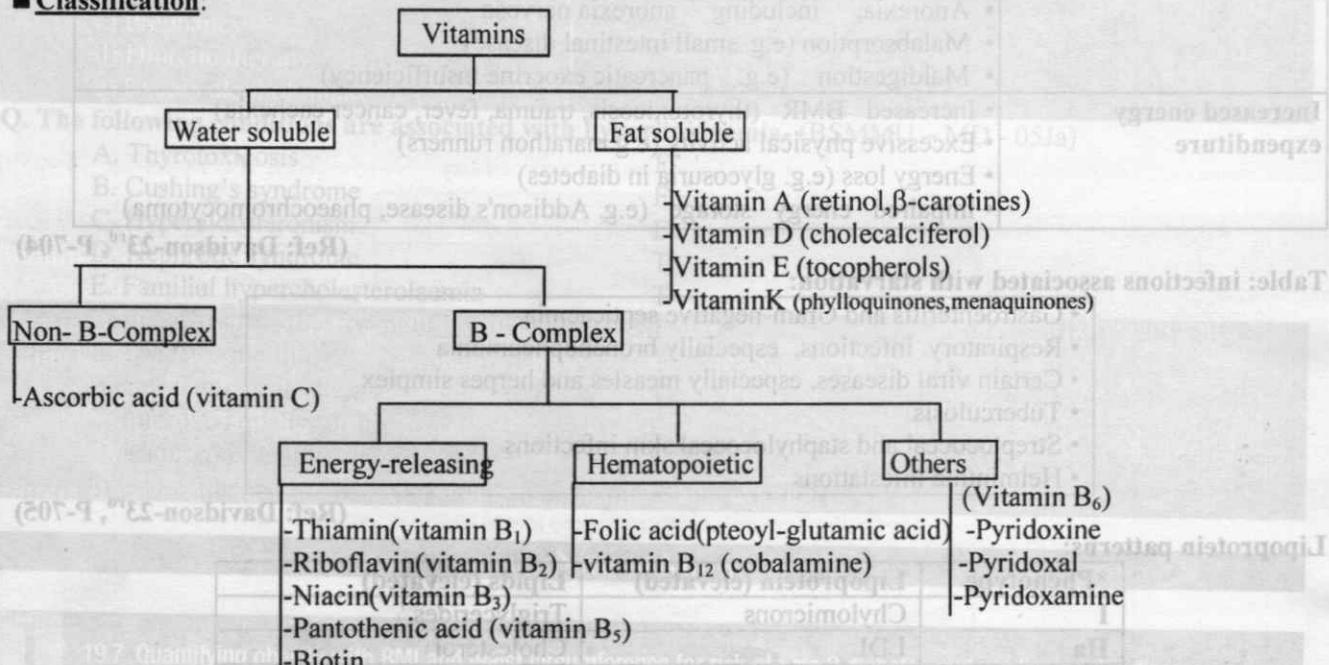
- a) Vitamin C
  - b) Vitamin D
  - c) Folic acid
  - d) Vitamin B<sub>12</sub>
  - e) Vitamin E
- Ans. a)T b)F (fat soluble) c)T d)T e) F (fat soluble)

**Help Link:** Fat soluble vitamins are: **ADEK**

■ **Definition:** Vitamins are organic nutrients that are required in small quantities for a variety of biochemical functions which, generally cannot be synthesized by the body and must therefore be supplied by the diet.

(Ref: Harper-30<sup>th</sup>)

■ **Classification:**



**Q. Fat soluble vitamins are- (BSMMU – MD - 01Ja)**

- a) Vit. A T
- b) Vit – C F
- c) Vit. E T
- d) Vit D T
- e) Vit. B F

(Ref: Lippincott-7<sup>th</sup>, P-371)

**5.30 Summary of clinically important vitamins**

Vitamin	Sources*		Reference nutrient intake (RNI)
	Rich	Important	
<b>Fat-soluble A (retinol)</b>	Liver	Milk and milk products, eggs, fish oils	700 µg men 600 µg women
<b>D (cholecalciferol)</b>	Fish oils	UV exposure to skin Egg yolks, margarine, fortified cereals	10 µg if > 65 yrs or no sunlight exposure
<b>E (tocopherol)</b>	Sunflower oil	Vegetables, nuts, seed oils	No RNI. Safe intake: 4 mg men 3 mg women
<b>K (phylloquinone, menaquinone)</b>	Green vegetables	Soya oil, menaquinones produced by intestinal bacteria	No RNI. Safe intake: 1 µg/kg
<b>Water-soluble B<sub>1</sub> (thiamin)</b>	Pork	Cereals, grains, beans	0.8 mg per 9.68 MJ (2000 kcal) energy intake
<b>B<sub>2</sub> (riboflavin)</b>	Milk	Milk and milk products, breakfast cereals, bread	1.3 mg men 1.1 mg women
<b>B<sub>3</sub> (niacin, nicotinic acid, nicotinamide)</b>	Meat, cereals		17 mg men 13 mg women
<b>B<sub>6</sub> (pyridoxine)</b>	Meat, fish, potatoes, bananas	Vegetables, intestinal microflora synthesis	1.4 mg men 1.2 mg women
<b>Folate</b>	Liver	Green leafy vegetables, fortified breakfast cereals	200 µg
<b>B<sub>12</sub> (cobalamin)</b>	Animal products	Bacterial colonisation	1.5 µg
<b>Biotin</b>	Egg yolk	Intestinal flora	No RNI. Safe intake: 10–200 µg
<b>C (ascorbic acid)</b>	Citrus fruit	Fresh fruit, fresh and frozen vegetables	40 mg

\*Rich sources contain the nutrient in high concentration but are not generally eaten in large amounts; important sources contain less but contribute most because larger amounts are eaten.

(Ref: Davidson-23<sup>rd</sup>, P-711)

**5.33 Biochemical assessment of vitamin status**

Nutrient	Biochemical assessments of deficiency or excess
<b>Vitamin A</b>	Serum retinol may be low in deficiency Serum retinyl esters: when vitamin A toxicity is suspected
<b>Vitamin D</b>	Plasma/serum 25-hydroxy vitamin D (25(OH)D): reflects body stores (liver and adipose tissue) Plasma/serum 1,25(OH) <sub>2</sub> D: difficult to interpret
<b>Vitamin E</b>	Serum tocopherol: cholesterol ratio
<b>Vitamin K</b>	Coagulation assays (e.g. prothrombin time) Plasma vitamin K
<b>Vitamin B<sub>1</sub> (thiamin)</b>	Red blood cell transketolase activity or whole-blood vitamin B <sub>1</sub>
<b>Vitamin B<sub>2</sub> (riboflavin)</b>	Red blood cell glutathione reductase activity or whole-blood vitamin B <sub>2</sub>
<b>Vitamin B<sub>3</sub> (niacin)</b>	Urinary metabolites: 1-methyl-2-pyridone-5-carboxamide, 1-methylnicotinamide
<b>Vitamin B<sub>6</sub></b>	Plasma pyridoxal phosphate or erythrocyte transaminase activation coefficient
<b>Vitamin B<sub>12</sub></b>	Plasma B <sub>12</sub> : poor measure of overall vitamin B <sub>12</sub> status but will detect severe deficiency Alternatives (methylmalonic acid and holotranscobalamin) are not used routinely
<b>Folate</b>	Red blood cell folate Plasma folate: reflects recent intake but also detects unmetabolised folic acid from foods and supplements
<b>Vitamin C</b>	Leucocyte ascorbic acid: assesses vitamin C tissue stores Plasma ascorbic acid: reflects recent (daily) intake

(Ref: Davidson-23<sup>rd</sup>, P-712)

#### **Summary of clinically important vitamins:**

Recommended name (alternative name)	Deficiency	Excess
<b>FAT-SOLUBLE</b>		
<b>Vitamin A (retinol)</b>	Xerophthalmia, night blindness, keratomalacia, follicular hyperkeratosis	Liver damage, bone damage, teratogenesis
<b>Vitamin D (cholecalciferol)</b>	Rickets, osteomalacia	Hypercalcaemia
<b>Vitamin E (tocopherol)</b>	Haemolytic anaemia, ataxia	
<b>Vitamin K (phylloquinone, menaquinone)</b>	Coagulation disorder	
<b>WATER-SOLUBLE</b>		
<b>Vitamin B<sub>1</sub> (Thiamin)</b>	Beri-beri, Wernicke-Korsakoff syndrome /W. encephalopathy. <i>Loss of appetite.</i> <i>Impaired digestion of starch and sugar.</i> <i>Diarrhoea or constipation.</i>	
<b>Vitamin B<sub>2</sub> (Riboflavin)</b>	Glossitis, stomatitis Growth impaired. <i>Anaemia.</i> <i>Photophobia.</i> <i>Cataracts.</i> <i>Dermatitis seborrhoea</i>	
<b>Vitamin B<sub>3</sub> (Niacin, (Nicotinic acid, nicotinamide))</b>	Pellagra	
<b>Vitamin B<sub>6</sub> (Pyridoxine)</b>	Polyneuropathy	Polyneuropathy
<b>Biotin (Vitamin B<sub>7</sub>)</b>	Dermatitis, alopecia, paraesthesiae	
<b>Folate (Vitamin B<sub>9</sub>)</b>	Growth failure & megaloblastic anaemia Glossitis Gastrointestinal disturbances	
<b>Vitamin B<sub>12</sub> (Cobalamin)</b>	Megaloblastic anaemia (dietary deficiency) Pernicious anaemia (intrinsic factor deficiency) neurological degeneration <i>Methylmalonic aciduria.</i>	A nimetIV B nimetIV
<b>Vitamin C (Ascorbic acid)</b>	Scurvy	3 nimetIV

(Ref: Davidson-23<sup>rd</sup>)

<b>Vitamin B-complex</b>	<b>Active form</b>
<b>Thiamine (Vit-B<sub>1</sub>)</b>	<ul style="list-style-type: none"> <li>• Thiamine pyrophosphate (TPP)</li> </ul>
<b>Riboflavin (Vit-B2)</b>	<ul style="list-style-type: none"> <li>• Flavin mononucleotide (FMN)</li> <li>• Flavin adenine dinucleotide(FAD)</li> </ul>
<b>Niacin</b>	<ul style="list-style-type: none"> <li>• Nicotinamide adenine dinucleotide (NAD<sup>+</sup>)</li> <li>• Nicotinamide adenine dinucleotide phosphate (NADP<sup>+</sup>)</li> </ul>
<b>Pyridoxine</b>	<ul style="list-style-type: none"> <li>• Pyridoxal phosphate</li> </ul>
<b>Folic acid</b>	<ul style="list-style-type: none"> <li>• Tetrahydrofolate (THF)</li> </ul>
<b>Vitamin-B<sub>12</sub></b>	<ul style="list-style-type: none"> <li>• 5'- Deoxyadenosyl cobalamin</li> <li>• Methylcobalamin</li> </ul>
<b>Non-B complex</b>	<b>Active form</b>
<b>Vitamin C</b>	<ul style="list-style-type: none"> <li>• Ascorbic acid</li> <li>• Dehydroascorbic acid</li> </ul>

Vitamins	Functions
<b>Vit-B<sub>1</sub>(Thiamin)</b>	<ol style="list-style-type: none"> <li>Acts as a coenzyme.</li> <li>Pyruvate → Thiamin → Acetyl Co-A</li> <li>Causes rapid glucose oxidation within CNS.</li> <li>Essential for good appetite and normal digestion.</li> <li>Helps in transmission in nerve impulse.</li> </ol>
<b>Vit-B<sub>2</sub> (Riboflavin)</b>	<ol style="list-style-type: none"> <li>Acts as coenzymes in oxidation reduction reactions in different biochemical reactions.</li> <li>Formation of certain enzymes.</li> <li>Participates in light adaptation.</li> <li>Involved in protein, fat &amp; CHO metabolism.</li> </ol>
<b>B<sub>3</sub>(Niacin)</b>	<ol style="list-style-type: none"> <li>It acts as coenzyme in the forms of NAD &amp; NADP in electron transfer reactions carried out by dehydrogenase enzymes.</li> <li>Essential for normal functioning of skin, intestinal tract &amp; nervous system.</li> </ol>
<b>Vit B<sub>5</sub></b>	It forms a part of coenzyme A(CoA), the coenzyme in acylation reactions. CoA represents the only known functional form of this metabolism.
<b>Vit B<sub>6</sub></b>	<ol style="list-style-type: none"> <li>Acts as coenzyme for transaminases in transamination reaction.</li> <li>Essential for dehydration &amp; desulphydratation of amino acids.</li> <li>Increases the transport of amino acid &amp; K<sup>+</sup> into cells against gradient.</li> <li>Essential for the metabolism of tryptophan.</li> <li>It is believed to be involved in the metabolism of unsaturated fatty acids.</li> </ol>
<b>Vit-B<sub>12</sub></b>	<ol style="list-style-type: none"> <li>Essential for maturation of RBC.</li> <li>Necessary for the synthesis of DNA.</li> <li>Produces remission in pernicious anaemia.</li> <li>Essential for protein metabolism.</li> </ol>
<b>Biotin</b>	<ol style="list-style-type: none"> <li>It is required in CO<sub>2</sub> fixation reactions (eg. Pyruvate → Oxaloacetate)</li> <li>Essential in carboxylation reactions.e.g. Acetyl CoA → Malonyl CoA (fatty acid synthesis)</li> </ol>
<b>Folic acid</b>	<ol style="list-style-type: none"> <li>Acts as coenzyme for the transfer of 1-carbon units (eg. methyl, formyl) for the biosynthesis of a variety of bio-molecules (eg. methionine, serine etc).</li> <li>It is involved in tyrosine metabolism and formation of RBC.</li> <li>Early fetal neural tube development.</li> </ol>

Adults	5000 IU
During pregnancy and lactation	6000-8000 IU
Children	2000-3000 IU

β-Carotene (plant origin)

↓ β-Carotene dioxygenase (Liver)

Retinaldehyde (retinal, Vit. A)

↓ Retinaldehyde reductase



### 19.29 Nutrition in pregnancy and lactation

- Energy requirements:** increased in both mother and fetus but can be met through reduced maternal energy expenditure.
- Micronutrient requirements:** adaptive mechanisms ensure increased uptake of minerals in pregnancy, but extra increments of some are required during lactation (see Box 19.32). Additional increments of some vitamins are recommended during pregnancy and lactation:

**Vitamin A:** for growth and maintenance of the fetus, and to provide some reserve (important in some countries to prevent blindness associated with vitamin A deficiency). Teratogenic in excessive amounts.

**Vitamin D:** to ensure bone and dental development in the infant. Higher incidences of hypocalcaemia, hypoparathyroidism and defective dental enamel have been seen in infants of women not taking vitamin D supplements at > 50° latitude.

**Folate:** taken pre-conceptually and during the first trimester, reduces the incidence of neural tube defects by 70%.

**Vitamin B<sub>12</sub>:** in lactation only.

**Tiamine:** to meet increased fetal energy demands.

**Riboflavin:** to meet extra demands.

**Niacin:** in lactation only.

**Vitamin C:** for the last trimester to maintain maternal stores as fetal demands increase.

**Iodine:** in countries with high consumption of staple foods (e.g. brassicas, maize, bamboo shoots) that contain goitrogens (thiocyanates or perchlorates) that interfere with iodine uptake, supplements prevent infants being born with cretinism.

Vitamin	Description
Vit-B <sub>1</sub> (Thiamine)	1. Acts as a coenzyme 2. Causes lipid peroxide oxidation 3. Essential for blood glucose transport 4. Helps in transmission of nerve impulses
Vit-B <sub>2</sub> (Riboflavin)	1. Acts as coenzyme in oxidation-reduction reactions 2. Reduces lipid peroxidative lesions 3. Promotes intestinal absorption 4. Involved in biosynthesis of CHO metabolites
Vit-B <sub>3</sub> (Niacin)	1. It acts as coenzyme in the biosynthesis of steroid hormones 2. Involved in metabolism of proteins, carbohydrates and lipids
Vit-B <sub>6</sub>	1. It acts as coenzyme in the biosynthesis of proteins, carbohydrates and lipids
Vit-B <sub>12</sub> (Cobalamin)	1. It acts as a coenzyme in oxidation-reduction reactions 2. Involved in DNA synthesis for the biosynthesis of myelin 3. Essential for biosynthesis of TPN 4. Involved in biosynthesis of FMN

### 19.30 Vitamin deficiency in old age

- Requirements:** although requirements for energy fall with age, those for micronutrients do not. If dietary intake falls, a vitamin-rich diet is required to compensate.
- Vitamin D:** levels are commonly low due to reduced dietary intake, decreased sun exposure and less efficient skin conversion. This leads to bone loss and fractures. Supplements should be given to those at risk of falls in institutional care – the group at highest risk and most likely to benefit.
- Vitamin B<sub>12</sub> deficiency:** a causal relationship with dementia has not been identified, but it does produce neuropsychiatric effects and should be checked in all those with declining cognitive function.

(Ref: Davidson-23<sup>rd</sup>, P-712)

### Question Bank

**Q. Circulating homocysteine level can be reduced by supplementation of (BSMMU -Residency – MD, MS, Basic Science – March '18)**

- folic acid
- thiamine
- niacin
- pyridoxine
- methylcobalamin

Ans. a) T b) F c) F d) T e) T

Ref.

Vit B12

Folic Acid

Vit B6 or pyridoxine

(Ref: Davidson-23<sup>rd</sup>)

**Q. Erythropoietic vitamins are (BSMMU – Residency - Dentistry - March' 17)**

- B<sub>12</sub>
- B<sub>6</sub>
- D
- K
- folic acid

Ans. a) T b)T c)F d)F e)T

Methylcobalamin

Ascorbic acid

Dehydroascorbic acid

**Q. Serum homocysteine level can be reduced by dietary supplementation of (BSMMU – Non-Residency – MD, MS, Basic science – July '16)**

- |                    |   |  |
|--------------------|---|--|
| a) niacin          | F | 1. Function of Vitamin A:  |
| b) folic acid      | T | 1. Vision: It - Cris-tetrahydroxy-β,γ-dihydroxybutyrate is the initial part of hydroxylase in loss of the lens.          |
| c) thiamin         | F | 2. Anti-infective function: It has anti-infective properties. It is called anti-infective vitamin.                       |
| d) pyridoxine      | T | 3. Maintenance of epithelial cell integrity: It is essential for normal growth & development of skin & mucous membranes. |
| e) methylcobalamin | T | (Ref: Davidson's Medicine 25 <sup>th</sup> + Harper 30 <sup>th</sup> + Lippincott 22 <sup>nd</sup> )                     |

**Help link:**

**Causes of hyperhomocystinemia (vitamin A):**

1. Deficiencies of the vitamins B6 (pyridoxine), B9 and B12, folic acid,
2. Chronic consumption of alcohol

**Q. Vitamins can reduce circulating homocysteine level are (BSMMU – Residency – MD, MS, Basic science – March '16)**

- |                    |   |
|--------------------|---|
| a) folic acid      | T |
| b) niacin          | F |
| c) pyridoxine      | T |
| d) thiamine        | F |
| e) methylcobalamin | T |

**Q. Common features of fat soluble vitamins are (BSMMU – Non-Residency – MD, MS, Basic science, Dentistry – July '15)**

- |  |   |
|--|---|
| a) isoprene derivatives                        | T |
| b) absorption is linked to that of dietary fat | T |
| c) synthesized endogenously                    | F |
| d) transported in blood by some proteins       | T |
| e) act as enzyme cofactors                     | F |

## VITAMIN-A

**Sources:**

1. **Plant sources:** All pigmented (particularly yellow) vegetables and fruits (eg.- sweet potatoes, carrots, pumpkins, papayas, tomatoes, apricots and peaches) and the leafy green vegetables which supply provitamin-A (carotene) in the diet. Cereals also contain carotene.
2. **Animal sources:** Preformed vitamin-A (retinol) is supplied by foods of animal origin; they are liver, milk, butter, eggs, kidney, the fat of muscle meats and fish liver oil which is very rich in the vitamin.

(Ref: A.C. Deb-8<sup>th</sup>, P-180)

**Daily requirements:**

<b>Adults</b>	5000 I.U.
<b>During pregnancy and lactation</b>	6000-8000 I.U.
<b>Children</b>	2000-3000 I.U.
<b>Infants</b>	1500 I.U.
1 I.U. = 0.3 mg of retinol	
	= 0.6 µg of β-carotene

(Ref: A.C. Deb-8<sup>th</sup>, P-180)

**Activation of Vitamin A:**

β Carotene (plant origin)

↓ β-Carotene dioxygenase (Liver)

Retinaldehyde (retinal, Vit. A<sub>1</sub>)

↓ Retinaldehyde reductase

### Retinol (Active form of Vit. A)

#### Functions of Vitamin A:

1. **In vision:** 11 - Cis-retinaldehyde is the initial part of photoreceptor complex in rods of the retina.
2. **Anti-infective function:** It prevents infection, hence it is called anti-infective vitamin.
3. **Maintenance of epithelial cell integrity:** It is essential for maintenance of integrity of epithelial cells & glands.
4. **In normal growth:** It is essential for normal growth & fetal development.
5. **In fertility:** It helps in fertility.
6. **In haemopoiesis:** It helps in haemopoiesis
7. **Anti oxidative function:** β-carotene acts as an antioxidant.

#### Effects of deficiency of Vitamin A:

##### Eye changes:

Early:

- Retina: Night blindness
- Conjunctiva: Conjunctival xerosis, Bitot's spot.

Late:

- Corneal xerosis
- Corneal ulceration with xerosis
- Keratomalacia

##### Skin changes:

- Dryness & roughness of skin leading to itching
- Atrophy of hair follicles
- Atrophy of sweat & sebaceous glands.

##### Changes in GIT:

- Atrophy of the salivary glands & stop their secretion
- The mucous cells & the epithelial covering of the intestinal villi undergo necrosis & show ulceration with secondary infections leading to diarrhea.

##### Changes in respiratory-tract:

- Transformation of the columnar into stratified epithelium of the lining cells of the mucous membrane of the nasal cavity, nasopharynx, trachea & bronchi

##### Changes in genito urinary system:

- Epithelia of renal pelvis, ureter, bladder, vagina show metaplastic changes.
- The mesothelium of ovary also shows metaplastic changes, leading to failure of reproductive function.

##### Skeletal changes:

- Overgrowth of bones, more predominantly in the cranium & vertebral column which sometimes compresses the nerve trunk leading to the neurological manifestations.

**Active (functional) forms of Vitamin A:**

1. Retinol → Maintenance of vision and reproduction.
2. Retinal → Component of photopigment rhodopsin.
3. Retinoic acid → Maintenance of epithelium
4. β-Carotene → Antioxidant

(Ref: Davidson's Medicine-23<sup>rd</sup> + Harper-30<sup>th</sup> + Lippincott's-7<sup>th</sup>)

**Toxic effects of Vitamin A (Hypervitaminosis A):**

1. **Scalp Hair:** Alopecia
2. **Skin:** Desquamated, dry, Pruritic
3. **Liver:** Liver damage, enlarged, cirrhotic
4. **CNS:** Increased intracranial pressure
5. Nausea, Headache caused by acute over dose
6. Long bones: Thickening of the long bones (Hyperostosis)
7. Hypercalcemia
8. Soft tissue: Calcification of soft tissues
9. Fetus: Fetal malformation (Teratogenic effect done by retinol not by β-carotene)
10. Excessive intake of β-carotene causes Hypercarotinosis

**Note:** Vit. A supplementation is contra-indicated in pregnancy due to its teratogenic effects.

**The Vitamins having antioxidant properties:**

- Vitamin E (Tocopherol)
- Vitamin C (Ascorbic acid)
- β-Carotene

**Note:** Flavonoids also act as antioxidant.

**Prevention of Vitamin A deficiency:**

- Improvement of diet
- Intake of Vitamin A fortified food
- Prophylactic use of high potency oral Vitamin, A capsule in the high risk children
- Health education of the people.

(Ref: Davidson's Medicine-23<sup>rd</sup> + Harper-30<sup>th</sup> + Lippincott's-7<sup>th</sup>)

**Question Bank****Q. Vitamin A deficiency causes (BSMMU-Residency - MD, Dentistry - March '18)**

- a) corneal ulceration
- b) night blindness
- c) photodermatitis
- d) gum bleeding
- e) hyperkeratosis

Ans. a) T b) T c) F d) F e) T

(Ref. ABC Biochemistry Page-503)

**Q. Vitamin A deficiency causes (BSMMU-Residency - Dentistry - March '18)**

- a) corneal ulceration
- b) gun bleeding
- c) photodermatitis
- d) night blindness
- e) Smooth tongue

Ans. a) T b) F c) F d) T e) F

(Ref. ABC Biochemistry Page-503)

**Q. The risk of vitamin A deficiency increases in (BSMMU – Residency – MD, Basic Science – March' 15)**

- a) vegetarian diet
- b) malabsorption syndrome
- c) zinc deficiency
- d) iron deficiency
- e) congenital cataract

3. Ans. a) F b) T c) T d) T e) F

It is essential for maintenance of integrity of epithelial glands.  
(Ref. ABC Biochemistry-6<sup>th</sup>, P-477)

**Q. Regarding vitamin A (BSMMU – Residency - MD/MS, Basic science – March' 14)**

- a) is stored primarily in the retina
- b) is fat soluble
- c) overdose can cause optic disc swelling
- d) milk is a poor dietary source
- e) deficiency can be caused by renal disease

Ans. a) F b) T c) T d) F e) F

(Ref. ABC Biochemistry-6<sup>th</sup>, P-474)

**Help link:**

■ **Functions:**

A. **Function as dietary component:**

1. Necessary for the formation of visual pigment **rodopsin** in rod cell and **iodopsin** in cone cells & therefore prevents night blindness.
2. Helps in normal growth especially skeletal growth and central nervous system.
3. Essential for normal reproduction, supporting spermatogenesis in male and preventing fetal resorption in female.
4. It is essential for normal differentiation of epithelial tissues and mucus secretion.
5. Resists infection.

B. **Function as therapeutic agent:**

1. Carotenes- decreases the risk for certain cancers. e.g. lung cancer.
2. All trans retinoic acid-
  - Treatment of psoriasis
  - Treatment of polymyelocytic leukaemia (experimental)
3. 13-cis Retionic acid – Treatment of severe acne.

(Ref: Lippincott-7<sup>th</sup>)

**Q. Clinical features of vitamin-A deficiency include: (BSMMU – Residency – MD – March' 13)**

- |                                 |   |
|---------------------------------|---|
| a) Hyperkeratosis               | T |
| b) Night blindness              | T |
| c) Corneal ulceration           | T |
| d) Raised intracranial pressure | F |
| e) peripheral neuropathy        | F |

(Ref. ABC Biochemistry-6<sup>th</sup>, P-477)

**Help link:**

■ **Deficiency symptoms:** can be described under the following sub-headings:

1. On eye:

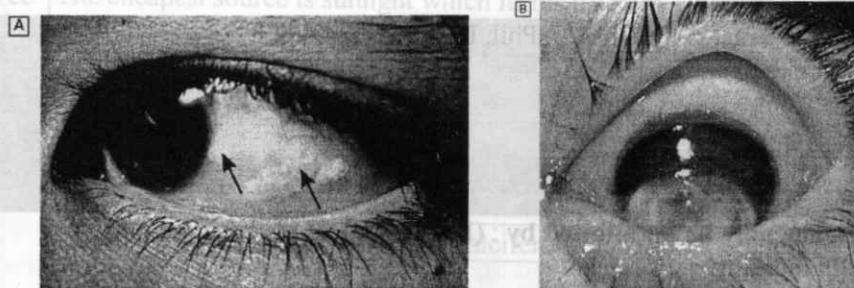
**Xerophthalmia (Dry eye):** The term 'Xerophthalmia' comprises all the ocular manifestations of vitamin A deficiency ranging from night blindness to keratomalacia. It has following stages-

**WHO classification of xerophthalmia:**

Classification code	Clinical description
X <sub>N</sub>	Night blindness
X <sub>1A</sub>	Conjunctival xerosis
X <sub>1B</sub>	Bitot's spot
X <sub>2</sub>	Corneal xerosis
X <sub>3A</sub>	Corneal ulceration/keratomalacia involving less than 1/3 of the corneal surface

X <sub>B</sub>	Corneal ulceration/keratomalacia involving more than 1/3 of the corneal surface
X <sub>S</sub>	Corneal scar
X <sub>F</sub>	Xerophthalmic fundi (white retinal lesion)

- **Night blindness:** Inability to see in dim light.
- **Conjunctival xerosis:** It is the first clinical sign of vitamin A deficiency. Conjunctiva becomes dry, wrinkled, muddy & unwettable.
- **Bitot's spots:** These are triangular, pearl-white or yellowish, foamy, spots on the bulbar conjunctiva on either side of the cornea.
- **Corneal xerosis:** The corneal surface becomes dull, dry, non-wettable and eventually opaque.
- **Corneal ulceration** with xerosis.
- **Keratomalacia:** Keratomalacia or corneal liquefaction is a medical emergency. The cornea of the eye becomes soft and loses its transparency. The softening may affect a part or whole of the cornea. If not promptly treated, it leads to complete collapse or destruction of the eyeball, results in blindness.



**Fig. Eye signs of vitamin A deficiency.** **A** Bitot's spots in xerophthalmia, showing the white triangular plaques (arrows). **B** Keratomalacia in a 14-month-old child. There is liquefactive necrosis affecting the greater part of the cornea, with typical sparing of the superior aspect.

## 2. On skin:

- Skin becomes dry & scaly especially over the outer aspect of the limbs, called follicular hyperkeratosis (phrynoderm).
- Atrophy of hair follicles.
- Atrophy of sweat and sebaceous glands.

## 3. On GI tract:

- Atrophy of salivary glands and they stop secretion.
- Infections, diarrhoea.

## 4. On respiratory tract:

Metaplasia of the epithelial lining (i.e. transformation of columnar to stratified squamous)

## 5. On genito-urinary tract:

Metaplasia of the epithelium.

## 6. On urinary tract:

Stone.

## 7. Growth failure.

**Q. Changes that occur in vitamin-A deficiency are:** (BSMMU – M. Phil, Diploma (Non-Residency) – 11Ju, DMC & others – MD/MS – 11Ju)

- squamous metaplasia
- toad skin.
- peripheral neuropathy.
- megaloblastic anaemia.
- xerophthalmia.

T

T

F

F

T

T

F

F

T

T

F

T

F

T

T

T

F

F

T

T

F

T

F

T

T

T

F

F

T

T

F

T

F

T

T

T

F

F

T

T

F

T

F

T

T

T

F

F

T

T

F

T

F

T

T

T

F

F

T

T

F

T

F

T

T

T

F

F

T

T

F

T

F

T

T

T

F

F

T

T

F

T

F

T

T

T

F

F

T

T

F

T

F

T

T

T

F

F

T

T

F

T

F

T

T

T

F

F

T

T

F

T

F

T

T

T

F

F

T

T

F

T

F

T

T

**Q. Vitamin A deficiency causes metaplastic changes in following organs – (BSMMU – MD/MS (Residency)-11Ja)**

- |                            |   |
|----------------------------|---|
| a) ocular epithelium       | F |
| b) upper respiratory tract | T |
| c) urinary tract           | T |
| d) gastro-intestinal tract | F |
| e) salivary gland          | F |

**Q. Vitamin A: (BSMMU - M. Phil, Diploma, July-08)**

- |  |   |
|--|---|
| a) is stored primarily in the retina         | F |
| b) is fat soluble                            | T |
| c) overdose can cause optic disc swelling    | T |
| d) has poor dietary source                   | F |
| e) deficiency can be caused by renal disease | F |

**Q. Vitamin A deficiency causes: (DMC – M. Phil, Diploma July, 2008)**

- |                          |   |
|--------------------------|---|
| A. Conjunctival xerosis. | T |
| B. Xerosis of sclera.    | F |
| C. Keratomalacia         | T |
| D. Anorexia              | T |
| E. Bony deformities.     | F |

**Q. Vitamin A deficiency may be manifested by : (BSMMU – MD - January, 2008)**

- |                                    |   |
|------------------------------------|---|
| A. lower child mortality           | F |
| B. hyperkeratosis .                | T |
| C. increased intracranial pressure | F |
| D. bone pain                       | F |
| E. corneal ulceration              | T |

**Q. Vitamin-A deficiency causes: (DMC – M.Phil, Diploma - 05Ju)**

- |  |   |
|--|---|
| a) Nyctalopia  | T |
| b) Squamous metaplasia                                   | T |
| c) non-stratified squamous epithelium becomes stratified | F |
| d) Hyper keratinization of the keratinized epithelium    | T |
| e) Hemeralopia   | F |

**Q. Functions of Vit. A include: (DMC – MD/MS - 04Ja)**

- |  |   |
|--|---|
| A. Maintenance of vision.                | T |
| B. Helps in wound healing.               | F |
| C. Differentiation of epithelial tissue. | T |
| D. Acts as a co-enzyme.                  | F |
| E. Essential for normal reproduction.    | T |

**Q. Vitamin A deficiency causes: (DMC – MD/MS - 04Ja)**

- |                          |   |
|--------------------------|---|
| A. Conjunctival xerosis. | T |
| B. Xerosis of sclera.    | F |
| C. Keratomalacia         | T |
| D. Anorexia              | T |
| E. Bony deformities.     | F |

**Q. The following statements regarding Vit. A are: (DMC – MD/MS – 04/03/00Ja)**

- |   |   |
|---|---|
| a) breast milk is not a satisfactory source                       | F |
| b) zinc is required for its mobilization                          | T |
| c) daily dose for infant is 100 microgram                         | F |
| d) keratomalacia is a reversible condition                        | F |
| e) Hypervitaminosis A may cause benign intracranial hypertension. | T |

**Q. Vitamin A (BIRDEM-04)**

- a) Is stored primarily in the retina.
- b) Deficiency can cause renal disease
- c) Is water soluble
- d) Overdose can cause optic disc swelling
- e) Is absent in cow's milk

F  
T  
F  
T  
F

**VITAMIN-D****Source:****Table: In the active form, vitamin-D is not well distributed in nature:**

<b>Rich sources</b>	The liver and viscera of fish and the liver of animals which feed on fish.
<b>Good sources</b>	Eggs and butter.
<b>Poor sources</b>	Milk. The amount of the vitamin can be increased by providing additional vitamin D in the cow's diet.
<b>Cheapest source</b>	The cheapest source is sunlight which forms O <sub>3</sub> from 7-dehydrocholesterol in the skin.

(Ref. A.C. Deb-8<sup>th</sup>, P-184)**Daily requirements:**

Infants and children	400 I.U.
Adults	200 I.U.
Women during pregnancy and lactation	400 I.U.
1 I.U. = 0.025 µgm of cholecalciferol	

(Ref. A.C. Deb-8<sup>th</sup>, P-184)**Biosynthesis of Vitamin D:**

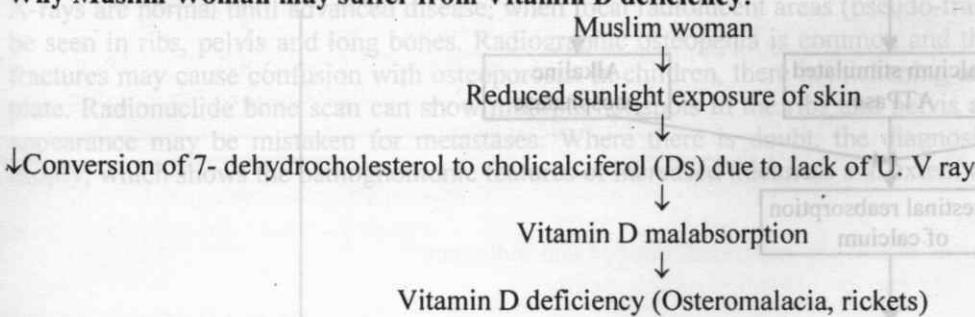
Vitamin D is synthesized in the skin from 7-dehydrocholesterol in an ultraviolet light mediated, non-enzymatic proteolytic reaction.

**Skin:** 7-dehydrocholesterol  
↓ U.V

Cholecalciferol (D<sub>3</sub>)

**Liver:**  
Cholecalciferol  
↓ 25-hydroxylase  
25(OH) D<sub>3</sub> (Calciferol)

**Kidney:**  
25(OH) D<sub>3</sub>  
↓ 1α-hydroxylase  
1, 25(OH)<sub>2</sub> D<sub>3</sub> (Calcitriol, active form of Vitamin D)  
↓ 24-hydroxylase  
24, 25(OH)<sub>2</sub> D<sub>3</sub> (24, 25 dihydroxy- cholecalciferol less active metabolite)

**Why Muslim Woman may suffer from Vitamin D deficiency:**

### Functions of Vitamin-D (Calcitrol):

#### 1. Bone:

- Calcium & phosphate mobilization from bone in presence of PTH
- ↑ Calcification
- ↑ Bone resorption

#### 2. Intestine: Promotes intestinal absorption of calcium phosphate.

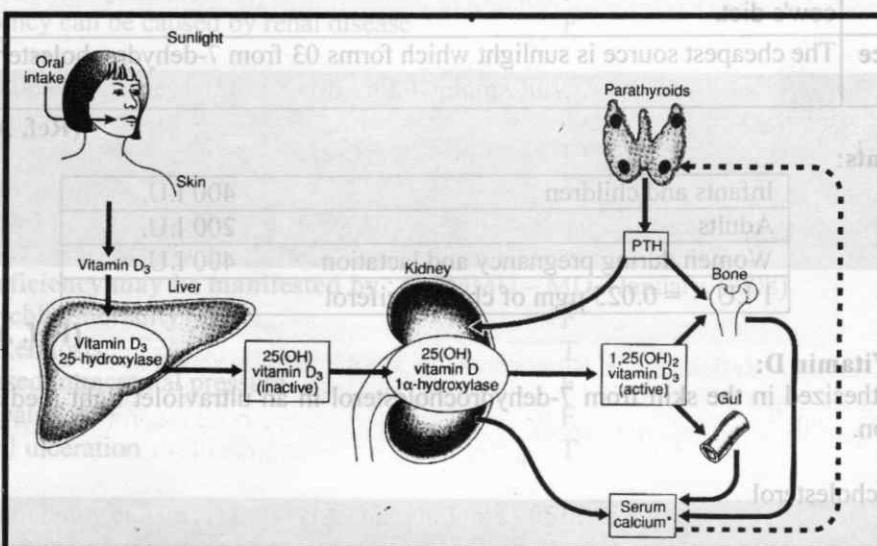
#### 3. Parathyroid glands:

- Calcitriole along with PTH helps in new bone formation & bone remodeling
- Calcitriole also may augment the actions of PTH on renal calcium reabsorption

#### 4. Kidney: Increases calcium & phosphate reabsorption

#### 5. Teeth: Helps in development of normal teeth

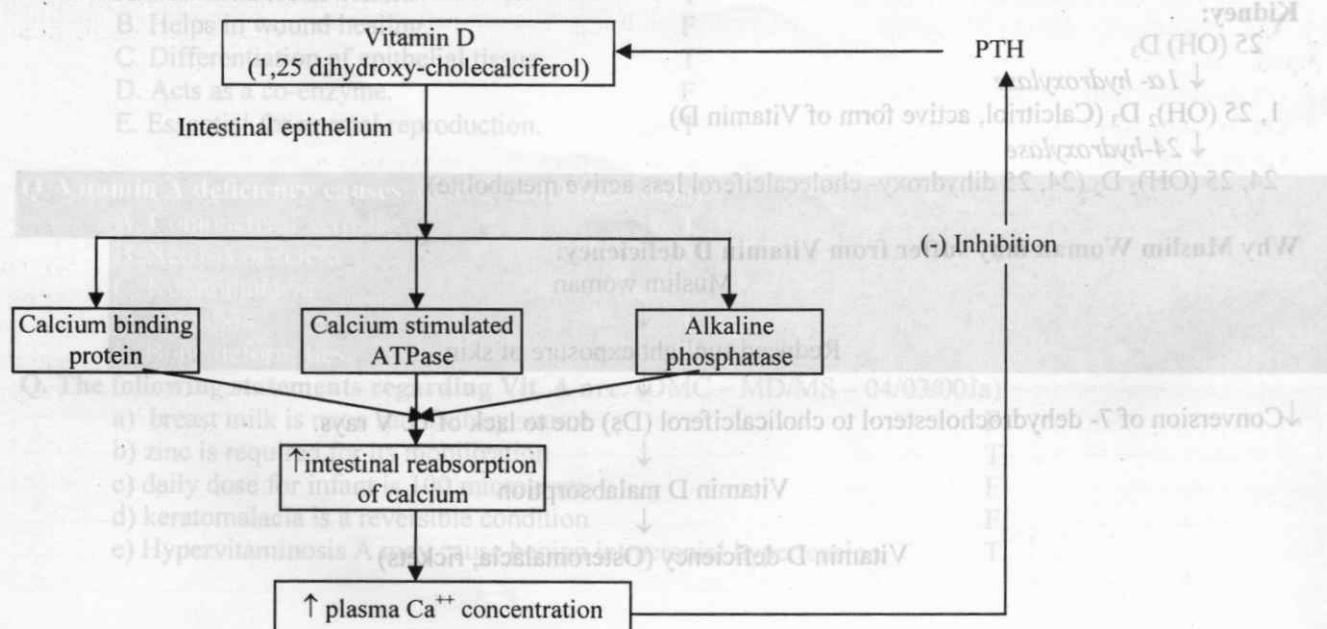
#### 6. Normal growth: Permits normal growth & development of human body.



**Fig.** Outline of calcium homeostasis showing interactions between parathyroid hormone (PTH) and vitamin D. 'Calcium in serum exists as 50% ionised ( $\text{Ca}^{++}$ ), 10% non-ionised or complexed with organic ions such as citrate and phosphate, and 40% protein-bound, mainly to albumin, it is the ionised calcium concentration which regulates PTH production.

(Ref: Davidson's Medicine-23<sup>rd</sup>)

### How Vitamin D maintains blood calcium Level:



**Note:** Vit. D is the most toxic among all the Vitamins.

#### Toxic effects of Vit. D:

1. GIT: Anorexia, nausea, digestive disturbances
2. Kidney: Polyuria, Irreversible damage to the kidneys
3. Soft tissue: Calcinosis-calcification of soft tissues
4. CNS: Headache, stupor
5. Hypercalcaemia

B. Tissues in its absence bones are weak and deformed (rickets).

#### Deficiency of calcium:

##### a) In case of children - Rickets –

- Incomplete mineralization of collagen matrix in bone.
- Soft & friable bones

##### b) In case of adult- Osteomalacia

- Defective & disportionate bone mineralization
- Spontaneous bone fracture

### VITAMIN D DEFICIENCY:

The most common cause is lack of sunlight exposure since maintenance of normal levels of vitamin D depends on UV sunlight exposure to catalyse synthesis of cholecalciferol from 7-dehydrocholesterol in the skin. Dietary deficiency can also play a role, but vitamin D occurs in only small quantities in most foods, except oily fish, so the amount present in average diets is insufficient to meet requirements. Lack of cholecalciferol results in reduced hepatic production of 25(OH)D<sub>3</sub> and thus reduced renal production of the biologically active metabolite 1,25(OH)<sub>2</sub>D<sub>3</sub>. The lack of 1,25(OH)<sub>2</sub>D<sub>3</sub> impairs intestinal calcium absorption and lowers serum calcium, which stimulates PTH secretion. This causes phosphate wasting and increased bone resorption in an attempt to maintain serum calcium levels within the normal range, causing progressive demineralisation of bone.

#### Clinical features:

Vitamin D deficiency in children causes delayed development, muscle hypotonia, craniotabes (small unossified areas in membranous bones of the skull that yield to finger pressure with a cracking feeling), bossing of the frontal and parietal bones and delayed anterior fontanelle closure, enlargement of epiphyses at the lower end of the radius, and swelling of the rib costo-chondral junctions (ricketty rosary). Osteomalacia in adults presents insidiously. Mild osteomalacia can be asymptomatic or present with fractures and mimic osteoporosis. More severe osteomalacia presents with muscle and bone pain, general malaise and fragility fractures. Proximal muscle weakness is prominent and the patient may walk with a waddling gait and struggle to climb stairs or get out of a chair. There may be bone and muscle tenderness on pressure and focal bone pain can occur due to fissure fractures of the ribs and pelvis.

#### Investigations:

The diagnosis can usually be made on a routine biochemical screen with measurement of serum 25(OH)D and PTH. Typically, serum alkaline phosphatase levels are raised, 25(OH)D levels are low or undetectable, and PTH is elevated. Serum calcium and phosphate levels may also be low but normal values do not exclude the diagnosis. X-rays are normal until advanced disease, when focal radiolucent areas (pseudo-fractures or Looser's zones) may be seen in ribs, pelvis and long bones. Radiographic osteopenia is common and the presence of vertebral crush fractures may cause confusion with osteoporosis. In children, there is thickening and widening of the epiphyseal plate. Radionuclide bone scan can show multiple hot spots in the ribs and pelvis at the site of fractures and the appearance may be mistaken for metastases. Where there is doubt, the diagnosis can be confirmed by bone biopsy, which shows the pathognomonic features of increased thickness and extent of osteoid seams.

**Management:**

Osteomalacia and rickets respond promptly to treatment with ergocalciferol (250-1000µg daily), showing rapid clinical improvement, an elevation in 25(OH)D and a reduction in PTH. Serum alkaline phosphatase levels sometimes rise initially as mineralisation of bone increases, but eventually fall to within the normal range as the bone disease heals. After 3-4 months, treatment can generally be stopped or the dose of vitamin D reduced to a maintenance level of 10-20 µg cholecalciferol daily, except in patients with underlying disease such as malabsorption, in whom higher doses may be required.

- Calcitriol along with PTH helps in new bone formation & bone remodeling
- Calcitonin may inhibit the actions of PTH on renal calcium reabsorption

4. Kidney: Increases calcium & phosphate reabsorption
5. Teeth: Helps in development of normal teeth

**Question Bank**

- Q. Vitamin D deficiency is associated with (BSMMU-Residency - Dentistry - March' 19)**

- a) hypocalcemia
- b) hyperphosphatemia
- c) elevated level of parathyroid hormone
- d) reduced alkaline phosphatase
- e) low serum concentration of 25 hydroxycholecalciferol

Ans. a) T b) F (hypophosphataemia) c) T d) F (raised) e) T

(Ref. Lippincott-7<sup>th</sup>, P-388)

- Q. Vitamin D maintains plasma calcium level by increased (BSMMU-Residency - Dentistry - March' 19)**

- a) secretion of parathyroid hormone
- b) intestinal uptake of calcium
- c) secretion of calcitonin
- d) renal reabsorption of calcium
- e) resorption of bone

Ans. a) F b) T c) F d) T e) T

**Help Link:****Calcitonin:**

- ✓ secreted by parafollicular cells of thyroid gland.
- ✓ The action of CT on calcium metabolism is antagonistic to that of PTH.
- ✓ calcitonin promotes calcification by increasing the activity of osteoblasts.
- ✓ It decreases bone reabsorption and increases the excretion of Ca into urine.
- ✓ therefore, has a **decreasing influence on blood calcium**.

(Ref. Sattanarayan-4<sup>th</sup>, P-407)

- Q. Following are the radiological presentation of rickets (BSMMU – Non-Residency – MD – July' 18)**

- a) increased distance between epiphysis and metaphysis
- b) periosteal elevation
- c) cupping and splaying of growing end of long bones
- d) Frankle's white line
- e) generalized osteopenia

Ans. a) T b) F c) T d) F (found in scurvy) e) T

(Ref: AH Mollah-5<sup>th</sup>, P-82)

**Help link:****• X-ray knee & wrist shows-**

- Widening, cupping and fraying of metaphysis.
- Wide gap between epiphysis and metaphysis.
- Density of shaft of bone is reduced (osteopenia).
- Deformity of long bone may be present.
- Green stick fracture may be present.

**• Chest X-ray shows**

- Chondral ends of ribs are expanded, cupped and indistinct.
- Rachitic rosary may be identified radiologically.

(Ref: AH Mollah-5<sup>th</sup>, P-82)

**Q. Vitamin D (BSMMU – Residency – Dentistry – March' 18)**

- a) increases intestinal absorption of  $\text{Ca}^{2+}$ .
- b) is essential for normal calcification of bones in childhood
- c) requires hepatic modification for activation
- d) can be synthesized in the body
- e) deficiency may result in hypoparathyroidism

**Help Link:**

- A. True** This occurs mainly in the upper small intestine.
- B. True** In its absence bones are weak and deformed (rickets).
- C. True** Initial (25-) hydroxylation occurs here.
- D. False** It can be produced in mammals by the action of ultraviolet light on 7-dehydrocholesterol in skin.
- E. False** (**hyperparathyroidism**) The low blood calcium level stimulates parathormone secretion.

(Ref. Roddy).

**Q. Osteomalacia is associated with (BSMMU – Residency – MD, Dentistry – March' 18)**

- a) reduced bone mineral density
- b) hypophosphataemia
- c) looser's zone in skull
- d) proximal myopathy
- e) reduced serum alkaline phosphatase

Ans. a) T b) T c) T d) F e) F

**Q. Which of the followings suggest the presence of vitamin D deficiency: (BSMMU – Residency – MD/MS – March' 13)**

- a) Hypocalcemia
- b) Hyperphosphatemia
- c) Elevated level of PTH
- d) Reduced alkaline phosphatase
- e) Low serum concentration of 25 hydroxy vitamin D

Ans: a) T b) F c) T d) F e) T

**Q. Radiological features of rickets are: (BSMMU - M. Phil, Diploma – July '10)**

- a) widened growth plate
- b) wimberger's sign
- c) subperiosteal haematoma
- d) trummer field zone
- e) fraying, splaying and cupping of the metaphysis

T  
F  
F  
F  
T**HELP LINK:****RADIOGRAPHIC FINDINGS IN RICKETS:**

The radiographic signs of rickets are the same regardless of the disorder responsible of under mineralization.

**1. Active rickets:****Knee and wrists:**

- Epiphyseal centers are indistinct or invisible
- Metaphyseal zones of provisional calcification have faint, irregular outlines-fraying.
- Ends of ulna and tibia are concave- cupping
- Ends of bones are widened-flaring
- Increased distance from the visible mineralized portion of the shafts to the epiphyseal centers is apparent
- Density of the bone shafts is reduced
- Deformity of long bones-may be present
- Green-stick fractures-may be present.

2. Cell Membrane: Tocopherols may protect cell membrane in general, particularly their unsaturated fatty acid constituents, from lipid peroxidation.

**Chest:**

- Ends of ribs are expanded, cupped, indistinct, and appear further than usual from the sternum
- Proximal humeri show changes listed for knee and wrists but lesser in degree because linear growth is slower.

**2. Healing rickets:** This differs from active rickets in that the line of provisional calcification is not frayed, but appears as a continuous dense line. This is the result of treatment. Vit-D and calcium salts, leading to mineralization of the provisional zone of calcification. So, in the healing rickets, the x-ray following features:

**Metaphysis shows:**

- Widening (broadening). Cupping (concavity)
- No fraying i.e. the line of provisional calcification is continuous

**The shaft:**

- The shaft still shows rarefaction, i.e. diminished density.
- The periosteum may show double periosteal line (due to subperiosteal deposition of osteoid tissue which is translucent)
- Deformities and green-stick fractures may present.

**3. Healed rickets:** With continuation of treatment all manifestations of activity disappear.

**The X-ray shows:**

- The shaft is calcified → normal density.
- The sub-periosteal osteoid tissue is calcified → no double periosteal line
- Broadening and cupping are corrected in addition to correction of fraying.

However, the difference between the x-ray of healed rickets and that of a normal bone is that in healed rickets the line of provisional calcification, the epiphyseal line is thick, dense and may be irregular, in addition, deformities may still be present but fractures are usually healed.

**Q. Nutritional rickets is characterized by (DMC – MD/MS - 08Ja)**

- |  |   |
|--|---|
| a) normal serum calcium                        | F |
| b) high serum phosphate                        | F |
| c) high alkaline phosphatase                   | T |
| d) thickening and widening of epiphyseal plate | T |
| e) low parathyroid hormone                     | F |

**Q. Biochemical changes in nutritional rickets are: (DMC – MD/MS - 05Ja)**

- |   |   |
|---|---|
| a) Hypocalcaemia                        | T |
| b) Hypophosphataemia                    | T |
| c) Hyper – parathyroidism               | T |
| d) Decreased serum alkaline phosphatase | F |
| e) Hyponatraemia                        | F |

**HELP LINK:****■ Changes in Rickets:**

1. Ca: normal or decreased.
2. Phosphate: decreased
3. Alkaline phosphatase: ↑
4. PTH: ↑
5.  $1,25(\text{OH})_2 \text{D}_3$ : N or ↓
6. X-ray:
  - Cupping, fraying, widening of ends of long bone.
  - ↑ Distance between epiphysis & diaphysis
  - ↓ Bone density

- Chest: ends of ribs are expanded, cupped and indistinct.  
- Rachitic rosary may be identified radiologically.

(Ref: AH Mollah-S, Page 10)

**Q. Calcium homeostasis is dependent for normal functioning of : (DMC – MD/MS - 02Ja)**

- A. Parathyroids
- B. Liver
- C. Kidney
- D. Adequate quantities of Vit D
- E. Adequate quantities of vitamin C

The average diet contains adequate amounts of vitamin-K and K<sub>1</sub> being synthesized by bacteria in the gut. So if the vitamin-K deficiency has not been reported in newborn babies in mother's milk when mother's diet has low vitamin-K content.

**Q. Agents used in the treatment and prevention of osteoporosis include: (BSMMU – MD - 00Ja)**

- A. Calcium.
- B. Calcitonin.
- C. Vitamin C.
- D. Vitamin D and analog.
- E. Sodium fluoride.

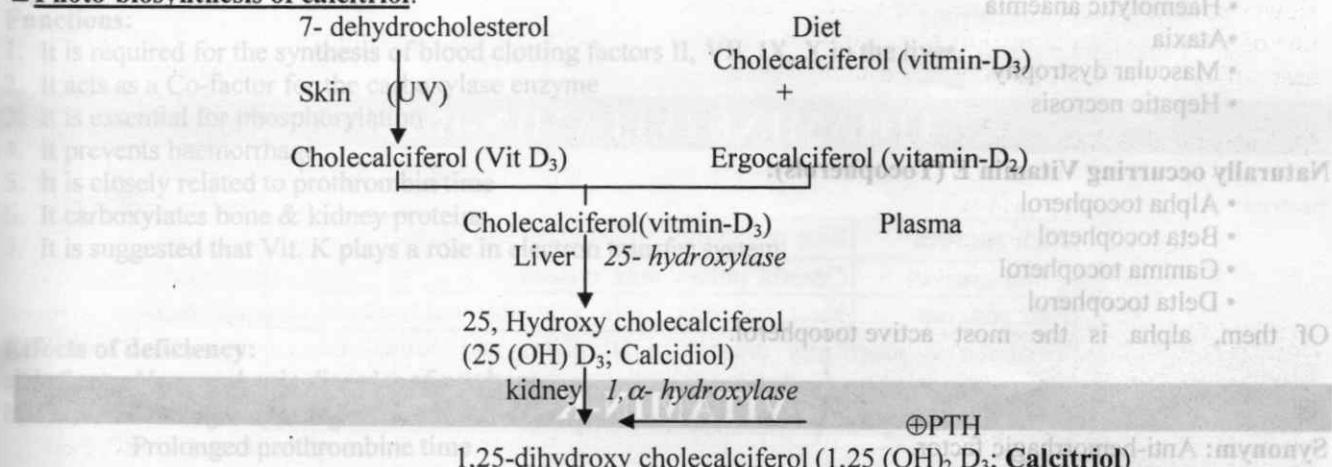
**Q. Ultraviolet ray converts 7- dehydrocholesterol into: (PG-96Ja)**

- A. Vitamin D<sub>3</sub>,
- B. Vitamin D<sub>2</sub>.
- C. Cholecalciferol
- D. Ergocalciferol.

**HELP LINK:**

■ **The active form of vitamin-D:** 1,25-Dihydroxycholecalciferol (calcitriol)

■ **Photo-biosynthesis of calcitriol:**



## VITAMIN-E

**Q. Vit-E deficiency may cause: (BSMMU - M. Phil, Diploma, July-09)**

- a) Decrease immunity
- b) Neuropathy
- c) Amyloidosis
- d) Malignancy
- e) Defective cell membrane structure

**Help link:**

**Good sources:** Eggs, meats, liver, fish, chicken, oatmeal, corn oil and cotton seed oil.

(Ref. A.C. Deb-8<sup>th</sup>, P-186)

**Daily requirements:** Adults: 25-30 mg. (Ref. A.C. Deb-8<sup>th</sup>, P-186)

**Functions of Vitamin E:**

1. **Antioxidative function:** They have got antioxidative effects & prevent unwanted oxidation in the body
2. **Cell Membrane:** Tocopherols may protect cell membrane in general, particularly their unsaturated fatty acid constituents, from lipid peroxidation.

3. **Other vitamins:** They prevent other vitamins present in food from oxidative destruction.
4. **Muscle:** It is essential for normal functions of muscle.
5. **Fertility:** They prevent sterility.
6. **Foetus:** Tocopherols are essential for normal fetal development.
7. **Connective tissue:** They have effects in maintaining the integrity of tissues which are mesodermal in origin. They have specific effect on fibrous connective tissues, so responsible for connective tissue metabolism.
8. **Protein metabolism:** It is concerned with protein metabolism & can prevent occurrence of protein deficiency.
9. **Antibrombotic function:** They have got some antithrombotic function.

#### Deficiency effects of Vitamin E:

##### a) Male:

- Degeneration of seminiferous tubules
- Atrophy of testes
- Sterility
- Deformities and green-stick fractures may present.

##### b) Female:

- Menstrual disturbances
- Death of fetus after implantation
- Habitual abortion

##### c) Both sexes:

- Haemolytic anaemia
- Ataxia
- Muscular dystrophy
- Hepatic necrosis

#### Naturally occurring Vitamin E (Tocopherols):

- Alpha tocopherol
- Beta tocopherol
- Gamma tocopherol
- Delta tocopherol

Of them, alpha is the most active tocopherol.

## VITAMIN-K

**Synonym:** Anti-hemorrhagic factor.

#### There are three naturally occurring forms of Vit. K:

- Vit. K1 (Phylloquinone 2-methyl-3-phytol-1,4-naphthoquinone)
- Vit. K2 (Menaquinones 2-methyl-3-N-isoprenyl-1,4-naphthoquinone)
- Vit. K3 (Menadione)

#### Source of Vit. K:

4. **Vit. K1:** Plant origin eg: Alfalfa, Cabbage, Cauliflower, spinach, green vegetable.
5. **Vit K2:** Animal origin eg: Putrefied fish meal, synthesized in the intestine by normal flora.
6. **Vit K3:** Synthetic derivative

**Daily requirement:** 70 -140 mg (estimated range)

**Sources:**

<b>Best sources</b>	Green leafy vegetables, eg.-alfalfa, spinach, cabbage, kale etc.
<b>Good sources</b>	Cauliflower, soyabean, wheat germ etc.

<b>Fair sources</b>	Carrots and potatoes.
<b>Poor sources</b>	Milk, meat and fish.
<b>Vitamin-K<sub>1</sub>:</b> Is produced by most bacteria present in the human intestine if it is not supplied in the diet.	

(Ref. A.C. Deb-8<sup>th</sup>, P-190)**Daily requirements:**

The average diet contains adequate amounts of vitamin-K<sub>1</sub> and K<sub>2</sub> being synthesized by bacteria in the intestine. So the vitamin-K deficiency has not been reported in healthy individuals except in new born infants fed on mother's milk when mother's diet has low vitamin-K content.

(Ref. A.C. Deb-8<sup>th</sup>, P-190)

**Absorption:** In upper part of the small intestine along with bile salts since it is fat soluble, vit. K require bile to be absorbed.

**Clinical significance:**

- In the new born, primary deficiency can occur, because -
  - Placental transfer of Vit. K is inefficient
  - The neonatal bowel has not yet acquired bacteria
  - Breast milk contains little of Vit. K.
 Vit. K is given routinely to newborn babies to prevent haemorrhagic disease of the newborn.
- In obstructive jaundice, dietary vit. K is not absorbed and it is very important to administer this vitamin in parenteral form before surgery.
- Warfarin & related anticoagulants act by antagonising Vitamin K.

**Functions:**

- It is required for the synthesis of blood clotting factors II, VII, IX, X in the liver.
- It acts as a Co-factor for the carboxylase enzyme
- It is essential for phosphorylation
- It prevents haemorrhage
- It is closely related to prothrombin time
- It carboxylates bone & kidney proteins
- It is suggested that Vit. K plays a role in electron transfer system.

**Effects of deficiency:**

a) **Infants:** Haemorrhagic disorder of newborn

b) **Adults:** Prolonged clotting time

(Prolonged prothrombine time)

**Question Bank**

**Q. Avitaminosis of K decreases synthesis of (BSMMU – Non-Residency – MD, MS, Basic science – July' 16 + March-2012)**

- a) fibrinogen F
- b) prothrombin T
- c) factor VII T
- d) factor VIII F
- e) factor IX T

(Ref: ABC Biochemistry-6<sup>th</sup>, P-481)

**Q. Vit. K is necessary for activation of: (DMC – M.Phil, Diploma - 05Ju)**

- a) prothrombin T
- b) factor-V F
- c) factor-IX T
- d) factor-VIII F
- e) factor-X T

**HELP LINK:**

**Vit. K is necessary for activation of Factor II (Prothrombin), Factor VII, Factor IX & Factor X**

■ **Role of vitamin K in the synthesis of these factors:** Factor II, VII, IX & X are synthesized in the liver in inactive form. These are carboxylated into active form in the presence of vitamin K. Vitamin K is converted into vit. K epoxide which is again reduced into vitamin K.

**There are three naturally occurring forms of Vit.K:**

- Vit. K1 (Phylloquinone 2-methyl - 3 phytol-1, 4-naphthoquinone)
- Vit. K2 (Menaquinones 2-methyl - 3-N-isoprenyl-1,4 naphthoquinone)
- Vit. K3 (Menadione)

**■ Functions of vitamin K:**

1. It catalyzes the synthesis of blood clotting factors II, VII, IX and X in the liver by carboxylation of glutamic acid residues.
2. It also carboxylates bone & kidney proteins.
3. It plays an important role in oxidative phosphorylation in the mitochondria.

**■ Vit. K in clinical use:**

1. Newborn
2. Obstructive jaundice before biliary surgery.

**■ Effects of vit. K deficiency:**

1. Haemorrhagic disorder of newborn
2. Prolonged clotting time
3. Prolonged prothrombin time

## THIAMINE (VITAMIN-B<sub>1</sub>)

Naturally occurring Vitamin E (Tocopherols):

**Source:** Alpha tocopherol

<b>Rich sources</b>	Rice polishings, wheat germ and yeast.
<b>Good sources</b>	Cereals, pulses, nuts, oilseeds.
<b>Fair sources</b>	Meat, fish, eggs, milk, vegetable and fruits.

Thiamine is practically present in all plants and animal tissues commonly used as food. The thiamine contained in these foods is destroyed with improper cooking.

Synonym: Anti-haemorrhagic factor.

(Ref. A.C. Deb-8<sup>th</sup>, P-193)

**Daily requirement:**

It is difficult to fix a single requirement of vitamin B<sub>1</sub>. The requirement is increased when metabolism is elevated as in fever, hyperthyroidism, increased muscular activity, pregnancy and lactation. Fat and protein reduce while carbohydrate increases the daily requirement of the "vitamin". Some of the thiamine is synthesized by the bacteria in the intestine. Deficiencies of the vitamin occur not only by poor dietary intake but also in persons suffering from organic diseases.

Source of Vit. B<sub>1</sub>:

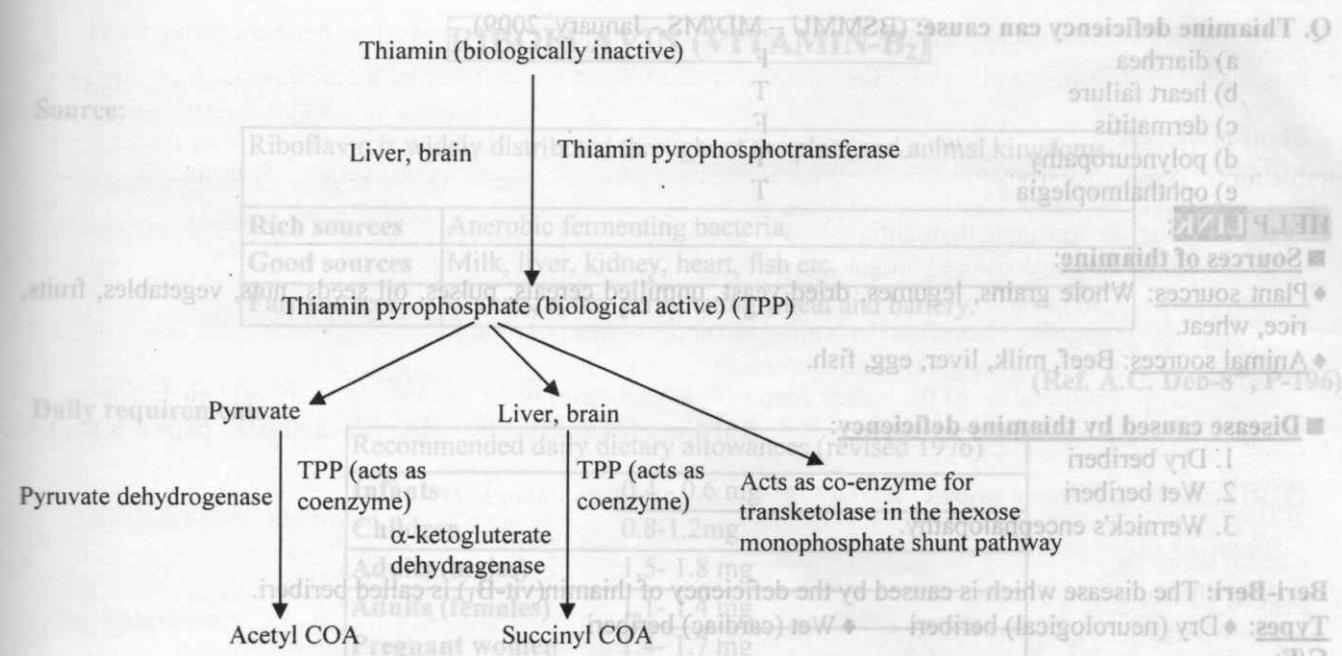
Vit. K1: Plant origin e.g. Alfalfa, Cabbage, Cauliflower, spinach, green vegetables.

Vit. K2: Animal origin e.g. Putrefied fish meal, synthesized in gut flora.

<b>Infants</b>	0.3 - 0.5 mg
<b>Children (Habit)</b>	0.7-1.2mg
<b>Adult (males)</b>	1.2-1.5 mg
<b>Adult (females)</b>	1.0-1.1 mg
<b>Pregnant women</b>	1.3-1.5 mg
<b>Lactating women</b>	1.3-1.5 mg

[Recommended daily dietary allowance (revised 1984)]

(Ref. A.C. Deb-8<sup>th</sup>, P-194)



**Beriberi:** The word 'Beri'- means 'I can not'. So beriberi signifies that the patient is too weak to do anything. Vitamin Bi (thiamin) deficiency leads to beriberi.

#### Types of beriberi:

##### Dry or neuro-logical beriberi

- Peripheral neuropathy: Tingling, Numbness, Wrists drop, Foot drop.
- Wernicke's encephalopathy: Confusion, Disorientation, Diplopia.
- Korsakoff's psychosis: Mental confusion, Loss of recent memory.

##### Wet or cardiac beriberi:

- Biventricular heart failure
- Pulmonary congestion
- Generalised oedema

##### Infantile beriberi:

Seen in exclusively breastfed infants of deficient mothers  
The condition is invariably fatal

#### Question Bank

Q. Thiamine deficiency may be associated with (BSMMU - Diploma - Dentistry - July '18)

- cardiac failure
- history of alcoholism
- history of smoking
- inhibition of enzyme aconitase
- neuropathies

Ans. a) T b) T c) F d) F e) T

Q. Thiamine deficiency leads to (BSMMU - Residency - MD, MS, Basic Science, Dentistry - March '18)

- confusion
- cardiac failure
- peripheral neuropathy
- ophthalmoplegia
- ostopenia

Ans. a) T b) T c) T d) T e) F

**Q. Thiamine deficiency can cause:** (BSMMU – MD/MS - January, 2009)

- a) diarrhea
- b) heart failure
- c) dermatitis
- d) polyneuropathy
- e) ophthalmoplegia

F  
T  
F  
T  
T

#### HELP LINK:

##### ■ Sources of thiamine:

- ♦ Plant sources: Whole grains, legumes, dried yeast, unmilled cereals, pulses, oil seeds, nuts, vegetables, fruits, rice, wheat.
- ♦ Animal sources: Beef, milk, liver, egg, fish.

##### ■ Disease caused by thiamine deficiency:

1. Dry beriberi
2. Wet beriberi
3. Wernick's encephalopathy.

**Beri-Beri:** The disease which is caused by the deficiency of thiamin(vit-B<sub>1</sub>) is called beriberi.

**Types:** ♦ Dry (neurological) beriberi      ♦ Wet (cardiac) beriberi

**C/F:**

■ **Dry beriberi:** It is manifested in chronic peripheral neuropathy with wrist and/ or foot drop and may manifest with korsakoff's psychosis and Wernicke's encephalopathy.

##### ■ Wernicke-korsakoff's syndrome:

- Confusion
- Ataxia
- Nystagmus
- Extra-ocular muscle weakness
- Dementia
- Disturbance of short term memory

■ **Wet beriberi:** Generalized oedema due to biventricular heart failure with pulmonary congestion.

1. Cardiac oedema (leg, face)
2. Palpitation.
3. Tachycardia
4. ↑Pulse pressure
5. Heart is enlarged

■ **Infantile beriberi:** Seen in infants between 2 & 4 months of age. The affected baby is usually breast-fed by a thiamin-deficient mother who commonly shows signs of peripheral neuropathy.

##### Treatment:

■ **Dry beriberi:** Responds to thiamin not uniformly good.

Multivitamin therapy seems to produce some improvement

■ **Wernicke's encephalopathy:** Treated with 50-100 mg thiamin hydrochloride solution IV injection followed by 50-100 mg IM daily for a wk.

■ **Wet beriberi:** It is an acute medical emergency requires treatment with IV thiamin.

(Ref: Davidson-23<sup>rd</sup>, P-714, A.C.Deb-8<sup>th</sup>)

**RIBOFLAVIN (VITAMIN-B<sub>2</sub>)**

Made of absorption of Vit. B<sub>2</sub>:  
Source: Take of food containing Vitamin B<sub>2</sub>.

Riboflavin is widely distributed throughout the plant and animal kingdoms.	
Gastric enzymes release Vit. B <sub>2</sub> from food.	
<b>Rich sources</b>	Aerobic fermenting bacteria.
<b>Good sources</b>	Milk, liver, kidney, heart, fish etc.
<b>Fair sources</b>	Cereals, roots, germinating wheat and barley.

(Ref. A.C. Deb-8<sup>th</sup>, P-196)**Daily requirements:**

Recommended daily dietary allowances (revised 1976)

<b>Infants</b>	0.4 - 0.6 mg
<b>Children</b>	0.8-1.2mg
<b>Adults (males)</b>	1.5- 1.8 mg
<b>Adults (females)</b>	1.1- 1.4 mg
<b>Pregnant women</b>	1.4- 1.7 mg
<b>Lactating women</b>	1.6- 1.9 mg

(Ref. A.C. Deb-8<sup>th</sup>, P-196)**Functions of Vit. B<sub>2</sub> (Riboflavin):**

- Cellular oxidation:** Riboflavin is a flavoprotein & is part of the oxidation chain in the mitochondria, acting as co-enzyme in oxidation reductions.
- Enzyme synthesis:** It acts as a co-factor for synthesis of certain enzymes
- Metabolism:** It helps in CHO, protein & fat metabolism
- Light adaptation:** It participates in light adaptation
- Normal growth:** It helps in normal growth
- Food addition:** Because of its intense yellow colour, riboflavin is widely used as a food additive.

**Deficiency effects of Vit. B<sub>2</sub>/ riboflavin:**

- Tongue:** Glossitis
- Lips:** Angular stomatitis, Cheilosis
- Genitalia:** Scrotal dermatitis, Vulval dermatitis
- Facial skin areas:** Nasolabial dyssebacea, Facial dyssebacea
- Eye:** Photophobia, Redness & burning sensation of the eyes, Vascularization of the cornea

**Q. Features riboflavin deficiency is/are (BSMMU – Non-Residency – MD, Basic Science, Dentistry – July '19)**

- cheilosis
- glossitis
- seborrhocic dermatitis
- dementia
- diarrhea

Ans. a) T b) T c) T d) F (niacin def) e) F (niacin def)

(Ref: DM Vasudevan-7<sup>th</sup>, P-480 + ABC Biochemistry-6<sup>th</sup>, P-483)**Help Link:****Riboflavin Deficiency****Causes:**

- ✓ Natural deficiency of riboflavin in man is uncommon, because riboflavin is synthesized by the intestinal flora.

- Q. This deficiency usually accompanies other deficiency diseases such as beriberi, pellagra and Kwashiorkor.

**Manifestations:**

Symptoms are confined to skin and mucous membranes.

- a) **Glossitis**
- b) Seborrhocic dermatitis
- c) Magenta colored tongue
- d) **Cheilosis**
- e) **Angular stomatitis** (inflammation at the corners of mouth)
- f) Circumcorneal vascularization
- g) Proliferation of the bulbar conjunctival capillaries is the earliest sign of riboflavin deficiency.

Ref: DM Vasudevan 7th 480+ ABC Biochemistry page 6th page 483

1. Dry beriberi

Q. Riboflavin deficiency causes (BSMMU -Residency - Dentistry – March '19)

- a) dermatitis
- b) dementia
- c) cheilosis
- d) anemia
- e) inflammation of tongue

Ans. a) T b) F c) T d) F e) T

Dry beriberi is which is caused by the deficiency of thiamine.

Help Link:

Riboflavin deficiency causes:

- ✓ Cheilosis, angular stomatitis, Glossitis, Seborrhoic dermatitis

vegetables, fruits,

(Ref. ABC-5<sup>th</sup>, P-535)

## Vitamin B<sub>12</sub>

Source:

Vitamin B<sub>12</sub> is present only in the foods of animal origin. It is not present in foods of vegetable origin. Bacterial synthesis of cobalamin occurs in the human colon but it is not absorbed. The only source of cobalamin in nature is via synthesis by micro-organisms in soil, water and the animal intestine.

<b>Richest sources</b>	Liver and kidney
<b>Good sources</b>	Meat, fish, eggs
<b>Fair sources</b>	Milk, cheese

Daily requirements:

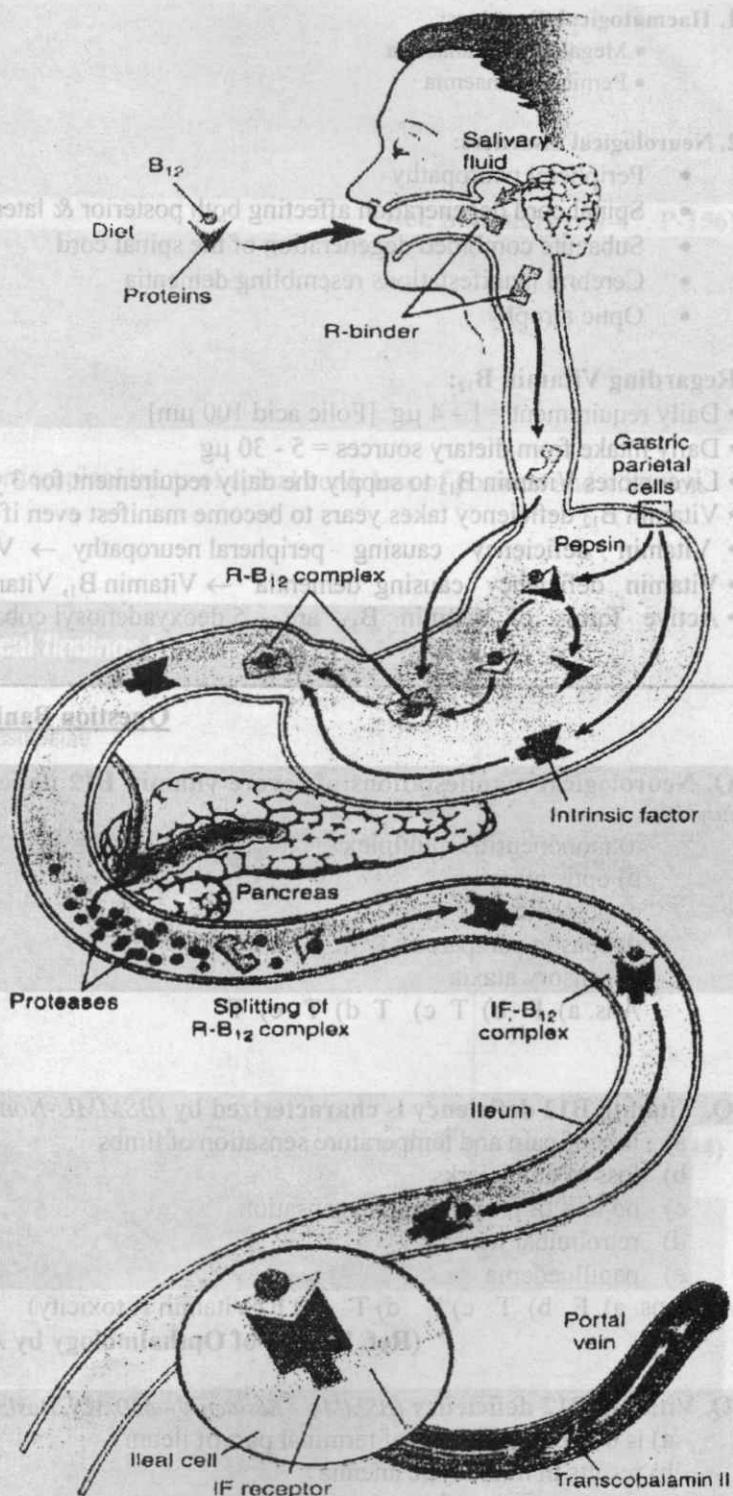
Recommended dietary daily allowances (revised 1974)

<b>Infants</b>	0.3 µg
<b>Children</b>	1-2 µg
<b>Adult (males)</b>	3.0 µg
<b>Adult (females)</b>	3.0 µg
<b>Pregnant women</b>	4.0 µg
<b>Lactating women</b>	4.0 µg

(Ref. A.C. Deb-8<sup>th</sup>, P-206)

### Mode of absorption of Vit. B<sub>12</sub>:

- Intake of food containing Vitamin B<sub>12</sub>  
 ↓  
 Gastric enzymes release Vit. B<sub>12</sub> from food in the stomach  
 ↓  
 At gastric pH binds to a carrier protein termed R protein  
 ↓  
 At pH 8, it is bounded to intrinsic factor which is a Vit. B<sub>12</sub> binding protein, secreted by parietal cells.  
 ↓  
 Switches of Vit. B<sub>12</sub> from the R protein to intrinsic factor  
 ↓  
 Formation of Vit. B<sub>12</sub> intrinsic factor complex in the intestine  
 ↓  
 The complex binds to specific receptors in the terminal ileum  
 ↓  
 Vit. B<sub>12</sub> is actively transported by the enterocytes to plasma leaving the intrinsic factor in the intestine  
 ↓  
 Vit. B<sub>12</sub> binds to a transport protein produced by the liver termed transcobalamin II  
 ↓  
 Transcobalamin II carries Vit B<sub>12</sub> to the tissues for utilization



**Fig. Schematic illustration of vitamin B<sub>12</sub> absorption.**

(Ref: Davidson's Medicine-23<sup>rd</sup> + Robbins)

- A. True     The B<sub>12</sub>/intrinsic factor complex is absorbed in the terminal ileum.

**Effects of deficiency of Vitamin B<sub>12</sub>:****1. Haematological disorders:**

- Megaloblastic anaemia
- Pernicious anaemia

**2. Neurological disorders:**

- Peripheral neuropathy
- Spinal cord degeneration affecting both posterior & lateral column
- Subacute combined degeneration of the spinal cord
- Cerebral manifestations resembling dementia
- Optic atrophy

**Regarding Vitamin B<sub>12</sub>:**

- Daily requirement = 1 – 4 µg [Folic acid 100 µm]
- Daily intake from dietary sources = 5 - 30 µg
- Liver stores Vitamin B<sub>12</sub> to supply the daily requirement for 3 years
- Vitamin B<sub>12</sub> deficiency takes years to become manifest even if all dietary intake is stopped
- Vitamin deficiency causing peripheral neuropathy → Vitamin B<sub>1</sub>, Vitamin B<sub>12</sub>, Vitamin B<sub>6</sub>
- Vitamin deficiency causing dementia → Vitamin B<sub>1</sub>, Vitamin B<sub>12</sub>, Niacin
- Active forms of Vitamin B<sub>12</sub> are - 5 deoxyadenosyl cobalamin & methylcobalamin.

**Question Bank**

**Q. Neurological manifestations of severe vitamin B<sub>12</sub> deficiency include (BSMMU-Non-Residency-Paediatrics-july'19)**

- a) mononeuritis multiplex
- b) optic atrophy
- c) dementia
- d) spastic paraparesis
- e) sensory ataxia

Ans. a) F b) T c) T d) T e) T

(Ref. Davidson-23<sup>rd</sup>, P-944)

**Q. Vitamin B<sub>12</sub> deficiency is characterized by (BSMMU-Non-Residency-Paediatrics-july'19)**

- a) loss of pain and temperature sensation of limbs
- b) loss of ankle jerks
- c) no loss of proprioceptive sensation
- d) retrobulbar neuritis
- e) papilloedema

Ans. a) F b) T c) F d) T e) F (Vitamin A toxicity)

(Ref. Review of Ophthalmology by A K Khorana-6<sup>th</sup>, P-109 + Davidson-23<sup>rd</sup>, P-944)

**Q. Vitamin B<sub>12</sub> deficiency (BSMMU-Residency - MD/MS, Basic science, Paediatrics - March' 19)**

- a) is caused by disease of terminal part of ileum
- b) results in microcytic anemia
- c) causes atrophy of gastric mucosa
- d) causes a reduction in circulating platelets
- e) causes pathological changes in CNS

Ans. a) T b) F(macrocytic/megaloblastic) c) F (is a cause but not effect) d) T e) T (Ref: Smidy)

(Ref. A.C. Deb-8<sup>th</sup>, P-208)

**Q. Vitamin B<sub>12</sub> deficiency causes (BSMMU – Residency - MD – March' 19)**

- a) megaloblastic anemia
- b) cerebellar syndrome
- c) dementia
- d) peripheral neuropathy
- e) papilloedema

Ans. a)T b) F c)T d)T e) F

(Ref. Sattanarayan-4<sup>th</sup>, P-156)

**Q. Vitamin B<sub>12</sub> deficiency is characterized by (BSMMU – Residency - Basic science – March' 19)**

- a) Loss of pain & temperature sensation of limbs
- b) Loss of ankle jerks
- c) No loss of proprioceptive sensation
- d) Retrobulbar neuritis
- e) Papilloedema

Ans.

- a) F (Degeneration of the posterior columns and corticospinal tracts of spinal cord: loss of position and vibration sense and sensory ataxia)
- b) T c) F d)T e) F (in Vitamin A toxicity)

**Help Link:**

**i 23.33 Neurological findings in B<sub>12</sub> deficiency**

**Peripheral nerves**

- Glove and stocking paraesthesiae
- Loss of ankle reflexes

**Spinal cord**

- Subacute combined degeneration of the cord
  - Posterior columns – diminished vibration sensation and proprioception
  - Corticospinal tracts – upper motor neuron signs

**Cerebrum**

- Dementia
- Optic atrophy

**Autonomic neuropathy**

(Ref. Davidson-23<sup>rd</sup>, P-944)

**Q. Vitamin B<sub>12</sub> contains (BSMMU – Residency – MD, MS, Basic Science – March' 18)**

- a) an iron atom
- b) a cobalt atom
- c) a magnesium atom
- d) a corrin ring
- e) a porphyrin ring

Ans. a) F b) T c) F d) T e) F

(Ref. ABC Biochemistry, Page – 512)

**Q. Vitamin B<sub>12</sub> deficiency may (BSMMU – Residency - Dentistry - March' 17)**

- a) result from disease of the terminal part of ileum
- b) result in anaemia with small RBCs well filled with hemoglobin
- c) cause wasting (atrophy) of the gastric mucosa
- d) cause a reduction in the circulating platelet level
- e) cause pathological changes in the central nervous system

Ans.

A. True The B12/intrinsic factor complex is absorbed in the terminal ileum.

- B. False** Lack of B12 results in a macrocytic hypochromic anaemia.  
**C. False** Gastric mucosa atrophy is a cause, not an effect, of B12 lack; gastric mucosa normally produces the 'intrinsic factor' required for B12 absorption.  
**D. True** B12 is used in the DNA synthesis required by platelet precursor cells.  
**E. True** Maintenance of myelin in neural sheaths also depends on vitamin B12.

(Ref: Roddy)

**Q. Causes of vitamin B<sub>12</sub> deficiency are (BSMMU – Residency - Dentistry - March' 17)**

- a) beriberi
- b) intrinsic factor of castle deficiency
- c) partial gastrectomy
- d) scurvy
- e) pernicious anaemia

**Ans.** a) F b) T c) T d) F e) T

**Q. The neurological manifestations of B<sub>12</sub> deficiency include (BSMMU – Non-Residency – MD, Basic science – July' 15)**

- a) mononeuritis multiplex F
- b) iritis F
- c) dementia T
- d) spastic paraparesis T
- e) sensory ataxia T

**Help link:**

**Neurologic manifestations of B<sub>12</sub> deficiency:**

- Higher functions-Dementia, psychosis
- Cranial nerves- Optic atrophy
- Pyramidal system- Spastic paraparesis
- Posterior columns- Paresthesia, diminished vibration sense, diminished loss of proprioception
- Peripheral neuropathy

**Q. Neurological complications of vitamin B<sub>12</sub> include: (BSMMU – Residency – MD – March'13)**

- a) Dementia
- b) Papilloedema
- c) Degeneration of anterior column of spinal cord
- d) Loss of vibration and position sense
- e) Autonomic disturbance

**Ans :** a) T b) F c) F d) T e) T

**HELP LINK:**

Vitamin B<sub>12</sub> deficiency is associated with:

Please try to remember the mnemonic— **SUPARSONIC**

Here:

S = Subacute combined degeneration of the spinal cord

U = Upper motor neuron signs due to degeneration of corticospinal tracts

P = Paraesthesia (gloves & stoking) Pernicious anaemia

A = Autonomic neuropathy R - Reduced sense of vibration and proprioception due to degeneration of posterior column of the spinal cord

S = Spinal cord degeneration affecting both posterior column & corticospinal tract.

O = Optic atrophy

N - Nutritional deficiency in strict vegetarians

I = Insidious, diffuse and uneven demyelination (in severe deficiency)

C = Cerebral manifestations resembling dementia

**Q. Recognized features of Vitamin B<sub>12</sub> deficiency include:** (BSMMU – Residency – MD – March '13)

- a) Degeneration of anterior spinal cord
- b) Paresthesia
- c) Optic atrophy
- d) Papilloedema
- e) Dorsal column lesion

Ans : a) F b) T c) T d) F e) T

(Ref. ABC Biochemistry-6<sup>th</sup>, P-485)

**Q. Vitamin B<sub>12</sub> deficiency is characterized by:** (BSMMU – M. Phil, Diploma (Non-Residency) – 12Ju, DMC & others – MD – 12Ju)

- a) loss of pain & temperature sensation of limbs
- b) loss of ankle jerks
- c) no loss of proprioceptive sensation
- d) retrobulbar neuritis
- e) papilloedema

Ans. a) F b) T c) F d) T e) F

**Q. Neurological complications of vitamin B<sub>12</sub> deficiency include:** (BSMMU – M. Phil, Diploma (Non-Residency) – 11Ju, DMC & others – MD/MS – 11Ju)

- |   |   |
|---|---|
| a) dementia                                       | T |
| b) papilloedema                                   | F |
| c) degeneration of anterior column of spinal cord | F |
| d) peripheral neuropathy                          | T |
| e) autonomic disturbance                          | T |

**Q. Vitamin B<sub>12</sub> deficiency may :** (BSMMU - M. Phil, Diploma – July '10)

- |   |   |
|---|---|
| a) result from disease of the terminal part of ileum  | T |
| b) result in anaemia with small RBCs                  | F |
| c) Causes wasting of gastric mucosa                   | F |
| d) causes reduction in the circulating platelet level | T |
| e) causes pathologic changes in CNS                   | T |

(Ref: Smiddy)

**Q. Vitamin B<sub>12</sub> deficiency:** (BSMMU - M. Phil, Diploma, July-09)

- |   |   |
|---|---|
| a) Causes demyelination   | T |
| b) Causes microcytic anaemia  | F |
| c) May cause progressive dementia   | T |
| d) May be due to gastric intrinsic factor deficiency                                      | T |
| e) May cause degeneration of both ascending and descending tracts of the posterior column | T |

#### HELP LINK:

##### Features of vit B<sub>12</sub> deficiency is/ are

- Megaloblastic anaemia
- Peripheral neuropathy
- Subacute combined degeneration of spinal cord
- Dementia
- Optic atrophy

(Ref: Davidson-20<sup>th</sup>, P-125)

#### Mode of absorption of Vit. B<sub>12</sub>:

Intake of food containing Vitamin B<sub>12</sub>



Gastric enzymes release Vit. B<sub>12</sub> from food in the stomach

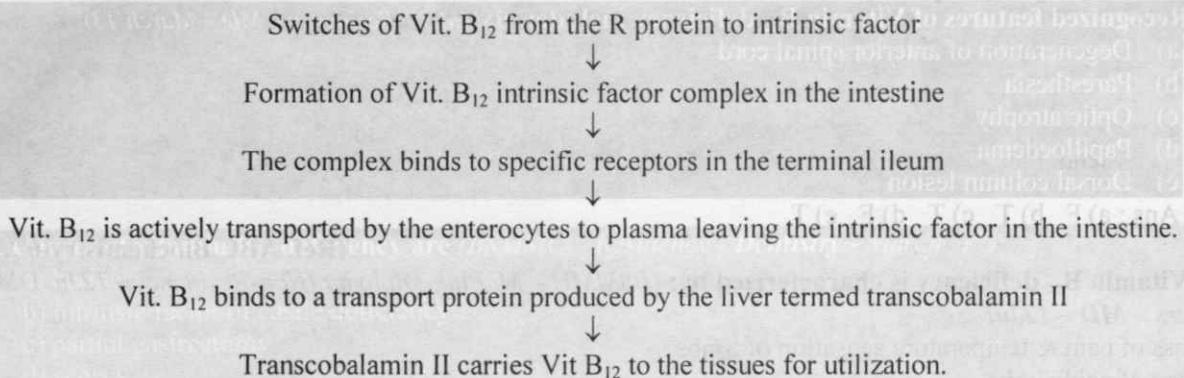


At gastric pH binds to a carrier protein termed R protein



At pH 8, it is bounded to intrinsic factor which is a Vit. B<sub>12</sub> binding protein, secreted by parietal cells.





**Q. Deficiency of vitamin B<sub>12</sub> may lead to:** (BSMMU – MD - January, 2009)

- a) glove and stocking paresthesia
- b) lower motor neuron type of paralysis
- c) optic atrophy
- d) autonomic neuropathy
- e) Wernicke's encephalopathy

T  
F  
T  
T  
F

**Q. Vitamin B<sub>12</sub> deficiency:** (BSMMU - M.Ph.Diploms, July-08)

- a) causes demyelination
- b) causes microcytic anemia
- c) may cause progressive dementia
- d) may be due to deficiency of gastric intrinsic factor
- e) may degenerate both the ascending tracts of the posterior column & descending pyramidal tract

T  
F  
T  
T  
T

**Q. Vitamin B<sub>12</sub> deficiency may result in –** (BSMMU – MD - January, 2007)

- a. sensory ataxia
- b. optic neuritis
- c. psychosis
- d. gloves and stocking anaesthesia
- e. microcytic anaemia

T  
T  
F  
T  
F

**Q. The cardinal features of vitamin-B<sub>12</sub> deficiency is/ are:** (DMC – M.Phil, Diploma - 06Ju)

- a) glossitis
- b) peripheral neuropathy
- c) MCV of 50 fl.
- d) MCH of 20 pg
- e) subacute combined degeneration of spinal cord

T  
T  
F (> 100 fl)  
F  
T

#### HELP LINK:

- Daily requirement = 1 - 4 µg; store in liver: 2 – 5 gm for 2-3 yrs.
- Daily intake from dietary sources = 5 - 30 µg
- Liver stores Vitamin B<sub>12</sub> to supply the daily requirement for 3 years
- Vitamin B<sub>12</sub> deficiency takes years to become manifest even if all dietary intake is stopped
- Vitamin deficiency causing peripheral neuropathy — Vitamin. B<sub>1</sub>, Vit. B<sub>6</sub>, Vit. B<sub>12</sub>.
- Vitamin deficiency causing dementia — Vitamin B<sub>1</sub>, Vitamin B<sub>12</sub>, Niacin.
- Active forms of Vitamin B<sub>12</sub> are — 5 deoxyadenosyl cobalamin & methylcobalamin.

Functions of vitamin B <sub>12</sub>	Deficiency features of vit B <sub>12</sub> deficiency
<ol style="list-style-type: none"> <li>Essential for maturation of RBC.</li> <li>Necessary for the synthesis of DNA.</li> <li>Produces remission in pernicious anaemia.</li> <li>Essential for protein metabolism</li> </ol>	<ol style="list-style-type: none"> <li>Megaloblastic anaemia (dietary deficiency)</li> <li>Pernicious anaemia (intrinsic factor deficiency)</li> <li>Methylmalonic aciduria.</li> <li>Peripheral neuropathy.</li> <li>Subacute combined degeneration of spinal cord.</li> <li>Optic atrophy</li> <li>Dementia</li> </ol>

**Q. Neurological complications of vitamin B<sub>12</sub> deficiency are:** (BSMMU – M. Phil, Diploma-06Ju)

- |   |   |
|---|---|
| a. Dementia                                       | T   |
| b. Papilloedema                                   | F   |
| c. Peripheral neuropathy                          | T   |
| d. Autonomic disturbance                          | T   |
| e. Degeneration of anterior column of spinal cord | F ( <i>Posterior column &amp; corticospinal tract</i> ) |

**HELP LINK:**

**Features of vit B<sub>12</sub> deficiency is/ are**

- Megaloblastic anaemia
- Peripheral neuropathy
- Subacute combined degeneration of spinal cord
- Dementia
- Optic atrophy

(Ref: Davidson-20<sup>th</sup>, P-125)

Red cell indices	Normal	Megaloblastic anaemia due to vit B <sub>12</sub> deficiency
MCV	83 - 101 femtolitres	> 120 femtolitre
MCH	27 – 32 picograms	↑
MCHC	31.5 – 34.5 gm/dl	Normal

**Q. The cardinal features of vit B<sub>12</sub> deficiency is/ are :** (DMC – MD/MS - 06Ja)

- |  |   |
|--|---|
| a. Glossitis                                     | T |
| b. Peripheral neuropathy                         | T |
| c. MCV of 50 fl.                                 | F |
| d. MCV of 20 pg                                  | F |
| e. Subacute combined degeneration of spinal cord | T |

Neural tube defect due to folic acid deficiency takes place 3-4 weeks after conception.

**Q. Causes of vit. B<sub>12</sub> deficiency -** (DMC – MD/MS - 03Ja)

- |  |  |
|--|--|
| a) Ulcerative colitis                    | F  |
| b) Crohn's disease                       | T  |
| c) Parasites such as schistoma infection | F (Adult <i>D. latum</i> can cause vitamin B <sub>12</sub> deficiency) |
| d) True vegans                           | T (Breast fed offspring of vegan mothers are at risk)                  |
| e) Secondary to low serum folate level   | T  |

**Q. Effect of Vit B<sub>12</sub> deficiency are -** (BSMMU – MD - 02Ja)

- |                                  |   |
|----------------------------------|---|
| a) Changes of epithelial surface | F |
| b) Sterility                     | F |
| c) Pancytopenia                  | T |
| d) Polychromatic macrocytosis    | T |
| e) Neuropathy                    | T |

**Help link:** Common features of megaloblastic anaemia is pancytopenia.

## FOLIC ACID

**Q. Folate deficiency occurs in (BSMMU – Non-Residency – MD – July '18)**

- a) tropical sprue
- b) celiac sprue
- c) pernicious anemia
- d) post-gastrectomy state
- e) small intestinal bacterial overgrowth

Ans. a) T b) T c) F d) F

e) F (in patients with blind loop syndrome presents with watery diarrhoea and or steatorrhoea with anaemia due to B12 deficiency. (Ref: Davidson-23<sup>rd</sup>)

**Q. Dietary sources of folate are- (BSMMU – MD - 02Ja)**

- |             |   |
|-------------|---|
| a) Spinach  | T |
| b) Fish     | F |
| c) Potatoes | F |
| d) Milk     | T |
| e) Kidney.  | T |

**Help link:**

**Source:**

<b>Richest sources</b>	Yeast, liver, kidney.
<b>Good sources</b>	Meat, fish, green leafy vegetables.
<b>Fair sources</b>	Milk, fruit.
Intestinal bacteria also synthesize folic acid.	

**Daily requirements:**

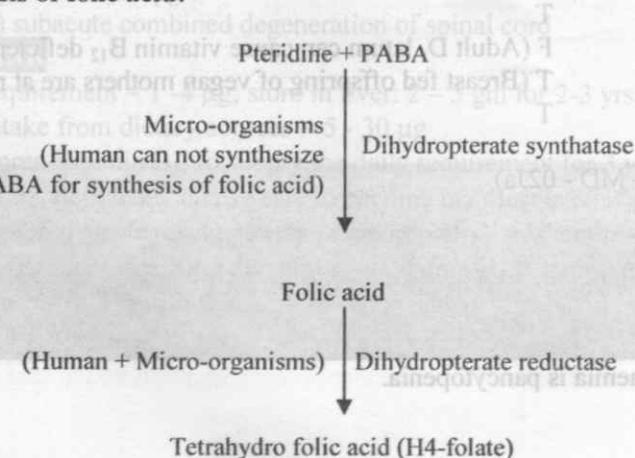
<b>Recommended dietary daily allowances (revised 1974)</b>	
<b>Infants</b>	50 µg
<b>Children</b>	100 -300 µg
<b>Adult (females)</b>	400 µg
<b>Pregnant women</b>	800 µg
<b>Lactating women</b>	600 µg

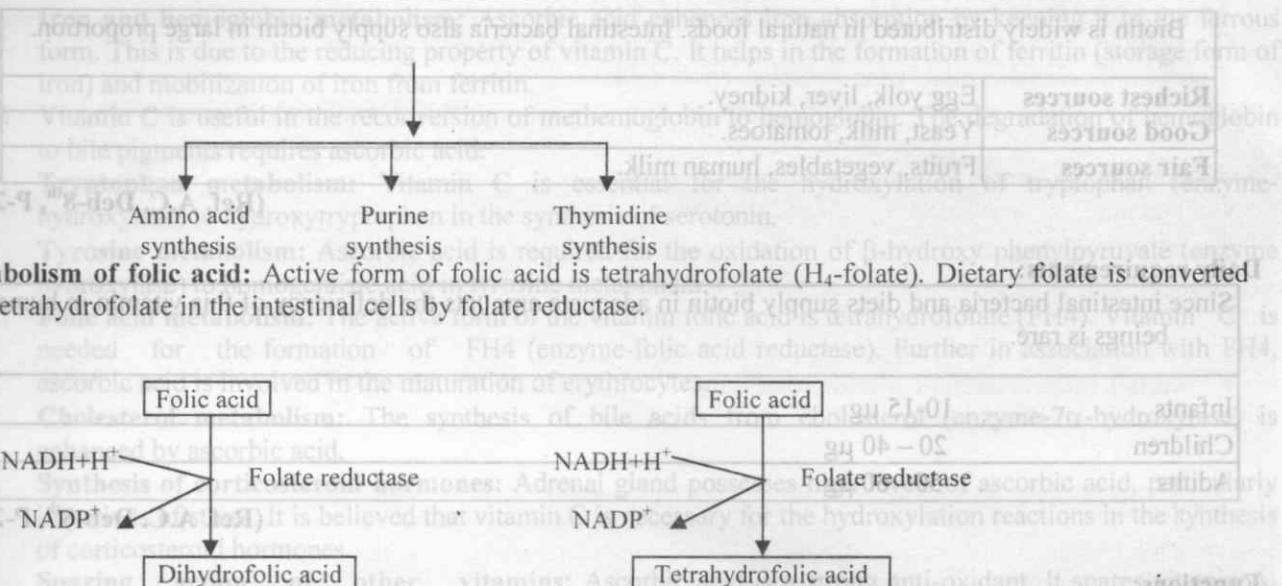
(Ref. A.C. Deb-8<sup>th</sup>, P-202)

**Structure:** Folic acid composed of three components-

- A pteridine (base)- two nitrogenous compound
- Para amino benzoic acid (PABA)
- Glutamic acid

**Biosynthesis of folic acid:**





#### Sources of folic acid:

- Animal : Liver, Kidney, Milk, Egg.
- Plant : Leafy Vegetable, beans, nuts & cabbage

#### Daily requirement: 0.4 mg

- During pregnancy: 0.8 mg
- During lactation: 0.5 mg

#### Deficiency effects of folic acid:

##### 1. Haematological disorders:

- Megaloblastic anaemia

##### 2. Neural tube defect

- Spina bifida
- Anencephaly
- Encephalocele

##### 3. GIT disorders

- Glossitis
- Infertility/ complete sterility (When deficiency is severe)

#### Regarding folic acid:

- Neural tube defect due to folic acid deficiency takes place 3-4 weeks after conception.
- Patients having history of neural tube defect in previous pregnancies should take 5 mg folic acid daily from before conception & throughout the first trimester of pregnancy.
- All women planning a pregnancy are advised to include good sources of folate in their diet. Liver is the richest source of folate which is also a richest source of Vitamin A. As Vitamin A supplementation is contraindicated in pregnancy due to its teratogenic effect, an alternative source of folate is advised in early pregnancy.

(Ref: Davidson's Medicine + Harper + Lippincott)

## BIOTIN

#### Synonym - Vitamin H

**Sources:** Liver, kidney, vegetables, egg yolk. Biotin is synthesized by intestinal flora in such large quantities that dietary source is probably not necessary. For that, biotin deficiency rarely occurs on a natural diet but is occasionally seen in patients consuming large quantities of raw eggs (unboiled eggs). Avidin in raw eggs binds to biotin in the intestine and inactivates it.

Biotin is widely distributed in natural foods. Intestinal bacteria also supply biotin in large proportion.

<b>Richest sources</b>	Egg yolk, liver, kidney.
<b>Good sources</b>	Yeast, milk, tomatoes.
<b>Fair sources</b>	Fruits, vegetables, human milk.

(Ref. A.C. Deb-8<sup>th</sup>, P-207)

#### Daily requirements:

Since intestinal bacteria and diets supply biotin in adequate amounts the deficiency of this vitamin in human beings is rare.

Infants	10-15 µg
Children	20 - 40 µg
Adults	50 - 60 µg

(Ref. A.C. Deb-8<sup>th</sup>, P-208)

#### Functions:

Biotin acts as a co-enzyme in carbohydrate, fatty acid & amino acid metabolism.

#### Effects of deficiency:

- Scaly dermatitis
- Alopecia
- Paraesthesia

## ASCORBIC ACID (VITAMIN-C)

#### Source:

<b>Richest source</b>	Amla
<b>Good sources</b>	Citrus fruits, tomatoes, green peppers, raw cabbage, guava, cauliflower, adrenal cortex.
<b>Fair sources</b>	Grapes, apple, banana, jackfruit, milk, liver, green leafy vegetable particularly salad greens, fresh potatoes, freshly killed meat, fresh raw fish, papaya.

Ascorbic acid is not synthesized in the body of the human beings. Dietary sources can only provide this vitamin. The artificial food or sterilised milk is devoid of vitamin-C.

(Ref. A.C. Deb-8<sup>th</sup>, P-192)

#### Daily requirement:

<b>Infants</b>	35 mg
<b>Children</b>	40 mg
<b>Adults</b>	45mg
<b>Pregnant women</b>	60 mg
<b>Lactating women</b>	80 mg

(Ref. A.C. Deb-8<sup>th</sup>, P-192)

#### Biochemical functions of vitamin-C:

Most of the functions of vitamin C are related to its property to undergo reversible oxidation reduction i. e., interconversion of ascorbic acid and dehydro-ascorbic acid.

1. **Collagen formation:** Vitamin C plays the role of a coenzyme in hydroxylation of proline and lysine while procollagen is converted to collagen (i. e. post-translational modification). The hydroxylation reaction is catalysed by lysyl hydroxylase (for lysine) and prolyl hydroxylase (for proline). This reaction is dependent on vitamin C, molecular oxygen and  $\alpha$ -ketoglutarate. Hydroxyproline and hydroxylysine are essential for the collagen cross-linking and the strength of the fiber. In this way, vitamin C is necessary for maintenance of normal connective tissue and wound healing process.
2. **Bone formation:** Bone tissues possess an organic matrix, collagen and the inorganic calcium, phosphate etc. Vitamin C is required for bone formation.

3. **Iron and hemoglobin metabolism:** Ascorbic acid enhances iron absorption by keeping it in the ferrous form. This is due to the reducing property of vitamin C. It helps in the formation of ferritin (storage form of iron) and mobilization of iron from ferritin.
- Vitamin C is useful in the reconversion of methemoglobin to hemoglobin. The degradation of hemoglobin to bile pigments requires ascorbic acid.
4. **Tryptophan metabolism:** Vitamin C is essential for the hydroxylation of tryptophan (enzyme-hydroxylase) to hydroxytryptophan in the synthesis of serotonin.
5. **Tyrosine metabolism:** Ascorbic acid is required for the oxidation of  $\beta$ -hydroxy phenylpyruvate (enzyme hydroxylase) to homogentisic acid in tyrosine metabolism.
6. **Folic acid metabolism:** The active form of the vitamin folic acid is tetrahydrofolate (FH4). Vitamin C is needed for the formation of FH4 (enzyme-folic acid reductase). Further in association with FH4, ascorbic acid is involved in the maturation of erythrocytes.
7. **Cholesterol metabolism:** The synthesis of bile acids from cholesterol (enzyme-7 $\alpha$ -hydroxylase) is enhanced by ascorbic acid.
8. **Synthesis of corticosteroid hormones:** Adrenal gland possesses high levels of ascorbic acid, particularly in periods of stress. It is believed that vitamin C is necessary for the hydroxylation reactions in the synthesis of corticosteroid hormones.
9. **Sparing action of other vitamins:** Ascorbic acid is a strong anti-oxidant. It spares vitamin A, Vitamin E, and some B-complex vitamins from oxidation.
10. **Cellular respiration:** Vitamin C is involved in the electron transport chain. Some components of ETC (e.g. cytochrome oxidase) exhibit optimum activity in the presence of ascorbic acid.
11. **Immunological function:** Vitamin C enhances the synthesis of immunoglobulins (antibodies) and increases the phagocytic action of leucocytes.
12. **Preventive action on cataract:** Vitamin C reduces the risk of cataract formation.
13. **Preventive action on chronic diseases:** Free radical are constantly produced in the normal metabolism. They cause serious damage to proteins, lipids, DNA and the cell membranes the free radicals are implicated in the development of cancer, heart diseases and also ageing. Vitamin C is a strong biological antioxidant, besides vitamin E and  $\beta$ -carotene. Supplementation of the diet with these three antioxidants has been found to decrease the incidence of chronic diseases such as cancer and coronary heart diseases. The antioxidants perform a common function to inactivate the toxic free oxygen radicals.

#### **Effects of deficiency of Vitamin C:**

##### **Mild case:**

- ↓ resistance to infection
- Gum bleeding
- Dental caries
- Joint tenderness

##### **Severe case**

- Scurvy
- Anaemia
- Haemorrhage

Helps in collagen synthesis.

#### Ques 10

##### **Regarding Vitamin C:**

- It is the most active reducing agent in the aqueous phase of the living tissues.
- It is easily destroyed by heat, pH & light
- Boiled milk contains no Vitamin C as traditional cooking methods reduce or destroy it.
- High dose of Vitamin C improves immune function including resistance to common cold (But such effect still remains unproven in controlled trials)
- Daily intake of more than 1 gm have been reported to cause diarrhoea & increase the formation of renal oxalate stones.
- Highest concentration of vitamin C is present in adrenal cortex, gut wall, aqueous & vitreous humors.

- Ascorbic acid is oxidised to dehydroascorbic acid. Both ascorbic acid & dehydro ascorbic acid have vitamin C activity.
- Human milk contains more vitamin C than cows milk.

(Ref: Davidson's Medicine + S. Narayan)

### Conditions when Vitamin C requirement is increased:

- Trauma
- Surgery
- Burns
- Infections
- Smoking
- Certain drugs: Adreno-corticosteroid, Aspirin, Indomethacin, Tetracycline
- Hospital admitted patient

### SCURVY:

Scurvy is the clinical manifestation of vitamin C deficiency characterized by abnormal formation of bone & teeth & hemorrhagic manifestations.

#### Cause:

- Intake of no fruits or vegetables for 2 - 3 months
- Infants fed on boiled milk (traditional cooking methods reduce or eliminate vitamin C)
- Adults with an inadequate diet

#### Types with clinical manifestations:

##### Adult scurvy:

- Swollen & spongy gum, which bleed easily
- Perifollicular, petechial or spontaneous bruising
- Haemorrhage into joints & GIT
- Anaemia
- Fresh wound fails to heal

##### Infant scurvy:

- Gingivitis
- Lassitude
- Anorexia
- Painful limbs
- Subperiosteal haemorrhage
- Enlargement of costochondral junctions

Infants	35 mg
Children	40 mg
Adults	45 mg
Pregnant women	60 mg
Nursing women	80 mg

### Question Bank

#### Q. Features of vitamin C deficiency are (BSMMU –Residency - Dentistry – March '19)

- prolonged prothrombin time
- normal bleeding time
- gum hyperplasia
- poor wound healing
- glossitis

Ans. a) F b) F(prolonged bleeding time) c) T d) T e) F

#### Help Link:

Bone formation: Bone tissues possess an organic matrix, collagen and the inorganic calcium, phosphate etc. Vitamin C is required for bone formation.

**Causes of glossitis:**

- ✓ Iron deficiency anaemia (painless glossitis)
- ✓  $B_{12}$  deficiency/ Megaloblastic anaemia (painful)- "beefy" or "fiery red and sore"
- ✓ Vitamin B1, 2, 3, 6 deficiency
- ✓ Many infection

**Q. Followings is/are feature/s of scurvy (BSMMU – Residency – MD, Basic Science, Dentistry – March' 18)**

- a) pencil point thinness of the cortex
- b) metaphyseal osteochondritis
- c) diaphyseal periostitis
- d) periosteal elevation
- e) positive Wimber sign

Ans. a) T b) F c) F d) T e) T

(Ref. Radiopedia)

**Q. Vitamin C (BSMMU – Residency - Dentistry - March' 17)**

- a) maintains prosthetic metal ions in their reduced form
- b) scavenges free radicals
- c) synthesized in humans
- d) deficiency causes cessation of bone growth
- e) daily requirement is 400 IU

Ans. a) T b) T c) F d) T e) T

H.L: Human guinea pigs, bats cannot synthesize ascorbic acid due to deficiency of a single enzyme name L-gulonolactone oxidase.

(Ref: A.C.Dep-187b + Periods of SMMU)

**Q. Vitamin C is required for the synthesis of (BSMMU – Residency – MD, MS, Basic – March' 15)**

- a) hydroxyproline
- b) hydroxylysine
- c) nor epinephrine
- d) coagulation factors
- e) thyroxine

Ans. a) T b) T c) T d) F e) F

**Q. Role of vitamin C: (BSMMU - M. Phil, Diploma – July '10)**

- a) formation of visual pigment F
- b) growth of the bones T
- c) treatment of pernicious anaemia F
- d) wound healing T
- e) pain relief F

**HELP LINK:****■ Functions:**

1. Helps in collagen synthesis.
2. It is required for degradation of tyrosine.
3. It is required for synthesis of epinephrine from tyrosine at the step of dopamine  $\beta$ -hydroxylase.
4. It is required for bile acid synthesis at the step of 7- $\alpha$ -hydroxylase.
5. It helps in adrenocorticosterone hormone secretion.
6. It helps in iron absorption from the intestine by reducing  $Fe^{+3}$  to  $Fe^{+2}$  ion..
7. It acts as an anti-oxidant.
8. It promotes the conversion of folic acid into its active form tetrahydrofolic acid, thereby takes part in the maturation process of RBC.
9. It plays an important role in wound healing.

(Ref: Harper-30<sup>th</sup>)

**Q. Ascorbic acid helps in – (DMC – MD/MS - 08Ja)**

- |                              |                     |
|------------------------------|---------------------|
| a) calcium absorption        | F (Iron absorption) |
| b) collagen synthesis        | T                   |
| c) iron absorption           | T                   |
| d) haemostasis               | F                   |
| e) oxidative phosphorylation | F                   |

**Q. Ascorbic acid: (BSMMU – M. Phil, Diploma July, 2004)**

- |   |   |
|---|---|
| A. Is a heat stable vitamin.                              | F |
| B. Is required as cofactor for the hydroxylation reaction | T |
| C. Deficiency causes easy bruising.                       | T |
| D. Is excreted in urine unchanged when taken large amount | T |
| E. In present in high concentration in cod-liver oil      | F |

**Help link:**

**Deficiency features:** Deficiency of vitamin C causes **scurvy** which is characterized by:

1. Hemorrhages from the mucous membrane of mouth, nose, GIT, gum bleeding, bleeding spot, purpural spot and muscles.
2. Muscular weakness.
3. Gums show swelling, tenderness, redness, ulceration and even gangrene.
4. Pain & swelling in the joints.
5. Delayed wound healing due to defective collagen synthesis.
6. Definitive defects in skeletal calcification.
7. Loosing of teeth and cessation of bone growth.
8. Susceptibility to infections, dental caries, pyorrhea.

(Ref: A.C.Deb-187p + Lecture of SSMC)

## NIACIN (NICOTINIC ACID) (VIT-B<sub>3</sub>)

**Sources:**

<b>Richest source</b>	Yeast, rice polishing.
<b>Good sources</b>	Meat, liver and poultry
<b>Fair sources</b>	Milk, eggs, tomatoes, leafy green vegetables.
<b>Poor sources</b>	Most fruits and vegetables.

The amino acid tryptophan present in the dietary proteins is converted into niacin in the body. 60 mg. of tryptophan produce 1 mg. of niacin. So tryptophan present in the foodstuff also provides additional niacin.

(Ref. A.C. Deb-8<sup>th</sup>, P-197)

**Daily requirements:**

Recommended daily dietary allowances (revised 1974).	
<b>Infants</b>	5-8mg
<b>Children</b>	9-16mcg
<b>Adult (males)</b>	16 - 20 mg
<b>Adult (females)</b>	12 - 16 mg
<b>Pregnant women</b>	14-18mg
<b>Lactating women</b>	16-20mg

(Ref. A.C. Deb-8<sup>th</sup>, P-197)

**Effects of deficiency of Niacin:****Functions of Niacin:**

1. Nicotinic acid & Nicotinamide have equal biological activity & are considered together in foods under the generic term 'Niacin'. Nicotinamide is an essential part of the two important pyridine nucleotides, nicotinamide adenine dinucleotide (NAD) & nicotinamide adenine dinucleotide phosphate (NADP) which play key role in intermediate metabolism.

2. NAD is also the enzyme of alcohol dehydrogenase.
3. Nicotinic acid lowers serum cholesterol
4. Niacin prevents pellagra
5. It is also essential for the normal functioning of the skin, intestinal tract & the nervous system.

**Q. Niacin deficiency leads to development of (BSMMU –Residency - MD/MS, Basic science, Paediatrics – March' 19)**

- a) scurvy
- b) pellagra
- c) peripheral neuropathy
- d) beriberi
- e) osteomalacia

Ans. a) F (vitamin C deficiency) b) T c) F (pyridoxine deficiency) d) F (thiamin deficiency)  
e) F (vitamin D deficiency)

**Help Link:** **Pelegra:** Diarrhoea, Dementia, Dermatitis

**Q. Characteristic features of pellagra include: (DMC – MD/MS - 05Ja)**

a) Dementia	T
b) Hypochromic microcytic anaemia	F
c) Depression	F
d) Diarrhoea	T
e) Pigmentation of the skin	F

**Help link:**

#### **Effects of deficiency of Niacin:**

##### **1. Pellagra:**

Pellagra means rough skin. The deficiency of niacin causes this disease. Pellagra is characterized by 3 Ds – dermatitis, diarrhoea and dementia and if untreated death (4<sup>th</sup> D).

##### **Dermatitis:**

- Erythema resembling severe sunburn
- Appears in the expose part of the body like in the neck & in the limbs
- Lesion may progress to vesication, cracking, exudation, crusting, ulceration
- Secondary infection may develop.

##### **Diarrhoea:**

- Diarrhoea associate with nausea, anorexia, glossitis dysphagia
- Diarrhoea ranges from a few . to several loose stool a day with blood & mucus

##### **Dementia:**

- In severe deficiency delirium develops acutely
- Dementia develops in chronic cases.
- i. Irritability, changes in disposition, depression, inability to concentrate are found in milder mental disturbances.
- ii. In mild cases, poor memory is common.
- iii. In chronic cases, spasticity, ataxia etc. are seen.

##### **2. Glossitis**

##### **3. Stomatitis**

Vitamin B6 is pyridoxal phosphate.

- Vitamin B6 deficiency is very rare in human but may occur during lactation therapy.
- The drug which frequently cause vitamin B6 deficiency are – isoniazide (ID), penicillamine.
- It is the only vitamin whose deficiency & excess both cause peripheral neuropathy.
- Large doses of vitamin B6 have an anti-carcinotic effect in radiotherapy induced dermatitis.

Q. Ascorbic acid helps in – (DMC – MDMS - 0813)

- a) calcium absorption
- b) collagen synthesis
- c) iron absorption
- d) oxidative phosphorylation
- e) oxidative phosphorylation



**Fig. Dermatitis due to pellagra (niacin deficiency)**

(Ref: Davidson's Medicine + Harper)

## PYRIDOXINE (VITAMIN B<sub>6</sub>)

### Sources:

<b>Rich sources</b>	Yeast, rice polishings, certain seeds such as a wheat and corn.
<b>Good sources</b>	Milk, meat, leafy vegetables, liver.
<b>Fair sources</b>	Fish, fruits, vegetables.

Intestinal bacteria can also synthesize this vitamin.

### Daily requirements:

<b>Recommended daily dietary allowances (revised 1974)</b>	
<b>Infants</b>	0.3 mg
<b>Children</b>	0.6-1.2 mg
<b>Adults (males)</b>	1.6 - 2.0 mg
<b>Adults (females)</b>	1.6-2.0 mg
<b>Pregnant women</b>	2.5 mg
<b>Lactating women</b>	2.5 mg

(Ref. A.C. Deb-8<sup>th</sup>, P-199)

Pyridoxine, pyrioxal and pyridoxamine are three closely related compounds with similar physiological actions. The active form of the Vitamin B<sub>6</sub> in human is pyridoxal 5-phosphate.

### Functions of vitamin B<sub>6</sub> (Pyridoxine):

1. It acts as co-enzyme and involves in transmutation for the synthesis of amino acids.
2. It is essential for metabolism of tryptophan.

### Effects deficiency of Vitamin B<sub>6</sub>:

#### Neurological:

Peripheral neuropathy

Personality changes

Convulsions

1. Nicotinamide & nicotinamide have equal biological activity & are considered together in foods under the generic term Niacin. Nicotinamide is an essential part of the two important pyridine nucleotides, nicotinamide adenine dinucleotide phosphate (NADP) which play key role in

#### Dermatological disorders:

Dermatitis around the eyes

Dermatitis around the mouth

**GIT disorders:**

Anorexia

Nausea

Vomiting

(Ref: Davidson's Medicine + Lippincott)

**Haematological disorders:**

Sideroblastic anaemia

**Regarding Vitamin B6:**

- Active form of Vitamin B6 is pyridoxal phosphate
- Vitamin B6 deficiency is very rare in human but may occur during lactation, alcoholics, during certain drug therapy.
- The drugs which frequently cause vitamin B6 deficiency are - Isoniazid (Anti TB), penicillamine
- It is the only vitamin whose deficiency & excess both cause peripheral neuropathy
- Large doses of vitamin B6 have an anti-emetic effect in radiotherapy induced nausea.
- It has become popular for the treatment of nausea in pregnancy, carpal tunnel syndrome & premenstrual syndrome (But there is no convincing evidence of benefits)
- Some cases of sideroblastic anaemia respond to treatment with pyridoxine.

(Ref: Davidson's Medicine + Lippincott)

**Question Bank****Q. Vitamins that act as coenzyme are (BSMMU – Residency – MD, MS, Basic Science, Dentistry – March '18)**

- ascorbic acid
- vitamin D
- vitamin E
- vitamin K
- pyridoxine

Ans. a) T b) F c) F d) T e) T

(Ref. ABC Biochemistry Page-84)

**Q. Features of vitamin B<sub>6</sub> deficiency are (BSMMU – Non-Residency – MD/MS, Basic science – July '14)**

- microcytic anaemia
- increased δ-ALA
- increased ferritin
- decreased serum iron
- sideroblasts in bone marrow

Ans. a) T b) F c) F d) F e) T

**Q. Pyridoxine deficiency may occur in: (BSMMU – MD – January, 2010)**

- Beriberi
- Wernicke's Korsakoff syndrome
- Isoniazid therapy
- Use of oral contraceptives
- Turner's syndrome

F

F

T

F

F

**HELP LINK:**

- Active form of Vitamin B6 is pyridoxal phosphate.
- Vitamin B6 deficiency is very rare in human but may occur during lactation, alcoholics, during certain drug therapy.
- The drugs which frequently cause vitamin B6 deficiency are — Isoniazid (Anti TB), penicillamine.
- It is the only vitamin whose deficiency & excess both cause peripheral neuropathy.
- Large doses of vitamin B6 have an anti-emetic effect in radiotherapy induced nausea.

- It has become popular for the treatment of nausea in pregnancy, carpal tunnel syndrome & premenstrual syndrome (But there is no convincing evidence of benefits)
- Some cases of sideroblastic anaemia respond to treatment with pyridoxine..

(Ref: Davidson's Medicine-23<sup>rd</sup> + Lippincott-7<sup>th</sup>)

**Q. Pyridoxine deficiency may occur in:** (DMC – M.Phil, Diploma - 07Ju)

- |                                  |   |
|----------------------------------|---|
| a) beriberi                      | F |
| b) Wernicke's Korsakoff syndrome | F |
| c) isoniazid therapy             | T |
| d) use of oral contraceptive     | F |
| e) Turner's syndrome             | F |

### **PANTOTHENIC ACID (VIT. B<sub>5</sub>)**

**Source:**

<b>Richest source</b>	Jelly
<b>Rich sources</b>	Yeast, liver, rice polishings and wheat germ.
<b>Good sources</b>	Milk, meat, eggs and leafy vegetables.
<b>Fair sources</b>	Fruits and other vegetables.

(Ref. A.C. Deb-8<sup>th</sup>, P-200)

**Daily requirements:**

<b>Infants</b>	1-2mg
<b>Children</b>	4-5mg
<b>Adults (males &amp; females)</b>	5-10mg
<b>Pregnant &amp; lactating women</b>	10-15mg

(Ref. A.C. Deb-8<sup>th</sup>, P-200)

**Physiological functions:**

Pantothenic acid is essential for the growth of infants and children.

**Coenzyme activities:**

1. Pantothenic acid as a constituent of coenzyme a is required for several fundamental reactions in metabolism.
2. Coenzyme a combines with acetate to form "active acetate" (acetylcoenzyme A) which is directly utilized by combination with oxaloacetic acid to form citric acid which initiates the citric acid cycle.
3. Acetyl-CoA derived from carbohydrates, fats or many of the amino acids undergoes further metabolism through the "common metabolic pathway".
4. In the form of active acetate, acetic acid also combines with choline to form acetylcholine or with the sulfonamide drugs which are acetylated prior to excretion.
5. The decarboxylated product of  $\alpha$ -ketoglutarate in the citric acid cycle is a coenzyme a derivative called "active succinate" (succinyl-CoA). Succinyl-CoA and glycine are involved in the first step leading to the biosynthesis of heme. So anemia occurs in the deficiency of this vitamin.
6. In lipid metabolism, coenzyme a has got significant role. In the first step of oxidation of fatty acids, the fatty acids are to be activated by coenzyme a catalyzed by the enzyme thiokinase. In each turn of the P-oxidation cycle, one molecule acetyl-CoA is released. This acetyl-CoA directly enters the citric acid cycle for degradation to carbon dioxide and water or two molecules of acetyl-CoA condense to form ketone bodies.
7. A significant amount of the cellular pantothenic acid is protein bound. This form is contained in a compound known as acyl carrier protein, a coenzyme required in the biosynthesis of fatty acids.
8. Coenzyme a is also involved in the metabolism of propionate and of branch chain fatty acids.

**Deficiency symptoms:**

1. Deficiency of this vitamin in man results in nausea, vomiting, certain gastrointestinal disorders, irritability, inadequate growth, anemia, fatty liver, failure in gaining weights.
2. Pantothenate deficiency causes burning foot syndrome in prisoners of war and is associated with reduced capacity for acetylation.

(Ref: A.C. Deb-8<sup>th</sup>, P-200)**Antioxidant vitamin**

**ANTIOXIDANTS:** During normal metabolism of oxygen free radicals are generated. The free radicals which are produced in human body are-

- OOH (peroxide radical)
- OH (Hydroxyl radical)
- O<sub>2</sub> (Superoxide radical)
- NO (Nitric oxide)

These free radicals are harmful for human body. Fortunately a considerable amount of protection exists in the body in the form of antioxidant, which combat free radicals. Food spices also contain antioxidant substance.

Principal dietary antioxidants are -

- Vitamin E
- Vitamin C
- β-carotene
- Flavanoids

**Tocopherol-as antioxidant:**

Vitamin E (tocopherol) is the most important natural antioxidant, which is effective in high oxygen concentrations. So it tends to be concentrated in those lipid structures that are exposed to the highest O<sub>2</sub> partial pressures, eg: RBC membrane, the membranes of the respiratory tree & retina.

Vitamin E is non-toxic and acts both inside & outside the cell. Vitamin E appears to be the first line of defense against lipid peroxidation. The beneficial effects are -

- Prevention of atherosclerosis
- Stoppage of the degeneration of germinal epithelium
- Protection from degenerative changes of dorsal column.

**Ascorbic acid - as antioxidant:**

Ascorbic acid is a strong reducing agent and functionally similar to both Vitamin & glutathione in lipid peroxidation & other oxidative conditions.

It inhibits nitrosamine-induced carcinogenesis by directly reducing these compounds. It is good scavenger for many free radicals & detoxifies inhaled oxidizing air pollutant.

**β-Carotene- as antioxidant:** β-Carotene being an antioxidant plays role in trapping peroxy free radicals (-OOR) in tissues at low partial pressure of oxygen.

But antioxidants effects of β-carotene is still controversial. Moreover it causes tachycardia & increases the risk of other cardiovascular diseases & causes cancer mortality in smokers.

(Ref: Harper-30<sup>th</sup>)**Question Bank**

Q. Following are the examples of antioxidant vitamins: (BSMMU – MD/MS - January, 2009)

- |                            |   |
|----------------------------|---|
| a) Vitamin D               | F |
| b) Vitamin B <sub>12</sub> | F |
| c) Folic acid              | F |
| d) Vitamin A               | T |
| e) Vitamin C               | T |

**Help link:**

■ **Antioxidant:** A number of intracellular reducing agents are able to reduce and, thus, detoxify oxygen intermediates in cells. These are called antioxidants.

(Ref-Lippincott-7<sup>th</sup>)

■ **Anti-oxidant vitamins:**

1. Vitamin A ( $\beta$ -carotin)
2. Vitamin C (ascorbic acid)
3. Vitamin E. (Tocopherol)

(Ref: Davidson's Medical Nutrition Therapy, 2005)

■ **Health importance of anti-oxidant vitamins:** Strong powerful oxidants such as superoxide ( $O_2^-$ ), hydrogen peroxide ( $H_2O_2$ ), peroxy radicals ( $ROOO'$ ) and hydroxyl radicals ( $OH'$ ), are produced during metabolism, through reactions with drugs and environmental toxins. They can cause severe damage to DNA, protein, unsaturated lipids resulting in cancer, inflammatory diseases, aging, and hemolytic anemia. Antioxidants reduce and, thus, detoxify these oxidants and prevent their consequences.

(Ref: Lippincott-7<sup>th</sup>, Harper-30<sup>th</sup>)

Note: Flavanoids also act as antioxidant

**Q. Following are the examples of antioxidant:** (BSMMU - M. Phil, Diploma, July-08)

- |                  |   |   |
|------------------|---|---|
| a) ascorbic acid | T | Yeast, liver, rice polishings and wheat germ. |
| b) vitamin E     | T |   |
| c) vitamin B     | F | Milk, meat, eggs and leafy vegetables.        |
| d) zinc          | F |   |
| e) copper        | F | Fruits and other vegetables.                  |

**Q. The following are the biological antioxidants:** (M. Phil, Diploma, July-06)

- |                  |   |
|------------------|---|
| a) beta carotene | T |
| b) vitamin-D     | F |
| c) vitamin-E     | T |
| d) vitamin-K     | F |
| e) vitamin-C     | T |

**Q. Substances having antioxidant effects is/ are:** (M. Phil, Diploma-05July)

- |              |   |
|--------------|---|
| a) Selineum  | T |
| b) Vitamin-A | T |
| c) Vitamin-K | F |
| d) Vitamin-E | T |
| e) Thiamin   | F |

**Q. Anti oxidant vitamins are:** (DMC – MD/MS -05Ja)

- |                  |   |
|------------------|---|
| a) Beta carotene | T |
| b) Vitamin D     | F |
| c) Vitamin E     | T |
| d) Vitamin K     | F |
| e) Folic acid    | F |

**Q. The following vitamins have antioxidant property:** (DMC – MD/MS - 04Ja)

- |                          |   |
|--------------------------|---|
| A. Vit. D                | F |
| B. Vit. C                | T |
| C. Vit. E                | T |
| D. Vit. K                | F |
| E. Vit. $\beta$ carotene | T |

**Q. Antioxidant vitamins are (M. phil, Diploma – 03Ju)**

- a) Beta carotene  
 b) Ascorbic acid  
 c) Tocoferol  
 d) Folic acid  
 e) Cholecalciferol

**Q. Vitamin having anti oxidant properties includes: - (DMC – MD/MS - 03Ja)**

- a) Retinal F
  - b) Beta-carotene T
  - c) Vitamin - K F
  - d) Vitamin - E T
  - e) Vitamin- C T

#### **HELP LINK:**

### ■ Other antioxidants:

- Ferritin, Transferrin, lactoferrin, ceruloplasmin
  - Glutathion peroxidase
  - Glutathione
  - Catalase

Table 1 • Elements believed essential for life

**Q. The following agents act as antioxidants (BSMMU – MD - 02Ja)**

- a) Vitamin E
  - b) Vitamin D
  - c) Ascorbic acid
  - d) Glutamic acid
  - e) Glutathione

## Others

**Q. Derivatives of following vitamins act as cofactors (BSMMU –Residency – MD, MS, Basic Science – March' 15)**

- BENEFITS OF FOLLOWING VITAMINS**

  - a) niacin
  - b) ascorbic acid
  - c) retinol
  - d) phylloquinone
  - e) cobalamine

Ans. a) T b) T c) F d) F e) T

(Ref. ABC Biochemistry-6<sup>th</sup>, P-92)

**O.** Glossitis occurs in deficiency of - (DMC - MD/MS - 09 Ja)

- |                                     |   |
|-------------------------------------|---|
| sitis occurs in deficiency of - (B) |   |
| a. vit B <sub>12</sub>              | T |
| b. folic acid                       | T |
| c. copper                           | F |
| d. vit-A                            | F |
| e. iron                             | T |

**HELP LINK**

Causes of glossitis
<b>Very common</b>
<ul style="list-style-type: none"><li>• Smoking</li><li>• Trauma</li></ul>
<b>Common</b>
<ul style="list-style-type: none"><li>• Anaemia</li><li>• Food allergy - allergy to food such as food coloring</li><li>• Psoriasis</li></ul>

<b>Very rare</b>
<b>Glucagonoma</b>

**Q. Following vitamins have protective role against cancer- (DMC – MD/MS - 08Ja)**

- a) Vitamin B2 F
- b) Vitamin C T
- c) Vitamin E T
- d) Vitamin D F
- e) Vitamin A T

**Q. Vitamins synthesized in the body: (DMC – MD/MS - 03Ja)**

- a) Vitamin —A F
- b) Vitamin —D T
- c) Vitamin —K T
- d) Biotin T
- e) Ascorbic acid F

**Q. Deficiency of vitamin: (DMC – MD/MS - 02Ja)**

- A. B<sub>1</sub> (Thiamine, Aneurine) leads to beriberi T
- B. B<sub>2</sub> (Riboflavin ) leads to inflammation of the mouth T
- C. B<sub>6</sub> (Pyridoxine) leads to pellagra F
- D. B<sub>12</sub> (Cyanocobalamin) leads to macrocytic anemia T
- E. E (Tocoferol) leads to azospermia. F

**Q. Gum bleeding is due to : (DMC – MD/MS - 02Ja)**

- A. Scurvy. T
- B. Rickets F
- C. Uraemia. F
- D. Lead poisoning. F (Blue line at the gum)
- E. Agranulocytosis. F (stomatitis)

**Q. Vitamin: (DMC – MD/MS - 01Ja)**

- A. It gives calorie to the body F
- B. Some vitamins are produced in the body T
- C. Vitamin A prevents respiratory tract infection in children T
- D. All fat soluble vitamins are anti-atherosclerotic F
- E. Vit. B has got antioxidant activity F

**Q. Regarding vitamins- (BIRDEM-04)**

- a) Liver stores vitamin – A
- b) Fresh citrus fruits are source of vitamin C
- c) Biotin is present in white portion of raw egg
- d) Riboflavin is present in green leafy vegetables
- e) Polished rice contains thiamine

Ans. a) T      b) T      c) F (egg yolk, liver, tomato)      d) F (liver, milk)  
e) T (liver, unrefined & cereal grains)

## MINERALS

**Table: Required daily amounts of minerals:**

Minerals	Required per-day
Na	3.0 gm
K	1.0 gm
Cl	3.5 gm
Ca	1.2 gm
P	1.2 gm
Fe	18.0 mg
I	150 µg
Mg	0.4 gm
Co	Unknown
Cu	Unknown
Mn	Unknown
Zn	15 mg

(Ref: Guyton & Hall)

**Table: Trace elements believed essential for life:**

Arsenic	Manganese
Chromium	Molybdenum
Cobalt	Nickel
Copper	Selenium
Fluorine	Silicon
Iodine	Vanadium
Iron	Zinc

(Ref: W. F. Ganong)

**Table: Summary of clinically important minerals:**

Mineral	Sources <sup>1</sup>	Reference nutrient intake (RNI)
<b>Calcium</b>	<b>Rich:</b> milk and milk products, tofu <b>Important:</b> milk, boned fish, green vegetables, beans	700 mg <sup>2</sup>
<b>Phosphorus</b>	Most foods contain phosphorus <b>Rich:</b> Marmite® and dry-roasted peanuts <b>Important:</b> milk, cereal products, bread and meat	550 mg <sup>2</sup>
<b>Magnesium</b>	<b>Rich:</b> wholegrains, nuts <b>Important:</b> unprocessed and wholegrain foods	300 mg men 270 mg women <sup>2</sup>
<b>Iron</b>	<b>Rich:</b> liver, red meat (haem iron) <b>Important:</b> non-haem iron from vegetables, wholemeal bread	8.7 mg 14.8 mg women < 50 yrs
<b>Zinc</b>	<b>Rich:</b> red meat, seafood <b>Important:</b> dairy produce, wholemeal bread	9.5 mg men 7 mg women <sup>2</sup>
<b>Iodine</b>	<b>Rich:</b> edible seaweeds <b>Important:</b> milk and dairy products	140 <sup>3</sup> g
<b>Selenium</b>	<b>Rich:</b> fish, wheat grown in selenium-rich soils <b>Important:</b> fish	60 µg women <sup>2</sup> 75 µg men
<b>Copper</b>	<b>Rich:</b> shellfish, liver <b>Important:</b> bread, cereal products, vegetables	1.2 mg <sup>2</sup>
<b>Fluoride</b>	Drinking water, tea	No RNI. Safe intake: 0.5 mg/kg
<b>Potassium</b>	<b>Rich:</b> dried fruit, potatoes, coffee <b>Important:</b> fresh-fruit, vegetables, milk	3500 mg

<b>Sodium</b>	<b>Rich:</b> Table salt, anchovies <b>Important:</b> processed foods, bread, bacon	160&mg-
---------------	---	---------

- 1 Rich sources contain the nutrient in high concentration but are not generally eaten in large amounts; important sources contain less but contribute most because larger amounts are eaten.  
 2 Increased amounts are required in women during lactation.

(Ref: Davidson-23<sup>rd</sup>)

### Question Bank

**Q. Trace elements include (BSMMU – Residency - MD/MS, Basic science, Paediatrics – March' 19; Residency – MD, MS, Basic science, Dentistry – March' 16; M. Phil, Diploma (Non-residency) – 11Ju, DMC & others – MD/MS – 11Ju)**

- a) iron
- b) sodium
- c) selenium
- d) magnesium
- e) phosphorus

Ans. a) T b) F c) T d) F e) F

(Ref. ABC-6<sup>th</sup>, P-462 + Sattanarayan-7th, P-405)

#### HELP LINK:

1. **Principal/Major elements (macrominerals):** These are the minerals required in large amounts in the body (greater than 100 mg/day). They are 7 in number –  
 Sodium, Potassium, Calcium, Magnesium, Phosphorus, Sulphur and Chlorine.

2. **Trace elements (microminerals):** These are the minerals required in small amount in the body (less than 100 mg/day).

These are – Iron, Iodine, Copper, Cobalt, Zinc, Manganese, Molybdenum, Selenium, Chromium, Fluorine, Nickel, Vanadium and Silicon.

(Ref: Harper-30<sup>th</sup> + Ganong-25<sup>rd</sup>)

**Q. The following are trace elements - (BSMMU – MD/MS -11Ja)**

- |               |   |
|---------------|---|
| a. sodium     | F |
| b. magnesium  | F |
| c. iron       | T |
| d. selenium   | T |
| e. phosphorus | F |

(Ref. ABC-6<sup>th</sup>, P-462 + Sattanarayan-7<sup>th</sup>, P-405)

**Q. Major minerals of human body are (DMC – md/ms - January, 2010)**

- |               |   |
|---------------|---|
| a. calcium    | T |
| b. iron       | F |
| c. phosphorus | T |
| d. iodine     | F |
| e. sodium     | T |

**Q. Trace elements are - (DMC – MD/MS - 09Ja)**

- |              |   |
|--------------|---|
| a. sodium    | F |
| b. potassium | F |
| c. calcium   | F |
| d. iodine    | T |
| e. iron      | T |

Element	Major functions	Deficiency disease/symptoms	Recommended dietary allowance	Major sources
Iron	Constituent of heme e.g. hemoglobin, myoglobin, cytochromes; involved in O <sub>2</sub> transport and biological oxidation.	Hypochromic, microcytic anemia	10–15 mg/d	Organ meats (liver, heart), leafy vegetables, iron cookware
Copper	Constituent of enzymes e.g. cytochrome C oxidase, catalase, tyrosinase; in iron transport.	Anemia, Menkes disease	2–3 mg/d	Organ meats cereals, leafy vegetables
Iodine	Constituent of thyroxine and triiodothyronine	Cretinism, goiter, myxedema	150–200 µg/d	Iodized salt, sea foods
Manganese	Cofactor for enzymes e.g. arginase, pyruvate carboxylase; glycoprotein synthesis.	Almost unknown	2–8 mg/d	Cereals, leafy vegetables
Zinc	Cofactor for enzymes e.g. alcohol dehydrogenase, carbonic anhydrase, lactate dehydrogenase.	Growth retardation, poor wound healing, hypogonadism	10–15 mg/d	Meat, fish, milk
Molybdenum	Constituent of enzymes e.g. xanthine oxidase	Almost unknown	75–250 µg/d	Vegetables
Cobalt	Constituent of vitamin B <sub>12</sub> , required for the formation of erythrocytes	Pernicious anemia (as in vitamin B <sub>12</sub> deficiency)	5–8 µg/d	Foods of animal origin
Fluorine	Helps in the proper formation of bones and teeth	Dental caries, osteoporosis	2–4 mg/d	Drinking water
Selenium	Involved in antioxidant function along with vitamin E; constituent of glutathione peroxidase and selenocysteine	Muscular degeneration, cardiomyopathy	50–200 µg/d	Organ meats, sea foods
Chromium	Promotes insulin function (as glucose tolerance factor)	Impaired glucose tolerance	10–100 µg/d	Brewer's yeast, meat, whole grains

(Ref. Sattanarayanan-7th, P-405)

## CALCIUM

### Dietary sources of calcium:

- Milks, Cheeses, Yoghurt, Eggs
- Fish eaten with bone, eg: Sardines, Pilchards
- Some Shellfish
- Some nuts eg: Almonds, Peanuts
- Some Legumes, eg: Chick peas, beans
- Fortified bread

### Distribution of Calcium:

Serum (9–11 gm/100 ml):

- Ionized or diffusible (50%)
- Plasma protein bound (40%)

C.S.F (4.5–5 gm/100 ml): Combined with substance other than plasma protein eg- Citrate, phosphate (10%)

Muscle: 7 mg/ 100 ml

**Nerve:** 15 mg/ 100 ml

#### Factors influencing blood calcium level:

- **Parathyroid hormone:** Regulate blood  $\text{Ca}^{++}$  level by increasing or decreasing the concentration according to the need of the body.
- **Vitamin-D:** Enhances absorption of calcium from gut & thus maintains the "normal plasma calcium concentration."
- **Plasma protein:** About 40% of the blood calcium is bound to plasma protein chiefly albumin. So ↓ plasma protein → ↓ blood calcium level.
- **Plasma phosphate:** There is an inverse relationship between blood phosphate & calcium level. ↑ serum phosphate → ↓ serum calcium level.
- **Calcitonin:** ↑ Ionized calcium level → ↑ production of calcitonin → ↑ Deposition of calcium in bone → ↓ blood calcium level → calcium homeostasis.
- **pH of intestinal lumen:** Acidic pH enhances whereas alkaline pH retards intestinal absorption.
- **High protein diet:** Helps in calcium absorption.
- **High fatty meal:** Retards calcium absorption.

(Ref: Harper + Robbins + Davidson's Medicine)

#### Route of excretion & deficiency symptom of calcium:

- **Main channel** (Bowel along with feces): 0.4 - 0.8 gm is excreted daily
- **Minor channel** (Kidney through urine): 120 - 150 gm is excreted daily

#### Deficiency symptom of calcium:

- Children: Rickets
- Adults: Osteomalacia

#### Hormonal control of calcium homeostasis:

##### PTH:

- ↑  $\text{Ca}^{++}$  mobilization from bone
- ↑  $\text{Ca}^{++}$  reabsorption from kidney
- ↑ intestinal  $\text{Ca}^{++}$  absorption

**Effect:** ↑ Plasma calcium

##### Calcitriol:

- ↑  $\text{Ca}^{++}$  reabsorption from kidney
- ↑  $\text{Ca}^{++}$  mobilization from bone
- Augmentation of PTH action

**Effect:** ↑ Plasma calcium

##### Calcitonin:

- ↓ osteoclastic activity
- ↑ osteoblastic activity
- ↑ renal  $\text{Ca}^{++}$  excretion
- ↑  $\text{Ca}^{++}$  deposition in bone

**Effect:** ↑ Plasma calcium

##### Growth hormone:

- ↑  $\text{Ca}^{++}$  absorption from intestine.
- ↑  $\text{Ca}^{++}$  excretion excretion through kidney.

**Effect:** Absorption > excretion, positive  $\text{Ca}^{++}$  balance.

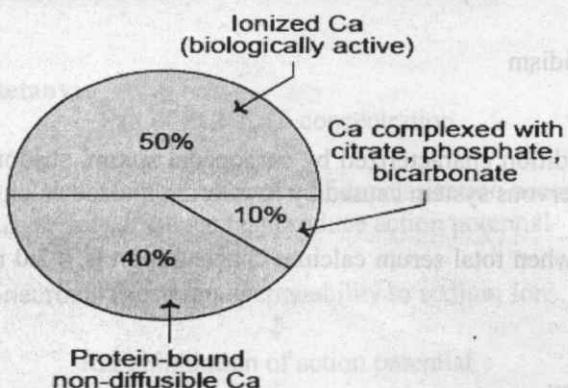
(Ref: Ganong + Guyton)

Q. Calcium ion (BSMMU –Residency - Dentistry – March' 19)

- a) deficiency causes spastic contraction of the heart
  - b) plays a powerful role in exciting the contractile process of the myofibrils
  - c) causes vasodilatation in higher concentration
  - d) constitutes 41% of the plasma calcium
  - e) controls the formation of 1, 25 dihydroxycholecalciferol

Ans. a) F b) T c) F d) F e) T (negative feedback)

**Help Link:**



**Fig. 18.1 : Different forms of circulating calcium.**

## Biochemical functions

- 1. Development of bones and teeth :**
  - 2. Muscle contraction:**
    - ✓  $\text{Ca}^{2+}$  interacts with troponin C to trigger muscle contraction.
  - 3. Blood coagulation:** (factor IV).
  - 4. Nerve transmission:**
  - 5. Membrane integrity and permeability :**
  - 6. Activation of enzymes:**
    - ✓ activation of lipase (pancreatic), ATPase and succinate dehydrogenase.
  - 7. Calmodulin mediated action of  $\text{Ca}^{2+}$ :**
    - ✓ Calmodulin is a calcium binding regulatory protein. Ca-calmodulin complex activates adenylate cyclase,
  - 8. Calcium as intracellular messenger:**
    - ✓ **second messenger** for hormonal action e.g. epinephrine in liver glycogenolysis.
    - ✓ **third messenger** for some hormones e.g. antidiuretic hormone (ADH) acts through cAMP, and then  $\text{Ca}^{2+}$ .
  - 9. Release of hormones:** insulin, PTH, calcitonin
  - 10. Secretory processes:**
    - ✓  $\text{Ca}^{2+}$  regulates microfilament and microtubule mediated processes such as endocytosis, exocytosis and cell motility.
  - 11. Contact inhibition:**
  - 12. Action on heart:**  $\text{Ca}^{2+}$  acts on myocardium and prolongs systole.

(Ref. Sattnarayan-4<sup>th</sup>, P-406)

## HYPOCALCAEMIA

Decreased blood calcium level less than its normal level is called hypocalcaemia.

### Causes of hypocalcaemia:

1. Hypoalbuminaemia

2. Alkalosis

- Respiratory eg. hyperventilation

- Metabolic eg. Conn's syndrome

3. Vitamin D deficiency

4. Chronic renal failure

5. Hypoparathyroidism

6. Pseudohypoparathyroidism

7. Acute pancreatitis

**Tetany:** Tetany is clinical condition characterized by carpopedal spasm, stridor & convulsions due to increased excitability of the peripheral nervous system caused by low serum ionized calcium concentration.

**When occurs:** Tetany occurs when total serum calcium concentration is < 2.0 mmol/L (in- adults, in absence of alkalosis)

### Types:

- Overt (manifest) tetany

- Latent tetany (no signs of overt tetany)

### Clinical features of overt tetany:

#### Children:

- Classical triad

- Carpopedal spasm

- Stridor

- Convulsions

#### Adults:

- Tingling & numbness of face, fingers & toes

- Painful carpopedal spasm

### Carpopedal spasm:

The characteristic position of the hand in carpopedal spasm -

- The metacarpophalangeal joints are flexed
- The interphalangeal joints of the fingers & thumb are extended
- Opposition of the thumb
- Toes are planter-flexed and the ankle joints extended (pedal spasm)

### Stridor:

It is due to paralysis of the respiratory muscles

**Convulsions:** It is due to tetany of brain. Latent tetany (Neuromuscular hyper excitability) can be demonstrated by eliciting following signs-

**Trousseau's sign:** Inflation of the sphygmomanometer cuff above the diastolic blood pressure for 3 minutes induces tetanic spasm of the fingers & wrist.

**Chvostek's sign:** Gentle tapping over the facial nerve at the angle of jaw causes twitching of the facial muscles.



Fig. Hypocalcemic tetany in the hand, called **carpopedal spasm**.

#### MAGNESIUM

The adult body contains about 20g magnesium, 70% of which is found in bones in connective tissue.

#### Mechanism of development of tetany:

Fall of ECF  $\text{Ca}^{++}$  concentration



↑ excitability of nerve & muscles by decreasing the amount of depolarization necessary to initiate changes in  $\text{Na}^{++}$  &  $\text{K}^{+}$  conductance that produce action potential



↑ neuronal membrane permeability to sodium ions.



Rapid initiation of action potential



The peripheral nerve fibre become excitable & begin to discharge impulses spontaneously



Impulses pass to the peripheral skeletal muscles



Tetanic contraction of muscles

## **HYPERCALCAEMIA**

Increased blood calcium level more than its normal limit.

Normal serum concentration of Mg is 2-3 mg/dl. It is present in the ionized form.

#### Causes of hypercalcaemia:

##### With normal or elevated PTH level

- Primary or tertiary hyperparathyroidism
- Lithium induced hyper parathyroidism
- Familial hypocalciuric hypercalcaemia

##### With low PTH level:

- Malignancy (eg. Lung, breast, renal, ovarian, colonic, thyroid carcinoma)
- Multiple myeloma
- ↑ Calcitriole level
- Thyrotoxicosis
- Paget's disease with immobilization
- Milk-alkali syndrome
- Thiazide diuretics
- Addison's disease

**Note:** In secondary hyperparathyroidism blood  $\text{Ca}^{++}$  level is low because secondary hyperparathyroidism occurs due to increased PTH secretion to compensate prolonged hypocalcaemia.

(Ref: Davidson's Medicine)

**Blood calcium Level:**

- 2.2 - 2.6 mmol / L → Normal
- > 3.5 mmol / L → Mild to moderate hypercalcaemia
- > 3.5 mmol / L → Severe hypercalcaemia

**PHOSPHORUS****PHOSPHORUS**

An adult body contains about 1 kg phosphate and it is found in every cell of the body. Most of it (about 80%) occurs in combination with Ca in the bones and teeth. About 10% of body P is found in muscles and blood in association with proteins, carbohydrates and lipids. The remaining 10% is widely distributed in various chemical compounds.

**Biochemical functions:**

1. Phosphorus is essential for the development of bones and teeth.
2. It plays a central role for the formation and utilization of high-energy phosphate compounds e.g. ATP, GTP, creatine phosphate etc.
3. Phosphorus is required for the formation of phospholipids, phosphoproteins and nucleic acids (DNA and RNA).
4. It is an essential component of several nucleotide coenzymes e.g.-  $\text{NAD}^+$ ,  $\text{NADP}^+$ , pyridoxal phosphate, ADP, AMP.
5. Several proteins and enzymes are activated by phosphorylation.
6. Phosphate buffer system is important for the maintenance of pH in the blood as well as in the cells.
7. Phosphate is necessary for the absorption and metabolism of carbohydrates.

**Dietary requirements:**

The recommended dietary allowance (RDA) of phosphate is based on the intake of calcium. The ratio of Ca: P of 1:1 is recommended (i.e. 800 mg/ day) for an adult. For infants, however, the ratio is around 2:1 which is based on the ratio found in human milk. Calcium and phosphate are distributed in the majority of natural foods in 1:1 ratio. Therefore, adequate intake of Ca generally takes care of the P requirement also.

**Sources:**

Milk, cereals, leafy vegetables, meat, eggs.

**Absorption:** Phosphate absorption occurs from jejunum:

1. Calcitriol promotes phosphate uptake along with calcium.
2. Absorption of phosphorus and calcium is optimum when the dietary Ca: P is between 1:2 and 2:1.
3. Acidity favours while phytate decreases phosphate uptake by intestinal cells.

**Serum phosphate:**

The phosphate level of the whole blood is around 40 mg/ dl while serum contains about 3-4 mg/ dL. This is because the RBC and WBC have very high content of phosphate.

The serum phosphate may exist as free ions (40%) or in a complex form (50%) with cations such as  $\text{Ca}^{2+}$ ,  $\text{Mg}^{2+}$ ,  $\text{Na}^+$ ,  $\text{K}^+$ . About 10% of serum phosphate is bound to proteins. It is interesting to note that the fasting serum phosphate levels are higher than the postprandial. This is attributed to the fact that following the ingestion of carbohydrate (glucose), the phosphate from the serum is drawn by the cells for metabolism (phosphorylation reactions).

**Excretion:**

About 500 mg phosphate is excreted in urine per day. The renal threshold is 2 mg/ dl. The reabsorption of phosphate by renal tubules is inhibited by PTH.

Dietary requirements: About 3-4 g/ day

#### Disease states:

1. Serum phosphate level is increased in hypoparathyroidism and decreased in hyperparathyroidism.
2. In severe renal diseases, serum phosphate content is elevated causing acidosis.
3. Vitamin D deficient rickets is characterized by decreased serum phosphate (1-2 mg/dl).
4. Renal rickets is associated with low serum phosphate levels and increased alkaline phosphatase activity.
5. In diabetes mellitus, serum content of organic phosphate is lower while that of inorganic phosphate is higher.

(Ref: Satyanarayana-4<sup>th</sup>)

## MAGNESIUM

### MAGNESIUM

The adult body contains about 20g magnesium, 70% of which is found in bones in combination with calcium and phosphorus. The remaining 30% occurs in the soft tissues and body fluids.

#### Biochemical functions:

1. Magnesium is required for the formation of bones and teeth.
2.  $Mg^{2+}$  serves as a cofactor for several enzymes requiring ATP. e.g.- hexokinase, glucokinase, phosphofructokinase/ adenylate cyclase.
3.  $Mg^{2+}$  is necessary for proper neuromuscular function. Low  $Mg^{2+}$  levels lead to neuromuscular irritability.

#### Dietary requirements:

Adult man : 350 mg/ day (flattened waves with inverted T wave).

Adult woman : 300 mg/ day

Sources: Cereals, nuts, beans, vegetables (cabbage, cauliflower), meat, milk, fruits.

#### Absorption:

Magnesium is absorbed by the intestinal cells through a specific carrier system. About 50% of the dietary Mg is normally absorbed. Consumption of large amounts of calcium, phosphate and alcohol diminish Mg absorption. PTH increases Mg absorption.

#### Serum Mg:

Normal serum concentration of Mg is 2-3 mg/ dl. It is present in the ionized form (60%), in combination with other ions (10%) and bound to proteins (30%).

#### Disease states:

1. Magnesium deficiency causes neuromuscular irritation, weakness and convulsions. These symptoms are similar to that observed in tetany (Ca deficiency) which are relieved only by Mg. Malnutrition, alcoholism and cirrhosis of liver may lead to Mg deficiency.
2. Low levels of Mg may be observed in uremia, rickets and abnormal pregnancy.

(Ref: Satyanarayana-4<sup>th</sup>)

## SODIUM

### SODIUM

Sodium is the chief cation in the extracellular fluid. About 50% of body sodium is present in the bones, 40% in the extracellular fluid and the remaining (10%) in the soft tissues.

The daily requirement of chloride as NaCl is 5-10 g. Adequate intake of sodium will satisfy the body's needs.

#### Biochemical functions:

1. In association with chloride and bicarbonate, sodium regulates the body's acid-base balance.
2. Sodium is required for the maintenance of osmotic pressure and fluid balance.
3. It is necessary for the normal muscle irritability and cell permeability.
4. Sodium is involved in the intestinal absorption of glucose, galactose and amino acids.
5. It is necessary for initiating and maintaining heart beat.

**Dietary requirements:**

For normal individuals, the requirement of sodium is about 5-10 g/ day which is mainly consumed as NaCl. For persons with a family history of hypertension, the daily NaCl intake should be less than 5 g. For patients of hypertension, around 1 g/ day is recommended. It may be noted that 10g of NaCl contains 4g of sodium. The daily consumption of Na is generally higher than required due to its flavour.

**Sources:**

The common salt (NaCl) used in the cooking medium is the major source of sodium. The ingested foods also contribute to sodium. The good sources of sodium include bread, whole grains, leafy vegetables, nuts, eggs and milk.

**Absorption:**

Sodium is readily absorbed in the gastrointestinal tract and, therefore, very little of it (< 2%) is normally found in feces. However, in diarrhea, large quantities of sodium is lost in feces.

**Plasma sodium:**

In the plasma (serum), the normal concentration of sodium is 135-145 mEq/l. Sodium is an extracellular cation, therefore, the blood cells contain much less (35 mEq/l). The mineralocorticoids, secreted by adrenal cortex, influence sodium metabolism. A decrease in plasma sodium and increase in its urinary excretion is observed in adrenocortical insufficiency.

**Excretion:**

Kidney is the major route of sodium excretion from the body. As much as 800g Na/day is filtered by the glomeruli, 99% of this is reabsorbed by the renal tubules by an active process. This is controlled by aldosterone. Extreme sweating also causes considerable amount of sodium loss from the body. There is, however, individual variation in sodium loss through sweat.

**Disease states:**

1. **Hyponatremia:** This is a condition in which the serum sodium level falls below the normal. Hyponatremia may occur due to diarrhea, vomiting, chronic renal diseases, adrenocortical insufficiency (addison's disease). Administration of salt free fluids to patients may also cause hyponatremia. This is due to overhydration. Decreased serum sodium concentration is also observed in edema which occurs in cirrhosis or congestive heart failure.

The manifestations of hyponatremia include reduced blood pressure and circulatory failure.

2. **Hypernatremia:** This condition is characterized by an elevation in the serum sodium level. It may occur due to hyperactivity of adrenal cortex (cushing's syndrome), prolonged administration of cortisone, ACTH and/or sex hormones. Loss of water from the body causing dehydration, as it occurs in diabetes insipidus, results in hypernatremia. Rapid administration of sodium salts also increases serum sodium concentration. It may be noted that in pregnancy, steroid and placental hormones cause sodium and water retention in the body, leading to edema.

The symptoms of hypernatremia include increase in blood volume and blood pressure (hypertension).

(Ref: Satyanarayana-4<sup>th</sup>)

## POTASSIUM

**POTASSIUM**

Potassium is the principal intracellular cation. It is equally important in the extracellular fluid for specific functions.

**Biochemical functions:**

1. Potassium maintains intracellular osmotic pressure.
2. It is required for the regulation of acid-base balance and water balance in the cells.
3. The enzyme pyruvate kinase (of glycolysis) is dependent on K<sup>+</sup> for optimal activity.
4. Potassium is required for the transmission of nerve impulse.
5. Adequate intracellular concentration K<sup>+</sup> is necessary for proper biosynthesis of proteins by ribosomes.
6. Extracellular K<sup>+</sup> influences cardiac muscle activity.

**Dietary requirements:** About 3-4 g/ day.

**Sources:**

Banana, orange, pineapple, potato, beans, chicken, liver. Tender coconut water is a rich source of potassium.

**Absorption:**

The absorption of  $K^+$  from the gastrointestinal tract is very efficient (90%) and very little is lost through feces. However, in subjects with diarrhea, a good proportion of  $K^+$  is lost in the feces.

**Plasma potassium:**

The plasma (serum) concentration of potassium is 3.4 - 5.0 mEq/l. The whole blood contains much higher level of  $K^+$  (50 mEq/l), since it is predominantly an intracellular cation. Care should, therefore, be taken to avoid hemolysis of RBC for the estimation of serum  $K^+$ .

**Excretion:**

Potassium is mainly excreted through urine. The maintenance of body acid-base balance influences  $K^+$  excretion. Aldosterone increases excretion of potassium.

**Disease states**

**Hypokalemia:** Decrease in the concentration of serum potassium is observed due to overactivity of adrenal cortex (cushing's syndrome), prolonged cortisone therapy, intravenous administration of  $K^+$ -free fluids, treatment of diabetic coma with insulin, prolonged diarrhea and vomiting.

The symptoms of hypokalemia include irritability, muscular weakness, tachycardia, cardiomegaly and cardiac arrest. Changes in the ECG are observed (flattened waves with inverted T wave).

**Hyperkalemia:** Increase in the concentration of serum potassium is observed in renal failure, adrenocortical insufficiency (addison's disease), diabetic coma, severe dehydration, intravenous administration of fluids with excessive potassium salts.

The manifestations of hyperkalemia include depression of central nervous system, mental confusion, numbness, bradycardia with reduced heart sounds and, finally, cardiac arrest. Changes in ECG are also observed (elevated T wave).

(Ref: Satyanarayana-4<sup>th</sup>)

## CHLORINE

**CHLORINE**

Chlorine is a constituent of sodium chloride;. Hence, the metabolism of chlorine and sodium are intimately related.

Fig. Iron absorption, uptake and distribution in the body.

**Biochemical functions:**

1. Chloride is involved in the regulation of acid-base equilibrium, fluid balance and osmotic pressure. These functions are carried out by the interaction of chloride with  $Na^+$  and  $K^+$ .
2. Chloride is necessary for the formation of HCl in the gastric juice.
3. Chloride shift involves the active participation of  $Cl^-$ .
4. The enzyme salivary amylase is activated by chloride.

**Dietary requirements:**

The daily requirement of chloride as NaCl is 5-10 g. Adequate intake of sodium will satisfy the chloride requirement of the body.

**Sources:**

Common salt as cooking medium, whole grains, leafy vegetables, eggs and milk.

**Absorption:** In normal circumstances, chloride is almost totally absorbed in the gastrointestinal tract.

**Plasma chloride:**

The normal plasma concentration of chloride is 95-105 mEq/l. Cerebrospinal fluid (CSF) contains higher level of  $\text{Cl}^-$  (125 mEq/l). This is due to the fact that protein content is low in GSF and, therefore,  $\text{Cl}^-$  is higher in order to maintain donnan membrane equilibrium.

**Excretion:**

There exists a parallel relationship betweencretion of chloride and sodium. The renal threshold for  $\text{Cl}^-$  is about 110 mEq/l.

**Disease states:**

- Hypochloremia:** A reduction in the serum  $\text{Cl}^-$  level may occur due to vomiting, diarrhea, respiratory alkalosis, Addison's disease and excessive sweating.
- Hyperchloremia:** An increase in serum  $\text{Cl}^-$  concentration may be due to dehydration, respiratory acidosis and cushing's syndrome.

(Ref: Satyanarayana-4<sup>th</sup>)

**SULFUR**

Sulfur of the body is mostly present in the organic form. Methionine, cysteine and cystine are the three sulfur-containing amino acids present in the proteins. Generally, proteins contain about 1% sulfur by weight.

**Biochemical functions:**

- Sulfur-containing amino acids are very essential for the structural conformation and biological function of proteins (enzymes, hormones, structural proteins etc.) The disulfide linkages (-S-S-) and sulfhydryl groups(-SH) are largely responsible for this.
- The vitamins thiamine, biotin, lipoic acid, and coenzyme a of pantothenic acid contain sulfur.
- Heparin, chondroitin sulfate, glutathione, laurocholic acid are some other important sulfur containing compounds.
- Phosphoadenosine phosphosulfate (PAPS) is the active sulfate utilized for several reactions e.g.-synthesis of glycosaminoglycans, detoxification mechanism.
- The sulfur containing amino acid methionine (as S-adenosylmethionine) is actively involved in transmethylation reactions.

**Dietary requirements and sources:**

There is no specific dietary requirement for sulfur. Adequate intake of sulfur containing essential amino acid methionine will meet the body needs. Food proteins rich in methionine and cysteine are the sources of sulfur.

**Excretion:**

The sulfur from different compounds is oxidized in the liver to sulfate and excreted in urine. The urine contains inorganic sulfate (80%), organic or gated or ethereal sulfate (10%) and sulfur (10%). The unoxidized sulfur is in the form of sulfur containing amino acids, thiocyanates etc.

(Ref: Satyanarayana-4<sup>th</sup>)

**IRON****Dietary sources of Iron:****Haem Iron:**

- Muscle meat (red more than white)
- Organ meat
- Fish
- Shell fish
- Potassium is required for the transmission of nerve impulse.
- Adequate ionization of central nervous system by potassium.
- Extracellular K<sup>+</sup> influences cardiac muscle activity.

### Non-haem Iron:

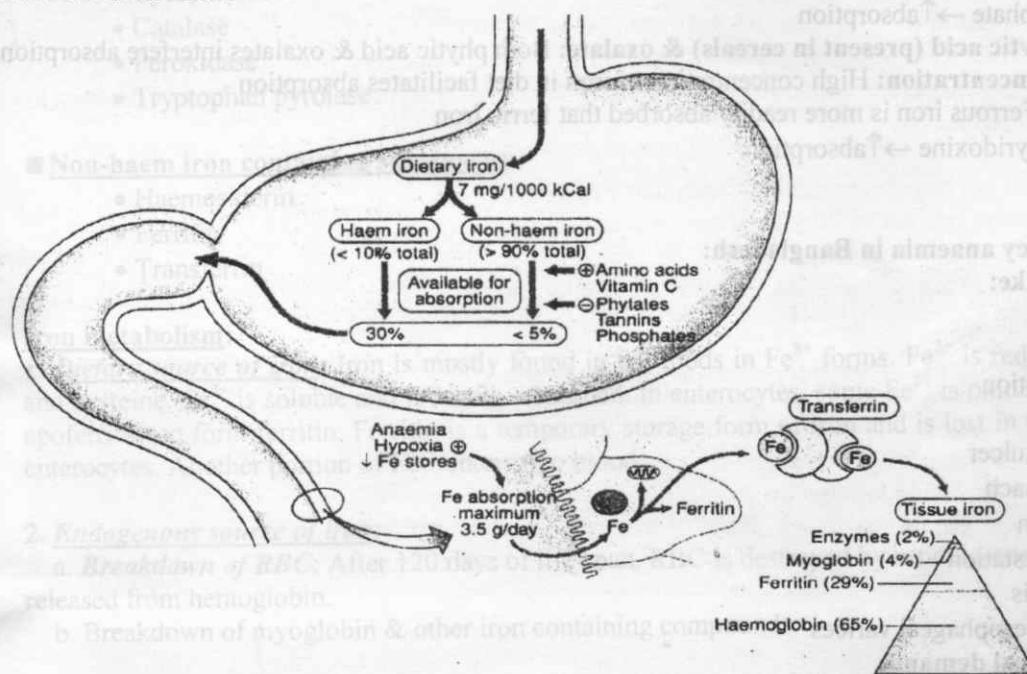
- Oat meal
- Legumes (peas, beans), nuts, fruits
- Whole meal bread
- Iron-fortified cereal foods
- Red wine
- Chocolate

The total content of iron in an adult body is 3.5 g. About 70% of this occurs in the erythrocytes as haemoglobin. At least 5% of body iron is present in myoglobin of muscle. Heme is the most bioavailable form of iron.

### Daily requirement of iron:

- Male: 8-10mg
- Female: 15 -18 mg
- A regular loss of only 2 ml of blood per day doubles the iron requirement.
- About 30 mg of iron is lost during menstruation.

### Distribution of Iron:



**Fig. Iron absorption, uptake and distribution in the body.**

(Ref: Davidson's Medicine)

### Total body iron is about 4 gms (100%):

- Hemoglobin (65%)
- Myoglobin (4%)
- Various heme compound that promote intracellular oxidation (1%)
- Combined with protein transferrin in the blood plasma (0.01%)
- Stored in the liver in the form of ferritin & hemosiderin

### Deficiency features of iron:

Iron deficiency usually results from either loss of iron due to blood loss, inadequate intake or malabsorption. The symptoms & signs of iron deficiency are mainly those of anaemia. These are -

- Anorexia
- Weakness, lassitude, fatigue
- Smooth tongue (loss of papillae)

- Brittle finger nails
- Angular stomatitis, glossitis
- Koilonychia

### Deficiency disorders:

- Microcytic hypochromic anaemia
- Dental caries
- Osteoporosis

### Factors affecting iron absorption:

1. **Acidity of stomach:** ↑ Acidity of stomach → ↑ reduction ferric iron to ferrous iron → ↑ absorption through mucosal epithelium.
2. **Presence of reducing substances:** Reducing agents like Vit C glutathione, S-H group of sulphate containing amino acids helps in iron absorption.
3. **Phosphate in diet:**
  - Low phosphate → ↑ absorption
4. **Presence of phytic acid (present in cereals) & oxalate:** Both phytic acid & oxalates interfere absorption
5. **Dietary iron concentration:** High concentration of iron in diet facilitates absorption
6. **Form of iron:** Ferrous iron is more readily absorbed than ferric Iron
7. **Pyridoxine:** ↑ Pyridoxine → ↑ absorption.

### Causes of iron deficiency anaemia in Bangladesh:

#### 1. Inadequate iron intake:

- Poor diet
- Anorexia
- Impaired absorption

#### 2. Chronic blood loss:

- Bleeding peptic ulcer
- Carcinoma stomach
- Carcinoma colon
- Hook worm infestation
- Uncreative colitis
- Rupture of the oesophageal varices

#### 3. Increased physiological demand:

- Menstruation
- Pregnancy
- Lactation
- Growing up children

• Combined deficiency anaemia is most common in Bangladesh.

### Question Bank

**Q. Dietary inorganic iron absorption is increased by (BSMMU –Residency – MD, MS, Basic Science, Dentistry – March '18)**

- a) vitamin C
- b) calcium
- c) fructose
- d) alcohol
- e) hepcidin

Ans. a) T b) F c) T d) T e) F

(Ref. ABC Biochemistry Page-559)

**Q. Iron (BSMMU – M. Phil, Diploma July, 2007)**

- |  |   |
|--|---|
| a) stored primarily in liver, spleen and bone marrow | T |
| b) excreted in urine in ferrous form                 | F |
| c) absorbed in ferric form                           | F |
| d) absorbed mainly in duodenum                       | T |
| e) transported as transferrin                        | T |

**HELP LINK:**

The total content of iron in an adult body is 3-5 g. About 70% of his occurs in the erythrocytes of blood as a constituent of hemoglobin. At least 5% of body iron is present in myoglobin of muscle. Heme is the most predominant iron-containing substance.

**■ Haem iron containing substances:**

- Haemoglobin
- Myoglobin
- Cytochromes
- Catalase
- Peroxidase
- Tryptophan pyrolase

**■ Non-haem iron containing substances:**

- Haemosiderin
- Ferritin
- Transferrin

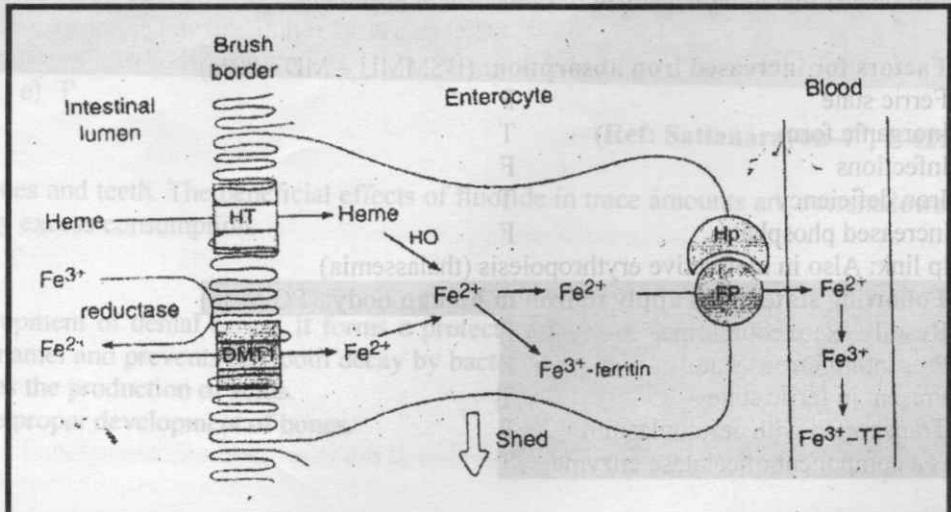
**Iron metabolism:**

**1. Dietary source of iron:** Iron is mostly found in the foods in  $\text{Fe}^{3+}$  forms.  $\text{Fe}^{3+}$  is reduced to  $\text{Fe}^{2+}$  by vitamin C and cysteine.  $\text{Fe}^{2+}$  is soluble and is readily absorbed. In enterocytes, some  $\text{Fe}^{2+}$  is oxidized to  $\text{Fe}^{3+}$  that binds with apoferritin to form ferritin. Ferritin is a temporary storage form of iron and is lost in the feces after shedding of enterocytes. Another portion of  $\text{Fe}^{2+}$  enters into blood.

**2. Endogenous source of iron:**

- Breakdown of RBC:** After 120 days of life span, RBC is destroyed by reticulo-endothelial system and iron is released from hemoglobin.
- Breakdown of myoglobin & other iron containing compounds.

**3. Transport of Iron:** In plasma,  $\text{Fe}^{2+}$  is oxidized to  $\text{Fe}^{3+}$  form.  $\text{Fe}^{3+}$  binds with apotransferrin to form transferrin, which is then transported in the plasma. Iron is loosely bound to transferrin and so, can easily be released to any cell when required.



**Fig: Mechanism of iron absorption.**

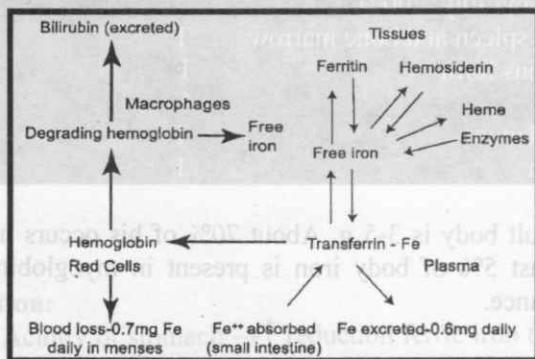


Fig. Metabolism of iron

4. **Utilization of Iron:** Transferrin enters into erythroblasts in the bone marrow by receptor mediated endocytosis. Here Iron is used in hemoglobin synthesis.
5. **Storage of Iron:** Iron is stored in liver, spleen and bone marrow in the form of ferritin and hemosiderin. Ferritin is the principal storage form of iron. When the quantity of iron in plasma falls very low, iron is removed from ferritin quite easily but from hemosiderin much less easily. The iron is then transported in the form of transferrin in plasma to the site where it is needed.

#### 6. **Loss of Iron from body:**

- About 0.6 mg of Iron is lost per day through bile, sweat, hair loss.
- A normal lady of reproductive age (or of 20 yrs. of age) has an additional iron loss of about 0.7 mg/day through menstruation.

So she has total iron loss of about 1.3 mg/day. So she must take increased amount of iron to maintain iron balance.

(Ref: Guyton-13<sup>th</sup>, Satyanarayana-4<sup>th</sup>)

**Q. The following diseases may result from a dietary deficiency:** (BSMMU – M. Phil, Diploma July, 2007)

- a) Marrusmus
- b) Xerophthalmia
- c) Pernicious anaemia
- d) Simple goiter
- e) Addison's disease

Ans.

- a) T (*it occurs due to protein deficiency*)
- b) T (*it occurs due to vitamin A deficiency*)
- c) F (*it is an autoimmune disease*)
- d) T (*it occurs due to iodine deficiency*)
- e) F (*it occurs due to deficiency of adrenocortical hormones*)

**Q. Factors for increased iron absorption:** (BSMMU – MD - 00Ja)

- A. Ferric state
- B. Inorganic form
- C. Infections
- D. Iron deficiency
- E. Increased phosphate

Help link: Also in ineffective erythropoiesis (thalassemia)

**Q. Following statements apply to iron in human body:** (PG-97Ja)

- A. Readily excreted in urine F
- B. Present in ferrous state F
- C. Present in ferric state T
- D. Transported with ceruloplasmin F
- E. Is a component of catalase enzyme T

(Ref: ABC Biochemistry)

## IODINE

**Sources of iodine:**

- Sea Fish
- Sea Weed
- Most plant foods grown near the sea
- Cod liver oil
- Ionized salts

**Daily requirement:** 150 µg

**Pregnancy:** + 25 µg

**Lactation:** + 50 µg

**Excretion:**

1. Inorganic iodine is mostly excreted by the kidneys, liver, skin, lungs and intestine and in milk.
2. About 10 percent of circulating organic iodine is excreted in feces. This is entirely unabsorbed food iodine.
3. 40 to 80 per cent is usually excreted in the urine; of which 20 to 70 µg. daily in adults and 20 to 35 µg in children. The urinary elimination is largest when the intake is lowest.
4. Urine iodine is increased by exercise and other metabolic factors.

**Iodine deficiency in human beings:**

1. In adults, the thyroid gland is enlarged, producing the disease goitre. If treatment is started very early, the thyroid becomes normal. If treatment is delayed, the enlargement of the gland persists.
2. In children, severe iodine deficiency results in the extreme retardation of growth which is known as **cretinism**.

**Prevention of goitre:** Goitre can be prevented by the regular use of iodide salt or iodide added to the drinking water in the concentration of 1: 5000 to 1: 2,00,000.

**Function of iodine:** It is essential for synthesis of thyroid hormones.

(Ref: A.C. Deb-8<sup>th</sup>, P-442)

## FLUORINE

**Q. Regarding fluoride metabolism (BSMMU-Residency – Dentistry – March '18)**

- a) blood-brain barrier is permeable to fluoride
- b) fluoride in the stomach diffuses across the gastric mucosa
- c) in younger teeth the enamel surface has low concentrations of fluoride
- d) fluoride in excess of 20mm/kg in the human adult regarded as lethal
- e) fluoride ions can be transferred into body secretions

Ans. a)T b)T c) F d) T e) T

(Ref: Sattanarayon-4<sup>th</sup>, P-421)

**Help link:**

Fluoride is mostly found in bones and teeth. The beneficial effects of fluoride in trace amounts are overshadowed by its harmful effects caused by excess consumption.

**Biochemical functions:**

1. Fluoride prevents the development of dental caries. It forms a protective layer of acid resistant fluoroapatite with hydroxyapatite of the enamel and prevents the tooth decay by bacterial acids. Further, fluoride inhibits the bacterial enzymes and reduces the production of acids.
2. Fluoride is necessary for the proper development of bones.

3. It inhibits the activities of certain enzymes. Sodium fluoride inhibits enolase (of glycolysis) while fluoroacetate inhibits aconitase (of citric acid cycle).

#### Dietary requirements and sources:

An intake of less than 2 ppm of fluoride will meet the daily requirements. Drinking water is the main source.

#### Disease states:

- Dental caries:** It is clearly established that drinking water containing less than 0.5 ppm of fluoride is associated with the development of dental caries in children.
- Fluorosis:** Excessive intake of fluoride is harmful to the body. An intake above 2 ppm (particularly  $> 5$  ppm) in children causes mottling of enamel and discoloration of teeth. The teeth are weak and become rough with characteristic brown or yellow patches on their surface. These manifestations are collectively referred to as dental fluorosis.
- Highly excessive intake of fluorine (over 10 parts per million) results in increased density and hypercalcification of the bone of spine, pelvis and limbs.

#### Prevention of fluorosis:

Fluorosis can be prevented by removing fluorides from the water by treatment with activated carbon or by some other suitable absorbents.

(A.C. Deb-8<sup>th</sup>, P-443 + Satyanarayana-4<sup>th</sup>)

## Zinc

#### Sources of Zinc:

- Liver
- Pancreas
- Shell fish
- Most animal tissues
- Wheat germ
- Meat
- Legumes
- Eggs
- Sea foods
- Milk

(Ref: Guyton-13<sup>th</sup>, S. D. Johnson-13<sup>th</sup>)

#### Daily requirement:

- Adults: 15 mg
- Pregnancy: 20 mg
- Lactation: 25 mg
- Infants: 3-5 mg
- Children: 10 mg

T (s) T(b) T (s) T(d) T(s) anA

#### Distribution:

It is widely distributed in the tissues of the body. The whole body (70 kg. weight) contains 1.4 to 2.3 gms. zinc. 20 per cent of the total is present in skin. A certain amount is also present in the bones and teeth. High concentrations of zinc are present in spermatozoa, prostate and epididymis. The highest concentration occurs in the choroid of the eye.

#### Blood zinc:

- Zinc is present in higher concentration in erythrocytes than in plasma.
- Normal plasma contains about 20 per cent of the zinc present in whole blood.

3. The concentration of zinc of human blood, plasma and erythrocytes are 0.8 mg., 0.12 mg. and 1.44 mg/100 ml, respectively.
4. About 3 per cent of zinc ion is contained in leukocytes. In certain types of chronic leukemia, there is a marked fall in the zinc content of peripheral leukocytes.
5. Most of zinc in erythrocyte is present in carbonic anhydrase.
6. The plasma concentration of zinc of human falls to 10 per cent of the normal level during later part of pregnancy and among those taking oral contraceptives.

(A.C. Deb-8th, P-444)

#### **Functions of Zinc:**

1. It is an essential component of many enzymes including carbonic anhydrase, alcohol dehydrogenase & alkaline phosphatase
2. It maintains normal concentration of Vitamin A in plasma
3. It is required for the preparation of insulin & increases the duration of insulin action when given by injection. Zinc is used in the P-cells of the pancreas to store & release insulin as required.
4. It acts as an antioxidant
5. It is concerned with wound healing
6. Its use has been popular with the children for prevention of diarrhoea

#### **Deficiency states of zinc:**

- Acute zinc deficiency has been reported in patients receiving prolonged zinc-free parenteral nutrition and causes diarrhoea, mental apathy, a moist eczematoid dermatitis especially around the mouth, the loss of hair.
- Zinc deficiency is responsible for the clinical features seen in the very rare congenital disorder known as **acrodermatitis enteropathica** (growth retardation, hair loss and chronic diarrhoea).
- Chronic deficiency has been described in association with **dwarfism** and **hypogonadism**.
- Zinc deficiency has also been observed secondary to protein energy malnutrition (PEM), malabsorption syndromes, and alcoholism and associated hepatic cirrhosis.
- In PEM, associated zinc deficiency causes thymic atrophy (zinc supplements may accelerate the healing of skin lesions, promote general well-being, improve appetite and reduce the morbidity associated with the malnourished state).

#### **Zn toxicity:**

- ✓ seen in welders due to inhalation of zinc oxide fumes.
- ✓ nausea, gastric ulcer, pancreatitis, anaemia, excessive salivation

(Ref: Davidson's + Ganong + Harper)

#### **Question Bank**

**Q. Zinc deficiency causes (BSMMU – Non-Residency – MD, MS, Paediatrics, Basic Science – July' 19; Residency – MD/MS, Basic science, Paediatrics – March' 19; MD, January-11)**

- a) skin ulcer
- b) peptic ulcer
- c) hypothyroidism
- d) depressed immune response
- e) hypogonadal dwarfism

Ans. a) T (Acrodermatitis enteropathica) b) F c) F d) T e) T

#### **Help Link:**

#### **Zn deficiency associated with:**

- ✓ Growth retardation, Poor wound healing
- ✓ Depressed wound healing and immune response,
- ✓ Anaemia, loss of appetite, diarrhoea, Impaired night vision,
- ✓ Loss of taste sensation, Impaired spermatogenesis/hypogonadism/infertility
- ✓ Depression, dementia, Neuropsychiatric manifestation of chronic alcoholism partly Zn def.

- ✓ Acrodermatitis enteropathica (rare inherited metabolic disease due to defect in absorption from duodenum, rash in the eye, mouth, nose, anus)
- ✓ Dermatitis

(Ref. Robbins & Cotrans-9<sup>th</sup>, P-443 + Sattarayon-4<sup>th</sup>, P-419 + ABC-5<sup>th</sup>, P-516)

**Q. Important features of zinc deficiency are (BSMMU-Non-Residency-Paediatrics-july'19)**

- a) perioral ulceration
- b) raw beef tongue
- c) mental retardation
- d) hypoproteinemia
- e) diarrhea

Ans. a) T b) F (occurs in B12 def) c) T d) F e) T

(Ref. Robbins & Cotrans-9<sup>th</sup>, P-443 + Sattarayon-4<sup>th</sup>, P-419 + ABC-5<sup>th</sup>, P-516)

**Q. Features of severe zinc deficiency are: (BSMMU - M. Phil, Diploma, July-08)**

- |                             |   |
|-----------------------------|---|
| a) impaired taste and smell | T |
| b) hair loss                | T |
| c) diarrhea                 | T |
| d) mental retardation       | T |
| e) night blindness          | F |

**Q. Important features of zinc deficiency are- (BSMMU – MD - 05Ja)**

- |                             |   |
|-----------------------------|---|
| A. Periorificial ulceration | T |
| B. Raw beef tongue          | F |
| C. Mental retardation       | T |
| D. hypoproteinemia          | F |
| E. Diarrhoea                | T |

#### **HELP LINK:**

##### **■ Causes of deficiency:**

1. Intestinal disease
2. Nephrotic syndrome
3. Ch. Alcoholism
4. Burn
5. Anorexia nervosa
6. Haemodialysis
7. DM
8. Ch. Febrile illness

##### **Features of zinc deficiency:**

1. A distinctive rash, most often around the eyes, nose, mouth, anus and distal parts, called **acrodermatitis enteropathica**.
2. Anorexia, often accompanied by diarrhea.
3. Growth retardation in children
4. Impaired wound healing
5. Hypogonadism with diminished reproductive capacity
6. Altered immune function
7. Impaired night vision related to altered vitamin A metabolism.
8. Depressed mental function
9. An increased incidence of congenital malformations in infants of zinc-deficient mothers.

(Ref: Robbins & Cotrans-9<sup>th</sup>)

##### **■ Deficiency features:**

1. Skin ulcer
2. Depressed immune response

3. Hypogonadal dwarfism.
4. Loss of taste acuity.
5. Decreased wound healing.
6. Delayed closure of epiphysis.
7. Anaemia.
8. Hepatosplenomegaly.
9. Thymic atrophy.

#### Important features of zinc deficiency

1. Diarrhoea.
2. Mental apathy.
3. A moist eczematoid dermatitis specially around the mouth.
4. Loss of hair.
5. Acrodermatitis enteropathica (growth retardation, hair loss, chronic diarrhoea).
6. Impaired taste & smell ( $\downarrow$  appetite).
7. Night blindness (severe zinc deficiency).
8. Impaired wound healing.

**Q. Zinc deficiency can cause:** (DMC – MD/MS - 05Ja)

- |                       |   |
|-----------------------|---|
| a) Poor wound healing | T |
| b) Infertility        | T |
| c) Hypertension       | F |
| d) Dwarfism           | T |
| e) Lichen planus      | F |

**Q. Zinc deficiency produces-** (BSMMU – MD - 03Ja)

- |                          |   |
|--------------------------|---|
| a) Hypogonadism          | T |
| b) Growth retardation    | T |
| c) Alopecia              | T |
| d) Delayed wound healing | T |
| e) Constipation.         | F |

## Magnesium

**Regarding Mg the following statements are correct:**

- The major part of magnesium (Mg) (65%) is present in the bones. The remaining (35%) is present in the cells.
- Plasma concentration usually follows that of calcium and potassium.
- Causes of Mg deficiency are severe diarrhea, ketoacidosis. It is often associated with hypocalcemia, hypokalemia and hypophosphatemia.
- Patients present with paresthesia, tetany, arrhythmias and fits. Treatment with magnesium salt, orally or intravenously (8 mmol MgSO<sub>4</sub> intravenous) given over 3 minutes to 2 hours depending upon severity.
- Hypermagnesemia is usually iatrogenic due to (i) excessive consumption of antacids containing magnesium and (ii) renal failure. It manifests with decrease in blood pressure (BP), neuromuscular depression, central nervous system (CNS) depression and coma.

**Q. Serum magnesium level is reduced in:** (BSMMU – M. Phil, Diploma (Non-Residency) – IJJu, DMC & others – MD/MS – IJJu)

- |                              |   |
|------------------------------|---|
| a) severe diarrhoea.         | T |
| b) chronic dialysis.         | T |
| c) acute renal disease.      | F |
| d) hyperthyroidism.          | F |
| e) idiopathic hypercalcemia. | F |

**HELP LINK:**

## MAGNESIUM

- Cofactor for many enzyme reactions and involved in control of muscular contractions.
- Average daily intake (10 mmol) and average daily requirements (8 mmol).
- The majority is distributed in bone and intracellular fluid.

### Abnormalities of serum magnesium levels:

#### Causes of hypomagnesaemia:

1. Malnutrition
2. Malabsorption or severe diarrhoea
3. Alcohol abuse
4. Inadequate intake (parenteral nutrition)
5. Renal tubular acidosis and diabetic ketoacidosis
6. Chronic diuretic therapy or dialysis
7. Acute pancreatitis and hepatic cirrhosis

#### Causes of hypermagnesaemia:

1. Acute renal failure
2. Chronic renal failure
3. Excess intake (parenteral nutrition)

#### Regarding nutritional value of selenium:

- It is important and essential element having antioxidant property.
- It is required for the anti-oxidant glutathione peroxidase which reduces harmful free radicals.
- It has also anti-thrombotic property and is required for sperm motility proteins.
- Its deficiency may lead to atheroma formation, increase chances of neoplasia, may cause cardiomyopathy.
- Selenium is present in cereals, nuts and meat.

## Others

**Q. Skin changes may result from deficiency of (BSMMU – Residency - MD/MS, Basic science, Paediatrics – March 19)**

- a) zinc
- b) vitamin D
- c) vitamin A
- d) pyridoxine
- e) fluoride

Ans.

- a) T (dermatitis)
- b) F
- c) T (toad skin/keratinization of skin/ keratinizing squamous metaplasia)
- d) F (peripheral neuropathy, anemia, defect in amino acid metabolism, hypercholesterolemia and atherosclerosis)
- e) F (Dental caries)

2. Depressed immune response