Paper I - August 2008

1. Explain the steps of beta oxidation of palmitic acid. Add note on Energetics. [Aug 2006 Essay]

- **Site of occurrence** : All tissues , prominent in liver and skeletal muscle.
- Intracellular location: M**itochondria**.
- Substrate: fatty acids.
- Product: acetyl Co A, NADH, FADH2

Steps in fatty acid oxidation:

I. Activation of fatty acids

II. Transport of fatty acids across mitochondrial membranes into mitochondrial matrix

III. Beta oxidation of fatty acids.

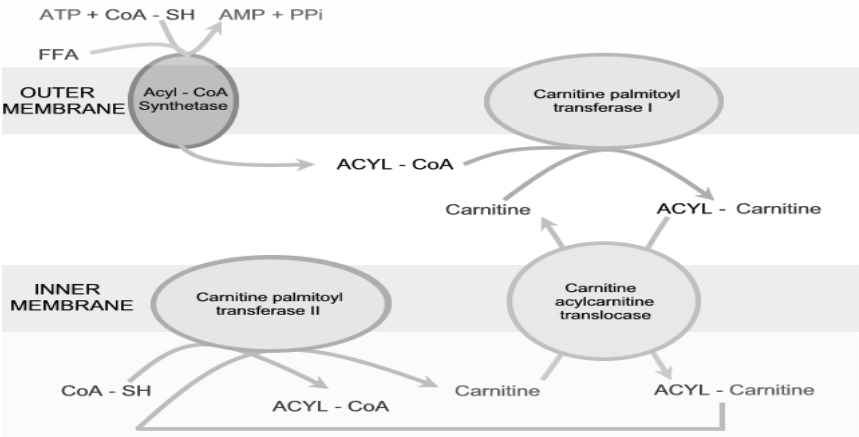
I. Activation of fatty acids

Fatty acid + ATP + CoA ---> Acyl-CoA + PPi + AMP

II. Carnitine as a Carrier

- Synthesized from **lysine & methionine in liver and kidney**
- Carnitine carries fatty acyl groups across the inner mitochondrial membrane

Carnitine shuttle



4 steps involved in beta oxidation:

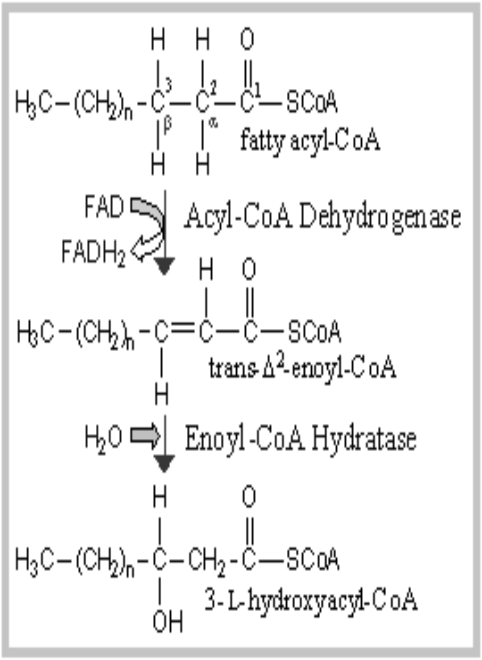
1. Dehyrogenation

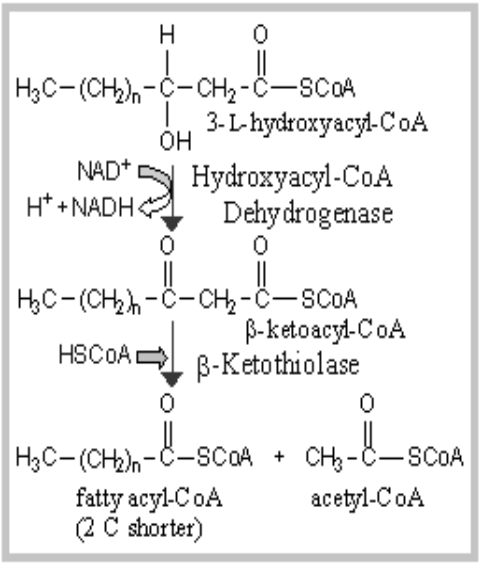
2. Hydration

3. Dehyrogenation

4. Thiolytic Cleavage

<u>Beta oxidation of fatty acids:</u>





Energetics of palmitic acid

• **From palmitoyl CoA to acetyl CoA**:		ATP
Acyl CoA dehydrogenase	7 FADH2	14
Beta-OH dehydrogenase	7 NADH	21
• **From 8 acetyl CoA**		96
• Total energy yield		131
ATP are used for activation of FA		-2
Hence net gain of ATP		**129**

2. What is Gluconeogenesis? Describe the pathway involved in gluconeogenesis. Add a note on regulation. [Feb 2007 Essay]

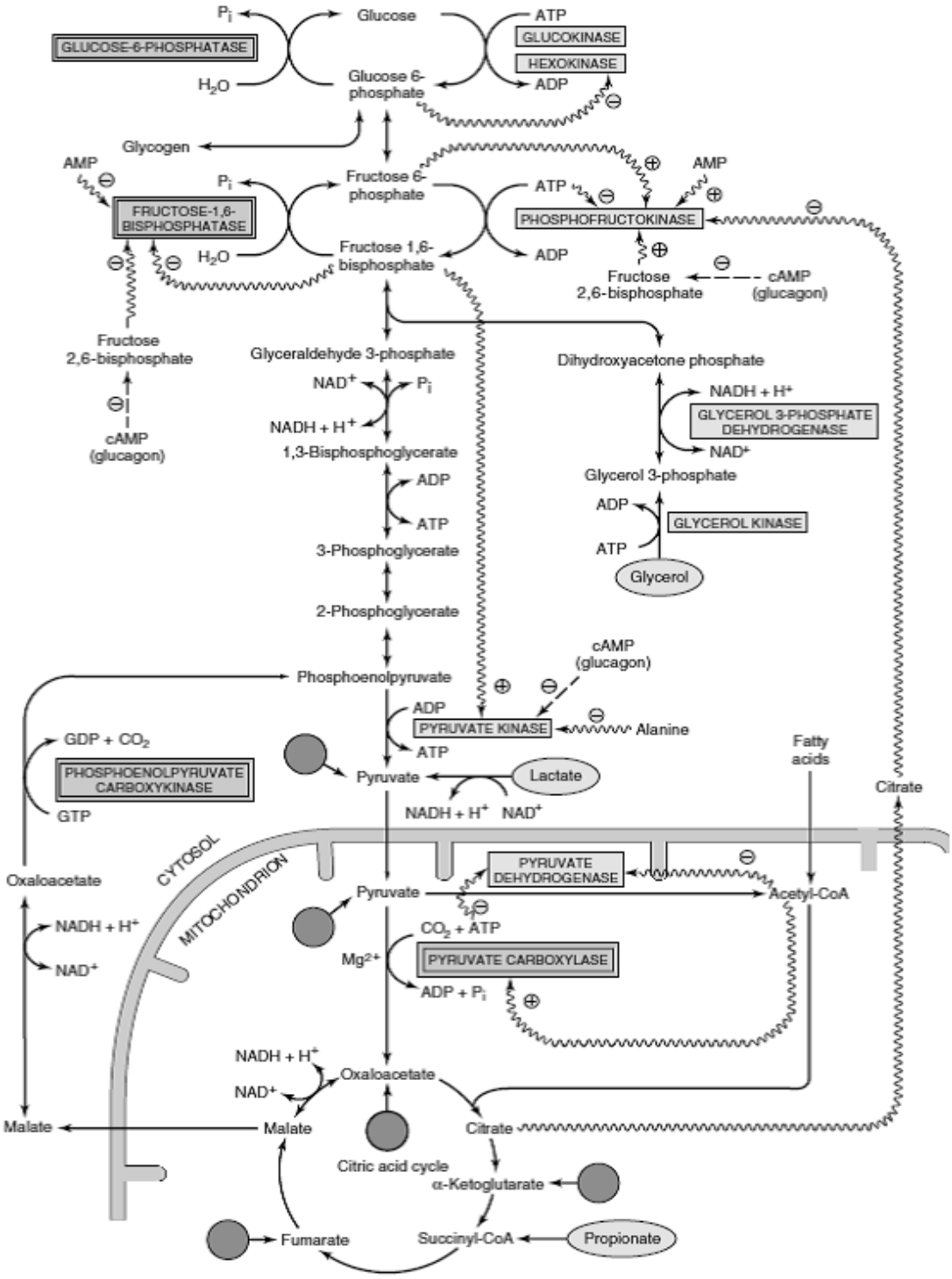


Fig Gluconeogenesis

Definition: Synthesis of Glucose from non-carbohydrate substrates

- Organs – Liver and Kidney (Cortex)
- Substrates : Pyruvate, Lactate, Amino acids (Glucogenic), Propionate, Glycerol
- **Key enzymes in gluconeogenesis:**
    - ✓ Glucose 6 phosphatase
    - ✓ Fructose 1,6 bisphosphatase
    - ✓ Phophoenol pyruvate carboxy kinase
    - ✓ Pyruvate carboxylase

Reciprocal regulation of glycolysis and gluconeogenesis:

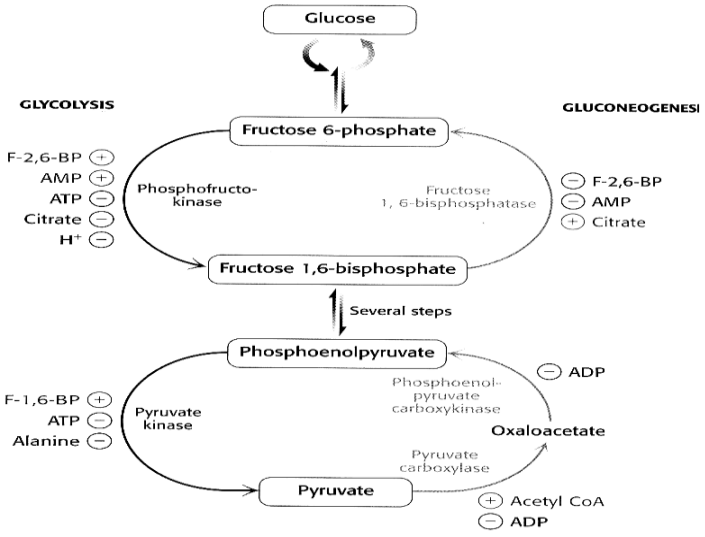


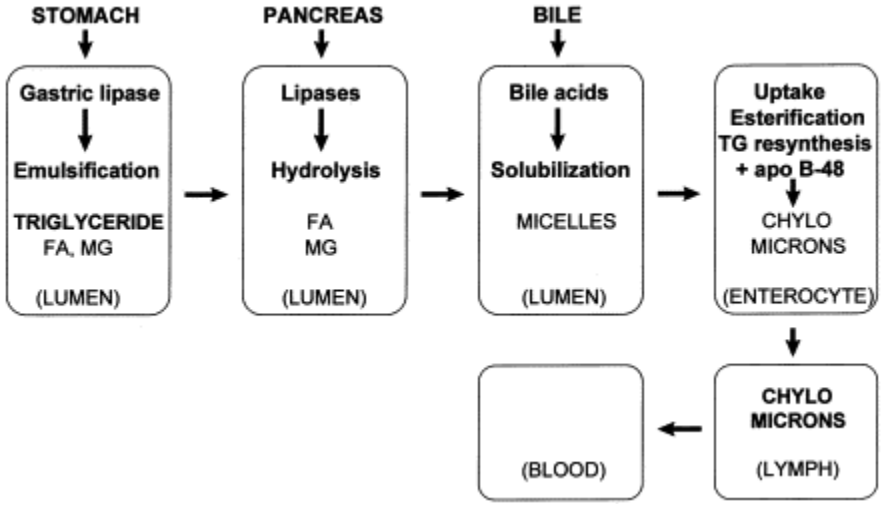
Fig Regulation of gluconeogenesis

II. Write short notes on (5 marks)

1.Functions of Vit C [Aug 2005 essay, aug 2008 SN]

- Very essential for bone formation
- Iron metabolism
- Tryptophan & Tyrosine metabolism
- Antioxidant
- Met-hemoglobin to hemoglobin
- Immune functions
- Needed for Folic acid metabolism
- Collagen synthesis, Cataract prevention, Cancer prevention, Cellular respiration, Cholesterol metabolism

2.Digestion and absorption of lipids.[Aug 2010 SN]



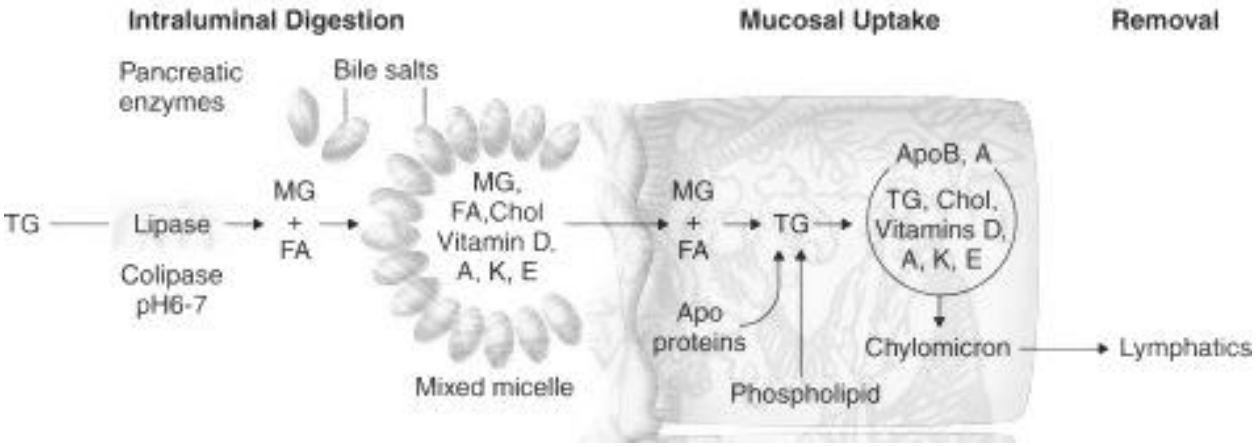


Fig Absorption of lipids

3. Haemoglobin S [march 2002, Sep 2012 SN]

Haemoglobin is a conjugated protein made up of a prosthetic group called heme and protein part globin. Globin is a complex tertiary structure composed of two alpha and two beta chains. The genes for these proteins are located in 16 and 11 respectively. Any mutation in these genes gives raise to abnormal structure of haemoglobin which shows altered haemoglobin function. There are plenty abnormal Hb is discovered yet.

Hemoglobinopathies

HbS: Sickle Cell Hb –

- The glutamic acid in the 6^{th} position of beta chain of Hb is changed to valine. This change of aminoacid causes sikling of RBC.
- The sickled RBC plugs in capillaries and may cause occlusion of major vessels and lead to infarction of organs.

4.Isoenzymes[Feb 2007 essay]

They are physically distinct forms of the same enzyme activity.

Assays of these enzymes are useful in diagnosis of diseases. They are

- ✓ Creatine kinase (CK)
- ✓ Lactate dehydrogenase (LDH)
- ✓ Cardiac Troponin I and Cardiac Troponin T
- ✓ ALP

Creatine Kinase: Normal level – 15-100 U/L

In MI, CK starts to rise within 3-6 hrs of infarction.

Isoenzyme	Subunits	Origin	Electrophoretic mobility
CK3	MM	Skeletal muscle	Least
CK2	MB	Heart	Intermediate
CK1	BB	Brain	Maximum

ADVANTAGE:

It is useful to detect early cases where ECG changes may be ambiguous.

It is not increased in hemolysis or in congestive heart failure. Therefore CK has an advantage over LDH.

LDH: Normal level – 100-200 U/L

It will convert pyruvte to lactate. It is increased in hemolytic anemia, carcinomas.

Isoenzymes of LDH:

Isoenzyme	Origin	Subunits	Electrophoretic mobility
LDH 1	Heart	H4	Fastest
LDH 2	RBC	H3M1	Faster
LDH 3	Brain	H2M2	Fast
LDH 4	Liver	H1M3	Slow
LDH 5	Skeletal muscle	M4	Slowest

[In MI, total LDH activity is increased, where LDH 1 is increased 5 -10 times. Normally, LDH 2 conc. in blood is greater than LDH 1; but this pattern is reversed in MI. This is called **flipped pattern.]**

AST: Normal level – 8-20 U/L

Other name: serum glutamate oxaloacetate transaminase

It is increased significantly in MI.

Cardiac Troponins:

Troponin I: it is increased in blood within 4 hours after onset of symptoms, peaks at 14-24 hrs & remains elevated for 3-5 days.

Troponin T: It is increases after 6 hrs of MI, peaks at 72 hrs and then remains elevated up to 7-10 days

ALP (alkaline phosphatase):

Zinc is a constituent ion of ALP. Its optimum pH is 9 to 10.
It is activated by magnesium and manganese.

It is of 4 major forms.

1. Bone ALP
2. Liver ALP
3. Kidney ALP
4. Fetal ALP

5. Structure of Cell membrane.[april 2001 SN]

Cell membrane is also called as plasma membrane.

- It protects the intracellular organelles from outer environment and provides selective permeability for cell function.
- The structure of cell membrane was described by singer and Nicolson and is accepted

Fluid mosaic model:

- ✓ The membrane is complex structure and is made up of lipids, proteins and carbohydrates etc
- ✓ The PL are arranged in bilayer with polar head groups oriented towards the exracellular side and cytoplasmic side with a hydrophobic core
- ✓ Choline rich PL – external layer
- ✓ Ethanolamine and serine rich PL – inner layer
- ✓ Proteins present in membrane divided into three categories
- ✓ Peripheral – these proteins attached to polar heads of outer of plasma membrane lipids through ionic/polar bonds -
- ✓ Transmembrane – these proteins span the whole membrane – eg. Receptors
- ✓ Dimensions: Single layer thichness – 25 A; Total thickness – 50 – 80 A^{o}
- ✓ Properties of PM: free lateral moments are seen hence it is fluid in nature, semipermiability

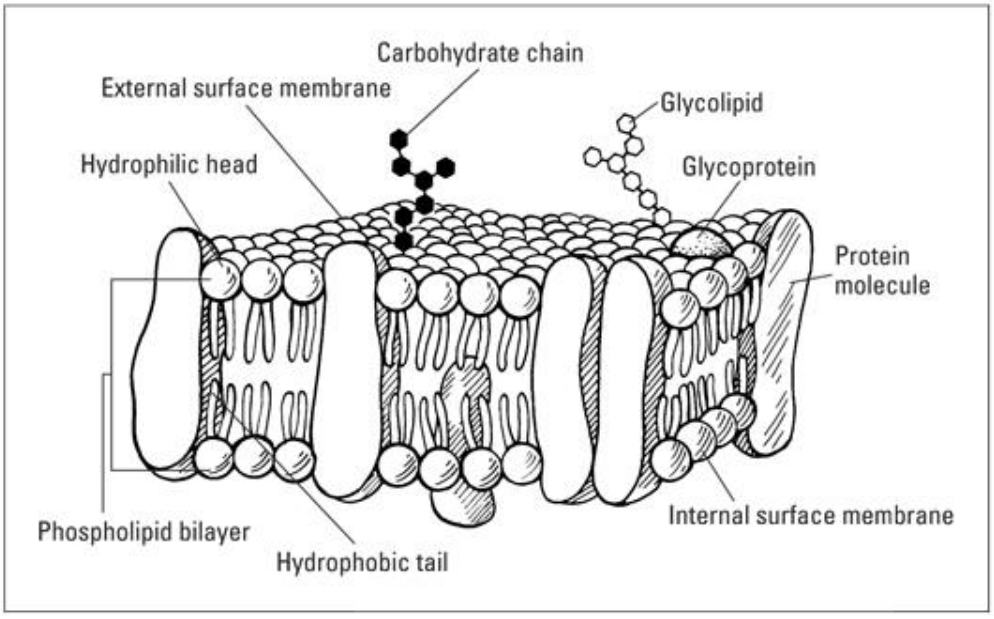


Fig Cell membrane

6. Define BMR. What are the factors that can affect BMR?[Aug 2005, Aug 2007 SN]

Definition: The energy required by a awaken individual during physical, emotional and digestive rest.

It is the minimum amount of energy required to perform vital functions such as circulation, respiration, working of heart etc.

Normal Value: Men - 34-37 k cal/m^2/hr
Women - 30-35 k cal/m^2/hr

Factors affecting BMR:

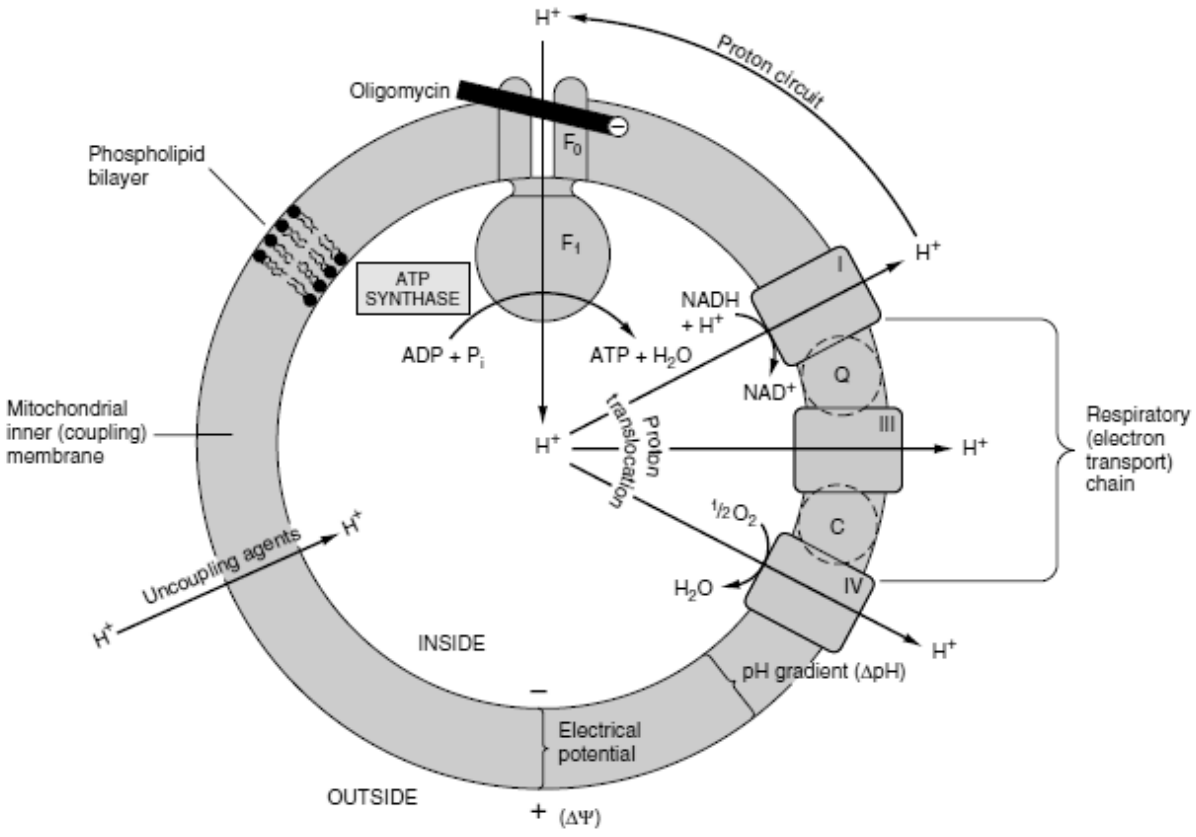
1**. Age**: In old age, BMR is lowered
2. **Sex:** Males have a higher value than females
3. **Temperature:** BMR increases in cold climate.
4. **Exercise:** It increases during exercise
5. **Fever**: 12% increase during fever
6. **Thyroid hormones**: BMR is raised in hyperthyroidism.

7. Define Oxidation Phosphorylation. Explain Chemiosmotic theory.[April2001, Feb 2006, Sep 2002 SN]

The coupling of oxidation with phosphorylation is termed oxidative phosphorylation. Peter Mitchell in 1961 proposed chemiosmotic theory to explain oxidative phosphorylation.

- The ultimate transfer of electrons from the reducing equivalents NADH and $FADH_2$ to oxygen through iron and hemes, is the driving force for forming ATP in mitochondria.
- The electron transport is coupled to the oxidative phosphorylation of ATP via the protons pumped during ETS.
- The linkage of these two systems is explained by the chemiosmotic hypothesis.
- In this theory the differences in both pH and membrane potential created on opposite sides of the inner mitochondrial membrane drives the phosphorylation of ATP by the Fo/F1 subunits of ATP synthetase.

Fig Chemiosmotic theory



8. Galactosemia

Increased amount of free galactose in blood.

It is an inborn error of metabolism

Incidence: 1 in 35,000 births

Defect: Deficiency of galactose 1 phosphate uridyl transferase enzyme

Features:

1. Hypoglycemia

2. Unconjugated bilirubin is increased

3. Enlargement of liver (jaundice)

4. Mental retardation

5. Congenital Cataract: Due to enzyme deficiency, Galactose is reduced to dulcitol. It accumulates in lens causes cataract.

6. Amino aciduria

Diagnosis:

Presence of galactose in urine (galactosuria).

Treatment:

Lactose free diet.

9. Ketogenesis[April 2001 SN, Feb 2005 SN]

[The acetyl co A formed from fatty acids can enter and get oxidized in TCA cycle only when carbohydrates are available. During starvation and diabetes mellitus, the acetyl co A takes the alternate fate of formation of ketone bodies.]

Level of KB in blood is **less than 1 mg/dl.**

Site of formation: Liver

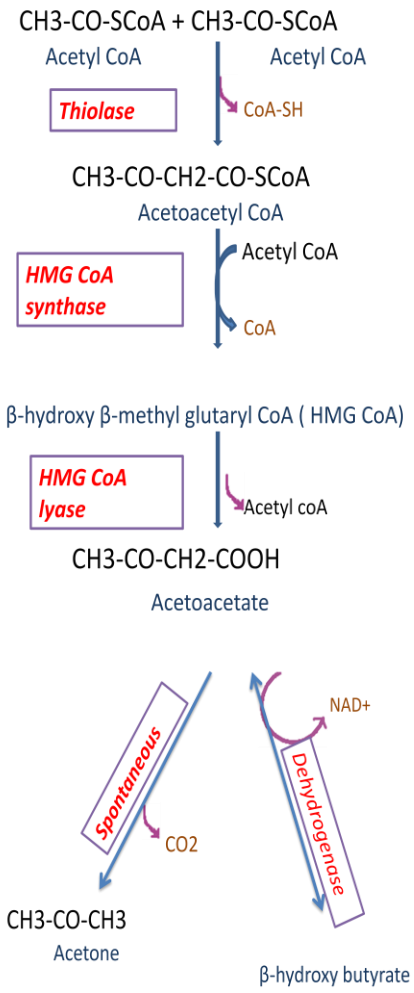
Site of ultization of KB: Extrahepatic tissues

Uses:

During starvation, it is the major fuel for brain, heart & muscles

Brain gets 75% of energy from KB during starvation.

ketogenesis



10. Glucose Tolerance Test:(GTT)

It is is used to diagnose diabetes mellitus in doubtful cases.

Indications of GTT:

- Fasting value in between 110 and 126 mg/dl
- To rule out renal glycosuria

Contra Indications of GTT:

- It should not be done in ill patients
- No role in follow up of diabetes

Procedure:

1. Patient should not take food after 8 PM.
2. Next day at 8 AM, fasting blood sample is collected. Also urine is collected.
3. 75 g of glucose in 300 ml of water is given.
4. Then blood and urine samples are collected at ½ an hour intervals for next 2 ½ hours.(total six samples including fasting sample)
5. Glucose level is estimated.
6. Graph is plotted.

Sugar level in GTT in normal and Diabetic patients:

	Normal	Criteria for Diabetes
Fasting	<110 mg/dl	>126 mg/dl
1 hr peak	<160 mg/dl	--
2 hr after	<140 mg/dl	>200 mg/dl

SHORT ANSWERS

1. Name the essential Fatty acids [aug 2007 SN]

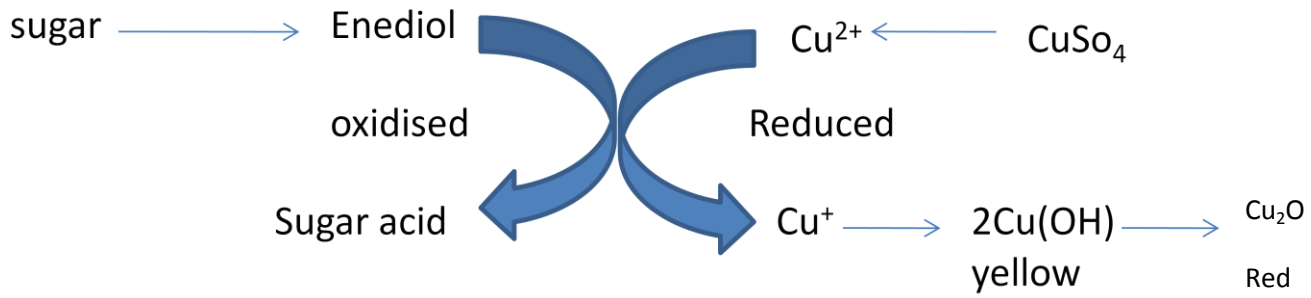
Ans. 1. Linoleic acid and Linolenic acid

2. Significane of HMP shunt:[Aug 2010 SN]

- Produces NADPH which serves as hydrogen and electron donor in reductive biosynthesis
- Produces 5 carbon sugar (Ribose) which is a component of DNA, RNA, ATP, NAD, FAD, CoA SH
- It doesn't yield energy.

3. Benedicts Test:

Ans. This is the test for reducing sugar. Benedict's reagent contains sodium carbonate, copper sulphate, and sodium citrate. The red precipitate is due to the formation of cuprous oxide. This test is carried out in mild alkaline medium.



4. Inhibitors of TCA cycle:

Ans. 1. Aconitase – It converts citrate to aconitate. It is inhibited by fluoro acetate

2. Alpha keto glutarate dehydrogenase – It converts alpha keto glutarate to succinyl CO A. It is inhibited by Arsenite

3. Succinate dehydrogenase – It converts succinate to fumarate. It is inhibited by malonate.

5. Chloride shift

Ans. When CO_2 is taken up, HCO_3^- conc within the cell increases. This would diffuse out into the plasma. Simultaneously, chloride ions from the plasma would enter in the cell to establish electrical neutrality. This is called chloride shift or Hamburger effect.

6. Functions of calcium[Feb 2009 SN]

Ans. [Normal level – 9-11 mg/dl]

- ✓ Activation of Enzymes : Calcium-Calmodulin complex causes activation of enzymes eg:Adenylcyclase, Phospholipases
- ✓ Nerve impulse transmission
- ✓ Triggers contraction of skeletal & cardiac muscles
- ✓ Helps in bone mineralization.
- ✓ Secretion of hormones into the blood
- ✓ Acts as a second messenger
- ✓ Required for blood coagulation, membrane formation, capillary permeability.

7. Lipotrophic factors[Sep 2002 SN]

Ans. They are required for the normal mobilization of fat from liver. Deficiency of these factors results in fatty liver.

Eg

1. **Choline**
2. **betaine**
3. **Lecithin**
4. **Methionine**
5. **Vit E and selenium**
6. **Omega 3 fatty acids.**

8. Normal blood levels of cholesterol, Bilirubin, Sodium, Potassium

Total cholesterol	140-200mg/dl
Bilirubin (unconjugated)	0.2-0.6 mg/dl
Bilirubin (conjugated)	0-0.2 mg/dl
Sodium	136-145 mmol/litre
Potassium	3.5-5 mmol/litre

9. Phospholipids

Ans. They contain glycerol, fatty acids and a nitrogenous base. They are amphipathic (both hydrophilic and hydrophobic). Eg. Lecithin, Cephalin, Phosphotidyl inositol, Plasmalogens.

10. Fluorosis[Aug 2009 SN]

Ans. Fluoride is the trace element. It helps to prevent tooth decay. The safe limit is 1 ppm in water Fluoride level more than 20 ppm is toxic , leading to alternate areas of osteoporosis and osteosclerosis with brittle bones. This is called **fluorosis**.

Characteristic feature:

- Genu valgum
- Blood fluoride increases to 50 microgram/100 ml. [normal- 4microgram/dl]
- Excretion of hydroxy proline in urine is enhanced.

Prevention: To provide fluoride free water, restriction of intake of jowar, supplementation of vit c and avoid fluorinated toothpaste.