Paper I- August 2009

I. ESSAY

1. What are porphyrias? Classify different types of porphyrias and give the enzyme defect and biochemical findings.[April 2001, Aug 2006, Feb 2006 SN]

Porphyrias are a group of inborn errors of metabolism associated with biosynthesis of heme. These are characterized by increased production and excretion of porphyrins and/or their precursors.

Porphyrias are:

1. **Acute intermittent porphyria-Uroporphyrinogen I synthase deficiency**

   This leads to secondary increase in activity of ALAs. The levels of ALA and PBG are elevated in blood and urine. Urine is dark on voiding due to photo oxidation of PBG to phorphobilin. Symptoms appear intermittently. Patients will have acute abdominal pain. An attack is precipitated by starvation and symptoms are relieved by glucose infusion. Patients may have neurological abnormalities like sensory and motor disturbances, agitation and confusion. Patients may have neuropsychiatric problems.

2. **Congenital erythropoietic porphyria**- Uroporphyrinogen I synthase deficiency . autosomal recessive disorder. Photosensitivity and dark urine are the symptoms.

3. **Porphyria cutanea tarda** -uroporphyrinogrn decarboxylase deficiency. Here patients are more prone for photosensitivity. The urobilinogens accumulate and when patients come under light they spontaneously form urobilin which is a potent oxidant and destroys skin cells and causes scarring. Patients have gross skin malformations leading to monster like appearance, and they prefer night. Sunscreens are mildly effective.

4. **Hereditary coproporphyria-coproporphyrinogen oxidase deficiency**

5. **Variegate porphyria - protoporphyrinogen oxidase deficiency**

6. **Erythropoietic proto porphyria- ferrochelatase deficiency**

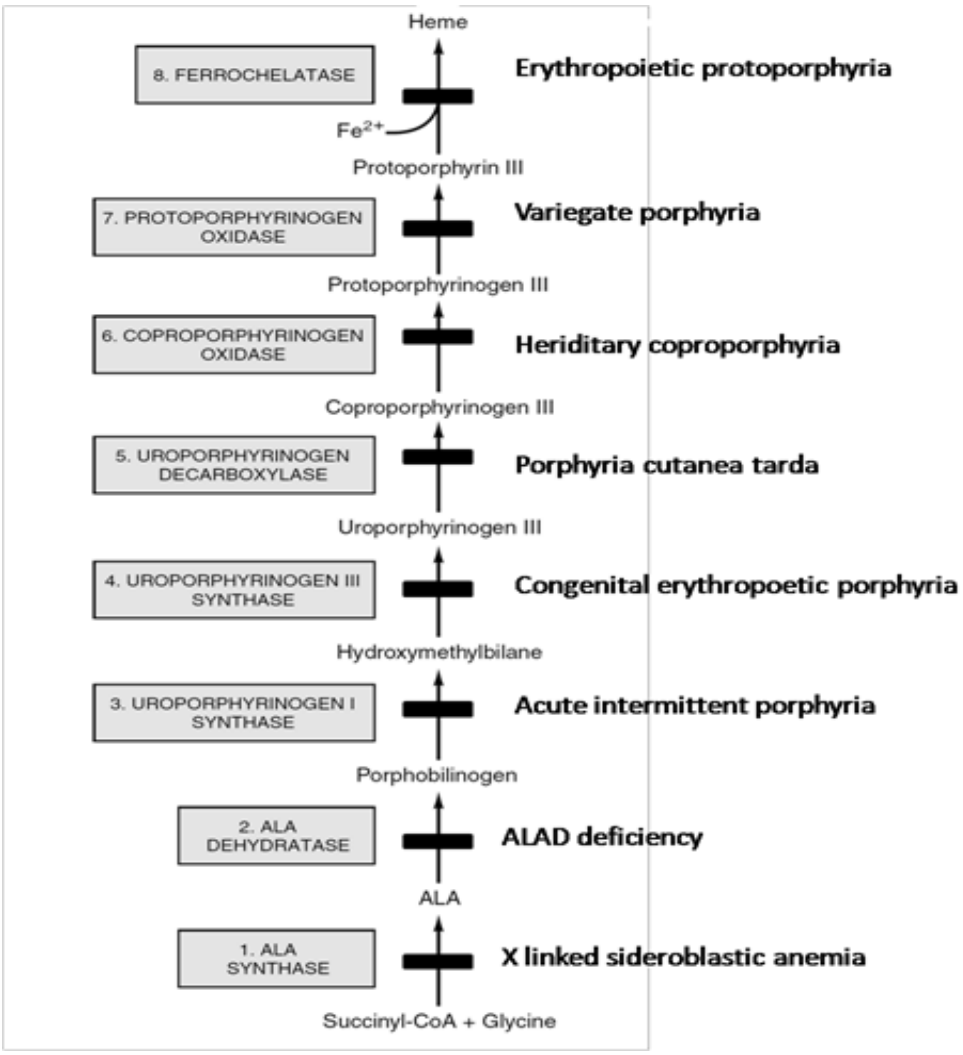


Fig Pophyrias

2. What is oxidative phosphorylation. Discuss the steps and significance.[April 2001, sep 2002 SN]

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

Oxidative phosphorylation is comprised of the following processes

1) Oxidation of reducing equivalents (NADH and $FADH_2$)
2) Electron transfer through 3 protein assemblies (Complex I, III, and IV) to O_2
3) Transport of H^+ into inter membrane space.
4) Transport of H^+ into the mitochondrial matrix
5) Synthesis of ATP.

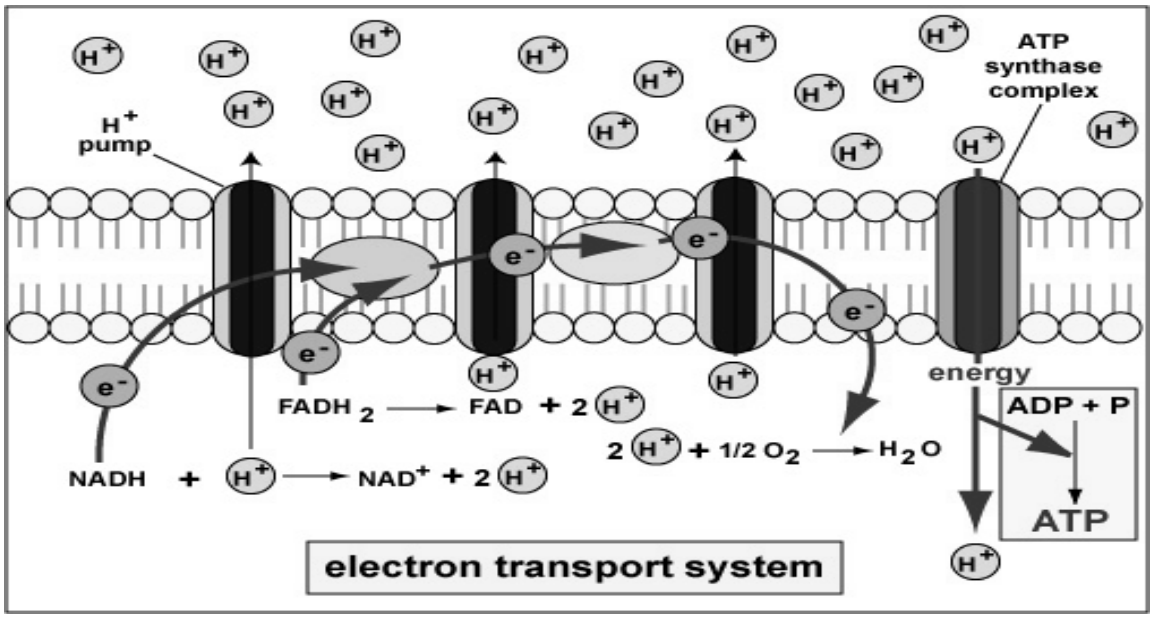
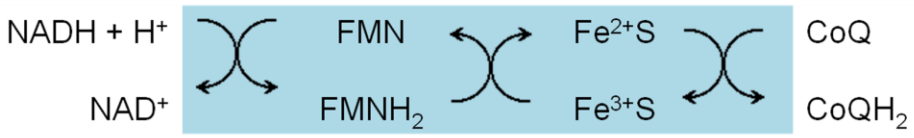


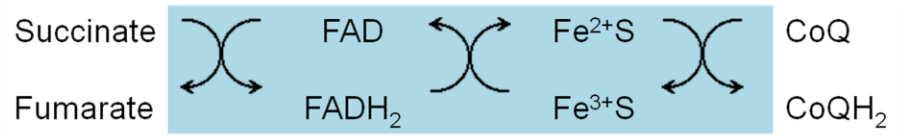
Fig ETC

- In ETC, the electrons are transferred from NADH to a chain of electron carriers.
- All components of ETC are situated in inner membrane of mitochondria. They are
- **Complex I - NADH dehydrogenase, also called NADH Coenzyme Q reductase.**
- **Complex II - Succinate - Coenzyme Q reductase.**
- **Complex III - Coenzyme Q - cytochrome c reductase.**
- **Complex IV - Cytochrome c oxidase.**

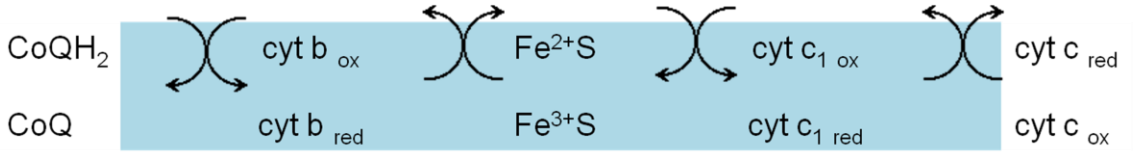
Complex I



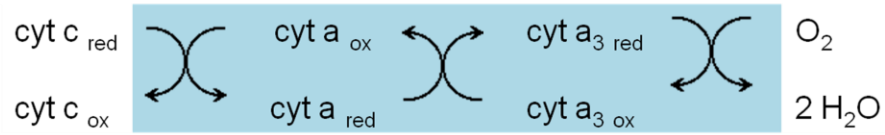
Complex II



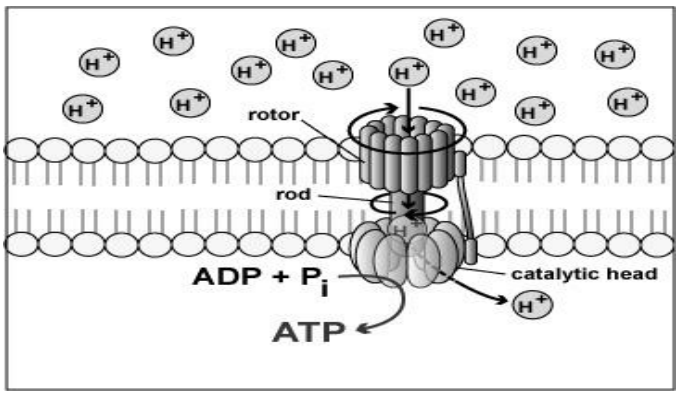
Complex III



Complex IV



Complex V (ATP synthase complex)



Salient features:

- Complexes I, III, and IV are proton pumps.
- Complex II is part of the Krebs cycle and does not pump protons
- Complex IV is the terminus of the electron transfer chain, consuming oxygen and making water.
- **ATP Yield: NADH = 3 ATP (entry at Complex I)**
  $FADH_2$ = 2 ATP (entry at Complex II)

II. Write short notes on (10*5=50)

1. Classify RNA and explain the functions.

Cellular RNAs are of 3 major types

- Messenger RNA of m RNA
- Transfer RNA of t RNA
- Ribosomal RNA or r RNA

m RNA:

It acts as messenger of information from gene to ribosomes.

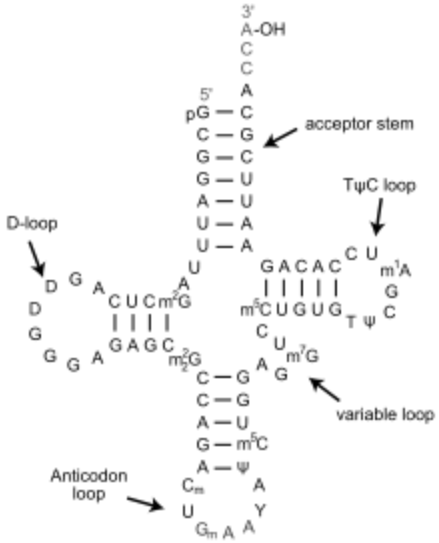
It carries message in the form of triplet code.

m RNA is the complementary copy of the template strand of DNA

t RNA:

other name: **Solube RNA or Adaptor RNA**

- They transfer amino acids from cytoplasm to the ribosomal protein synthesizing machinery. Hence the name t RNA
- It is **clover leaf** in shape
- It contains unusual bases like pseudo uridine, dihydro Uracil, hypoxanthine. Moreover many bases are methylated.
- It contains 5 arms
    1) Acceptor arm: It carries amino acid
    2) Anticodon arm: It recognizes triplet nucleotide codon present in m RNA.
    3) D arm: It is having recognition site for enzymes which add amino acids.
    4) Pseudouridine arm: involved in binding t RNA to ribosomes.
    5) Variable arm.



r RNA:

It is the protein synthesizing machinery.

2. Hyper uricemia

When uric acid levels increase in the blood it tends to get deposited as crystals in synovial fluid of joints leading to inflammation and acute arthritis. This disease is called Gout

- **primary gout**
    - 5-phosphoribosyl amidotransferase- there will be increased production of purines due to absence of regulation on this enzyme. It's a genetic defect
    - Abnormal PRPP synthase- there will be increased production of PRPP due to absence of regulation on PRPP synthase. It's a genetic defect.
    - Salvage pathway enzyme deficiencies-there would be more availability of PRPP leading to production of purines→ uric acid
    - Von Gierke's Disease- due to G-6-Pas deficiency, G-6-P is not converted to glucose. So it goes through HMP shunt resulting in more nucleotide bases, increasing urate production.
- **Secondary Gout:**
    - Increased production of uric acid- malignancy- lymphomas, leukemias; after treatment of cancer, cancer cells breakdown, leading to hyperuricemia; trauma-tissue damage; starvation-where catabolism is increased
    - Reduced excretion- renal failure, thiazide diuretics- which inhibits urate secretion, lactic acidosis and Ketoacidosis- interferes with urate secretion

Clinical features:

Uric acid gets deposited in the cooler areas of body like distal joints to form tophi. Hypeuricemia leads to increased excretion of uric acid through the kidneys, so uric acid crystals gets deposited in the urinary tract leading to renal calculi.

Treatment:

1. Dietary purine intake should be reduced, alcohol should be restricted
2. Uricosuric drugs which increases the excretion of uric acid like probenecid should be used
3. For calculi Allopurinol can be used. It inhibits xanthine oxidase and reduces the formation of uric acid. It's a type of suicide inhibition like aspirin, where the enzyme becomes completely functionless.
4. Colchicine, an anti-inflammatory drug used in RA can be used to reduce inflammation in joints.

3. Renal Glycosuria [Aug 2007 SN]

Normal renal threshold for glucose 175-180 mg/dl

If it rises above, it starts appear in urine.

Physiological cause:

Pregnancy

Pathological cause:

Fanconi syndrome

4.Cardiac troponin [Feb 2008 SN]

Cardiac Troponins:

Troponins are markers of MI.

The troponin complex consist of 3 components.

Troponin C: C for calcium binding

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. It is not increased in muscle injury, whereas CK2 may be elevated.

Troponin T (TnT): it increases within 6 hours of MI, peaks at 72 hours and then remains elevated upto 7-10 days.

5. Structure of cholesterol and its importance [Feb 2009 Essay]

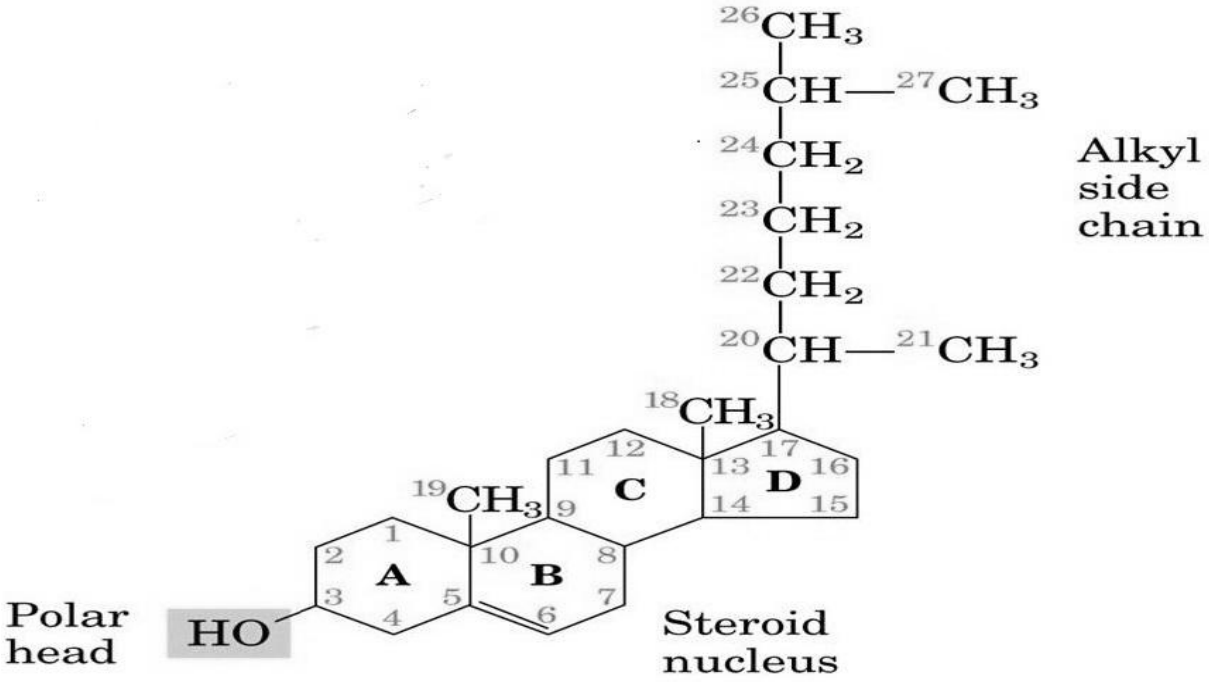


Fig Structure of cholesterol

- Other name: Animal sterol
- Cholesterol means '*solid bile alcohol*'
- It derives its name from Greek word '*cholesterine'* means Bile solid..
- It was 1st isolated from human gall stones
- Cholesterol has a crucial role in
    - Structure of membranes
    - Precursor of steroid hormones and bile acids

6. Beri beri [Aug 2007 Essay]

1. **Wet beri-beri:**
   - ✓ It related to edema of face, trunk, and serous cavities.
   - ✓ Breathless ness, palpitation, swollen calf muscles, elevated systolicpressure, fast and bouncing pulse are seen.
   - ✓ The heart becomes weak.
2. **Dry beri-beri:**
   - ✓ It is not related to edema, and mostly related to degeneration ofnervous system (peripheral neuritis).
   - ✓ Muscles are weak and unable to movement and patients arebecome bedridden.
3. **Infantile beri-beri:**

✓ the child has symptoms like sleeplessness, restlessness, vomiting, convulsions, and death.

8. Flurosis [Aug 2008 SN]

i. Fluoride is the trace element. It helps to prevent tooth decay.
ii. The safe limit is 1 ppm in water (parts per million)
iii. 1 ppm = 1 g of fluoride in millions of water, this is equal to 1 mg/1000 ml)
iv. 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 of flurosis:

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

Prevention:

- Flurosis is highly prevalent in areas where jowar is the staple diet. Even ordinary toothpaste contains fluoride about 700 ppm.
- Prevention is to provide fluoride free water, restriction of intake of jowar, supplementation of vit c and avoid fluorinated toothpaste.

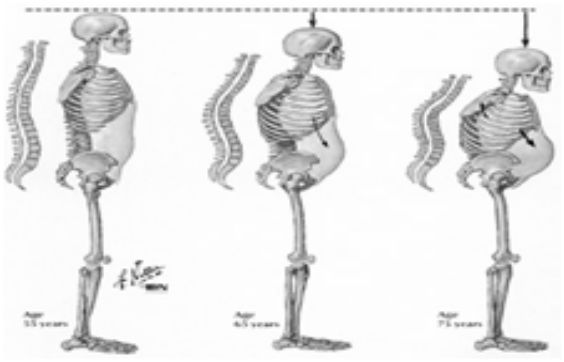
TOXICITY

Skeletal fluorosis - This occurs when the intake of fluorine is 5-20 ppm.

Phase 1 – sporadic pain, stiffness of joints, osteosclerosis of pelvis and vertebral column.

Phase 2 – chronic joint pain, arthritic symptoms, calcification of ligaments , osteoporosis of long bones.

Phase 3 – crippling deformities of spine and major joints,muscle wasting, neurological defects, compression of spinal cord.



Advanced flourosis results in **genu valgum**

9. What is PEM? Types and its important features.

It predominantly affects children.

1. Marasmus: It results due to continued severe deficiency of both dietary energy and protein

2. Kwaskiorkor: It is due to continued severe deficiency of protein alone.

Biochemical alterations in PEM:

1. Metabolic rate is decreased
2. Hypoalbuminemia
3. IgG increases
4. Fatty liver in kwashiorkor
5. Hypokalemia
6. Hypomagnesmia

	Marasmus	**Kwaskiorkor**
Age of onset	Below 1 year	1-5 year
Appearance	Shrunken	Plump due to edema
Attitude	Irritable	Lethargic
Skin	Dry	Dermatitis
Cause	Calorie deficiency	Protein deficiency
Serum albumin	2 to 3 g/dl	<2 g/dl
Serum cortisol	Increased	Decreased
Growth retardation	Marked	Present

Treatment:

1. Diet providing 150-200 k cal/kg body weight and 3-4 g of protein/kg body weight

2. Diet rich in 3 parts of vegetable protein and one part of milk protein is effective.

10. Functions of vit C [Feb 2012 Essay]

- 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

III. SHORT ANSWERS

1. Effect of temperature on enzyme activity.

The velocity of enzyme catalysed reaction is increases parallel upto a particular temperature due to supplying of activation energy and slowly falls in higher temperature due to degradation of enzyme molecule. The temp at which maximum amount of the substrate is converted to the product per unit is called the optimal temperature. Most of the enzymes works at optimal temparatures ranges betwee 37-50^{o}C ,except some eg. Thermobacillus (Taq pol II). When we draw the plot a graph for velocity vs temp, we will get the bell shaped curve

2. Define Epimer. Name two.

When sugars are different from one another, only in configuration with regard to a single carbon atom, other than the reference carbon atom, they are called epimers. Eg.

- ✓ Glucose and mannose are an epimeric pair which differ only with respect to carbon 2.
- ✓ Glucose and galactose differ with respect to carbon 4.

3. Phosphotidyl inositol importance.

It acts as 2^{nd} messenger.

It has a crucial role in structure of membranes.

4. Functions of Selenium

Ans.

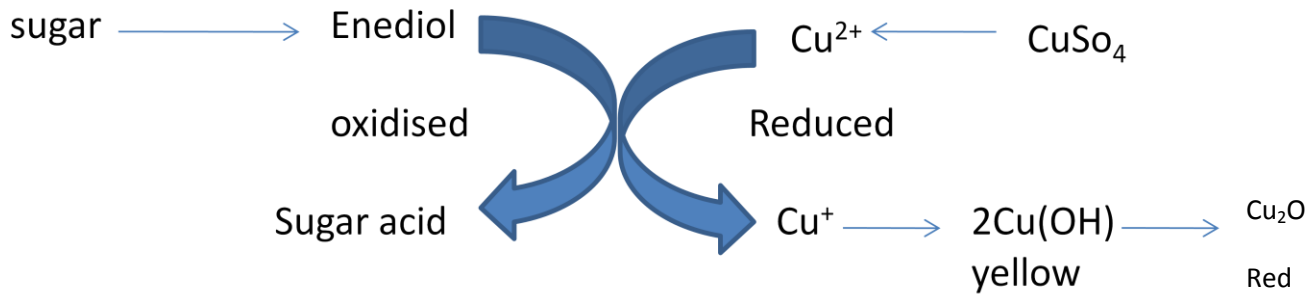
It is a non specific intracellular anti oxidant.

This action is complementary to vit E. Hence, vit E reduces the ‘se’ requirement.

Se deficiency causes liver necrosis, cirrhosis, cardiomyopathy.

5. Benedicts test [Aug 2008 – 2 marks]

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.



7. **Ribose and deoxy ribose**

   Ribose is a pentose sugar. Deoxy ribose is also a pentose but it contains one oxygen atom less than ribose.

8. Lysosomes [Aug 2010 SN]

It is a cell organelle. Other name: suicidal bag. It contains hydrolases enzymes.

8. Bence Jones proteins.

Monoclonal light chains are excreted in urine. This is due to asynchronous production of H and L chains or due to deletion of portions of L chains, so that they cannot combine with H chains. These proteins block kidney tubules.

Properties:

When these proteins are heated between 45^0 C and 60^0 C; it redissolving at higher than 80^0 C and lower than 45^0 C.

Diagnosis: Bradshaw's test:- urine + HCl ----> white precipitate.

9. Bile salts

Sodium and potassium salts of glycocholic acid and tauroglycocholic acid.

Functions:

1. facilitate digestion of lipids
2. they form micelle which bring about the absorption of lipids.
3. It keeps the cholesterol in solution.

10. Cori cycle:

Other name: Lactic acid cycle.

Definition: Transferring lactate from tissue to liver and synthesis of glucose is known as cori's cycle.

- **Effects**
    - It rescues lactate for further use (gluconeogenesis)
    - It counteracts lactic acidosis.
    - It is of less importance in starvation but important in more normal situations esp in certain cells such as matured RBC, medulla, retina which are lacking mitochondria and virtually anaerobic.
    - unlike alanine cycle it does not consume any energy