# Concepts

Active Space

- Fed state: Within 2 hours of food intake
- Fasting state: No food intake for 12 – 18 hours
- Starvation: No food intake for 1 – 3 days
- Anabolism: Synthesis → In fed state
- Catabolism: Breakdown → In fasting and starvation

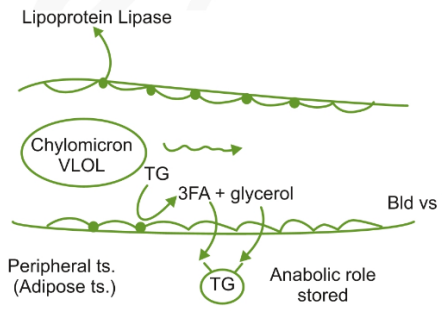
## SMILE FORMULA

02:07

1) Smile formula 1:

| Anabolic pathways or enzymes | Catabolic pathways or enzymes |
|---|---|
| Glycogenesis | Glycolysis |
| HMP | Link reaction (Pyruvate dehydrogenase reaction) |
| Fatty acid synthesis | Glycogenolysis |
| Cholesterol synthesis | Glycogenolysis |
| TG synthesis | Beta oxidation of fatty acids |
| Lipoprotein lipase | Gluconeogenesis |
| | Ketone body synthesis |
| | Ketone body utilization / breakdown |
| | Hormone sensitive lipase |

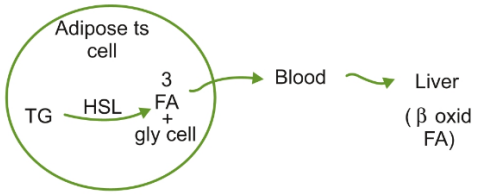
- Lipoprotein lipase:
  - Present in the endothelium of blood vessels
  - It is an anabolic enzyme



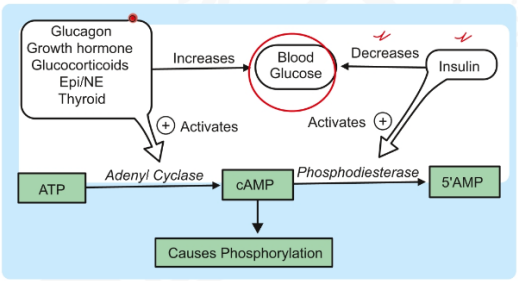



Pinch to zoom

- Hormone sensitive lipase:




2) Smile formula 2: Hormones relationship
   - Insulin is active in fed state → Anabolic
   - Glucagon is active in fasting / starvation state → Catabolic
   - Insulin activates all anabolic pathways / enzymes but it also activates 2 catabolic pathways:
     - Glycolysis
     - Link reaction
   - Glucagon activates all catabolic pathways except glycolysis and link reaction




   - Insulin decreases cAMP (dephosphorylation) and glucagon increases cAMP (phosphorylation)
3) Smile formula 3: Any pathway / enzyme which is activated by insulin, will be active in its dephosphorylated state
4) Smile formula 4: Pathway / compartment
   - Anabolic – cytoplasm
   - Catabolic – mitochondria
   - 2 exceptions: Glycolysis and glycogenolysis are two catabolic pathways which occur in cytoplasm
   - 3 pathways occur in both mitochondria (where is starts) and cytoplasm:
     - Urea cycle

Active Space

- Haem synthesis
- Gluconeogenesis

Active Space

Q1: What are the sources of blood glucose:

i. Food
ii. Liver glycogen (12 – 18 hours)
iii. Gluconeogenesis

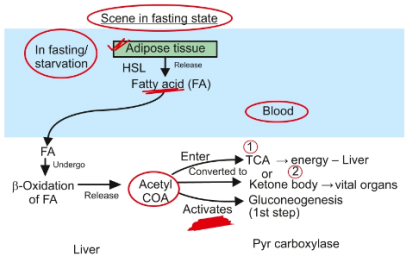
Q2: Preferred / main fuel for body?

→ 1st Carbohydrate → Fats → Proteins / AA

- Fats can never be converted to carbohydrates: 2 exceptions:
  - Glycerol
  - Propionic acid

Glycerol-3-P —(Glycerol-3-P Dehydrogenase)→ DHAP → Glucose

- Odd chain FA → Propionyl CoA (3C) → D-methyl malonyl CoA (4C) ($CO_2$ is added with the help of enzyme: Propionyl CoA Carboxylase which uses Biotin / Vitamin B7 as cofactor)
- D-methyl malonyl CoA is converted to L-methyl malonyl CoA (4C) by racemase enzyme
- L-methyl malonyl CoA (4C) is converted to Succinyl CoA by Methyl malonyl CoA mutase. It uses Vitamin $B_{12}$ as cofactor
- Succinyl CoA is an intermediate of TCA → OAA → Glucose
- L-methyl malonyl CoA appears in urine B12 deficiency and it is responsible for peripheral neuropathy
- Propionic acid appears in urine in biotin deficiency



Active Space

- Acetyl CoA is never gluconeogenic
- In diabetes, there is deficiency of insulin:
  - Blood glucose is unable to enter peripheral tissues
  - Cells will behave as if they are in fasting state and active all catabolic pathways of body
  - Catabolic activities that will be activated are: HSL, lipolysis, $\beta$-oxidation of FA, gluconeogenesis, ketone body synthesis
  - Anabolic pathways that are activated in chronic diabetes:
    - Lipolysis → Excess acetyl CoA in liver → Diverted to fat synthesis in liver: FA, TG, VLDL, Cholesterol
- Fuels used in different situations in body:

| | Fed | Fasting | starvation |
|---|---|---|---|
| Brain | Glucose | Glucose | Ketone bodies |
| Heart | Fatty acids | Fatty acids | Ketone bodies |
| Liver | Glucose | Fatty acids | Amino acids |
| Muscle | Glucose | Fatty acids | Fatty acids and KB |
| Adipose tissue | Glucose | Fatty acids | Fatty acids |
| RBC | Glucose | Glucose | Glucose |

- Fetal heart uses glucose as primary fuel
- In heart failure: Fuel is glucose
- In fasting state:
  - Brain uses glucose because FA cannot cross BBB
  - RBC uses glucose because RBC cannot utilize FA

## DIET *33:28*

- Normal diet:
  - 60 – 70% carbohydrate
  - 15 – 20% Fats → Exogenous fat → Chylomicron
  - Remaining proteins
- Of total carbohydrate intake:
  - 50% is used for energy
  - Remaining 50% is stored:
    - 10% glycogen
    - 40% is converted into fats → Endogenous fat is synthetized in liver → VLDL

- Patient on diet for weight loss → Exogenous fat is stopped but endogenous fat will increase → Increased VLDL
- Atkin's diet: Low calorie / low carbohydrate diet
- Honey, Juice contains fructose → Most lipogenic sugar
- Thermogenic effect / Thermic / SDA [Specific Dynamic Action]: Amount of energy required to digest, absorb, transport and metabolize:
  - Maximum for Proteins > Carbohydrates > Fats

Active Space

## ENZYME CLASSIFICATION *39:03*

I. Oxidoreductases
II. Transferases
III. Hydrolase (water used to break bond)
IV. Lyases: Do not use water or ATP
V. Isomerase
VI. Ligases: Uses ATP to make bond

- + $O_2$ → Oxidation
- + $H_2$ / Electron / Reducing equivalent → Reduction
- Dehydrogenases:
  - Removal of $H_2$ → Oxidation

$$A \xrightarrow{\text{Dehydrogenase}} A\ (\text{Oxidized})$$

  - $H_2$ can be taken up by either:
    - NAD → NADH → 2.5 ATP
    - FAD → FADH2 → 1.5 ATP
    - NADP → NADPH → No ATP; Involved in Anabolic Pathway: Reductive biosynthesis
- NADPH:
  - Synthetized from:
    - HMP (Major)
    - Malic enzyme
    - Cytoplasmic Isocitrate Dehydrogenase

    } Cytoplasm
  - Used in:
    - Reductive biosynthesis: NADPH donates $H^+$

$$A \xrightarrow{\text{Reductase}} A\ (\text{Reduced})$$

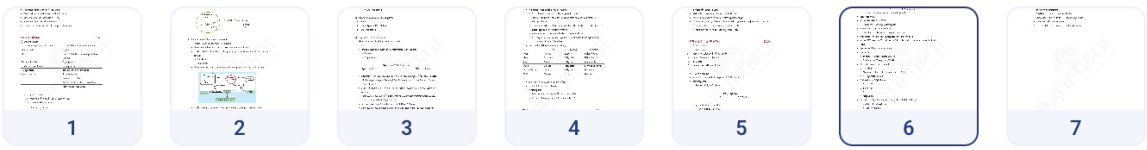
- Hence, Dehydrogenase belongs to Enzyme EC I

- Reductase → EC I
- Kinase: Transfer P → EC II
  - Kinase transfers organic Phosphate
- Phosphatase: Transfer P → EC II
  - Phosphorylase transfers inorganic Phosphate
- Phosphatase → Removal of phosphate with water → EC III
- Kinase: ATP used or ATP produced → Substrate level phosphorylation (without using ETC)
- ETC → Oxidative phosphorylation
- Synthesis:
  - Synthase: No ATP required (EC IV)
  - Synthetase: ATP required (EC VI)
- All synthases are lyases except:
  - NOS → EC I
  - Glycogen synthase, citrate synthase → EC II
  - ATP synthase → EC III
- Carboxylase (+$CO_2$): It uses:
  - ATP: EC VI
  - Biotin / B7
  - $CO_2$
  - Magnesium
- Removal of $CO_2$ is known as decarboxylation which is of 2 types:
  - Oxidative decarboxylation
    - Uses Vitamin $B_1$
    - EC I
    - Dehydrogenase enzyme is used (oxidative)
  - Simple decarboxylation
    - Uses Vitamin $B_6$
    - EC IV
    - $CO_2$ is removed without using hydrogen or water
    - Eg: Amine formation from amino acids by removal of $CO_2$
      - Histidine → Histamine
      - Tryptophan → Tryptamine
      - Tyrosine → Tyramine

Active Space







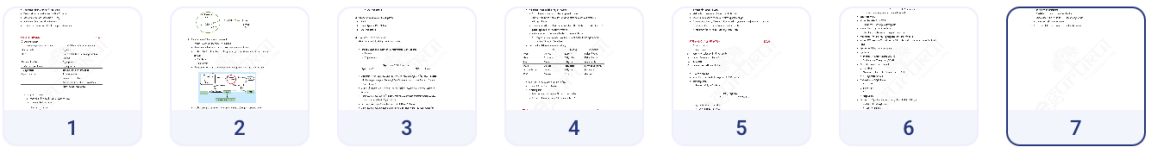
- Dopa → Dopamine
- Serine → Ethanolamine
- Cysteine → $\beta$-Mercapto ethanolamine
- Glutamate → GABA (acid) - $\gamma$ - amino butyric acid
- Lysine → Cadaverine (diamine)

▪ Amino acid → In amine group removed: $\alpha$-keto acid

**Active Space**







# Rate Limiting Enzymes

Active Space

1) Glycolysis: 3 regulatory / irreversible enzymes –
   i. Hexokinase / glucokinase
   ii. PFK1 → Rate limiting enzyme
   iii. Pyruvate kinase

Fructose 6 phosphate —PFK – 1→ Fructose 1, 6 Bisphosphate

- Activators of PFK-1:
  - Fructose 2, 6 bisphosphate
  - AMP
- Inhibitors of PFK-1:
  - ATP
  - Citrate

2) Gluconeogenesis: 3 enzymes are RLE
   i. Pyruvate carboxylase
   ii. PEPCK
   iii. Fructose 1, 6 Biphosphatase

3) Kreb's cycle / TCA: 3 RLE
   i. Citrate synthase
   ii. $\alpha$-Ketoglutarate dehydrogenase
   iii. Isocitrate dehydrogenase → Most important

- Activators of IDH: ADP
- Inhibitors of IDH: ATP, NADH

4) Glycogenesis:
   - RLE: Glycogen synthase – EC II
   - It is activated by insulin and glucose-6-phosphate and inhibited by glucagon and epinephrine

5) Glycogenolysis:
   - RLE: Glycogen phosphorylase – EC II
   - It is activated by cAMP, Kinase, 5'AMP, Glucagon/Epinephrin/NE, calcium and calmodulin
   - It is inhibited by Insulin, phosphatase, ATP, Glucose, Glucose-6-phosphate and fructose-6-phosphate

6) HMP
   - RLE: G6PD → 1st most common human enzyme deficiency
   - 2nd most common human enzyme deficiency → Pyruvate kinase

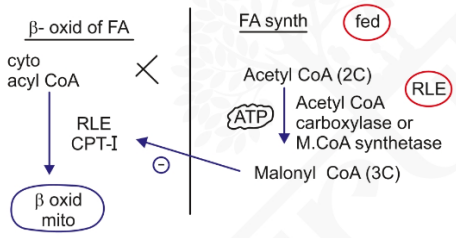
7) Purine synthesis (Denovo) → PRPP glutamyl amido transferase





- It is inhibited by AMP, GMP and IMP

8) Purine catabolism:
   - RLE: Xanthine oxidase (does not require Copper)
   - Allopurinol is a suicide inhibitor of this enzyme
9) Pyrimidine synthesis:
   - RLE: CPS-II (Eukaryote) - Carbamoyl Phosphate Synthetase (eukaryote) → Present in cytoplasm
   - In prokaryote: RLE is ATC (Aspartate Trans Carbamoylase)
10) Urea cycle: RLE → CPS-I (mitochondria)
   - Activator: N-Acetyl Glutamate (NAG)
11) $\beta$ - oxidation of FA and FA synthesis:

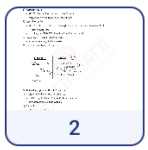



12) Ketone body synthesis: HMG-CoA synthase
13) Cholesterol synthesis: HMG CoA reductase
   - Inhibited by Mevalonate, Statins, Cholesterol and BA
   - Stimulated by insulin and thyroxine
14) BA synthesis:
   - RLE: 7$\alpha$-Hydroxylase
15) Catecholamine synthesis:
   - RLE: Tyrosine hydroxylase
16) Vitamin D synthesis:
   - 1 - $\alpha$ - hydroxylase
17) Niacin synthesis:
   - QPRTase (Quinolate Phosphoribosyl Transferase)

Active Space

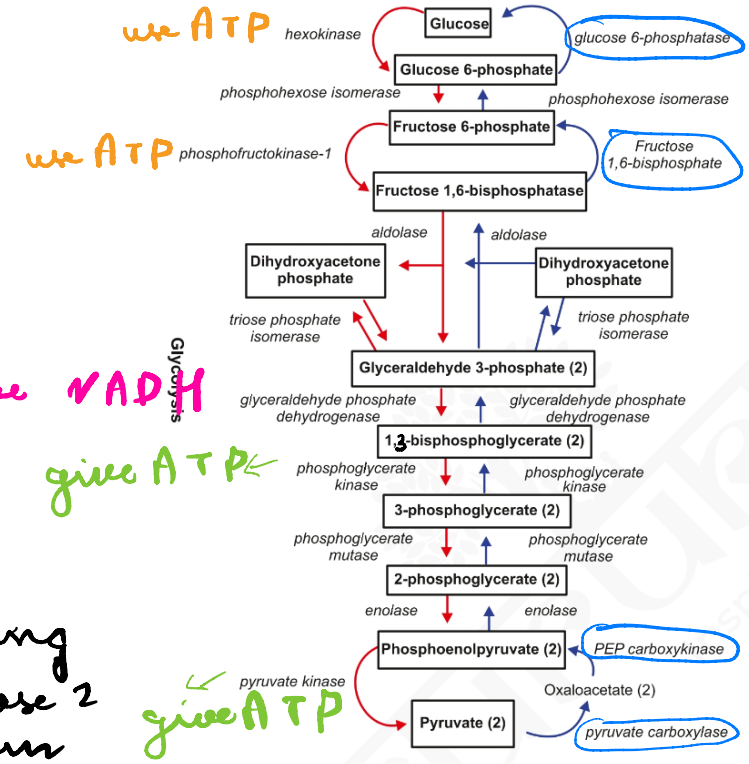






# Energetics

Active Space




give ATP
give NADH
give ATP
4 Enzymes different from glycolysis

I. Glycolysis (Glucose → 2 pyruvate)

- 2 ATP are used by Hexokinase and Phosphofruckinase - 1
- Substrate level phosphorylation: +4 ATP - PG kinase and Pyruvate kinase
- 2 NADH are produced by glyceraldehyde-3-phophate dehydrogenase → 5 ATP in ETC
- Total ATP produced: 4 + 5 - 2 = 7 ATP (aerobic glycolysis)
- Anaerobic glycolysis: Pyruvate is converted into lactate by LDH. 2 NADH is converted back to NAD by LDH
  - Energetics: 4 - 2 = 2 ATP
  - Purpose: Regeneration of NAD , again used in aeroleic glycolysis

anything in phase 2 i.e from DHAP to pyruvate is multiplied by 2.
4 ATP by SLP
- 5 ATP from 2 NADH via ETC in mitochondria

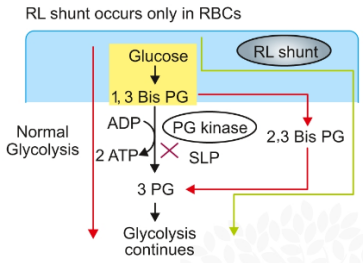
LDH is reverse dehydrogenase, convert NADH to NAD

Q1: In anaerobic glycolysis, end product is:
→ 2 ATP + 2NAD

Q2: In anaerobic glycolysis, there is gain of
→ 2 ATP

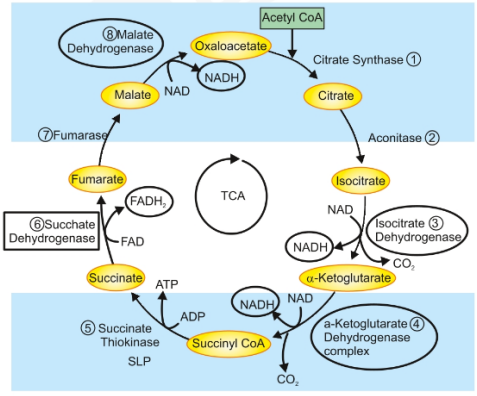
NAD is produced and used, so No net gain

- In RBC:
  - There are no mitochondria: ETC cannot produce 5 ATP from NADH
  - Energetics: 4 – 2 ATP = 2 ATP
- Rapaport Leubering Shunt (RL Shunt)




  - No ATP produced
  - 2, 3 Bis PG is produced which helps unloading of $O_2$ from HbA
- In RBC:
  - 90% of glucose undergoes anaerobic glycolysis
  - 10% of glucose enters RL shunt to form 2, 3 BPG
- If no RL shunt in RBC → 2 ATP
- If 1 triose enters RL shunt → 1 ATP
- If both triose enters RL shunt → 0 ATP

II. TCA cycle energetics




Active Space

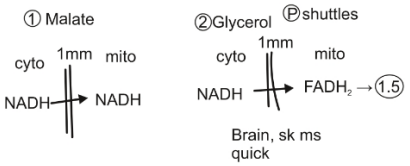
Active Space

- 3 NADH: 7.5 ATP
- 1 $FADH_2$ : 1.5 ATP
- 1 ATP from substrate level phosphorylation
- Hence, from 1 acetyl CoA: 10 ATP are produced

- Complete breakdown of glucose:
  - Glycolysis: 7 ATP
  - Link reaction: 2 NADH → 5 ATP
  - TCA cycle: 20 ATP

  } 32 ATP
- Pasteur's effect:
  - Occurs in normal cells of body
  - If oxygen is present, then anaerobic glycolysis will not occur
- Warburg effect:
  - Cancerous cells of body
  - Glucose will be converted to lactate irrespective of whether oxygen is present or absent → Anaerobic glycolysis with no oxidative phosphorylation
- In ETC:
  - NADH:
    - I → $4H^+$
    - III → $4H^+$
    - IV → $2H^+$

    } $10H^+$ → 25 ATP
  - $FADH_2$: 6 $H^+$ → 1.5 ATP
    - II → No $H^+$
    - III → $4H^+$
    - IV → $2H^+$
- Shuttles (NADH): From Cytoplasm to mitochondria so that NADH can take part in ETC:
  - Malate
  - Glycerol Phosphate shuttle: Present in brain and skeletal muscles because it is quick in supply of ATP



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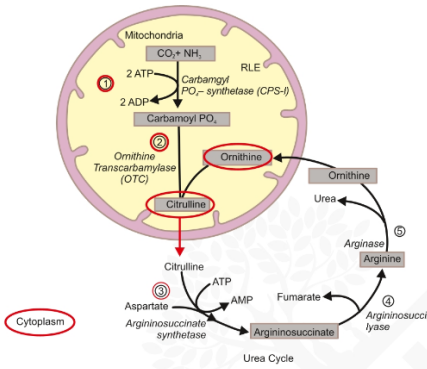
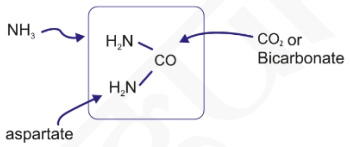
- Shuttle is not required for TCA and link reaction as they are already occurring in mitochondria

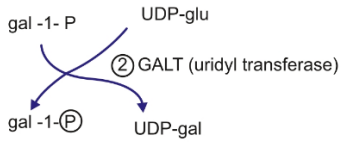
- If aerobic glycolysis uses glycerol shuttle, how many ATPs are formed:
  - − 2 + 4 + 3 = 5 ATPs
- Urea Cycle:




  - 4 ATP or 3 ATP but 3 high energy phosphate bonds are used
- Source of components of Urea:




- Energetics of galactose metabolism:
  - Galactose is converted into Galactose-1-P by Galactose kinase by utilization of 1 ATP
  - Then:




  - UDP-galactose is converted into UDP-glucose by Epimerase

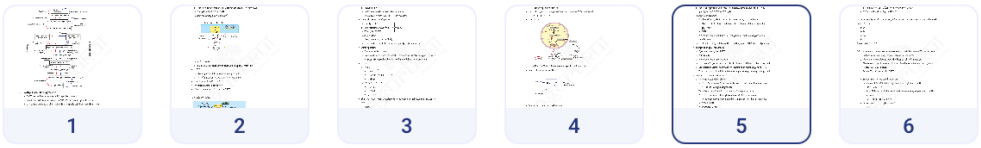
Active Space

- Glucose-1-P → Glucose-6-P → Enters glycolysis (no hexokinase is required)
- Hence, energetics of Galactose is completely same as Glucose (7 ATP by glycolysis and 32 ATP by TCA cycle)

- Energetics of fructose:
  - Fructose (Kinase) → Fructose-1-P: Converted by aldolase B into:
    - Glyceraldehyde → Glyceraldehyde-3-P by kinase → Enter phase II of glycolysis
    - DHAP
  - 2 ATPs are used by 2 kinases → Energetics of fructose and glucose are exactly same
  - Fructose is rapidly metabolized because it bypasses PFK-1 step of glycolysis
- Energetics of gluconeogenesis:
  - Pyruvate carboxylase: 2 ATP
  - PEPCK: 2 GTP
  - Phosphoglycerate kinase: 2 ATP
  - Thus, when 2 pyruvate are converted to glucose, 6 high energy bonds are used
  - Conversion of lactate to pyruvate OR alanine to pyruvate require no ATP. Thus, conversion of lactate and alanine to glucose require 6 high energy bonds
- Energetics of beta oxidation of FA:
  - Cytoplasm: Activation of FA:
    - FA → Acyl-CoA by Acyl-CoA synthetase / thiokinase with conversion of ATP to AMP (2 high energy bonds)
  - For entry of acyl CoA into mitochondria, 3 enzymes are used:
    - CPT-I (Carnitine Palmitoyl Transferase) → Present on outer mitochondrial membrane and is the RLE. It is activated in fasting state
    - CPT-II (IMM)
    - Translocase (IMM)
  - In liver mitochondria:
    - For breakage of bond between $\alpha$Carbon and $\beta$Carbon, 4 enzymes are required:
      - Dehydrogenase: 1 $FADH_2$ → 1.5 ATP
      - Hydratase
      - Dehydrogenase: 1 NADH → 2.5 ATP
      - Thiolase
    - Palmitic acid: 8 acetyl CoA → TCA (80 ATPs) → KB → Gluconeogenesis
- Energetics of palmitic acid:
  - 7 cleavage x 4 ATP = 28 ATP







- 8 Acetyl CoA x 10 ATPs = 80 ATP
- Final ATP = 108 – 2 (used for activation) = 106 ATP

- 18 Carbon Stearic acid gives 120 ATP

Q1: In beta oxidation of palmitic acid, if final product formed is acetoacetate, then net gain of ATP is:

a) 21
b) 26
c) 106
d) 129

Answer: 28 – 2 = 26 ATP

Q2: If muscle glycogen is used for anaerobic glycolysis, how many ATPs are formed?

- End product of muscle glycogen is Glucose-6-phosphate
- Glucose-6-phosphatase is present in liver but absent in muscles
- Glucose-6-phosphatase does not require hexokinase after entering glycolysis. Hence, 1 ATP will be saved.
- Total ATP produced: 4 – 1 = 3 ATP

- Energetics of ketone body breakdown:
  - Acetoacetate (4C) → 2 Acetyl CoA (1 succinyl CoA is used)
    Net ATP: 20 – 1 = 19 ATP
  - Beta-OH butyrate → Acetoacetate (by enzyme dehydrogenase and NADH is produced
    Net ATP: 19 + 25 = 215 ATP
- Pathways which do not yield any ATP:
  - HMP
  - Uronic acid
  - RL shunt
  - Oxidation of VLCFA
  - Alpha oxidation of FA

**Active Space**

# Diseases

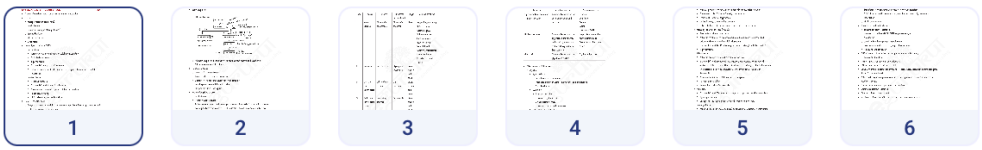
Active Space

## LYSOSOMAL STORAGE DISEASES 00:18

- They are hydrolases and they break many macromolecules
- They are:
  - Mucopolysaccharidosis (MPS)
  - I-cell disease
  - Pompe's (Glycogen storage disease)
  - Sphingolipidoses
  - Wolman's disease
  - Cystinosis
- Mucopolysaccharidosis (MPS):
  - Hurler disease
    - Dermatan sulphate and Heparan sulphate accumulate
    - Reilly body inclusions
    - Inguinal hernia
    - Enzyme deficiency: $\alpha$-L-Iduronidase
    - Corneal clouding, skeletal abnormalities, Hepatosplenomegaly, Mental retardation
  - Hunter disease
    - X-linked recessive
    - Enzyme deficient: Iduronate sulfatase
    - Dermatan sulphate and Heparan sulphate accumulate
    - No corneal clouding
    - Mild Hurler + aggressive behaviour
- I-cell / Inclusion body:
  - Enzyme deficient: N-acetyl glucosamine phosphotransferase (golgi apparatus)
  - Hydrolases do not reach lysosomes
  - Protein targeting disorder
  - Clinical features same as MPS but more severe
  - Serum hydrolases are raised
- Pompe's disease:
  - Hypotonia, hepatomegaly, cardiomegaly
  - Enzyme deficient: Acid maltase
- Cystinosis:
  - Defect: Transporter in lysosomes for cystine transport
  - Cystine deposits
  - Treatment: Cysteamine chelates cystine

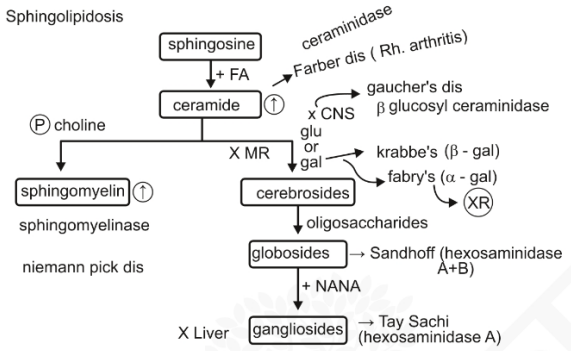






- Cyanide Nitroprusside test is positive

- Sphingolipidosis:




  - All sphingolipidosis have cherry red spots except Fabry's and Gaucher's
  - Fabry's disease: Angiokeratoma
- Wolman's disease:
  - Lysosomal storage disease
  - TG and cholesterol esters are raised
  - Characteristic feature: Calcification of adrenals
  - Hepatosplenomegaly, failure to thrive
  - Enzyme deficient: Acid lipase
- Protein targeting disorders:
  - I-cell disease
  - Primary hyperoxaluria
  - Zellweger syndrome: Most severe peroxisomal biogenesis disorder – Peroxisomes are empty: Ghost peroxisomes → $\alpha$-oxidation FA and Oxidation of VLCFA are affected

    VLCFA and Branched chain FA like Phytanic acid are accumulated
  - Familial hypercholesterolemia
  - Cystic fibrosis
- Garrod's tetrad:
  - Cystinuria
  - Alkaptonuria
  - Albinism
  - Essential pentosuria

**Active Space**

## GLYCOGEN STORAGE DISEASE

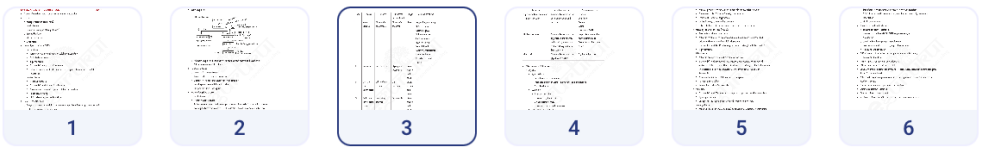
13:53

Active Space

| Type | Disease | Enzyme | Substrate accumulated | Organ | Clinical features |
|---|---|---|---|---|---|
| I | Von-Gierke's | Glucose-6-phophatase | Glucose-6-phophate | Liver | Severe hypoglycemia, Ketosis, Massive hepatomegaly, Kidney enlarged, Lactic acidosis, Hyperuricemia, hyperlipidemia, hypertriglyceridemia, Moon like facies / Dolls like / round facies |
| II | Pompe's | Acid maltase | Glycogen in lysosomes | Liver, muscle and brain | |
| III | Cori's / Limit Dextrinosis | Debranching enzyme | Limit dextrins | Liver, muscle and brain | |
| IV | Anderson / Amylopectinosis | Branching enzyme | Amylopectins | Liver, muscle and brain | |
| V | McArdle's | Muscle phosphorylase | Muscle glycogen | Muscle | Exercise intolerance, lactate normal after exercise |
| VI | Her's | Liver phosphorylase | Liver glycogen | Liver | Hepatomegaly with mild hypoglycemia |







## AMINO ACID TRANSPORTER DEFECT

17:18

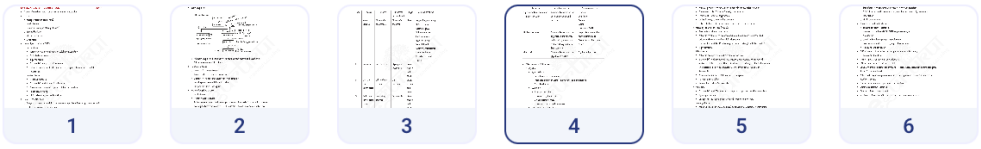
Active Space

| Disorder | Defect in transporter | Amino acid in urine |
|---|---|---|
| Cystinuria (most common transporter defect) | Common transporter for basic amino acids and cysteine | Cysteine<br>Ornithine<br>Arginine<br>Lysine<br>Mnemonic: COAL |
| Hartnup's disease | Common transporter for tryptophan and neutral amino acid (mono-amino mono-carboxy amino acid transporter) | Tryptophan (mainly) and neutral amino acids<br>Serum tryptophan is not raised |
| Glycinuria | Common transporter for glycine and proline | Glycine and proline |

- Other Amino acid disorders:
  - Glycine:
    - Hyperoxaluria
      - Defect: Glycine transaminase
      - Increased oxalate in urine + extra renal oxalate deposits
      - Oxalate stones
    - Glycinuria
      - Transporter defect
      - Increased glycine in urine
      - Urine oxalate normal
      - Increased risk for oxalate stones
    - Non-ketotic hyperglycinemia
      - Defect in glycine cleavage system
      - Increased glycine in serum, urine and CSF
      - Mental retardation, seizures
  - Phenylketonuria:
    - Enzyme deficient: Phenylalanine hydroxylase which converts Phenylalanine into tyrosine
    - Tyrosine becomes essential
    - Hypopigmentation: Melanin is not formed
    - Increased phenylalanine → Phenyl – pyruvate, phenyl – acetate and phenyl – lactate







- Phenyl – alanine enters brain and it leads to mental retardation
- Phenyl – pyruvate → $FeCl_3$ positive test → Phenyl ketone in urine
- Phenyl – acetate → Mousy / musty odour of urine
- Treatment: Tyrosine, tryptophan
- Restrict phenylalanine and aspartame
- THB (Tetrahydro biopterin) maybe beneficial in few patients

○ Maple Syrup Urine Disease (MSUD):
- Sweet odour urine / burnt sugar
- Defect in catabolism of branched chain amino acids and branched chain ketoacids → Ketosis and mental retardation
- Enzyme deficient: BCKA dehydrogenase or decarboxylase (B1 dependent)
- High mortality

○ Alkaptonuria:
- Defect in phenylalanine and tyrosine catabolism
- Enzyme deficient: Homogentisate oxidase / dioxygenase → Homogentistic acid accumulates → turns black → polymerized in body leading to formation of alkapton bodies → accumulate in connective tissue bluish black discoloration
- Accumulates in intervertebral disc → Back pain
- No mental retardation
- Joints → Arthritis: Oochronosis

○ Albinism:
- Enzyme deficient: Tyrosinase – It requires copper because it is an oxidase
- Hypopigmentation
- Vitiligo: Patchy hypopigmentation but tyrosinase is normal

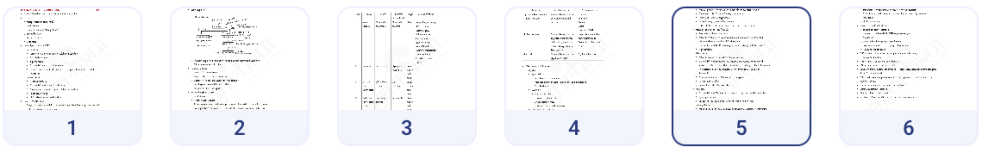
○ Homocystinuria:
- Acquired (B6, B9 or B12 deficiency) or genetic (CBS defect: Cystathionine Beta Synthase)
- Cysteine becomes essential
- Homocysteine (SH) is increased in blood
- In urine, it gets oxidized to homocysteine (S = S)
- In:
  - B6 deficiency: Xanthurenic acid accumulates
  - B9 deficiency: FIGLU accumulates
  - B12 deficiency: L-methyl malonic acid will accumulate in urine

• Galactosemia:
○ Minor galactosemia: Galactokinase – oil drop cataract

Active Space







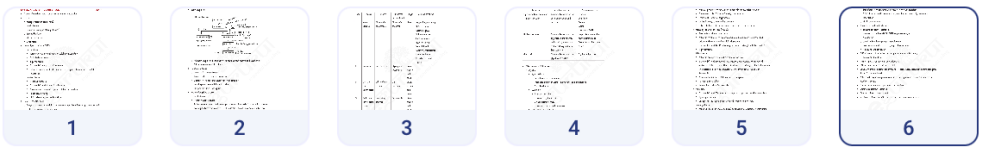
- Classic galactosemia: Enzyme deficient – GALT (Galactose-1-phosphate uridyl transferase) → converts Galactose-1-P → UDP galactose
- Clinical features: Oil drop cataract, jaundice, hepatomegaly and mental retardation
- Most common type

- Hereditary fructose intolerance:
  - Enzyme deficient: Aldolase B
  - It converts fructose-1-P to DHAP & glyceraldehyde
  - No cataract
  - Jaundice, hepatomegaly and hypoglycemia
  - Fructose-1-p inhibits liver glycogen phosphorylase
  - Kidney failure can occur
- CNS, skin and hair affected → Multiple carboxylase deficiency
  - Tom cat urine odour
- CNS + hypopigmentation: Phenylketonuria
- CNS + burnt sugar like odour → MSUD
- Child with stroke, skeletal abnormalities: Knock knees, pectus carinatum, elongated limbs → Homocystinuria
- Patient with organomegaly, easy bruising, bony pain and frequent fractures → Gaucher's disease
- Coarse facial features: Lysosomal storage disease
- Snow flake cataract: Diabetes
- Oil drop cataract: Galactosemia
- Sunflower cataract with KF ring: Wilson's disease of copper excess

**Active Space**







# Carbohydrate Chemistry

Active Space

- Carbohydrates are Polyhydroxy aldehydes or Ketones
  - Either aldehydes or ketones are the functional groups
  - Polyhydroxy means they have many OH groups
  - If a carbohydrate has 6 carbons, then number of OH groups will be 5 (6C = 5OH)
  - If a carbohydrate has 5 carbons. Then number of OH groups will be 4 (5C = 4OH)

## ISOMERISM IN CARBOHYDRATES *01:00*

- Isomers have the same molecular formula
- Isomerism is possible in carbohydrates because of asymmetric or Chiral carbon having all four valencies occupied by different atoms or group of atoms

  $R_1$, $R_2$, $R_3$ = Three different group of atoms

  H = Hydrogen atom

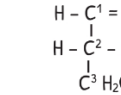
  C here is Chiral carbon

- 2 types of isomerism exists
  - Structural isomerism: Have different structure
  - Optical isomerism: Have different optical properties
- Optical isomers
  - We have small 'd' and small 'l'
  - Small 'd' represented by plus '+' sign when light is rotated towards right side that is when plane polarized light is passed through a solution of carbohydrate, if it is rotated towards right side, it is called Dextrorotatory or '+' sign
  - If light is rotated towards left side, it is Levorotatory, represented by l or '-' sign
  - Racemic mixture means equal 'd' and 'd' present
  - Racemase enzyme is that enzyme which interconvert the isomers
    - It is a misnomer
    - It is not converting 'd' and 'l' into each other, but rather
    - It converts 'D' and 'L' into each other
- Structural isomers
  - They are of 4 types → Functional, Enantiomerism
    1. Functional: Functional group is different i.e., one is having aldehyde and the other a ketone group

Ex:

3C Aldehyde

Glyceraldehyde



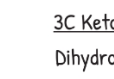
$1^{st}$ – Functional group is added to the $1^{st}$ carbon i.e., Aldehyde in this case

$2^{nd}$ – To the terminal carbon, $H_2OH$ group is added

$3^{rd}$ – In all left over places, OH added on right side and H on left side

3C Ketone

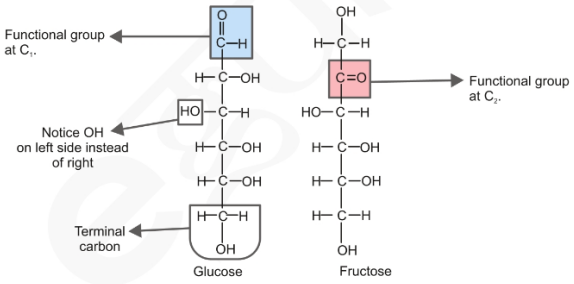
Dihydroxy acetone



$1^{st}$ – Ketone group is added to $2^{nd}$ atom i.e., C = O

$2^{nd}$ – On terminal carbon i.e., $C_3$, $H_2OH$ is added

$3^{rd}$ – $C_1$ is also terminal carbon and $H_2OH$ is added there too




- What are the asymmetric carbons in these carbohydrates?

  Ex:

Active Space

3C Aldehyde

Glyceraldehyde

$H - C^1 = O$ → This functional carbon is symmetric because 2 valencies are occupied by same atom that is Oxygen

$H - C^2 - OH$

$C^3\ H_2OH$

Asymmetric

↓

Symmetric because it has two Hydrogen atoms

3C Ketone

Dihydroxy acetone

$C^1 - H_2OH$

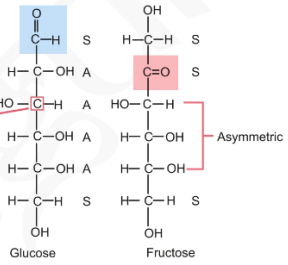
$C^2 = OH$

$C^3\ H_2OH$

Symmetric because there are two hydrogens

Symmetric because it's a functional group

Symmetric because there are 2 hydrogens




On left, it has OH group

On Right, it has H

On 3rd side, it has a group with 2 carbons

On 4th side, it has a group with 3 carbons

For carbon, look at whole group present on that side of valency

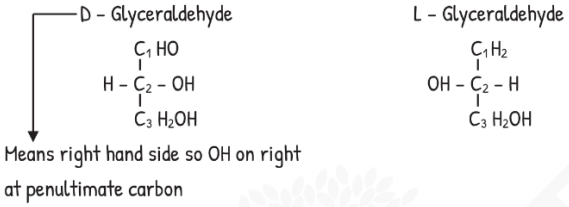
→ One valency has 2 groups of carbons, while

→ Other has 3 groups of carbon making it asymmetric

Active Space

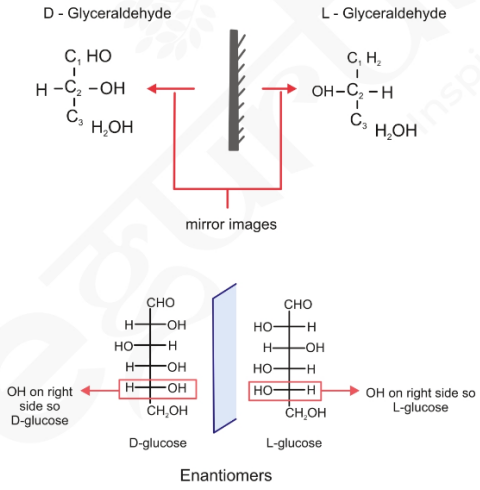
2. Enantiomerism

- These are capital 'D' and 'L' isomerism
- Also called mirror images
- Enantiomerism is different H and OH orientation at the penultimate carbon on 2nd last carbon




Means right hand side so OH on right at penultimate carbon

- If a mirror is placed in between them, then the penultimate carbons are mirror images of each other




MCQ → Which form of carbohydrate is abundant? D or L? In cell, nature, plasma, body etc.?

→ D is abundant

MCQ → Which form of Amino Acid is abundant? D or L?

→ L is abundant

**Active Space**

So, Amino acid in protein is L form

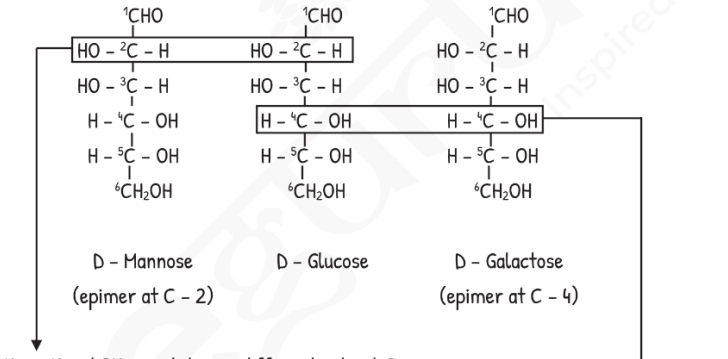
- But, there may be free Amino Acids in body which are not present in protein
- This free amino acid may be D or L
- Amino acid that is synthesized in body is always L

Source of D – Amino acid is always exogenous because it cannot be synthesized in body

- Exogenous source can be diet or intestinal bacterial flora
- Ex D-serine, D-Aspartate → Found in Brain

MCQ – Which form of Amino Acid present in body → Both D and L
MCQ – Which form of Amino acid present in protein → Only L

3. Epimerism
   - Different H and OH orientation around only one carbon other than penultimate carbon




Here, H and OH orientation is different only at $C_2$
So, mannose is epimer of glucose at C-2

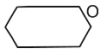
Differ only in one carbon that is $C_4$
So, Galactose is epimer of glucose at C-4

   - Are mannose and galactose epimers of each other?
     - They differ at $C_2$ and $C_4$
     - So, they are not epimers of each other

4. Anomerism
   - Exists only for cyclic structures
   - It is different H and OH orientation at functional carbon

Active Space

- Because in cyclic structures, functional carbon is also asymmetric
- For making cyclic structures, oxygen is shared between functional carbon and 2nd last carbon
- There are 2 types of cyclic structures
  i. Pyranose:
  It is a 6 membered ring with oxygen present at the particular question

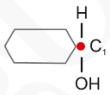



  ii. Furanose:
  It is a 5 membered ring with oxygen present at that particular position

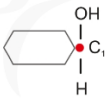

- Glucose is a Pyranose structure
- Fructose is a Furanose structure
- For Hexoses, both Pyranose and Furanose exist
- For Pentoses, only Furanose exists

MCQ – How many carbons are present in Pyranose?
→ 5
→ Because one position is occupied by Oxygen

- Anomers are of two types – $\alpha$ and $\beta$
  i. At functional carbon, if OH is downward then it is $\alpha$ (Alpha)




  ii. At functional carbon, if OH is upward then $\beta$ or beta




## GLUCOSE TRANSPORT *18:20*

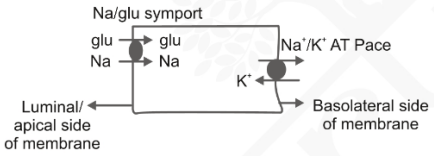
- It is of two types
  - Active Transport
  - Facilitative Transport
- Active transport
  - It is Sodium dependent Glucose Transport (SGLT)
  - It is active so II is against the concentration gradient
  - It allows glucose to go only in one direction, mostly inside the cell
  - SGLT is of two types

Active Space

Active Space

- SGLT – 1:
  - This is for both glucose and galactose transport
  - Present in intestine and kidneys
  - Mutation leads to Glucose and Galactose malabsorption
- SGLT – 2:
  - This is only for glucose
  - Present only in kidneys
  - Mutation causes Familial Renal Glycosuria

- In active transport, when glucose is entering the cell, then sodium enters too
  - So, also called Sodium Glucose Symport
  - And, when glucose enters this way then ATP is not used here
  - But, ATP is indirectly used by $Na^+$ / $K^+$ ATP are pump on other side of cell and that pump uses ATP
  - This transport is also called Secondary Active Transport




- Facilitative Transport / GLUT
  - Also called as GLUT transporters
  - Main glucose transporters of the body
  - This transport is Bidirectional which means via GLUTs, glucose can enter into the cell and leave as well
  - Transport is down the concentration gradient like passive transport
  - This transport does not use sodium so it is sodium independent glucose transport
  - Types of GLUTs:
    - GLUT – 1:
      - In RBC, kidneys, placenta, brain
      - Function is Basal Glucose uptake means the glucose uptake occurs irrespective of any state in body
      - Occurs also in fasting state because brain, placenta, RBCs require glucose to function

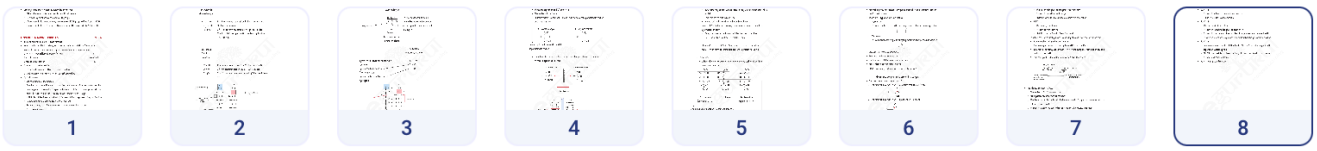
- Kidneys require glucose for reabsorption

- GLUT – 3:
  - Present in kidney, placenta, brain, neurons
  - Function is Basal Glucose Uptake
- GLUT – 2:
  - This one works in fed state
  - Present in intestine for glucose absorption
  - Present in pancreas so glucose enters into pancreas and release insulin
  - Present in liver because glucose enters into liver for glycogen formation
- GLUT – 4:
  - Pancreas releases insulin → It activates GLUT – 4 participating in insulin dependent Glucose uptake
  - GLUT 4 is on peripheral tissues of body like muscles like skeletal, cardiac muscles and Adipose tissue
- GLUT – 5: Fructose transport

**Active Space**







# Carbohydrate Metabolism

Active Space

## GLYCOLYSIS 00:20

- Also called Embden Mayerhoff Pathway
- Glycolysis has 3 regulatory / irreversible steps
  - Hexokinase
  - Phosphofructokinase – 1 / PFK 1
  - Pyruvate kinase
- Pyruvate kinase is irreversible, Regulatory and Substrate level phosphorylation step too.
- Another substrate level phosphorylation step is phosphoglycerate kinase
- Pyruvate kinase deficiency is second most common human deficiency
- G6PD deficiency is 1st most common human enzyme deficiency
  - In pyruvate kinase and G6PD deficiency, Hemolysis is present
  - To distinguish both of these deficiencies, we check for Heinz bodies which are present only in G6PD deficiency
- Inhibitors of Glycolysis:
  - Iodoacetate: Inhibits Glyceraldehyde – 3 – P – Dehydrogenase enzyme
  - Arsenate:
    - Inhibits Glyceraldehyde – 3 – P – Dehydrogenase enzyme
    - Pathway is not inhibited and Pyruvate is formed but ATP is not formed
  - Sodium Fluoride:
    - Inhibits enolase enzyme
    - Used in Blood glucose estimation

## LINK REACTION 03:08

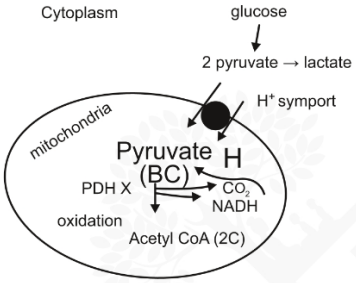
- Occurs in mitochondria:
  - In cytoplasm, glucose gets converted to 2 pyruvate via glycolysis
  - Pyruvate has to enter mitochondria and has to cross inner mitochondrial membrane which is semi-permeable
  - So, the polar compound pyruvate needs a transporter, pyruvate proton symport and it takes pyruvate and proton inside mitochondria
  - Link reaction occurs where pyruvate is converted to Acetyl CoA by using pyruvate dehydrogenase complex
  - Dehydrogenase reaction signifies oxidation occurring and removal of carbon dioxide occurring so this oxidative decarboxylation and coenzyme for this is $B_1$
  - In $B_1$ deficiency that is Beri-Beri, lactic acidosis occurs

Active Space

- Because oxidative decarboxylation step does not occur, leading to excess pyruvate
- Pyruvate excess goes to cytoplasm
- Pyruvate forms excess of lactate - Lactic Acidosis

- There is formation of NADH as well

- Link Reaction is irreversible:
  - That's why fats can never be converted to carbohydrates because Acetyl CoA can never be converted to pyruvate and so cannot be converted to glucose




## TCA CYCLE

05:34

- Occurs in mitochondria
- It is not affected by any hormones
- It is not affected by fed / fasting state of body
- TCA cycle depends on two things
  - Energy status of cell: If there is enough ATP in cell then TCA won't occur
  - Availability of oxaloacetate:
    - Oxaloacetate acts as limiting factor
    - Only if oxaloacetate is present, then TCA will occur
    - It is the carrier of TCA or 1st substrate of TCA
    - It plays a catalytic role in TCA because TCA starts with oxaloacetate and there is addition of Acetyl CoA to make citrate and so on until oxaloacetate is formed again and not used up
- TCA cycle occurs in aerobic state
  - It cannot occur in anaerobic state because ETC won't occur and NADH, $FADH_2$ which are produced through TCA cycle, they cannot enter ETC
  - So, there's feedback regulation from NADH and $FADH_2$ in anaerobic situation which will stop TCA cycle
- Only 1 substrate level phosphorylation step exists in TCA
  - By enzyme Thiokinase
  - Thiokinase mostly produces ATP

- It produces GTP in liver and kidney for gluconeogenesis during fasting or starvation

- Acetyl CoA is not an intermediate of TCA cycle and all other molecules in TCA are intermediates
- In TCA cycle, 2 carbon dioxide are removed
  - They are removed from oxaloacetate and Acetyl CoA
- Inhibitors of TCA
  - Fluro citrate: It is a competitive inhibitor of enzyme Aconitase
  - Fluoroacetate: it is non-competitor inhibitor of enzyme Aconitase
  - Arsenate: Inhibits alpha keto glutamate dehydrogenase enzyme
  - Malonate: Inhibits succinate dehydrogenase
- Malonate / Malonyl CoA
  - It is a three carbon compound
  - Malate, on the other hand is 4 Carbon compound and intermediate of TCA
  - Malonate is also inhibitor of 3 pathways in body:
    - TCA cycle
    - ETC
    - Beta oxidation of fatty acid

PYQ: Why do we take Vitamins when we are low on energy or feeling lethargic?

- There is an important biochemical relationship between Vitamins and energy
- 5 coenzymes are required for link reaction and TCA
- Both of these require lots of energy
- The 5 coenzymes are: Lipoic acid, Vitamin $B_1$, Vitamin $B_2$, Vitamin $B_3$ and Vitamin $B_5$

## ELECTRON TRANSPORT CHAIN / ETC *12:24*

- Occurs in inner mitochondrial membrane
- Basically electrons are being transported from one molecule to other
- Components of ETC
  - Protein complexes

    I

    II

    III

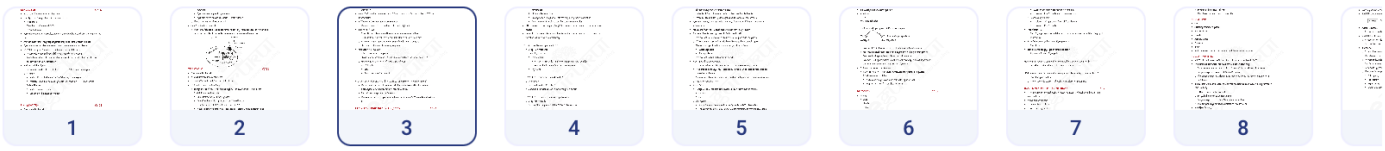
    IV

    V

Active Space







Active Space

    - The protein complexes are fixed in the membrane and cannot move but mobile carriers can
  - 2 mobile electron carriers
    - Coenzyme Q / Ubiquinone: It is the only non-protein member of ETC
    - Cytochrome C: It is also a peripheral membrane protein
- ETC is known as oxidative phosphorylation because oxidation and phosphorylation are coupled
- Uncoupling is when oxidation and phosphorylation are not coupled or not occurring together but can occur independently

PYQ: What are the uncouplers in ETC?
- Drug – Dinitrophenol
- Naturally occurring
  - Thermogenin
    - Present in Brown fat in hibernating animals and neonates
    - Responsible for non-shivering thermogenesis
  - Thyroxine

PYQ: ADP to ATP conversion is inhibited by?
- Oligomycin
- Because it inhibits Complex 5
- Complex 5 is responsible for converting ADP to ATP

PYQ: ADP to ATP transfer is inhibited by which drug?
- Drug Atractyloside
- Because this compound inhibits ADP-ATP translocase

- Inhibitors of ETC
  - Complex I – Rotenone, Phenobarbitone
  - Complex II – Malonate
  - Complex III – Pnenformin
  - Complex IV – Cyanide, Carbon monoxide, Hydrogen sulphide, Sodium azide

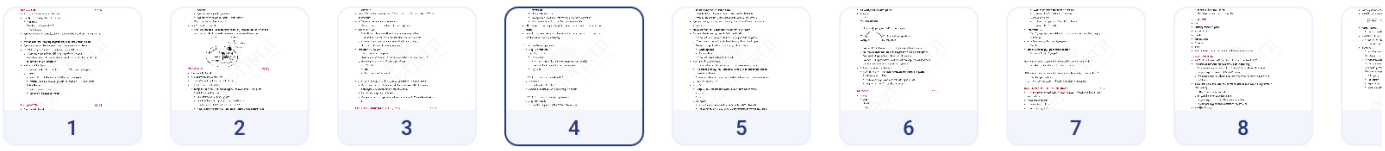
## GLUCONEOGENESIS

*17:00*

- It is the conversion of two molecules of pyruvate to 1 molecule of glucose
- This pathway share all enzymes with glycolysis except 4 of them:







- Instead of Pyruvate kinase, gluconeogenesis has pyruvate carboxylase and phospho enol pyruvate carboxy kinase
- Instead of PFK-1, gluconeogenesis has fructose 1, 6 bisphosphate
- Instead of Hexokinase, gluconeogenesis has Glucose 6-phosphatase

- Pyruvate carboxylase is activated by Acetyl CoA, it uses ATP and is present in mitochondria
- PEPCK and fructose 1, 6 Bisphosphate is present in Cytoplasm
- Glucose 6 phosphatase is present in Endoplasmic reticulum
  - It is present in ER because it breaks glucose 6 phosphate to glucose
  - If the enzyme is present in cytoplasm then glycolysis cannot happen
  - Glucose 6 phosphatase is a common enzyme to 2 pathways:
    - Gluconeogenesis
    - Glycogenolysis
  - It is present in liver and absent in muscles
- Substrates of gluconeogenesis
  - Pyruvate and lactate: Because lactate can be converted to pyruvate
  - Propionic acid and Glycerol: These are two breakdown product of fats which are converted to glucose
  - Amino acids: Glucogenic amino acids and both ketogenic and ketonic amino acids
  - Any intermediate of TCA
- Amino Acids:
  - Ketogenic: The ones that form Ketone body / Acetyl CoA in the end
    - Leucine
    - Lysine
  - Glucogenic:
    - Any amino acid which in end forms Pyruvate or TCA intermediate
    - The vest of the amino acids out of 20 are remaining is that are glucogenic
    - Most glucogenic of them: Alanine
  - Both Ketogenic and Glucogenic: Mnemonic – TIP
    - Tyrosine, Tryptophan, Threonine
    - Isoleucine
    - Phenylalanine

## RECIPROCAL REGULATION *23:00*

- Any two opposite pathways will not occur together that is they are reciprocally regulated

Active Space

- If one occurs, then other is inhibited and vice versa
- Ex: Glycolysis and Gluconeogenesis
- In fed state

  ↓

  PFK – II is activated

  ↓

  Fructose, 2-6 bisphosphate → Reciprocal regulator

  PFKI ⊕ Glycolysis

  ⊖ Fructose 1-6 bisphosphatease Gluconeogenesis

  - Fructose 1, 6 bisphosphate is the molecule involved in glycolysis
  - Fructose 1, 6 bisphosphatase is the enzyme involved in gluconeogenesis
  - Fructose 2, 6 bisphosphate is the reciprocal regulator
  - Fructose 2, 6 bisphosphatase is not present normally in cells but present in cancerous mutations and it suppresses glycolysis
- $P_{53}$ tumor suppressor mechanism
  - TIGAR protein or TP-53 induced Glycolysis and Apoptosis Regulator
  - TIGAR regulates two things:
    - It will decrease glycolysis and help with repair of cell
    - Proptosis occurs if repair does not occur

## GLYCOGEN 27:42

- Storage
  - Liver
  - Muscle
  - Brain
- End product
  - Of liver glycogenosis is free glucose and purpose of liver glycogenolysis is to provide blood glucose
  - Of muscle is glucose 6 phosphate and purpose is giving energy to muscles
- Glycogen synthesis
  - Rate limiting enzyme is glycogen synthase
- Glycogen Breakdown / Glycogenolysis
  - Glycogen Phosphorylase
    - Rate limiting enzyme is Glycogen phosphorylase

Active Space

- Glycogen phosphorylase releases 90% glucose in form of Glucose 1 phosphate
- Glycogen phosphorylase requires Vitamin $B_6$
- It breaks $\alpha$ (1 – 6) bonds in glycogen molecule

  - Debranching enzyme
    - It releases 10% glucose in form of free glucose
    - It breaks $\alpha$ (1 – 6) bonds
- Transferase – 2
  - Both Glycogen synthase and Glycogen phosphorylase belong to this category of Transferase
- Site of Glycogen synthesis and Glycogenolysis
  - Cytoplasm
- Requirements for glycogen synthesis to occur
  - A primer – Protein Glycogenin

MCQ: Which enzyme is common between glycolysis and glycogen synthesis?
- Hexokinase / Glucokinase which phosphorylates glucose

MCQ: Which enzyme is common between glycogenolysis and glycogen synthesis?
- Phosphor gluco mutase
- It interconverts glucose 1 phosphate and Glucose 6 phosphate

## HEXOSE MONOPHOSPHATE PATHWAY *31:17*

- It is called Hexose monophosphate because Glucose-6-Phosphate is the starting material here
- It occurs in cytoplasm
- It is an anabolic pathway
- It is activated by insulin
- Rate limiting enzyme is G6PD (Inactive in phosphorylated state and Active in dephosphorylated state)

### PRODUCTS OBTAINED FROM HMP PATHWAY

- Another name of HMP is Pentose Phosphate Pathway (PPP) because Ribose 5 phosphate is a Pentose phosphate and synthesized by this pathway
  - The only source of Ribose 5 phosphate is HMP
  - Ribose 5 phosphate is synthesized in Phase II of HMP which is a non-oxidative and Reversible phase

Active Space

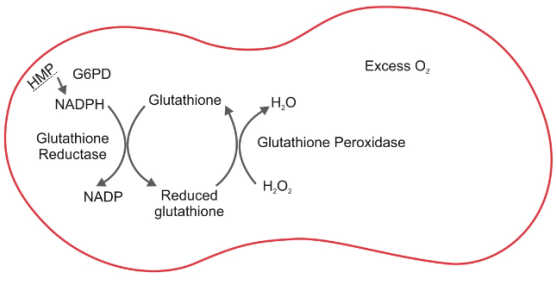
- NADPH is also obtained from HMP
  - Synthesized in Phase 1 of HMP
  - This phase is oxidative and irreversible

## SITES OF HMP

- Liver
- Lactating mammary glands
- Adipose tissue
- Gonads
- Adrenal glands
- Placenta
- RBCs
- HMP can never occur in skin and non lactating mammary glands

## ROLE OF HMP IN RBC

- In RBC, HMP will make NADPH and the main enzyme involved in G6PD
- NADPH will be converted into NADP with oxidation occurring
  - On other hand, glutathione will be reduced and forms oxidized glutathione
  - Enzyme required here is Glutathione Reductase
  - This enzyme requires Vitamin $B_2$ as coenzyme and is the marker enzyme for $B_2$ deficiency
- In RBC, there is always excess $O_2$ and free radicals are continuously being formed in RBC like $H_2O_2$
  - $H_2O_2$ is reduced to $H_2O$ (water)
  - So, glutathione can be oxidized again
  - Enzyme required for this is Glutathione peroxidase
  - This enzyme requires selenocysteine at its active site
- In G6PD deficiency
  - NADPH, Reduced Glutathione not formed
  - $H_2O_2$ is accumulated in excess which damages RBC membrane leading to Hemolysis




ROLE OF HMP IN RBC

Active Space

## SORBITOL PATHWAY

36:26

Active Space

- Glucose gets converted to sorbitol in presence of enzyme Aldose Reductase
- Sorbitol gets converted to fructose in presence of enzyme Sorbitol Dehydrogenase


- Aldose Reductase
  - Present in all cells
- Sorbitol dehydrogenase
  - Present in liver, testis
  - Because fructose is energy for sperms
- In diabetics,
  - Excess glucose present
  - This glucose enters few cells of body like Retina, nerves, glomerulus of kidneys
  - In those cells, Aldose reductase being present forms sorbitol in excess
  - But, Sorbitol dehydrogenase is not present so sorbitol stored in excess
  - Sorbitol is Hygroscopic, it will absorb water and it will cause cell swelling
  - This leads to complication of Diabetes that is:
    - Retinopathy
    - Neuropathy
    - Nephropathy
    - Snow flake cataract

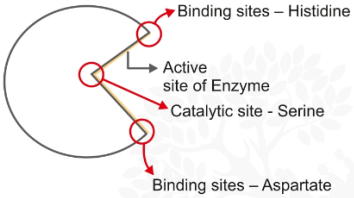
# Enzymes

Active Space

- All enzymes are proteins with exception – Ribozyme in which RNA acts as an enzyme

## SERINE PROTEASES 00:36

- Examples:
  - Chymotrypsin, Trypsin, Elastase, Thrombin, Plasmin, clotting factors III, XI, Prostate Specific Antigen
- Amino acids at active sites



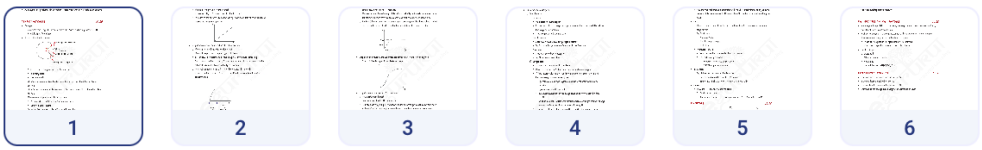

  - At Active site of Enzyme, we have three sites:
    - 2 Binding sites
    - 1 catalytic site
  - With help of amino acids at binding site, the enzyme will hold the substrate / protein
  - With the help of amino acid at catalytic site, the enzyme will cut the substrate / protein
  - The amino acids present at these sites are:
    - Binding sites – Histidine and Aspartate at each
    - Catalytic site – Serine
  - Serine proteases have a role in Tumor cell migration
- Which Amino acid do serine proteases cut at?
  - Chymotrypsin – Cut at carboxy terminase of large hydrophobic bulky amino acids like Tryptophan, Phenylalanine
  - Trypsin – Cut at Carboxy terminals of Basic amino acids like lysine, Arginine
  - Elastase – Cut at carboxy terminals of small neutral amino acids like Glycine, Alanine

## ENZYME KINETICS 04:27

- In enzyme kinetics we learn shapes of different graphs

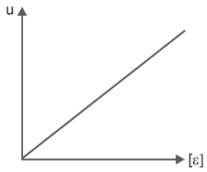




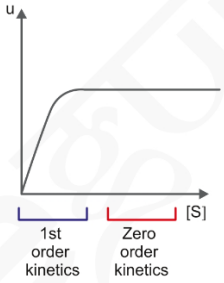


Active Space

- Graph between velocity and enzyme concentration
  - This is a straight line or linear graph
  - It says velocity ∝ Enzyme concentration ($u \propto [\varepsilon]$)
  - It means as the enzyme will be increasing, velocity or date of reaction will be increasing in same proportion



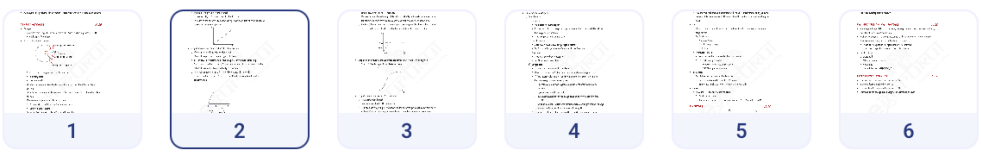

- Graph between velocity and substrate concentration
  - This is also called Michelis Menten Graph
  - Shape of graph is Rectangular Hyperbola Graph
  - So, initially when substrate is increasing, velocity is also increasing
  - But, In later portion of graph, Enzyme is saturated with substrate so further substrate will not influence velocity of reaction
  - In initial portion of graph, it is 1st order kinetics where $u \propto [S]$
  - In later portion of graph, it is zero order Kinetic where u is independent of [S] concentration




- $K_m$ and $V_{max}$ in case of rectangular hyperbola graph
  - $V_{max}$ is the maximum velocity possible
  - Half of $V_{max}$ is $V_{max}$ / 2
  - If $V_{max}$ is then extrapolated X axis – $K_m$ value is achieved
  - $K_m$ is Michelis Menten constant
  - $K_m$ is that substrate concentration at which velocity is half of $V_{max}$
  - $K_m$ is called signature of Enzyme because it is a constant value, it does not change with change in enzyme concentration or change in substrate concentration
  - $K_m$ is affected by affinity between enzyme and substrate and its an inverse relationship

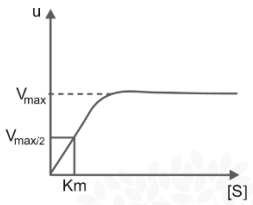






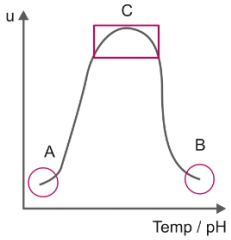
Active Space

- In case of competitive inhibition, affinity between enzyme and substrate diminishes, in that case $K_m$ increases
- This rectangular hyperbola graph is between velocity and substrate concentration for simple enzymes that are those enzymes that have only one active site
- For Regulatory or Allosteric enzymes are those enzymes that hove active site but also have allosteric site where activated or inhibitor of enzyme can bind



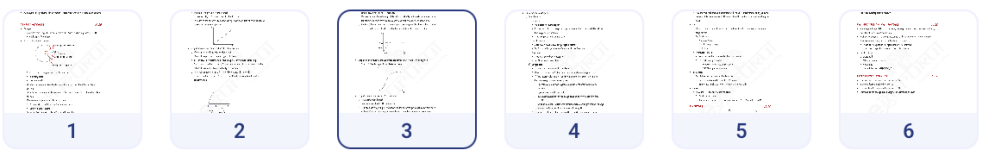

- Graph between velocity and substrate concentration for allosteric enzymes
  - Graph plotted is sigmoidal or S-shaped graph


- Graph between temperature / pH and velocity
  - It is a Bell shaped graph
  - Point A is very low in pH / temperature
  - Point B is very high in pH / temperature and enzymes get denatured at this point
  - At Point C, velocity is in good amount and is called optimum temperature and optimum pH
  - Optimum temperature for human enzymes is 37° C
  - Optimum pH for human enzymes is 5 - 9
  - Velocity is maximum at optimum temperature and pH







## ENZYME CLASSIFICATION

11:00

Active Space

- Oxidoreductase category:
  - Subcategories:
    a) Oxidases:
      - All oxidases require copper
      - 2 oxidases that do not require copper are Xanthine oxidase, sulfite oxidase that require Molybdenum
      - Uses oxygen as hydrogen acceptor

    b) Dehydrogenases
      - Uses NAD / NADP / FAD as hydrogen acceptor
      - Eg: Pyruvate Dehydrogenase Complex of Link Reaction

    c) Peroxidases
      - Uses $H_2O_2$ as Hydrogen acceptor
      - Eg: Glutathione peroxidase

    d) Oxygenases
      - Incorporate oxygen into the substrate
      - They can incorporate 1 atom or 2 atoms of molecular oxygen
      - If they incorporate 1 atom then they are mono-oxygenases or mixed function oxygenases or hydroxylase
        - Eg: Phenyl alanine hydroxylase which converts phenyl alanine to tyrosine
        - Tyrosine has one OH present
        - But, hydroxylases are mono-oxygenases so only 10 is added in this reaction
        - So, if asked what is difference between molecular weight between phenyl alanine and tyrosine, the difference will be by 16
      - If two atoms of molecular oxygen added then it is Dioxygenase enzyme
        - Eg: Glutathione reductase which will add hydrogen and will do reduction

    e) Reductase
      - Eg: Glutathione reductase which will add hydrogen and will do reduction

- Transferases
  - Eg: Kinase which transfer organic phosphate
    Phosphorylase which transfer inorganic phosphate
    Amino transferase
    Methyl transferase
- Hydrolase
  - They use water to break the band

Active Space

- Eg: Phosphatase – the enzyme that phosphate
- Any enzyme that breaks macromolecule bond like carbohydrate, so any enzyme breaking this like Amylase, Maltase etc. then it is adding water and breaking the bond

- Lyase
  - These enzymes can make or break a bond but do not require water and do not require ATP
  - Eg: Synthases
    Aldolase A and B
    Simple decarboxylases
    Hydralase
  - Hydrolase – EC No 4
    - Water is added or removed but bond not broken
    - Eg: Enolase of glycolysis
      Fumarase, Aconitase of TCA cycle
      PEPCK of gluconeogenesis
- Isomerases
  - Eg: Mutase does intramolecular transfer
    Racemase which will connect L – D isomers
    Epimerase which will connect epimers into each other
- Ligase
  - They are ATP and they make the bond
  - Ex: Synthetase enzyme,
    Carboxylase enzyme: They carboxylase uses ATP, Biotin, $CO_2$ and Mg

## INHIBITORS *19:50*

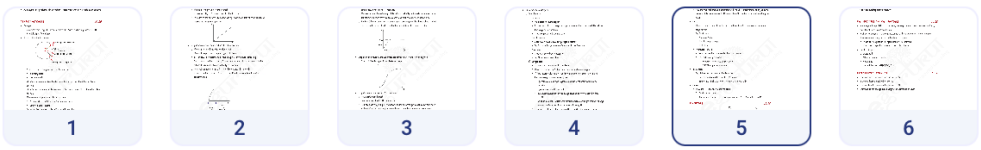
| | $K_m$ | $V_{max}$ |
|---|---|---|
| Competitive inhibition | ↑ | - |
| Non competitive inhibition | - | ↓ |
| Uncompetitive inhibition | ↓ | ↓ |

## ELECTROPHORETIC MOBILITY OF ISOENZYMES *20:30*

- For example
  - LDH has 5 isoenzymes (1 to 5)
  - CK has 3 isoenzymes (1 to 3)







- So, always the 1st isoenzyme has most electrophoretic mobility and the last one has the least Electrophoretic mobility

Active Space

## CO – ENZYMES AND CO – FACTORS *21:20*

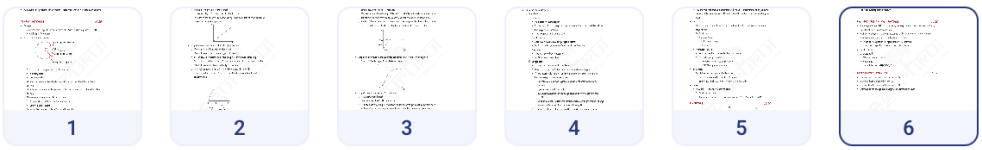
- Any enzyme is a protein but most enzymes require a non protein as well and only then the enzyme is active enzyme
- Such active enzyme is known as holoenzyme where protein portion is known as Apoenzyme and non protein portion is of two types:
  - If non protein portion is organic then it is coenzyme
  - If non protein portion inorganic then it is cofactor
- Ex of coenzymes:
  - Lipoic acid
  - All water soluble vitamins
  - Vitamin K
  - Nucleotides: NAD, NADP, FAD, FMN

## PROPERTIES OF ENZYMES *23:00*

- Enzymes increase velocity or rate of reaction
- Enzymes decrease activation energy
- Enzyme do not change equilibrium of reaction
- Enzymes do not change free energy of substrate or product

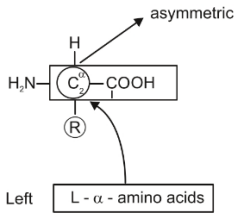




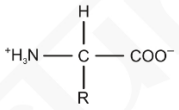


# Amino Acids and Proteins

Active Space




- All amino acids have 1 asymmetric carbon except:
  - 0 → glycine
  - 2 → Isoleucine and threonine → Essential in diet
- There are:
  - 8 essential amino acids
  - 2 semi-essential amino acids: Arginine > histidine
- Histidine is essential in children but not in adults.
- Amino acid stays in the form of Zwitterion/ampholyte with net charge zero. It is precipitated and insoluble.

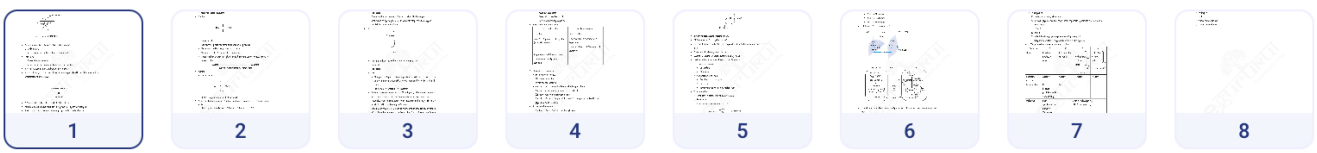


Zwitterion

- PI/Isoelectric pH is that pH at which Zwitterion exists.
- Acidic amino acids have more carboxy group → Negatively charged.
- Basic amino acids have more amino groups → Positively charged.
- In acidic medium, protein or amino acids exist as positively charged structures.
- In basic medium, protein or amino acids exist as negatively charged structures.
- Charge on:
  - Cathode: negative
  - Anode: positive
  - Cation: positive
  - Anion: negative
- Classification of amino acids:
  - Aliphatic: Glycine, alanine, valine, leucine, isoleucine
    - All are non-polar



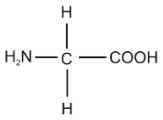




- Least non-polar: Glycine
- Most non-polar isoleucine

Active Space

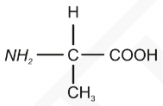
- Glycine:



  - Non-essential
  - Flexibility of proteins: turns and bends (Also proline)
  - Glycine and proline are present in β-turns
  - Glycine is smallest and simplest amino acids.
  - Uses: creation of creatine, glutathione, haem and serine. Hence, Serine is non-essential.

$$\text{Glycine} \xrightarrow[\text{Serine Hydroxy Methyl Transferase}]{} \text{Serine}$$

- Alanine:
  - Non-essential



  - Most glucogenic amino acid (3 carbons)
- Branched chain amino acids: Valine, Leucine and Isoleucine → Essential amino acids
  - Maple Syrup Urine Disease: Defect in catabolism of BCAA

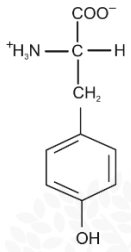
$$BCAA \xrightarrow{Transamination} BCKA \xrightarrow[\text{BCKA Dehydrogenase complex OR Decarboxylase}]{Oxidative\ decarboxylation\ (B1)}$$

  - BCKA decarboxylase is deficient in MCUD → Ketosis, Brain (Mental Retardation) → Maple syrup like odor of urine, abnormal muscle tone → Coma, death → High mortality rate
- Aromatic AA:

i. Phenylalanine

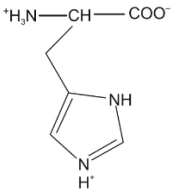
- Essential
- Non-polar
- Phenylalanine gets converted into tyrosine with the help of phenylalanine hydroxylase. → Irreversible step, requires oxygen, NADPH, Tetrahydro Biopterin.

ii. Tyrosine



- Contains indole ring → blue color on any reaction
- Essential
- Non-polar
- Uses:
  a. 60mg of tryptophan makes 1mg of Niacin (Vitamin $B_3$). Vitamin $B_3$ and Vitamin D are atypical vitamins which can be synthetized in the body.
  b. Formation of serotonin → Melatonin
- Hartnup's disease: Aminoaciduria (Tryptophan) without a corresponding increase in its serum levels. Amino acids for neutral amino acids especially tryptophan is defective in intestines and kidneys. There will be Niacin deficiency leading to Pellagra.
- Carcinoid syndrome: Too much of tryptophan is used for the synthesis of serotonin leaving very little tryptophan for the formation of niacin leading to Pellagra.
- 5-Hydroxy Indole Acetic Acid (5-HIAA) is increased in patients of Carcinoid syndrome which is an end product of Serotonin.

iii. Histidine:



Active Space

- It has imidazole ring
- Polar but less polar
- Essential but semi-essential
- Maximum buffering capacity

Active Space

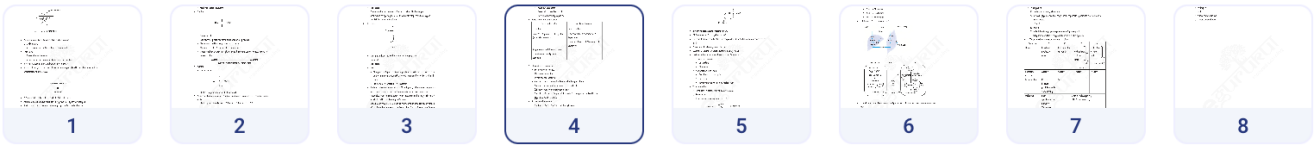
- Basic and Acidic amino acids

| Basic amino acids | Acidic amino acids |
|---|---|
| Essential | Non-essential |
| Polarity: Arginine (+++) > lysine (++) > Histidine (+) | Oxyloacetate → Aspartate → Asparagine<br>$\alpha$-Ketoglutarate → Glutamate → Glutamine |
| Arginine and histidine are semi-essential whereas lysine is essential | |

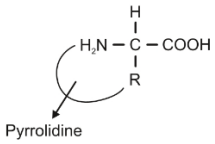
- OH containing amino acids:
  - Serine: non-essential
  - Threonine: essential
  - Tyrosine: non-essential
  - AA which has maximum tendency to bind to phosphate
  - AA which is responsible for covalent modifications (phosphorylation/dephosphorylation)
  - AA which is involved O-glycosidic bonds. Asparagine is involved in N-glycosidic bond -CONH).
- Sulphur containing AA
  - Cysteine (HS-C): Contains sulfhydryl group.
  - Methionine (C-S-C)
  - Methionine (essential) is converted into cysteine (non-essential) in body.
  - Cysteine is polar (Sulfhydryl group); methionine is non-polar.
  - Methionine → homocysteine → Cysteine. Serine and $B_6$ are also required.
- Imino acids: Proline
  - Amino group is not free.
  - It is part of pyrrolidine ring
  - Secondary amine
  - Non-polar and non-essential
  - It can be synthesized from Ornithine.



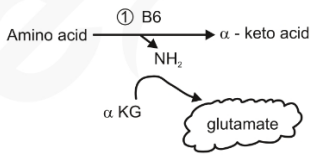




Active Space



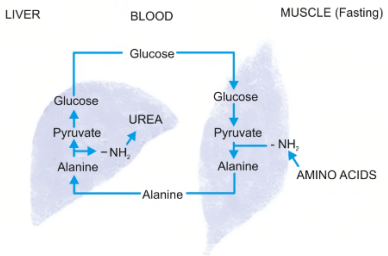

- 21st amino acid: Selenocysteine → UGA
- 22nd amino acid: Pyrrolysine → UAG
- Co-translational modifications of stop codons lead to formation of these amino acids.
- Precursor of Selenocysteine: Serine
- Glycine → Serine → Selenocysteine and Cysteine
- Derived amino acids do not have a codon. Some are:
  - Present in protein:
    - OH-proline
    - OH-lysine
  - Not present in protein:
    - Ornithine, Citrulline } Urea cycle
    - Homocysteine: Methionine metabolism
- Transamination:
  - First step in catabolism of all amino acids
  - Reversible
  - Transamination enzymes: SGOT, SGPT

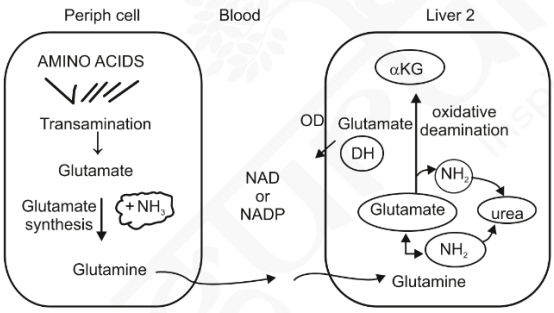



  - Only α-$NH_2$ takes part. Except δ-amino of ornithine take part in formation of proline with the help of enzyme Ornithine Amino transferase.
  - 17 AA take part in transamination.
  - 3 AA do not take part in transamination:
    i. Proline
    ii. Lysine
    iii. Threonine

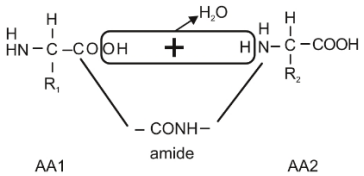
Active Space

- Transport of ammonia from:
  - Body → Glutamine
  - Brain → Glutamine
  - Muscles → Alanine
- Cahill cycle / Glucose Alanine Cycle:




- Transdeamination: Transamination (peripheral cells) + oxidative deamination (liver cells)
- Proteins:
  - Peptide bond: amide bond present in protein. It is a strong covalent bond and it has partial double bond character (trans)



- Structures of protein:
  - 1°: sequence
  - 2°: folding of primary structure:
    a. α-helix: glycine, proline, tryptophan, aspartate, glutamate and valine are never found.
    b. βSheet
    c. βturn
  - 3°: fully folded single polypeptide chain. Eg: myoglobin
  - 4°: fully folded multiple polypeptide chain. Eg: Hemoglobin
- Difference between various protein structures:

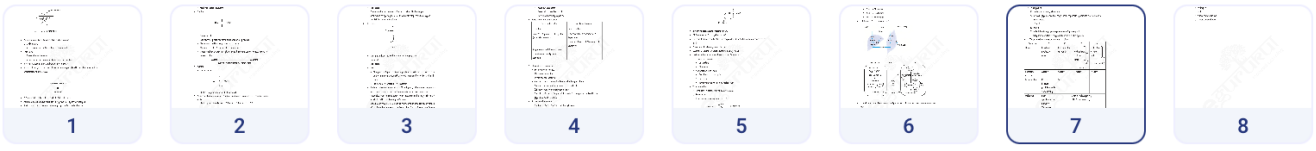
| Features | 1° | 2° | 3° | 4° |
|---|---|---|---|---|
| Bond | Covalent / Peptide / Amide | Hydrogen-bond (H-bond) | S-S<br>Hydrophobic<br>Hydrogen<br>Ionic<br>HHI<br>(Mnemonic) | Hydrophobic<br>H-bond<br>Ionic<br>HHI<br>(Mnemonic) |
| Functional activity | Absent | Absent | Present | Present |
| Denaturation | Retained because peptide bond is very strong | Lost | Lost | Lost |
| Detection | Mass spectrometry<br>Edman's Technique | X-ray crystallography<br>NMR spectrometry | | |
| • Ionic bond is also known as electrostatic bond<br>• S-S stands for disulphide bond | | | | |

  - NMR spectrometry is best for non-crystallizable proteins
- Bonds in Enzyme-substrate interaction:
  - Hydrogen
  - Hydrophobic
  - Ionic
  - Sometimes covalent
  - Never Vander Waals forces

Active Space





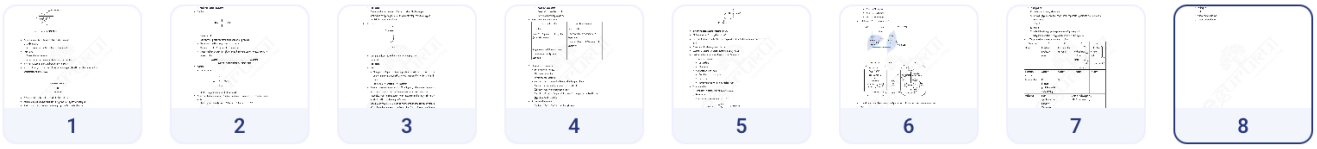


- Bonds in Protein-DNA interactions:
  - Hydrogen
  - Ionic
  - Vander Waals forces
  - Never covalent bonds

**Active Space**



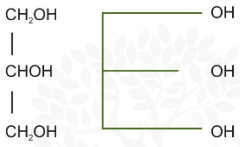


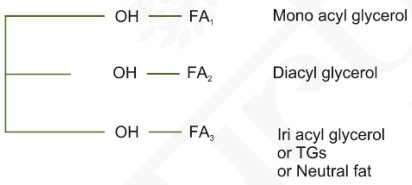


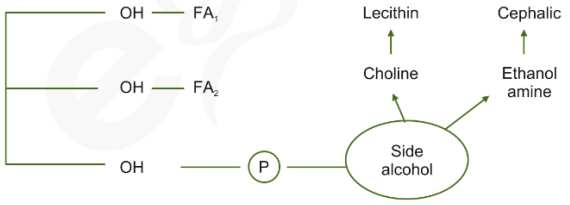
# Lipids

Active Space

- They are non-polar: not soluble in polar solvents
- It is made of alcohol (-OH: Polar) and fatty acids (-COOH: Polar) → Fat / Ester / Lipid (non-polar) [Water is removed]
- Classification of lipids:
  - Simple: FA and alcohol
  - Complex: FA + alcohol + other component (phosphate [Phospholipid] or carbohydrate [Glycolipid])
    - Phospholipid and glycolipid have both polar and non-polar → Amphipathic
- Main alcohol in lipids: Glycerol

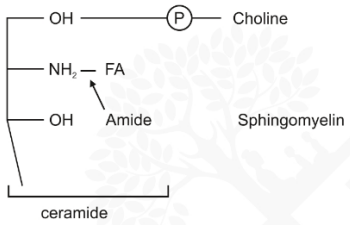



  - Phospholipases $A_1$, $A_2$, C and D breakdown phospholipids.
- Cardiolipin is a complex phospholipid - Glycerol is attached to 2 phosphatidic acid (1 glycerol + 2 FA + 1 phosphate). Due to its complexity, it can sometimes act an antigen → antiphospholipid syndrome:
  - Anti-cardiolipin antibodies
  - Recurrent abortions

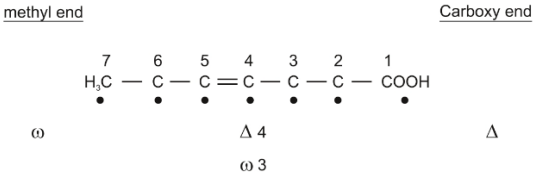
- Pro-thrombotic condition
- Phospholipids are of two types:
  - Glycerophospholipids: alcohol is glycerol
  - Sphingophospholipids: alcohol is sphingosine
- Sphingosine:
  - Long carbon skeleton
  - Amino group at second position
  - It is an unsaturated amino-alcohol
- Sphingophospholipid: Alcohol (Sphingosine) + FA + P
  - Sphingomyelin is the only Sphingophospholipid of concern in human body.




- Glycolipids:
  - Glycerol is never present. → Glycosphingolipid
  - Phosphate and its side alcohol is also not present
  - Sphingosine + FA + Glucose: Glucocerebroside/Glucosyl ceramide

Ceramide

  - Glucocerebroside is never found in CNS, it is found only in extra neural tissues
  - Sphingosine + FA + Galactose → Galactocerebroside/Galactosyl ceramide - Found in CNS
- PUFAs/Polyunsaturated Fatty Acids:
  - 2 or more doble bonds
  - Essential in diet (EFA)

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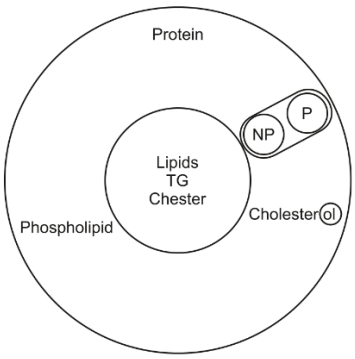
- PUFAs/EFA maybe of 2 varieties:
  - Omega-3:
    - Cervonic Acid/ Docosahexaenoic acid (DHA) [22C, 6=]
      - Important component of breast milk: required for brain development of child.
      - Also present in fish oil.
    - Alpha-Linolenic acid [18, 3=]
      - Present in flaxseed oil, soyabean oil
      - It is precursor of DHA and Timnodonic acid.
    - Timnodonic acid [20C, 5=]
      - Present in fish oil
      - It is also called as Eicosa Pentaenoic acid
  - Omega-6:
    - Gamma-Linolenic acid (18C, 3=)
      - Present in oil of evening primrose.
    - Linoleic acid [18C, 2=]
      - Present in Safflower oil
    - Arachidonic acid [20C, 4=]
      - Present in animal fats
      - Important for synthesis of prostaglandins in body.
- Most essential fatty acid: Linoleic acid.
- Cardioprotective PUFA: Omega 3

Active Space

## LIPID TRANSPORT *18:58*

- Lipids are transported in blood in the form of lipoprotein.
- Lipids present in blood are:
  - Triglyceride: Non-polar
  - Phospholipid: amphipathic
  - Cholesterol: amphipathic
  - Cholesterol ester: Non-polar



| | Lipoprotein | Lipid | Protein / Apoprotein |
|---|---|---|---|
| Density ↓ | Chylomicron | Exogenous triglycerides | Apo B48 |
| | Chylomicron remnant | TG + Cholesterol | Apo B48 + ApoE |
| | VLDL | Endogenous triglycerides | Apo B100 |
| | VLDL – Remnant / IDL | TG + Cholesterol | Apo B100 + ApoE |
| | LDL | Cholesterol | Apo B100 + ApoE |
| | HDL | Cholesterol ester | Apo A, C and E |

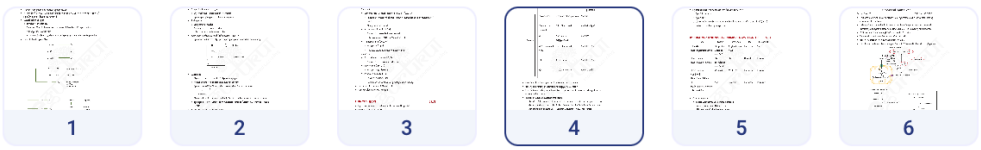
Active Space

- Density is directly proportional to percentage of proteins.
- Density is inversely proportional to triglyceride content.
- Density is inversely proportional size of lipoprotein: chylomicron is largest in size whereas HDL is smallest.
- HDL does reverse cholesterol transport:
  - HDL adds FA to cholesterol to form cholesterol ester which is transported to liver.
  - HDL has maximum phospholipids: Lecithin donates this FA to form Lysolecithin with the help of enzyme LCAT: Lecithin Cholesterol Acyl Transferase.
  - LCAT:
    - Apo $A_1$: activator
    - Apo $A_2$: inhibitor
- Chylomicrons transport exogenous triglycerides from intestines to peripheral tissues.
- VLDL transports endogenous triglycerides from liver to peripheral tissues.
- LDL transports cholesterol from liver to peripheral tissue.
- HDL transports cholesterol from peripheral tissue to liver.
- Anabolic:

Chylomicron and VLDL —(Lipoprotein lipase removes TG)→ Chylomicron and VLDL remnant







- TG gets stored in adipose tissue.

- Ligands on lipoproteins are present for uptake by liver:
  - Apo E: Remnants
  - Apo A: HDL
  - LDL receptors mediate receptor mediated endocytosis of LDL. Apo B100 (main) and Apo E are the ligands present.

Active Space

## HYPERLIPOPROTEINEMIA / FREDRICKSON CLASSIFICATION 30:14

| Type | Defect | Lipoprotein | TG | Cholesterol |
|---|---|---|---|---|
| I: Familial Hyperchylomicronemia | Lipoprotein lipase or Apo C-2 | Chylomicrons, VLDL | Increased | Normal |
| II (a): Familial Hypercholesterolemia | LDL receptor or Apo B-100 | LDL | Normal | Increased |
| II (b): Familial Combined Hyperlipoproteinemia | Unknown | VLDL, LDL | Increased | Increased |
| III: Dysbetalipoproteinemia / Broad $\beta$ disease | Apo E | Remnants | Increased | Increased |

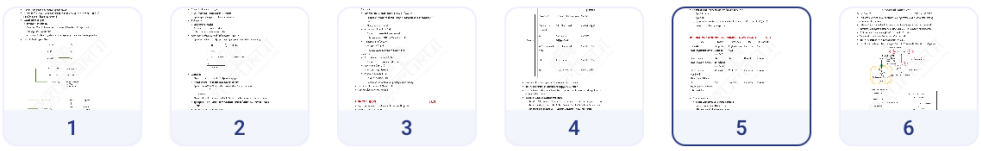
- Clinical features:
  - Tendon Xanthoma: Cholesterol increased
  - Eruptive Xanthoma: TG increased
  - Milky plasma: Chylomicron increased
  - Acute pain abdomen (Acute Pancreatitis): TG increased
  - Plasma and tuberoeruptive xanthoma: Chylomicron remnant, VLDL remnant
- Lipoprotein 'X' (abnormal):
  - Increased in LCAT deficiency + cholestatic states.
  - Rich in amphipathic lipids.
  - Poor in neutral lipids

## FATTY ACID SYNTHESIS 35:20

- Anabolic pathway which occurs in cytoplasm



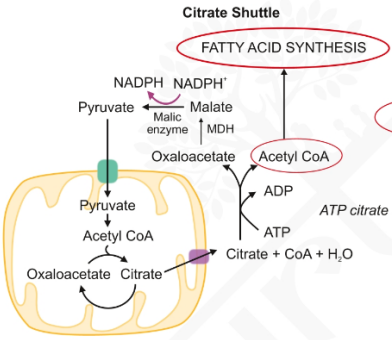


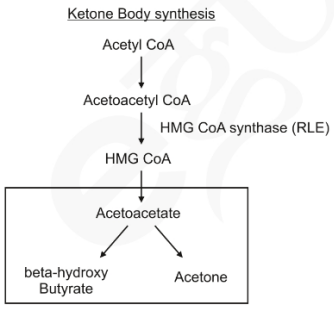


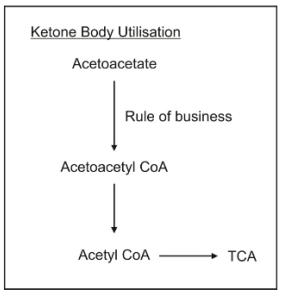
- Activated by insulin and occurs in fed state of body

$$\text{Acetyl CoA (2C)} \xrightarrow{\text{Acetyl CoA Carboxylase } (+CO_2)} \text{Malonyl CoA (3C)}$$

- This enzyme is also known as Malonyl CoA synthetase and it is the rate limiting enzyme of this pathway.
- Malonyl CoA is converted to Fatty Acid Synthase Complex which has 2 subunits containing 6 enzymatic activities each. Extra $CO_2$ is removed by this enzyme.
- Both acetyl CoA and malonyl CoA are used in FA synthesis.
- FA is synthetized from the carbons of Acetyl CoA.
- Donor of carbons for FA synthesis: Manolyl CoA.
- Citrate shuttle is used from bringing Acetyl CoA from mitochondria to cytoplasm.




- Thiolase is common to 4 pathways:
  - Ketone body synthesis
  - Ketone body utilization
  - Cholesterol synthesis
  - β-oxidation of FA

Active Space

# Molecular Biology

Active Space

## NUCLEIC ACIDS 00:45

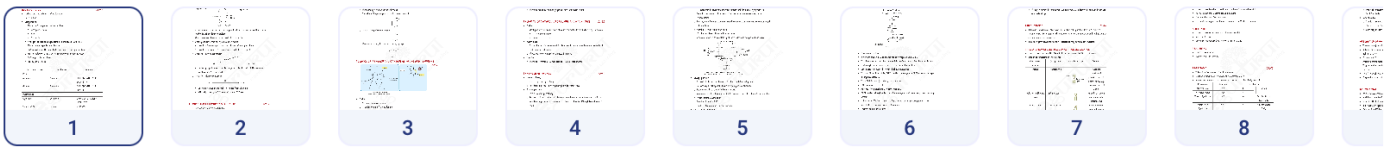
- Nucleic acids are polymers of nucleotides
  Ex: DNA, RNA
- Components
  - There are 3 components of nucleotides
    - Nitrogenous base
    - Sugar
    - Phosphate
  - Nitrogenous base and sugar combined are called Nucleoside
  - There is no phosphate in nucleoside
  - DNA has Adenine, Thymine, Cytosine, Guanine nitrogenous bases
  - RNA has Adenine, Uracil, Cytosine, Guanine nitrogenous bases
  - DNA sugar is Deoxyribose
  - RNA sugar is Ribose

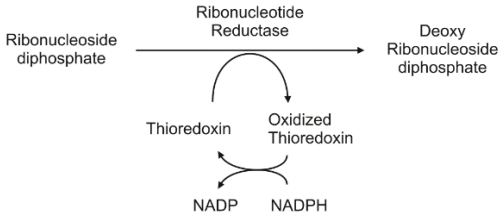
| Nitrogenous Base | Nucleoside | nucleotide |
|---|---|---|
| Purines | | |
| Adenine | Adenosine | HMP, ADP, ATP, dAMP, dADP, dATP |
| Guanine | Guanosine | GMP, GDP, GTP, dGMP, dGDP, dGTP |
| Pyrimidines | | |
| Cytosine | Cytidines | CMP, CDP, CTP, dCMP, dCDP, dCTP |
| Uracil (RNA) | Uridine | UMP, UDP, UTP |
| Thymine (DNA) | Thymidine | dTMP, dTDP, dTTP |

- Formation of Deoxyribose Sugar
  - Formed via HMP pathway
  - Ribose from gets converted to deoxyribose form into DNA
  - This conversion only occurs at Diphosphate level that is when Ribonucleoside diphosphate then at this level it is converted to Deoxy Ribo nucleoside diphosphate
  - Enzyme involved is Ribonucleotide reductase



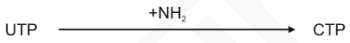







- On other hand, Thioredoxin is getting oxidised to Thioredoxin (oxid) and enzyme involved is Thioredoxin Reductase
- Ribose to deoxyribose occurs at level of diphosphate
- Uracil gets converted to Thymine and Cytosine
  - Uracil to Thymine gets converted at level of monophosphate
  - Uracil to Cytosine gets converted at level of triphosphate
- Uracil to Thymine conversion


  - Methyl group obtained from Tetrahydrofolate with help of Thymidylate synthase and ATP not used
- Uracil to Cytosine conversion



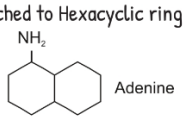

  - One amino group added that is obtained from Glutamine
  - With help of enzyme CTP synthetase and ATP used

## PURINES AND PYRIMIDINES STRUCTURE 08:50

- Purines are Adenine and Guanine

• Purine structure

- Structure is one Hexacyclic Ring joined to one Pentacyclic Ring
- If an amino group is attached to Hexacyclic ring – Adenine

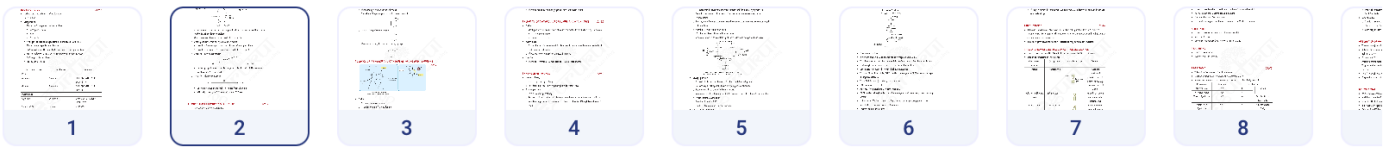



- If amino group not present, then Guanine


Active Space



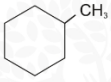




- Pyrimidine structures
  - There are cytosine, uracil and thymine
  - Cytosine – Single ring and an amino group present

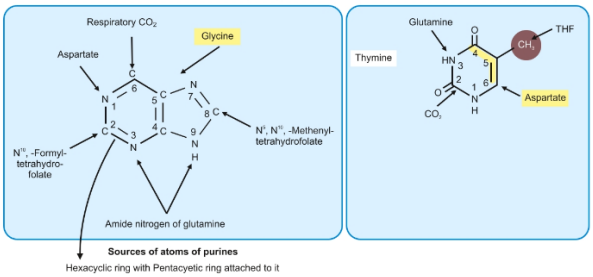

  - Uracil – Single hexacyclic ring

  - Thymine – Hexacyclic ring with Methyl group




## SOURCES OF NITROGEN AND CARBONS OF PURINE AND PYRIMIDINE

09:51




- Purines
  - $N_1$ comes from Aspartate
  - $N_3$ and $N_9$ coming from Glutamine
  - $N_7$ coming from Glycine
  - $C_4$ and $C_5$ coming from Glycine
  - $C_2$ from Tetrahydrofolate
  - $C_8$ is also from Tetrahydrofolate
  - $C_6$ is from carbon dioxide
- Pyrimidines
  - Single hexacyclic ring
  - $N_1$ is from Aspartate
  - $N_3$ is from Glutamine
  - $C_4$, $C_5$, $C_6$ is form Aspartate

Active Space

- $C_2$ is from carbon dioxide
- Thymine has an extra methyl group from Tetrahydrofolate

Active Space

## PRODUCTS OF CATABOLISM OF PURINE AND PYRIMIDINES 11:52

- Purines
  - When purines are broken down, they are converted to purine like ring – Uric acid
    - It is soluble in water
    - Excreted from body
- Pyrimidines
  - Pyrimidines are broken down into pieces so there are more than one products of hydrolysis or catabolism
  - These are Ammonia, carbon dioxide, $\beta$-alanine
- Thymine
  - Thymine – Ammonia, Carbon dioxide, $\beta$ amino isobutyrate

## SYNTHESIS OF PURINES 12:50

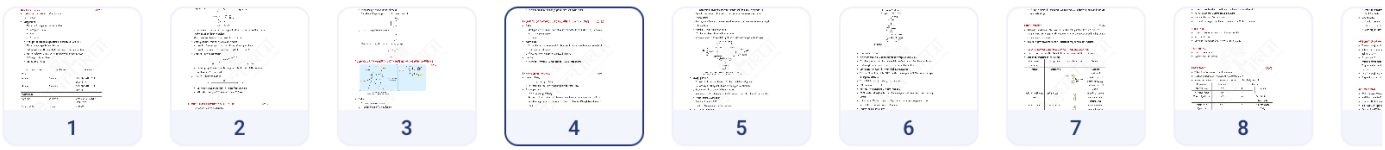
- Denovo pathway
  - It is a high energy pathway
  - Rate limiting step is PRPP glutamyl amide transferase
- Salvage pathway
  - It is a low energy pathway
  - Purines that are catabolized, they are taken back into body by salvage pathway
  - Rate limiting enzyme is Hypoxanthine Guanine Phosphor Ribonyl Transferase / HGPRT

## PURINE CATABOLISM 14:17

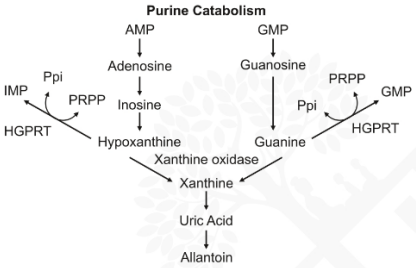
- Catabolic pathway
  - AMP and GMP go into catabolic pathway
  - Phosphate is removed from them to form Nucleoside – Adenosine and Guanosine
  - Sugar is removed from Guanosine to form Guanine
  - Adenosine forms Inosine by removal of amino group from Adenosine and enzyme is Adenosine deaminase / ADA
    - The ADA enzyme increases in Tuberculosis







- If ADA enzyme decreased then patient has SCID / Severe Combined Immuno Deficiency because this enzyme is important for B and T lymphocytes
- From inosine, sugar will be removed and we get nitrogenous base, we get Hypoxanthine
- Both hypoxanthine and guanine taken by enzyme Xanthine oxidase converting it into Xanthine
- Xanthine converted into uric acid
- Xanthine oxidase is Rate limiting enzyme
- Uric acid convaled to allantoin by enzyme uricase in non primate animals



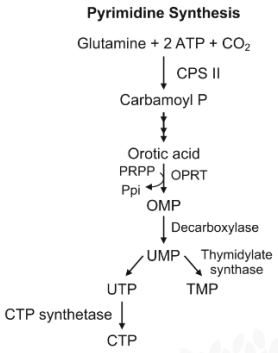

Complete def of HGPRT- LESCH NYHAN Syndrome
Partial def of HGPRT- KELLEY SEEGMILLER Syndrome

- Salvage pathway
  - At level of nitrogenous bases that is hypoxanthine and guanine
  - So, lets say 10 nitrogenous bases are going into catabolism
  - But only 5 will be allowed to foam uric acid
  - Remaining 5 will be taken up back into body and converting them to nucleotides
  - Hypoxanthine will make IMP
  - Guanine will make GMP
  - HGPRT is the common enzyme involved
- Lesch Nhyan Syndrome
  - Complete deficiency of HGPRT
  - Patient has gout because if pathway is not occurring, all purine nitrogenous bases are converted to uric acid. This causes Hyperuricemia.
  - Self mutilation behaviour because of increase PRPP
- Kelley Seegthisler Syndrome
  - Partial deficiency of HGPRT
  - Patient has gout

Active Space

## PYRIMIDINE SYNTHESIS *18:00*

Active Space




- Occurs in cytoplasm
- 2 ATP and carbon dioxide and source of nitrogen is Glutamine
- That forms carbamoyl phosphate with help of carbamoyl phosphate synthetase II
- Carbamoyl phosphate is converted to orotic acid or orotate
- Orotic acid is converted to OMP which is a nucleotide
- From orotic acid / orotate, PRPP is added and enzyme is OPRT / orotate phospho Ribosyl Transferase
- From OMP to UMP, Decarboxylase is involved
- UMP is converted to TMP
- At level of triphosphate UTP converted to CTP
- OPRT and Decarboxylase is bifunctional enzymes and there are present on single protein
- If there are effected, patient will have orotic acid uria where patients have megaloblastic anemia, Growth retardation
- Treatment is giving uridine

## RIBOSE AND DEOXYRIBOSE SUGAR *20:31*

- Structure:
  - Furanose farm with oxygen on top
    $C_1$, $C_2$, $C_3$, $C_4$, $C_5$ is out of the ring
    At $C_1$ – H and OH present
    $C_2$ – H and OH present
    $C_3$ – H and OH present
    $C_4$ – H present
    $C_5$ – $CH_2OH$ present

- At position 2, if oxygen is removed then called $2^1$ deoxyribose present in DNA
- If oxygen removed from number 2 and 3 then $2^1 3^1$ dideoxy ribose is used then DNA synthesis stopped

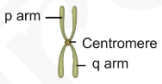
Active Space

## CHROMOSOMES 21:46

- In human, somatic cells they have 2n / diploid configuration that is 23 pairs of chromosomes where 1 pair of chromosomes are sex chromosomes and rest 22 pair of chromosomes are acetosomes
- In case of germ cells, there are n / haploid so they have 23 chromosomes

### TYPES OF CHROMOSOMES BASED ON CENTROMERS LOCATION

- Centromere location – It is the middle or central constriction of chromose
- Ends of chromosome are telomeres

| Centromere location | Designation | Metaphase shape | Example |
|---|---|---|---|
| Middle | Metacentric |  | These are considered primitive type of chromosomes e.g. chromosome no. 1 and 3 |
| Between middle and end | Submetacentric |  | Majority of human autosomes, X-chromosome |
| Close to end | Acrocentric |  | Y-chromosome, some autosomes (13, 14, 15, 21, 22) |
| At end | Telocentric |  | Not in humans |

### MENTACENTRIC

- If centromere is in the middle then it is mentacentric
- P arm and Q arm are of exact size
- These are primitive chromosomes
- Only chromosome 1 and 3 are mentacentric

Active Space

## SUBMETACENTRIC

- If centromere is between middle and end then it is submetacentric
- Most common chromosome found in humans
- P arm is short and Q arm is long
- They make up majority of human autosomes and X-chromosomes

## ACROCENTRIC

- If centromere very close to end then Acrocentric
- Very short P arm
- Only 5 autosomes are like this → 13, 14, 15, 21, 22

## TELOCENTRIC

- Centromere is at end
- Does not exist in humans

## BARR BODY *23:45*

- This is inactive condensed X chromosome
- Number of Barr body = Number of X chromosome – 1
- In a normal female – 2 X chromosome present so 1 Barr body present

| Phenotype | Genotype | Barr bodies | |
|---|---|---|---|
| Normal Male | XY | 0 | Normal |
| Normal Female | XX | 1 | |
| Turner Syndrome | X0 | 0 | Female with no Barr Body |
| Klinefelter Syndrome | XXY | 1 | Male with Barr Body |
| Super Female | XXX | 2 | Female with two Barr Bodies |

- Normal male, XY genotype so 0 Barr body
- Normal female, XX genotype so 1 Barr body
- Turner Syndrome:
  - Female with no Barr body, genotype X0
  - No Barr body
- Klinefelter Syndrome:
  - Phenotype is male with Barr body

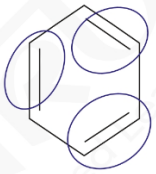
- Genotype is XXY
- Two X chromosomes
- So, 1 Barr body

- Super Female:
  - S and X chromosomes in genotype
  - Phenotype is of female
  - Barr body present is 2

Active Space

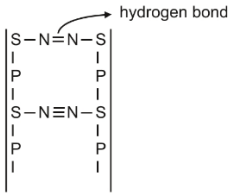
## ABSORPTION OF UV LIGHT BY NUCLEIC ACIDS *25:10*

- There are conjugated double bonds causing light absorption
- In DNA, it is because of nitrogenous bases and absorb UV light at 280 nm
- Proteins and Amino acids absorb at 280 nm because of Aromatic amino acids and maximum absorption is by Tryptophan because is the only aromatic amino acids having two rings
- NAD / NADP absorb light at 840 nm
- Porphyrins absorb at 400 nm and absorption band is known as Soret band



## BONDS IN DNA *26:07*

- DNA is double stranded
- Back bone is made of sugar and phosphate
- Sugar is attached to nitrogenous base
- In between nitrogenous base, hydrogen bond formed
- Between A and T, there are two hydrogen bonds
- Between C and G, there are three hydrogen bonds
- The bond between N and S, there is $\beta$-N glycosidic bond
- This bond is between $C_1$ of sugar and $N_9$ of purine and $N_1$ of pyrimidine and it is covalent bond
- Bond between sugar and phosphate, it is $3'5'$ phosphodiesters bond and it is covalent bond
- In RNA, size it is single stranded these are no hydrogen bonds



## DNA 27:48

- DNA is double stranded in both Prokaryotes and Eukaryotes
- In prokaryotes, it is circular double stranded and there are no introns
- In eukaryotes, it is linear double stranded and have introns
- Introns can prevent mutation in eukaryotic DNA
- In Eukaryotes, mitochondria is present and it is same like prokaryotes that is circular double stranded with no introns
- There are more chances in mutations

## PALINDROME 28:52

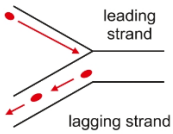
- Palindrome is same sequence on both strands
- For example
  a) GGCC
  b) TAAT
- Which among both is a palindrome?
  - a) is the answer
  - palindrome is present in DNA which is double stranded so we check both strands
  - TAAT is 5'TAAT 3' and when direction not mentioned then obviously left is 5'
    - 5' TAAT 3'
    - 3' ATTA 5'
    - Second strand reading from 5' is ATTA and not same, not a Palindrome
  - GGCC
    - 5' GGCC 3'
    - 3' CCGG 5'
  - This should always be read from 5' → 3'

## DNA REPLICATION 30:40

- Helicase
  - This causes strand separation
  - Uses ATP for strand separation
  - When separating strand, creates positive supercoils
- Topoisomerase
  - Relieves positive supercoils be cause only replication fork can move forward then
- Single Strand DNA binding proteins
  - They prevent reannealing of two strands
  - They are unwinding proteins and unwind double strands

Active Space

- Primase
  - Synthesize RNA primers
  - 1 primer – leading strand
  - Multiple primers – lagging strand
  - The small fragments are Okazaki fragments




- DNA polymerase III
  - DNA dependent DNA polymerase
  - This enzyme makes leading and lagging strand
- DNA polymerase I
  - It removes RNA primers from both leading and lagging primers
  - Then it fills the gap with DNA only on lagging strand
  - The gap on leading strand will be left
- DNA ligase
  - Joins the fragments
  - Uses ATP
  - Creates phosphodiester bond
  - Works on lagging strand

Active Space

## PROKARYOTIC AND EUKARYOTIC DNA POLYMERASES *34:57*

Comparison of Prokaryotic and Eukaryotic DNA Polymerases

| E.coli (Prokaryotes) | Eukaryotes | | Function |
|---|---|---|---|
| DNA Polymerase I | Nucleus:<br>• RNase H<br>• FEN-1 (Flap endonuclease)<br>• $\delta$-polymerase (minor role) | Mitochondria<br>• RNase H<br>• FEN-1 (Flap endonuclease) | Remove primer and fill the gap |
| DNA Polymerase II | $\beta$<br>$\gamma$ | | DNA proof reading and repair<br>DNA repair<br>Mitochondrial DNA synthesis |

Active Space

| | | |
|---|---|---|
| DNA Polymerase III | $\varepsilon$<br>$\delta$ | Leading strand synthesis<br>Lagging strand synthesis |
| DNA-G protein | $\alpha$ | Primase (synthesize Primers) |

## PROOFREADING AND REPAIR *37:13*

- Telomere shortening
  - 7 enzymes play a role in Replication
  - With each replication, a gap is left and some DNA lost
  - So, somatic cells have limited number of divisions after n no. of divisions, somatic cells die
  - At some point, very less DNA and cell cannot survive

| | Proofreading | Repair |
|---|---|---|
| Writer | Mail during synthesis | Correction after synthesis |
| Enzymatic activity | 3' → 5' exonuclease activity | Mostly endonuclease, 5' → 3' exonuclease activity sometimes |
| Enzyme in prokaryotes | DNA polymerase II | DNA polymerase II |
| Enzyme in eukaryotes | All DNA Polymerase can do proofreading except alpha and beta polymerase | $\beta$ - Polymerase (main)<br>$\varepsilon$ - Polymerase (minor role) |
| Phase of cell cycle | S-phase | Most repairs occur in G1 phase |

## RNA DEPENDENT DNA POLYMERASE *39:45*

- Germ cells and stem cells have infinite divisions
- Because they have an extra enzyme - Telomerase enzyme
- This enzyme has protein portion acts as enzyme
  - Has RNA portion - acts as template
  - Taking the RNA as template, DNA is synthesized on it
  - The gap that was created is filled like this





- Enzyme responsible is RNA dependent DNA polymerase or Reverse transcriptase
- It is not Ribosome since no enzymatic activity from RNA but acts as template
- Its activity increases in cancer and decreases with aging

Active Space

## DNA REPAIR *40:00*

| DNA Repair | Phase of cell cycle | Damage | Cause | Disease |
|---|---|---|---|---|
| Nucleotide excision repair | G1 | Thymine-Thymine dimers (T-T dimers) | UV radiation | Xeroderma pigmentosa |
| Base excision repair | G1 mainly but can occur in any phase | Cytosine deaminated to uracil | Spontaneous, heat, infra red rays, viral infection, Nitrous Oxide | MUTYH associated polyposis |
| Mismatch repair | G2 | Mismatched base | Proofreading error | HNPCC (Hereditary Non Polyposis Colorectal Cancer) |

## TRANSCRIPTION *42:48*

- Synthesis of RNA on DNA
- DNA is taken as template and RNA synthesized on it
- Enzyme is DNA dependent RNA polymerase
- But in replication, Primase enzyme that is also DNA dependent RNA polymerase

## RNA POLYMERASE 43:39

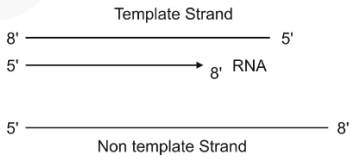
RNA Polymerase contains 5 different subunits

| Subunit | Nuclear | Function |
|---|---|---|
| $\alpha, \omega$ | Alpha and omega | Required for enzyme assemble |
| $\beta$ | Beta | Has catalytic activity |
| $\beta'$ | Beta' | For template binding |
| $\sigma$ | Sigma | For initiation (recognize promotor) |

## RNA POLYMERASES IN EUKARYOTES 44:34

| Eukaryotic RNA polymerase | RNA synthesized |
|---|---|
| Type I | All rRNA except 5s rRNA |
| Type II | mRNA, mi-RNA, inc-RNA, few snRNA and snoRNA |
| Type III | 5s rRNA, tRNA, few snRNA and snoRNA |
| Mitochondrial RNA Polymerase | Mitochondrial RNA |

- Template strand and non template strand
  - For transcription, the two strands are unwinded
  - Suppose, there is gene on strand one that will be template strand on which RNA will be synthesized
  - Template strand is also known as Antisense or non coding strand or minus strand
  - Strand number 2 is non template strand, it is coding strand because codons matches with RNA with difference bring U in RNA, T in DNA
  - Also called sense strand since same sense of direction as new RNA




## RIBOZYMES 47:14

- RNA acting as enzyme
- Ribozyme types:

Active Space

- 23s rRNA in prokaryotes
  28s rRNA in eukaryotes
  - Peptidyl transferase enzymatic activity
  - Involved in elongation and termination in translation
- Role in splicing – snRNA / small nuclear RNA
  - SnRNAs type – $U_1$, $U_2$, $U_4$, $U_5$, $U_6$
  - U is used because uracil rich
  - Help in splicing which is removal of introns
  - SnRNA + Proteins → SNRNPs / Small nuclear Ribo nucleo protein
- Ribonuclease P → Cleaves tRNA

Active Space

## CODONS 49:22

- Nucleotide triplets i.e., three bases make one codon
- Total 4 bases used to make codons – A U CG
- $4^3$ = 64 codons are possible

PYQ: if 4 bases make one codon then what combination is possible?
$4^4$ = 256 codons
Not possible, hypothetical question

- We have 64 codons
  - 3 out of these are stop codons
    - UAA
    - UAG
    - UGA
  - Stop codons means they won't code for amino acids
    - 61 codons for 20 amino acids
    - Each amino acid has roughly 3 codons
    - This property is called Degeneracy of codons / Redundancy
    - 2 amino acids do not show Degeneracy
      → Methionine, (only 1 codon: AUG)
      → Tryptophan

## TRANSLATION 51:40

- Activation of amino acid with tRNA
  - Then initiation of translation
  - Elongation
  - Translation termination
- In activation
  - Amino acid attached to tRNA
  - Enzyme involved is Amino acyl tRNA synthetase
  - 2ATP used
  - This enzyme is only point of proof reading in translation
  - Responsible for fidelity or accuracy of translation
  - The enzyme has 20 isoenzymes, one for each amino acids

## FACTORS IN TRANSLATION IN PROKARYOTES AND EUKARYOTES 53:29

MCQ – In translation, how many ATP, GTP used to add 1 amino acid in growing polypeptide chain?

- 2 ATP, 2 GTP
- 2 ATP in attachment of amino acid at tRNA – Activation of amino acid
- 2 GTP
  - 1 in elongation step for adding amino acid
  - 1 in translocation
- 4 high energy phosphates used

## CRISPR CAS – 9 SYNDROME 56:20

- Clustered regulatory interspersed short pallindromic repeats
- Cas 9 is Endonuclease enzyme and it cuts CRISPR associated sequences
- System is used to create double strand DNA breaks
- Now technology
- Cheap and easy method to create breaks in DNA
- CRISPR system is naturally present immune systems in bacteria against viruses – Bacteriophages saved as memory and passed to progeny
- System was used in Covid 19 testing:
  - FELUDA
  - FN Cas 0 Editor linked Uniform Detection array
  - Detects genomic sequence of SARS Covid virus
  - Accurate, quick round trip
  - Simple paper strip test

Active Space

PYQ: For genome editing, CRISPR which repair mechanism used?

→ Non homologous end joining repair

Active Space

## PCR / POLYMERASE CHAIN REACTION *01:00:58*

- This DNA amplification
- Components required in PCR:
  - Double stranded DNA to be amplified
  - 2 primer one for each strand
  - Enzyme Tag polymerase from Bacteria Thermos aquaticus
  - Substrate – Deoxyribonucleotides
  - Magnesium ions in a buffer medium
- High temperature required for DNA strand separation

## REAL TIME PCR / QUANTITATIVE PCR

- This tells quantity of DNA in real time
- Five original components + SYBR green dye as well
- SYBR green dye gives fluorescence when bound to ds DNA
- As ds DNA getting amplified and increasing. Fluorescence is also increasing and can be detected
- Quantity of DNA measured by machines

## RT – PCR *01:04:07*

- Reverse transcriptase PCR
- Helps amplify RNA
- First, RNA converted to DNA by Reverse transcriptase
  - The DNA is called cDNA or complimentary DNA
  - cDNA amplified using normal PCR that is Polymerase enzyme
  - cDNA by transcription converted to RNA which is abundant
- RT – PCR has enzyme 7$^{th}$ polymerase and it has activity of Reverse transcriptase enzyme and DNA polymerase as well

## GENOMIC IMPRINTING *01:05:20*

- In this gene is inhibited, so transcription or translates won't occur
- Most common method
  - DNA methylation at CG site will inhibit genes
- Other method, Histone post translational modifications like Histone methylation or Deacetylation
- DNA methylation affected by Sodium bisulfide method
- Post translational modification of histone detected by ChIP – Chromatin Immuno Precipitation
- Diseases due to genomic imprinting
  - Prader Willi Syndrome – Paternal allele of gene is detected and maternal allele imprinted
  - Angelman Syndrome – Maternal allele of gene is detected and paternal allele imprinted

## MICROARRAY *01:08:19*

- OR chip
- Small chip is there in this technique where lots of DNA sequences can be placed and multiple mutation can be detected
- Multiple gene expression analysis can be done as well
- Comparative genomic hybridization done
- Can also detect – SNIPS – Single Nucleotide is variable in different population i.e., Single nucleotide polymorphism
- Microarray cannot detect Aneuploidy
- Other methods

  Karyotyping best for detecting monosomy and trisomy
  - FISH can detect aneuploidy in any phase and also tells location of gene on chromosome, microdeletion, amplification, complex translocation

## MENDELIAN INHERITANCE DISORDERS *01:11:39*

- Single gene disorders
- AR, AD, XR, XD, Y linked disorders

- Autosomal dominant
  - Familial Hyper cholestrolemia

Active Space

- Autosomal Recessive (AR)
  - All mucopolysaccharidosis except Hunter
  - All urea cycle disorders except Ornithine Transcarbamylase deficiency
  - All sphingolipidoses except Fabry disease
  - All amino acid disorders
  - All glycogen storage disorders
  - Orotic aciduria
  - Willson's disease
  - ADA deficiency
  - Hemochromatosis
- X linked Recessive Disorders
  - Hunter's Disease
  - Fabry's Disease
  - Ornithine Transcarbamylase deficiency
  - Menke's Disease
  - Lysch Nyhan syndrome
  - G6PD deficiency

Active Space

## DETERMINE INHERITANCE PATTERN *01:14:19*

- Family history given and both male and female affected with equal frequency → Autosomal
- If at least one parent affected with disease → Dominant pattern
- Neither of parent has disease → Recessive pattern
- All sons and father affected - Y linked inheritance
- Mother affected and all offsprings affected → Mitochondrial inheritance
- No male - male transmission - X linked
- More males affected and affected sons born to unaffected mother → X linked Recessive inheritance

## KLENOW FRAGMENT *01:17:00*

- DNA polymerase 1 enzyme is involved in DNA replication
- It has 3 activities:
  - Primer removal activity
  - Synthetase activity
  - Proofreading activity

- We have Exonuclease activity on terminal side and other activities on carboxy terminal side
- With bacteria Bacillus subtills, there is toxin subtilisin that can cut so there is small fragment on left side and larger on right side which is Klenow fragment which is formed by removal of 5' – 3' exonuclease activity

Active Space

## SEVERITY OF DAMAGE IN POINT MUTATION

- Frameshift mutation more severe because the whole frame of codon shifted and many amino acids down the line can be changed
- In Frameshift mutation, nitrogenous bases are added or deleted which are not in multiple of 3 that's why codon shifted
- Non sense mutation – Some amino acid replaced by stop codon and early protein termination
- Missense mutation – One amino acid changed with another

# Miscellaneous

Active Space

## RESPIRATORY QUOTIENT 00:32

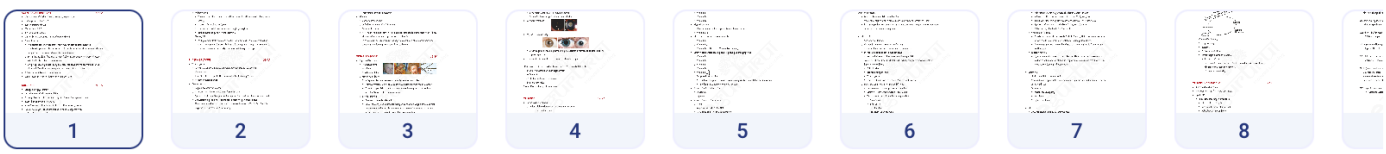
- RQ is amount of Carbon dioxide produced/oxygen used
- Carbohydrates → 6/6 = 1
- RQ for proteins → 0.8
- RQ for fats → 0.7
- RQ for alcohol → 0.66
- RQ for diet excess or rich in carbohydrate → > 1
- RQ in diabetes
  - In a normal person, in fed state, main fuel for body is carbohydrates
  - In a diabetic person, it is considered that body is in fasting state because cells are not getting glucose due to low or deficient insulin
  - So, in fasting state, fats are the main fuel, so RQ in diabetes decreases because RQ of fat is less than carbohydrates
  - On giving insulin, glucose will again enter into cells and the body will be in fed state and RQ will increase on giving insulin in a diabetic patient
- RQ decreases in Diabetes and Alkalosis
- RQ increases in Acidosis, during fever and exercise

## COLLAGEN 03:39

- Collagen is a glycoprotein
- Most abundant of all human proteins
- Primary structure of collagen is $(Gly\text{-}X\text{-}Y)_n$ repeated again and again
- Every third amino acid is Glycine
- X and Y can be proline, lysine, hydroxyproline, hydroxy lysine
- Types of collagen – There are around 28 and few important are:
  - Type 1 – Present in skin
  - Type 2 – Connective tissue
  - Type 3 – Arteries, CVS, healing and granulation tissue
  - Type 4 – Basement membrane of glomerulus in kidneys
- If Type 4 is defective – Alport Syndrome
  - Hematuria
  - If not treated, end state renal disease occurs
- Type 7
  - Present at junction of dermis and epidermis
  - Defect in Type 7 – Epidermolysis bullosa in which there are skin blisters







- Post Translational Modification of collagen
  - Hydroxylation
    - There are function of numerous collagen bonds in collagen making the protein strong
    - It occurs for proline and lysine
    - Enzymes are prolyl hydroxylase and lysyl hydroxylase
    - Both enzymes require iron and vitamin C
  - Glycosylation
    - Adding carbohydrate and on its addition, bond formed is Aldole condensation which is intramolecular cross links in collagen giving strength to the molecule
    - Enzyme responsible here is lysyl oxidase which requires copper

Active Space

## PLASMA PROTEINS *08:05*

- Transthyretin
  - Earlier named pre-albumin as it moved further ahead of Albumin in electrophoresis
  - Transthyretin transports Thyroxine and Retinal Binding Protein
  - Present in blood and CSF
- Ceruloplasmin
  - Helps in transport of copper
  - Its precursor - Apo ceruloplasmin formed in liver
  - Apo - ceruloplasmin then joins with 6 copper atoms and then forms ceruloplasmin
  - Ceruloplasmin goes into blood and takes copper to peripheral tissue
  - The enzyme also has ferroxidase activity where it converts $Fe^{+2}$ to $Fe^{+3}$. So, it is required for iron transport in the body.

## MENKE AND WILSON DISEASE *10:07*

- Menke's:
  - Copper deficiency in body
  - Deflective protein is ATP-7A protein
  - X linked Recessive
  - Protein that is deficient in Menke's disease is present in intestine for absorption of Cu
  - Copper absorption won't be done leading to copper deficiency
  - Ceruloplasmin is the protein that transports copper and it is formed in liver

- Ceruloplasmin will also be decreased because there is not enough copper to be incorporated into ceruloplasmin
- Wilson's:
  - Copper excess in body
  - Defective protein is ATP-7B protein
  - Autosomal recessive
  - ATP-7B protein is present in liver and is responsible to throw copper out of body via bile and incorporate copper into ceruloplasmin
  - In this disease, Cu will increase in body and copper won't be incorporated into ceruloplasmin, leading to decreased ceruloplasmin

Active Space

## MENKE'S DISEASE 13:10

- Signs and Symptoms:
  - Premature birth
  - Hypotonia
  - Growth retardation
  - Mental retardation

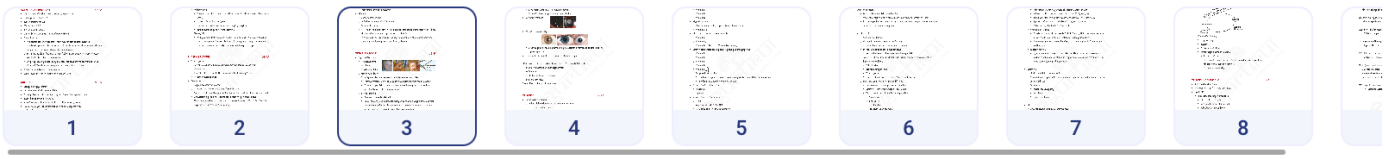

  - Grey Depigmented hair because enzyme Tyrosinase is affected
    - Enzyme tyrosinase is an oxidase and all oxidase enzymes require copper
    - There is copper deficiency in Menke's disease leading to tyrosinase being affected thus affecting pigment melanin
  - Brittle kinky hair
    - Because collagen is affected
    - One of the enzyme required for collagen synthesis is lysyl oxidase and that requires copper too but there is copper deficiency. So, enzyme not working properly and so not enough strength in protein collagen
    - Because of this, disease is AKA Menke's Kinky hair syndrome
  - There will be decreased copper in blood and urine

## WILSON'S DISEASE 15:15

- Increased copper in blood and urine
- Copper increased in:
  - Liver - leading to liver damage
  - From liver to extrahepatic tissues leading to this damage
  - Brain - neurological degeneration







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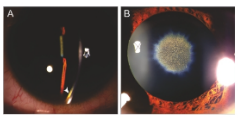
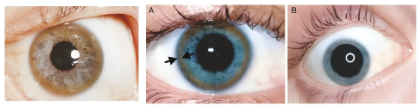
- Kidneys – Renal damage, urolithiasis
- Bone marrow and RBCs – Hemolytic anemia
- Eyes – Sunflower shaped cataracts and KF rings

- Sunflower cataract:



- Kayser – Fleischer Rings:



  - Green or golden brown pigmented ring in Descemet's membrane of cornea, due to copper deposition
- Treatment – Rx Penicillamine because it chelates copper

MCQ: in which of the following disorder, ATP 7A protein is deficient?

a) Wilson's hepatolenticular degeneration
b) Selenosis
c) Menke's kinky hair syndrome
d) Bronze Diabetes

Ans: c) Menke's kinky hair syndrome

## VITAMINS *17:32*

- Water soluble vitamins
  - Water soluble vitamins act as coenzymes in body
    - They are not stored in body
    - Exception is Vitamin B12 that is stored in body in liver
- Fat soluble vitamins
  - Vitamin A, D, E, K
  - They are stored in body
  - They can have toxic effects as well if they are taken in excess
  - They don't act as coenzymes with one exception Vitamin K which is a fat soluble vitamin which act as coenzyme in the body
  - Vitamin K is a fat soluble vitamin which has a water soluble form that is menadione also called Vitamin $K_3$ and is a synthetic form
- Vitamins synthesized by intestinal bacterial flora

- Vitamin $B_2$
- Vitamin $B_5$
- Vitamin $B_7$
- Vitamin K

- Atypical vitamins
  - Those vitamins that are synthesized by human enzymes
  - Vitamin D, $B_3$
- Vitamins not present in vegetarian diet
  - Vitamin D
  - Vitamin $B_{12}$
  - Vitamin $B_{12}$ deficiency > Vitamin D deficiency
- Vitamin deficiencies causing neurological signs and symptoms
  - Vitamin $B_1$
  - Vitamin $B_3$
  - Vitamin $B_6$
  - Vitamin $B_{12}$
  - Vitamin E

  Peripheral neuropathy:
  - Can be distinguished because $B_{12}$ deficiency will have megaloblastic anemia too
  - In vitamin E deficiency, Hemolysis present
- Site of vitamin B9 absorption
  - Duodenum
  - Jejunum
- Site of vitamin B12 absorption
  - Ileum
  - Requires Intrinsic Factor (IF)
  - Deficiency of IF → Pernicious Anemia
- Vitamin deficiency anemias
  - Microcytic Hypochromic Anemia
    - Due to Vitamin C deficiency or Vitamin $B_6$ deficiency
    - Vitamin C required for iron absorption
    - Vitamin $B_6$ is coenzyme for rate limiting step of heme synthesis – ALA synthase
  - Megaloblastic Anemia
    - Due to vitamin $B_9$ or $B_{12}$ deficiency
    - No neurological symptoms in $B_9$ deficiency but peripheral neuropathy which is progressive and found in $B_{12}$ deficiency

Active Space

PYQ: A person consumes raw eggs and one day he fell unconscious due to hypoglycemia. What is the reason?

- Raw eggs have a protein named Avidin
- Avidin binds tightly with Vitamin $B_7$ and won't allow absorption of Biotin
- $B_7$ is an important coenzyme for carboxylase enzymes and pyruvate carboxylase is the first step in gluconeogenesis

Active Space

- Vitamin A
  - Active form – Retinal
  - Absorbed from intestine in form of retinal
  - It reaches liver and stored in form of retinal esters
  - Stored in bio cells or peri sinusoidal cells
  - In liver, retinol esters joined to retinol binding protein
  - From liver, it goes into circulation and Ternary complex is formed so three things are joined here
    - Retinal ester
    - Retinol binding protein
    - Transthyretin
    - This complex is made so Vitamin A is not lost in urine
  - Signs and symptoms in Vitamin A deficiency
    - Most common cause of preventable blindness
    - Vitamin A is involved in Wald's Visual Cycle
    - First, there is loss of sensitivity to green light
      - Night blindness
      - Bitot spots
      - Keratomalacia
      - Follicular Hyperkeratosis
      - Corneal ulceration
      - Xeropthalmia
      - Immunosuppression
  - Excess Vitamin A – Vitamin A toxicity
    - Causes pseudotumour cerebri
    - A condition that resembles brain tumour and there is increased intracranial tension and headache

- Vitamin D
  - Synthesis of Vitamin D occurs in body

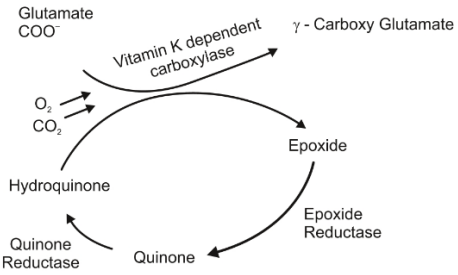
Active Space

- Organs involved are skin, liver and kidneys
- With help of UV rays, synthesis of Vitamin D starts in skin
- In liver, reaction occurs with help of enzyme 25, Hydroxylase
- In kidneys, rate limiting step occurs with enzyme 1-$\alpha$-Hydroxylase
- Synthesis of Vitamin D starts from 7-dihydrocholesterol
- Active moiety of Vitamin D - Calcitriol

- Vitamin D deficiency
  - Rickets in children where there is Rachitic Rossery, Hot cross bun appearance of head due to non-closure of fontanelle, Bow legs knock knees
  - Osteomalacia in adults where they have soft bones leading to fractures and Waddling gait
- Excess Vitamin D
  - Hypervitaminosis D in which the patient has Hypercalcemia, Hypercalciuria leading to Renal calcium stones and deposition of calcium in soft tissues like blood vessels leading to hypertension

- Vitamin E
  - Most potent lipid phase antioxidant
  - Vitamin E works synergistically with selenium, glutathione and Vitamin C for its antioxidant role
  - Deficiency:
    - Peripheral neuropathy
    - Hemolysis
    - Ophthalmoplegia

- Vitamin K
  - Only fat soluble which has coenzyme role
  - It has coenzyme role in activation of clotting factors 2, 7, 9, 10
  - These clotting factors have glutamate in them
  - Vitamin K will do more carboxylation of these glutamate residues in clotting proteins making $\gamma$-carboxy glutamate
    - Vitamin K helps there so hydroquinone is active form of Vitamin K involved and gets converted to Epoxide form of Vitamin K
    - Epoxide form is converted to Quinone form by adding one Hydrogen to Epoxide
    - Adding another hydrogen to Quinone makes Hydroquinone




- Vitamin K deficiency
  - Easy bruising
  - Bleeding
  - ↑ Prothrombin time
  - Hemorrhagic disease of newborn
    - Preterm infants >
    - Because intestinal system is sterile and no bacteria to synthesize
      → Breast milk poor in Vitamin K
      → Hepatic immaturity

## VITAMIN C DEFICIENCY *33:49*

- Increased bleeding time
- Diet poor in citrus fruits and vegetables
- Cyclic GMP:
  - Is a second messenger involved in:
    - Vitamin A visual cycle
    - Nitric oxide vasodilatory effect
    - Activation of ANP and BNP

Q1: Corneal transparency is due to which Glycosaminoglycan (GAG)?
→ Keratan sulfate

Q2: Which lipid deficiency causes Retinitis Pigmentosa?
→ DHA

Q3: Apo $B_{48}$ is synthesized from Apo B 100 gms in intestine and this formed due to?
→ RNA editing which is a post transcriptional modification

Active Space

Q4: HbA1C, best method of detecting it?
→ Ion exchange chromatography

Q5: Best investigation for any inborn error of metabolism?
→ Mass spectrometry

Q6: When is buffer most effective?
→ When pH = pKa

Q7: Maximum buffering range?
→ pH = pKa ± 1

Q8: Minimum buffering is at which point?
→ When pH = Isoelectric pH

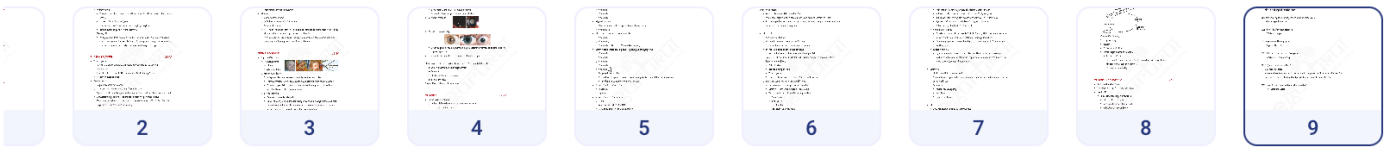
Q9: Major extracellular buffer?
Bicarbonate buffer
Also considered an ideal buffer because both components of bicarbonate buffer. Can be affected for maintaining blood pH which is why considered ideal buffer

Q10: Major intracellular buffer / urinary buffer?
→ Phosphate buffer

Active Space







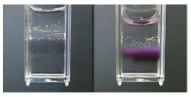
# Image Based Discussion

Active Space

## TEST TUBES

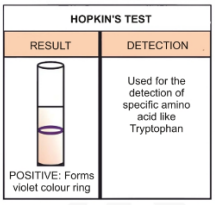
00:42

- Molisch Test
  - It is a general test for all carbohydrates
  - But no. of carbons must be 5 or more
  - So, a 3 carbon or 4 carbon carbohydrate will not give a positive Molisch test
  - The positive test is a purple coloured ring at junction of two liquids



- Rothera's Test
  - Rothera's test is for Ketone bodies
  - We have a purple coloured ring


- Hopkin's Test
  - This is for detection of specific amino acid Tryptophan
  - It also gives a purple ring at junction of two liquids




- Biuret Test
  - It is a purple coloured solution which is a positive test
  - It is for proteins and peptides
  - Free amino acids or dipeptide will not give Biuret test positive
  - Because in Biuret test, minimum two peptide compounds to give a positive test and these are present in Tripeptide and other higher proteins and peptides

- Ninhydrin Test
  - It is for $\alpha$-Amino acids
  - It is not positive for Proline and Hydroxyproline

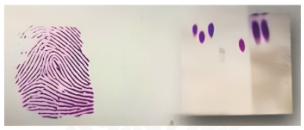
- Ninhydrin Test
  - Used for painting fingerprints





Active Space

- A ninhydrin spray is available and we spray this on the person's fingers or hands and a fingerprint is obtained
- The reaction occurs as follows:
  - Ninhydrin spray contains ninhydrin reagent
  - In our fingers, there is sweat
  - Sweat has amino acid
  - Free amino acid will react with ninhydrin reagent to give this purple colour and that gives us fingerprints



- Also used in paper Chromatography
  - Thin layer of silica and there are purple stains
  - Amino acids are applied on the paper on bottom
  - During chromatography process, amino acids move upward
  - It can be interpreted in various ways

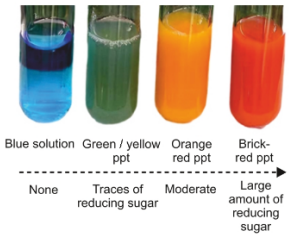
- Million's Test
  - Used for Tyrosine (Aromatic Amino Acid)

- Pauly's Test
  - Gives red colour
  - This is positive for Tyrosine and Histidine

- Sakaguchi Test
  - This for Arginine (Basic amino acids)

- Benedict Test
  - Gives positive for Reducing sugars
  - All monosaccharides are reducing in nature like Glucose, galactose, fructose
  - Some disaccharides are reducing in nature like maltose, isomaltose and lactose
  - Benedict test is also called a semi quantitative test because it gives various colours and the colours tell the amount of sugar present in the sample
    - In the first test tube the Benedict sample is blue in colour
    - But after boiling it blue remains blue means negative and no sugar present
    - Look at colour spectrum

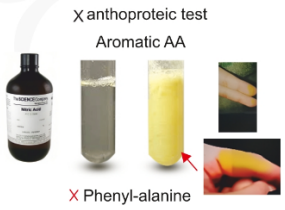
- V X } Not needed
- I X }
- Blue means negative
- Green means ⊕
- Yellow means ⊕ ⊕
- Orange means ⊕ ⊕ ⊕
- Red means ⊕ ⊕ ⊕ ⊕




- This means the amount of sugar is increasing as colour is increasing in colour spectrum range

- Non sugar substances that give Benedict test positive
  - Because these substances are reducing in nature
  - These substances are:
    - Uric acid
    - Ascorbic acid
    - Homogentisic acid
    - Salicylates eg. Aspirin
    - Glutathione
    - Creatinine

- Nitric Acid
  - Hands turn yellow when handling nitric acid because of Xanthoproteic Reaction occurring
  - Xanthoproteic test gives yellow colour
  - It is for aromatic amino acids
  - All Aromatic amino acids give positive except phenyl alanine



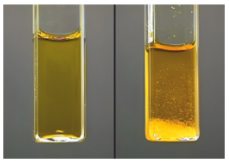

- DNPH / Dinitro Phenyl Hydrazine Test
  - Positive test is orange / yellow crystalline derivatives
  - This test is done for diagnosis of phenylketonuria and Maple Syrup Urine Disease
  - The test defects $\alpha$-Keto acid in urine
  - In Phenylketonuria, $\alpha$ keto acid in urine is Phenyl pyruvate

Active Space

Active Space

- In MSUD, $\alpha$ keto acid in urine is alpha keto acids

Orange/yellow crystalline derivatives



a negative test (left) and a positive test (right)

Which is the biochemical method of Blood Glucose Estimation?

- Inside the glucometer, the test happening is GOD – POD enzymatic method
- GOD stands for Glucose oxidase
- POD stands for Peroxidase

- Cyanide Nitroprusside Test (CNT)
  - Positive test is magenta colour
  - This test is positive for any substance containing Sulfhydryl group or disulfide bond
  - For Ex. Cysteine, Cystine, Homocysteine, Homocystines
    - Cystine has disulfide bond
    - Cysteine or Homocysteine, there is sulfhydryl group
  - This test will be positive in Homocystinuria, Cystinuria and Cystinosis

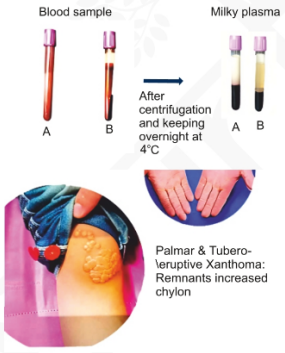

- Sulfur Test
  - It has sulfur containing amino acid
  - The positive colour is black or brown colour
  - There are two sulfur containing amino acids – Cysteine and Methionine
  - Sulfur test is positive for cysteine but not for methionine because sulfur is attached to two carbons and is not exposed outside so the sulfur is not easily released and methionine will not give sulfur test

- Heat Coagulation Test
  - Method: Protein solution is taken and filled in 2/3rd of tube
  - It is boiled and heated
  - Proteins are coagulated

Active Space

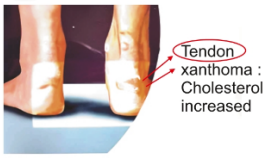
## MILKY PLASMA 15:50

- Blood sample when taken from the patient is red in colour
- After centrifugation, to check if patient has milky plasma we have to keep sample overnight at 4° C
- In the morning, milky plasma seen also called Lipemic plasma
- It interprets that chylomicrons have floated to the top and formed a creamy layer
- Hyperlipoproteinemia:
  - Palmar and Tubero eruptive Xanthoma: These occur when remnants are increase which are Chylomicron remnant and VLDL remnant / IDL




## TENDON XANTHOMA 18:03

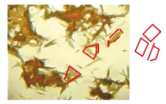
- It means Cholesterol is increased




## OSAZONES 18:13

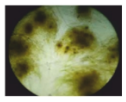
- Only reducing sugar will make crystals or osazones which can be seen under microscope

- Needle shaped
  - Or broomstick appearance
  - Occurs in case of glucose, fructose and mannose
- Galactosazone
  - They will be Rhombic plate like
- Maltasazone
  - These are typical yellow or black colour sunflower shaped typically
- Lactose
  - It is hedgehog or powder puff shaped



Galactosazone crystals as viewed under the microscope (Rhombic plates)

Sun flower shaped Maltosazone crystals as viewed under the microscope

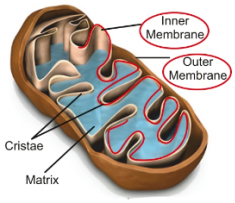



Powder puff/hedge hog shaped crystals of loctose as viewed under the microscope

Needle shaped glucosazone crystals as viewed under the microscope

## ORGANELLES 19:57

- Mitochondria
  - In mitochondria, all catabolic pathways occur except Glycolysis and Glycogenolysis
    - Vital pathways - TCA, ETC
    - Replication, transcription and translation of mitochondrial DNA
    - Activation of Apoptosis



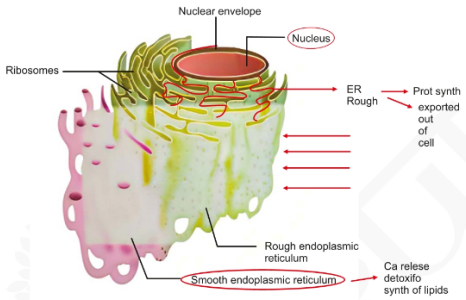

  - 3 pathways occur both in mitochondria and cytoplasm and they all start from mitochondria
    - Urea cycle
    - Heme synthesis
    - Gluconeogenesis

- Nucleus
  - There is a nuclear envelope
  - Continuation of nuclear envelope is Endoplasmic reticulum

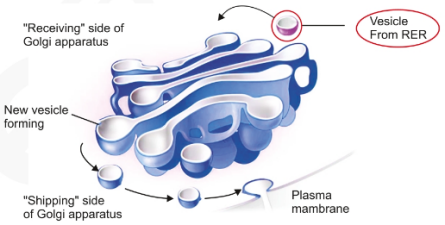
**Active Space**

Active Space

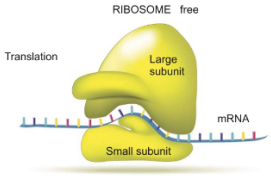
- When we have large number of chromosomes attached, then it is Rough Endoplasmic Reticulum. When protein synthesis occurs and proteins which are to be exported out of the cell
- Smooth ER when no ribosomes are attached and it is involved in:
  - Detoxification
  - Synthesis of lipids
  - Calcium release and
  - Sequestration




- Golgi apparatus
  - This receives proteins from Endoplasmic reticulum and mainly Rough Endoplasmic Reticulum
  - When vesicle is formed, this protein needs to be exported out of cell and 1st it will come to Golgi apparatus
  - On sides of Golgi apparatus, vesicles are getting formed
  - These vesicles will go towards plasma membrane and this side is known as shipping side




- Ribosome
  - Free ribosome function is to synthesize those proteins that are inside the cell in cell metabolism



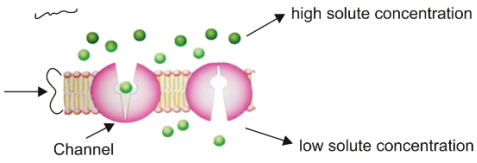



Pinch to zoom

## CELL MEMBRANE TRANSPORT

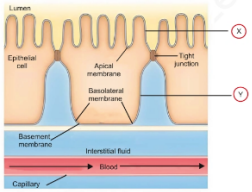
24:58

Active Space

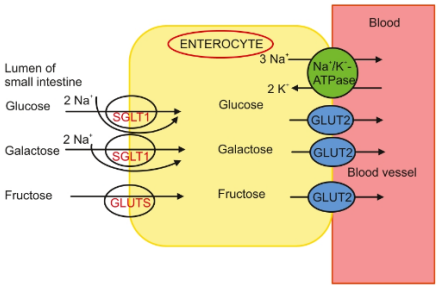



- The work of transporter or channel is to take solute from area of higher concentration to area of lower concentration
- Mechanism followed is ping pong mechanism
- This basically means the protein can change its structure
- In Image A, opening of channel is towards the Higher concentration side and one solute comes and gets attached here, then the protein changes its combination and the side closes from other side to open and released
- Ping pong mechanism is followed in → Glucose transporters, GLUTs

- Intestinal cell
  - Which transporter is present at position X and Y?
    - At apical side, transporter is SGLT-1 and that is Sodium dependent glucose transporter – 1
    - At Basolateral side, it is GLUT-2 present



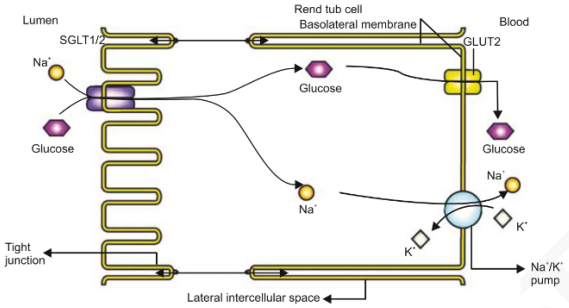

- Enterocyte cell
  - In enterocyte
  - There is lumen side where there is SGLT-1 and it transport sodium and via this transporter both glucose and galactose transported
  - There is GLUT-5 for fructose transport
  - On basolateral side, GLUT-2 is present which can transport glucose, galactose and fructose
  - At basolateral side, there is sodium potassium pump too which transports 2 sodium out of cell and 3 sodium inside the cell





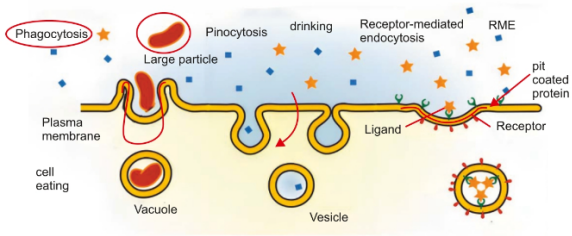

Pinch to zoom

- Renal tubular cell
  - On lumen side, SGLT-1 and SGLT-2
  - On basolateral side, sodium potassium ATPase pump
  - On blood side, GLUT-2




## PHAGOCYTOSIS 28:53

- Phagocytosis is cell eating, some solid particle when taken inside cell via cytosis of plasma membrane
- Pinocytosis is cell drinking when some solute or liquid when taken inside the cell
- Receptor mediated endocytosis where there is a pit in the membrane is coated by special protein CLATHRIN
  Eg: LDL Receptors on liver cells and they will uptake LDL from blood via Receptor Mediated Endocytosis




## UNIPORT, SYMPORT, ANTIPORT 30:20

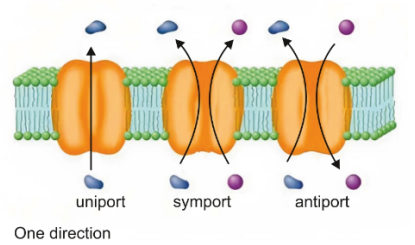
- Uniport means only in one direction and only one substance is taken from one side of membrane to other
- Symport and Antiport are co-transport methods which means two molecules are transported together
- In symport, both molecules are going in same direction
- In antiport, two molecules are going in opposite direction

Active Space



Pinch to zoom

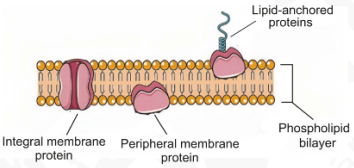
Active Space



One direction

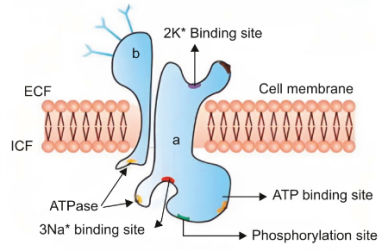
## LIPID BILAYER MEMBRANE 31:05

- Proteins in lipid bilayer membrane
- Integral membrane protein covers entire length of membrane
  Eg: Sodium Potassium ATPase pump
- Peripheral membrane proteins and that is outside of the cell
- Lipid anchored proteins and are G-proteins and there are anchored within cell membrane via lipid that is phosphatidyl inositol



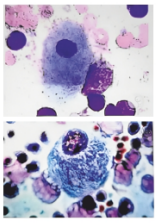

## SODIUM POTASSIUM ATPASE PUMP 32:00

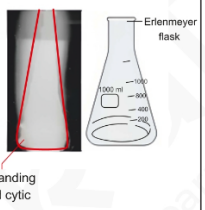
- It has two subunits – $\alpha$ and $\beta$
- $\alpha$ is main subunit
- $\beta$ is for anchoring this protein in membrane
- $\alpha$ portion has
  - Sodium binding site
  - Potassium binding site
  - Phosphorylation site
  - ATP binding site
- $\beta$ subunit has Glycosylation sites on it towards outside of membrane



## GAUCHER'S CELL / DISEASE *33:00*

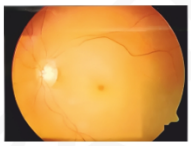
- Most common lysosomal storage disease
- Peculiar feature - Crumpled tissue paper appearance of Gaucher cell
- Patient has:
  - Hepatosplenomegaly
  - Bony pain and pathological fracture
  - Pancytopenia
  - Thrombocytopenia (Easy bruising)
  - X-Ray long bones:
    - Evlenmeyer flask deformity
    - Because end of long bones are expanding and cytic
    - Because Gaucher's disease is a sphingolipidosis
  - No mental retardation
  - No cherry red spots





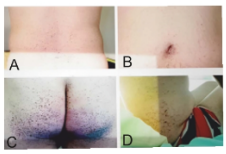

## MACULAR CHERRY RED SPOT *34:48*

- All sphingolipidoses have cherry red spot except Tabry's and Gaucher's Disease



## ANGIOKERATOMA *35:00*

- Benign cutaneous lesions of capillaries
- It results in small masks of red to blue colour
- Characterized by hyperkeratosis
- Found in Fabry's disease and GM1 Gangliosidoses




## FARBER'S DISEASE *35:46*

- Sphingolipidoses resembling Rheumatoid arthritis

Active Space



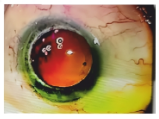
Pinch to zoom

Active Space

## CALCIFICATION OF ADRENALS IN WOLMAN'S DISEASE *36:15*

- Lysosomal storage disease
- Not a sphingolipidoses
- Lipids are getting accumulated in this disease
- Enzyme deficient is Lysosomal acid lipase
- Clinical features:
  - Watery green diarrhoea
  - Vomiting, failure to thrive
  - Hepatosplenomegaly
- Also known as cholesterol ester storage disease

## CATARACTS *36:56*



- Snow flake cataracts
  - Diabetes
  - Due to excess of Alcohol sorbitol
- Oil drop cataract
  - Galactosemias
  - Excess of alcohol Galactitol or Dulcitol
- Sunflower cataract
  - Wilson's disease

## LESCH NHYAN SYNDROME *37:38*

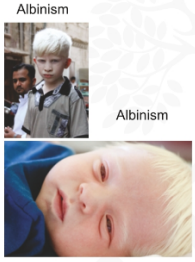
- Self mutilation by patient – Neuro psychiatric symptom
- Enzyme Hypoxanthine Guanine Phospho Ribosyl Transferase affected
- Patients also have gout

## ALKAPTONURIA *38:18*

- Urine turns black in colour on standing
- It is due to oxidation of homogentisic acid
- Discoloration of ear cartilage
- Bluish discoloration of sclera
- Bluish spots on eyes
- Damage to calcification of intervertebral disc
- Chronic back pain
- Bluish black discoloration of skin


## ALBINISM *39:07*

- Patients have milky white skin due to Tyrosine deficiency
- Tyrosinase helps in formation of melanin pigment
- If patchy skin then vitiligo




## PHENYLKETONURIA *39:49*

- In this amino acid Phenyl alanine cannot form Tyrosine so that cannot form pigment melanin
- Patients have:
  - Mental retardation
  - Hypopigmentation
  - Bluish sclera


## HOMOCYSTINURIA *40:32*

- Patients have:
  - Dislocated lens
  - Genu valgum
  - Short stature
  - Peches carinatum

Active Space

- Osteoporosis
- Patients can have myocardial infection, stroke and vascular diseases

Active Space

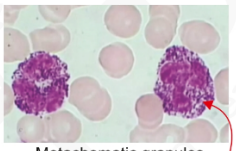
## MUCOPOLYSACCHARIDOSIS 41:09

- Hurter Disease – Type 1 polysaccharidosis
- Hunter Disease – Type 2 polysaccharidosis
- Hurler Disease
  - Corneal clouding
  - Coarse facial features
  - Mucinous discharge
  - Bullet shaped phalanges
- Hunter Disease
  - Clear vision
- Mucopolysaccharidosis have Broad and Proximally shaped metacarpals and Bullet shaped phalanges
- Mucopolysaccharidosis have Reilly body inclusions and these are large coarse purple granules in neutrophils
- Found mainly in Type 1 / Hurter's Disease


Hurler's disease


Hunter's disease




Metachomatic granules surrounded by a clear zone

Reilly body inclusions

## ZELLWEGER SYNDROME 42:40

- Child has:
  - Up standing eyes
  - High forehead
  - Skin folds along nasal borders
- It is most severe peroxisomal biogenesis disorder where there are empty paroxysomes also known as Ghost perioxisomes

## VON GIERKE'S DISEASE 43:20

- It is Type 1 Glycogen storage disease
- Most common Glycogen storage disease in children
- Doll like facies due to:
  - Hypolipidemia
  - Hepatomegaly
  - Lactic acidosis

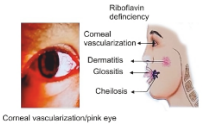
- Hyperuricemia
- Hypoglycemia

Active Space

## VITAMIN B2 DEFICIENCY 43:56

- Riboflavinosis
- Patient has:
  - Magenta tongue / glossitis
  - Corneal vascularization / Pink eye
  - Inflammation of corners of mouth

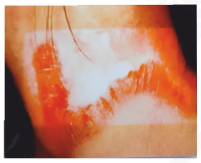
Glossitis/magenta tongue



Corneal vascularization/pink eye

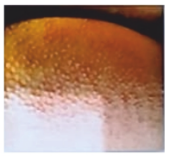
## CASHL'S NECKLASE 44:28

- Dermatitis occurring in Pellagra / $B_3$ deficiency
- Photosensitive Dermatitis


Casal's necklace

## VITAMIN A DEFICIENCY 45:10

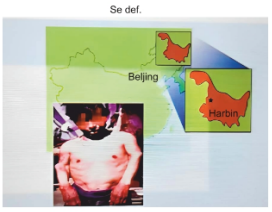
- Bitot spots are seen which is superficial deposition of keratin in conjunctive
- Follicular Hyperkeratosis

## KESHAN'S DISEASE 45:32

- Selenium deficiency
- Mainly affects children and women of child bearing age
- Patients have: Cardiomyopathy, muscle weakness, muscular dystrophies, inability to gain weight, Hypothyroidism, Hypertension, eczema, arthritis
- Selenium poor soil corelates with high incidence of cancer

- Selenium required for enzyme Glutathione peroxidase that helps destroy free radicals




## WILSON'S DISEASE 46:40

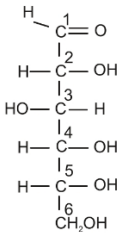
- Golden brown pigmented ring in Descemet's membrane of cornea
- Because of excess copper in body


## MENKES DISEASE 47:06

- There is copper deficiency
- Light hair and skin colour
- Mental retardation
- Hypopigmentation is because copper required for enzyme tyrosine and it makes melanin

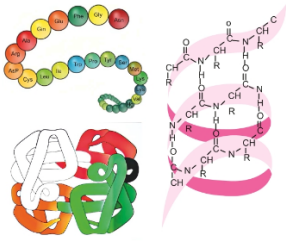

## GLUCOSE 47:46

- Six carbon sugar
- Aldehyde sugar
- 1st carbon – Aldehyde CHO
- Terminal carbon – $CH_2OH$
- All other carbons
  - H on left side
  - OH on right side
- At $C_3$ – OH on left hand side



Active Space

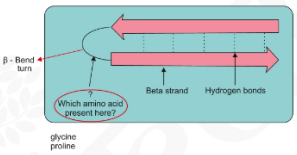
## PROTEIN STRUCTURE 48:36



- All amino acids in sequence – Primary structure
- $\alpha$-Helix – Secondary structure
- Four folded polypeptides – Quaternary structure
- Single fully folded polypeptide chain – Tertiary structure

## $\beta$-BEND 49:18

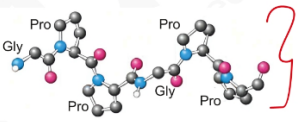
Which amino acid present mostly at beta bond?




- Glycine and proline
- Usually no. of amino acids present there are four

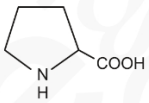
## COLLAGEN 49:42

- Many glycine and proline proteins are present here
- In primary structure of collagen every 3rd amino acid is glycine
- Primary structure is (glycine – X – Y)$_n$

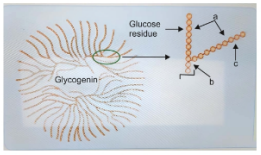



## PROLINE 50:13

- It is a secondary amino acid




## GLUCOSE RESIDUES 50:51




- Central portion of glycogen and surrounding it are glucose residues
- Which bond is present at point A, B, C?
  - At Point A, it is linear structure and that is $\alpha$(1-4) bond
  - Point C is also linear structure and that is $\alpha$(1-4) bond
  - Point B is branch point and that is $\alpha$(1-6)

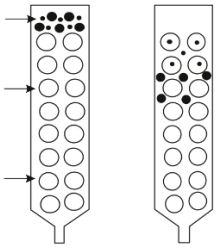
Active Space



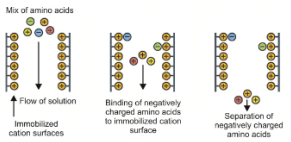
Pinch to zoom

## CHROMATOGRAPH AND ELECTROPHORESIS 51:35

- Gel Filtration / Size Exclusion Chromatograph
  - There are larger and bigger molecules going down in this column
  - Gel filtration type of column chromatography
  - The bigger proteins are quickly going downwards while smaller protein are entering gel and going downward slowly

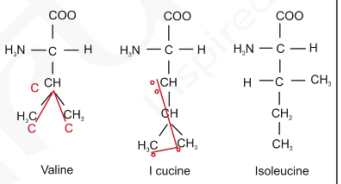


- Ion Exchange Chromatography
  - A column where positive ion is attached to the column and mixture of positive and negative amino acids going down
  - Negative amino acid is attached to column and positive amino acids are put out

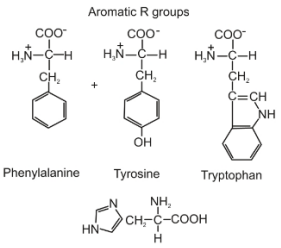



## AMINO ACIDS 53:00

- Valine, Leucine, Isoleucine
  - Valine, leucine, isoleucine have a common group on top
  - Valine forms V
  - Leucine forms an L shape
  - Isoleucine has same number of carbons as leucine but position different




- Aromatic Amino Acids
  - Phenylalanine has a phenylalanine ring and a carbon
  - Tyrosine has OH added to structure of phenylalanine
  - Tryptophan – there are two rings which are indole ring or nucleus
  - Histidine having side chain, one carbon and a ring inside chain and there are 2 nitrogens in the ring that is imidazole ring




- Aspartate, Glutamate, Asparagine, glutamine
  - Asparagine and glutamine, $NH_2$ group added
  - There are 4 carbons in Aspartate and asparagine

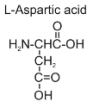
Active Space



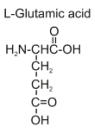
Pinch to zoom

- 5 carbons in glutamate and glutamine

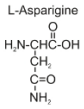
L-Aspartic acid



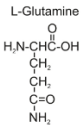
L-Glutamic acid



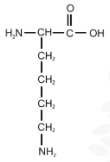
L-Asparigine



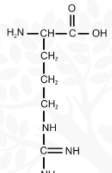
L-Glutamine



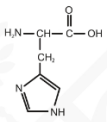
- Glycine, Arginine
  - Glycine after basic structure has 4 carbons and 1 amino group
  - Arginine has 8 carbons and a guanidino group which has central each on with 3 nitrogens



Lysine



Arginine



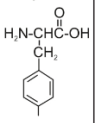
Histidine

- Serine, Threonine
  - Serine, after basic structure there is $CH_2OH$
  - Threonine, there are 2 carbons and 1 OH

L-Serine

L-Threonine

L-Tyrosine

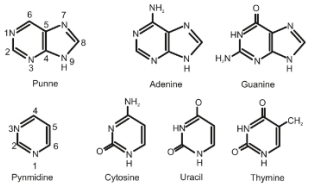


## N – BASE STRUCTURES

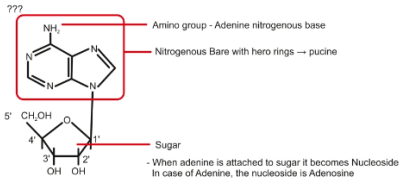
56:00

- Purine, pyrimidine structures
- Purine has 2 rings
- 2 rings + amino group on top - Adenine
- 2 rings + amino group with oxygen - Guanine
- Pyrimide, one ring
- Cytosine, one amino group present
- Uracil, no amino and no methyl present
- Thymine is matching with methyl

N-base structures




What is this structure?




Active Space

## KARYOTYPE

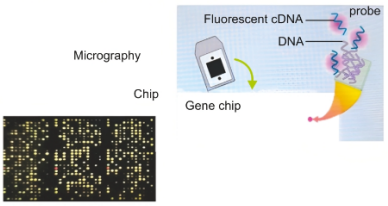
57:59

- It is karyotype where all 23 pairs of chromosomes are shown
- Best for detecting monosomy and trisomy

## MICROGRAPHY

58:24

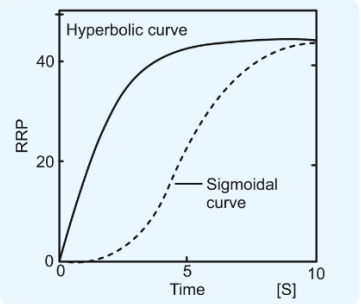
- Also called gene chip
- Patient's DNA and fluorescent complimentary DNA is probe
- On a chip, we can have loads of materials
- 1st probe is placed on chip and minimal amount of sample added and multiple mutations can be detected




## GRAPH BETWEEN SUBSTRATE CONCENTRATION AND VELOCITY

59:16

- Rectangular hyperbola graph for simple enzymes
- Sigmoidal graph for Halosteric or Regulatory enzymes




Active Space