India Connecting Continents (ICC)

Study materials for FMGE

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BIOCHEMISTRY

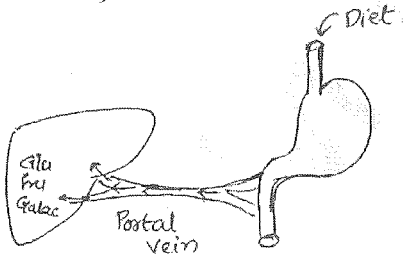
CARBOHYDRATE METABOLISM

Maltose - rice, wheat, veg, fruits.
Sucrose - in sweets.
Milk - Lactose

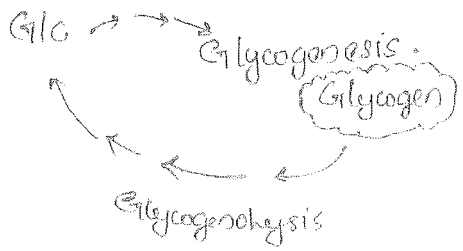
Maltose = Glucose + Glu
Sucrose = Glu + Fructose
Lactose = Glu + Galactose
(Disaccaride, Monosaccharide, Monosaccharide)

Enzyme
Maltose → Maltase.
Sucrose → Invertase
Lactose → Lactase

Q. End product of digestn of carbohydrates:
- Large amount of Glu
- Galactose, fructose, - Little.

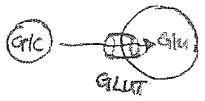


Liver monitor - blood glu level.
Additional Glc can't be stored as Glc → so converted into Glycogen
Glycogen - stored form of Glc.



Glycogenesis
Glycogenolysis } In Liver.

Glc → Blood → cell → Energy.
Glc can't enter cell directly ∴ A transporter - GLUT
(Glucose Transporter)



Glucose Transporters

Name	Location	Feature
• GLUT-1	Brain & RBC's specially	• Basal uptake of glc.
• GLUT-3		

They have the ability to attract the glc even in hypoglycemic state
↳ Basal uptake of glc.

$K_m \propto \frac{1}{\text{Affinity}}$ Km = Michaeli's Menten Constant.

- GLUT-1, GLUT-3 have ~~high~~ low Km, ie high affinity.

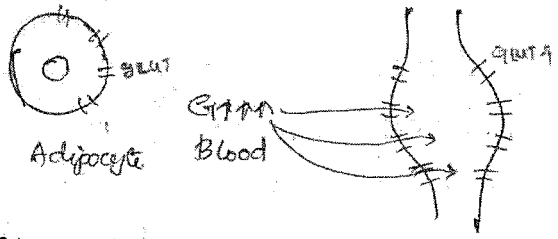
GLUT-2 • Liver
• β cells of Pancreas
• kidney

Allows both entery and release of glucose.
For GLUT-2 (eg: Liver)
• high Km
Low Affinity

In Liver cell, low affinity to attract Glc bcoz ↑ glc in blood : Affi ↓.
∴ ↑ Km.

GLUT-4 Skeletal Mb, Adipocyte, Heart
* Insulin dependent transporter
Km value moderate

After food → ↑↑↑ Glc in blood → Insulin released from Pancreas (Brain)

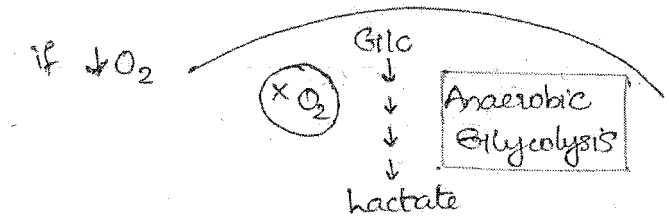


↑↑↑ Glc in blood
→ Insulin released
it uses GLUT-4 in
Adipocyte surface, ske M surface
Glc → move to Adipocyte, ske. M.
thus ↓ Glc in blood.
∴ GLUT-4 : Insulin dep Transporter.

Insulin act on SIM
GLUT-4 ↑↑
Glc to SIM
↓ Glc in blood.

***
* GLUT-5 Spermatozoa ★ Transport Fructose
Testes
Intestine

GLUT-7 Endoplasmic Reticulum



Lactic acid → Lactate (solid)

- No further metabolism for LACTATE.
- Lactate get accumulated → Lactic acidosis : Muscle weakness, fatigue

If hypoxia → anaerobic glycolysis
→ Lactate accumulate →
Lactic Acidosis. (Metabolic Acidosis)

Basics

1. Oxidation : ↑ in oxidation no:
   addition of O_2
   Removal of H_2
   Removal of e^-

eg : Fe — Fe^{2+} ferrous
Fe^{3+} ferric

* $Fe^{2+} \rightarrow Fe^{3+}$. (in ferrous metabolism)
oxidation rn.

I^- - Iodide ion

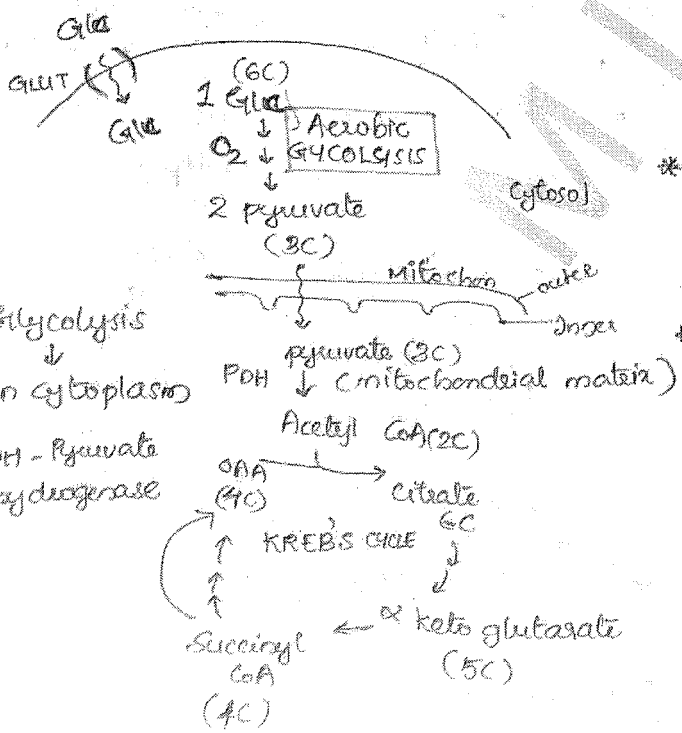
* $I^{-1} \rightarrow I^{0}$ (Thyroid hormone products)
Iodide ion — Iodine (Atoms - neutral)
oxidation

Substrate —oxidn→ pdt.
(removal of H_2)
$-H_2$

if H_2 removed → H_2 accepted by
NAD^+, FAD^+
{Hydrogen acceptors} NAD^+, FAD^+

NAD^+ Nicotinamide Adenyl dinucleotide → $NADH + H^+$
FAD^+ → $FADH_2$
(Flavin adenine dinucleotide)

***
* Overview



Glycolysis
↓
in cytoplasm

PDH - Pyruvate dehydrogenase

* Pyruvate to Acetyl CoA - Cytosol
Mitochondrial Matrix

* Glcn → pyruvate - Cytosol
3 Steps for complete Glcn metabolism
1) Aerobic glycolysis 2) Pyru → Acetyl CoA 3) Krebs cycle.

$NADH + H^+$
$FADH_2$
↓ Electron transport chain
(ATP)

* Oxidation – dehydrogenase enzyme

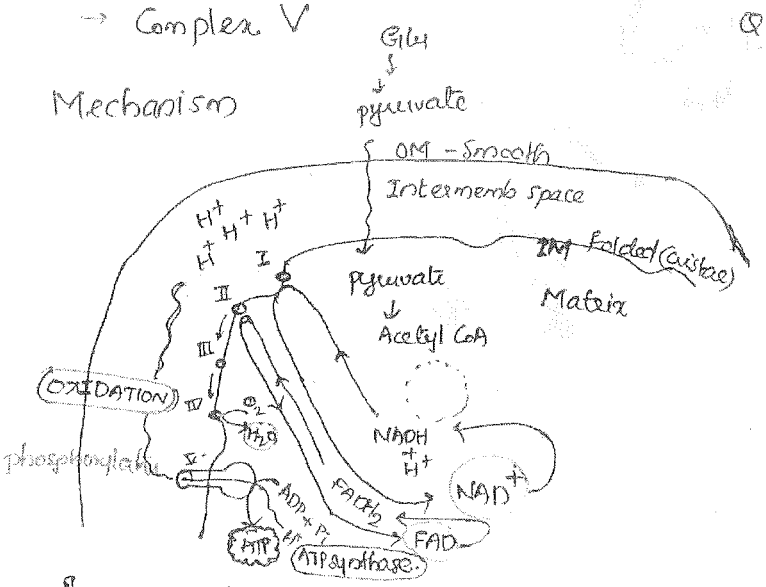
Electron Transport Chain (ETC)

* Site : Inner Membrane of Mitochondria

It consist of 5 protein complex.

→ Complex I
→ Complex II
→ Complex III
→ Complex IV
→ Complex V

Mechanism



Inner memb contain protein - Complex.

if any oxidation occur it is accepted by $NAD^+ \longrightarrow NADH + H^+ \longrightarrow$ always give to Complex I → give

Complex V :
phosphorylation

$ADP + Pi \xrightarrow[\text{synthase}]{ATP} ATP$

Q. $NADH + H^+$ only give H^+ to → Complex I

Q. *In ECT → ∉ ℘ ATP produced by oxidative phosphorylation.

Q. Final acceptor of H_2 in ETC → O_2.

Q. Complex IV – oxidation

Q. H_2O formation – Complex IV

Q. phosphorylation – Complex V

Q. Coupling – Oxidation + phosphorylation

Complex I – $NADH + H^+$ enter

Complex II – $FADH_2$

Imp

Barbiturate
Rotenone
↓⊖
$NADH + H^+$ → Complex I / NADH dehydrogenase → NAD^+
↓ H^+

Malonate
↓⊖
$FADH_2$ → Complex II / Succinate dehydrogenase → FAD^+

Coenzyme Q / Ubiquinone (carrier)
↓
Complex III / Cytochrome reductase
↓
Cytochrome C (carrier)
↓
CO, CN^-, H_2S } ⊖ → Complex IV / Cytochrome oxidase — O_2 → H_2O [OXIDATION]

* final acceptor of H_2 in ETC → Oxygen

Oligomycin ⊖
[PHOSPHORYLATION] Complex V / Fo - F1 particle — ADP + Pi → ATP [ATP SYNTHASE]

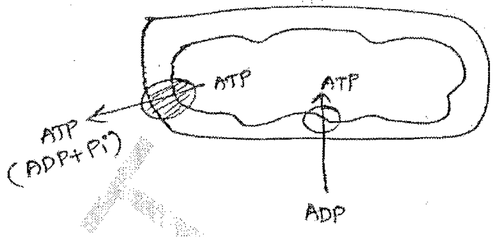
* H_2S - hydrogen sulphide

* Barbiturates, Rotenone } - inhibit the Complex I

~~Complex I~~

* Malonate - inhibit Complex II

* Oligomycin - inhibit Complex ~~IV~~ V



- on membrane of mitochondria ATP - ADP transporter
- ATP - ADP transporter inhibited by "ATRACTYLOSIDE"

Synthesis of ATP (2 methods)
- Oxidative phosphorylation (OP)
  - In ETC
  - Mitochondria (inner memb)
- Substrate level phosphorylation (SLP)

Mobile Carriers of ETC

- CoQ / Ubiquinone - b/w Comp I, II & Complex III
- Cyto C - b/w Complex III & IV

* From 1 molecule of $NADH + H^+$
↳ 2.5 ATP's

* From 1 molecule of $FADH_2$
↳ 1.5 ATP's

Inhibitors of ETC

Complex IV (Cyto-oxidase) is inhibited by - CO.

* CO - carbon monoxide

* CN^- - cyanide

Uncouplers

Definition: It uncouples oxidation & phosphorylation in ETC

∴ ↓ synthesis of ATP.

eg: 2,4 DNP - 2,4-Dinitro phenol.
2,4 DNP bind with H^+ → cross the membrane and enter the cell matrix → Energy produce → can't trap in form of ATP.
Aspirin (NSAID) - uncouples - ↓ ATP synthesis

(Imp)
- Thermogenin
- Thyroxine

} physiological uncouplers produced inside body.

GLYCOLYSIS

- also k/a - EMBDEN MAYERHOFF PATHWAY. (EMP)

def: Glu → → Pyruvate

Site: Cytosol

Glucose
C-C-C-C-C-C

↓ ATP → ADP Hexokinase / Glucokinase

Glu-6-p
C-C-C-C-C-C-Ⓟ

This Ⓟ from ATP.

Note:
- if there is transfer of Ⓟ from one molecule to another molecule → KINASE enzyme.
- All kinase need Mg^{2+}

↓ Isomerase Enzy

Fruc-6-p

Glucose = $C_6H_{12}O_6$

Fructose = $C_6H_{12}O_6$

Same formula but different structure → Isomerization

Fru-6-P
C-C-C-C-C-C-Ⓟ

↓ ATP → ADP phospho fructo kinase 1 (PFK-1)

Fruc 1,6, bisphosphate
Ⓟ-C-C-C-C-C-C-Ⓟ

↓ Aldolase

DHAP (3C) Dihydroxy Acetone phosphate ⇌ G-3P (3C) Glyceraldehyde 3-phosphate

DHAP ↓ Isomerase, NADH+H

G-3P ↓ NAD, Pi, G3P dehydrogenase (oxidation) (Remove Hp)

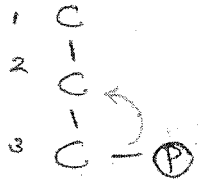
G-3P
1,3 bisphospho glycerate
C-Ⓟ
C
C-Ⓟ

Only one oxidation reaction in Glycolysis.

↓ phosphoglycero KINASE, ADP + Pi, SLP, ATP

3 phosphoglycerate

- Here phosphorylation occur directly → SLP [substrate level phosphorylation]
- Oxidative phosphorylation - only in ETC there NAD & FAD are formed



↓ Mutase

2 - phospho glycerate

- On single molecule, if change the position of Ⓟ from 2 to another C

↓ MUTASE

↓ Enolase ⊖ H_2O

phospho enol pyruvate (PEP)

Pyruvate kinase

↓ ADP + Pi, SLP → ATP

Pyruvate

Energetics - Calculation of ATP

Enzy	Mech	No: of ATP
G-3-P DH	2 NADH + H^+ × 2.5 ATP	+ 5 ATP
phospho glycero kinase	SLP	+ 2 ATP
pyruvate kinase	SLP	+ 2 ATP
HK/GK		- ATP
PFK-1		- ATP

- Oxidation occur @ G-3-P dehydrogenase.
- Splitting - Aldolase.
- SLP @ Pyruvate kinase, phosphoglycero kinase.

- Net gain of ATP in Glycolysis 7 ATP.

Regulation of Glycolysis

Depend on condition of cell

Need to Regulate - ↑ or ↓ speed.

* Rate limiting Enzyme

PFK-1

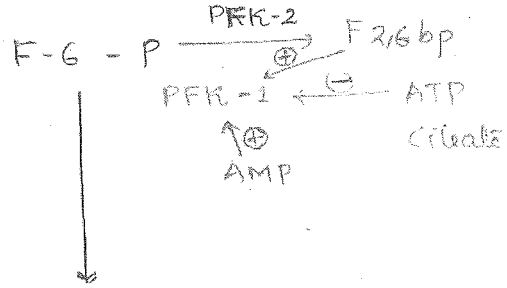
This Enzy regulate the entire glycolysis.

Glu

↓

Glu-6-pho

↓



ATP & Citrate	⊖	PFK-1
AMP & F 2,6 bp	⊕	PFK-1

* Indication of energy rich cell

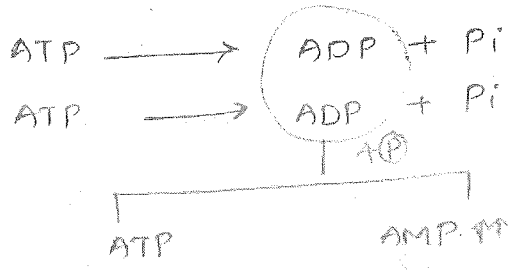
↑ ATP

↑ Citrate

So we inhibit the glycolysis.

ATP & citrate ⊖ → PFK-1

* Indication of Energy poor cell.



Then AMP get accumulated in cell - in energy low condition

AMP ⊕ → PFK-1

Thus stimulate glycolysis.

Same F-6-P → F 2,6 bp

F 1,6 bp

Insulin -

- will not act on PFK-1
- Act on Glucokinase / ~~Hexokinase~~

Insulin → stimulates Glycolysis

Thus ↓ Glu level in blood.

Irreversible Rxns of Glycolysis

- HK / GK
- PFK-1
- PK (pyruvate kinase)

Glycolysis - irreversible on.

Inhibitors of Glycolysis

FLOURIDE ⊖ → Enolase.

Q. NaF inhibits Enolase

Q. What is added into blood to estimate accurate blood glu level.

NaF in test tube

NaF ∴ inhibit Glu metabolism.

- Glu → (HK / GK) → Gl-6-P

	Hexokinase	Glucokinase
Imp		
occurs in	All tissues	Liver
Substrate:	Can metabolise all 6-C substrates eg: Glu Fru Galactose	Only metabolise Glucose
Inhibitor	Glu-6-P	Fru-6-phos
Km value	Km low Km $\propto \frac{1}{\text{Affinity}}$	Km high

- RBC rich in O_2 but no mitochondria } Anaerobic glycosis

Glu
↓ ← ATP
Glu-6-P
↓
Fruc-6-P
↓ ← ATP
Fru 1,6 bp

DHAP → G-3P → 1,3 bpg → 3pg → 2pg → PEP → pyruvate → Lactate

G-3-P → 1,3 bpg → 3pg → 2pg → PEP → pyruvate → Lactate (3C)

NAD+ / NADH+H+ (G-3-P → 1,3 bpg)
ATP (1,3 bpg → 3pg)
ATP (PEP → pyruvate)
NADH+H+ / NAD+ (pyruvate → Lactate)
NADH+H+ / NAD+ (pyruvate → Lactate)

- Insulin stimulates Glucokinase

Aerobic Glycolysis:
In presence of O_2 & Mitochondria.

Anaerobic Glycolysis:
In absence of O_2, Mitochondria.

- Glycolysis in RBC

Glycolysis in RBC
↳ Anaerobic Glycolysis

Net gain of ATP in Anaerobic Glycolysis 2 ATP

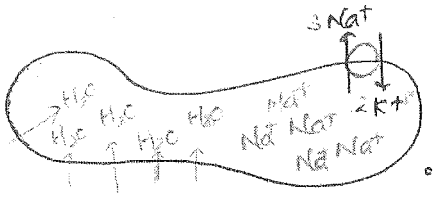
★★ In Anaerobic Glycolysis - pdt formed 2ATP, 2 Lactate (3C)
No CO_2 release

Clinical Correlation.

pyruvate kinase ↓ses

- Deficiency of pyruvate kinase leds to ↓

Hemolytic Anemia.



- Na+ efflux
- K+ influx

No Heinz bodies

↳ in deficiency of pyruvate kinase

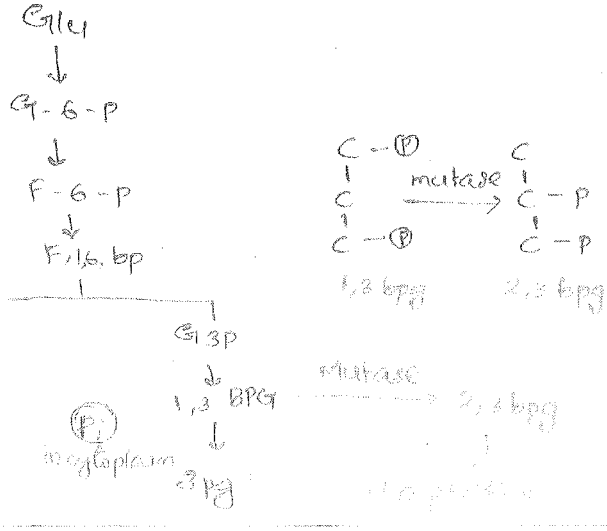
Condensation of Hb - Heinz bodies

- In RBC - already anaerobic Gly ∴ ↓ ATP produced.
- if pyruvate kinase deficiency → ATP further reduces → $Na^+ K^+$ ATPase pump will not work → Na^+ accumulate → H_2O enters → RBC burst → Hemolytic Anemia.

Rapaport - Luebering Cycle

Site: Exclusively in RBC.

- formation of 2,3 bisphosphoglycerate (2,3 BPG)

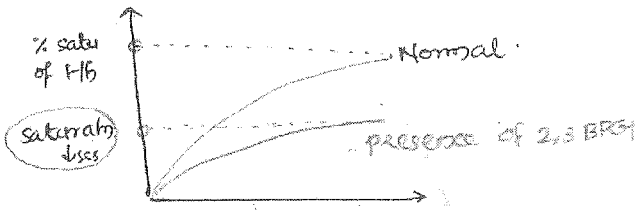


Removal of Ⓟ → phosphatase.

- Ⓟ free in cytoplasm after removal.

Correlation with physiology.

ODC : Oxygen dissociation curve.



O_2 attachment to Hb - saturation

if PO_2 ↑ses - ↑ % saturation of O_2 to Hb.

In presence of 2,3 bisphoglycerate

↓

↓ saturation of Hb

↓

Right shift of ODC.

In high altitude, Atm pressure ↓, Lungs get ↓ O_2.

↓

RBC help to deliver O_2 faster to cell by help of 2,3 bpg.

↓ saturation of O_2 with Hb in presence of 2,3 BPG.

↓

Right shift of ODC.

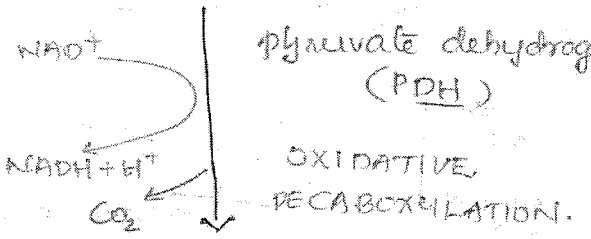
High altitude

Hypoxia

Anaerobic

Conversion of pyruvate to Acetyl CoA

Pyruvate 3C



Acetyl CoA 2C

Addition of C or removal of C
→ in form of CO_2

Here

CO_2 removal - decarboxylation.

Pyr dehydrogenase - oxidation.
action

* Pyruvate get convert to AcetylCoA by the process
↓
Oxidative decarboxylation

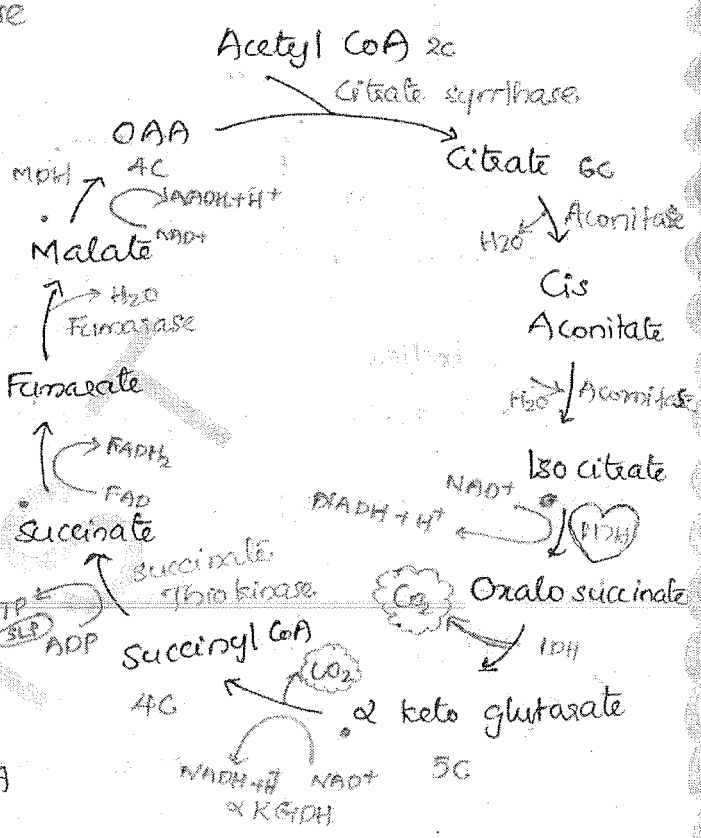
Pyruvate Dehydrogenase Complex

need Coenzyme - 5

- Lipoic Acid
- Thiamine pyrophosphate (TPP)
- Coenzyme A
- NAD+
- FAD

Kreb's Cycle / TCA cycle / Tricarboxylic Acid cycle / Citric Acid Cycle

Site : Mitochondrial Matrix



- Isocitrate dehydrogenase - IDH

From "isocitrate" - all female steps will be oxidation.

Oxidation - 4

1. Isocitrate dehydro
   $NAD^+ \longrightarrow NADH + H^+$
2. α ketoglutarate deby
   $NAD^+ \longrightarrow NADH + H^+$
3. Succinate deby
   $FAD \rightarrow FADH_2$
4. Malate deby $NAD^+ \rightarrow NADH + H^+$

Substrate level phosph - 1 Succinate thiokinase

Energetics

Net gain of ATP.

3 × 2.5	$NADH+H^+$	→ 7.5
1 × 1.5	$FADH_2$	→ 1.5
1 × 1	ATP	→ 1
		10 ATP

Enzy	Mech	No: of ATP
IDH	$NADH+H^+$ 2.5 ATP	2.5
αKGDH	$NADH+H^+$ 2.5 ATP	2.5
SDH	$FADH_2$ 1.5 ATP	1.5
MDH	$NADH+H^+$	2.5
Succinate deh thio kinase	SLP	1
		10 ATP.

Net gain of ATP in krebcycle is 10 ATP from 1 molecule of Acetyl CoA.

Rate limiting enzy in krebs cycle
↓
IDH.

Q. Isocitrate → oxalosuccinate → α keto glutarate : one step.
Oxalosuccinate — intermediate thing/pdt
decarboxylation also occurs

*** αKGDH - oxidative decarboxylation

similar to pyruvate dehydrogenase

αKGDH - also need 5 coenzyme.

Lipoic acid.

TPP ← from Vit B_1

CoA ← from Vit B_5

NAD^+ ← from Vit B_3

FAD ← Vit B_2.

- Vit B_3 - Niacin, Nicotinic acid.
- Vit B_5 - CoA (pantothenic acid)
- Vit B_2 - Riboflavin

Nicotinamide adenyl dinucleotide.

Flavin adenyl dinucleotide

- Vit B_1 - Thiamine.

Q. Vitamins Required for Kreeb's cycle.

Vit B_1, B_5, B_3, B_2.

Inhibitors of TCA cycle

Malonate ⊖→ SDH

Arsenite ⊖→ αKGDH

Fluoroacetate ⊖→ Aconitase

GLUCONEOGENESIS

def: Formation of glc from Non carbohydrate source.

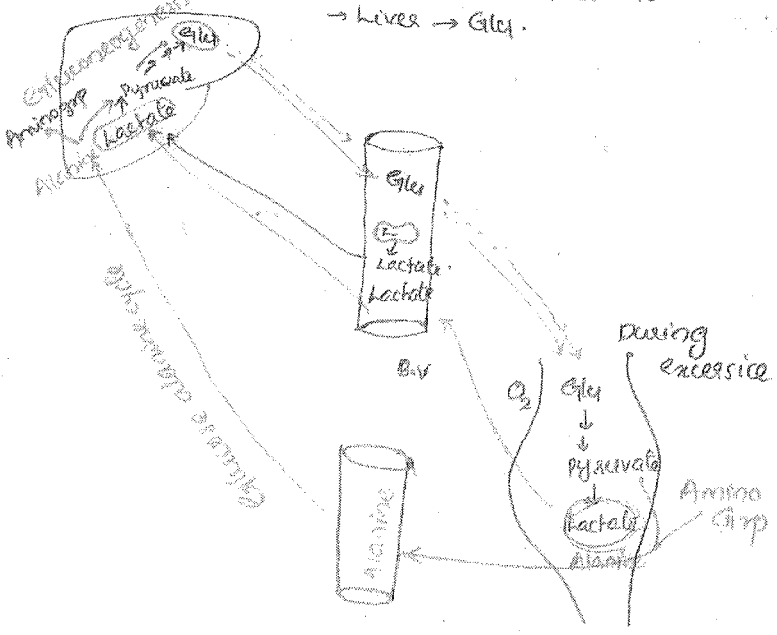
eg: 1) Amino acid
Total - 20 AA
All AA will form Glucose except:
Leucine, Lysine } only form ketone bodies → ketogenesis.

2) Pyruvic acid.
3) Lactic acid
4) Glycerol.

Site: Liver 90%
Kidney 10%

Gluconeogenesis: cytosol & Mitochondria

CORI'S CYCLE: Pyruvate from skeletal Mls. → Liver → Glu.



During excersise → Skeletal Muscle need more O_2.
in such cases Anaerobic resp → Lactate accumulate
↓
Muscle Fatigue.

Lactate → release to Blood

Source of Pyruvate

- CORI'S CYCLE
- Glucose Alanine Cycle
- From Anaerobic Respiration of RBC.

Gluconeogenesis

Glu
↓
Glu-6-P
↓
Fru-6-P
↓
F-16-bispho

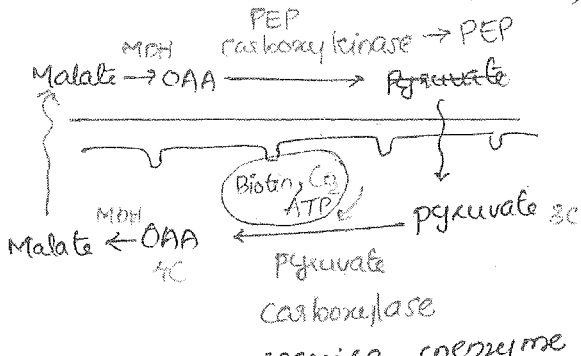
3 - irreversible step

All others are reversibles.

F-16-bispho
↓
G-3-P
↓
1,3 bisphospho glycerate
↓
3pg
↓
2pg
↓
PEP
↓
pyruvate

Gluconeogenesis :

Pyruvate C in mitochondrial Matrix)



* Only 3 enzyme use : BIOTIN
  1. pyruvate carboxylase (one of the 1st enzyme)

* if reversible m - no change in enzyme.

From :

F 1,6 - bp
↓ Fructose 1,6 biphosphatase
F-6-ph
↓
Glu-6-ph
↓ Glucose-6 phosphatase
Gluc

Rate limiting enzyme in Gluconeogenesis - Fructose 1,6 bisphosphatase

* Gluconeogenesis doesn't occur in Skeletal Mls - dlt absence of G-6-phosphatase

Glycogen Metabolism

Structure of glycogen :

Glycogen - storage form of glc

Glycogen is polymer of Glc

G1 - G1 - G1 - G1 — G1 - G1
G1 - G1 - G1

α(1→4) glycosidic bond.

Glycogen : Branched tree like structure

α (1,4) glycosidic bond.

Glucose — 2 Anomeric form
α Glc β Glc.

→ 1st C of 1 glc with 4th C of another glc.

→ Where that branch begins :
α (1,6) glycosidic bond.

In glycogen all the bond will be α 1,4 glycosidic bond except at the branching point
↓
α (1,6) glycosidic bond.

Skeletal Muscle - more glycogen storage than Liver.

GLYCOGENESIS

def : formation of Glycogen from Glc

Site : Liver > Kidney

Glu

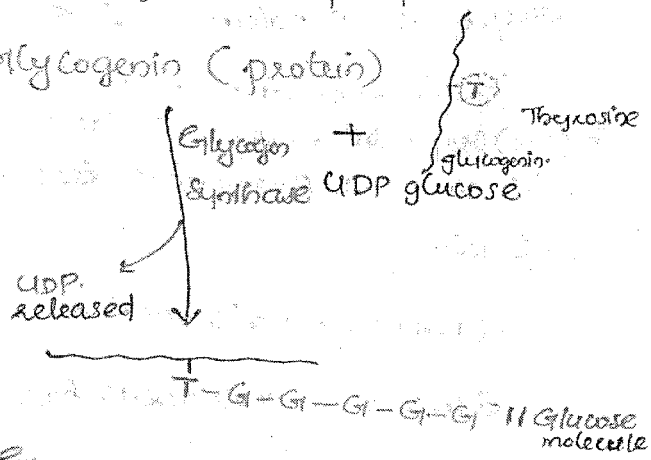
↓ Activation

↓

UDP glucose (activated Glc)

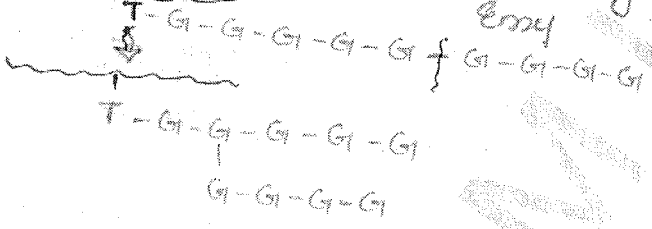
UDP - Uridine diphosphate.

Then Glycogenin (protein)



• Glycogen synthase - Enzy formation of linear chain.

To form the branches - Branching Enzy



Branching Enzy = 4,6 Transferase

* By alternate work of Glycogen synthase & Branching Enzy the tree like glycogen structure formed.

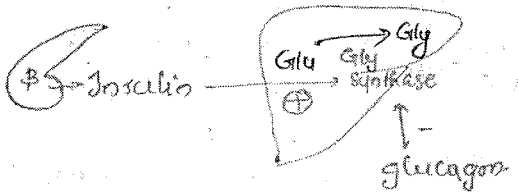
Rate limiting Enzy

↓

Glycogen Synthase.

→ Insulin — stimulate the Gly synthase

When Glc ↑↑↑ in blood

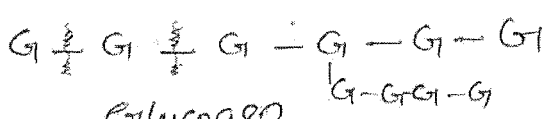


if Insulin, ATP - Glycogen synthase
AMP, Glucagon → Glycogen synthase

Glycogenolysis

def : glycogen ⟶ glc

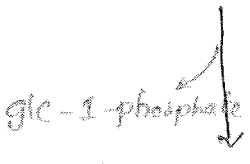
Site : Liver Cytosol.



Glycogen

↓ Glycogen phosphorylase

Glycogen phosphorylase act at end, and release glc-1 phosphate



Gly phosphorylase stop working 4 Glc molecule before branching

Glycogen phosphorylase - only have ability to release glc-1 phosphate from linear chain

Can't remove glc-1-phosphate from branch. ie can't break branch. (α1,6 glycosidic bond)

Debranching Enzy : Break the branch @ α, 1,4 glycosidic bond

G1 G1 G-G-G

G-G-G-G-G-G-G-G-G-G

↓ then add the G-G-G to linear chain.

G1

G-G-G-G-G-G-G-G-G-G-G-G

Debranching Enzy : 4,4 transferase

Bifunctional enzy :

1) Break the α1,4 glycosidic bond & attach by forming α1,4 glycosidic bond.

2) Break α1,6 glycosidic bond.

↳ ~~brea~~ release free glucose (Little amount)

glucose ←

G-G-G-G-G-G-G-G-G-G

↓ Glycogen phosphorylase

Glu-1-p

↓ Mutase

Glu-6-p

↓ Glucose-6-phosphatase

Glu

Glycogen phosphorylase

↓

Rate limiting enzyme.

Branching Enzy → GLYCOGEN → Glycogen phosphorylase

Linear chain

Glycogen synthase

UDP Glu

↑ Activate

Glu

Limit Dextrin

Debranching Enzy

Linear chain

Glu ↓ phosphorylase

Glu-1-ph

↓ Mutase

Glu-6 ph

Glucose-6-phosphatase

Glu.

Deficiency of Enzyme → Glucose-6-phosphatase

→ ↑ Glu-6-pho

→ prevent break down of glycogen

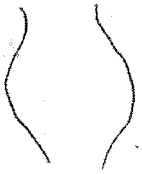
∴ Glycogen storage disease

Gly stor disease	Enzy deficiency
Type I VON GIERKE'S dis	Glu-6-phosphatase
Type III CORI's disease	Debranching Enzy
Type VI Hers disease	Gly phosphorylase

Glycogen

↓ Hepatic Gly phosphorylase deficiency

HER's dis
Type VI



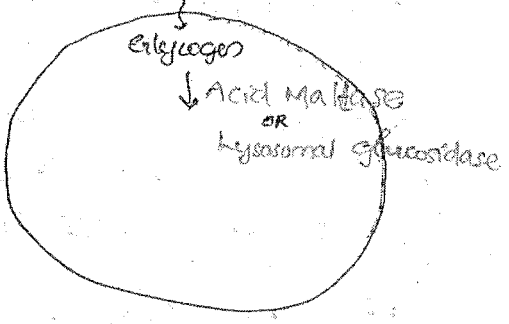
Glycogen

↓ Muscle Gly phosphorylase deficiency.

Mc Ardle's dis
Type V

In cytosol

Lysosome Glycogen



Acid maltase:
Breakdown glycogen in lysosome

This enzy deficiency

↓

Type II
Pop pompe's disease

Skeletal Mls

Liver

Glycogen

↓

↓

Glu-6-p

↓ Glu-6-phosphatase

Glu

This Glu can be utilized by all tissue

Glycogen

↓

↓

↓

Glu-6-p

↓ Glu-6 pho

Glu

not present

Muscle use the Glu-6-phosphate by itself.

So others can't get

Anderson
• def of Branching
Type IV
improper glycogen formed.

Cori's → defn of Debranching
Type III

HMP Shunt

also k/a - pentose phosphate Pathway

- Hexose Mono phosphate pathway.

Imp products of HMP shunt:

① NADPH (diff NADH)

② Ribose 5-phosphate

Ribose 5 phosphate - necessary for formation of DNA & RNA.

NADPH

1. Helps in fatty acid synthesis also help in formation of steroids Cholesterol, Steroid hormones.

- Cholesterol → hormones (steroids)

2. NADPH has role in RBC
3. WBC - Neutrophil

Site of HMP shunt: TALE

- Testes
- Thyroid gland
- Ovaries
- placenta
- Adrenal gland (cortex)
- Adipocyte
- Liver - central organ for FA synthesis.
- Erythrocytes, Lens of eye
- Lactating mammary gland

Inside the cell:

HMP shunt occurs in Cytosol

Reactions:

Glu-6-phosphate (starting substrate)

Glu-6-phosphate dehydrogenase (G6PD) ↓ → $NADP^+$ → $NADPH + H^+$

6-phosphogluconate

↓

Ribulose 5-P

Transketolase — Coenzyme - TPP, Vit B_1 deficiency

Transaldolase ↓

Ribose 5-Phosphate

↓

↓

Fructose-6-phosphate.

1st reaction:

Glu-6-phosphate : oxidation.

Enzy : Glu-6-phosphate dehydrogenase.

NADPH formed.

Glu

↓

Glu-6-P

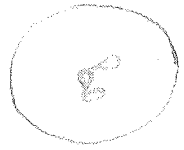
↓ Isomerase

Fru-6 ph

HMP shunt

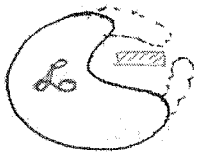
Role of NADPH in Neutrophil:

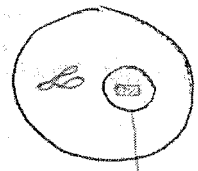
Neutrophil - fn: phagocytosis



35 lobed PMN cells

Neutrophil will engulf bacteria.





phagosome.

C5a
LTB4

Inside the neutrophil : HMP shunt occur.

Glu-6-P → (G6PD, NADP+ → NADPH + H+) → product + O_2 → H_2O_2

hydrogen peroxide free radicle

↓

kill bacteria

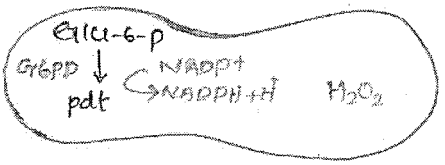
* O_2 dependent killing.

* If G6PD deficiency → unable to kill bacteria

↓

prone to recurrent inf

Role of NADPH in RBC



Extra O_2 can cause — superoxide free radicle

O_2
Drugs
Fava beans.
Infection
} H_2O_2 inside RBC

H_2O_2 → breakdown of RBC membrane.

But normally body prevents the breakdown.

Inside RBC, HMP shunt occur.

Glu-6-P → (G6PD, NADP+ → NADPH + H+) → pdt

Inside RBC - Glutathione

Reduced Glutathione + H_2O_2 → H_2O + Oxidised Glutathione

Oxidised Glutathione + NADPH → Reduced Glutathione

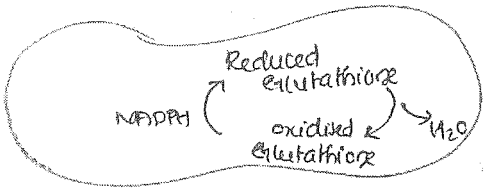
RBC contain glutathione + NADPH

→ Reduced glutathione (contain H_2) + H_2O_2

↓

Oxidised Glutathione

NADPH help to release H_2O_2 with help Glutathione.



NADPH removes the free radical ie (H_2O_2) from RBC's.

∴ stabilises the memb of RBC.

NADPH reduces glutathione.

Clinical Corelation

1) G6PD deficiency:

Led to Hemolytic Anemia.

Heinz bodies.

- Urea differentiate P.K deficiency & G6PD def.

Q: G6PD def - MCC enzy deficiency

⇒ Leading to hemolytic Anemia.

Q. Vit B_1 deficiency - MCC is alcohol

2) Alcoholism (MCC)

↓

Vit B_1 defi

↓

TPP ↓

↓

∴ Transkelolase enzy defective

Wernicke Korsakoff syndrome.

Glycolysis

Cytosol

ATP — synthesis / utilize

No Loss of CO_2 in glycolysis

HMP shunt

Cytosol

Q. No role of ATP

Q. CO_2 produced (3 CO_2 molecule)

G6PD Enzy

↓

RLE.

★ Rate Limiting Enzyme

Glu-6-phosphate dehydrogenase

Chemistry of Proteins

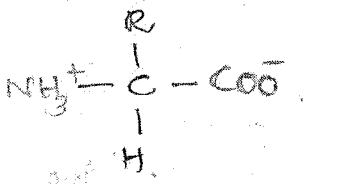
Ions → +ve → Cation
Ions → -ve → Anion.

Q. Proteins : polymers of L-α Aminoacid

In human beings:
AA - in L form
gle - in D form
or
sugar.

Proteins are formed by peptide bond. → polypeptides ⇒ made of many AA.

No branches - in protein.



∴ AA are Zwitter Ion / Hybrid Ion.

• Net charge on AA is Zero.

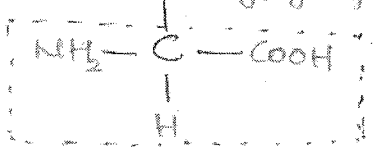
eg: LEUCINE
Zwitter ion. @ pH-6

Leucine having Zwitter ion @ pH = 6
This pH - Isoelectric pH

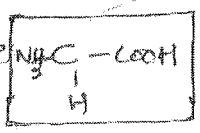
AA

def: organic compound which consist of Carboxylic acid group - COOH & Amino gap - NH_2

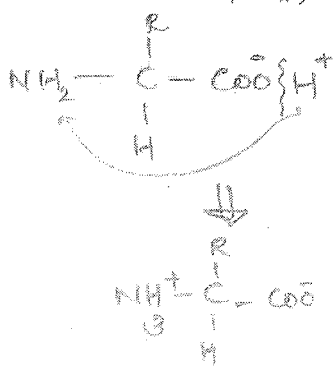
R/ Alkyl group.



• C - tetravalent

• All 20 - AA have same  only R group change.

Exact form of AA in body.



Isoelectric pH
It is the pH @ which AA exists in form Zwitter ion.

Every AA have their own Isoelectric pH.

Classification of AA

I. Structural classificatn
7 groups of AA.

I. Aliphatic AA
Glycine - Simplest AA
Alanine
Valine
Leucine
Isoleucine.

II. hydroxyl Gpp (-OH) Containing AA
Serine
Threonine

III Sulphur containing AA
- Cysteine
- Methionine

IV Acidic AA:
- Aspartate / Aspartic acid.
- Glutamine
- Asparangine
- Glutamic acid. / Glutamate.

V Basic AA:
- Lysine
- Arginine
- Histidine

VI Aromatic AA
- Thyrosine
- Tryptophan
- Phenylalanine.

VII Imino Acid
- Proline.

II Based on Nutritional Requirmt

Essential AA
- Not produced inside body
- ∴ We have to take essentially through diet.

Non Essential AA:
- produced in body.
- No need to take by food.

Essential AA:
- Valine
- Leucine
- Isoleucine
- Threonine
- Methionine
- Lysine
- Arginine
- Histidine
- Tryptophan
- phenyl alanine.

Semi essential AA:
- Arginine
- Histidine

Not synthesised in body.
Not required, only required in Childhood (Growing children)

III Based on Metabolic fate.

1. Ketogenic AA (6)
   AA which forms ketone bodies
   - Lysine
   - Leucine

2. Glucogenic & Ketogenic AA (4)
   - Tyrosine
   - Tryptophan
   - phenyl alanine
   - Isoleucine.

   } Aromatic AA

3. Glucogenic AA: 14 - pure glc
   Rest all AA - 18 AA

21st AA - Seleno cysteine
formed from Serine
UGA

22nd AA - Pyrrolysine
Codon: UAG

Stop codon

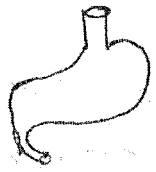
UAA
UAG
UGA

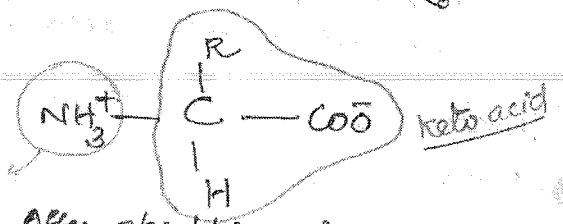
Except for selenocysteine
Pyrrolysine

Metabolism of Proteins

Overview:

Protein rich diet consume → digestion → form AA (large mol → small)
→ AA absorbed into body.





After absorption of AA

Deamination :

NH_3^+ is removed as Ammonia (NH_3)

Remaining AA – ketoacid.
ie Remaining 'C' skeleton.

NH_3 - have no function, also toxic to body.

if NH_3 ↑ in blood
↓
Hyperammonemia
↓
lead to Cerebral edema.
- Convulsion
- Coma

∴ Need to excrete NH_3.

NH_3 is toxic → insoluble

In liver

NH_3
↓ Urea cycle.
Urea (soluble)
↓
excreted

Urea cycle / Ornithine cycle / Krebs Hanseleit Cycle

Site : liver Cytosol & Mitochondria

NH_4^+ Ammonium ion.
+
CO_2
↓ Carbamoyl phosphate synthase 1
Carbamoyl Phosphate

Ornithine → OTC (Ornithine trans Carbamoylase) → Citrulline

Citrulline → Aspartate (Argino succinate synthase) → Argino Succinate

Argino Succinate → Breakdown (Argininosuccinase) → Arginine + Fumarate

Arginine → Urea + Ornithine (Arginase / Breakdown)

Q. Urea – $NH_2 - CO - NH_2$
OR
$CO(NH_2)_2$

Sources of Urea

- 1st NH_2 from NH_4^+
  IInd NH_2 from Aspartate
  CO ' CO_2

$NH_2 - CO - NH_2$

↑ Ammonium ion — ↑ CO_2 — ↑ Aspartate

* 1st 2 reactions - takes place in Mitochondria
* Last 3 rxns - in cytosol.

- Citrulline forms in mitochondria → enter cytosol then + aspartate

* Rate limiting enzyme in Urea cycle CPS - 1

Q.

CPS - I	CPS - II
Urea cycle	pyrimidine synthesis
Mitochondrial Enzyme	* Cytosol Enzyme
$NH_4^+ + CO_2$ → (CPS I) CAP	Glutamine + CO_2 → (CPS II) CAP

QA Source of NH_3:

NH_4^+ ion	Glutamine

Metabolism of Aromatic AA

1) Metabolism of phenyl alanine & Tyrosine :

Only 1 fn of phenylalanine
↓
convert to Tyrosine

* phenylalanine —(PAH phenylalanine hydroxylase)→ Tyrosine
  Addition ⊕ OH^- hydroxylation

* From Tyrosine → Melanine
  → T_3, T_4
  → Catacholamines (DA, Epi, NEpi)

* Then degradation of Tyrosine

Conversion of phenyl alanine to Tyrosine

Phenylalanine —(PAH phenylalanine hydroxylase)→ Tyrosine
↑ OH^-

OH^- added by Tetrahydro Biopterin (H_4)
After addition of H_2
↓
Dihydro Biopterin (H_2)

Clinical Corelation C/C :

* phenyl alanine hydroxylase deficiency → phenyl alanine ↑
  ⟹ phenyl ketonuria (PKU)

phenyl ketonuria (PKU)

Enzy def : PAH

C/F :
→ pale skin
no Tyrosine → no melanine
Melanine in skin

→ if melanine deficiency in ~~skin~~ hair
↳ Blonde hair.

→ No Tyrosine — No T_3, T_4
T_3, T_4 essential for brain development
↳ Mental Retardation.

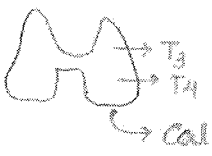
→ Mousy odour

Formation of Melanine

Tyrosine —(Tyrosinase)→ Melanin

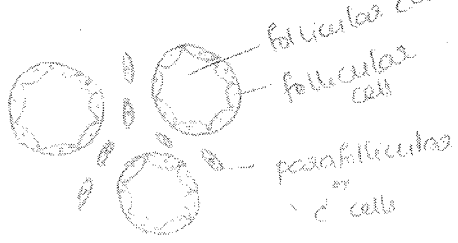
if Tyrosinase deficiency / absence
↳ Leucoderma
- White patches
starting from surrounding from lip, or starting from finger
→ Vitiligo
→ Albinism

Formation of thyroid hormones



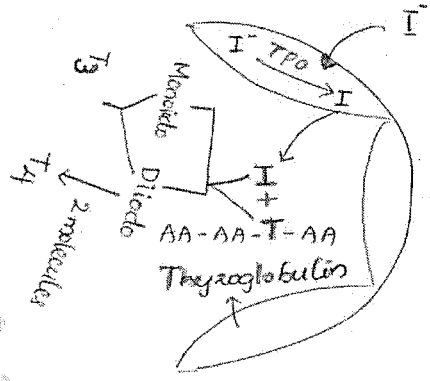
Calcitriol – Vit D

Thyroid gland → made up of Thyroid follicles → lined by follicular cells, inside cavity follicular cavity.



- Calcitonin – produced from parafollicular cells OR 'C' cells

T_3, T_4 – produced by follicular cells.



follicular cells
① produce a protein – Thyroglobulin

Thyroglobulin
AA – AA-AA – T – AA – AA
↓
transported to follicular cavity

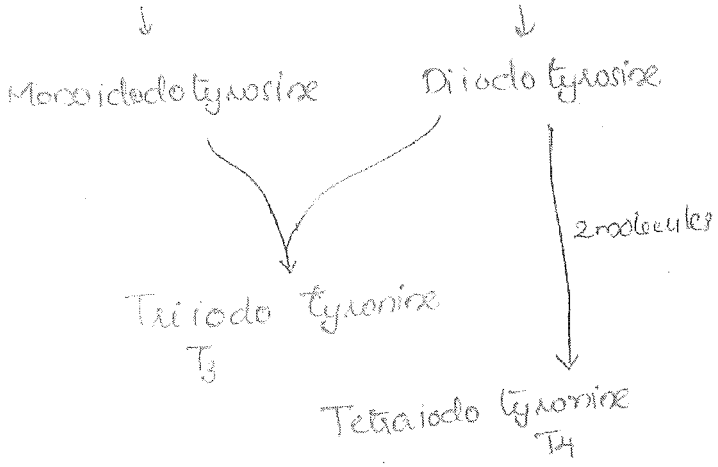
② Outside the follicle
Iodide ion
Stage I : Trapping of Iodide
Stage II : oxidation

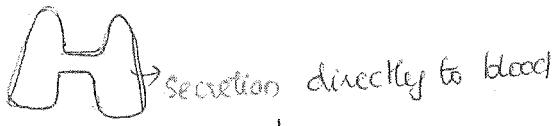
TPO – Thyroperoxidase

Stage III : Transport into cavity.

In cavity : Stage IV : coupling
Iodine combine with Tyrosine in Thyroglobulin

1 Iodine + Tyro — 2 Iodine + Tyro





↓ Transport

(O) Tissues.

T_4 ⟶ Thyroxine

T_4 ⟶ secreted more, than T_3.

* Thyroid hormones bind to TBG (Thyroid Binding globulin) then transport to tissue.

Conversion of T_4 ⟶ T_3

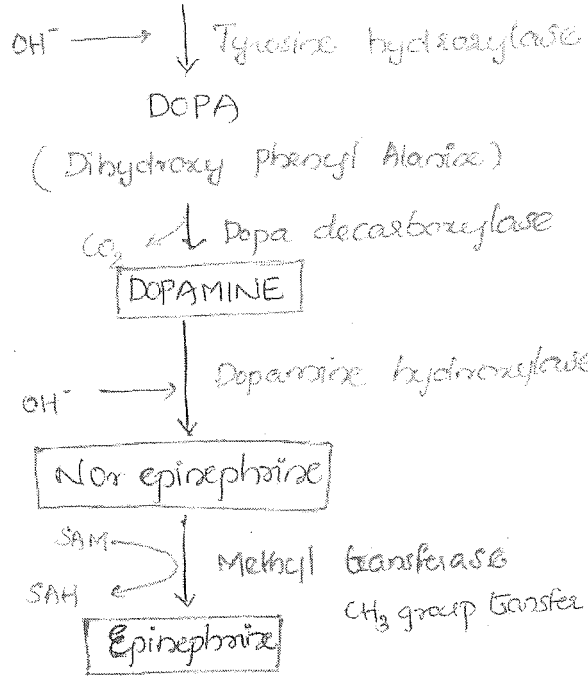
T_4 —(5' deiodinase)→ T_3 (Active T_3)

T_4 —(5 deiodinase)→ reverse T_3 / γ-T_3 / Inactive T_3

Formation of Catecholamines

DA, Epi, nEpi

phenyl alanine —(OH⁻)→ Tyrosine



SAM = S-adenosyl Methionine

SAH = S-adenosyl homocysteine

SAM - methyl group donor.

* Basal ganglion → NT is dopamine

Dopamine def — parkinsonism.

In Parkinsonism → dopamine ↓ Ach ↑

Doc — Levodopa + Carbidopa

Anticholinergic:

Prototype: Atropine - not given because non specific

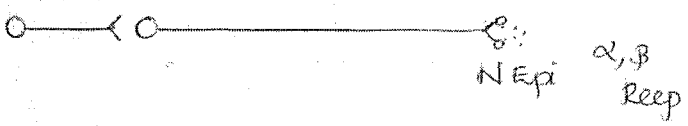
block all cholinergic Resp

* Anticholinergic drug ∈ Anti parkinsonism: Benzhexol (Specific)

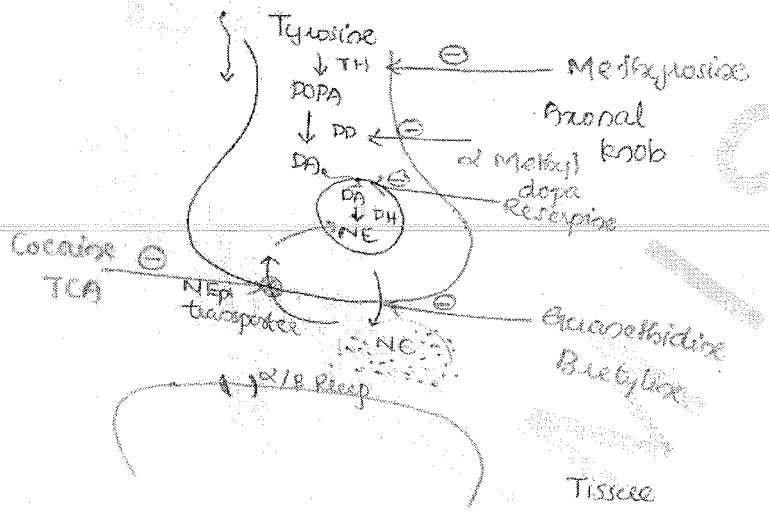
Correlation:

Parasym:

Sym N:



Sympathetic postganglionic Nerve ending



* At Nerve ending - No Methyl transferase

Nor Epi

↓ X

Epi

* ↓ reuptake, NEpi ↓

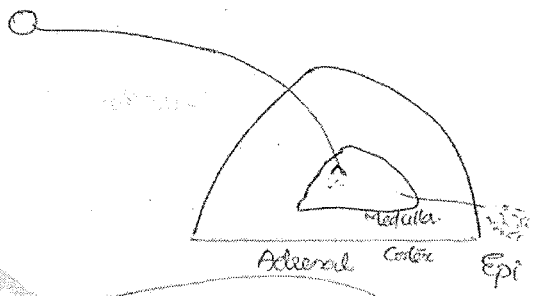
↓

Depression

* So gave TCA → prevent the reuptake of NEpi → stimulate mood.

* α methyl DOPA - HTN in pregnancy.

Sym N.S



No ganglion in bw Sym NS & Adrenal Medulla.

Degradation of Tyrosine

Tyrosine

↓

Homogentisate

↓ Homogentisate oxidase

Maleyl acetoacetate

↕

Fumaryl acetoacetate

↓

Fumarate | Acetoacetate

Fumarate is carbohydrate → Glucogenic AA

Acetoacetate is ketone body → ketogenic AA

After metabolism Tyrosine

form carbohydrate ketone body.

* if Homogentisate Oxidase deficiency, Homogentisate level ↑↑

Test: Long standing urine
↓
Black urine.

Clinical Correlation

Alkaptonuria / Black urine dis:

Enzyme: homogentisate oxidase deficiency.

Black colour / Coke colour urine.

- if Homogentisate (acid) get deposited in cartilage → Black cartilage
↓
Ochronosis.

Tryptophan

1. Serotonine / 5 hydroxy tryptamine
5 HT
S - mediator of inflammation

$5HT_3$ antagonist : Ondansetron

2. Melatonin
Pineal gland.

3. Niacin → Vit B_3

Q. Vit B_3 forms coenzyme
NAD^+, $NADP^+$

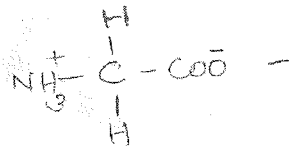
NAD^+ formed from Tryptophan

Metabolism of Aliphatic AA

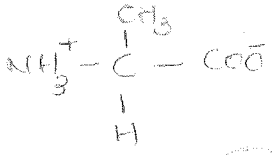
Aliphatic AA	Aromatic AA
Glycine	Tyrosine
Alanine	Tryptophan
Valine	Phenyl alanine
Leucine	
Isoleucine	

Aliphatic - open chain

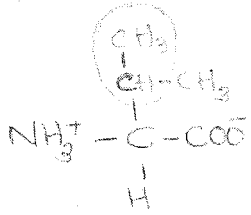
Aromatic - 



→ Glycine
Simplest AA



Alanine



- Valine
- Leucine
- Isoleucine

} Branched chain AA

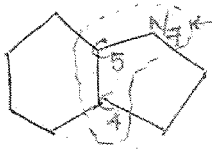
Metabolism of Aliphatic AA

Glycine:

1. Required for Heme synthesis

Succinyl CoA + Glycine
↓
δ ALA
↓
Heme

2. Purine Ring synthesis: Gl, A



← By glycine

∴ C_4, C_5, N_7 → Glycine

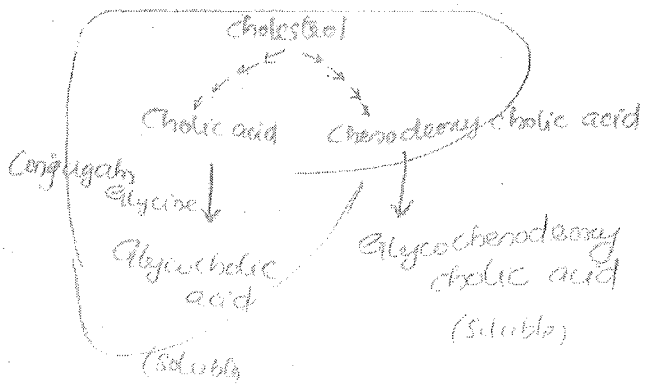
3. Creatine
4. Creatinine
5. Glutathione (Tripeptide)

Glutamate - Cysteine - Glycine

6. Required for Conjugation Rn

Bile → Bilirubin, bile salt, bile acid

- Bilirubin — is bile pigment
- Bile acids formed from Cholesterol in Liver
- Bile acid: (1° bile acid.)
  - Cholic acid
  - Chenodeoxycholic acid.



Bile: Emulsification of fat & Absorption

Fn: of bile acid.

To reach intestine → cholic acid & chenodeoxycholic acid: shld dissolve

Cholic & chenodeoxy cholic acid
↓
insoluble
(from cholesterol)

∴ shld Conjugate with Glycine, to make them soluble in Liver

- Glycocholic acid (Soluble)
- Glycochenodeoxy cholic acid. (Soluble)

Q. Conjugation ↑ solubility

* Conjugated form reach → Normal flora of intestine

Normal flora — convert → 2° bile acid

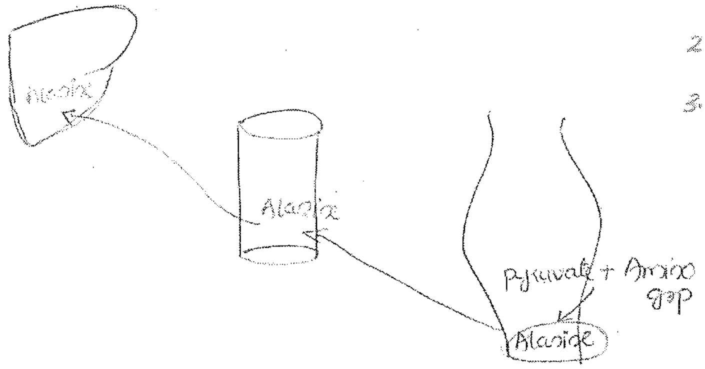
Glycocholic acid	Glyco chenodeoxy cholic acid
↓ Intestine	↓
2° Bile acid: Deoxycholic acid	Deoxy Lithocholic acid.

7. Neurotransmitter

Glycine - both

Alanine:

1. Glucose Alanine Cycle:



Q. Most of Amine is transported to Liver from ~~intestine~~ skeletal Muscle in the form of Alanine

Valine, Leucine, Isoleucine:

Valine, Leucine, Isoleucine } —Brached chain keto acid dehydrogenase→ Metabolites

if enzyme deficiency: Maple syrup urine disease.

Clinical correlation

Maple syrup Urine disease:

Bcoz urine smells like Burnt sugar.
(Caramelization)

Brached chain keto acid dehydrogenase.
↓
5 coenzymes needed.

Lipoic acid
Thiamine pyrophosphate
Coenzyme A
NAD+.
FAD

1. Pyruvate dehydrogenase
2. α Keto glutarate dehydrogenase
3. Branched chain keto acid dehydrogenase

} 5 coenzyme needed.

Metabolism of sulphur containing AA

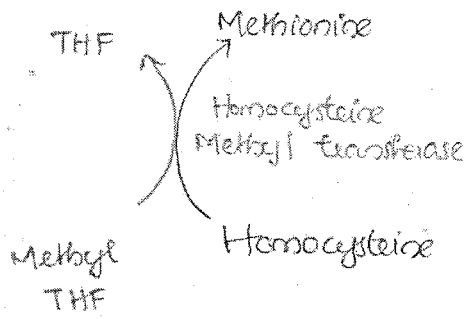
Cysteine, Methionine

Megaloblastic Anemia.
↓
Vit B_{12} OR folic acid deficiency

SQ
Nor epinephrine
SAM → SAH
↓
Epinephrine

Usually in methylation → methyl grp formed by SAM
∴ Regeneration of SAM

SAM → SAH ——→ Homocysteine
↓
Methionine



Methyl tetrahydrofolate - add $-CH_3$ group during regeneration into ~~H~~omocysteine

↓ Homocystein methyl Transferase need Vit B_{12}

Methionine

* Vit B_{12} - needed for 2 Rxns
coenzyme

- One on is - Homocystein methyl transferase

* V Valine
O Odd chain FA
M Methionine
I Isoleucine
T Threonine

End product of Metabolism of VOMIT

↓↓

Propionyl CoA → (CO_2) (ATP, CO_2 / BIOTIN) propionyl CoA Carboxylase

Methylmalonyl CoA

propionyl CoA Carboxylase require BIOTIN

Methylmalonyl CoA

↓ Methylmalonyl CoA Mutase / Vit B_{12}

Succinyl CoA

This is propionic acid pathway.

Megaloblastic Anemia

Vit B_{12} ↓ → Homocysteine ↑, Methylmalonyl CoA

Folic acid ↓ → Homocysteine ↑

if Vit B_{12}

Basic AA

Arginine :

1) Arginine $\xrightarrow{NOS}$ NO

Nitric oxide Synthase.

NO : potent vasodilator

NTG - prodrug → forms NO → vasodialator.

2) Arginine $\xrightarrow{Arginase}$ urea + ornithine

Urea cycle.

Histidine :

1) for formation of histamine.

mediator of Infla, Allergy.

Histamine :

- Vasodialator → more blood.
- Bronchoconstriction - asthma.
- ↑ permeability - more fluid leak out → edema
-

Asthma

IgE → attach to Mast cell → degranulation → Histamine → Bronchoconstriction

Histamine

SERINE :

1st AA → sclerocystosine (TCA)

Clinical corelation

Hartnup's diseases :

↓ absorption of AA from intestine.

Tryptophan - ↓ level

Tryptophan - for Vit B_3 ↑ pellagra like symptoms - C/F

CHEMISTRY OF LIPIDS

Lipids :

Esters of fatty acid & glycerol

Inorganic :

Acid + Base → Salt + H_2O

Neutralization.

Organic

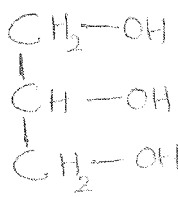
Carboxylic acid + Alcohol → Ester + H_2O

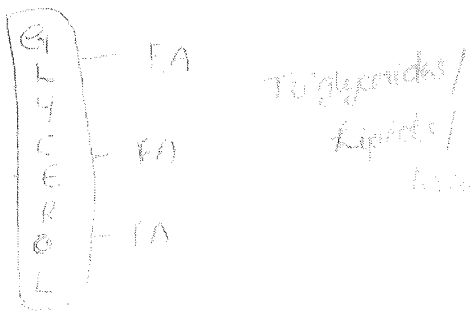
$-COOH$ $-OH$ $-\overset{O}{\overset{\|}{C}}-O-$

Esterification.

Fatty acid + Glycerol → Lipid (Ester)

Glycerol





Triglycerides / Lipids / Fats

Fatty acid

def:

- Long chain of C attached to -COOH acid. (Carboxylic acid)
- Long chain carboxylic acid

Classification

FA — Saturated / Unsaturated

C – C
C = C
C ≡ C

- if no multiple bonds in C chain if FA – saturated FA.
- if multiple bonds (double) present – Unsaturated FA.
  - ↳ MUFA – only one = bond
  - ↳ PUFA – if more than 1 multiple bond.
- if more than 1 unsaturation – PUFA
- only 1 unsaturation – MUFA

Based on Nutritional Requirement

Essential FA

- LINOLEIC ACID
- LINOLENIC ACID
- ARACHIDONIC ACID

Linoleic Acid

18:2 (9, 12)

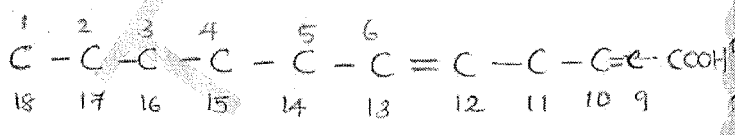
- 18:2 → No: of C → 18 C
- 18:2 → No: of Unsaturation
- (9, 12) → position of unsaturation

Linolenic Acid : 18:3 (9,12,15)

Arachidonic Acid : 20:4 (5, 8, 11, 14)

Olden Nomenclature

Linoleic Acid – 18:2 (9,12)



Count the C from excl. when = found

eg: Linoleic Acid – $\omega 6$

Linolenic Acid – $\omega 3$

Arachidonic Acid – $\omega 6$

Non essential FA

Remaining FA other than essential FA.

Essential FA:

Human beings lacks the enzy which can incorporate the = bond after 9th C

So can't produced in body supplied through diet.

Linoleic acid. Most essential FA

Lipid metabolism

Overview:

Lipid
↓
Fatty acid. Glycerol.
↓
↓ β oxidation of FA. - process
↓
Acetyl CoA
↓ ketogenesis
↓
Ketone bodies

β oxidation of fatty acid.

3 stages:

1. Activation → Cytosol
2. Transport
3. β oxidation Proper → Mitochondria

I Activation

in cytosol

Fatty acid

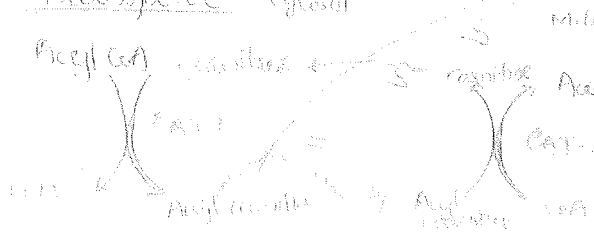
2 ATP → activation (Acyl CoA synthase)

Acyl CoA:

C – C – C – C – CoA

Acetyl CoA - contain only 2C
Acyl CoA - " long chain C.

II Transport



CAT - Carnitine Acyl transferase

Carnitine Shuttle : help in transport of Acyl CoA

Q. Carnitine shuttle operates in β oxidation of FA.

β oxidation proper

- Mitochondrial Matrix
- Starting substance : Acyl CoA
- 4 stages

Acyl CoA (eg: 16C)

FAD → / FADH₂ ← ↓ Oxidation

delta-2 transenoyl CoA

↓ Hydration

β hydroxy Acyl CoA

NAD⁺ → / NADH+H⁺ ← ↓ Oxidation

β keto acyl CoA

↓ Cleavage

Acyl CoA (eg: 14C) + Acetyl CoA eg (2C)

If β oxidation proper occur for once

1 NADH

1 FADH₂

Q. In human being FA undergo metabolic event reaction

↓

PALMITIC ACID (16C)

if we start with palmitic acid (16C)

7 cycles of β oxidation proper

7 FADH₂ + 7 NADH

Energetics

palmitic acid - 16C

β oxidation proper - 7 times

7 $FADH_2$ × 1.5 ATP = 10.5 ATP

7 NADH + H^+ × 2.5 ATP = 17.5 ATP

No: of Acetyl CoA - 8 molecules.

Each molecule of Acetyl CoA
↳ 10 ATP (Kreb's cycle)

8 Acetyl CoA × 10 ATP = 80 ATP

108 ATP
− 2 ATP (Activation of FA)

106 ATP

* No: of times of β oxidation proper = $\frac{n}{2} - 1$

n = no: of carbons.

Fatty Acid	End product
Even chain FA	Acetyl CoA (2C)
Odd chain FA	propionyl CoA (3C)

Acyl CoA
↓ Acyl CoA dehydrogenase
Δ^2 transenoyl CoA
↓
β hydro
↓
↙ ↘

Q. Calculate no: of ~~acid~~ ATP Arachidonic acid - 20C

20C

β oxidation proper - 9 times

9 $FADH_2$ × 1.5 ATP - 13.5 ATP

9 NADH × 2.5 ATP - 22.5 ATP

Acetyl CoA - 10 molecules

10 Acetyl CoA × 10 ATP = 100 ATP

136 ATP
− 2 ATP

134 ATP

Clinical Correlation:

Lactation:

Baby has to be ~~feed~~ fed - 2 hrs.

Feed @ ~~8 hrs~~ 8 o'clock
↓ didn't feed
Morning

Milk Lactose → Glu + Galactose

if didn't feed

Adipocyte (Lipid → Fa + Gly)

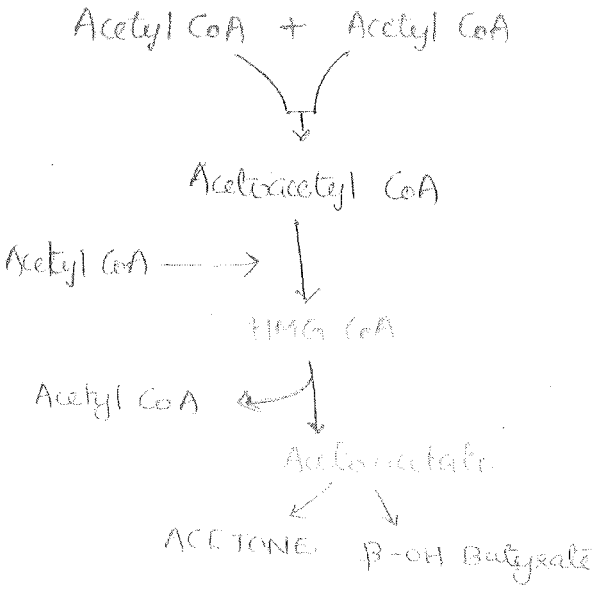
FA → in cell
Activation
Transport - carnitine
β oxidation proper
↓
if baby have Acyl CoA dehydrogenase deficiency.
No ATP will be produced.
↓
The baby died.

Condition:
Sudden Infant Death syndrome (SIDS)
Baby dies overnight, dlt no feeding.

Ketone bodies

1. Acetoacetate
2. Acetone
3. β hydroxy butyrate

Ketogenesis



Q. 1° ketone body
↳ Acetoacetate

Q. ketogenesis → Liver
Site: Mitochondria *

• Ketone bodies - Source of Energy.

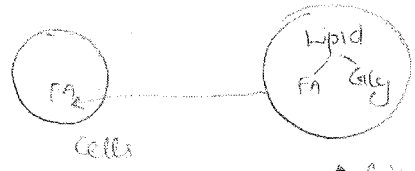
Q. Liver can't utilize ketone bodies
all other organs can use.

Q. Which ketone bodies exhaled out?
Acetone (fruity smell)

HMG CoA
(β hydroxy β Methyl Glutaryl CoA)

Diabetes Mellitus

Hyperglycemia.
↑↑Glu.



In diabetic people
Glu ↑↑, cells not get Glu, cells depend on adipocyte
→ ↑ FA in cells

FA
↓
Acetyl CoA
↓
Ketone bodies
Type 1 diabetes

Diabetic ketoacidosis

Fatty acid synthesis

Acetyl CoA —(Acetyl CoA Carboxylase, Biotin; CO_2)→ Malonyl CoA

- Acetyl CoA Carboxylase utilise Biotin
- This rxn require
  - ATP
  - Biotin
  - CO_2

Malonyl CoA —(Fatty acid Synthase Complex)→ Fatty Acid palmitic acid (16C) (Imp)

↓ to Enzy

* Rate limiting enzyme

↓

Acetyl CoA Carboxylase.

↑ ⊕ Citrate, Insulin

Insulin : Anabolic hormone, it helps in formation of Enzyy Glycogen, Fatty acid.

Also citrate stimulate.

Fatty acid synthesis in human body → Palmatic acid

* Fatty acid → formed in cytosol

→ enter into Endoplasmic reticulum

Inside formation ER:

1. Elongation
2. Desaturation

Rough ER : formation of protein.

CHOLESTEROL Metabolism

Synthesis of Cholesterol:

5 stages

Acetyl CoA + Acetyl CoA

↓

Acetoacetyl CoA

Acetyl CoA →

↓

HMG CoA — 1st stage

HMG CoA Reductase ⊖ — statin

↓

Mevalonate — 2nd

↓

Isoprenoid Unit — 3rd

↓

Squalene — 4th

↓ 19 rxns.

Cholesterol

Q. Rate limiting Enzy of cholesterol synthesis

↳ HMG CoA Reductase.

if hypercholesterolemia, to ↓ FA by inhibition of HMG CoA Reductase

↓

Statin drug

Degradation of Cholesterol

Cholesterol

All steroid Hormones | Vit D | Bile acid

1) Mineralocorticoids

Major Mineralocorticoid

Aldosterone - help in Na, H_2O retension.

↓

Concentrate of Urine

2) Glucocorticoids :

Major Glucocorticoid

Cortisol - energy metabolism

3) Testosterone

4) ♀ sex ~~organ~~ hormones :

Estrogen.

Progesterone.

- All other steroid hormones

Lipoproteins

Contain lipid part - triglycerides & Cholesterol

\+

protein part - Apoprotein

Apo protein

Apo B48

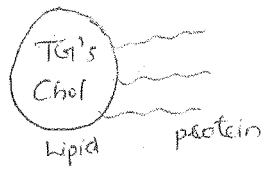
Apo B100

Apo C

Apo E

Apo A

Lipid + protein = Lipoprotein



Types :

Chylomicron

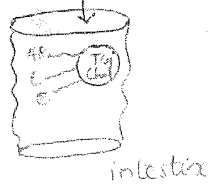
VLDL

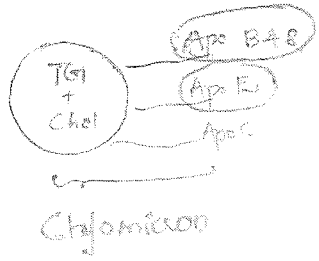
HDL

LDL

IDL

Dietary / Exogenous fat





- All exogenous fat forms Chylomicron in intestine

- Chylomicrons are not absorbed by Blood. (Lacteals) absorbed by Lymph → finally drain into blood.

In the blood chylomicron comes in contact with peripheral tissue eg: Adipocyte

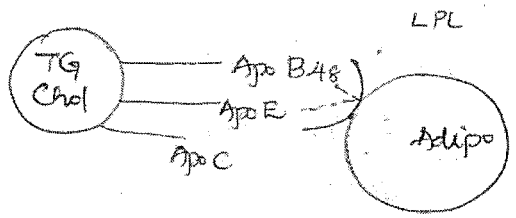
The chylomicron receptor on Adipocyte is identified by

Apo B_{48}

Apo E

Near the tissue → Enzyme

LPL (Lipo protein Lipase)



After attaching, Apo C activate LPL. (Lipo protein Lipase)

★ LPL breakdown Lipid on Chylomicron.

Then stored in Adipocyte → fat stored.

Not all Cholesterol chylomicron stored.

VLDL → B100, E, C

Q. Exogenous fat (syn in Liver) - VLDL

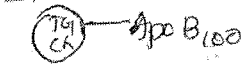
Q. Dietary fat metabolised by Chylomicrons

Q. Int to tissue - Chylomicron

Q. Liver to tissue - VLDL

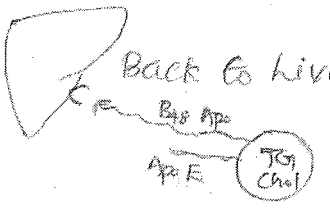
Density is determined by protein → Apoprotein.

From intermediate lipoprotein remove protein → LDL



HDL:

Chylomicron remnant



Apo B48 } identify
Apo E } liver R.

Composition

Lipoprotein	Apoprotein
Chylomicron	ApoB48, E, C
VLDL	ApoB100, E, C
IDL	ApoB100, E
LDL	Apo B100
HDL	Apo A, E, C

Out of all Lipoprotein

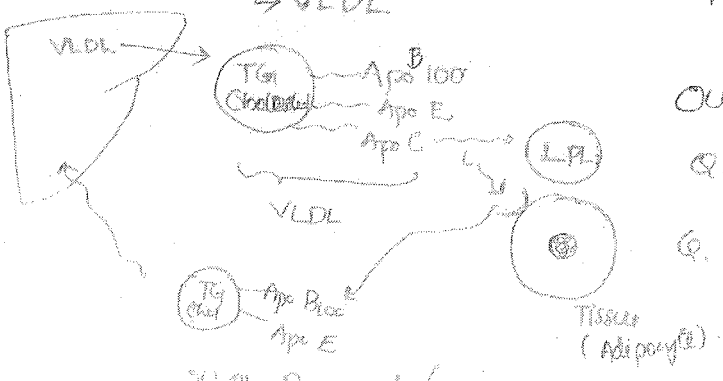
Q. Highest Cholesterol

Q. Highest TG's

Metabolism of VLDL

Liver synthesis which Lipoprotein

↳ VLDL



VLDL Remnant / IDL

Functions of Apoprotein

Apo B 48, Apo B100, Apo E } Receptor & Lipoprotein interaction

Apo C — Activation of LPL

Apo A — " " LCAT (Lecithin cholesterol acyl transferase)

ENZYMES

Def: Enzyme are substance which ↑ velocity / catalyses / ↑ rate of reacn.

Classifications:

6 Classes:

Class I — Oxidoreductases
" II — Transferases
" III — Hydrolases
" IV — Lyases
" V — Isomerases
" VI — Ligases

Universal Classificatn.

Class I:
Include all enzymes which do Oxidatn & Reduction.
eg:

Class II:
eg: Glucokinase / HK
Alanine transaminase

Class III:
Breakdown in presence of H_2O

Class IV:
Absence of H_2O – breakdown.

Class V:
Same struc diff structure formula.

Class VI:
Ligases – unite.

Nature of Enzymes

Enzy. Protein + Non protein
↓ Holoenzy — ↓ Apoenzyme — ↓ Prosthetic Grp / Coenzyme / Cofactor

Coenzyme – no protein part of Enzyme.

Holo Enzyme = Apo Enzy + Coenzyme

Factors affecting Enzyme

1. Concentratn of Enzy
2. " " Substrate
3. " " product
4. Temperature
5. pH.

Concentratn = rate of

$S \xrightarrow{E\uparrow} P$

if E↑ – velocity ↑

Concentration of Enzy ∝ Velocity

Concentration of substrate

$\uparrow S \xrightarrow{E} P$

↑S ∝ V↑

Con of S ∝ velocity.

Concentration of product

$S \xrightarrow{E} P\uparrow$

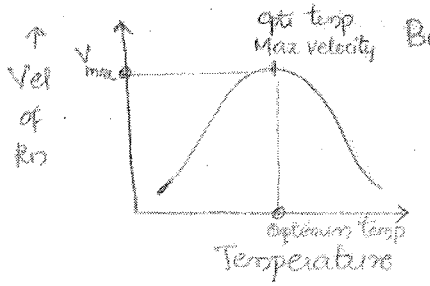
Con of Pdt↑ → Velocity ↓

∝ 1/Velocity.

Temperature

When temp ↑ → velocity ↑

After an optimum temp the further ↑ temp, Enzyme → denaturation.



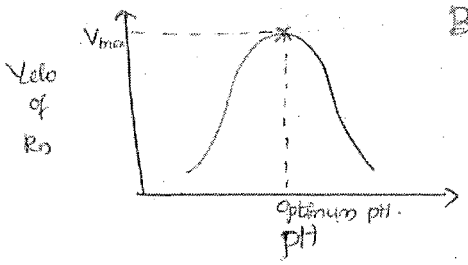
Bell shaped graph

Optimum temp : 40 – 45°C

max velocity @ optimum temp

pH

pH 1 → 14



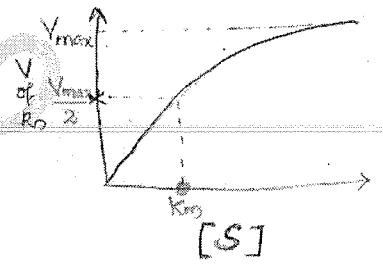
Bell shaped graph.

Optimum pH – 6 to 8 pH.

pH @ which Velocity Maximum.

** Q Michaelis Menten Graph

[S] ∝ velocity of reaction



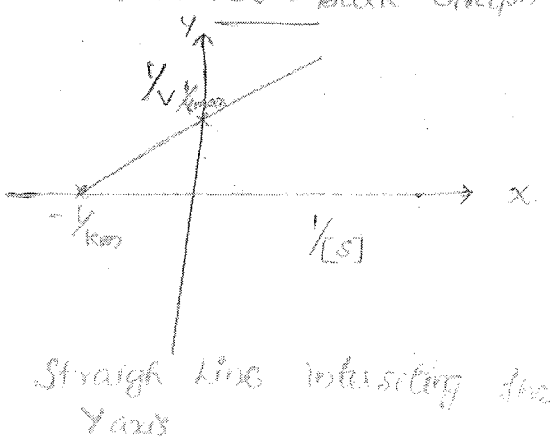
Parabolic Graph.

[S]↑ ∝ V↑ parabolic graph.

Michaelis Menten Constant (K_m)

Q. It is substrate concentration @ half the Max velocity.

Q. Lineweaver – Burk Graph



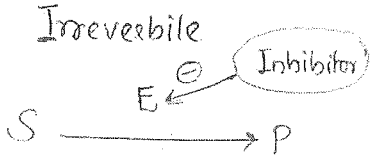
Straigh line intersecting the Y axis

The straight line intersecting the Y axis
That point - $1/V_{max}$

The straight line intersecting the X axis
that point - $-1/K_m$

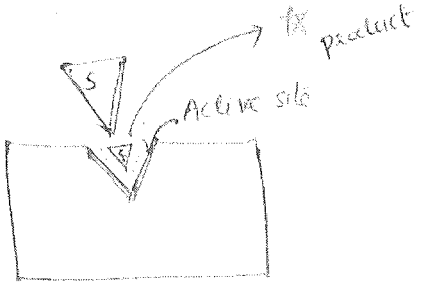
Enzyme Inhibition

2 types:
- Reversible
- Irreversible



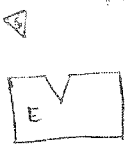
Inhibition inhibit the Enzy - Rn stopped, After sometime Inhibitor release → Rn again happen.
↳ Reversible Inhibition.

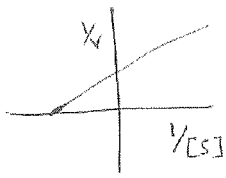
Irreversible:
Inhibitor ~~Enzy~~ permanently bind to Enzy



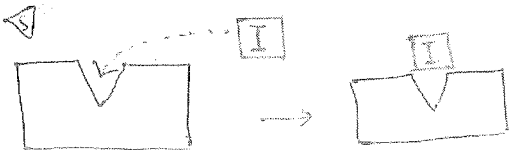
$S + E \rightleftharpoons SE \longrightarrow E + P$

Reversible Inhibition:
- Competetive I
- Non competetive I

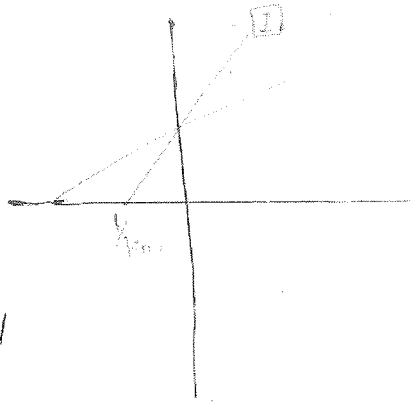




Normal Rn.



No Reaction.



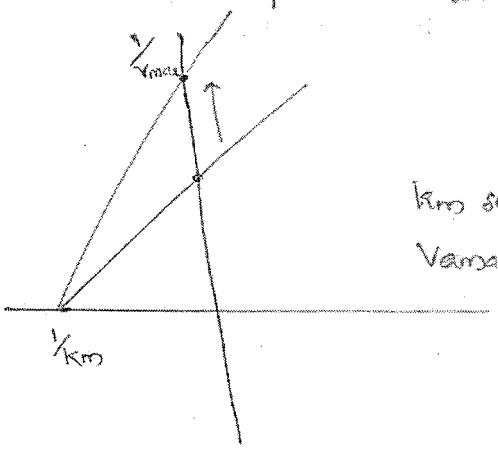
V_{max} same
Km ↑

Competetive Inhibition:

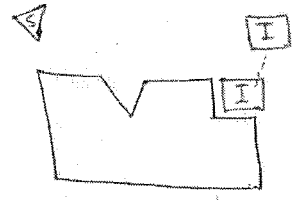
Q. V_{max} - what happened?
V_{max} - Remains same

Q. K_m ?

Non competetive Inhibitor.



Km same
Vamax ↓ses



On enzyme, seperate site for inhibitor - Allosteric site

I Not depend on S → Non competetive I

↓

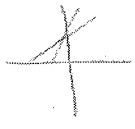
Rn steps

Q. Km same

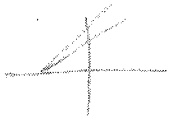
Vmax ↓ses

here $\frac{1}{V_{max}}$ ↑ses ∴ V_{max} ↓ses

Competetive Inhibition - Crossing



Non competetive Inhibition - Not Crossing



Isoenzyme

Lactate dehydrogenase - LDH

Isoenzyme	Subunits	Location
LDH_1	H_4	Heart
LDH_2	H_3M	Heart
LDH_3	H_2M_2	Brain
LDH_4	HM_3	Muscle
LDH_5	M_4	Muscle

Creatinine kinase - CK

CK - BB	Brain
CK - MM	Muscle
CK - MB	Heart

NUCLEIC ACID

DNA — RNA

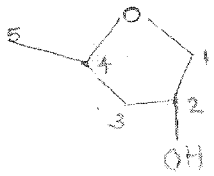
double stranded helical structure

Strand:
Each strand of dna - polymer of Nucleotide

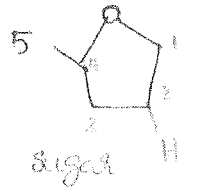
Nucleotide:
① Sugar
② phosphate
③ Nitrogenous base

Sugar

Ribose (5C)



Remove -O from C_2



deoxy Ribose sugar

Nitrogen Bases

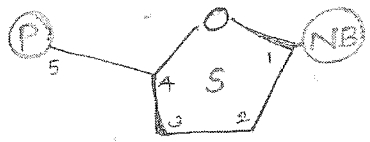
Purine
Adenine
Guanine

Pyrimidines
Cytosine
Thymine

Major Purines
Adenine, Guanine.

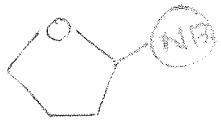
Minor Purines:
Hypoxanthine
Xanthine
Uric acid

Nucleotide



Nucleoside

S + NB



Nucleotide = S + P + NB
Nucleoside = S + NB

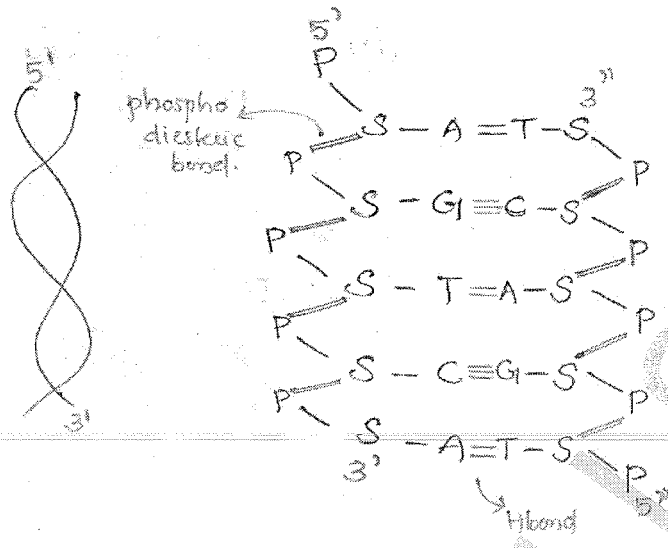
Nucleoside = NT - P
Nucleotide = NS + P.

Nitrogenous Bases (NB)	NB+S Nucleoside.	NB+S+P Nucleotide
Pu — Adenine	Adenosine [S+A]	AMP, ADP, ATP
Pu — Guanine	Guanosine	GMP, GDP, GTP
Py — Cytosine	Cytidine	CMP, CDP, CTP
Py — Thymine	Thymidine	TMP, TDP, TTP

ATP - Nucleotide
&
Energy rich molecule

Structure of DNA

Watson & Crick DNA
B- DNA.



Sugar of 1 NT combine ⓟ of another NT.

Phospho diester bond.

↓

Strong bond.

→ if T, pH ↑ses - it will not affect phosphodiester bond.

Chargaff's rule

1) No: of purines = No: of pyrimidine

$A + G = C + T$

$\frac{A+G}{C+T} = 1$

Complementary Law

2) Purines — A, G
Pyrimidine — C, T

- H bond - weak bond. changes with Temp & pH.

Two strands join together by - Hydrogen bond.

Single strands - phospho diester bond.

protein - peptide bond.
Carbohydrate - glycosidic bond.
Lipids - Ester bond.

DNA

→ ds
→ Helical
→ Complementary
→ Antiparellel.

Nucleases

Exo nucleases
Endo nucleases

Enzymes to break Nucleic acid
(to break phosphodiesteric bond)

Types of DNA

- A DNA
- B DNA

C DNA

D DNA

E DNA

Z DNA

B DNA

Watson & Crick. DNA

ds

Right hand helix.

In B DNA - 10 bps/helix

2 helix = 360°.

Length of 1 helix

34 Å

Distance blw base pairs

3.4 Å

Diameter of DNA.

20 Å

Q. In a DNA if A is 30%, Then C = ?

A + G = C + T

50%

if A = 30%

30% 30%

20% 20%

G = C

Z DNA

ds

Zig zag

Left hand helix

Z DNA

12 bps / helix

Q. In DNA, if T = 65% Then G?

65% + 65% = 120%.

T = A

Ans: Our DNA is 100%.

DNA does not exist.

OR

Can be a single stranded DNA

then chargaff rule not exist

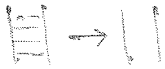
Q. Denaturation / Melting of DNA

When Temp or pH ↑ses (alkali added)

→ H bond break

and denaturation or

Melting of DNA occurs.



Q. Renaturation or Annealing

When Temp ↓ses

Organization of DNA

chromatic material

String of beads.

Bead = Nucleosome

Nucleosome:

Nucleus protein

Histone protein

Octamer

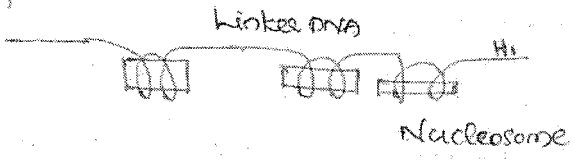
Nucleosome

8 Histone proteins ⇒ Octamer of Histone.

2 Copies

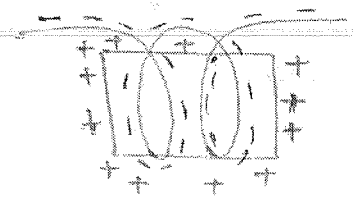
H_{2A}	H_3
H_{2B}	H_4

Nucleosome - linked by Linker DNA assoc ē H_1 histone protein



DNA

Negative charge



Q. Histone protein contain large amount of lysine (Basic AA) Arginine

Basic AA ∴ positive charge in histone.

In Basic AA - R group contain NH_3^+ ⇒ gives +ve

In Acidic AA → R group contain COO^- ⇒ gives -ve

~~On DNA~~

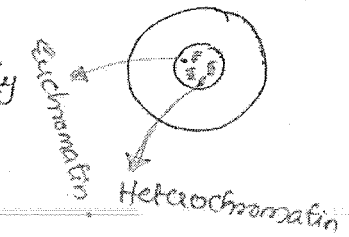
Q. DNA coils on Histone protein 1.75 terms

Euchromatin	Heterochromatin
• Lightly stained	• Darkly stained
• Loosely coiled	• Tightly coiled ∴ Take stain more.

Genetic Expression for this gene shld be expressed

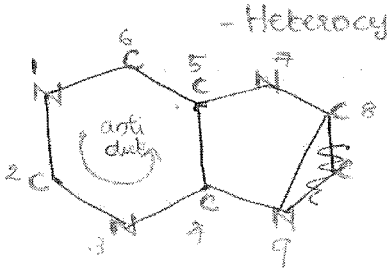
↳ for that Loosely arranged.

DNA → RNA.



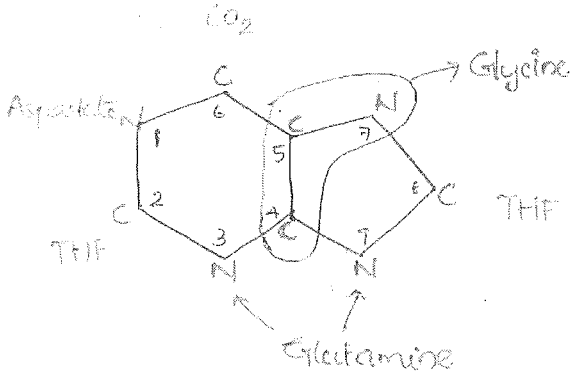
Metabolism of Nucleotide

Purine Ring - Double ring
- Heterocyclic



Homocyclic - only one element i.e C

Heterocyclic C + N



Nitrogen - only contributed by AA (protein)

THF -

overview Synthesis of purines

DeNovo Synthesis — Salvage pathway.

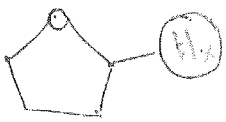
IMP shunt → Ribose 5 - (P)

↓

IMP

AMP — GMP

IMP - Inosine Mono phosphate



Inosine

Inosine Mono phosphate

Ribose - 5 - phosphate - formed from IMP shunt

for formation of DNA & RNA

DeNovo Synthesis

① Ribose - 5 - phosphate

ATP → AMP (PRPP Synthase)

phosphoribosyl pyrophosphate (PRPP)

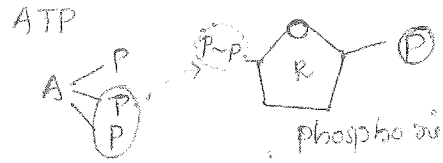
← Glutamine (NH_2) — Amidotransferase

phosphoribosyl Amine

↓

IMP

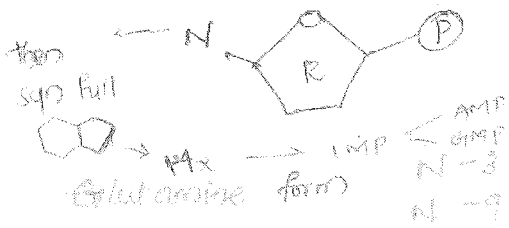
AMP — GMP



P_i → pyrophosphate

↓

Glutamine came remove (P~P) then added (N) from NH_2

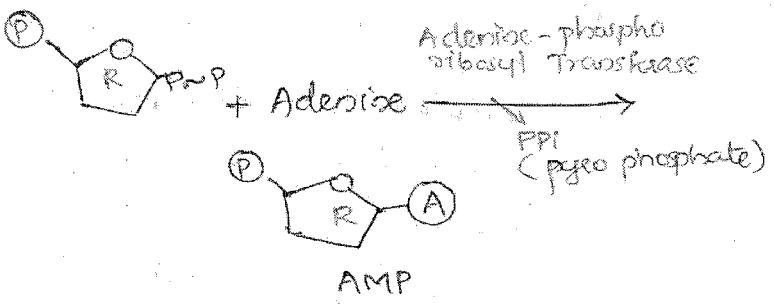


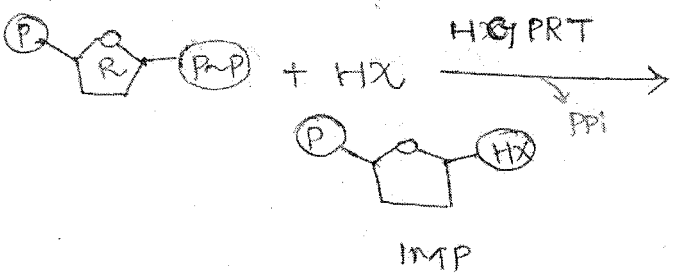
N_1 - Aspartate

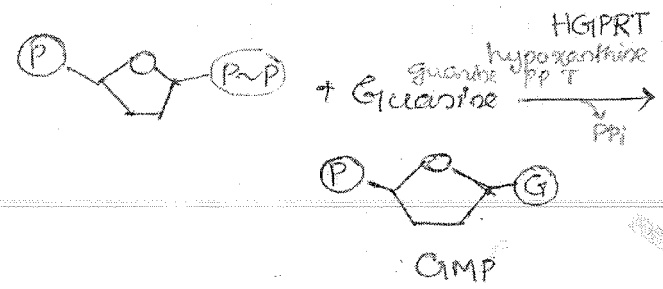
C_2, C_8 - THF

C_4, C_5, N_7 - Glycine

Salvage pathway







Clinical Correlate:

Lesch - Nyhan Syndrome

Enzyme deficiency: HGPRT

↑ products, ↓ utilization → ↑ uric acid.

C/F:

Gout

Neurological disorder

* SELF MUTILATION

- Chewing the fingers
- Bleeding

Lesch Nyhan Sy - X linked Recessive Disorder

End products of Purine

AMP GMP IMP

↘ ↓ ↙

Hypoxanthine

↓ Xanthine oxidase

Xanthine

↓ Xanthine oxidase.

Uric acid.

C/C:

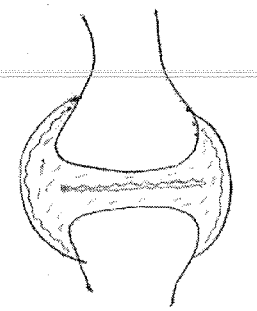
GOUT

uric acid ↑

Hyperuricemia.

uric acid → MSU crystal

(Mono Sodium Urate)



MSU crystal - Needle shaped crystal

MSU crystal deposited in synovial joint → irritate joints → inflammation

GOUTY ARTHRITIS

Pseudo Gout:

"Calcium pyrophosphate" deposited.

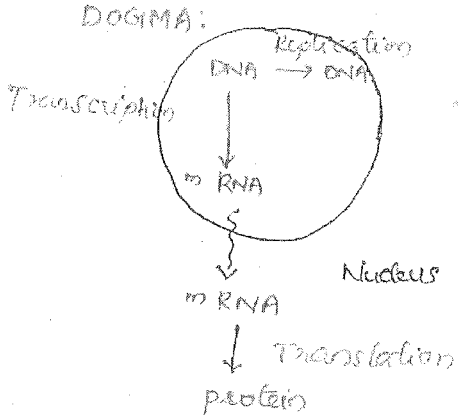
Q. End Product

Purine ⟶ Uric acid

Pyrimidines ⟶ NH_3, CO_2, β alanine like

MOLECULAR BIOLOGY

CENTRAL DOGMA:



Replication, Transcription – Nucleus
Translation – cytoplasm

Enzyme for Replication : DNA polymerase

" " Transcription : RNA polymerase.

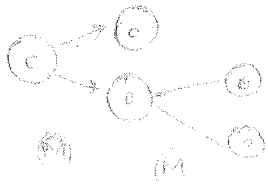
Replication ☆

Def : formation of a DNA from DNA.

DNA ⟶ (DNA dependent DNA polymerase) ⟶ DNA

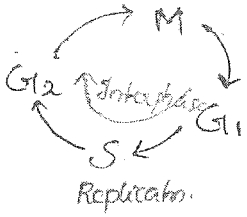
Site : Nucleus.

Occurs during 'S phase' of cell cycle

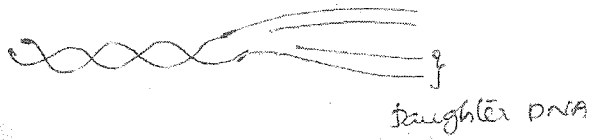


Interphase.

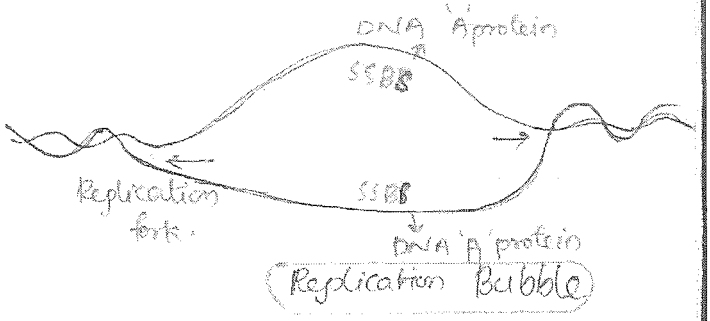
M ⟶ (Interphase: G_1 S G_1) ⟶ M



S phase → Replication.



Daughter DNA:
Half of parent is conserved
∴ Replication is a semi conservative process.



SSBP – protein
Single strand binding protein
Stabilises the single strand

SSBP – stabilizer

SSBP – prevent the attack of Nucleases in single strand.

For Replication of entire DNA – opening of Replication fork → by unwinding the DNA

Helicases - start to uncoil the DNA → but due to Super coil (more strong coils) → helicase stop function.

Topoisomerase : 2 types
uncoil the super coil

2 functions :

1. Nick - make cut and relax the coil.
2. Then attach.

Topoisomerase

Topoisomerase I

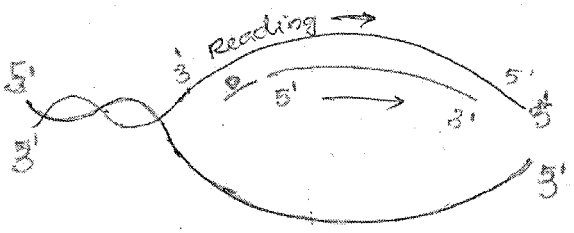
- Nick one strand

Topoisomerase II

- Nick both strand.
- DNA Gyrase ↓ in prokaryotes

Fluroquinolones - Antibacterial

Inhibit DNA Gyrase ↓ No DNA uncoiling ↓ No DNA Replicatn.



"DNA polymerase" enter but can't stabilise the whole single strand.

∴ RNA primer. small nucleotide

Thus DNA polymerase stabilized

RNA primer formed by PRIMASE

- Direction of Replication 3' → 5'
- Reading always in 3' → 5' by DNA polymerase.
- New strand formed 5' → 3'

DNA polymerase

1. Proof reading
2. Exonuclease Activity

It break the phosphodiester bond → Nucleases activity Exonucleases.

C T
G C

DP Read the strand, if any Correction → it cut the ends. act as Exonucleases.

PRIMER

Formation - Primase
Removal - RNase H in Eukaryote.

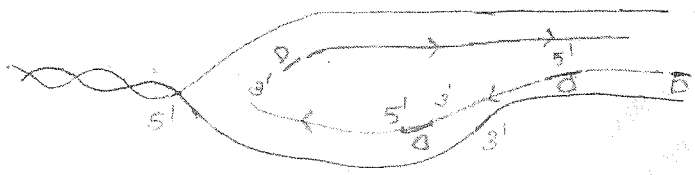
The gap filled by DNA polymerase I

Ligation: DNA Ligase

Replication: DNA polymerase III.

Q. The strand which move towards Replication fork: 

Leading strand.



Q. The strand which move away RF: Lagging strand.

The new DNA polymerase came DNA primer

Q DNA polymerase

Prokaryotes	Eukaryotes
DNA P - I	DNAP α - primase DNAP β - DNA repair
DNAP - II	* DNAP γ - Mitochondrial DNA replicate
DNAP - III	DNAP δ } Leading strand DNAP ε } Lagging strand

DNAP-III → form Leading strand
Lagging strand.

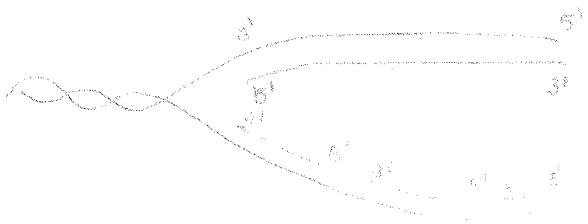
Continous strand: Leading strand.

Discontinous strand: Lagging strand.

DNAP-I Gap filling

DNAP II - DNA repair

OKAZAKI fragments:
fragments in Lagging strand.



Protein Synthesis

DNA
↓ Transcription.
hn RNA (heteronuclear RNA)
↓ post transcriptional modification.
m RNA

Q. post transcriptional modifications occur in Nucleus.

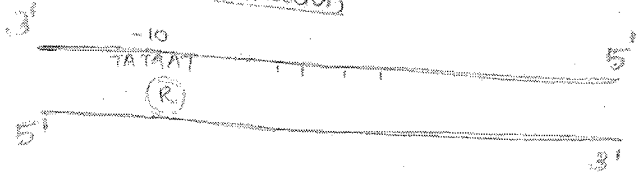
m RNA
↓ Translation.
protein

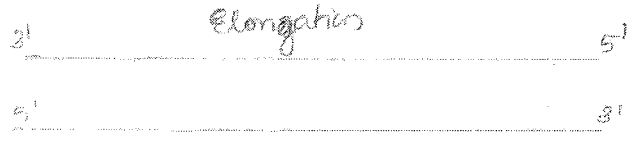
Post translational Modifications.

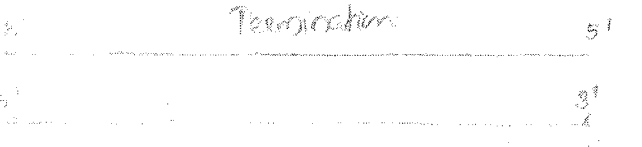
TRANSCRIPTION

Def: formation of RNA from DNA. DNA dependent RNA polymerase
DNA → RNA

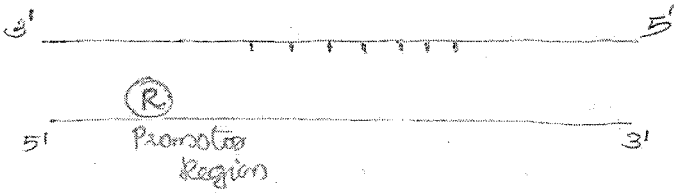
Site: Nucleus.







Initiation:



Attachment of RNA polymerase to DNA, in promotor Reg sequence before the sequence (upstream)

In prokaryotes attachment:

★ -10 Sequence.

TATAAT - Sequence of Promotor Reg

TATA Box / Pribnow Box.

★ -35 sequence. TTGACA

In Eukaryotes

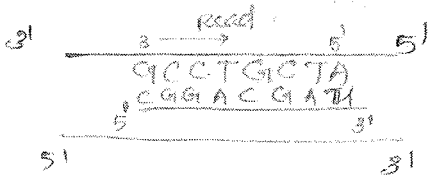
- -25 seq Hogness Box TATA
- -70 to -80 seq CAAT Box CAAT

Elongation

Then RNA polymerase move and read sequence.

Read → 3'→5' } in Entire Molecular Biology

Then form RNA



T = U

RNA polymerase

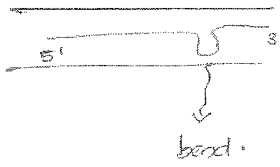
No proof Reading
No Exonuclease activity

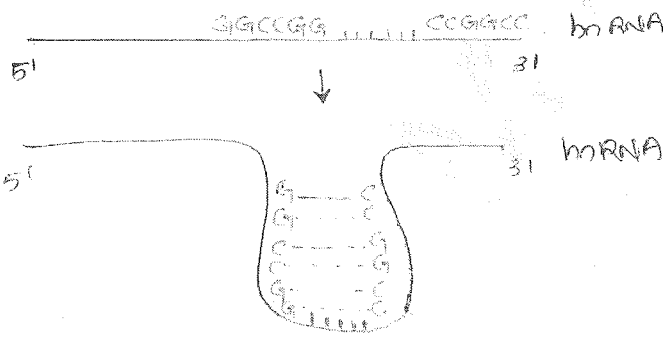
Termination

ρ - dependent

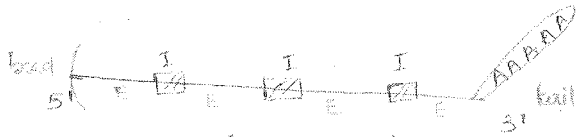
ρ - independent

- ρ dependent T
  - ρ protein
  - 2 functions:
    - Terminate the RNA.
    - Remove RNA
- ρ independent T
  - RNA forms a "bend" bcoz of palindromic sequence.





Post transcriptional Modification



hn RNA / 1° transcript

Modification:

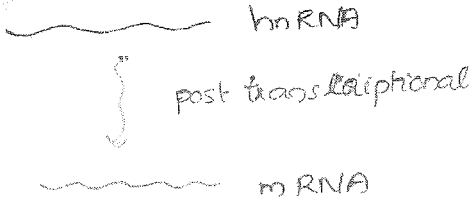
1) 5' Capping
   7 methyl Guanosine
   attach → 5' end.

2) On tail: 3' end.
   poly 'A' tail

3) Splicing:
   Removal of Intron
   Ligation of Exons

Introns - Non functional
Exons - functional.

Splicing: done by
Spliceosomes
OR
sn RNP's
OR
Snurps.



RNA POLYMERASE

Prokaryotes	Eukaryotes
RNAP	RNAP I
Subunits:	RNAP II
α α	RNAP III
β β'	
σ factor	

- σ factor - help to identify and attach to promoter region.

In Eukaryotes:
RNAP I → rRNA
" II → hn RNA, snRNA
" III → tRNA

Except 21st AA — UGA — Selenocysteine
22nd AA — UAG — Pyrrolysine

Q. RNAP - I - form all the * RNA except 5s rRNA → formed by RNAP III

Genetic Code / Codon.

def: Combination of 3 nucleotide which code for an amino acid.

AUG → Methionine

Pu — A, G Py — C, U

4 - Nitrogen bases
Codon - 3 NB

$\therefore (4)^3 = 4 \times 4 \times 4$
$= 64$ codon

*Q. If Codon has 4 nucleotide

$4^4 = 256$ Codon.

64 Codons

AUG
5' 3'
mRNA

AUG - Initiation Codon

UAA, UAG, UGA → Stop Codon / Termination C / Non sense C

Features

1) Universal
Same codon code for same AA for all species.

2) (No punctuations) comaless & Non overlapping.

3) Specific / Unambiguous

4) Degenerate: 1 AA can be coded by different codon.
Codon code for AA → 61

Ribosomes

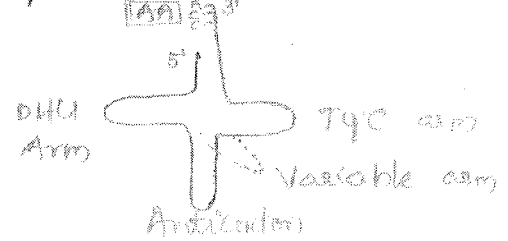
Prokaryotes — 70s → 50s, 30s
Eukaryotes — 80s → 60s, 40s

tRNA

smallest tRNA. (tiny)
Most abundant - rRNA

Structure:

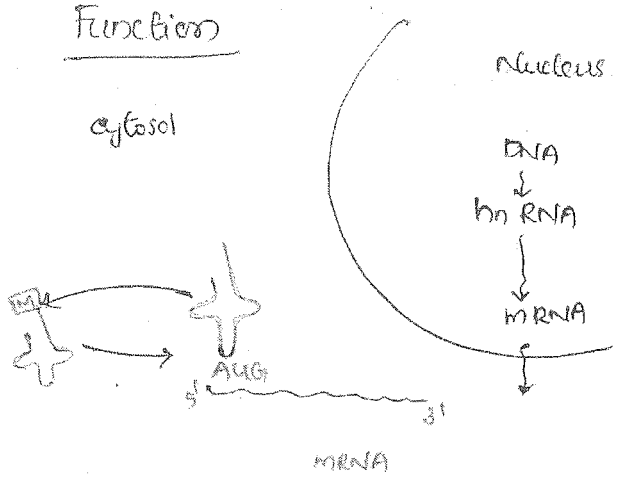
Shape - Clover leaf



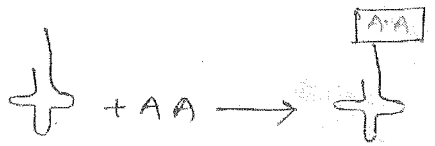
3' end - Acceptor arm

Anticodon arm - Read the mRNA.

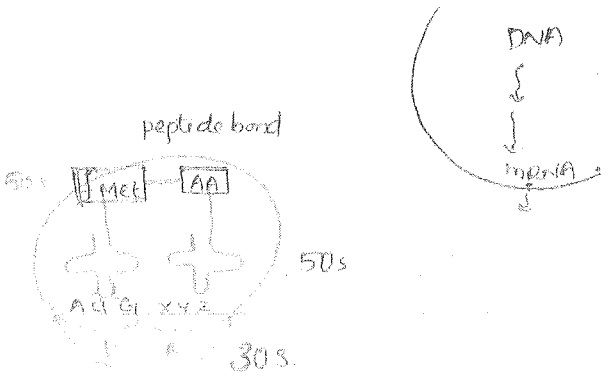
Function



tRNA - read the codon on mRNA and search for AA.
and help in transfer of AA from cytosol



Q. Drug that prevent Amino acyl tRNA.

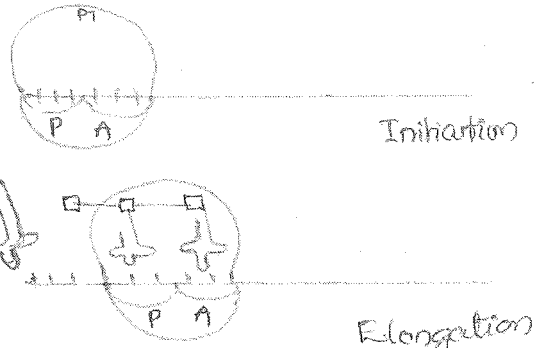


Initiation Complex:

Sandwiching of mRNA b/w 2 subunits of Ribosome.

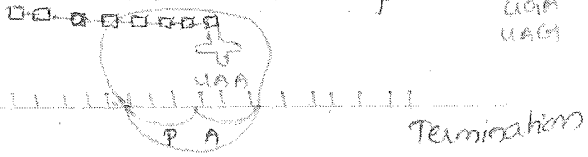
- fMet formyl Methionine - prokaryotes
- Met - Methionine - Eukaryotes
- Peptidyl transferase forms petide bond.
- peptidyl transferase - found in Larger subunit

After forming peptide bond, the tRNA detaches.



Translocation - 1 codon distance movement by Ribosome.

When reaches stop codon. UAA UGA UAG



Translation

1. Initiation
2. Elongation
3. Termination

Q. Insulin. -51 AA

• If deficiency of Cu
↓
Collagen triple helix not formed.

Post translational Modification & * Protein folding done by CHAPERONS

DNA
↓
mRNA
↓
protein

Proteins modified by
- Hydroxylation
- Glycosylation
- Carboxylation
- Methylation

if defective protein → Labelling of protein

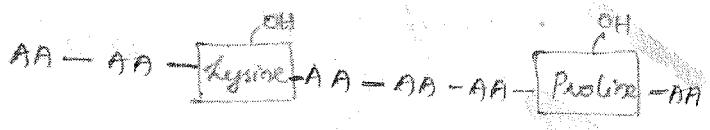
Q. Labelling by Ubiquitin

Q. if any protein attached to Ubiquitin
↓
abnormal Protein

Q. Proteasomes - breakdown the abnormal protein

Post transitational Modification of Collagen

Collagen - polymer of AA



Hydroxylation

Lysinyl hydroxylase - Coenzyme Vit C

Prolyl hydroxylase - Coenzyme Vit C

if Vit C defi → no hydroxylation
→ no Collagen

C/C:
• Bleeding gums
feature of scurvy.

* Triple Helix done by
Lysyl oxidase require Cu

Blotting Techniques

Analysis of

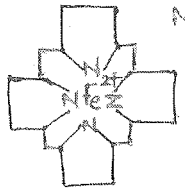
Northern blotting - RNA
Southern blotting - DNA
Western blotting - Protein

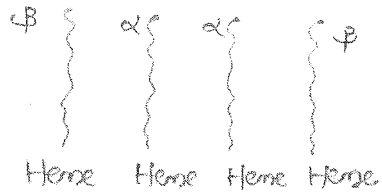
HAEMOGLOBIN

Haemoglobin
- Non protein
- protein

Structure of Heme.

Pyrrole Ring → Protoporphyrin + Fe^{2+} (ferrous ion) → Heme





globin chain.

Heimoglobin

Types of Hb

- HbA – $\alpha_2\beta_2$
- HbA_2 – $\alpha_2\beta_2$ $\gamma_2\delta_2$ } Adult
- Hb F – $\alpha_2\gamma_2$ – Foetus
- HbA_{1c} – $\alpha_2\beta_2$ – Glucose

glycosylated Hb
seen in Diabetes patients

Heme synthesis

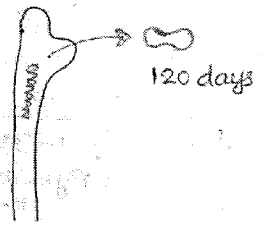
Succinyl CoA + Glycine
→ (ALA synthase, Coenzyme PLP (pyridoxine phosphate) Vit B_6)
→ δ ALA (δ-Amino levulonic Acid)
→ (H_2O, ALA Dehydratase)
→ Porphobilinogen (PBG).

* RLE of heme synthesis
ALA synthase.

PBG
↓
Cleo porphyrinogen
↓
Copro porphyrinogen
↓
Proto porphyrinogen.
protoporphyrin
- Fe^{2+} → Ferrochelatase → HEME
- -gen → means inactive
- active → gin

Lead poisoning inhibit Ferrochelatase
Lead (Pb) – inhibit Ferrochelatase
&
inhibit ALA dehydratase

Degradation of Heme



Red BM forms RBC → blood.
after 120 day → Old RBC →
Graveyard of RBC Spleen.

Hemolysis occur
↓
Hb release
Heme / Globin
Heme → Biliverdin → Bilirubin (end product of Heme degradation)
Globin → breakdown → AA → Reutilized bcoz somany functions.

Bilirubin - no function so excreted, but Insoluble.
∴ Taken to Liver → through blood.

Bilirubin + Albumin
complex
Insoluble
Bilirubin (Unconjugated B)
↓ ← UDP glucuronic acid
Bilirubin diglucuronide (Conjugated B)
Soluble
↓
To intestine
↓
Bilirubin → Normal flora → Urobilin (Urine) / Stercobilin (Feces)

Clinical correlation

- Hyperbilirubinemia (Jaundice)

(N) bilirubin = 0.5 – 1 mg/dL (>2 mg/dL - hyper)

1. Hemolytic J
   Hemolysis Ab (N)
2. Hepatic J - hepatic cause can't conjugate, UDP glucuronyl
3. Obstructive J
   - No. of RBC breaking (N)
   - Conjugation (N)
   - but due to obstruction: Cholelithiasis
     Conjugated B rises.

Vitamins

Fat soluble	Water soluble
A, E, K	B, C

Vit A

Retinol — OH

Retinal — CHO

Retinoic acid — COOH

Source:

* β carotene → 2 Retinal (Vit A)

(Pro Vit A)

Functions:

1. Vision:
2. Epithelium
3. Reproduction
4. Antioxidant - Vit ACE

• Retina

Rods

Cones

Rhodopsin = Opsin + 11 Cis Retinal

⇒ Walds Visual Cycle / Rhodopsin cycle.

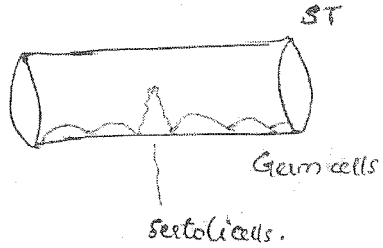
Light energy converted to Nerve Impulse

Epithelium

Growth & differentiation of Epithelium - Vit A required

Reproduction

Testis → Lobules → seminiferous tubules



Germ cells → Spermatozoa

flattened epi cells

if Vit A deficiency → abnormal epi cells → Oligospermia, Aspermia → Infertility

Deficiency diseases:

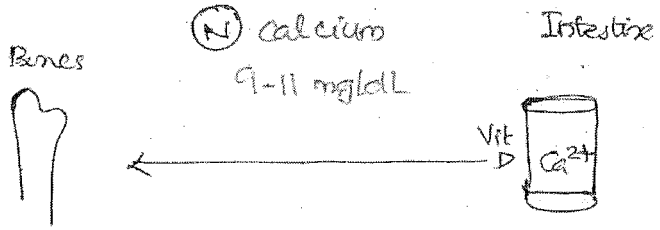
1) Night blindness / Nyctalopia
2) Xerophthalmia
3) Keratomalacia
4) Rough & dry skin
5) Infertility

Most potent antioxidant - Vit E.

Vitamin D

Vit D_1 - Calciferol
Vit D_2 - Ergocalciferol
Vit D_3 - Cholecalciferol

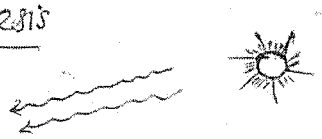
Function



Vit D is required for Ca^{2+} absorbtion from int & Deposition in Bone.

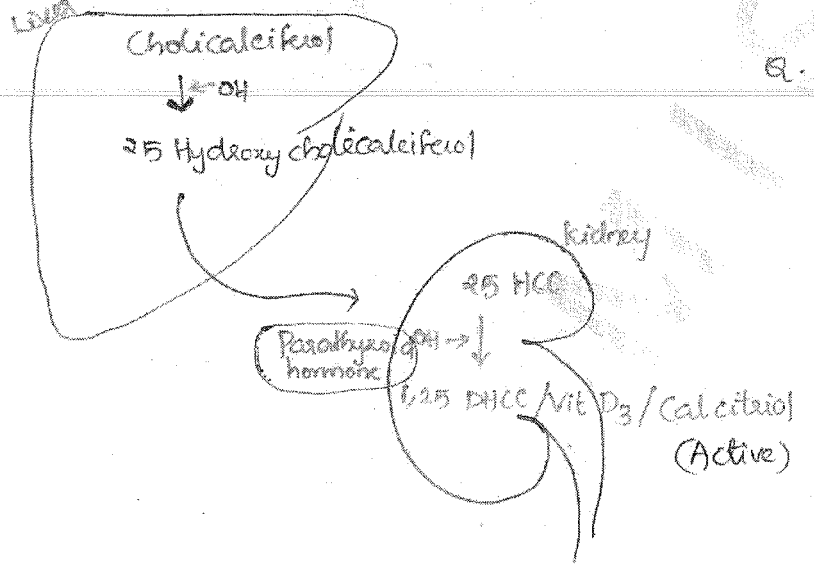
In children Ca def - Rickets
Adult Ca " - Osteomalacia

Synthesis



Skin

↓ 7 dehydro cholesterol
↓ U.V
Cholecalciferol



Synthesis

Skin → liver → Kidney.
PTH - essential for hydroxylation in Kidney or activation

Vit K

Q.

Vit K_1 phylloquinone
Vit K_2 Menaquinone
Vit K_3 Menadione

Function:

1. Coagulation

Clotting factor 2 7 9 10

CF 2 - prothrombin
CF 7 - stabilising factor
CF 9 - Christmas factor
CF 10 - Stuart factor

- Vit K required for
  γ Carboxylation at Glutamate
  These CF undergo carboxylation in modification (post translation)
  ↓
  post-translational modification

Deficiency disease

1. Bleeding
2. ↑ses prothrombin time (PT ↑)

Vit E / α tocopherol → active Vit E

Anti oxidant

def disease:
Rarely Neurological disorder

Water soluble

Vit B Complex

Vit B	Coenzyme	Enzy	Def dis
Vit B_1 Thiamine	TPP Thiamine diphosphate	• PDH • αKGDH • Branched chain ketoacid DH (5 Coenz Bcci)	Beri Beri
		• Transketolase ↓ need TPP (HMP shunt)	Wernicke Korsakoff Syndrome
Vit B_2 Riboflavin	FAD FMN	dehydrogenases	• Cheilosis • Angular stomatosis
Vit B_3 Niacin / Nicotinic acid	NAD+ NADP+	dehydrogenases 3D	pellegra ↓ dementia dermatitis diarrhea DEATH
Vit B_5 panthothenic acid	Coenzy A	—	Burning foot syndrome
Vit B_6 / pyridoxine	PLP	• ALA → Sideroblastic Anemia synthase • AST • ALT	
Vit B7 / Biotin / Vit H	Biotin	Pyruvate carboxylase propionyl CoA carboxylase Acetyl CoA Carboxylase	Alopecia

Q. Vit help in carboxylation ?
Vit B7 / Biotin

deficiency of B7 - d/t
Consumption of Raw Egg
Egg White - a protein
AVIDIN

if not boiled → Avidin
Combined with Biotin
→ excreted from body

- Biotin deficiency occur.

Deficiency disease

1. Megaloblastic Anemia
2. Neurological disorder.
   Neural tube defect
   MC defect: Spina Bifida

Vit B_9 / folic Acid

Liver, - Rich source of Vit 9, Vit 12
Spleen

folic acid absorbed from jejunum

Dihydro folate

folate → DHF → THF
(H_2 on folate→DHF; DHF reductase on DHF→THF; H_2)

THF + Methyl ($-CH_3$) / Formyl / Methylene
→ Methyl THF
Formyl THF
Methylene THF
" 1 C " Compound
↓
formation of DNA
RNA

Vit B_{12} / Cobalamine

Homocysteine Methyl transferase
Methyl Malonyl CoA Mutase

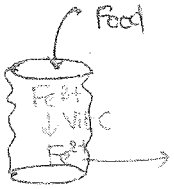
deficiency disease:
Megaloblastic Anemia
peripheral Neuropathy
(only asso c Vit B_{12}) not with folic acid defi

D Fe^{2+}
J Folic acid
I Vit B_{12}

Vit C / Ascorbic acid.

- Anti oxidant
- post translational modification of collagen
- Absorption of Fe

Vit C help in absorbtion of Fe.



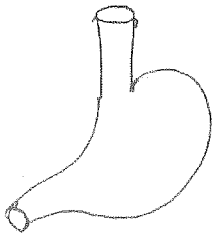
→ absorbed in Duodenum.

↓

Deficiency disease

Scurvy

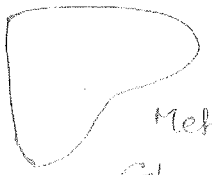
~~MINERALS~~



Carbohydrate rich meal will go to stomach → dig

→ Glu ↑ (more)
Fru
Galactose

To liver → by portal vein.



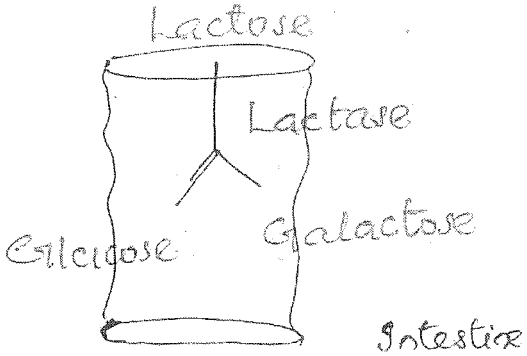
Metabolism of Glc, Fru, Galactose

Galactose metabolism

When consume milk or milk products

↓

it contain carbohydrate



From int Galactose absorbed it reach blood → distribute to various tissues

Glu → Glu-6-phosphate

The 1st rn of Glu inside cell is Glu

↓

Glu-6-phosphate

to keep Glu inside cell by trap

The galactose enter the tissue → 1st reaction

Galactose

ATP → ADP + Pi — Galactokinase

Galactose - 1 - phosphate

UDP glucose came

Exchange — Galactose - 1 - phosphate uridyl transferase occurs → UDP galactose

Glucose - 1 - phosphate

↓

Glycolysis

Glycogenesis

Glycogenesis

~~Glycolysis~~.

↑ Galactose in blood

↓

Galactosemia

Also went to Lens through blood

In Lens - an enzyme

Aldose reductase

Galactose ⟶ Galactitol

Aldose reductase

Deficiency of Lactase

ie lactose will not get digested

Bloating, diff in osmotic pressure - diarrhoea

Vomiting.

if def of Galactokinase

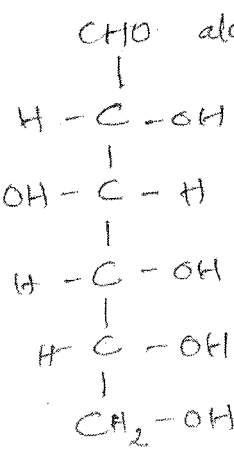
we can trap the galactose into cell. Gluc can't trap (P)

So galactose move out of cell

carbohydrates :

polyhydroxy aldehyde / ketones.

Glucose $C_6H_{12}O_6$



In Fructose - $C_6H_{12}O_6$

ketone - in group.

Alcohol $\xrightarrow{\text{oxidan}}$ aldehyde / ketone

aldehyde $\xrightarrow{\text{oxidan}}$ acid

In alcoholic person - Always Acidosis.

Galactose :- -CHO in group

Galactose $\xrightarrow[\text{Aldose reductase}]{\text{enzyme lens}}$ Galactitol in Lens

if Galactitol get accumulate in Lens → causes Cataract

ie cataract d/t to deficiency of Galactokinase (in early life → Cataract)

Non classical Galactosemia

↓

d/t to def of Galactokinase

No problem to tissue, bcoz not trapped into tissue

★ if deficiency Galactose 1-phos uridyl tran

get accu in tissue →

get acc in blood →

causes Classical Galactosemia

also cataract occur

bcoz when Gala-1-pho ↑ses ∴ Galactose ↑

∴ cataract occur in early lives

Galactose & Galactose-1-phosphate also get accumulated in

Lives

kidney

causes

Cirrhosis

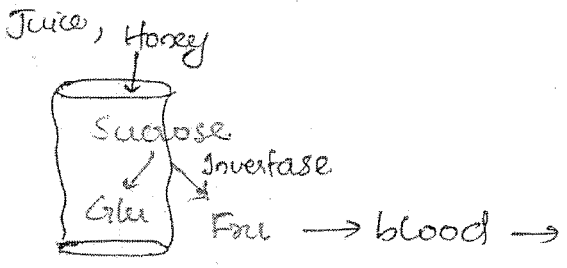
Renal tubular dis

+

also Cataract

also vomiting, lethargy

Fructose Metabolism



enter tissue

In cell:

Fructose

↓ Fructokinase

Fructose - 1 - phosphate

↓ Aldolase B

DHAP + Glyceraldehyde

Glycolysis

Glycogen metabolism

Fructose start accumulate in blood → excrete through urine

↓

Essential Fructosuria (No symptoms - Benign condition)

★ if Fructokinase def

→ ↑ fructose in blood → but not cause Cataract

bcoz -C=O group in fructose

deficiency of Aldolase B leads to

↓

Hereditary Fructose intolerance.

Liver get affected bcoz F-1-phosphate get accumulated.

Also in Brain - tremor also vomiting, diarrhoea.

MINERAL METABOLISM

Iron:

Q. Storage form of Fe in tissue

Q. " in intestinal mucosa

Fe → Fe^{+2} Ferrous

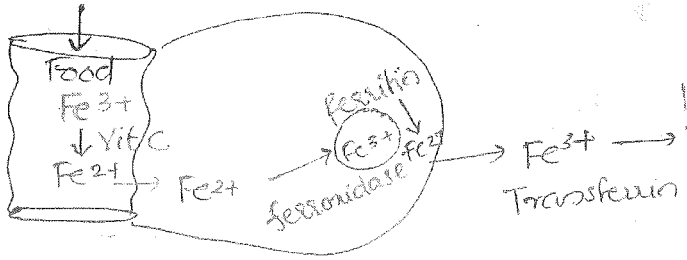
Fe → Fe^{3+} Ferric

$Fe^{2+} \xrightarrow[oxi]{} Fe^{3+}$

$Fe^{3+} \xrightarrow[reduction]{} Fe^{2+}$

When Fe moves across a memb in form of Fe^{2+}

Transport & storage always in Fe^{3+}



Food Fe in Fe^{3+} form → to cross memb need to change to Fe^{2+}

$Fe^{3+} \xrightarrow{Vit\ C} Fe^{2+}$

absorbed in cell of Duodenum & layer

Mucosa, sub M, Muscularis, Serosa

Once absorbed Fe^{2+} → transport and stored as Fe^{3+} form

by

$Fe^{2+} \longrightarrow Fe^{3+}$

Stored in intestinal & Mucosal cell → Ferritin

To absorb into cell from stored form again Fe^{2+} & enzyme

$Fe^{3+} \xrightarrow[Ferroreductase]{} Fe^{2+}$

Transfer of iron with help of protein

↓

Transferrin

↓

To tissue

eg: Bone marrow for hematopoiesis.

↓

stored Fe^{3+} in Tissue

hemosiderin

Q. Fe not excreted from body

1 way metabolism can come inside the body but can't excrete

bcz continuous erythropoiesis

Hemosiderosis
↓
Fe accumulation ↑ in body

Hemolysis → RBC lysis ← Heme, Glo – AA

Heme ← Fe^{2+} start accumulate in body – Hemosiderin
↓
excrete in urine
Hemosiderinuria

Coenzyme – no protein part of Enzyme.

Coenzyme from Vit B_{12}
Also Metalloenzyme
Cobalt — for Vit B_{12}

Q. Chromium — potentiate the action of Insulin

Q. Which will stabilize Insulin.
↓
Zinc

Fluoride — req for Ca & teeth

Iodine — Thyroid hormone

Molybdenum — For Xanthine oxidase

Q. Selenium — Coenzyme or Cofactor for
★ Glutathione peroxidase
★ Deiodinase

★ Thioredoxin Reductase.

Zinc — Cofactor for
★ Carbonic anhydrase
★ Lactate dehydrogenase
Q. ★ Alcohol dehydrogenase
★ Alkaline phosphatase

Manganese — Arginase
Carboxylase
Q. kinases Mg/Mn

Cu
★ Thyrosinase
★ In ETC – Complex 4 (cytochrome oxidase)

Lipid storage diseases

Lipid = FA + glycerol

Lipids

- Simple lipids
  - only FA + alcohol
    - FA + glycerol — eg: Fats/oils
    - FA + alcohol except glycerol — eg: Waxes.
- Complex Lipids

FA + Alcohol + 3rd sub

1) phosphate → phospholipid
2) Carbohydrate → Glycolipid.
3) Protein → Lipoprotein

phospholipid

FA + alcohol + phosphate

based on alcohol

- FA + Glycerol + pho → Glycerophospholipid.
- FA + sphingocine + (P) → Sphingophospholipid
  - eg: sphingomyelin
  - degrade by Sphingomyelinase
  - if this Sphingomyelinase enzy deficiency
  - ↓
  - Neiman pick disease.

Glycolipid

FA + sphingocine + Carbohy

based on carbohydrate

- FA + Sphi + Monosaccharide → Cerebrosides
- FA + sphin + Oligosaccharide → Gangliosides

Cerebrosides

FA + S + Monosaccharide

- FA + S + Glc → Glucocerebroside → enzyme: Glucocerebrosidase → Gaucher's dis
- FA + S + Galactose → Galactocerebrosidase → enzy: Galactocerebrosidase → Krabbe's dis

Ganglioside

- α Hexosaminidase → def → Tay Sach's dis
- β Hexosaminidase → def → Sand off's dis