BIOCHEM

ISTRY

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METABOLISM OF CHO

2 types of entry of glucose into cells:

① Insulin-independent ⇒ Hepatocytes, Erythrocytes, Brain

② Insulin-dependent ⇒ Muscle, Adipose tissue

GLUT-1	Brain, kidney, RBC, Retina, Colon, Placenta	Glucose uptake
GLUT-2	Liver, kidney, Small intestine, β-cells of pancreas	Quick uptake & release of glucose
GLUT-3	Brain; Placenta, kidney	Glucose uptake
GLUT-4	Heart, Muscle, Skeletal muscle, Adipose tissue	Insulin-mediated glucose uptake
GLUT-5	Small intestine	Absorption of fructose
GLUT-7	Liver	Release of glucose from ER to cytosol
SGLUT-1	Intestine, Kidney	Cotransport of Na^+ & glucose (against the conc. gradient)

GLYCOLYSIS

Glucose

ATP → ↓ Hexokinase OR Glucokinase

Glucose-6-Phosphate

⇌ Phosphohexose isomerase

Fructose-6-Phosphate

ATP → ↓ Phosphofructokinase

Fructose-1,6-bisphosphate

↑ Aldolase

DHAP ⇌ (Phosphotriose isomerase) Glyceraldehyde-3-Phosphate

Glyceraldehyde-3-Phosphate

NADH ← ⇌ G-3-P dehydrogenase

1,3-Bisphosphoglycerate

ATP ← ⇌ Phosphoglycerate Kinase

3-Phosphoglycerate

⇌ PG mutase

2-Phosphoglycerate

⇌ Enolase

PEP

ATP ← ↓ Pyruvate kinase

Pyruvate (enol) → Pyruvate (Keto) ⇌ (Lactate DH) Lactate

NAD⁺

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Hexokinase	Glucokinase
• Present in almost all tissues.	• In liver.
• Low km (0·1mM)	• High km for glucose (10mM)
• Inhibited by glucose-6-phosphate.	• Not inhibited.

Due to low km, Hexokinase can act on glucose even at low conc. of glucose
(low km → HIGH affinity)
& v.v.

In Glycolysis:

- Aerobic ⇒ 7ATPs (2ATPs + 2NADH)
- Anaerobic ⇒ 2ATPs
- If anaerobic but starts from glycogen ⇒ 3 ATPs (b/c glycogen directly produce glucose-1-phosphate without using ATP)

PASTEUR EFFECT

→ Inhibition of glycolysis by O_2 (aerobic condition)
→ ↑Citrate & ↑ATP b/c of O_2 inhibits phosphofructokinase.

CRABTREE EFFECT

→ Inhibition of O_2 consumption by the addition of glucose to tissues having high aerobic glycolysis.
→ OPPOSITE of Pasteur effect.

Pyruvate is converted to Acetyl-CoA
↳ Catalyzed by Pyruvate Dehydrogenase (PDH)

PDH requires 5 cofactors (The Real Life Never Pleases)

- TPP
- Lipoamide
- FAD (from Riboflavin)
- Co-A (from Pantothenic acid)
- NAD^+

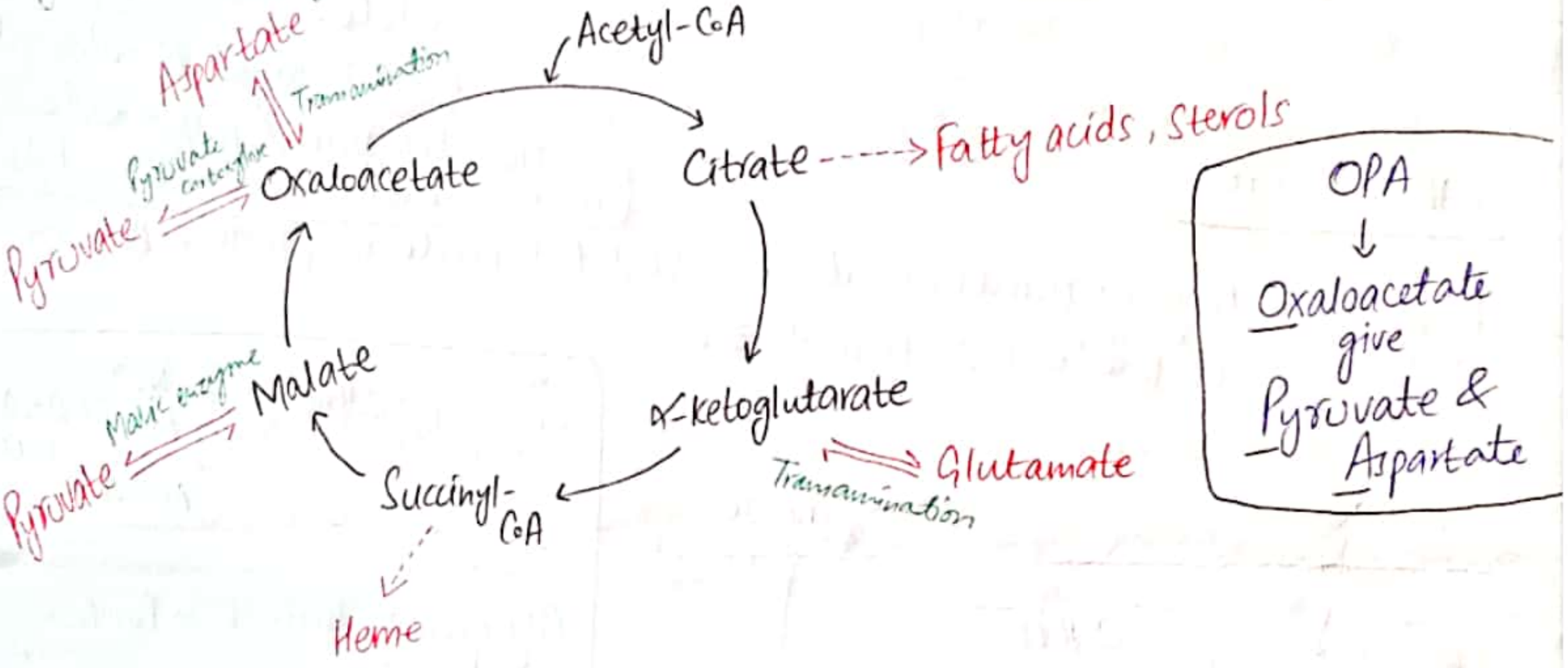
→ These same cofactors are also used by α-ketoglutarate DH complex in TCA cycle.

There is no direct participation of O_2 in Kreb's cycle but it is strictly aerobic b/c NAD^+ & FAD^+ required for the rxn are generated in ETC only in the presence of O_2.

1 acetyl CoA ⟶ KREB'S CYCLE ⇒ 10 ATPs (1 GTP + 3 NADH + 1 $FADH_2$)

NOTE

• Hyperammonemia withdraws α-ketoglutarate (from Kreb's cycle) to glutamate & glutamine ⇒ This leads to ↓ Kreb's cycle.



GLUCONEOGENESIS

→ Major substrates are lactate, pyruvate, glucogenic amino acids, propionate & glycerol.

→ Occurs in cytosol

→ Major sites are liver (1kg/day) & kidney matrix ($^1/_{10}^{th}$ of liver).

NOTE

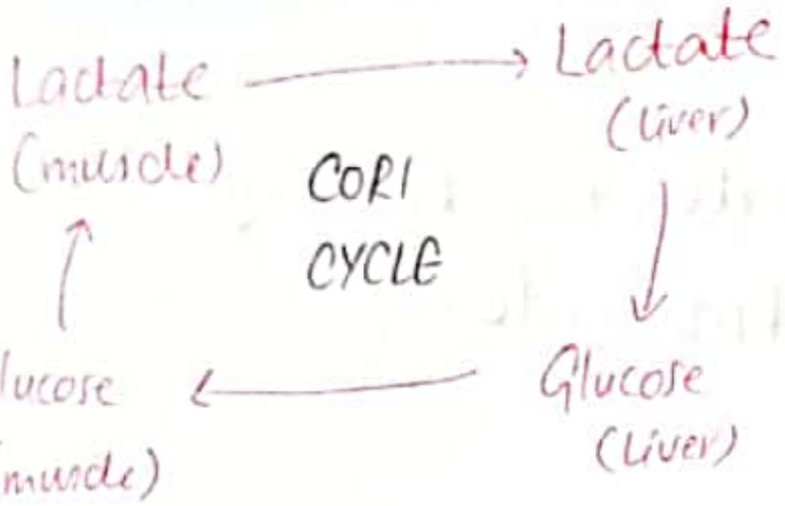
↳ Malate goes out of the mitochondria, into the cytosol where by Malate DH it forms oxaloacetate which then forms PEP & it reverses the glycolysis until Fructose-1,6-bisphosphate ⇒ use F-1,6-BPases ⇒ Glucose-6-P use Glucose-6-Pases to form Glucose.

Gluconeogenesis occur from amino acids & use a lot of energy ⇒ which come from β-oxidation of fats.

CORI CYCLE

Pyruvate $\xrightarrow[\downarrow NAD^+]{LDH}$ Lactate (in skeletal muscle during anaerobic)

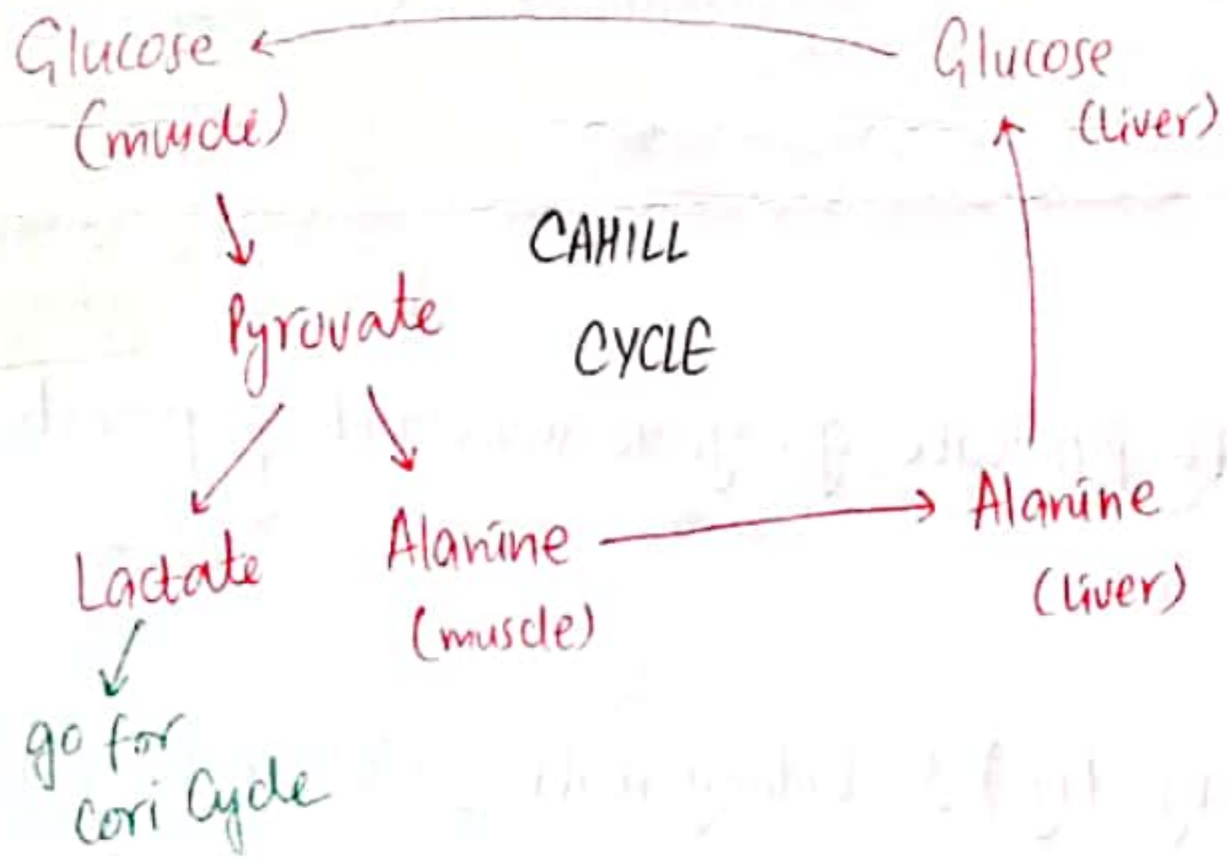
Skeletal muscles LACK the last 2 enzymes needed for gluconeogenesis i.e. glucose-6-phosphatase & fructose-1,6-bisphosphatase which are present in liver. Hence,



Animals can't convert fat → glucose b/c of absence of glyoxylate cycle.
EXCEPT Glycerol released from lipolysis & propionate from oxidation of odd-chain FAs

CAHILL CYCLE

Pyruvate undergoes transamination in Skeletal muscle to produce Alanine which goes to the liver & form glucose.



Glycogen Synthase 'a' → NOT PHOSPHORYLATED (ACTIVE)

Glycogen Synthase 'b' → PHOSPHORYLATED (INACTIVE)

NOTE
cAMP ↗ breaks glycogen
Insulin ⇒ DEPHOSPHORYLATE (remove phosphate)
⇓
promote Glycogenesis

HMP Shunt

→ Anabolic.
→ Synthesize NADPH & Pentoses. (→ e.g. Ribose-5-phosphate)
→ ATP is neither used nor generated.

Glucose-6-Phosphate Dehydrogenase (G6PD) deficiency

- → X-linked recessive
- → Mostly males
- → MOST COMMON GENETIC DISEASE
- → Affect all cells but mostly RBCs
- → HMP-shunt is the only source of NADPH in RBC
- → Causes HEMOLYTIC ANEMIA

b/c of shorter lifespan of RBC → The G6PD patient is RESISTANT TO MALARIA.

WERNICKE-KORSAKOFF SYNDROME

- → Genetic disorder associated with HMP shunt.
- → Mental disorder, memory loss, partial paralysis.
- → Symptoms are manifested in vitamin-deficient alcoholics.

URONIC ACID PATHWAY

- → Synthesize glucuronic acid, pentoses & vit. ascorbic acid (not in primates & guinea pigs)

NOTE

- L-Gulonate → precursor for vit. C
- Enzyme: L-gulonolactone oxidase which does this is absent in man, other primates & guinea pigs.

NOTE

Fructose-1-phosphate

↙ ALDOLASE B ↘

DHAP ⇌ Glyceraldehyde-3-Phosphate

Fructose → rapidly metabolized by liver compared to glucose b/c it skips the rate-limiting step of glycolysis.

Fructose enter into cell the same way as galactose independent of insulin. (both are independent)

Sorbitol / Polyol pathway is ABSENT in Liver

LIPIDS

conc. of lipids in plasma is: (Private Chores Tar Free)

Phospholipids > Cholesterol > Triglycerides > Free fatty acids

WOLMAN DISEASE ⇒ Accumulation of lipids ⇒ def. of enzyme lysosomal acid lipase.

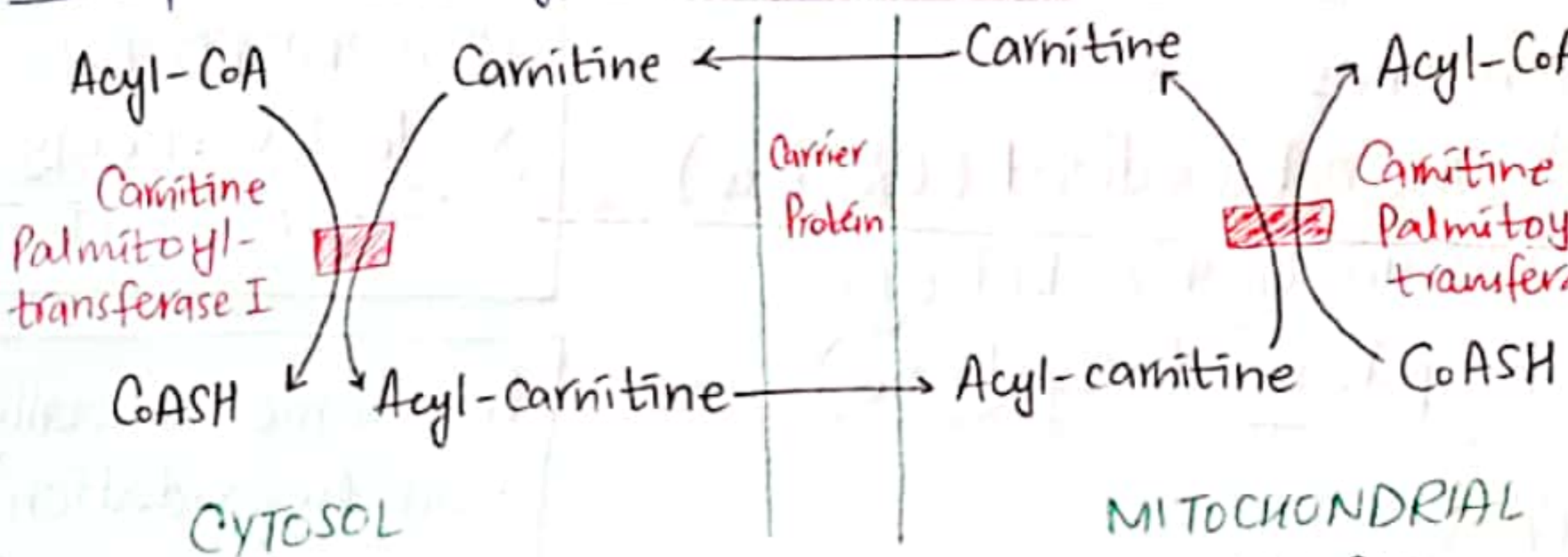
β-OXIDATION:

3 stages:

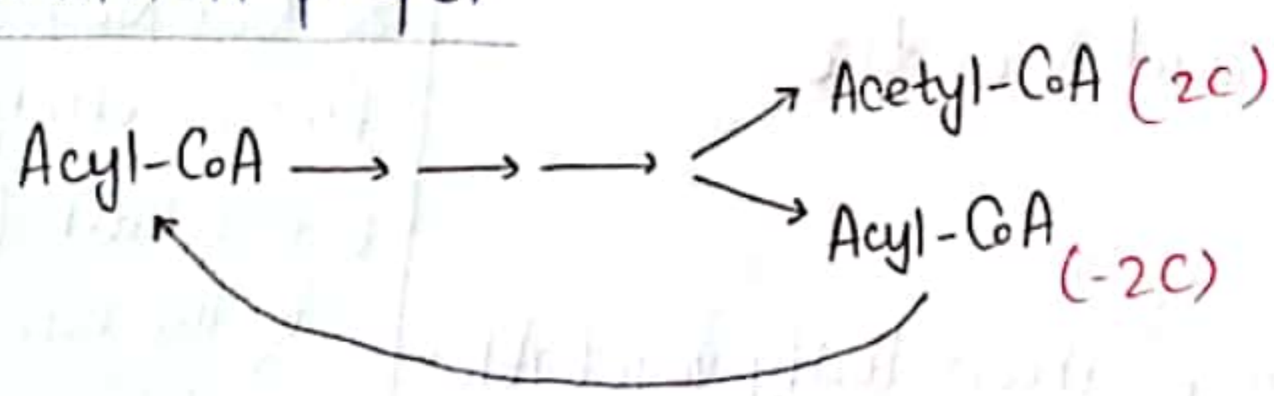
① Activation of fatty acids (in cytosol)

Fatty acid $\xrightarrow[ATP]{\text{Thiokinase}}$ Acyl-CoA

② Transport of fatty acids into mitochondria



③ β-Oxidation proper



Palmitoyl-CoA (18C)
↓
7 $FADH_2$ + 7 NADH + 8 acetyl-CoA
(1 acetyl-CoA = 10 ATPs)

Hence,
1 Palmitoyl-CoA = 10·5 + 17·5 + 80
= 108 ATPs
−2 (energy utilized for activation)
Net ⇒ 106 ATPs

Jamaican Vomiting Sickness is caused by eating unripe ackee fruit which contains HYPOGLYCIN A → inhibits acyl-CoA dehydrogenase

NOTE

- Carnitine deficiency ⇒ No fatty acid oxidation ⇒ Most of the energy is derived from glucose ⇒ Carnitine deficiency induces HYPOGLYCEMIA.
- CPT-I deficiency affects LIVER.
- CPT-II deficiency affects SKELETAL MUSCLE (& to some extent the liver).
- Sudden Infant Death Syndrome (SIDS) ⇒ Cause is mostly unknown but in 10% of the cases is due to def. of medium chain acyl-CoA dehydrogenase.

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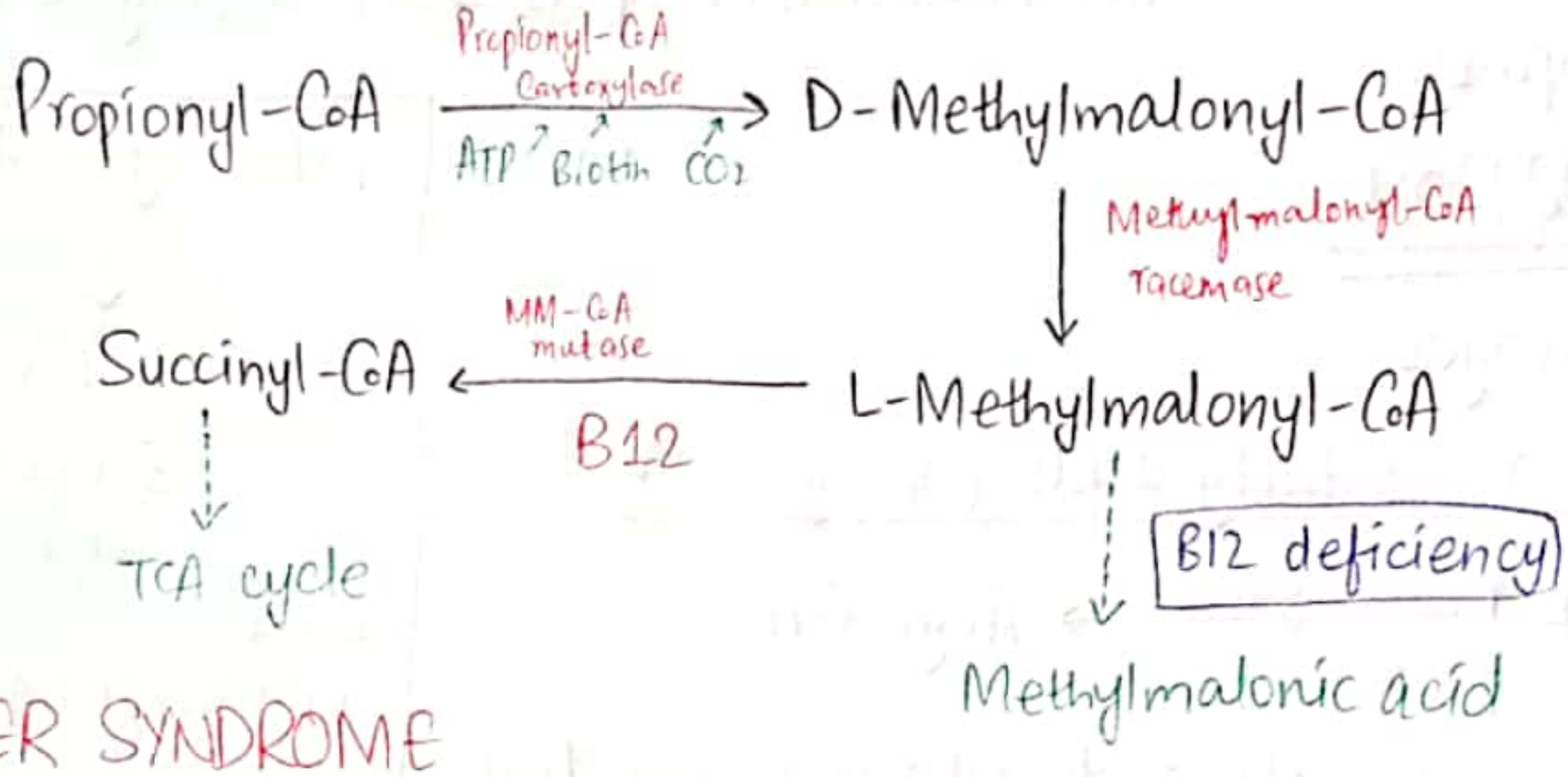
Oxidation of odd chain fatty acids:

→ Same as for that of even chain.

→ EXCEPT that the last 3 carbon atoms that are left behind (Propionyl CoA) through rxns form Succinyl-CoA.



ZELLWEGER SYNDROME

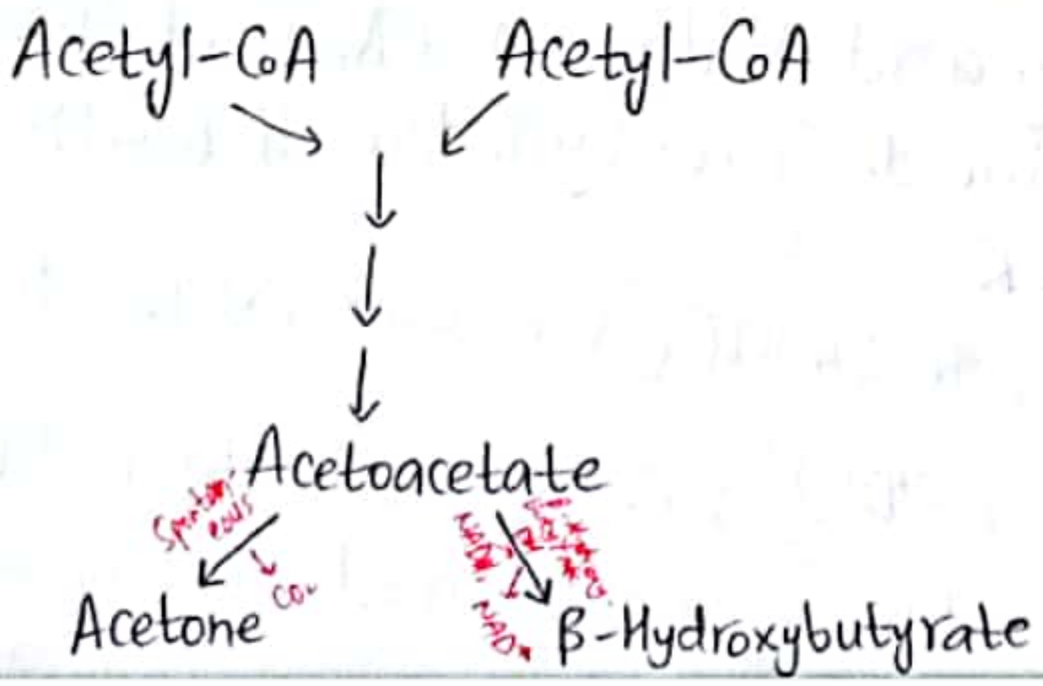
- Absence of peroxisomes.
- Long chain FAs are not oxidized ($C_{26}-C_{38}$)
- Accumulate in brain, liver & kidneys (Cerebrohepatorenal Syndrome).

REFSUM'S DISEASE

- Defect in α-oxidation.
- Lack of enzyme Phytanic acid α-oxidase.
- Phytanic acid conc. ↑
- Derived from chlorophyll.
- Patient should not consume green leafy vegetables.

UNSATURATED FAs provide less energy than SATURATED FAs

Peroxisomes initially start the oxidation of long chain fatty acids & does NOT ~~rele~~ produce energy. (it is later followed by the normal β-oxidation in Mitochondria).



Ketone bodies are:

- β-Hydroxybutyrate → energy (doesn't have a keto group)
- True ketones:
  - Acetone → No energy
  - Acetoacetate → energy

(BAA)

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NOTE · ketone bodies are degraded to supply energy.

β-Hydroxybutyrate ⟶ Acetoacetate ⟶ Acetoacetyl-CoA ⟶ Acetyl-CoA + Acetyl-CoA

(β-Hydroxybutyrate ⟶ Acetoacetate: NAD+ / NADH)

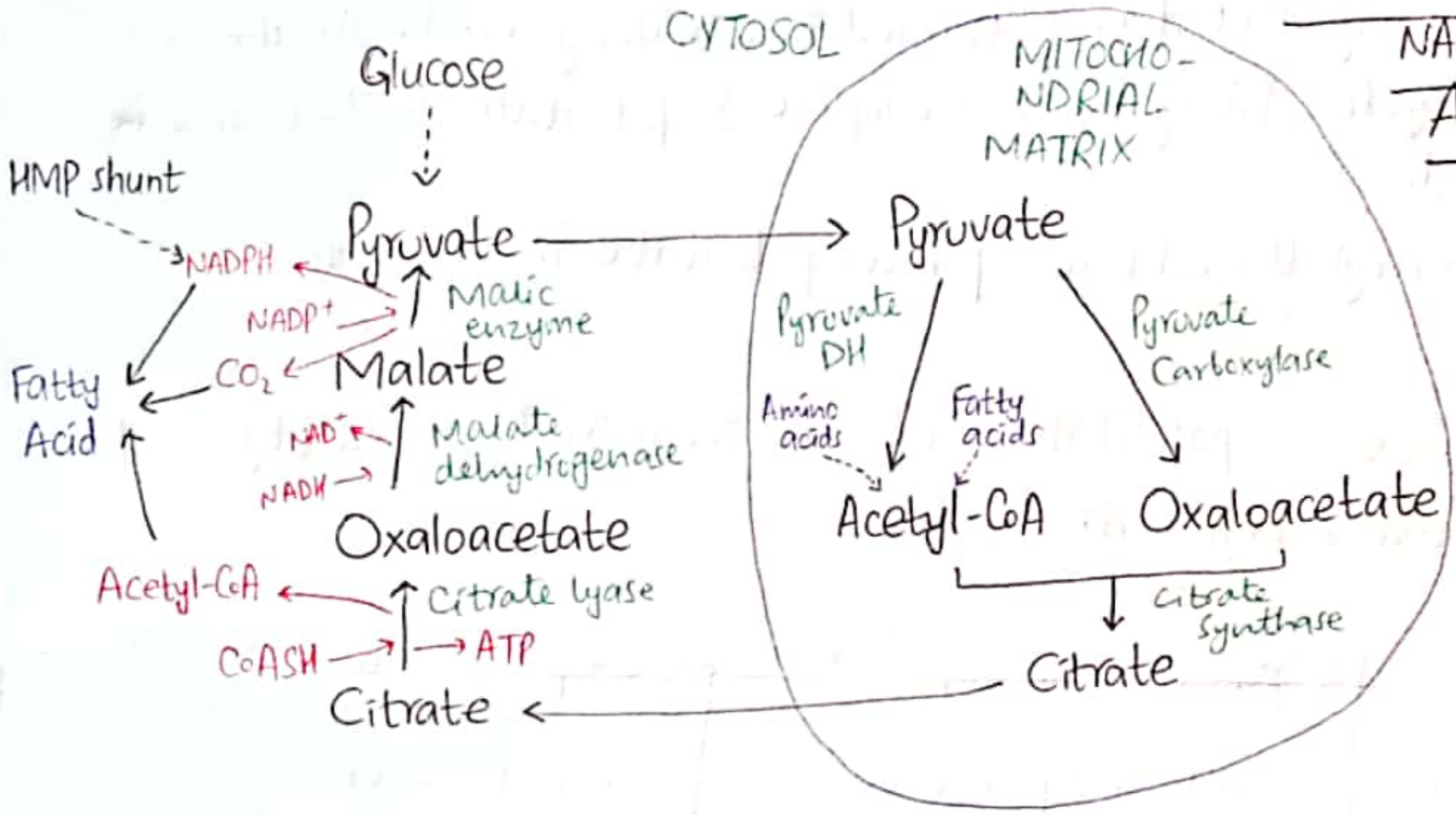
(Acetoacetate ⟶ Acetoacetyl-CoA: THIOPHORASE; Succinyl-CoA / Succinate)

(Acetoacetyl-CoA ⟶ Acetyl-CoA + Acetyl-CoA: Twiolase)

THIOPHORASE is absent in liver, hence ketone bodies are not utilized by liver.

FATTY ACID SYNTHESIS

① Production of NADPH & Acetyl-CoA



TRICKS

· P ⇒ $\overrightarrow{PAO}$ $\overleftarrow{CAO}$

(A, O, C)

· When citrate comes out into the cytosol, it goes up as $\overrightarrow{COMP}$.

Acetyl-CoA & NADPH (especially Acetyl-CoA, for carbons) are building blocks for fatty acid synthesis.

② Production of Malonyl-CoA

Acetyl-CoA ⟶ Malonyl-CoA

(CO_2, ATP, Biotin; Acetyl-CoA Carboxylase)

TRICK → almost every carboxylase use ABC
i.e ATP
Biotin
CO_2

③ Rxns of Fatty Acid Synthase Complex

FAS complex is a set of multifunctional enzyme ⇒ exists as a dimer ⇒ each monomer possesses the activities of 7 different enzymes & an acyl carrier protein (ACP) with 4'-phosphopantetheine-SH group.

NOTE

↳ In prokaryotes, ACP is SEPARATE from FAS complex.

When the rxn end once, it is repeated 6 more times & each time 2C are added to the fatty acid chain. (obtained from malonyl-CoA). At the end of the total 7 cycles, FA synthesis is complete & palmitate (16C)-bound to ACP is produced.

→ enzyme palmitoyl thioesterase separates palmitate from FA synthase.

NOTE

↳ Of the 16C of palmitate, 14 come from Malonyl-CoA (by 7 cycles) & 2 come from Acetyl-CoA.

	Fatty Acid Synthesis	β-Oxidation
① Major tissues	Liver, Adipose tissue	Muscle, Liver
② Subcellular site	Cytosol	Mitochondria
③ Precursor/Substrate	Acetyl-CoA	Acyl-CoA
④ End product	Palmitate	Acetyl-CoA
⑤ Intermediates are bound to	Acyl-carrier protein (ACP)	Coenzyme-A
⑥ Coenzyme require	NADPH	FAD^+ & NAD^+
⑦ Carbon units added/degraded	Malonyl-CoA	Acetyl-CoA
⑧ Transport system	Citrate (Mitochondria → Cytosol)	Carnitine (Cytosol → Mitochondria)
⑨ Inhibitor	Long chain acyl-CoA (inhibits acetyl-CoA carboxylase)	Malonyl-CoA (inhibits CAT-I)
⑩ Pathway increased	After rich CHO diet.	In starvation
⑪ Hormones that ↑	High ratio of insulin/glucagon	Low ratio of insulin/glucagon
⑫ Status of enzyme(s)	Multifunctional enzyme complex	Individual enzymes

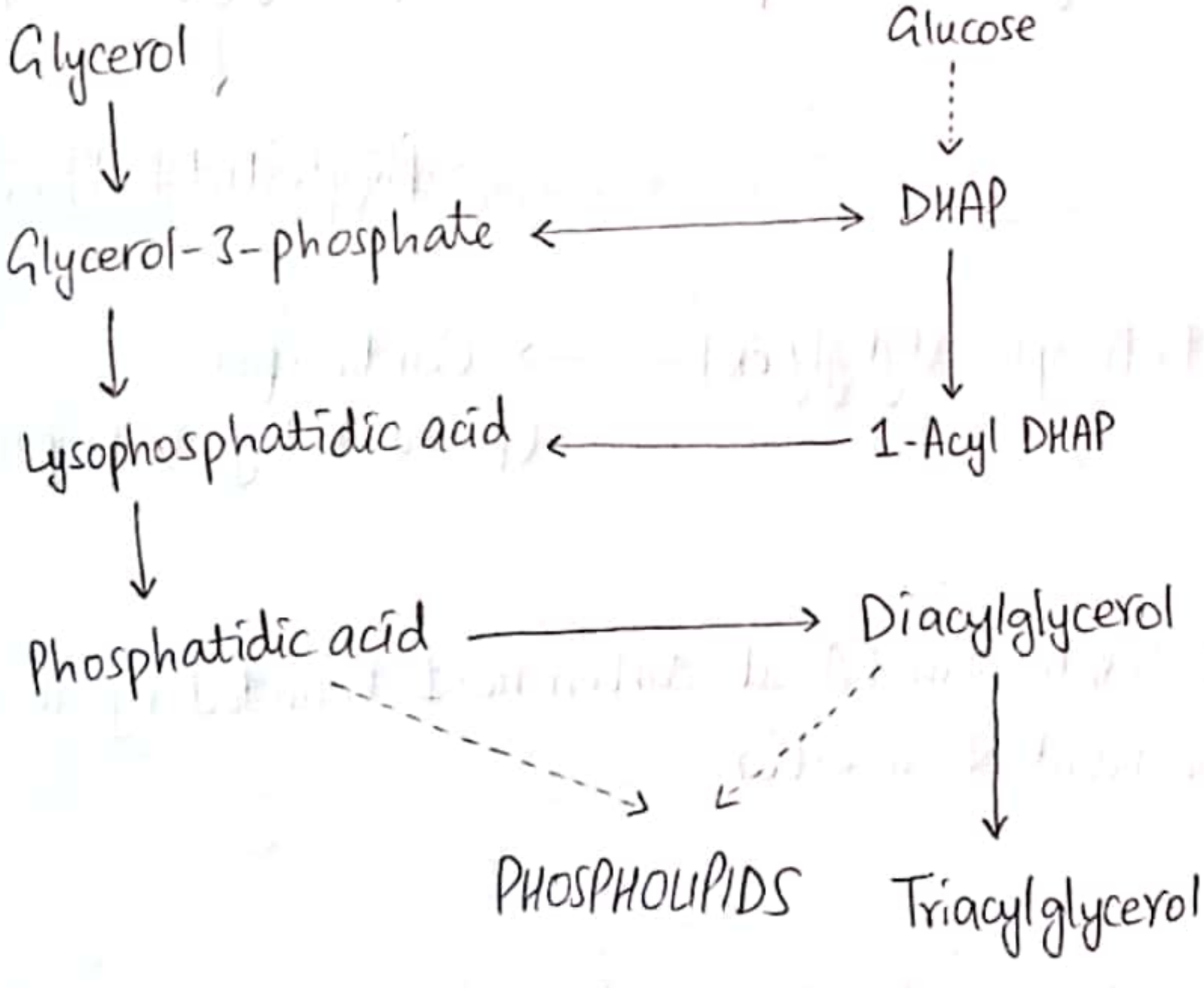
TAG

- In liver, glycerol kinase is present ⇒ Glycerol ⟶ Glycerol-3-Phosphate
It is absent in adipose tissue.
- In both liver & adipose tissue, glucose serve as a precursor for glycerol-3-phosphate via glycolysis.
- Glycerol-3-phosphate is imp. for synthesis of both TAG & Phospholipids

NOTE

↳ 3 fatty acids found in Triacylglycerol are not of the same type:

- Saturated FA → Carbon 1
- Unsaturated FA → Carbon 2
- Either of them → Carbon 3



PHOSPHOLIPIDS

- Lecithin & Cephalin

Choline & Ethanolamine get phosphorylated + CTP → CDP-choline, CDP-ethanolamine

CDP-choline + DAG ⟶ Phosphatidylcholine (Lecithin)

CDP-ethandamine + DAG ⟶ Phosphatidyl ethanolamine (Cephalin)

- **Phosphatidylserine**

phosphatidyl ethanolamine —(Serine)→ Phosphatidyl serine + ethanolamine

- **Phosphatidyl inositol**

CDP-diacylglycerol + Inositol ⟶ Phosphatidyl inositol

(imp for signal transmission across membranes)

- **Phosphatidyl glycerol & cardiolipin**

CDP-diacylglycerol + Glycerol-3-Phosphate ⟶ Phosphatidyl glycerol-3-phosphate ⟶ Phosphatidyl glycerol

Phosphatidyl glycerol + Phosphatidyl glycerol ⟶ Cardiolipin

(possess antigenic properties)

- **Plasmalogens**

These are phospholipids with FA at carbon no. 1 bounded by an ether linkage, instead of an ester.

NOTE

↳ An imp. plasmalogen ⇒ 1-alkenyl 2-acetyl glycerol-3-phosphocholine, causes blood platelet aggregation & is referred to as PLATELET ACTIVATING FACTOR.

TRICK

CDP + DAG → PHOSPHATIDYL

Sphingomyelins

Palmitoyl-CoA + Serine ⟶ ⟶ ⟶ Sphingosine

Sphingosine ⟶ Ceramide
(↑ acyl group)

Ceramide + CDP-choline ⟶ Sphingomyelin.

Phospholipase A1 → cleaves FA at C1 position of phospholipid.

" A2 → hydrolyzes FA at C2 position (rich sources are SNAKE & BEE VENOM)

" B → removes second acyl group at C2 position

" C → cleaves the bond b/w phosphate & glycerol

" D → hydrolyzes & remove nitrogenous base from phospholipids

NIEMANN-PICK DISEASE

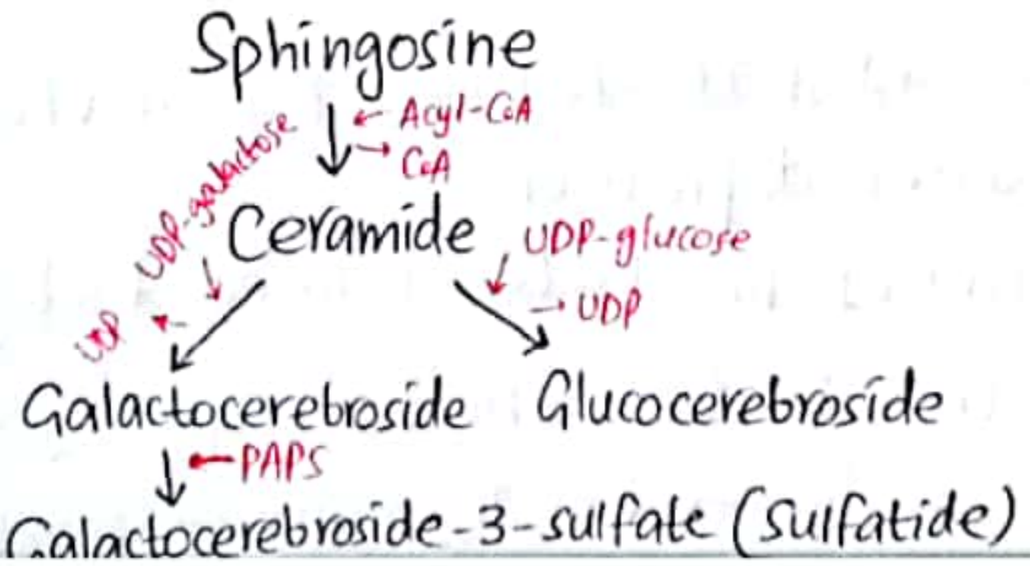
→ defect of enzyme Sphingomyelinase. → Mental retardation.
→ Sphingomyelin accumulate in liver & spleen ⇒ organs enlarge.

FARBER'S DISEASE

→ defect of enzyme Ceramidase.
→ Skeletal deformation. (muscle farbers are not working) TRICK

GLYCOLIPIDS

→ Derivatives of Ceramide (Sphingosine + FA)



Galactocerebroside is a major component of membrane lipids in the Nervous System (High in myelin sheath)

GAUCHER'S DISEASE

→ Defect in β-glucosidase. → Glucocerebroside ↑

Anemia
Pigmentation of skin
Osteoporosis
Enlargement of Liver & Spleen
Mental retardation

KRABBE'S DISEASE

→ Defect in β-galactosidase → Galactocerebroside ↑
→ Absence of myelin sheath.

LIPOTROPIC FACTORS are substances the deficiency of which cause fat (TG) to accumulate in Liver.
eg. Choline, Betaine, Methionine, Inositol, Folic acid, vit. B12, Glycine, Serine.

Lipoprotein-a (Lp-a) ⇒ identical in structure to LDL.
- Lp-a ⇒ INHIBITS fibrinolysin ⇒ ↑ CHD

Biochemical changes in alcoholism

① Metabolism of alcohol (by alcohol DH or MEOS) consume NAD^+ so, $NADH/NAD^+$ ratio ↑.

② High conc of NADH favours pyruvate ⟶ lactate (cause LACTIC ACIDOSIS)

③ ↓ Pyruvate ⟶ ↓ gluconeogenesis ⟶ HYPOglycemia

④ CAC is impaired b/c of ↓pyruvate, ↓ ~~fat~~ oxaloacetate & ↓NAD^+.
As a result, acetyl-CoA ↑ & gets diverted towards ketogenesis & synthesize lipids. (Fatty liver & Hyperlipidemia)

⑤ b/c of lactic acidosis, ↑ serum uric acid.

⑥ Acetaldehyde (Alcohol $\xrightarrow{\text{Alcohol DH}}$ Acetaldehyde) conc. ↑ ⇒ interferes with functioning of neurotransmitters ⇒ causes depression.

⑦ Acetaldehyde ↑ also causes headache, nausea, tachycardia, ↓BP.

⑧ Alcoholics are prone to vit. deficiencies (especially vit. B_1, B_6 & C)
(Wernicke-Korsakoff Syndrome ⟶ ↓ of Thiamine ⟶ common in alcoholics)

CHOLESTEROL

Precursor for: ① (My PAGE)

- Steroid Hormones
  - Mineralocorticoids
  - Progestins
  - Androgens
  - Glucocorticoids
  - Estrogen

② Bile salts & acids

③ Vit. D (7-dehydrocholesterol $\xrightarrow{\text{UV light}}$ cholecalciferol)

Women have ↓ conc. of cholesterol b/c of ↑ Estrogen.

Statin drugs ↓ conc of cholesterol by inhibiting HMG-CoA Reductase.

Hypercholesterolemia occurs in

- Diabetes Mellitus (↑acetyl-CoA => Synthesize ↑cholesterol)
- Hypothyroidism (↓HDL receptors on hepatocytes)
- Obstructive Jaundice (obstruction in excretion of cholesterol)
- Nephrotic Syndrome (↑ plasma globulin → ↑ cholesterol)

Hypocholesterolemia occurs in

- Hyperthyroidism
- Pernicious anemia
- Malabsorption syndrome
- Hemolytic jaundice

CHYLOMICRONS

→ Synthesized in the intestine
→ Transport exogenous (dietary) TAG to various tissues.
→ HIGHEST quantity of lipid (99%)
→ LOWEST " " protein (1%)

VLDL

→ Produced in liver & intestine.
→ Transport TG.

LDL

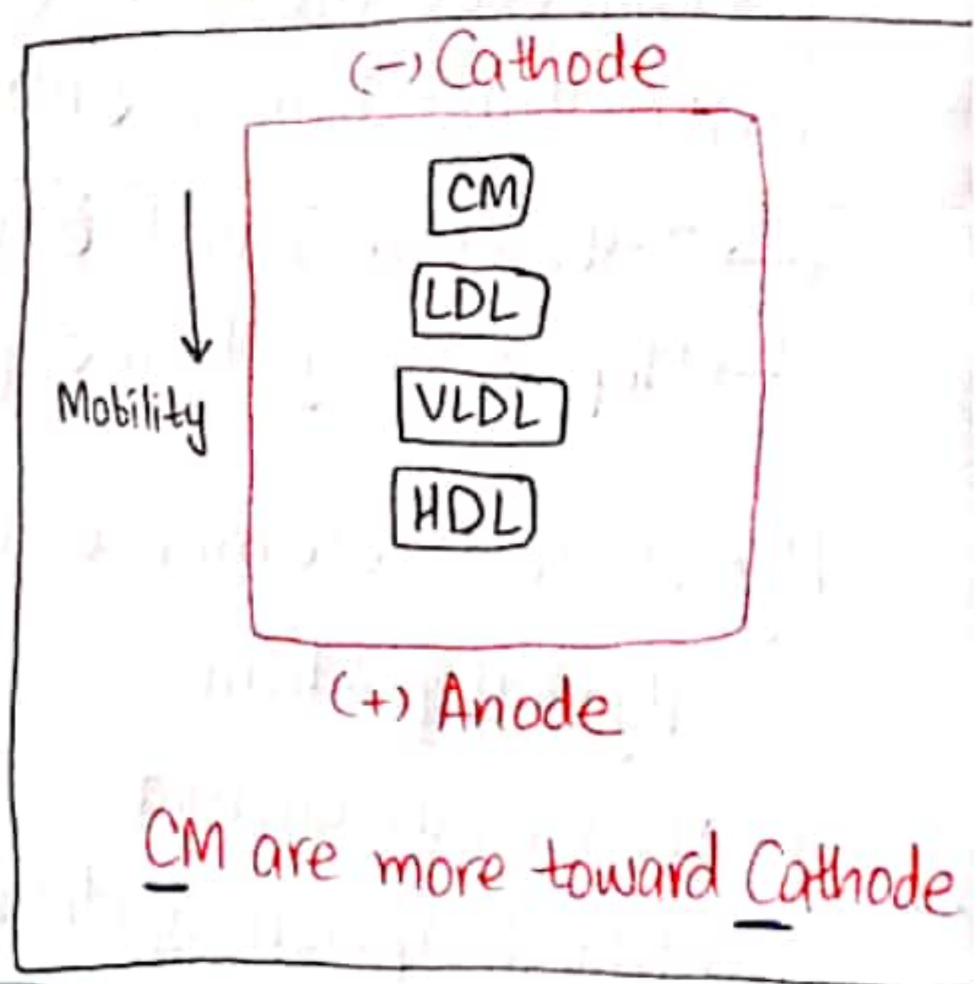
→ Formed from VLDL in blood circulation.
→ Transport cholesterol from liver to other tissues.

HDL

→ Mostly synthesized in liver.
→ Transport cholesterol from peripheral tissues to liver.
(Reverse cholesterol transport).

Free fatty acids - albumin
Lipids — protein

→ Each molecule of albumin can hold about 20-30 molecules of free fatty acids.

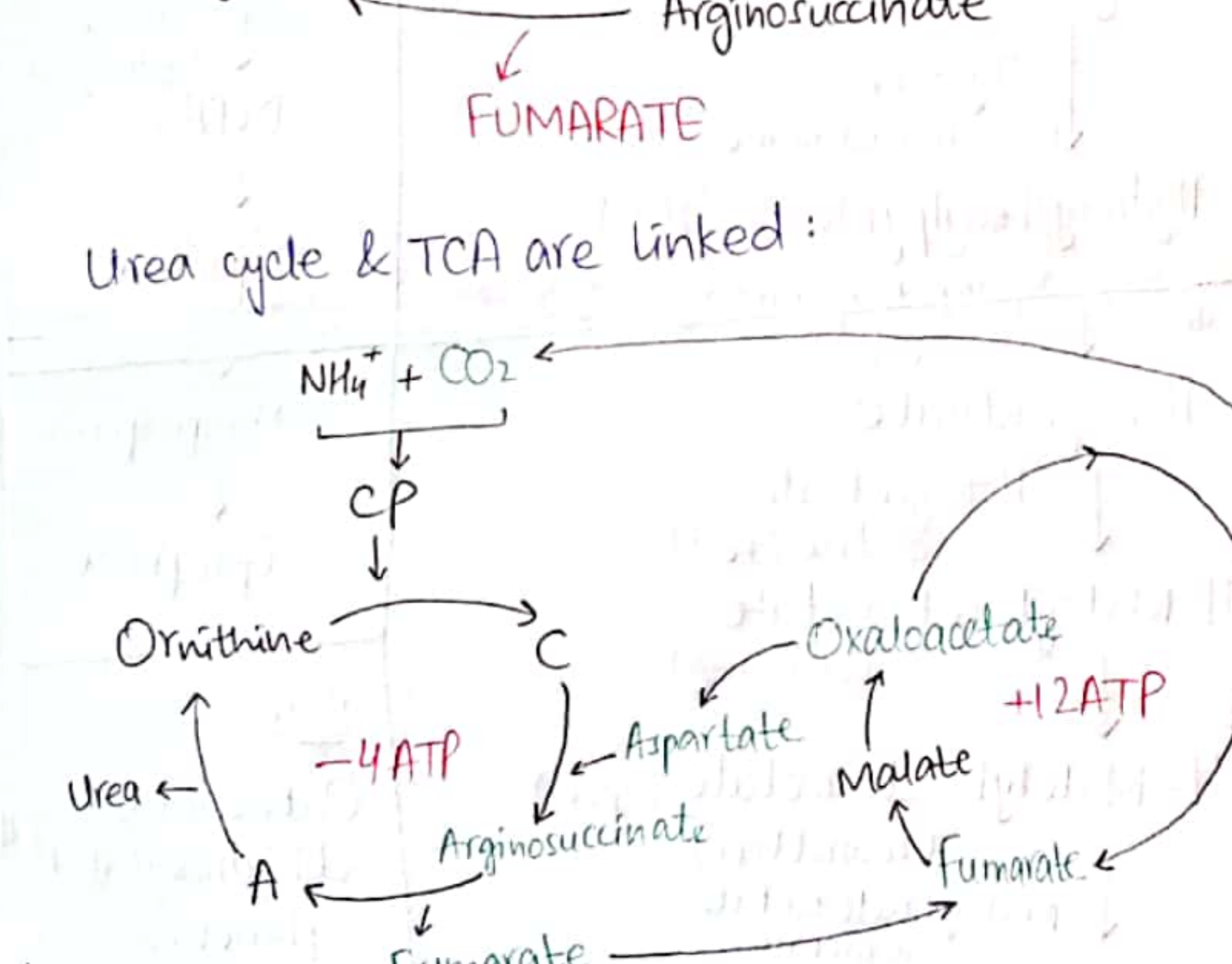


HYPER LPemias

CM	CM	CM	CM	CM	CM
VLDL	VLDL	VLDL	VLDL	VLDL	VLDL
IDL	IDL	IDL	IDL	IDL	IDL
LDL	LDL	LDL	LDL	LDL	LDL
HDL	HDL	HDL	HDL	HDL	HDL
Type I	IIa	IIb	III	IV	V

AMINO ACIDS

- All transaminases use PLP as coenzyme (derived from vit. B6).
- All a.as undergo transamination EXCEPT Lysine, Threonine, Proline & Hydroxyproline (Let The Proline Hit (the floor))



Urea cycle & TCA are linked:

①

②

③

④

GLYCINE

- → Creatine (GAM)
- → Glutathione (γ-Glu-Cys-Gly)
- → Heme (Succinyl-CoA + Gly ⟶ DALA)
- → Purines ()
- → Conjugated bile acids (Glycocholic acid & Glycochenodeoxycholic acid)

Transport of ammonia b/w various tissues & liver occur in form of GLUTAMINE (for most tissues) & ALANINE (from muscle to liver).

All of the enzymes of urea cycle are present in most tissues but ARGINASE is only present in liver, which is why urea cycle is specific to liver.

GAM synthesized creatine → remove H_2O to form creatinine (i.e. Glycine, Arginine & Methionine).

Glutathione is as tripeptide i.e. γ-Glutamyl-cysteinyl-glycine

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PHENYLALANINE → (Hydroxylation at para position) → TYROSINE

- → T_3 & T_4
- → Epinephrine & Norepinephrine
- → Dopamine
- → Melanin

Phenylalanine
↓ Phenylalanine hydroxylase
Tyrosine
↓ Tyrosine transaminase
p-Hydroxyphenylpyruvate (HPP)
↓ Ascorbate ⟹ p-HPP dioxygenase (Cu^{+2})
Homogentisate
↓ Homogentisate oxidase (Fe^{+2})
4-Maleylacetoacetate (close ring)
↓
4-Maleylacetoacetate (open) (rewritten)
↓ Maleylacetoacetate isomerase
4-Fumarylacetoacetate
↓ FAA hydrolase
Fumarate → TCA cycle / Glucose
Acetoacetate → Fat

PHENYLKETONURIA
↙
mousey odour of urine + ↓ melanin

TYROSINEMIA TYPE II

NEONATAL TYROSINEMIA
↙
Infant has cabbage-like odour

ALKAPTONURIA
↙
black colour urine + ochronosis (due to alkapton deposition)

TYROSINEMIA TYPE II (TYROSINOSIS)
↙
Infant has cabbage-like odour

Serum cre... is a more ... indicator o... function than serum urea.

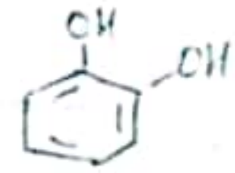
KRYPTO...

① Tyrosine
↓ Tyrosinase
DOPA
↓
↓
Melanin

② Tyrosine
↓ Tyrosine hydroxylase
DOPA
↓
Dopamine
↓
Norepinephrine
↓
Epinephrine

NOTE

Catechol is dihydroxylated phenol i.e.



Catechol

The amine derivatives of catechol are Catecholamines (i.e. dopamine, E & NE).

TRYPTOPHAN

- → NAD^+, $NADP^+$
- → Serotonin
- → Melatonin

Vitiligo → Hypopigmentation starts around mouth, nose, eyes, nipple.
Leucoderma → " " " hands & then spreads.

2 pathways for metabolism:
① Kynurenine Pathway ② Serotonin Pathway

↑ Xanthurenate in urine detects vit. B6 deficiency.
(Hence, in B6 def. ⇒ ↓ NAD^+ & $NADP^+$ synthesis ⇒ Pellagra-like symptoms).

- enzyme kynurenine hydroxylase is INHIBITED by Estrogen, hence women, in general, are more susceptible to pellagra.

NOTE

- Serotonin is 5-Hydroxytryptamine
- Normally, only 1% of tryptophan → serotonin.

Tryptophan induces sleep

- In mammals, large amount of serotonin is synthesized by INTESTINAL CELLS (by argentaffin cells of GIT) ⇒ when they develop a tumor called malignant carcinoma OR argentaffinomas, upto 60% of tryptophan → serotonin (normal → 1%) ⇒ called MALIGNANT CARCINOID SYNDROME.

HARTNUP'S DISEASE ⇒ Low plasma levels of Tryptophan & some other NEUTRAL AMINO ACIDS ⇒ elevated levels in urine.

CYSTEINE

- → Glutathione (Glu-Cys-Gly)
- → Taurine
- → Co-A
- → Active sulfate

METHIONINE

- → Active methionine
- → Creatine
- → Epinephrine
- → Polyamines

In cysteine synthesis
- → Sulfur is obtained from Homocysteine
- → Rest of the molecule " " " Serine

S-adenosyl methionine (SAM) has Sulfonium atom (S^+)

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CYSTINURIA => A specific carrier is present in kidney tubule for reabsorption of Cysteine, Ornithine, Arginine & Lysine (COAL). Defect of this transport system lead to excretion of all these 4 amino acids in urine.

Maple Syrup Urine Disease => Urine of affected individuals smell like maple syrup (burnt sugar). => enzyme defected is Branched chain α-ketoacid Dehydrogenase.

Isovaleric Acidemia => ~~Urine smell~~ Individual exhibit a "CHEESY" odour in breath & body fluids => ↑ isovalerate in urine => enzyme defected is isovaleryl-CoA dehydrogenase.

HISTIDINE

- → Histamine
- → N^5-Formimino-THF

ARGININE

- → Creatine
- → Nitric oxide

GLUTAMATE

- → GABA
- → Glutathione (γ-Glu-Cys-Gly)
- → γ-carboxyglutamate (clotting factors 2,7,9,10)

NOTE

- Histidine, Proline & Arginine (HAP) are converted in their metabolism to glutamate.
- α-ketoglutarate ~~serve~~ in TCA serve as immediate precursor of glutamate.

LYSINE

- → Carnithine (trimethyllysine serve as a precursor)

GLUTAMINE

- → Chief source of ammonia in kidneys (-NH_3 stored as glutamine)
- → Purines & Pyrimidines Synthesis
- → Amino sugars
- → Takes part in conjugation reactions.

Glutamate is decarboxylated to GABA ie. require PLP & vit B6 (def. of vit B6 results in ↓ GABA => convulsions => Stiff Person Syndrome (SPS)

ASPARTATE

- → Donates one amino group for urea synthesis (Other ~~amino~~ ~~group~~ come from ammonia)
- → Connects urea cycle with TCA.
- → Purines & Pyrimidines
- → Malate-Aspartate shuttle (transfer reducing equivalents (NADH) from cytosol → mitochondria)

β-ALANINE

→ Alanine transports pyruvate from muscle → Liver.

→ β-alanine synthesize CoA.

↑alanine in urine have increased risk for ↑ Blood Pressure

SERINE

→ Form N^5, N^{10}-methylene THF (most common one-carbon moiety)

→ Form pyruvate (by deamination)

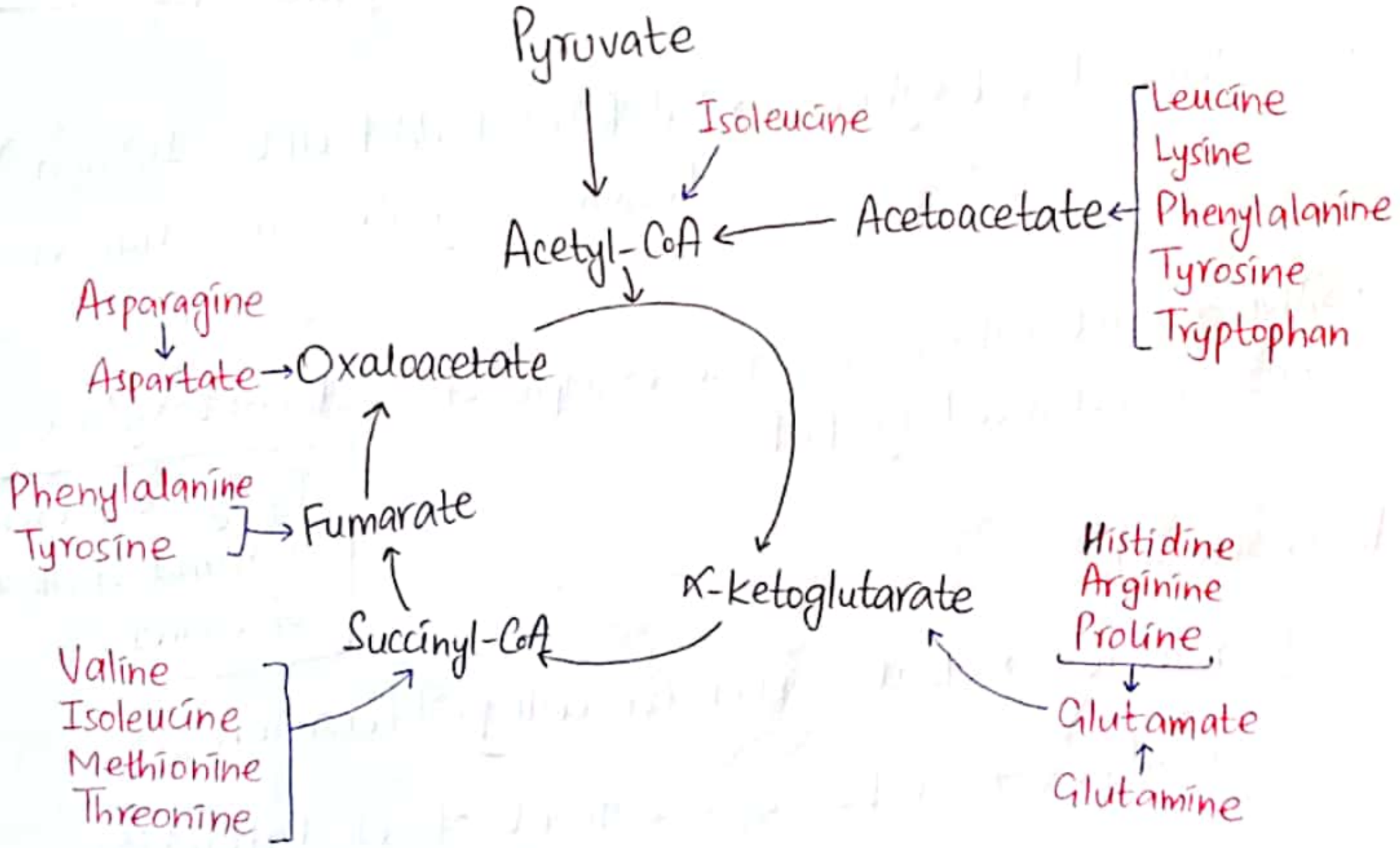
→ Form cysteine (Sulfur → by Homocysteine & rest of carbon skeleton → Serine)

→ Form selenocysteine (21st amino acid)

→ Synthesize sphingomyelins & cephalins

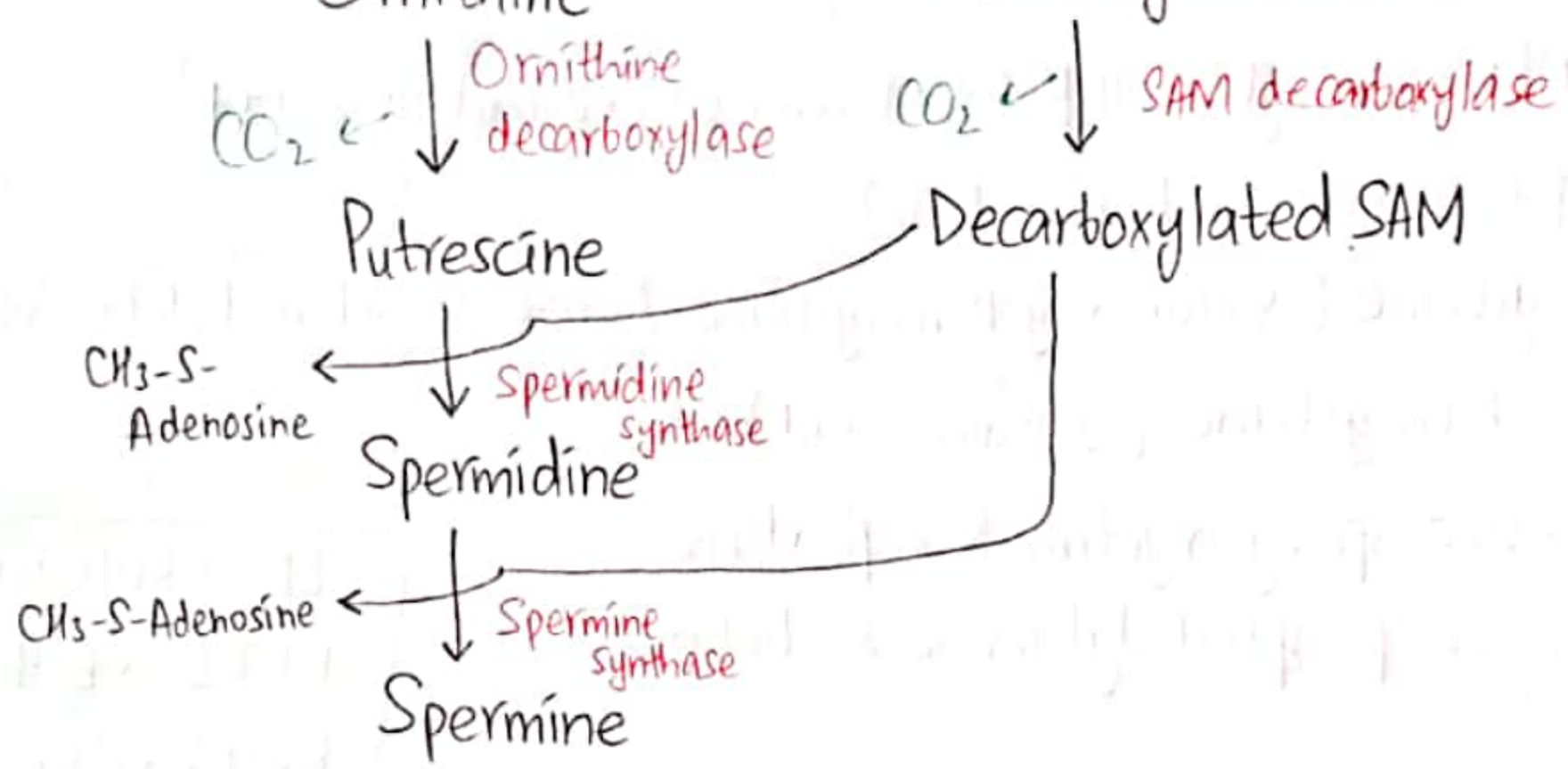
→ Synthesize phosphatidyl serine & choline

LL → Ketogenic
PTTI → Both
Rest → Glucogenic



Polyamines

Putrescine, Spermidine & Spermine



NOTE

- Ornithine decarboxylase ⟶ SHORTEST HALF LIFE (10 min.) known among all mammalian enzymes.
- SAM decarboxylase is a rare example of a decarboxylase enzyme not needing PLP.

↑ polyamine excretion is found in all types of cancer.

Diagnostically,

Putrescine → ideal marker for cell proliferation

Spermidine ⟶ suitable for assessment of cell destruction.

METABOLISM OF AMINO ACIDS

NOTE ⇒ Transaminases use vit B6 (PLP form) as coenzyme.

- All a.as undergo transamination EXCEPT:

  Lysine, Threonine, Proline, Hydroxyproline
  (Let The Proline Hit the floor)

- Glycine, Tryptophan ⇒ Form N^{10}- Formyl THF (Get The Chips Back)
- Choline, Betaine ⇒ Form N^{10}- Methyl THF

  (Histidine & Serine form N^5, N^{10}- Methenyl/Methylene THF)

Tyrosinosis (Tyrosinemia Type I) ⇒ CABBAGE-LIKE ODOUR

Isovaleric Acidemia ⇒ CHEESY ODOUR

Branched chain ketoacidosis ⇒ MAPLE SYRUP SMELL IN URINE

Putresciene ⇒ Marker for Cell Proliferation.

Spermidine ⇒ Marker for Cell Destruction.

MOLECULAR BIOLOGY

Replication of DNA occurs in 5'–3' direction.

DNA Helicase → separates strands like a zip opener.

Prokaryotes have:

① DNA pol. I → Joins Okazaki fragments (along with DNA ligase) + catalyzes DNA fragment that replaces RNA primer on LAGGING STRAND

② DNA pol. II → DNA repair.

③ DNA pol. III → Synthesis of new DNA strand + Proof-reading.

~~DNA~~ Type I DNA Topoisomerase → cuts SINGLE DNA strand to overcome problem of supercoils. & then reseal the strand.

Type II DNA Topoisomerase → " BOTH " " "

" " " " "

" " " " .

Stop codons

UAG → Amber
UAA → Ochre
UGA → Opal

There are 5 DNA pol in Eukaryotes:

① DNA pol α → Synthesis of RNA primer.
② " " β → Repair of DNA.
③ " " γ → Replication of mitochondrial DNA.
④ " " δ → Replication on leading strand of DNA + proof-reading.
⑤ " " ε → " " Lagging " " " " " .

4 phases of cell cycle & DNA replication:

In cancer, most of the cells are in S-phase

① G1 → Active protein synthesis.
② S → Replication of DNA (diploid genome converted into tetraploid)
③ G2 → Enlargement of cytoplasm + actual cell division.
④ G0 → Dormant phase.

Telomeres prevent loss of DNA at the end of chromosomes during each course of replication.

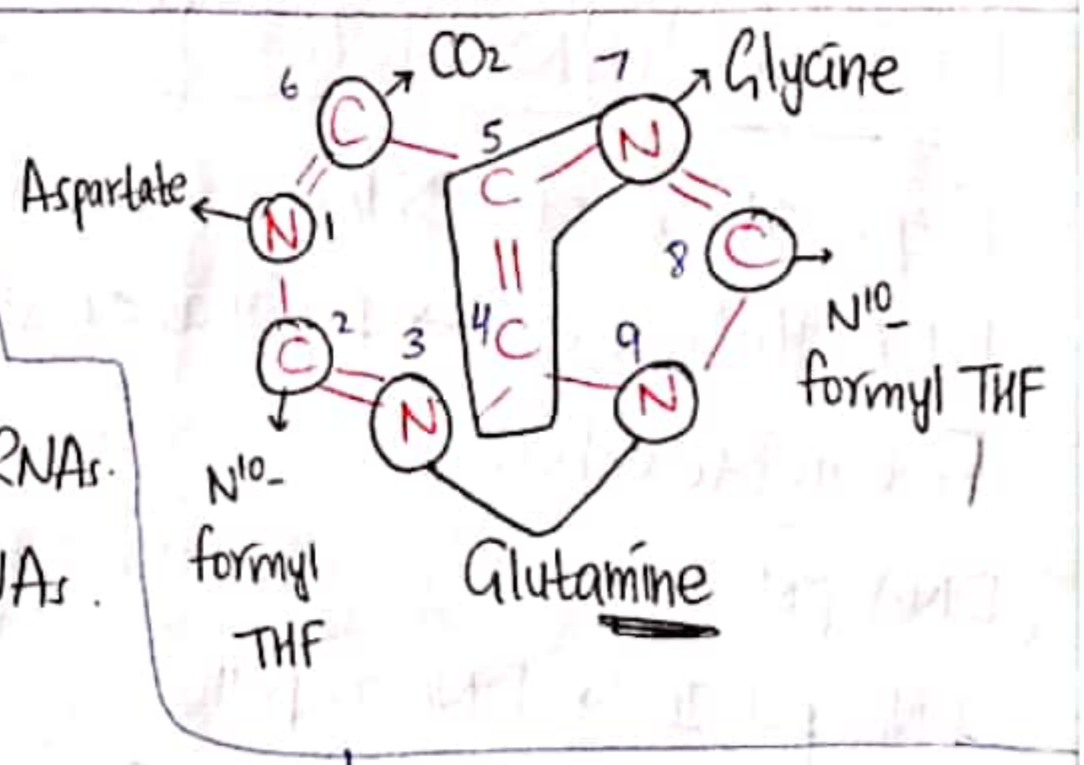
Human telomeres have a repeated sequence of TTAGGG

Xeroderma Pigmentosa → defect in Nucleotide excision-repair.

Hereditary Non-Polyposis Colon Cancer (HNPCC) → defect in Mismatch-repair.

3 RNA polymerases:

① RNA pol. I → Synthesize rRNAs.
② " " II → " mRNAs + snRNAs.
③ " " III → " tRNAs + srRNAs.



Blotting techniques helps identify:

① DNA (Southern blot)
② RNA (Northern blot)
③ Protein (Western blot)