Follic Deficiency Anemia
Megaloblastic Anemia

[DEPTH OF BIOLOGY]

↓ clinical condition

↓ due to low level of folate or follic acid

↓ leads to → Anemia & Neural tube malformation

#: folate or Vit B_9 → comes from green leafy vegetables and citrus fruits like lemon.

In these folic acid is present in the form of Polyglutamate

↓ chains of aminoacids called as Glutamic acid.

• chain is negatively charged [DEPTH OF BIOLOGY]

↓ due to the presence of carboxyl group

↓ makes it

- ↓ polar
- ↓ Soluble in H2O
- ↓ Not soluble in lipid

So, the polyglutamate residue of follic acid are almost Non-Absorbable from GI tract where all the cells are surfaced with the lipid cell membrains. [DEPTH OF BIOLOGY]

Now when, polyglutamate residue reaches a portion of the small intestine Jejunum.

↓ a special enzyme present at jejunal mucosa → this cuts down the polyglutamate residue to Monoglutamate

↓ Smaller, less negatively charged, can pass through cell Membrane [DEPTH OF BIOLOGY]

↓

These enters the Jejunal cells, where they are converted to Tetrahydrofollic acid or THF by the enzyme called Tetrahydrofolate reductase

[DEPTH OF BIOLOGY]

THF
↓
gets methylated → Methyl-THF (more soluble)

Once the methyl THF form they leave the Jejunal cells and enters blood stream.

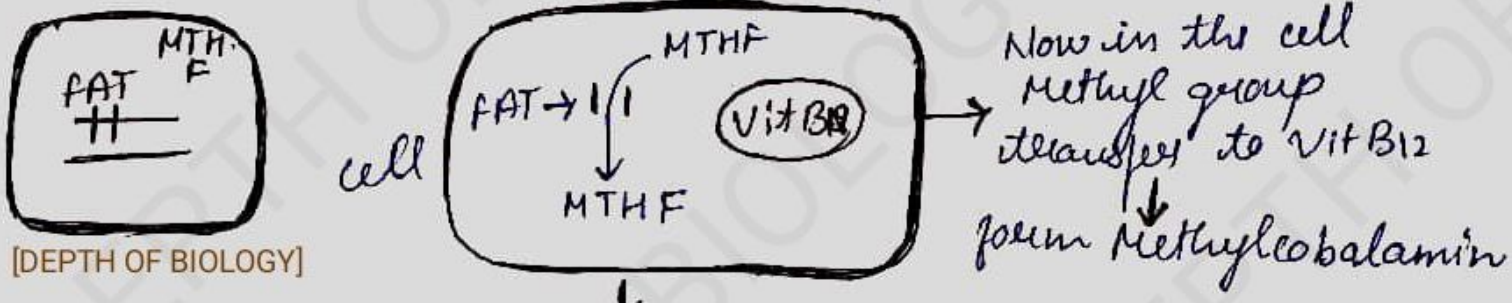
goes to liver and gets stored for short period of 2-3 months

while most of it used up for Metabolic activity inside various cells around the body

[DEPTH OF BIOLOGY]

Follic acid used to synthesize DNA Precursors
↓
essential for DNA replication and cell division.

On target cell, there's a specialized membrane protein called Follic acid transporter or. FAT
. This moves the circulating methyl THF inside cell.



[DEPTH OF BIOLOGY]

↓

free THF in the process inside the cell get extra methylene group (from serine) → an amino acid found within the cells.

↓
THF → THF with Methylene
↓

Transfers its methylene to a nucleotide called.. deoxyuridine monophosphate or d-UMP
↓
Now d-UMP after get methylene converted into d-TMP

[DEPTH OF BIOLOGY]

deoxyThimidine Monophosphate

[DEPTH OF BIOLOGY]

↓

Then converted into Thymidine (one of the nucleotide use to build DNA)

‡ Methyl Cobalamin transfer its Methyl group to Homocysteine

↓

and converts into essential amino acid called Methionine

‡ If Homocysteine ↓↓↓ ⟶ Harmful

→ Follic acid also play very Imp. role in foetal develop:

↳ development of CNS

- Follic Acid Deficiency →

Impaired cell ÷ (RBC, WBC and Platellets ÷ affected)

–Too much Homocysteine

- Neural tube defect in foetus. [DEPTH OF BIOLOGY]

Normally

Now, Inside the Bone Marrow RBC precursors are normally big and Plump ⟶ they undergo series of cell division which results in small mature RBC's.

‡ Folate Deficiency →

Bone Marrow pumps out larger but still mature RBC called Macrocytes

↓

This type of RBC destroy in the spleen

↓

cause ↓se in total RBC count Anemia

↓

. In Respons the Bone Marrow compensate loss by releasing Megaloblasts

↓ [DEPTH OF BIOLOGY]

abnormally developed RBC precursors into the blood.

↓

and the find result Macrocytic Megaloblastic anemia

. Also affect WBC production

→ The Bone Marrow releasing large, Immature Neutrophils

↓

Hypersegmented

Which means their nuclei has ≥ 6 lobes.

Finally ⇒ severe folate deficiency may also decrease Bone Marrow Production of Platellete precursors

↓

called Megakaryocytes

So when this 3 blood cell lines are affected

↓

Pancytopenia → RBC, WBC, Platellet ↓ only in case of severe folate deficiency.

In folate deficiency, old epithelial cells. (In tongue) are not replaced and this slow down the healing of normal wear and tear of the tongue

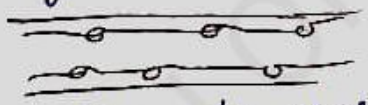
↓

which ultimately lead to Inflamation of the tongue known as Glossitis

Next → Homocystine ↑↑ (Body)

also builds up in the blood where it binds with endothelial cell lining blood vessle

Some of it excreted in urine called Homocystinuria

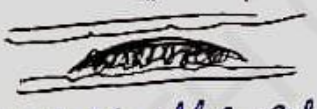


causing them to secrete molecule called Pro inflamatory Cytokines

↓

These attract Immune cells like leukocyte to the area and cause Inflamation.

↓ leads to Atherosclerosis or plaque build up inside the arteries.



This narrows the arteries and could lead to Ischemia of the tissue supported by them.

Homocysteine  Blood Clot → Homocysteine also binds to platellets and make them stick together to make blood clots.

• All these increase the risk of Ischemic Heart disease or Stroke.

Causes

(a) ⟶ ↑se demand
(b) ⟶ ↓se dietary intake
(c) ⟶ Impaired absceptian

Normally, we have supply of folate in body upto 2-3 months But this can use quicker during pregnancy because Need ↑se.

→ So Generally who have folate deficiency —
⟶ either pregnant
⟶ restricted diet for longer then six weeks

→ Excessive OH consumption and medication like Phenytoin often Interfere with folic acid absceptio -on from the Jejunum.

Sign and symptoms

⟶ Anemia
⟶ shortness of breath
⟶ Pallor
⟶ Easy fatigability
⟶ Soreness of tongue due to glossitis.

In some cases → Ischemic Heart Disease
⟶ Paralysis
⟶ chest pain
⟶ stroke
⟶ slurred speech.
⟶ Panchtopenia → in long and severe case.

Diagnosis

① → Peripheral Blood smear
(large RBC and hyper.segm. neutrophill)
→ Mean corpuscular vol. (MCV) → >100
Macrocytosis

(2) → Homocystiene level ↑↑↑ [DEPTH OF BIOLOGY]

(3) → Bone Marrow study (Megaloblastic changes in RBC precursors)

Cause with Treatment

(1) Dietary ——→ Oral Folate supplements

(2) Absorption ——→ Avoid Alcohal consumption, offending medications.

(3) Pregnancy ——→ Fallate supplements (Grain)

[DEPTH OF BIOLOGY]