Megaloblastic Anemia (Vit.-B12)

Vit B_{12} ↓↓ in body

→ Leads to variety of Problems ranging from Anemia to soreness of the tongue and Neurological dysfunction

Vit. B12 = Cobalamin → Is a complex organometallic compound found in animal and dairy products

↓

Broken in Stomach by Pepsin

↓

which is active form of gastric enzymes called pepsinogen to release B_{12}

Pep → Peps → A&DP → Vit B_{12}

→ Parietal cell made a protein in stomach called Intrinsic factor can bind to B_{12}

↓

and B_{12} – Intrinsic factor complex passes into the Intestines

↓

when the complex reaches the Terminal Ileum

↓

The enterocyte which are special cell lining the Intestine.

They recognise the Intrinsic factor and absorb whole the complex.

↓

Inside the enterocyte, Intrinsic factor gets removed and a special protein called Transcobalamin – II

↓

Binds the free B_{12} and transport it into the blood.

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from there to various target tissues

↓

Some of the transcobalamin-B12 complex gets to the liver where B12 can be stored for several years.

B12 used to synthesize DNA precursor

↓

which is essential for cell division.

↓

First, Vit B12 accepts a Methyl group from tetrahydro-folate or MethyTHF

↓

Making Methylcobalamin and free Tetrahydrofolate or THF in the process

THF ← Extra Methyl group (from serine)

THF-Methylene → Transfers the Methylene to a nucleotide called d-Ump

↓

d-Ump —(Methyl)→ T-ump.

Methylcobalamin —(transfer methyl group to)→ Homocystine —(converted into)→ Methionine

Cabone formed

- B12 is used by
  - mitochondria → in another active form called Adenosylcobalamin

↓

acts as a coenzyme for methylmalonyl co-enzyme A-mutase

↓

This enzyme converts

Methylmalonyl Co-A → Succino Co-A

↓

Reduces the level of Methylmalonic acid — Harmful if build up.

Consequences of B12 deficiency →

① Impaired cell division ⟶ affects rapidly dividing cell in the Bone Marrow like RBC, WBC as well as Platellete precursors

② Homocystine ↑↑

③ Methylmalonic acid ↑↑

Inside the Bone Marrow (RBC precursors are normally big and Plump), They undergo a series of cell division which results in small mature RBCs

↓

Now with deficiency of B12 at first, the Bone Marrow pump out large but still mature RBC called Macrocytes

↓

These RBC destroys in spleen.

↓

causes decrease in RBC count or Anemia

↓

In response the Bone Marrow compensate by releasing Abnormally developed RBC precursors called Megaloblasts (into the blood)

↓

Final result Macrocytic Megaloblastic Anemia

B12 deff also affect WBC production ⟶ so the bone Marrow start releasing.

- Large Immature Neutrophils with hypersegmented nuclei [has more then 5 lobes]

→ Vitamin B_{12} ↓ ⟶ ↓se the production of Megakaryocytes, which are the platellet precursors in the Bone Marrow.

↓↓↓ RBC, WBC, Platellet ⟶ affected ⟶ Pancytopenia

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

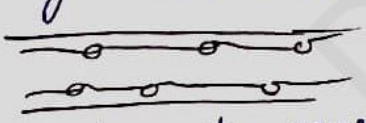
↓

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

↓

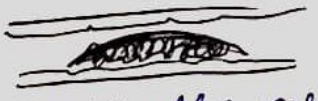


causing them to secrete molecule called Pro inflamatory Cytokines

↓

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.

Me of it excreted in urine called Homocystinuria

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→ In patient (B_{12}↓↓) ⟶ Methylmalonic acid ↑↑

↓

It builds up in the Neuron. – Especially in the Myelin sheath.

which degenerates

- Myelin help transmit electrical signal from one Neuron to another at very high speed.

But in B_{12}↓↓ communication b/w neuron is significantly slower

↓

which leads to Impaired Neurological & Muscle function

Vitamin B_{12} deficiency

- Impaired Absorption

eg:

① In pernicious anemia

↓

(↑)se production of overzealous IgA antibodies against Intrinsic factor or parietal cell

② In chron's Disease

→ enterocyte in the Ileum are danged

→ so B_{12} can't bind with transcobalamin

③ Gastric bypass ⟶ Ingested food passes through the stomach quickly.

→ Intrinsic factor can't bind with B_{12} (which get from food)

④ Bacterial overgrowth In bowl can also reduce absorption (lead to B_{12} deficiency)

Dietary Intake ↓↓

↓

→ Who avoid all animal production.

→ who Don't take Vit B_{12} supplement.

Sign and Symptoms

→ most comman anemia, shortness of Breath, Pallor and Easy fatigability as well as soreness of the tongue due to glossitis.

→ In some cases Ischemic heart diseases.

- chest pain
- stroke

- Paralysis
- slurred speech.

- In very severe cases → cause Impairment of Neural function
  - → loss of memory
  - → decreased reflexes.

Diagnosis :-

→ Methylmalonic acid level ↑↑

1. Peripheral Blood Smear
2. Homocystiene level ↑↑↑
3. Bone Marrow study. → Megaloblastic changes in RBC precursors.

Causes with Treatment :-

1. Absorption related → B12 dosage ↑↑ (Intramuscular B12 Injection). for a couple of months
2. Treatment of the underline → cause, when possible should also be started.