MEGALOBLASTIC ANEMIA:

→ defective or impaired DNA synthesis and defective megaloblasts in bone marrow in which the maturation of the nucleus is delayed relative to that of cytoplasm.

Causes: → folate deficiency
→ vitamin B12 deficiency }{ As they all essential factors for the synthesis of thymidylate normal DNA synthesis & nuclear maturation }

– Thymidine def causes Abnormality in Rapidly dividing cells.
↓
The hematopoietic precursor show nuclear cytoplasmic Asynchrony of progenitors undergo Apoptosis that lead to Anemia.

MEGALOBLASTIC ANEMIA

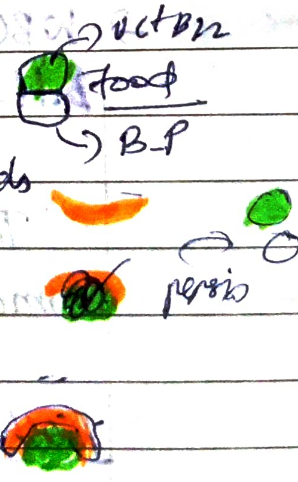
causes:

Vit B12 def
→ Malabsorption (pernicious A)
→ Poor dietary intake
→ surgical
→ ↑ demand (preg, hyperthyroid)

Folate def. → (Abs in jejunum)
– Poor dietary intake
– ↑ demand (haemolysis)
– Malabsorption
→ Antifolate drugs
– Redem

Mechanism of B12 Absorption:

Vit B12 bound to binding protein in food.
↓
Secretion of haptocorrin from salivary glands
↓
Pepsin Releases vit B12 from binding protein.
↓
Vit B12 form complex haptocorrin.
↓
This complex get split by proteases from Pancreas.
↓
B12 get Absorbed



formation of IF vit B12 complex

↓

Endocytosis of vit B12 with ~~transcobalamin~~ ileal enterocytes via cubilin Receptor.

↓

Association of B_{12} with transcobalamin II

↓

Delivery of vit B_{12} to tissue cells.

PATHOGENESIS:

Vit B_{12} FA deficiency

↓

impaired DNA synthesis
Normal cytoplasmic synthesis

↓

cell keeps on enlarging → (∵ nuclear maturation is delayed due to impaired DNA, so lags behind cytoplasmic maturation.)

↓

Megaloblasts > larger than normoblasts; All dividing cell in the body like, skin, GI tract, bone marrow) mucosa affected.

↓

Granulopoiesis & thrombopoiesis Also affected. ← patient p/c with pancytopenia, thrombocytopenia granulocytopenia

↓

Intramedullary death of erythroid precursor, myeloid precursor.

↓

Ineffective hemopoiesis, affecting erythropoiesis granulopoiesis & thrombopoiesis

↓

Anemia, leukopenia, thrombocytopenia.

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Lab Findings:

Pheripheal Blood:

Hb↓, PCV↓, MCV↑, MCH↑, MCHC – normal.

Pheripheral smear:

- Pancytopenia → ↓RBC, ↓WBC, ↓platelet.

RCB → Macroovalocytes (egg shaped)

- Lack of central pallor well Hemoglobinized
- Aniso poikilocytosis
- Basophilic stippling, Howell Jolly bodies (nuclear Remnants)
- Cabot Ring (Acidophilic)

WBC: ↓ count, Hypersegment neutrophil → 1st sign

Bone Marrow:

- Markedly hypercellular, Megaloblast ↑

M:E Ratio is Reversed from 1:1 to 1:6.

- Nuclear cytoplasmic asynchrony
- Ineffective erythropoiesis
- Delicate sieve-like chromatin

BIOCHEMICAL TEST:

LDH ↑, bilirubin ↑, Serum Fe, Ferritin ↑, homocysteine ↑

- Shilling test
→ Deoxyuridine suppression test
for Folic Acid

↳ FIGLU is urine

Clinical feature:

Onset: Insidious of progress

Classic triad of presentation: weakness, sore throat, paresthesia.

→ Painful Red beefy tongue.

– Neurological Manifestation

IRON DEFICIENCY ANEMIA:

→ Most common nutritional disorder → Fe deficiency

Dietary lack | Impaired Absorption | ↑Demand | Chronic Blood loss:

→ Serum ferritin → 15-300 ng/L.
below 12 indicate Anemia.

→ Hemosiderin → found in Reticuloendothelial cells.
appear as golden yellow granules in the cytoplasm of the cell.
t/t with prussian blue (Pearl's stain)
↳ hemosiderin takes blue-black color.
↓
due to iron Reacts with Potassium ferrocyanide

RDA = ~~10-20~~ 5-10 mg/day (M) 20 mg/day (F).

Absorption from duodenum & proximal jejunum.

PATHOGENESIS:

due to def of Iron causing defective heme synthesis

→ Produce - hypochromic microcytic Anemia

→ Progressive depletion of Hemosiderin ↓ ferritin Reserve lower serum Fe ↓ transferrin saturation level.

→ ↑ erythroid Activity.

Causes:

Dietary deficiency
- Inadequate (Dietary def)
- Impaired Absorption - celiac disease, chronic diarrhea
- ↑ Demand - Pregnancy, infancy, growing child
- Chronic Blood loss → Renal tumor, hemorrhoids, GI tract

Lab Findings:

Hb & PCV ↓

MCV ↓, MCH ↓ MCHC ↓

RDW ↑ (11.5-14.5%) normal > 15%. 1st sign of iron