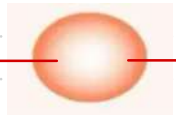
Morphological classification of Anemia

Microcytic

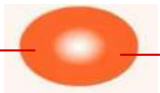


- It's color is hypochromatic
  - عرفنا هذا الإشي باستخدام Peripheral blood smear
- It's small in size < 80

Causes: TAILS

- Sideroblastic anemia
- Lead poisoning
- Thalasemia
- Iron deficiency anemia
- Anemia of chronic disease
- It's the most common cause

Normocytic

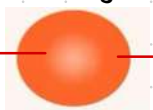


- It's color is normal
- It's size 80-100

haraba

- Aplastic anemia
- Bone marrow failure
- Hemolytic anemia
- Renal disease
- Anemia of chronic disease
- Acute blood loss

Macrocytic



- It's color is hyperchromatic
- It's size >100

Causes: MALM

- Myelodysplasia
- Liver disease
- Megablastic anemia
- Alcoholism

Macrocytic

**RBCs larger than normal

**MCV > 100 fl

Macrocytic

Megablastic anemia (Most common Cause)

- Folate (Vit B9) deficiency
- Cobalamin (Vit B12) deficiency
- Copper deficiency
- Orotic aciduria → autosomal recessive disease there will be deficiency in certain enzyme that leads to pyrimidine deficiency → So there will be increase in orotic acid in urine
- Drug-induced (Allopurinol)

Non- megablastic anemia

- Alcohol use disorder
- Liver disease
- Diamond-Blackfan anemia

Note:

The difference between megablastic anemia and non-megablastic anemia is:
The presence of hypersegmented neutrophils

Exist in megablastic anemia ↔ Don't exist in non-megablastic anemia

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Megablastic anemia

heterogeneous group of disorders that have:
Large cells with an arrest in nuclear maturation → Unbalanced cell growth and impaired cell division

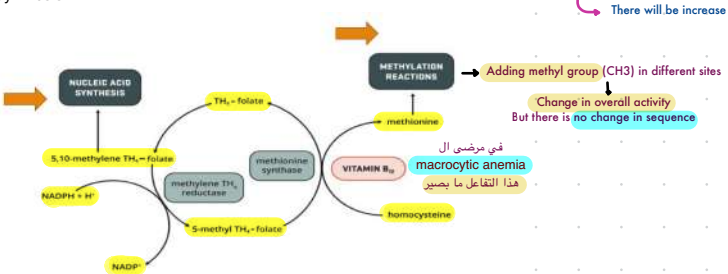
So there will be a defect in nucleus
That means there will be a problem in (DNA synthesis, to a lesser extent RNA and protein synthesis)

most apparent in rapidly dividing cells as:
Blood cells, gastrointestinal cells, skin and epithelial cells.

*So patients will have pancytopenia
" Anemia (↓RBCs), thrombocytopenia (↓Platelets) and granulocytopenia

*Red cells progenitors undergo apoptosis (intramedullary hemolysis)
There will be increase in bilirubin—> having jaundice

MC Causes:
① Vit B9, B12 deficiencies
② Medications
③ Direct interference with DNA Synthesis (HIV infection)



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Vitamin B12 (Cobalamin) Deficiency Anemia

Sources:

cobalt-containing vitamin

1- meat 2- fish 3- Dairy products

*Not exist in vegetables and fruits

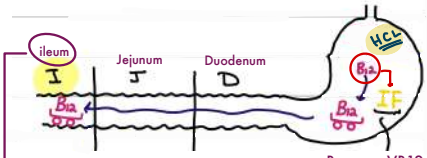
It is stored in the liver

Storage (reservation) is sufficient for (5 - 20)years

عشان هيك لما تظهر أعراض الdeficiency معناها كان هناك unrecognized malabsorption لعدّة سنوات

So Vit B12 deficiency has chronic onset

Vit B12 absorption:

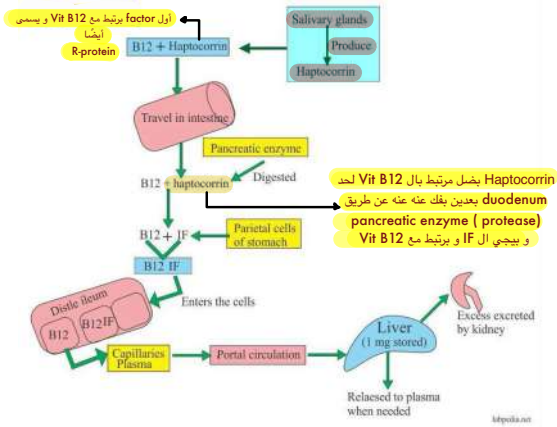


Vit B12 is absorbed in the terminal ileum

Because VB12 is sensitive to the HCL

So it's bind with intrinsic factor during it's passage through gastrointestinal tract

IF bind Vit B12 at duodenum, before that it's bind with haptocorrin



Things that affect Vit b12 absorption:

- pernicious anemia (Atrophic gastritis) (autoimmune disease) There will be destruction of parietal cells and intrinsic factor
- Gastrectomy (There will be loss of IF)
- ileal resection (Loss site of absorption)
- distal ileum disorders (Crohn disease)
- pancreatic insufficiency

مش رح يكون في حتى انه يصير في dissociation بين pancreatic enzymes (proteases) ال VB12 and Haptocorrin

Folate (Folic Acid) Deficiency Anemia

Causes:

- poor diet (poverty & the elderly)
- increased metabolic needs: *pregnant women *chronic hemolytic anemias
- Malabsorption or defect in metabolism
  - Absorption is inhibited by beans and legumes (البقوليات), acidic food
  - Drugs: phenytoin or methotrexate.
  - Malabsorptive disorders (celiac disease, tropical sprue)

Morphology of megaloblastic anemia

Bone marrow (BM):

Because of low hemoglobin–> continuous feedback of hypoxia–> Increase production of RBCs

1) hypercellular 2) Numerous megaloblastic erythroid and Granulocytic progenitors

1) larger than normal progenitors
2) Delicate, finely reticulated nuclear chromatin (indicative of nuclear immaturity)

peripheral blood (PB):

*hypersegmented neutrophils (>=5) appear before the onset of anemia

normally (3-5)lobes

To be hypersegmented neutrophils in smear there must be ;

- 1 neutrophil with >= 6 segments
- More than 5% of neutrophils have >= 5 segments

-The red cells typically include large, egg-shaped macroovalocytes.

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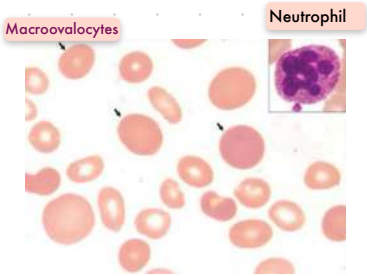
Megablastic anemia

Histologic changes



1) Larger cells
2) Loss of pale center (due to present of large nucleus)
3) hyperchromatic (arrested immature nucleus)

Clinical manifestation

1- Symptoms of anemia

2- Neurological abnormalities

-Changes in personality -Psychosis
-peripheral neuropathy

Cause:
VB12 is needed for myelin formation, so it's deficiency lead to demyelination of posterior and lateral column of spinal cord

Neurological symptoms appears according to the nerve involved

-Symmetric numbness
-Tingling
-Burning sensation
→ In feet and hands

-Unsteadiness of gait
-Loss of position sensation → Particularly in toes

Physical findings

Glossitis (Red, leafy tongue)

Smooth surface due to loss of papillae

caused by Cobalamin deficiency

Lemon yellow hue
(increased bilirubin level)

Cause: intramedullary hemolysis

hyperpigmentation (not common)

Cause: increased melanin synthesis
⇓
Due to increase activity of tyrosinase

Laboratory findings

- Complete blood count (CBC)
- Red blood cell (RBC) indices (Low Hemoglobin, increase MCV)
- Peripheral blood smear
- Serum cobalamin (decreased)
- Serum folate (decreased)

Note:

Treatment of megablastic anemia:
1) B12 or B9 supplements
(Depending to the cause of deficiency)

2- Parenteral supplementation
(when malabsorption is the cause)

**in increase demand or poor diet (tablets can be used)

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Non-megaloblastic anemia

(no hypersegmented neutrophils)

Causes:

Alcohol consumption (RBCs toxicity)

- Lead to arrest in nuclear maturation
- Resulted in large nucleus and RBC

hereditary spherocytosis (impaired volume regulation)

- Causing RBCs to be large
- Defect in carrying functional hemoglobin (anemia)

Hypothyroidism and liver disease

- Causing lipid deposition in cell membrane of RBC

Marked reticulocytosis (Very rare)

from states of:

1) Excess RBC consumption (hemolysis)

2) Turnover in pregnancy

3) Primary bone marrow disease
(reticulocytes are larger than the average RBCs)

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