Megaloblastic anemia (macrocytic)

It is a form of anemia characterized by very large red blood cells and a decrease in the number of those cells. It was result from inhibition of DNA synthesis during red blood cell production. When DNA synthesis is impaired, the cell cycle cannot progress from the G2 growth stage to the mitosis (M) stage. This leads to continuing cell growth without division, which presents as macrocytosis. The defect in red cell DNA synthesis is most often due to **vitamin B12 deficiency** or **folate deficiency**.

Pernicious anemia is a type of megaloblastic anemia in which the body isn't able to absorb vitamin B12 due to a lack of intrinsic factor in stomach secretions, that induced VB12 absorption, lead to inability of body to produce adequate number of RBC.

Folic acid (vitamin B9), also known as pteroylglutamic acid, the functional form of folate is tetrahydrofolic acid. The main dietary sources of folic acid are green vegetables, also it found in fruit. Daily adult requirements of folic acid range from 50 to 100 microgram. The body stores around 5 mg of folate between 3 and 4 months. Folate is primarily stored in the liver

It is mainly absorbed in the jejunum and ileum by passive transport, and by active transport after folate binds to reduced-folate transporter 1 and 2 (RFT-1 and RFT-2) and folate binding protein (FBP), which depend on concentration differences of it.

Excess intracellular folic acid can pass into the blood stream and then be filtered through the glomerulus, secreted into the proximal tubule, and eliminated in the urine at a rate of 2 - 5 mcg/day.

The biological functions of folic acid include: **purine and methionine synthesis** It important in the production of DNA and RNA.

Cobalamin (B12) is a highly complex, essential vitamin, owing its name to the fact that it contains the mineral, cobalt, and is necessary for DNA synthesis and cellular energy production. It is important to note that the recommended intake reported in the literature ranges from 2 to 5 microgram/day

The body stores between 2 to 5 mg of vitamin B12 for between 3 and 4 months. Like folic acid, it is mainly stored in the liver. The main dietary sources of vitamin B12 are animal foods, such as beef, fish, and dairy products. It is also found in some animals that ingest cobalamin-synthesizing bacteria, such as ruminants and oysters. Plant foods do not contain cobalamin.

It was absorbed in stomach, and three parts of small intestine (duodenum, jejunum, Ileum).

Megaloblastic anemia causes:

1-Vitamin Bl2 and Folate deficiency 2-Abnormalities of vitamin B12 or folate metabolism (e.g. transcobalamin deficiency, antifolate drugs) 3-Other defects of DNA synthesis (congenital enzyme deficiencies- acquired enzyme deficiencies).

Causes of vitamin B12 deficiency

1. Insufficient dietary intake: Strict vegetarians (‘vegans’)

2. Deficient absorption: Pernicious anemia, total or partial gastrectomy and diseases of small intestine (fish tapeworm).

Causes of folate deficiency

1- Insufficient dietary intake poor diet with lack of green vegetables 2-chronic alcoholics.

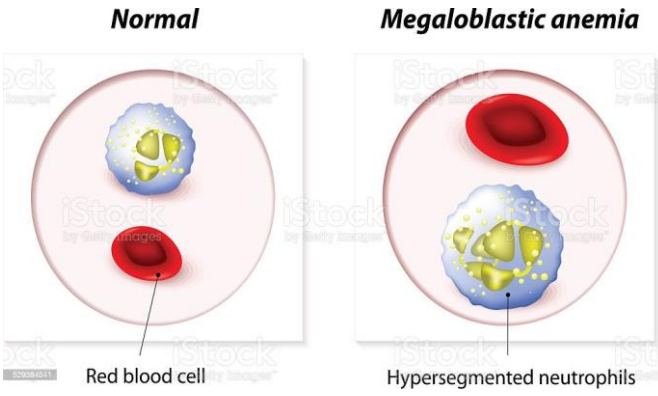
3- Deficient absorption (malabsorption syndromes) such as celiac disease.

4- Increased demand during pregnancy.

Symptoms of megaloblastic anemia:

1-pale skin **2**-decreased appetite **3**-irritabilitty 4- fatigue **5**-numbness or tingling in hands and feet (Vitamin B12 specific) **6**-lightheadedness upon standing or exertion **7**-swollen, red tongue **8**-bleeding gums**.**

Laboratory diagnosis:



1-CBC: MCV is increased, MCH is slightly increased, MCHC is within normal limits, low Hemoglobin and RBC shaped has large size and oval shaped (macrocytic)

2-the peripheral blood smear shows macrocytosis and many hypersegmentation of neutrophils (why).

3-leucopenia and thrombocytopenia. **4**-reticulocytes are not in comparison to the degree of anemia. **5**-already B12 and folate deficiency**.**

Metabolism of B12 and folate

The absorption of dietary vitamin B12, after combination with intrinsic factor (IF) produced by parietal cells of gastric mucosa, transported to the terminal part of **ileum** where receptors for IF are present on the epithelial cells.

Then IF is degraded, B12 attaches to another transport. protein called **Transcobalamin TC**, is the essential plasma protein for transferring Bl2 into the cells of the body, include two type first TCN1 produced from salivary gland, bind with cobalamin to protect it from stomach acid, second TCN2 that transport VB12 and enter it to the cells.

Folate absorption occurs through the duodenum and jejunum after conversion of all dietary forms to methyltetrahydrofolate **(methyl THF).**

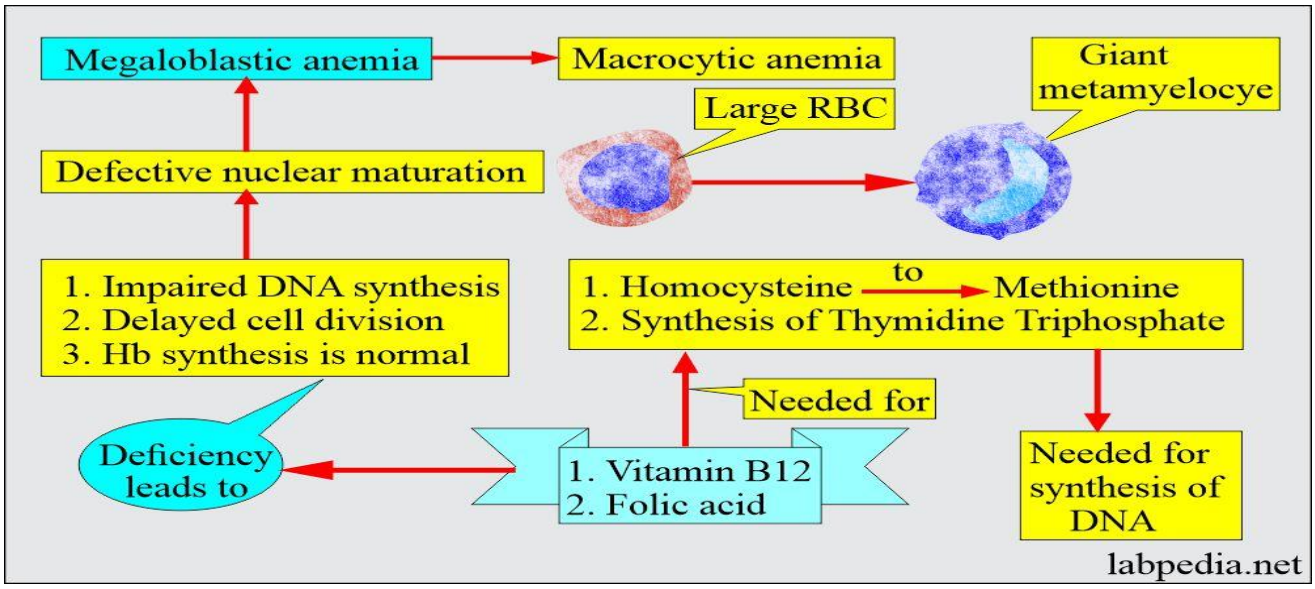


Figure 1Diagram explain the summary of Megaloblastic anemia

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