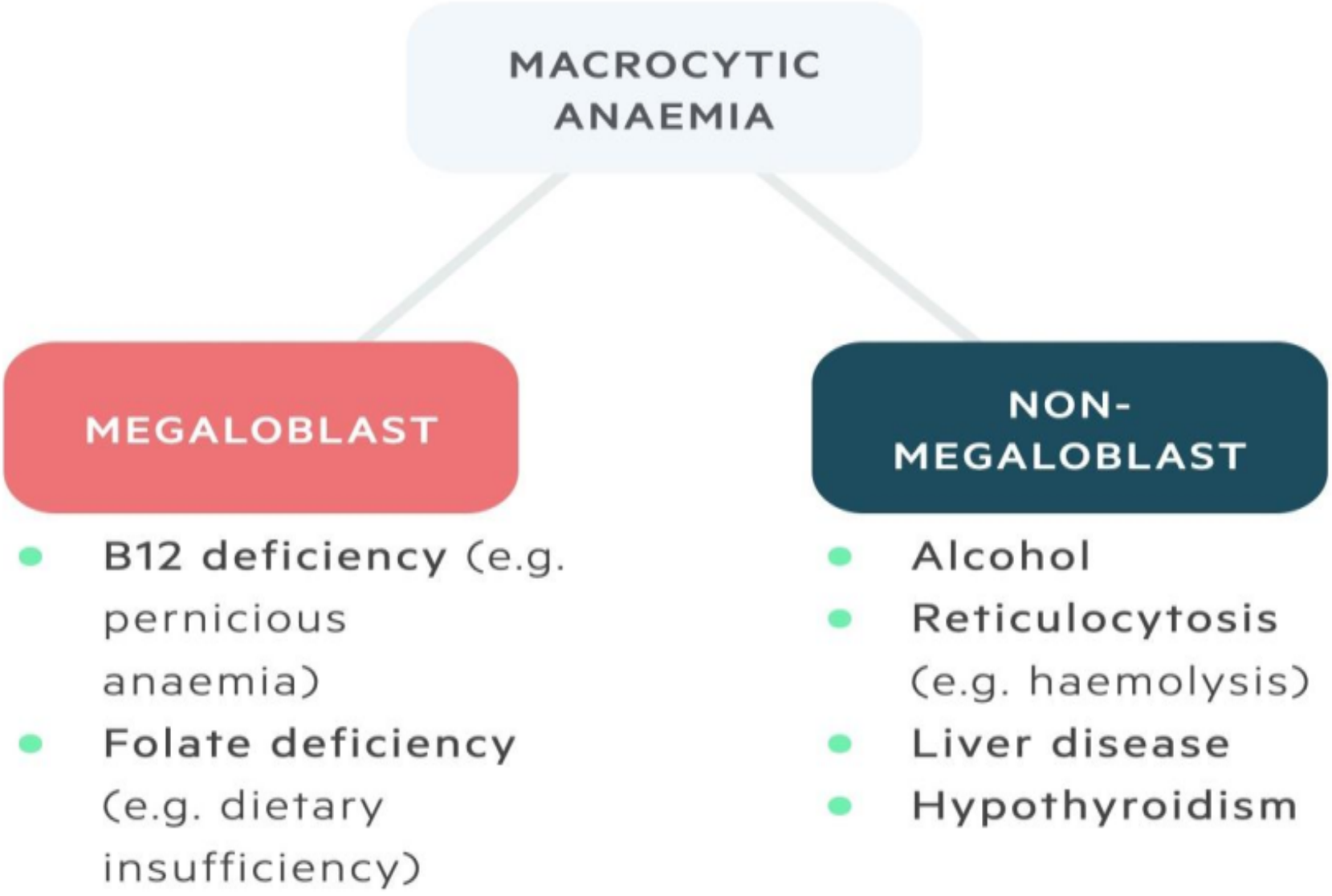
Hematology

Megaloblastic Anemia (macrocytic)

LEC 8

Dr. Mohamed kamel kudi

- 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.


MACROCYTIC ANAEMIA
MEGALOBLAST
B12 deficiency (e.g. pernicious anaemia)
Folate deficiency (e.g. dietary insufficiency)
NON-MEGALOBLAST
Alcohol
Reticulocytosis (e.g. haemolysis)
Liver disease
Hypothyroidism

- **Pernicious anemia** is a type of megaloblastic anemia in which the body is not able to absorb vitamin B12 due to a lack of intrinsic factor in stomach secretions, that reduced vitamin B12 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 50-100 μg. The body stores around 5 mg of folate between 3-4 months. Folate is primarily stored in the liver.

- It is mainly absorbed in the jejunum and ileum by passive transport, and by active transport. Excess intracellular folate can pass into the blood stream and then be filtered and eliminated in the urine at a rate of 2-5 μg/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 μg/day. The body stores between 2-5 mg of vit B12 for between 3-4 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.

- **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.

- **Causes of vitamin B12 deficiency**

- 1. **Insufficient dietary intake**: Strict vegetarians (‘vegans’)
- 2. **Deficient absorption**: Pernicious anemia, total or partial gastrectomy , diseases of small intestine, and fish tapeworm (*Diphyllobothrium latum)* .

- **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.

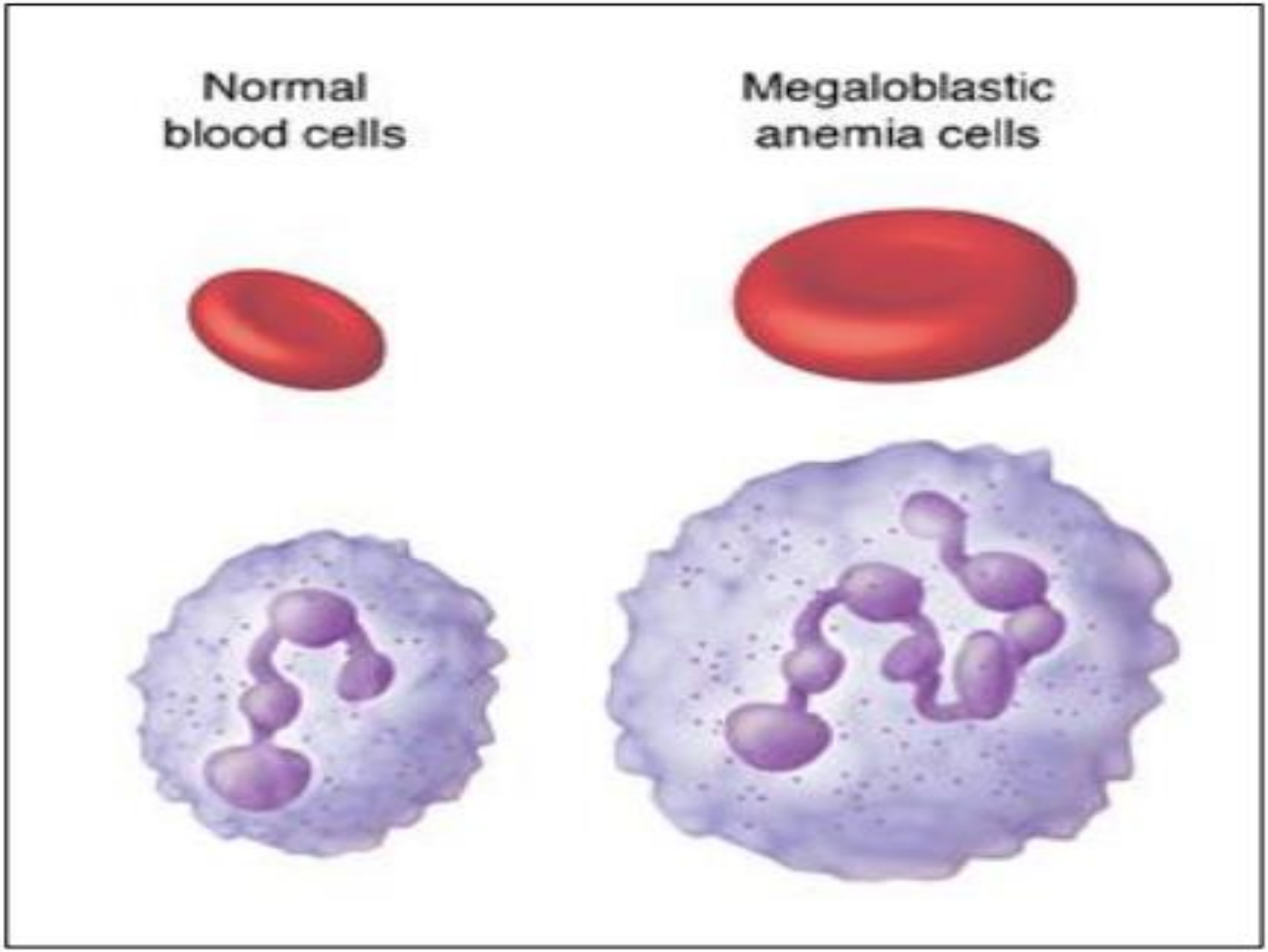
- 4- Increased demand during pregnancy.

Symptoms of megaloblastic anemia:

- 1- Pale skin
- 2- Decreased appetite
- 3- Irritability
- 4- Fatigue
- 5- Swollen, red tongue
- 6- Bleeding gums.
- 7- Numbness or tingling in hands and feet (Vitamin B12 specific)
- 8- Light headedness

- **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 blood smear shows macrocytosis and many hypersegmentation of neutrophils.
- 3- Leucopenia and thrombocytopenia.
- 4- Reticulocytes are not in comparison to the degree of anemia.
- 5- Decrease serum B12 and folate assay.


Normal
blood cells
Megaloblastic
anemia cells

- **Non- Megaloblastic anemia**

- There are many non-megaloblastic causes of macrocytic anemia. The mechanism for formation of large red cells in each of these conditions is unclear , increased deposition of lipids on erythrocyte membrane , the time of maturation in the marrow may be synaptic.
- There are some external causes that also contribute such as **alcohol**, some **toxic drugs**, **smoking** and others.

- **Metabolism of B12 and folate**

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

- Then **IF** is **degraded** and B12 attaches to another transport. A protein called Transcobalamin TC, is the essential plasma protein for transferring B12 into the cells of the body, including two type first TCN1 produced from salivary gland, binds 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).

Thank You For Listening