HLS
Red Cell Disorders
Anemia-II.

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Morphological Classification of Anemia

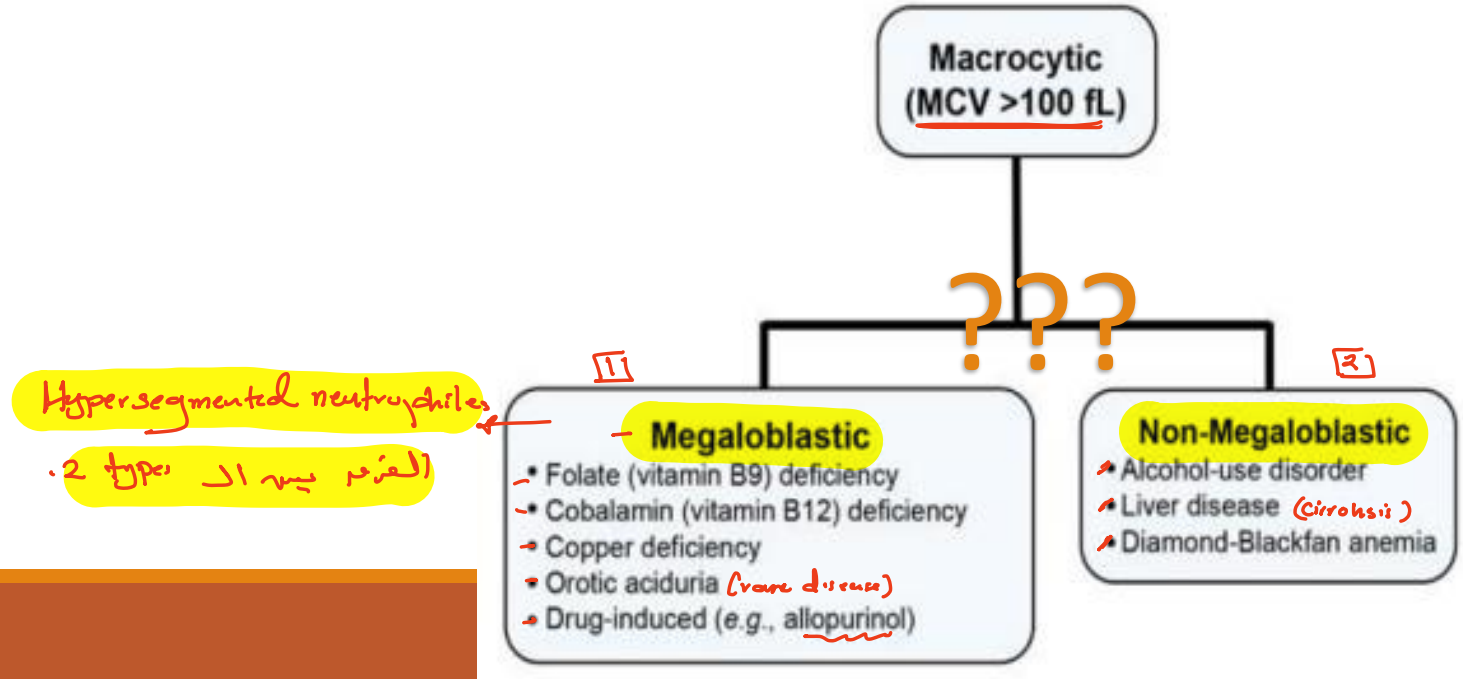
Morphological-classification-of-anemia

Morphology	Microcytic	Normocytic	Macrocytic
MCV (fL)	<80	80 - 100	>100
Disorders	**T**halassemia **A**nemia of chronic disease **I**ron deficiency anemia **L**ead poisoning **S**ideroblastic anemia	**H**emolytic anemia **A**nemia of chronic disease **R**enal disease **A**cute blood loss **B**one marrow failure **A**plastic anemia	**M**egaloblastic anemia **A**lcoholism **L**iver disease **M**yelodysplasia

III. Macrocytic anemia

- Macrocytic anemia is a term used to describe erythrocytes that are larger than normal, typically mean cell volume (MCV) greater than 100 fL.

- The most common cause of macrocytic anemia is megaloblastic anemia.



Megaloblastic anemia

- Megaloblastic anemia describes a heterogeneous group of disorders that share common morphologic characteristics: large cells with an arrest in nuclear maturation

- These abnormalities are due to impaired DNA synthesis and, to a lesser extent, RNA and protein synthesis

- Megaloblastic changes are most apparent in rapidly dividing cells such as blood cells and gastrointestinal cells

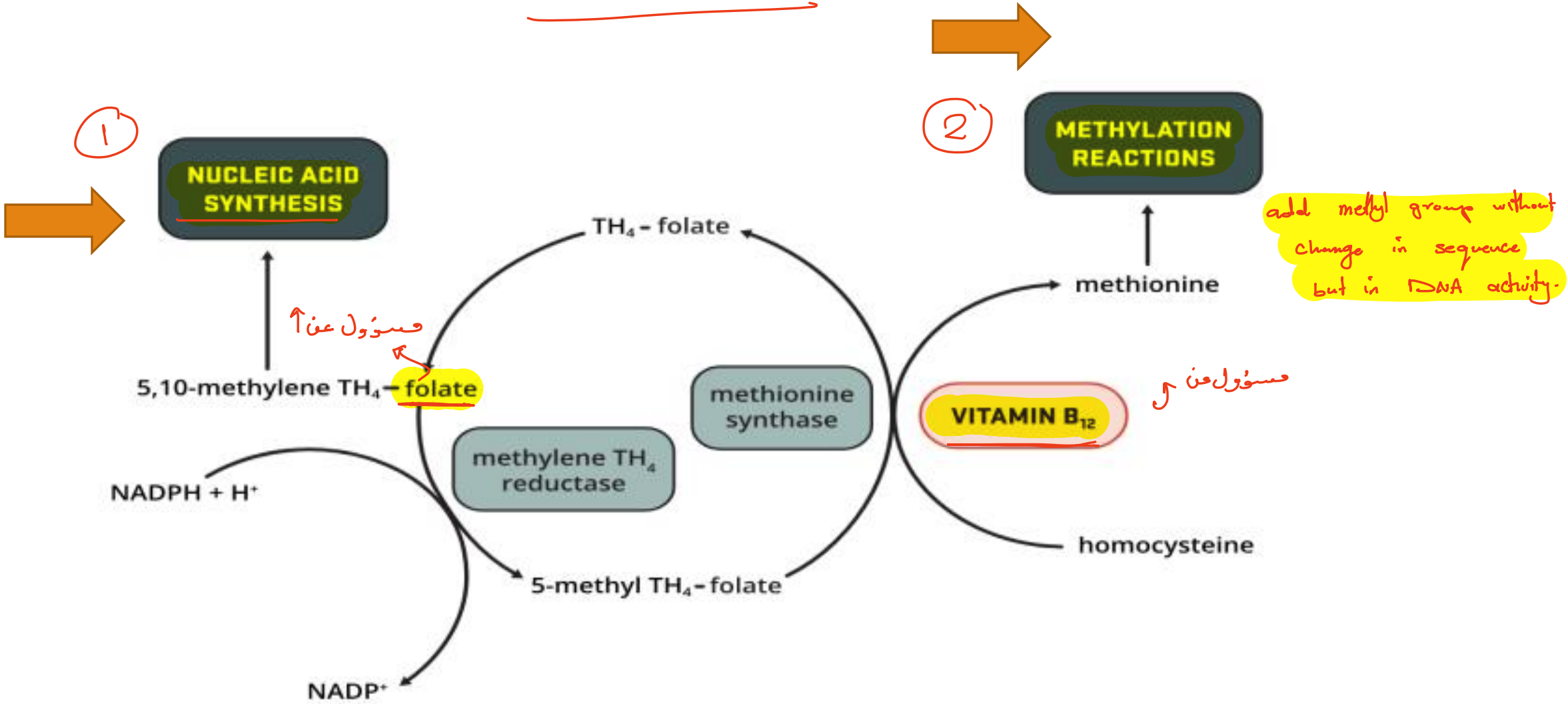
- The most common causes of megaloblastosis are:

- vitamin B12 and folate deficiencies.
- Medications.
- Direct interference of DNA synthesis by HIV infections.

- since nuclear maturation is arrested ……Unbalanced cell growth and impaired cell division occur and leading to:

- Many red cell progenitors are undergo apoptosis in the marrow (intramedullary hemolysis).
- Granulocyte and platelet precursors also are affected, most patients present with pancytopenia (anemia, thrombocytopenia, and granulocytopenia).

2 Process


1
NUCLEIC ACID SYNTHESIS
2
METHYLATION REACTIONS
add methyl groups without change in sequence but in DNA activity.
TH_4 - folate
methionine
مسؤول عن
5,10-methylene TH_4 - folate
methionine synthase
VITAMIN B_{12}
مسؤول عن
methylene TH_4 reductase
NADPH + H^+
homocysteine
5-methyl TH_4 - folate
$NADP^+$

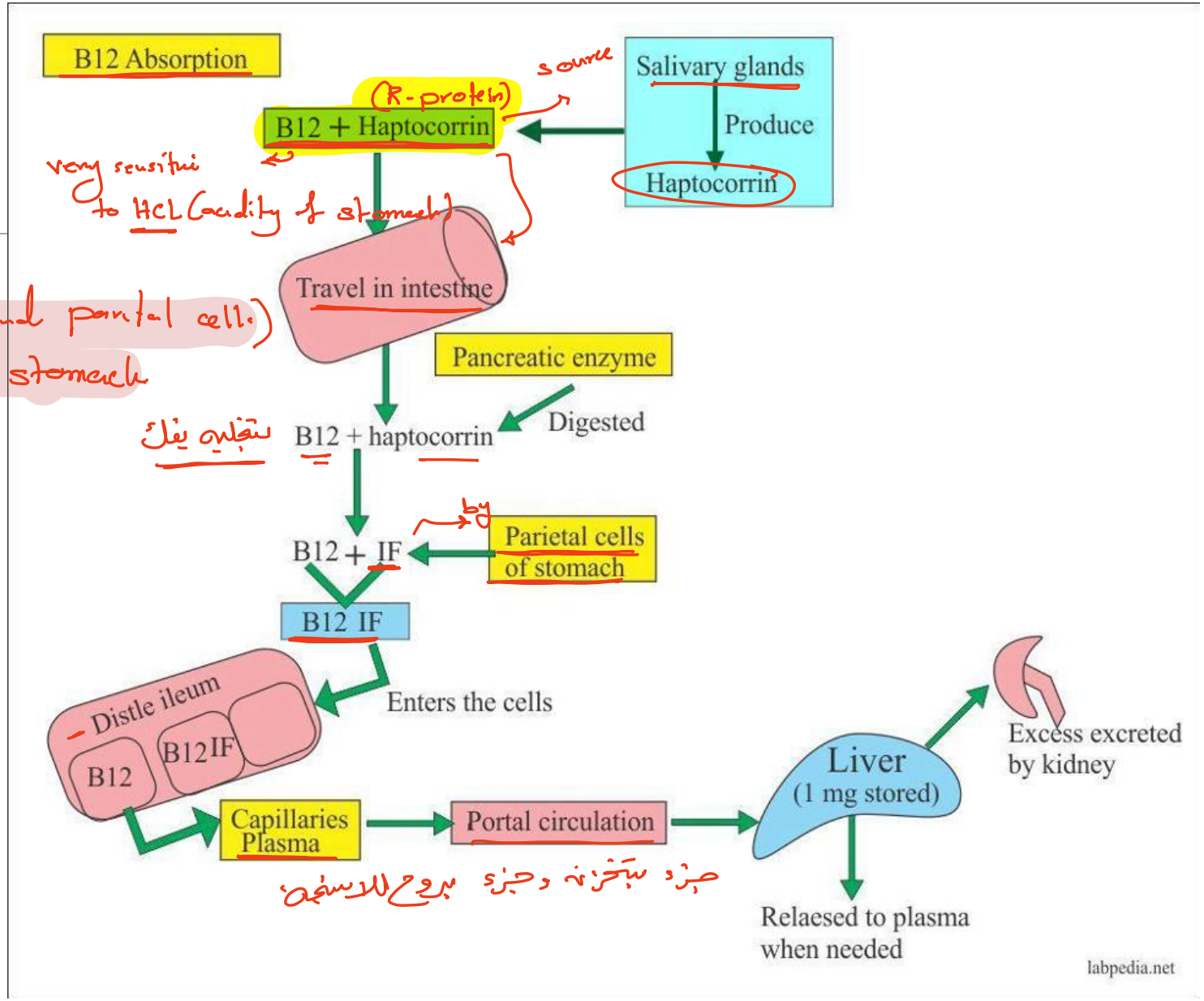
Vitamin B12 (Cobalamin) Deficiency Anemia

* The primary sources of cobalamin (Clb), a cobalt-containing vitamin, are meat, fish, and dairy products and not vegetables and fruit.

- It is stored in the liver, which normally contains reserves sufficient for 5-20 years→ clinical presentations typically follow years of unrecognized malabsorption.

- vitamin B12 has to be protected during its passage through the gastrointestinal tract to the distal ileum, the site of B12 absorption, by binding to intrinsic factor (IF)(used to stabilize cobalamin and transport it to the terminal ileum.

- pernicious anemia*.
- Gastrectomy.
- ileal resection.
- distal ileum disorders (Crohn disease).
- pancreatic insufficiency.



Folate (Folic Acid) Deficiency Anemia

- Result of inadequate dietary intake, sometimes complicated by increased metabolic demands.

- The risk is increased with:

1. poor diet (poverty & the elderly).
2. increased metabolic needs (pregnant women and patients with chronic hemolytic anemias).
3. Malabsorption or defect in metabolism, e.g:

1- Absorption is inhibited by beans & legumes. بقوليات

2- Drugs: phenytoin or methotrexate.

3- Malabsorptive disorders . (القمح, حساسية)

Morphology of megaloblastic anemia

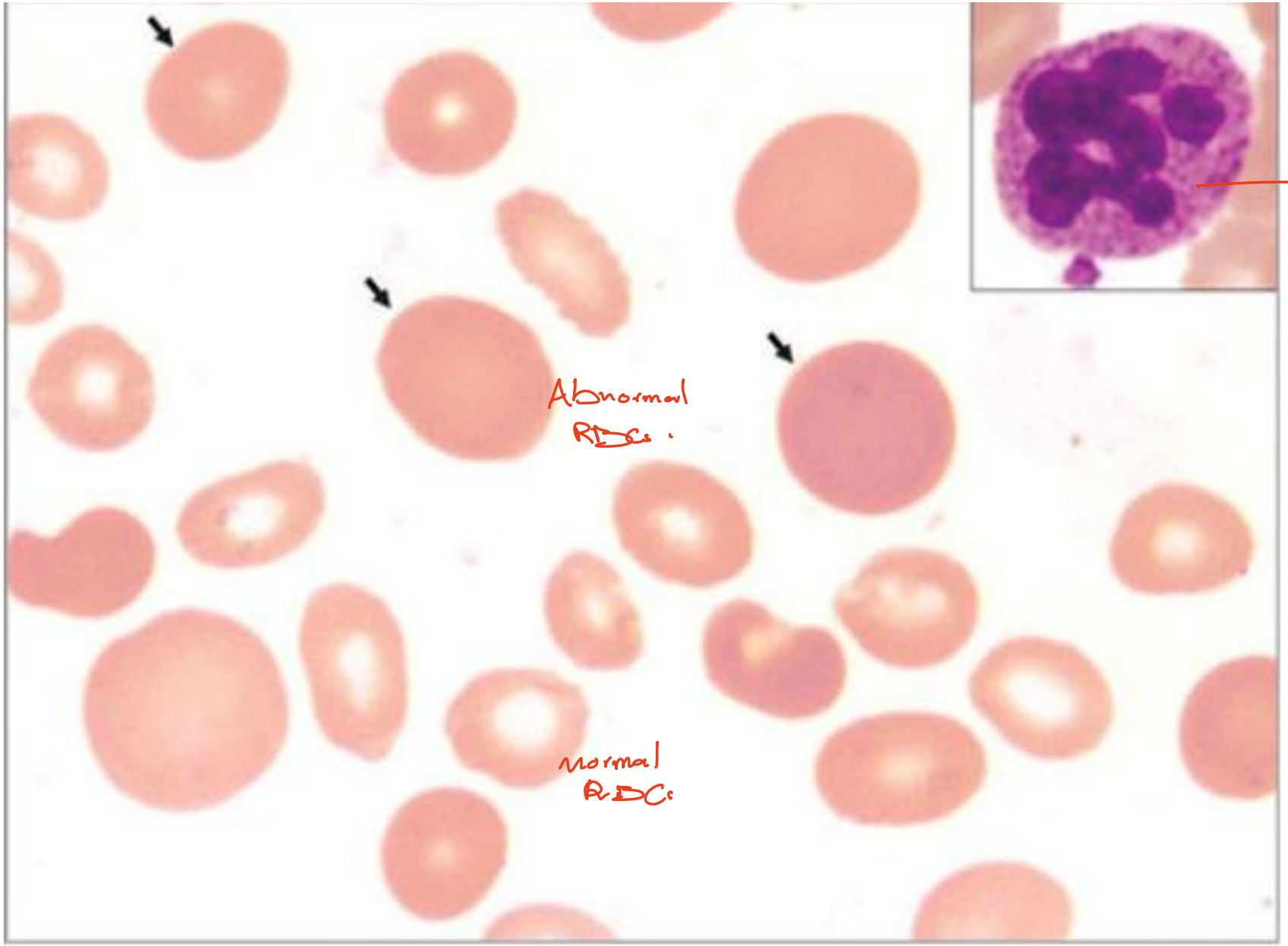
Bone marrow (BM): hypercellular with numerous megaloblastic erythroid & granulocytic progenitors

- Megaloblasts: larger than normal progenitors with delicate, finely reticulated nuclear chromatin (indicative of nuclear immaturity).

peripheral blood (PB):

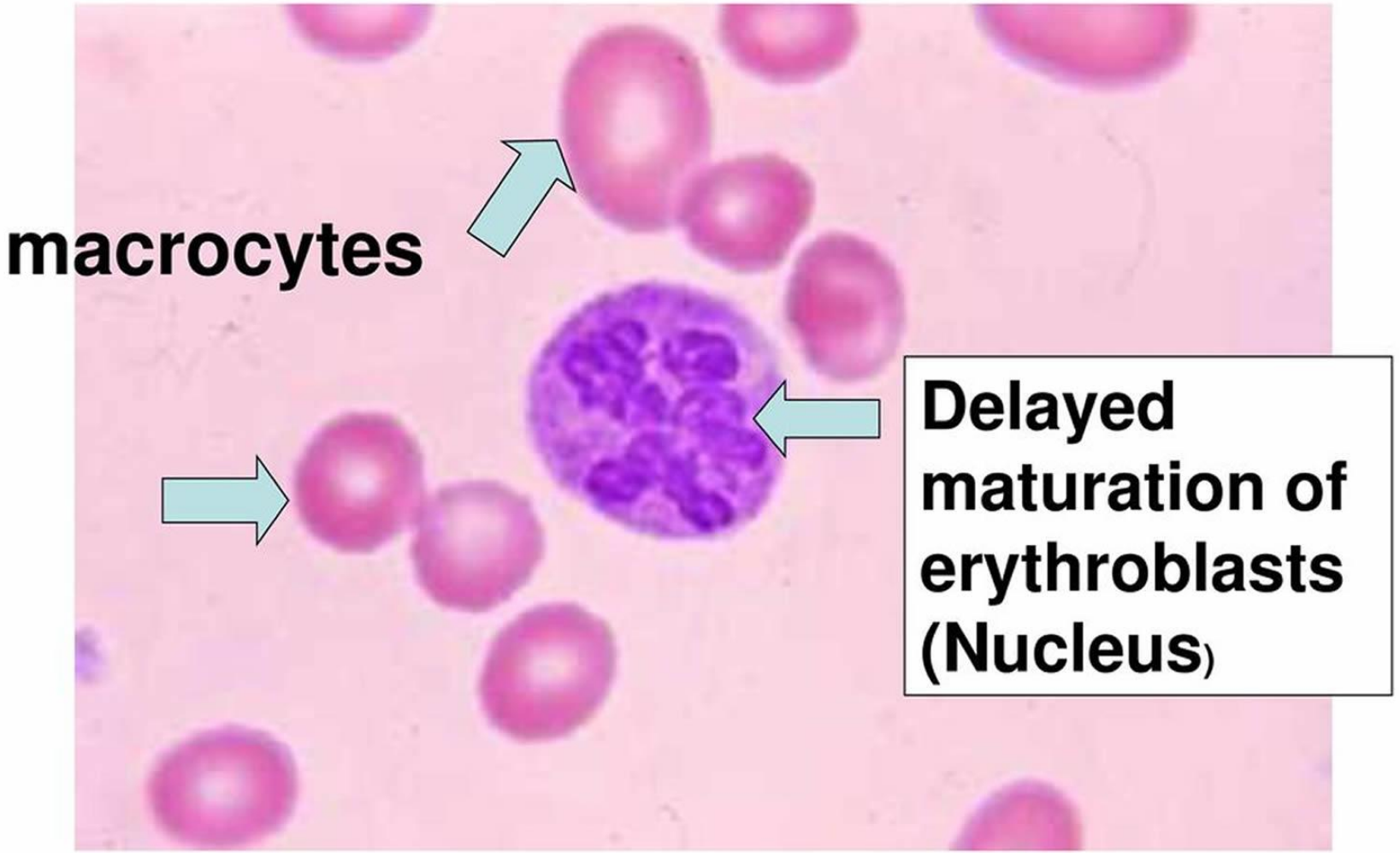
hypersegmented neutrophils (>=5) → which appear before the onset of anemia.

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



. 1.3: Peripheral blood smear showing macro-ovalocytes (arrows) and hypersegmented neutrophil (inset)

Megaloblastic Anemia



Clinical manifestation of megaloblastic anemia

- Patient with megaloblastic anemia may exhibit manifestations of:

*anemia: loss of appetite, weight loss, nausea, and constipation..

*neurological abnormalities: change in personality, psychosis and peripheral neuropathy.

- Why???

B12 deficiency lead to demyelination of the posterior & lateral columns of the spinal cord.

- Clinically:

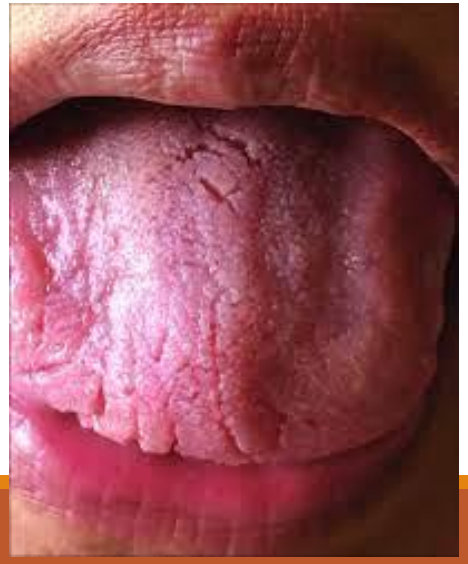
* symmetric numbness, tingling, & burning in the feet or hands, followed by unsteadiness of gait and loss of position sense, particularly in the toes.

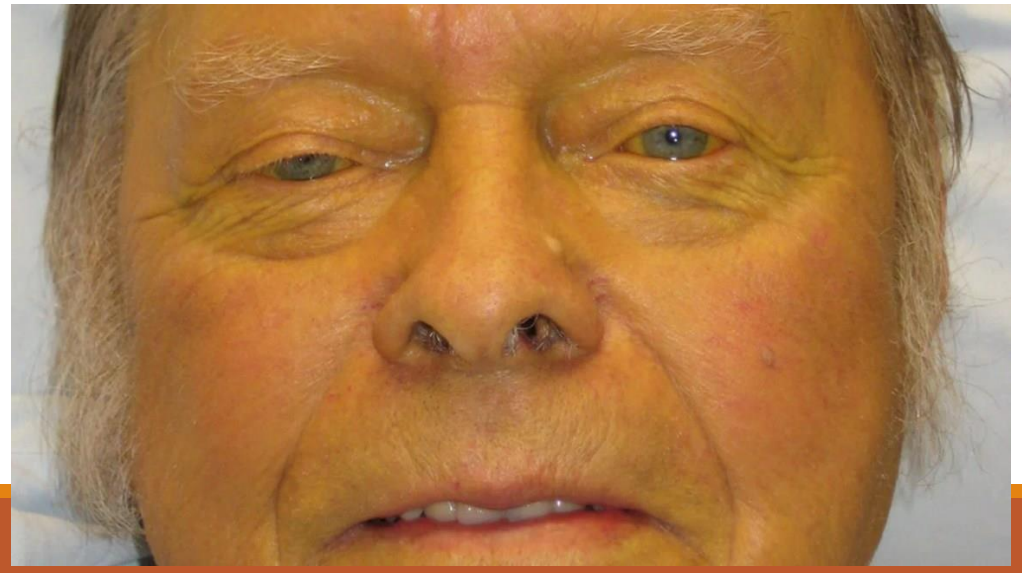
Physical findings

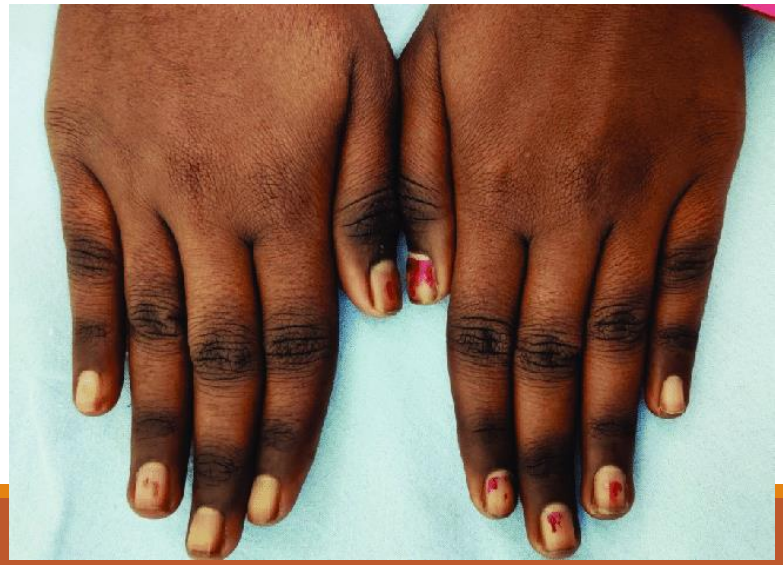
* Glossitis, characterized by a smooth tongue due to loss of papillae, occurs in persons with cobalamin deficiency.

* Patients may have a lemon-yellow hue due increased indirect bilirubin level (intramedullary hemolysis).

* hyperpigmentation of the skin (increased melanin synthesis).







LABORATORY FINDINGS OF MEGALOBLASTIC ANEMIA

low Hb, then → MCV (> 100 fl)

- Complete blood count (CBC)
- Red blood cell (RBC) indices
- Peripheral blood smear. → آخر خطوة
- Serum cobalamin
- Serum folate

Treatment

- Supplementation of B12 and folate.
- When malabsorption is a cause, parenteral supplementation is needed
- Treat the underlying cause

Non-megaloblastic anemia

- Non-megaloblastic anemia, in the absence of hypersegmented neutrophils, occurs in a variety of settings like :

- alcohol consumption (RBC toxicity).
- hereditary spherocytosis (impaired volume regulation increases red cell size).
- hypothyroidism and liver disease (due to lipid deposition in the cell membrane).
- marked reticulocytosis from states of excess RBC consumption such as hemolysis or turnover in pregnancy or primary bone marrow disease (reticulocytes are larger than the average RBCs).