SAWA UNIVERSITY

امراض الدم الكورس الأول

Macrocytosis and megaloblastic anemia

جامعـــــــة ســـــــــاوة الاهلية — Sawa University

كليـــــة التقنيـــات الصحيـة والطبيـة — College of health and medical techniques

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....المرحلـــــــــــــة .....الثالثة — . ..... Third ..... Stage

محاضرة رقم7

Lecture No. 7

الجانب النظري

Theoretical

تدريسي المادة : د وضاح علي حسين

Megaloblastic anemia

- The megaloblastic anemias are a group of disorders characterized by the presence of distinctive morphological appearances of the developing red .cells in the bone marrow
- The erythroblasts in the bone marrow show a characteristic abnormality

maturation of the nucleus being delayed relative to that of the) .(cytoplasm

This A synchrocy is due to defect in DNA synthesis

Causes of megaloblastic anemia

Cobalamin (Vitamin B12) deficiency or .1
.abnormalities of metabolism

.Folate deficiency or abnormalities of metabolism .2

Other defects of DNA synthesis (Ex: alcohol, .3
.therapy with drugs interfering with DNA synthesis)

Biochemical basis of megaloblastic anemia

- The common feature of all megaloblastic anemias is a defect in DNA synthesis that affects rapidly .dividing cells in the bone marrow and other tissues
- All conditions that give rise to megaloblastic changes share in common a reduced rate of synthesis or polymerization of the immediate precursors of DNA

In deficiencies of either folate or cobalamin there is a failure to convert deoxyuridine monophosphate (dUMP) to .deoxythymidine monophosphate (dTMP)

The coenzyme 5,10-methylene tetrahydrofolate polyglutamate is needed for this reaction and the availability .of this co-enzyme is reduced in either deficiency

This reflect the Cobalamin–folate relationship, that explains • the abnormalities of folate metabolism that occur in cobalamin deficiency and also why the anemia that occurs in .cobalamin deficiency will respond to folic acid in large doses

Clinical features of megaloblastic anemia

- The onset is usually insidious with gradually progressive symptoms and signs of anemia.
- Many asymptomatic patients are diagnosed when a blood count that has been performed for another reason reveals macrocytosis.
- The patient may be mildly jaundiced because of the excess breakdown of hemoglobin resulting from increased ineffective erythropoiesis in the bone marrow
- The serum unconjugated bilirubin and lactate) (dehydrogenase –LDH- are raised

Laboratory diagnosis of megaloblastic anemia

- **Anemia may be severe, mild or even absent, but the blood film and bone marrow appearances are always abnormal.**

Peripheral blood:

- **The anemia is macrocytic (MCV >100 fL) and the macrocytes are typically oval. If iron deficiency is also present the MCV may be normal.**
- **A proportion of the neutrophils show hypersegmented nuclei (more than five nuclear lobes).**
- **High unconjugated bilirubin**
- **High LDH**
- Reticulocyte count is low for degree of anemia.
- Total white cell and platelet counts may be moderately reduced, especially in severely anemic patients.

:Bone marrow

- .Bone marrow is usually hypercellular
- The most characteristic finding is dissociation between nuclear and cytoplasmic development in the erythroblasts, with the nucleus maintaining a primitive appearance (open, fine, lacy appearance) despite maturation and hemoglobinization of the cytoplasm. the cells are larger than normoblasts
- Giant and abnormally shaped metamyelocytes are characteristic

CAUSES OF VITAMIN B12 DEFICIENCY

.Dietary deficiency: only vegans .1

... Gastric factors : hypoclorhydria, gastrectomy. 2

: Pernicious anemia .3

this is an autoimmune disorder with loss of parietal cells causing .intrinsic factor deficiency

Anti-parietal cell a.b are present in over 90% of cases A positive result supports the diagnosis

Antibodies to intinsic factor are found in the serum of 60% of patients . .and are diagnostic

. Small bowel factors: pancreatic insufficiency .4

Infestation with the fish tapeworm .5

Inflammatory disease of the terminal ilium such as Crohn's disease or .6 .ileal resection can result in vit. B12 deficiency

-

Folic acid deficiency

.Most foods contain some folate

The highest concentrations are found in liver and yeast, spinach, other .greens and nuts

. The total folate content of an average diet is about 200-250 µg daily •

Daily requirements are about 100 µg

The stores about 10 µg are only sufficient for about 4 months . Largest store in the liver

Folate is easily destroyed by heating, particularly in large volumes of • water; over 90% may be lost

Stores are sufficient for about 4 months

Causes of folate deficiency

.Dietary deficiency

.Alcohol drinking

.Malabsorption : Gluten enteropathy

.Drugs as salazopyrine

-:Increased requirements

-pregnancy and lactation

-infancy

-chronic hemolysis

-malignancy

Hemodialysis

.Antifolate drugs: antiepileptic, alcohol, methotrexate

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:Absorption and transport

- The principal site of folate absorption is the upper ,small intestine
- .On average, about 50% of food folates is absorbed
- Folate is transported in plasma; about one-third is loosely bound to albumin and two-thirds is unbound

DIGESTION, ABSORPTION, TRANSPORT,AND STORAGE

- Before the polyglutamate forms of folate in foods can be absorbed, they must be hydrolyzed to the monoglutamate form.
- This hydrolysis or deconjugation is performed by at least two hydrolases or conjugases.

The conjugases found in human jejunal mucosa, pancreatic juice and bile

Once absorbed through the duodenum and jejunum , reduced and

.methylated to form MTHF

Transport and Storage

- Free in plasma: monoglyutamate derivatives, mainly THF.
- Uptake by the liver using carrier and converted to 5-methyl THF and 10- formyl-THF .
- Most of 5-methyl THF and 10-formyl THF is excreted into the bile.
- The liver stores about one-half of the body's folate. And polyglutamate form.

Transport and storage

- Blood:
- Folate is found as monoglutamate
- 2/3 bound to protein albumin,
- 1/3 free

- RBC- folate level is index of longer-term (2-3mo) folate status than dose plasma.

Function

Synthesis of DNA from its precursors (‘thymidine’ and **.1** ‘purines’)

Folate coenzymes are required for the **metabolism .2 of** several important **amino acids**, such as the synthesis of . .methionine from homocysteine

3. Prevents serious birth defects in the fetus and new-born such as neural tube defect

4. Red blood cells Megaloblastic Anemia.

5. Folic acid improving mental and emotional health.

.

Folic acid for a healthy pregnancy and baby

.Folic acid ihelps neural tube to grow healthy during pregnancy

The neural tube will become early brain and spinal cord. But if the neural tube doesn’t close properly , it can cause a very serious birth and spinal cord defect called a neural tube defect (NTD)

Folate structure

- Folate is made up of three distinct parts, all must be present for vitamin activity.
- pteridine or pterin
- P-aminobenzoic acid (PABA).
- L-glutamic acid to form folate
- Although humans can synthesize all the component parts of the vitamin, they do not have the enzyme necessary for the coupling of the pterin molecule to PABA to form pteroic acid.

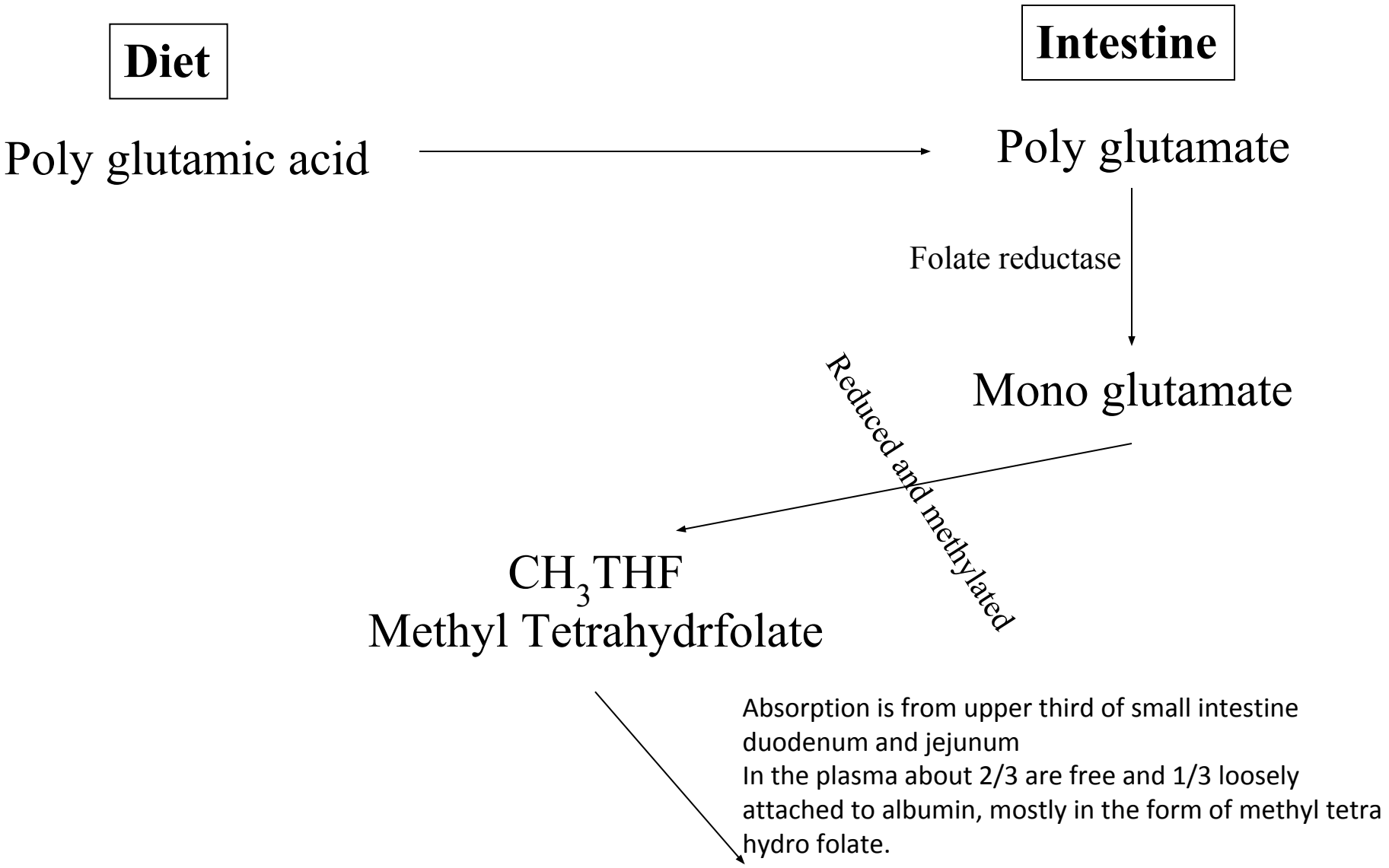
Absorption

Polyglutamates ingested in diet are converted

to monoglutamates and dihydrofolates are reduced to **tetrahydrofolates by Folate reductase**

then converted to **methyltetrahydrofolates** ,which enter the**.** .portal blood and then carried to liver

Absorption and metabolism



Clinical picture

Pallor

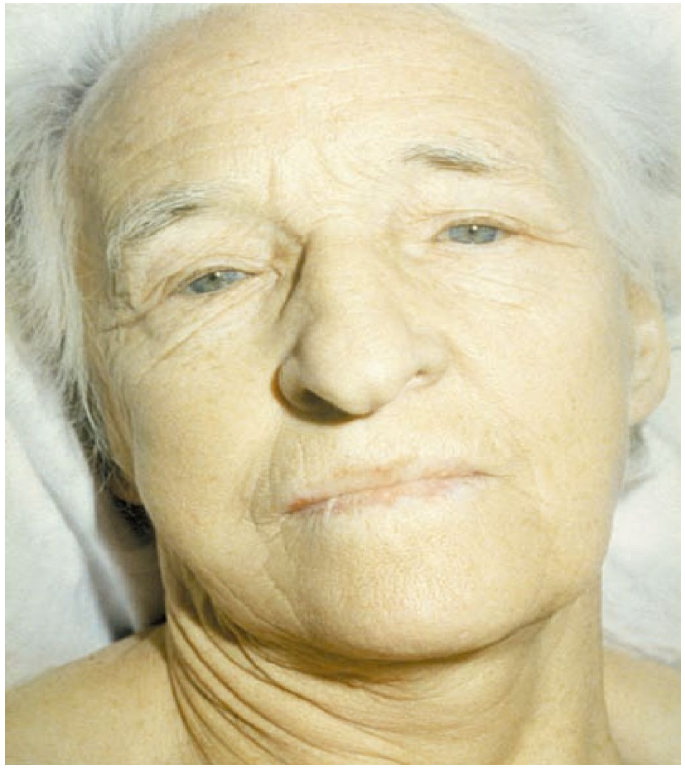
,Glossitis (a beefy-red sore tongue)

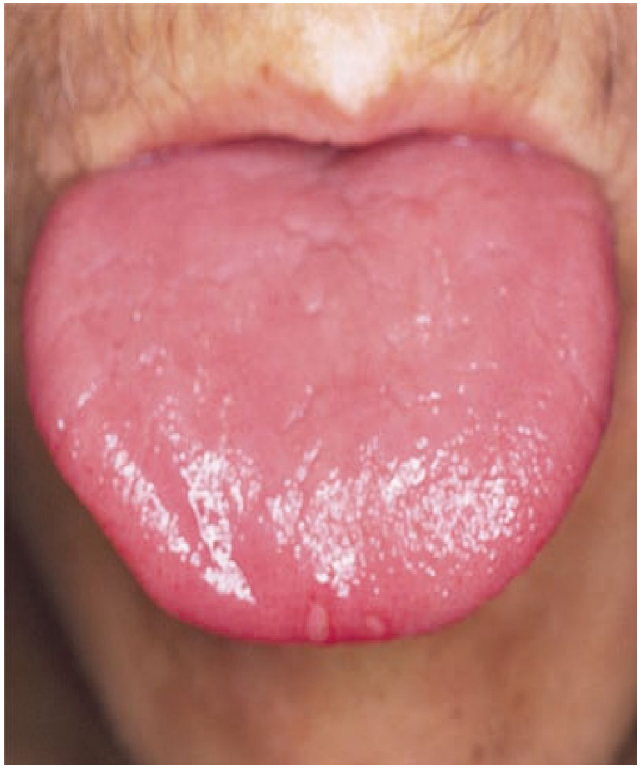
Angular stomatitis and mild symptoms of malabsorption with loss of weight may be present because of the .epithelial abnormality

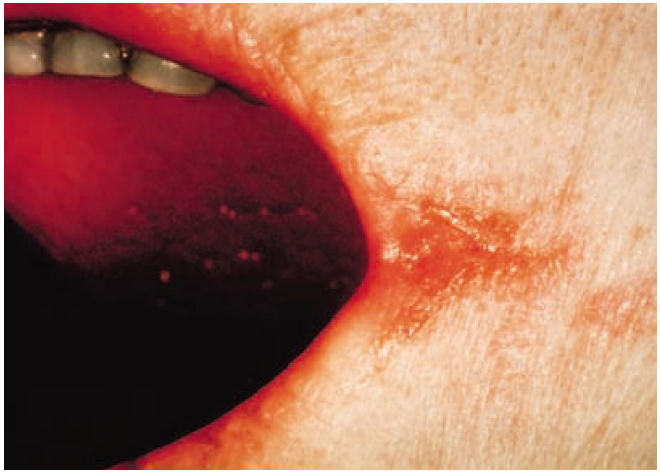
. Purpura as a result of thrombocytopenia •

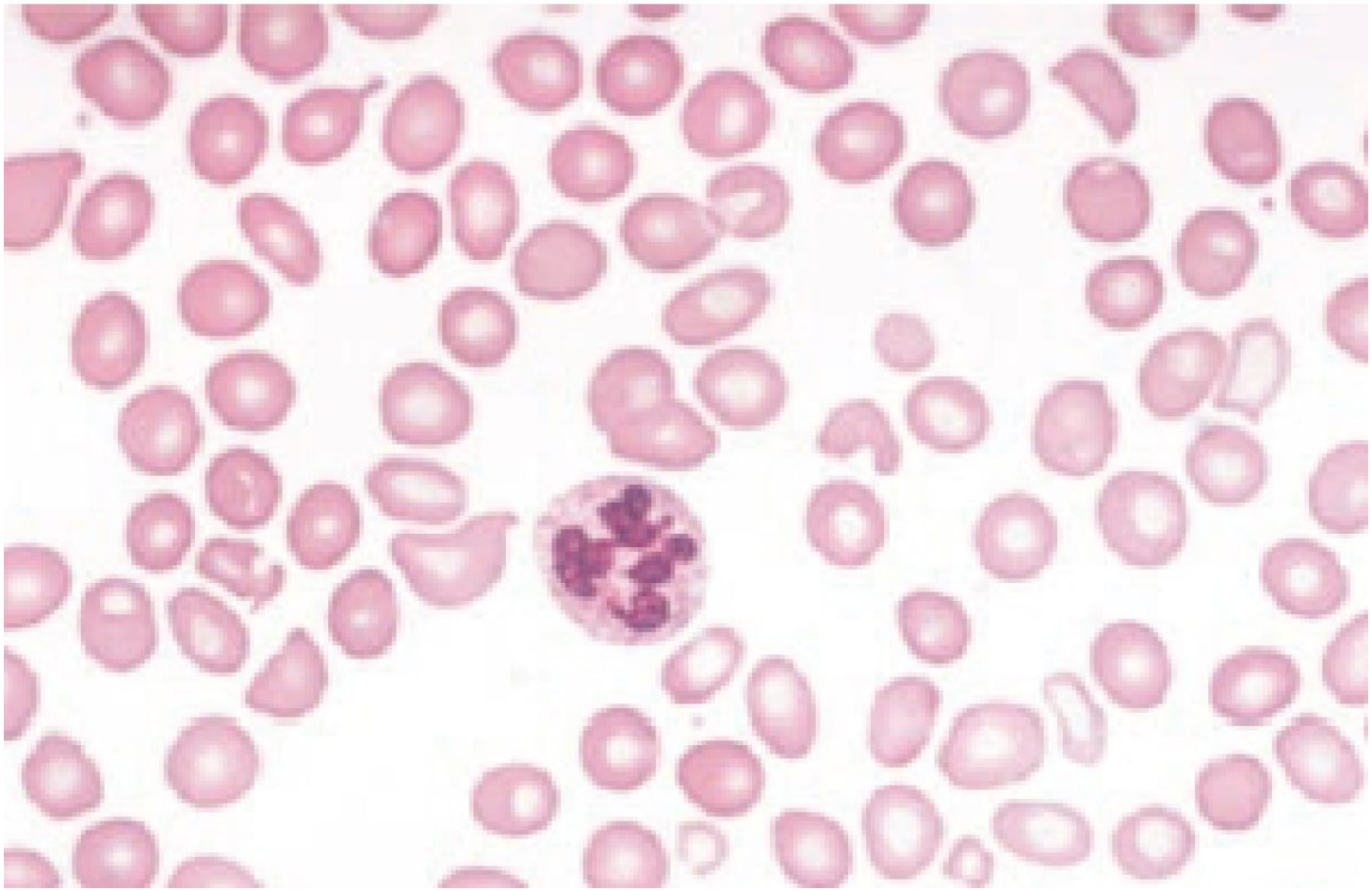
The anemia and low leukocyte count may predispose • to infections, particularly of the respiratory or urinary .tracts

Folate deficiency may cause mental changes such as • .depression and slowness



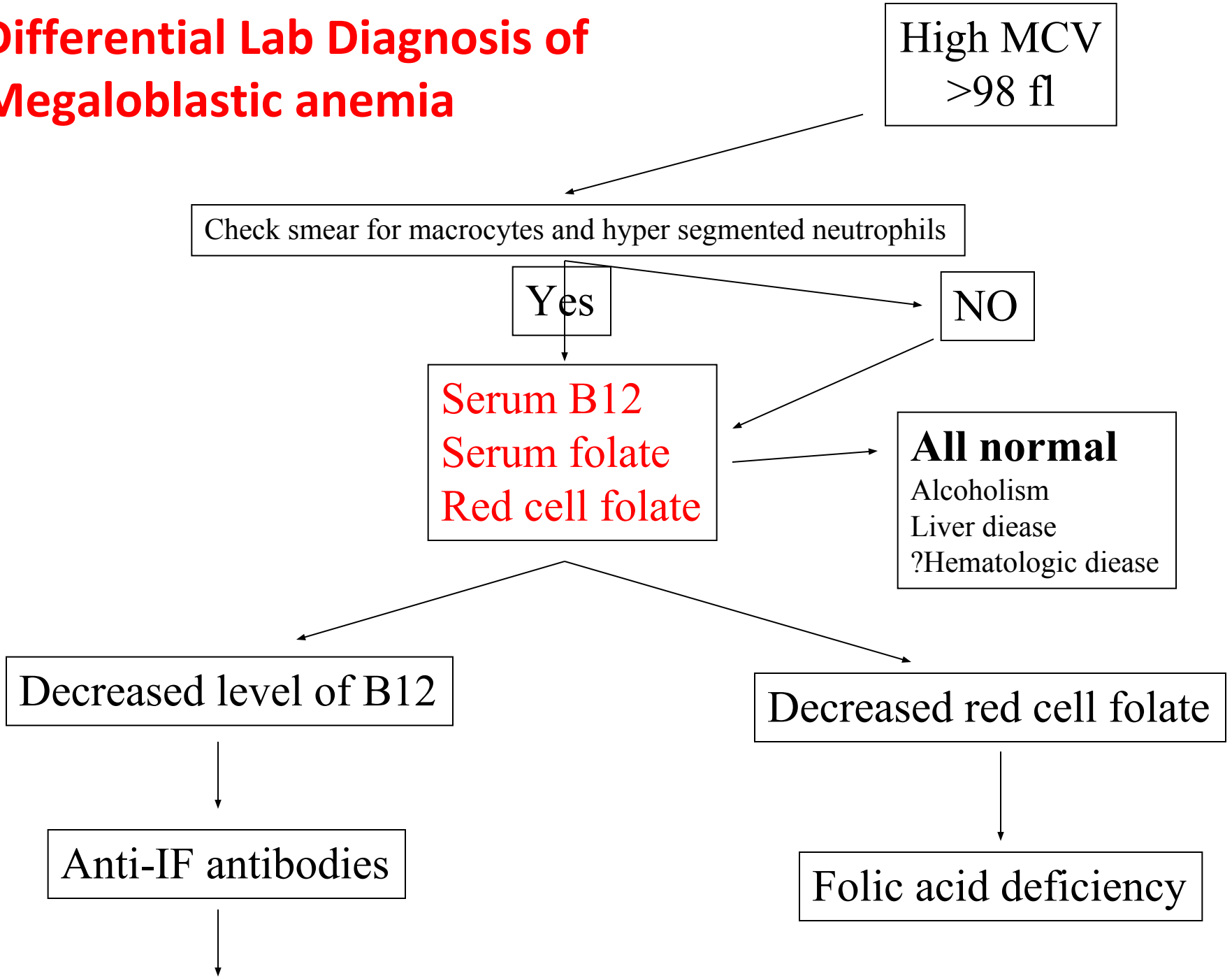






- Macrocytic anemia with typically oval macrocyte-
- Hyper segmented neutrophils

Differential Lab Diagnosis of Megaloblastic anemia



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Treatment

Folic acid 5mg tab orally

Q1

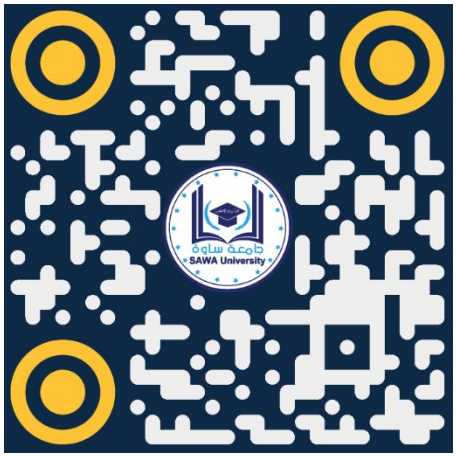
laboratory diagnosis of megaloblastic anemia

Q2

causes of megaloblastic anemia

Q3

causes of folic acid deficiency anemia



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