



محاضرة رقم 8

Lecture No. 8

الجانب النظري

Theoretical

امراض الدم الكورس الأول

pernicious anemia

Sawa University

College of health and medical techniques

Department of Medical Laboratories

..... Third Stage .

جامعة ساوة الاهلية

كلية التقنيات الصحية والطبية

قسم تقنيات المختبرات الطبية

....المرحلةالثالثة

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. due to defect in DNA synthesis.

These are caused by either vitamin B12 or folic acid deficiency, This deficiency leads to the production of cells with arrested nuclear maturation but normal cytoplasmic development:

proliferating cells will exhibit megaloblastosis; .

.Intramedullary hemolysis results in a raised bilirubin and LDH but no reticulocytosis.

.The mature red cells are large and oval.

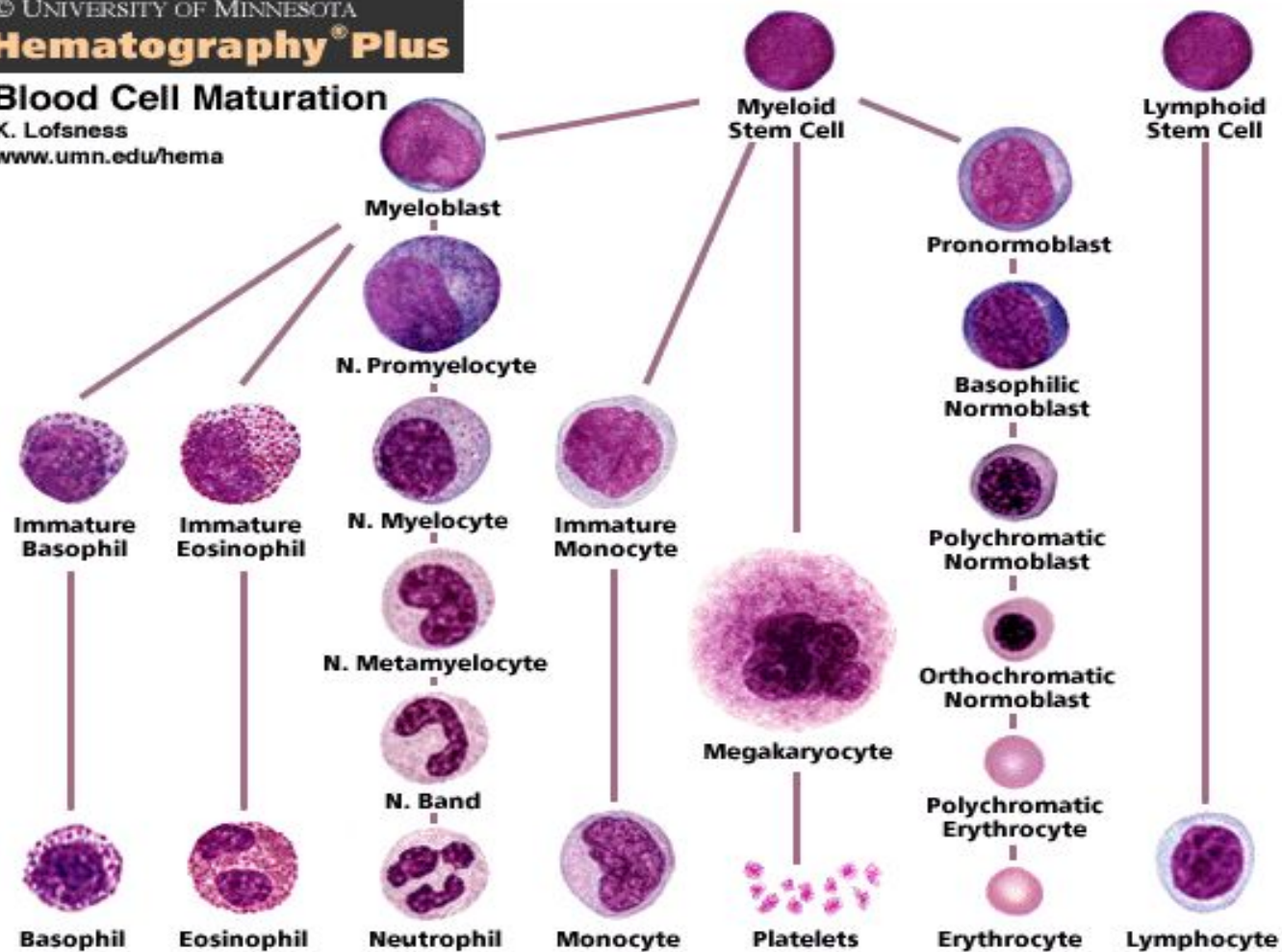
Giant metamyelocytes appear and contain a large nucleus .

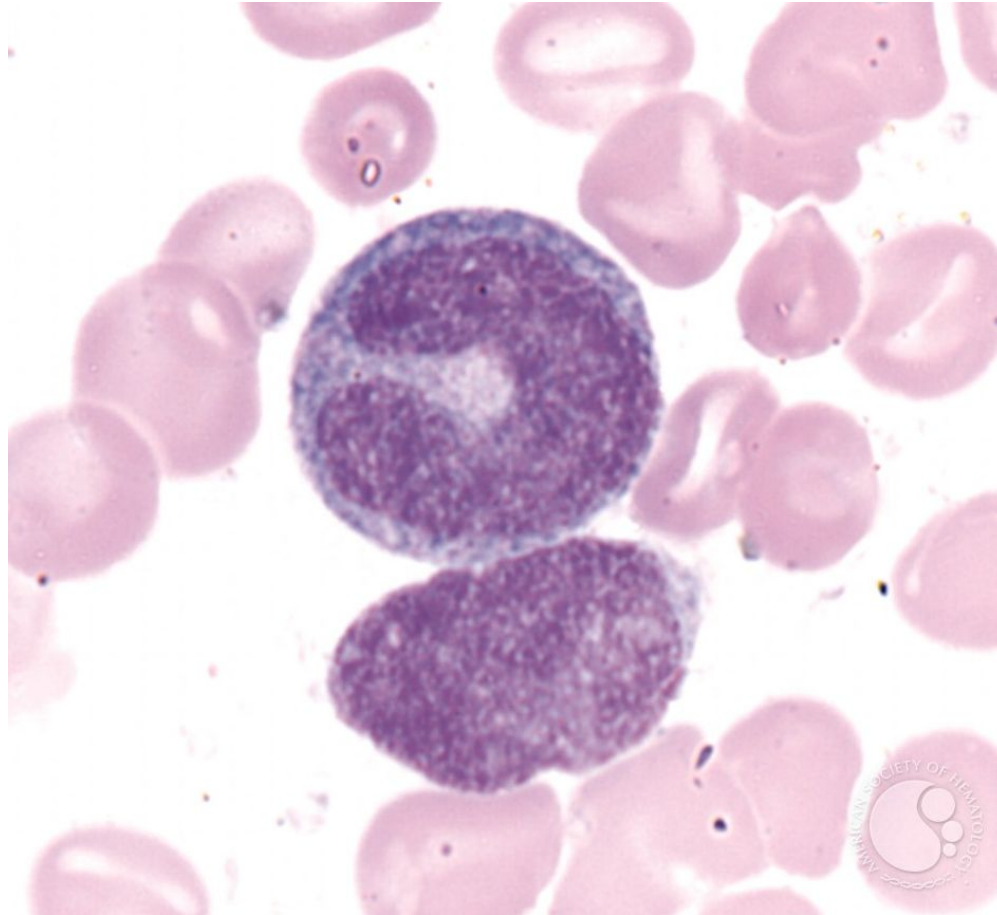
The mature neutrophils show hypersegmentation of their nuclei with some cells containig 6 or more lobes.

If severe, pancytopenia is present in the peripheral blood .

Blood Cell Maturation

K. Lofsness
www.umn.edu/hema





VITAMIN B12 ABSORPTION

The average daily diet contains 5-30ug of vit B12 mainly in meat, fish, eggs and milk.

The daily requirement of B12 is 1ug.

In the stomach, gastric enzymes release vit. B12 from food and at gastric PH it binds to a carrier protein termed R protein.

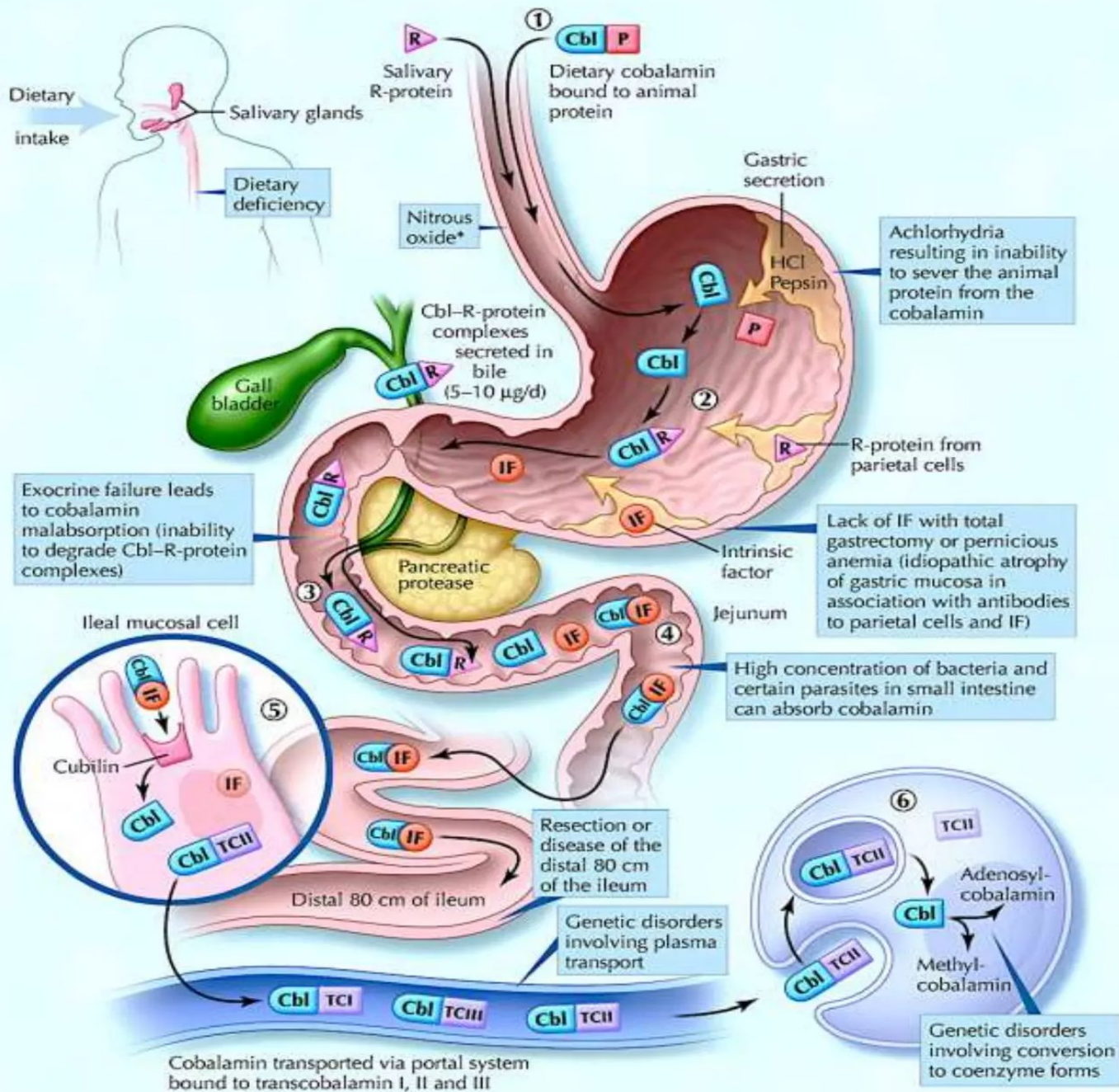
The gastric parietal cells produce acid and intrinsic factor.

Intrinsic factor is a B12-binding protein which optimally binds B12 at PH 8.

As gastric emptying occurs, pancreatic secretions raise the PH and B12 switches from R protein to intrinsic factor.

The vit. B12 intrinsic factor complex binds to specific receptors in the terminal ileum and vit. B12 is actively transported by the enterocytes to the plasma.

The liver stores enough B12 to supply the daily requirement for 3 years and t.



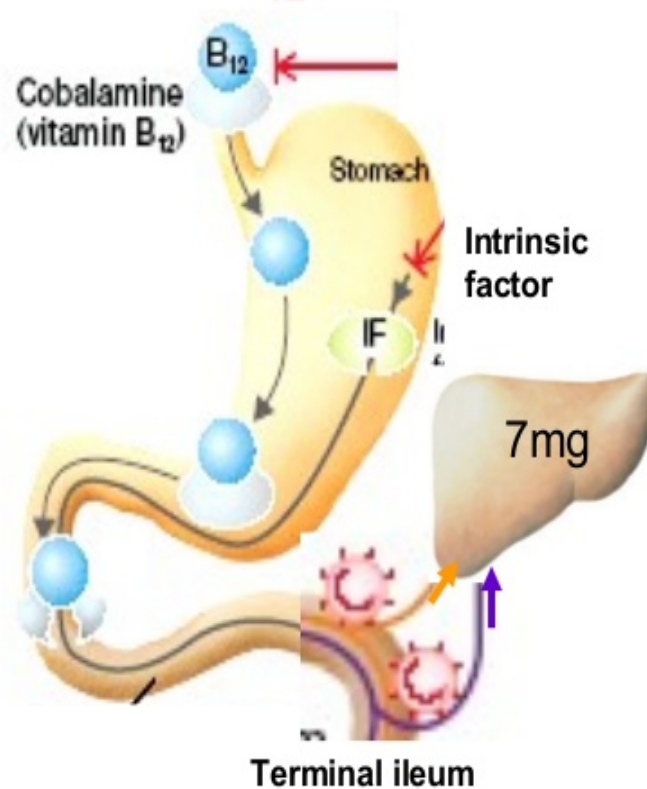
Absorption of vitamin B₁₂

Intrinsic factor is a glycoprotein of M.W. 4500.

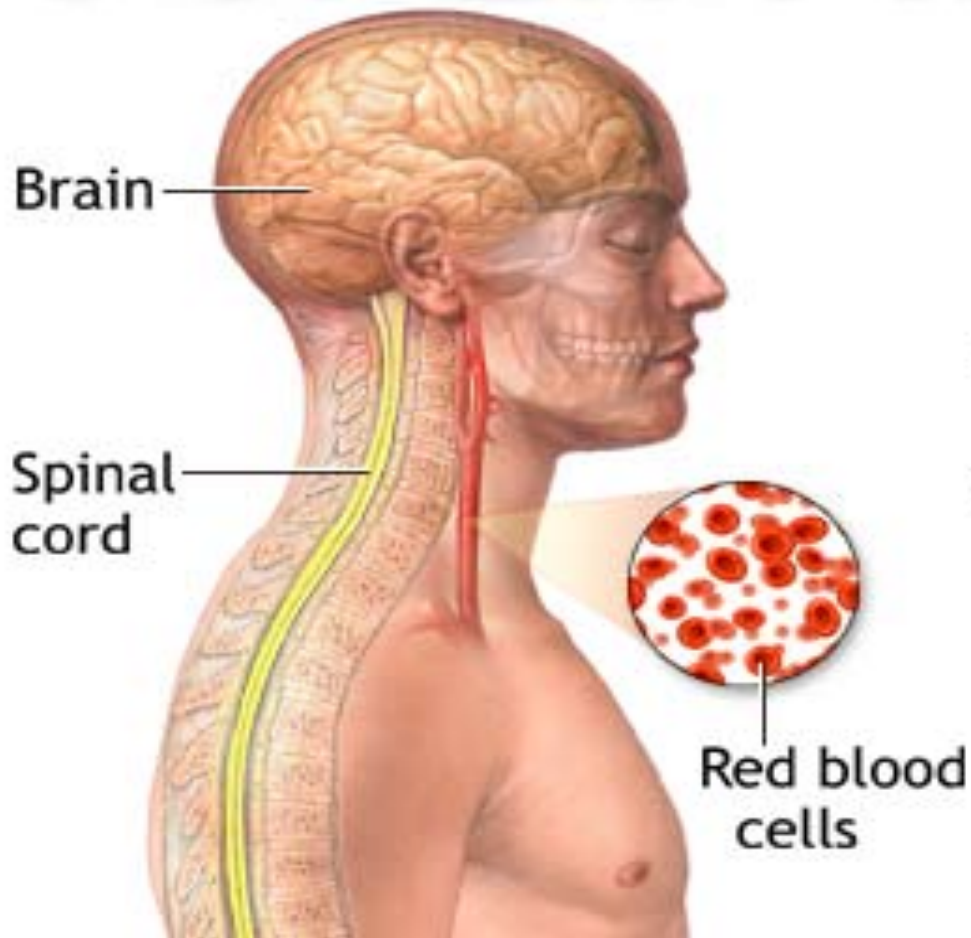
Vit. B₁₂ combine with intrinsic factor forming a complex that resist digestion by GIT enzymes.

This complex is absorbed at terminal ileum by pinocytosis.

Vit. B₁₂ is transported to the liver where it is stored.



Vitamin B₁₂



Vitamin B₁₂ is important for metabolism, the formation of red blood cells, and the maintenance of the central nervous system, which includes the brain and spinal cord

 ADAM.

CAUSES OF VITAMIN B12 DEFICIENCY

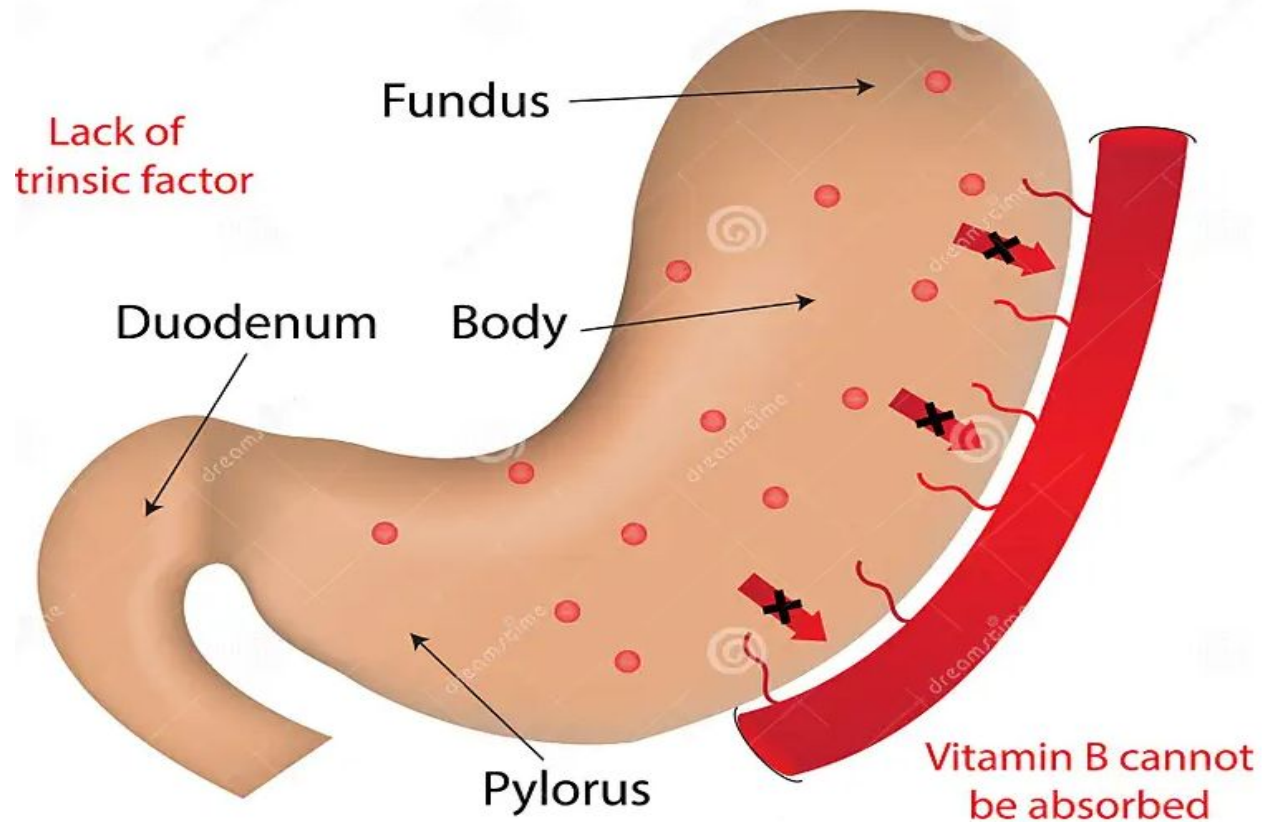
1. Dietary deficiency: only vegans.
2. Gastric factors : hypochlorhydria, gastrectomy ...
3. Pernicious anemia :
this is an autoimmune disorder with loss of parietal cells causing intrinsic factor deficiency.
Anti-parietal cell a.b are present in over 90% of cases A positive result supports
the diagnosis
- . Antibodies to intrinsic factor are found in the serum of 60% of patients and are diagnostic.
4. Small bowel factors: pancreatic insufficiency .
5. Infestation with the fish tapeworm
6. Inflammatory disease of the terminal ileum such as Crohn's disease or ileal resection can result in vit. B12 deficiency.

Pernicious anemia (PA)

- Defined as a severe lack of intrinsic factor due to gastric atrophy secondary to autoimmune attack on the gastric mucosa. .
- The ratio of incidence in men and women is 1:1.6 and the peak age of onset is 60 years.
- The disease occurs more in subjects or families with other organ-specific autoimmune diseases, in those with premature greying, blue eyes and vitiligo, and in persons of blood group A.
- There is also an increased incidence of carcinoma of the stomach in 2-3% of the patients (mainly in men).



Pernicious Anemia



Diagnosis of PA

- Intrinsic Factor antibodies (specific for PA)
- Parietal cell antibodies (non specific for PA).

It is present in the serum of 90% of adult patients with PA,

.

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)

- 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 and widespread melanin pigmentation are less frequent presenting features .
- The anemia and low leucocyte count may predispose to infections, particularly of the respiratory or urinary tracts. Cobalamin deficiency has also been associated with impaired bactericidal function of phagocytes.

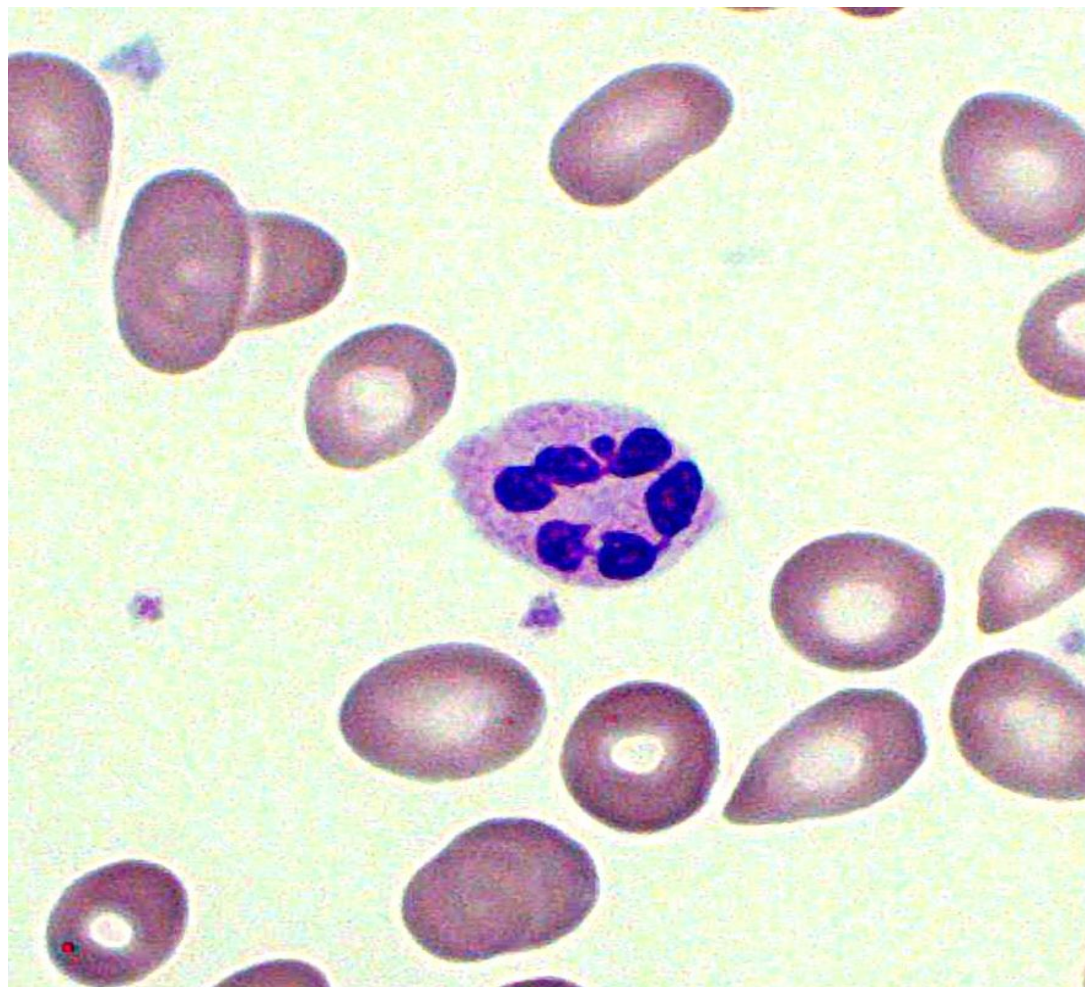
- **Neurological manifestations**

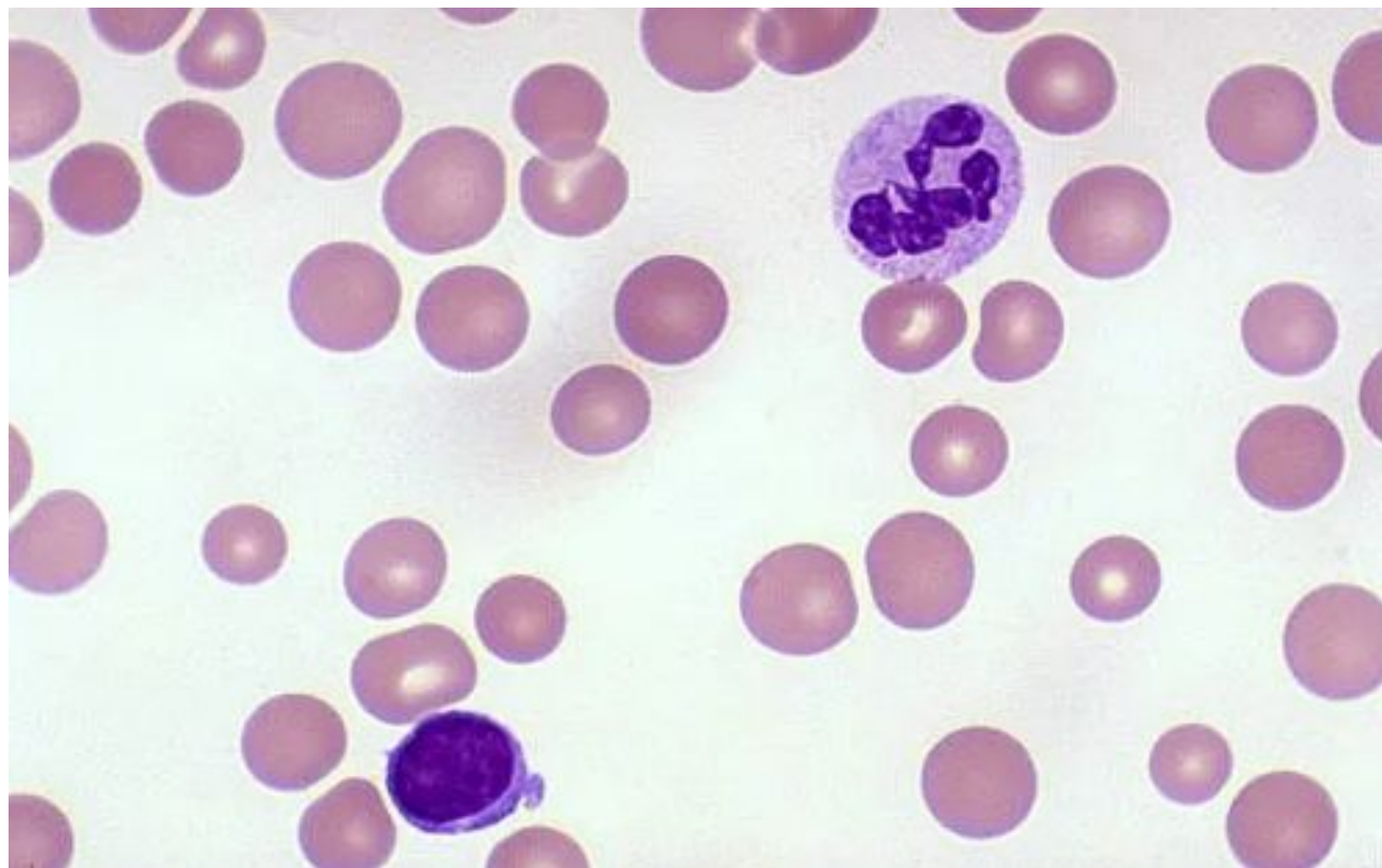
- Cobalamin deficiency may cause bilateral peripheral neuropathy or degeneration (demyelination) of the posterior and pyramidal tracts of the spinal cord and, less frequently, optic atrophy or cerebral symptoms..

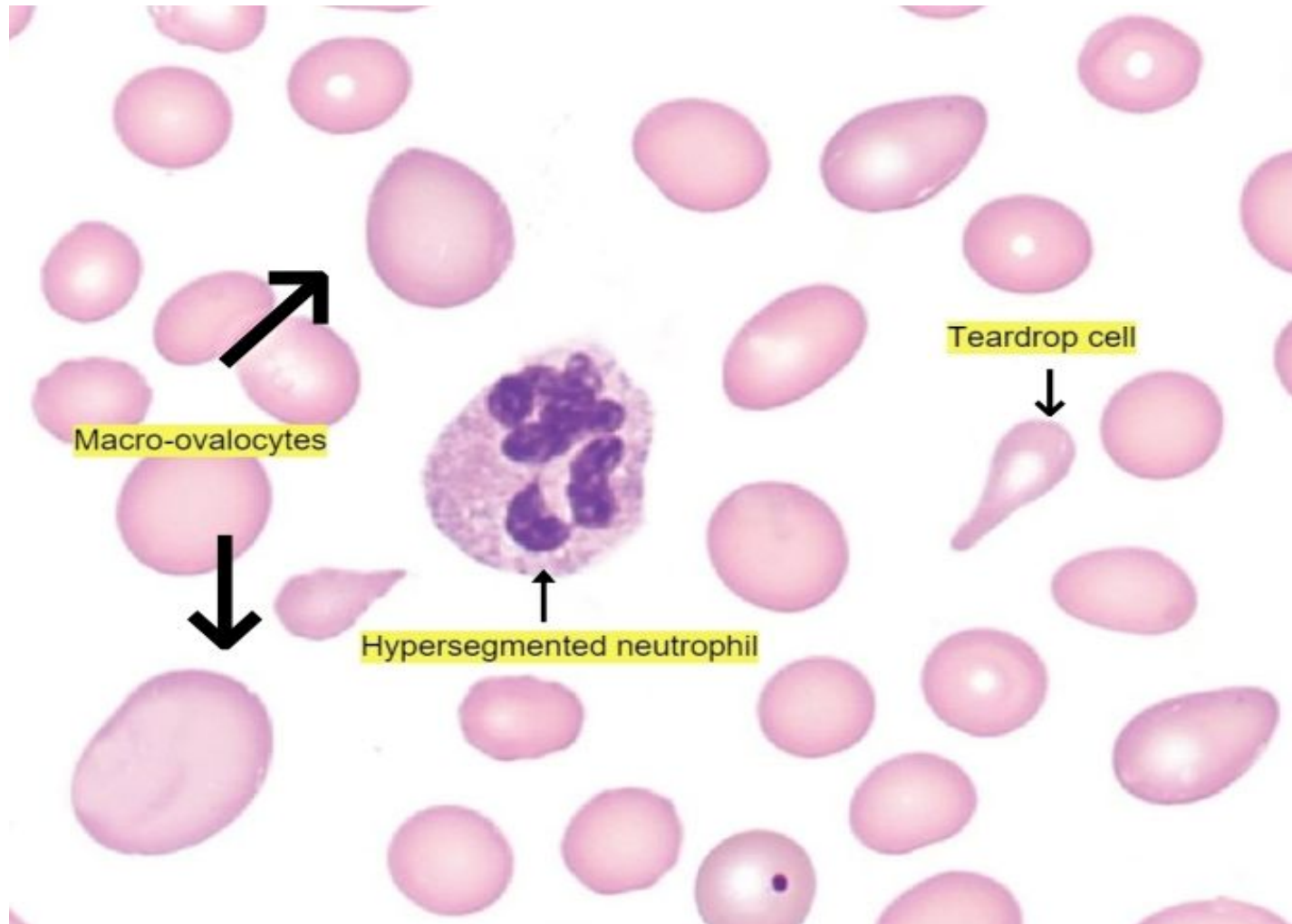
DIAGNOSTIC FEATURES

1. Hb: often reduced , may be very low.
2. MCV: usually raised, commonly above 120fl.
3. RBC count :low
4. Reticulocyte count :low for degree of anemia.
5. Leucocyte count :low or normal.
6. Platelet count : low or normal. (Thrombocytopenia)
7. Blood film: oval macrocytosis,poikilocytosis,red cell fragmentation,neutrophil hypersegmentation.
8. Bone marrow:increased cellularity,megaloblastic changes in erythroid series ,giant metamyelocytes,dysplastic megakaryocytes,increased iron in stores ,pathological non-ringed sideroblasts.
9. Plasma LDH: elevated ,often markedly.

*







Hematological findings

- Anemia may be severe, mild or even absent
blood film and bone marrow appearances are always abnormal.
- 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).
- 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.
- dissociation between nuclear and cytoplasmic development in the erythroblasts, with the nucleus maintaining a primitive appearance (open, fine, lacy appearance) despite maturation & hemoglobinization of the cytoplasm.
- Giant and abnormally shaped metamyelocytes are characteristic.

*

Q1 increased segmentation of nucleus of neutrophils more than 5 segment is a manifestation

Folate or vitamin B12 deficiency B. Iron deficiency C. Thalassemia D. Repeated blood transfusion

Q2 . Macrocytic have an MCV > than:

A. 80 fl B. 75 fl C. 90 fl D. 115 fl.

Q3 Vitamin B12 absorbed from

A) Ileum b) Liver c) Duodenum d. stomach

Q4 In pernicious anemia:

**(A) MCV less than 100 FL. (B) There is hypochromic microcytic anemia. (C). Reticulocyte count increased
(D) Decreased absorption of vitamin folic acid E. anti intrinsic factor antibody diagnostic**

Q5 . Macrocytic anemia due to decrease in

A) Iron B) Vitamin C c) B12 and . Folic acid D) G6PD enzyme deficiency

Q6 In a case of classic pernicious anemia, the patient has

A. leukopenia B. hyper segmented neutrophils C. thrombocytopenia D. all of the above

Q 7 In pernicious anemia:

**(A) The life span of R.B.C.s is longer than normal. (B) There is microcytic hyper chromic anemia.
• (C) The formation of reticulocyte is increased. (D) Decreased absorption of vitamin B12**

Q8 Macrocytic anemia due to decrease in

A) Iron B) Vitamin C c) B12 d) G6PD

*

Q9 Macrocytic anemia occurs by.....

A. folic acid deficiency. B. Vit B12 deficiency. C. Pernicious anemia. D. All of the above

Q10 Intrinsic factor essential for the absorption of :

a. Vit B 12 . b. Folate . c. Nicene . d. Vit C

Q11 Megaloblastic anemia related to folic acid deficiency is associated with

**A. abnormal absorption B. increased utilization
C. nutritional deficiency D. all of the above**

Q 12 Choose the feature that is not characteristic for B12 - deficiency anemia:

A. megaloblastic type of hematopoiesis

B. disorder of the intrinsic factor secretion C. anti-intrinsic factor antibody

D. Hyper segmented neutrophil E. Hypochromic microcytic anemia

Q13 the earliest hematological finding in megaloblastic anemia is

A. Hyper segmented neutrophils B. Decreased hemoglobin

C. Decreased hematocrit D. decrease MCV

Q 14 Pernicious anemia it is autoimmune disease against:

A- Intrinsic factor B- Parietal cell C- Chief cell D. A and B

Q 15 Blood tests in people with pernicious anemia may reveal:

A. Normocytic anemia with leukocytosis

B. B. Microcytic anemia with leukopenia C. Macrocytic anemia with leukocytosis

C. D. Microcytic anemia with leukocytosis E. Macrocytic anemia with leukopenia

*

Q 16 Laboratory diagnosis of megaloblastic anemia

- A. The anemia is macrocytic (MCV >100 fL) B . Neutrophils show hyper segmented nuclei C. Reticulocyte count is high. D. Increase thrombocyte count E. A and B**

Q17 Choose the feature that is not characteristic for B12 - deficiency anemia:

- A. Megaloblastic type of hematopoiesis. B. disorder of the intrinsic factor secretion.**
C. Anti-intrinsic factor antibody D. Hyper segmented neutrophil E. increased serum iron.

Q18 In patient with Pernicious anemia True or False:

- A. Loss of parietal cells of stomach B. Intrinsic factor deficiency**
C. Anti-parietal cell abs are present in over 90% of cases D. Antibodies to intrinsic factor diagnostic
E. Anemia is microcytic with MCV less than 80 FL F. Anemia associated with neurological symptoms

Q19 The peripheral blood smear in megaloblastic anemia shows following EXCEPT

- A. Macrocytic anemia B. Increased reticulocytes C. hyper segmented neutrophils**
D. Decreased platelets count

Q 20 A lack of which of these will result in a condition called megaloblastic anemia?

- A. Iron B. Vitamin C C. Vitamin B-12 and folic acid**
D. lead poisoning. E. hereditary spherocytosis

Q 21 The intrinsic factor is required for the absorption of:

- A. Iron B. Folic acid C. Vitamin B12. D. Zinc**

*

Q22. Which of the following is described as a "biconcave disc"

- a. Platelets b. Erythrocytes c. Leukocytes d. Monocytes

Q23 which one of the following cause folate deficiency?

- A- total gastrectomy B- veganism C- ileal resection D- long term dialysis

Q23 Blood tests in people with pernicious anemia may reveal:

- A. Normocytic anemia with leukocytosis
B. Microcytic anemia with leukopenia
C. Macrocytic anemia with leukocytosis
D. Microcytic anemia with leukocytosis (increased white blood cells)
E. Macrocytic anemia with leukopenia (decreased white blood cells)

Q24 Megaloblastic anemias can be caused by

- A. tapeworm infestation B. gastric resection C. nutritional deficiency D. all of the above

6. Blood tests in people with pernicious anemia may reveal:

- A. Normocytic anemia with leukocytosis
- B. Microcytic anemia with leukopenia
- C. Macrocytic anemia with leukocytosis
- D. Microcytic anemia with leukocytosis (increased white blood cells)
- E. Macrocytic anemia with leukopenia (decreased white blood cells)

Q18 Megaloblastic anemias can be caused by

- A. tapeworm infestation
- B. gastric resection
- C. nutritional deficiency
- D. all of the above



Scan to get the lecture