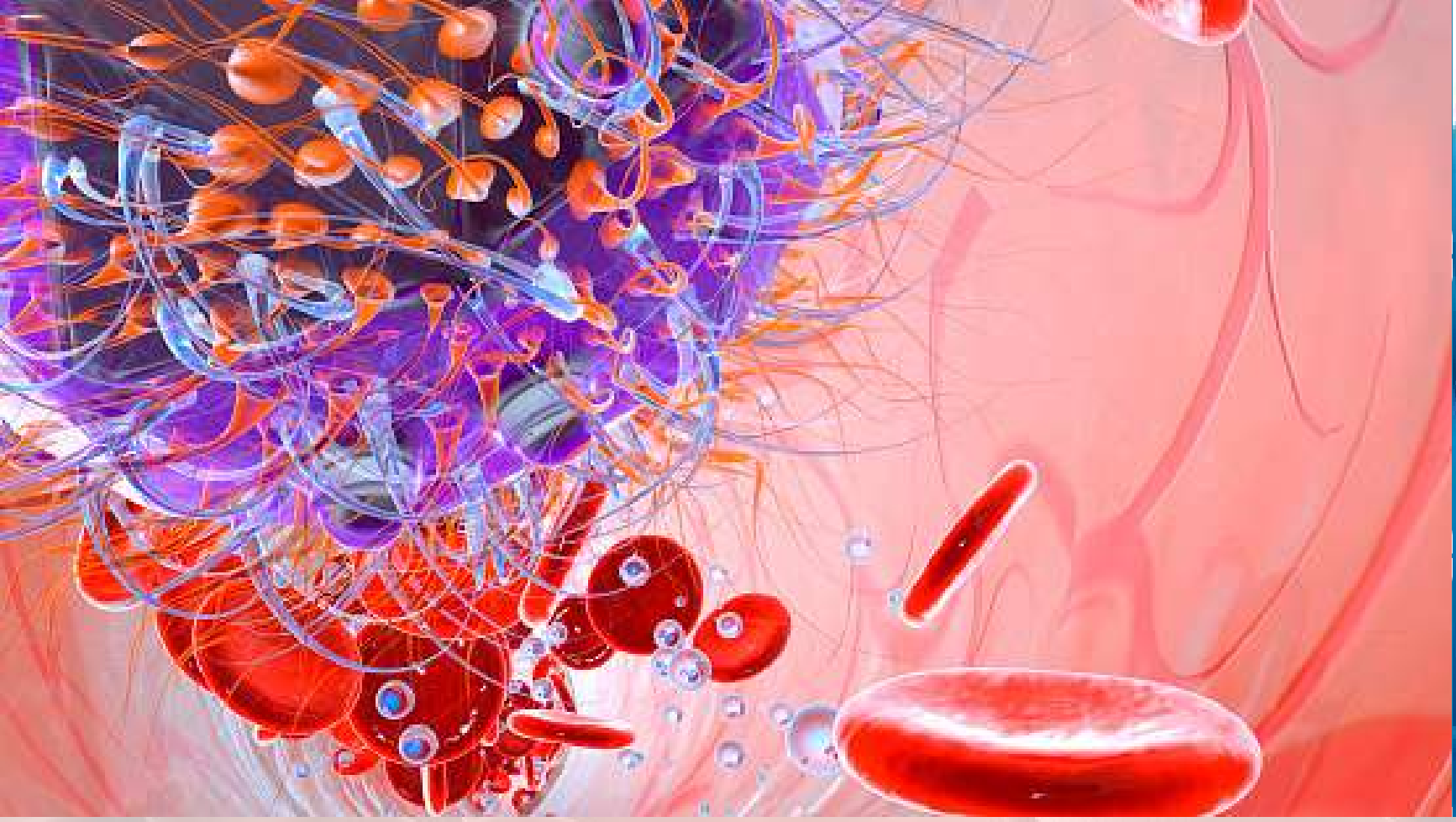

Hematology

"Haematology"

Dr. Abdulsalam A. Al-Ani
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IRON DEFICIENCY ANEMIA

- Iron is an essential element not only for the Hb synthesis, but also to many body enzymes.
- Although iron the most common elements in the earth's crust, its deficiency still the most common cause of anemia all over the world (about 1/2 of billion affected).
- Absorbed in a limit amount with excess of loss, mostly due to hemorrhage or inadequate intake.

➢Prevalence

- Globally, anemia affects about 1.62 billion people (33%) of the population all over the world, half of them due to iron deficiency.
- The highest prevalence is in preschool-age children (47.4%).
- The lowest in men (12.7%).
- Greatest number seen in non-pregnant women up to 49%, which due to menstrual blood loss.
- In Iraq the prevalence shows different results (about 20-30%).

Prevalence of Iron Deficiency Anemia among Adolescents Intermediate School Pupils in Ramadi District

Fakhri Jamel Dala Ali **MRCP**

Abdul-Salam Al-Ani **FICMS**

Abstract:

Objective: To find out the prevalence of iron deficiency anemia (IDA) among adolescents intermediate school pupils.

Subjects & Methods: A study was carried out on 520 (320 boys and 200 girls) intermediate school pupils. Boys of less than 15 years old and girls were characterized anemic if their packed cell volume (PCV) were < 36% , and < 39 in boys of 15 years old or above. Iron deficiency anemia was considered if anemic pupil shows TS < 5% or SF < 15% when TS were 5% or above.

Results: The prevalence of IDA was found to be 20.35% with a higher prevalence in girls than in boys. It is mostly noticed at age of 15 in girls and 17 in boys. IDA was diagnosed by TS > 5% in 56.19% pupils and low SF in 43.81%.

Conclusion: This study clarified that IDA is a health problem of moderate severity among adolescent intermediate school pupils in Ramadi district. To overcome this health problem we recommend to detect and treat the anemic pupils in addition to ensure them about the iron rich diet are important measures.

Key Words: Anemia, Iron deficiency, prevalence of iron deficiency anemia, adolescent, intermediate school pupil, Ramadi.

Prevalence of anemia among primary school children in Ramadi-Iraq

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Ahmad E. Al-Ani *MBChB*

Abstract

Objective: To estimate the prevalence of anemia in general and iron deficiency anemia (IDA) in particular among primary school children in Ramadi District.

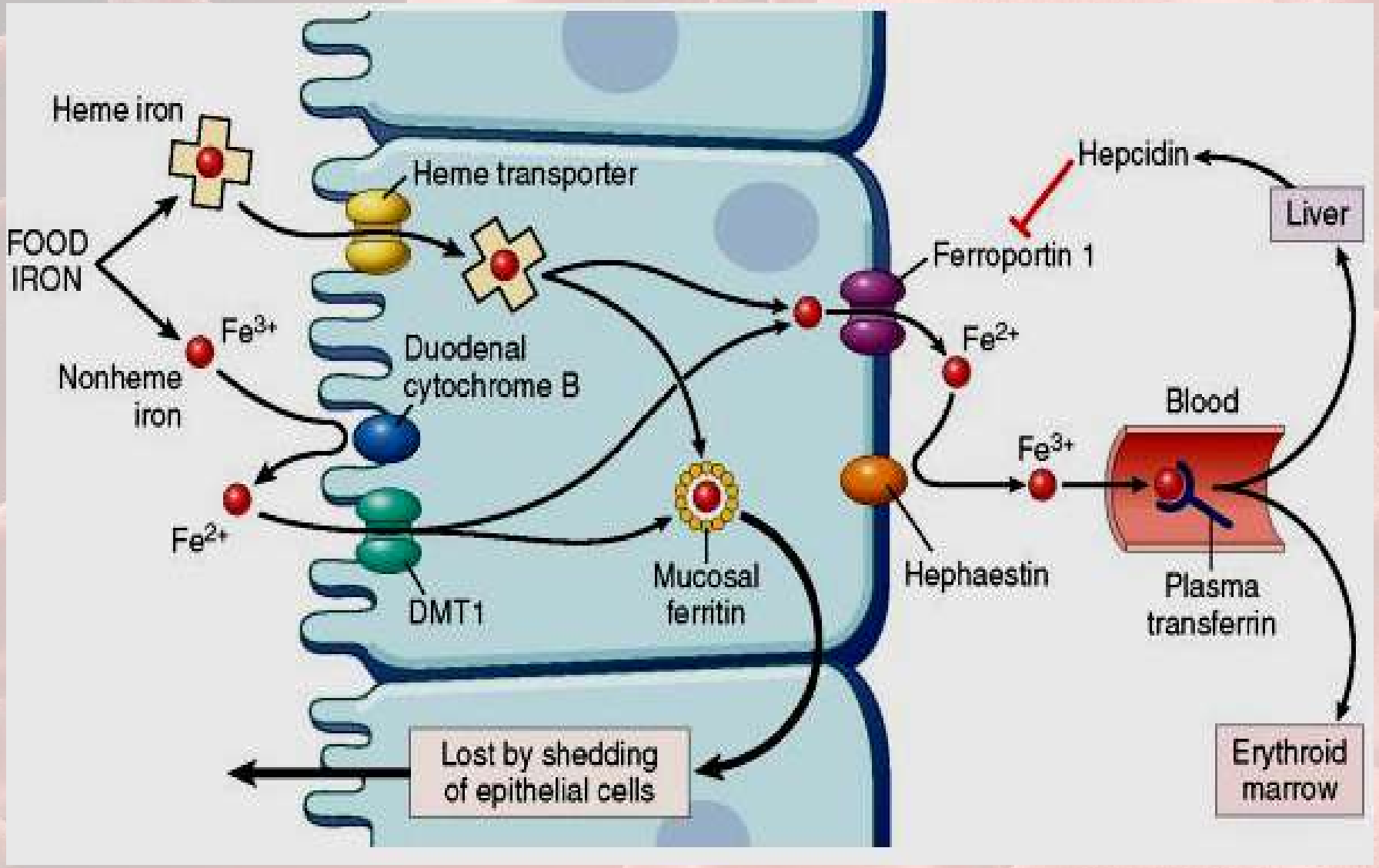
Subjects and methods: A total of 641 school children 6-12 years old (305 boys and 336 girls) were selected by random sampling for the study. Diagnosis of anemia was considered when the PCV is less than 36%. The value of hypochromia, serum iron (SI), total iron binding capacity (TIBC) and transferrin saturation (TS) were evaluated as screening tests for IDA.

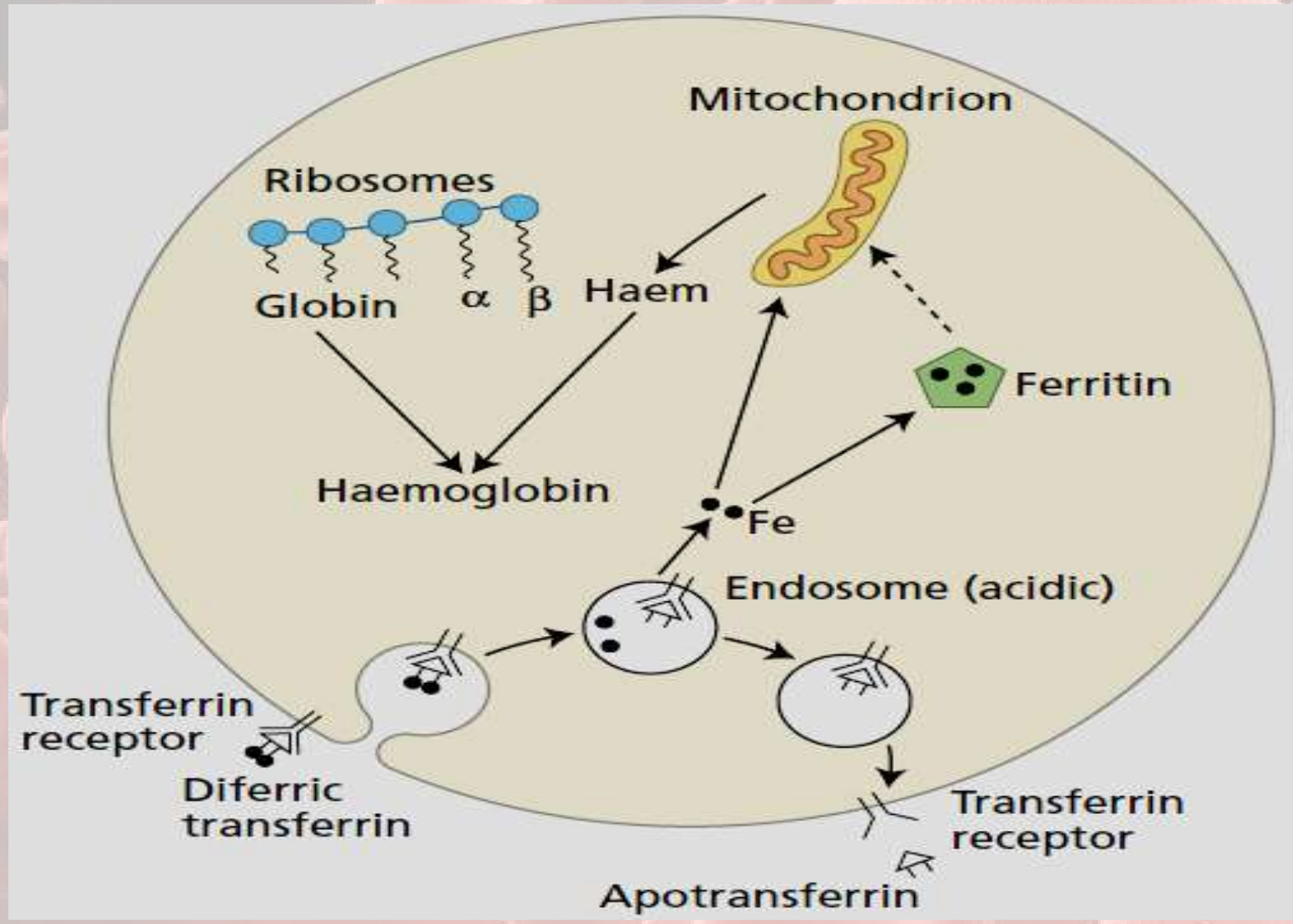
Results: Seventy of the studied children were found to be anemic (9.92%). Sixty children (9.36%) fulfilled the criteria of IDA, while 4 had Beta thalassemia minor. Hypochromia was found to be very useful screening test for IDA.

Conclusion: IDA still represents a major nutritional problem among primary school children in Ramadi District. We suggest giving courses of iron therapy to school children under the teachers' supervision and promotion of awareness about iron rich diet among mothers through launching campaigns.

➢Iron metabolism:

- Iron is absorbed mainly in the duodenum and upper jejunum, in a heme, the other part broken down partly to inorganic iron.
- About 5-10% of the normal 10-20 mg of dietary iron is absorbed each day, and this is sufficient to balance the 1-2 mg daily losses from desquamation of epithelia .
- Iron food found in a ferric and heme complexes. Meat iron is more absorbed the vegetable one.
- Iron absorption may be regulated both at the stage of mucosal uptake and at the stage of transfer to the blood.
- Absorbed iron is carried in the bloodstream by the glycoprotein named transferrin. Normally, about 20-45% of transferrin binding sites are filled (percent saturation).


Heme iron
Heme transporter
FOOD
IRON
Nonheme
iron
Fe^{3+}
Duodenal
cytochrome B
Fe^{2+}
DMT1
Mucosal
ferritin
Lost by shedding
of epithelial cells
Hepcidin
Liver
Ferroportin 1
Fe^{2+}
Blood
Fe^{3+}
Hephaestin
Plasma
transferrin
Erythroid
marrow

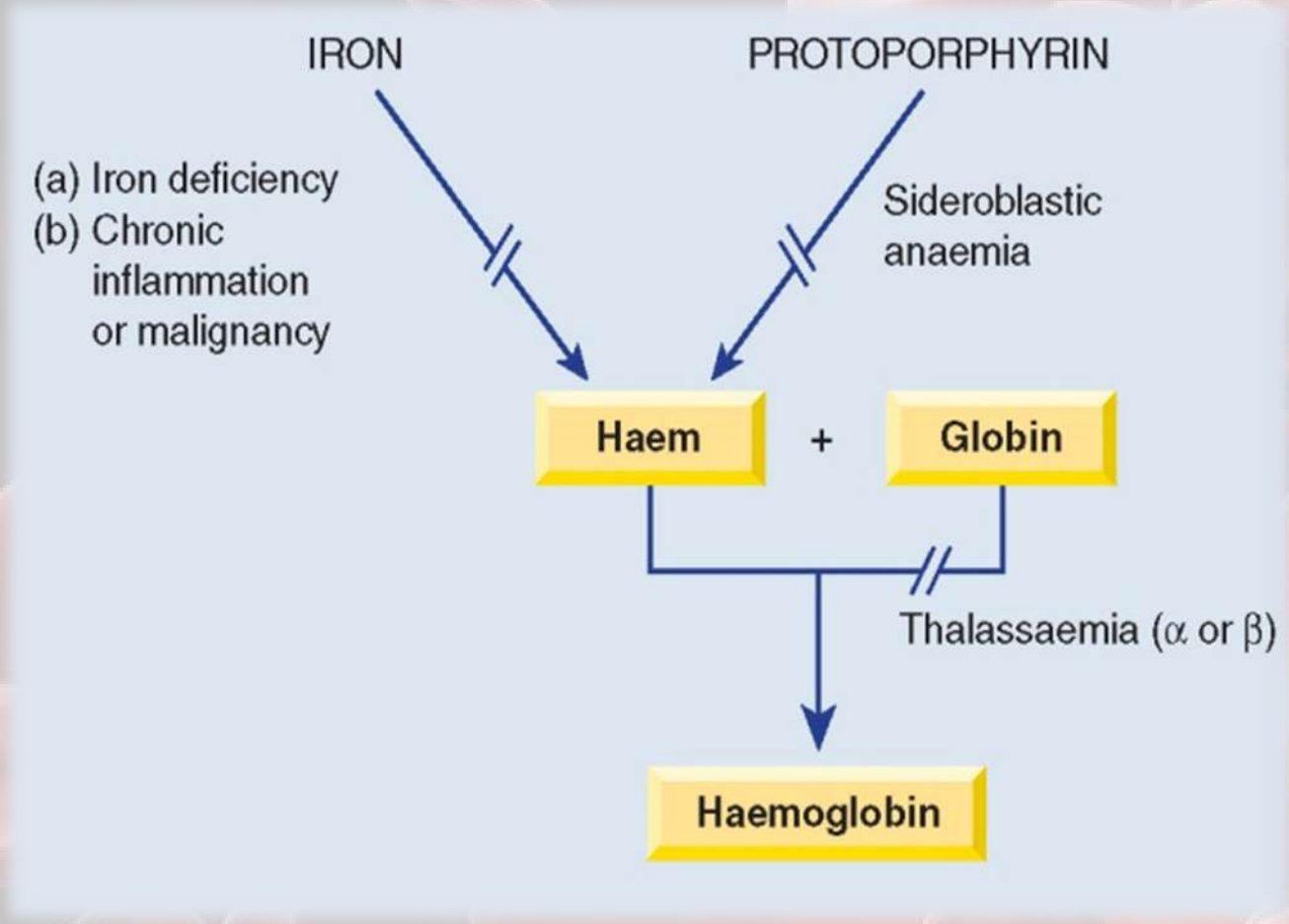


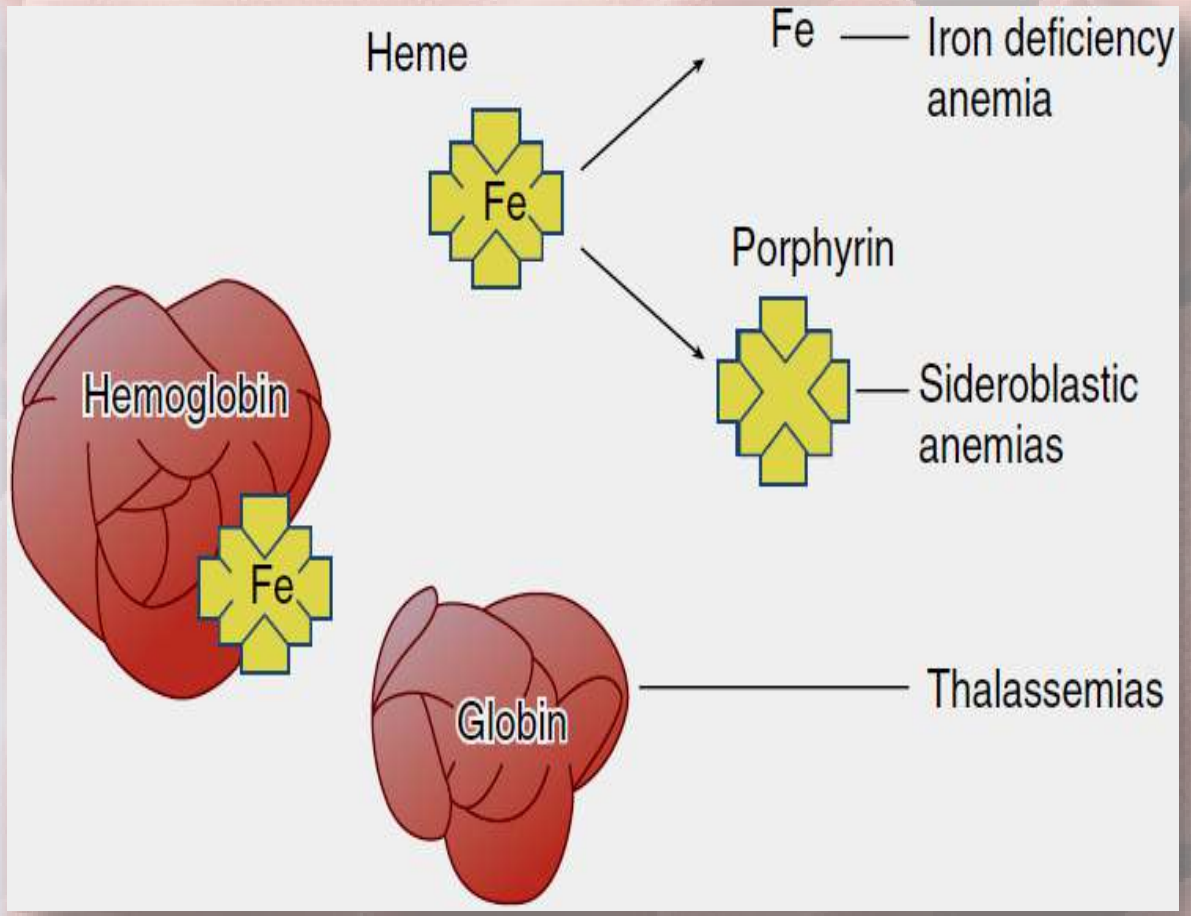
Incorporation of iron from plasma transferrin into hemoglobin in developing red cells. Uptake of transferrin iron is by receptor-mediated endocytosis.

- **Factors affecting iron absorption**

Factors favouring absorption	Factors reducing absorption
Haem iron	Inorganic iron
Ferrous form (Fe^{2+})	Ferric form (Fe^{3+})
Acids (HCl, vitamin C)	Alkalis – antacids, pancreatic secretions
Solubilizing agents (e.g. sugars, amino acids)	Precipitating agents – phytates, phosphates, tea
Reduced serum hepcidin	Increased serum hepcidin
Ineffective erythropoiesis	Decreased erythropoiesis
Pregnancy	Inflammation

- Deficiency of iron leads to defect in the heme synthesis with subsequent Hb synthesis.
- Usually of hypochromic microcytic (low MCV and MCH).
- Crucial proteins for iron synthesis; transferrin, ferritin and transferrin receptor 1 (TfR1).
- **Hepcidin** is a regulatory hormone important for iron release from macrophages and intestinal epithelial cells. Recently used as an important test in cases of hypochromic anemia, especially to differentiate it from anemia of chronic diseases.





Defects of Hb synthesis lead to hypochromic anemia

➢ Causes of Iron Deficiency:

1- Poor diet;

A major factor in many developing countries but rarely the sole cause in developed countries

2- Chronic blood loss;

- ❑ Uterine
- ❑ Gastrointestinal, e.g. peptic ulcer, oesophageal varices, aspirin (or other non-steroidal anti-inflammatory drugs) ingestion, partial gastrectomy, GIT carcinomas, hookworm, angiodysplasia, colitis, piles, diverticulosis
- ❑ Rare; hematuria, hemoglobinuria, pulmonary hemosiderosis, self-inflicted blood loss

3- Increased demands;

- ❑ Prematurity
- ❑ Growth
- ❑ Pregnancy
- ❑ Erythropoietin therapy

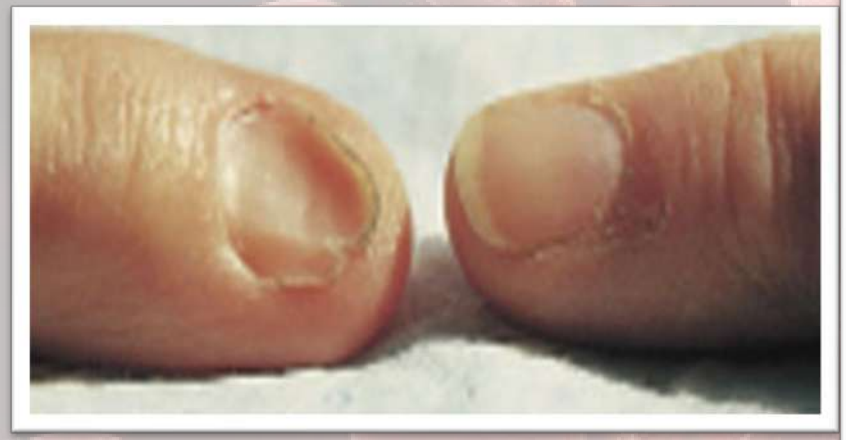
4- Malabsorption;

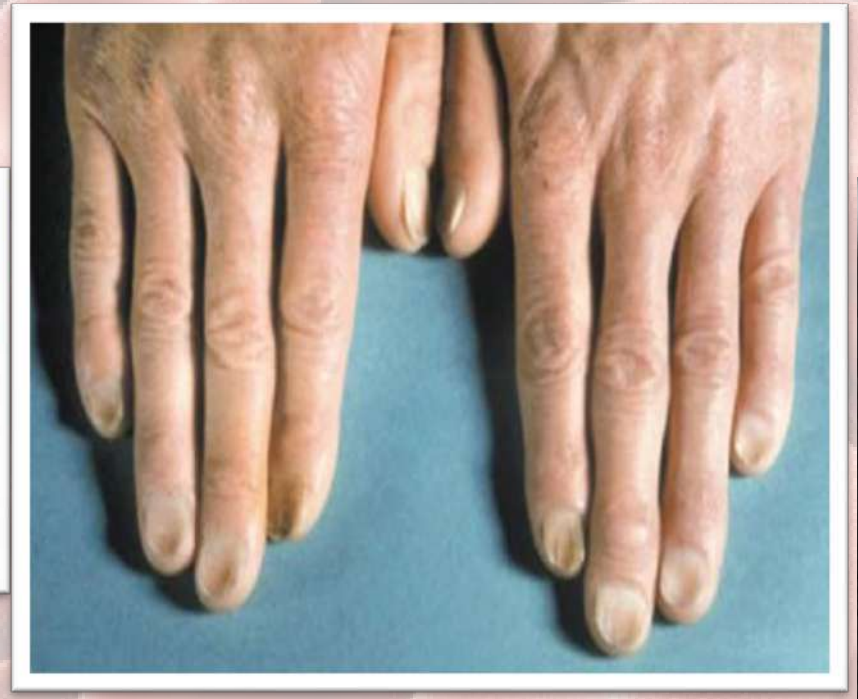
Gluten-induced enteropathy, gastrectomy, autoimmune gastritis

➢Clinical Features:

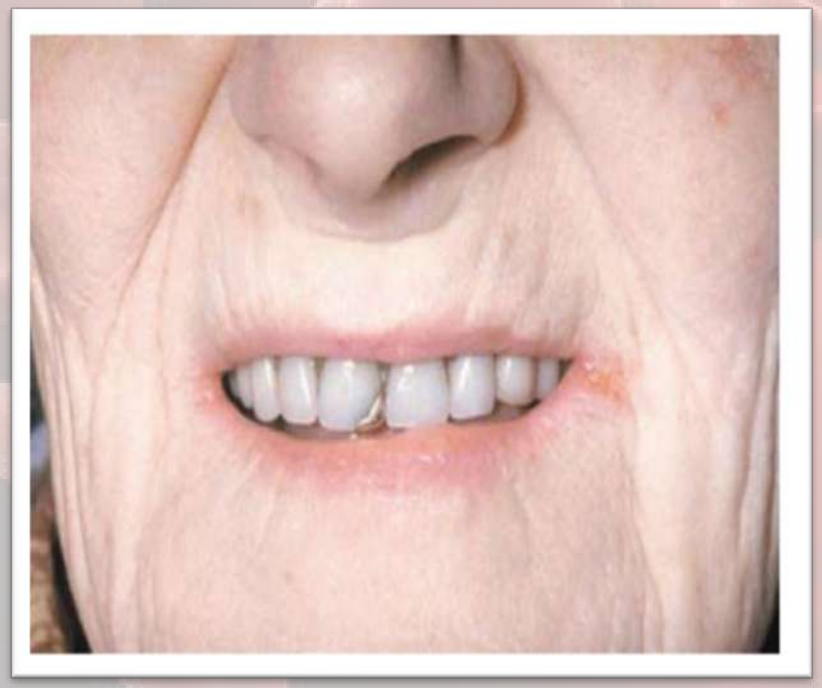
- General features of anemia.
- Painless glossitis, angular stomatitis.
- Koilonychia (ridged or spoon like nails).
- Dysphagia due to pharyngeal web (Paterson-Kelly or Plummer-Vinson syndrome).
- Abnormal dietary craving (pica), such as ice, chalk or paper.
- Children; irritability, poor cognition, declining of psychomotor development.

Koilonychia “spoon nails”

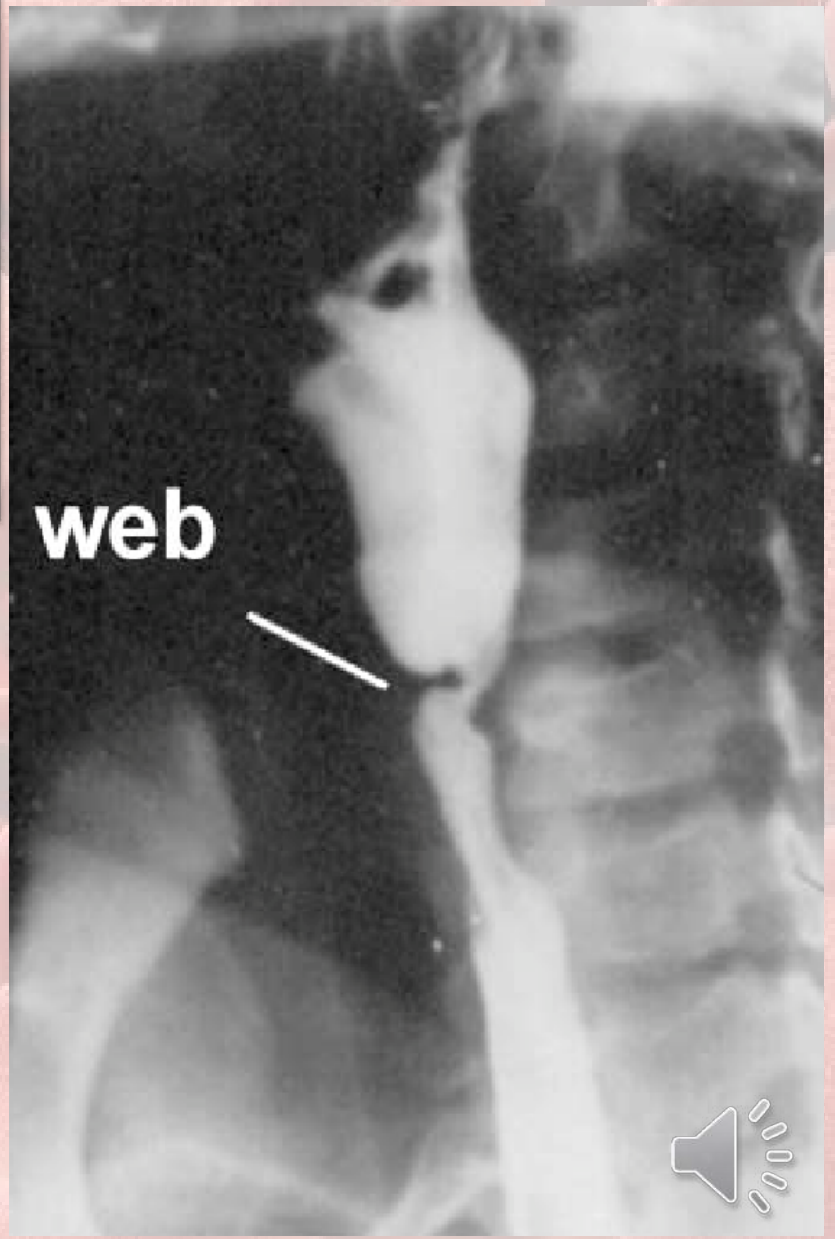




Angular stomatitis

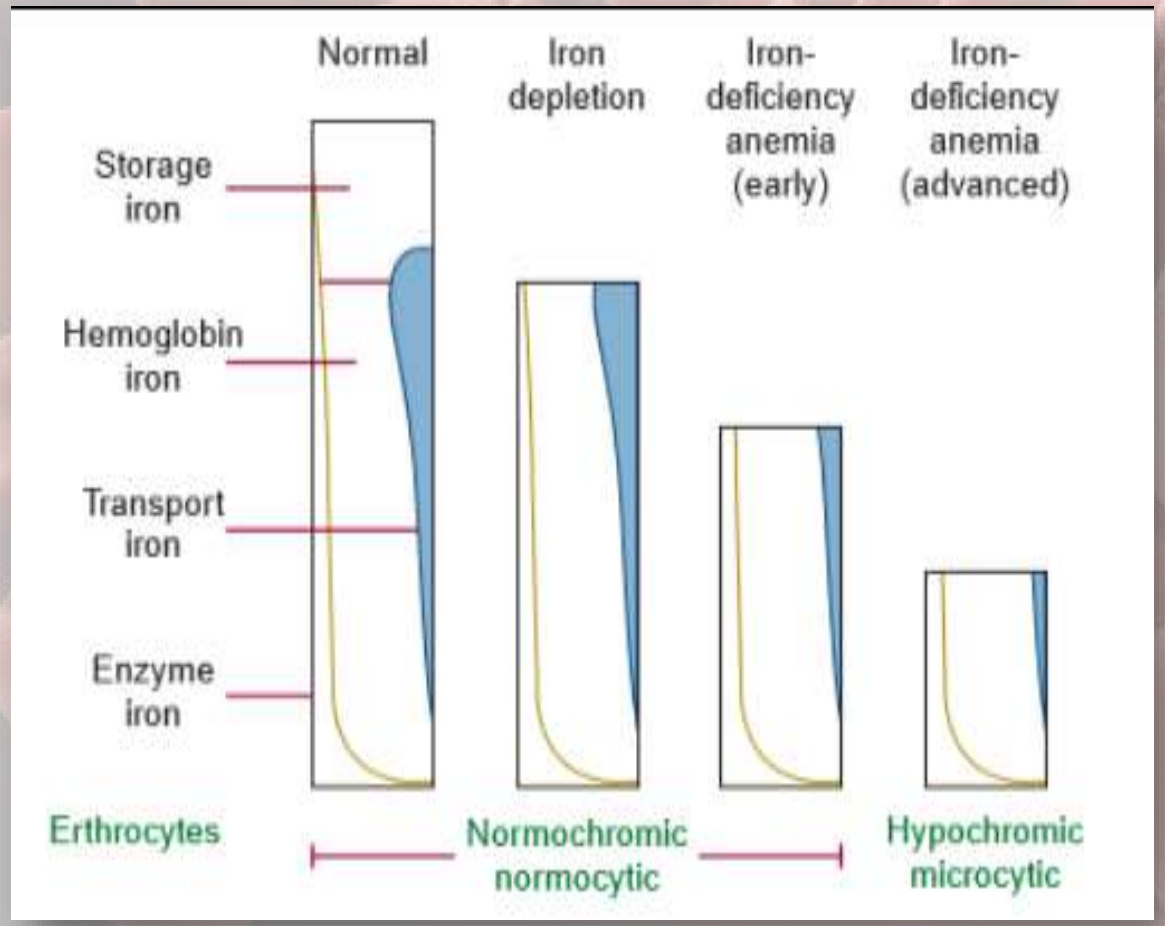


Barium swallow X-ray of pharyngeal web in Paterson-Kelly (Plummer-Vinson) syndrome



➢ Laboratory Findings:

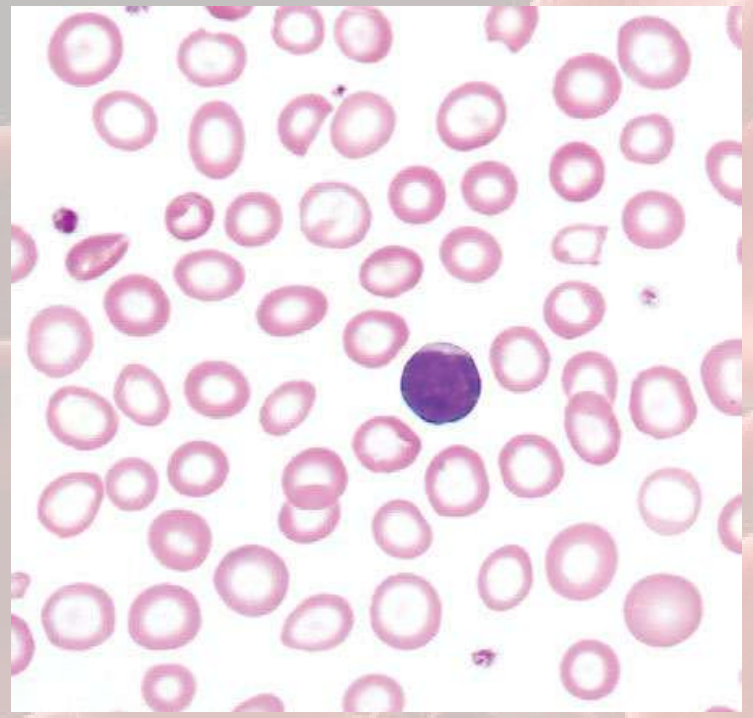
- The state of iron store depletion, called latent iron deficiency, with association of low transferrin usually precedes the state of anemia.
- Low serum ferritin and transferrin (< 15 μg/L) is the most sensitive tests for the iron deficiency.

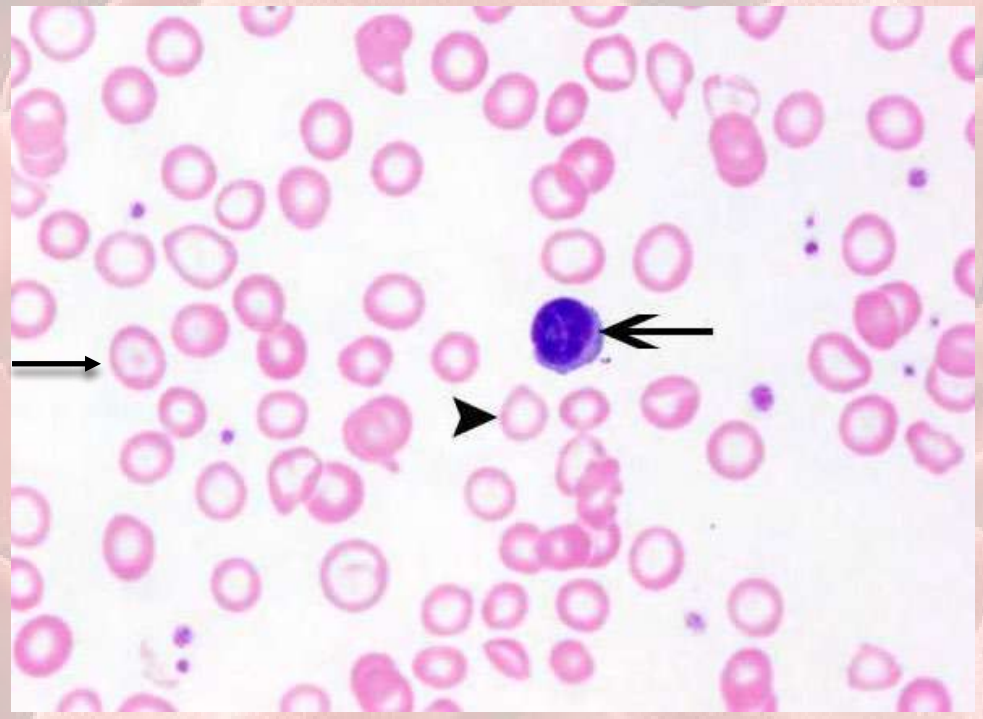


	Normal	Latent iron deficiency	Iron deficiency anaemia
Red cell iron (peripheral film and indices)	Normal	Normal	Hypochromic, microcytic MCV↓ MCH↓
Iron stores (bone marrow macrophage iron)	++	0	0

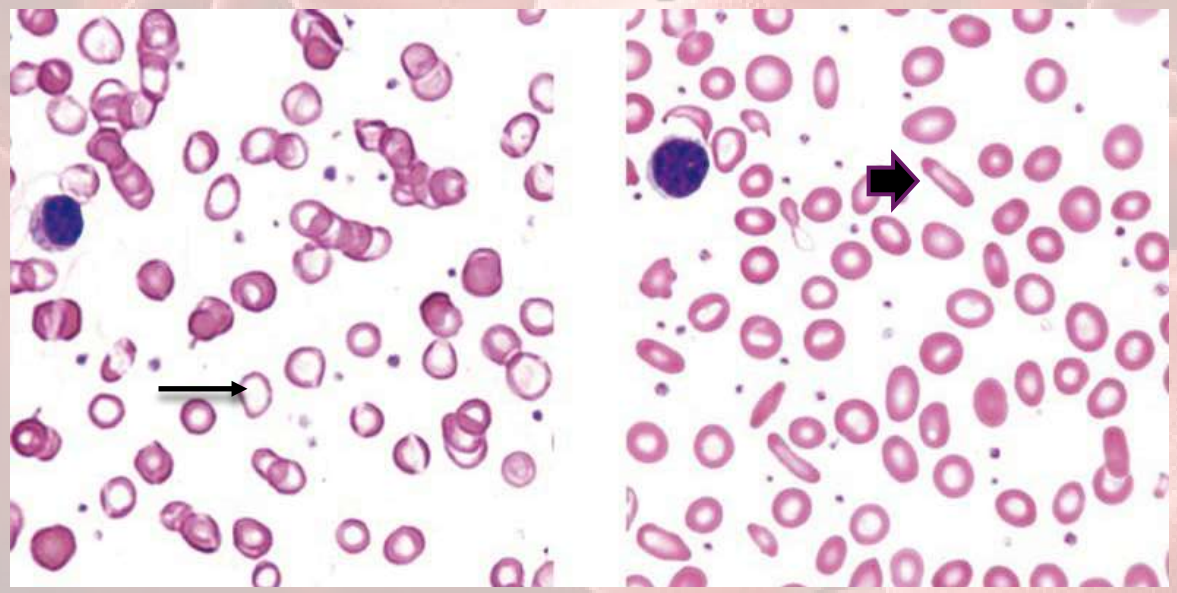
Red cell indices and Bd film;

- Low MCV and MCH; usually correlate with the severity of the anemia. Can be normal if there is a concomitant macrocytic anemia
- Blood film shows hypochromic microcytic with occasional target cells and anisocytosis (difference in cells size) and poikylocytosis (difference in cells shape), such as pencil-, or cigar-shape cells.
- Reticulocyte count usually low in relation to anemia (corrected reticulocyte count).
- Platelets; moderately increased.





Moderate and sever IDA with the Comparison to a normal lymphocyte



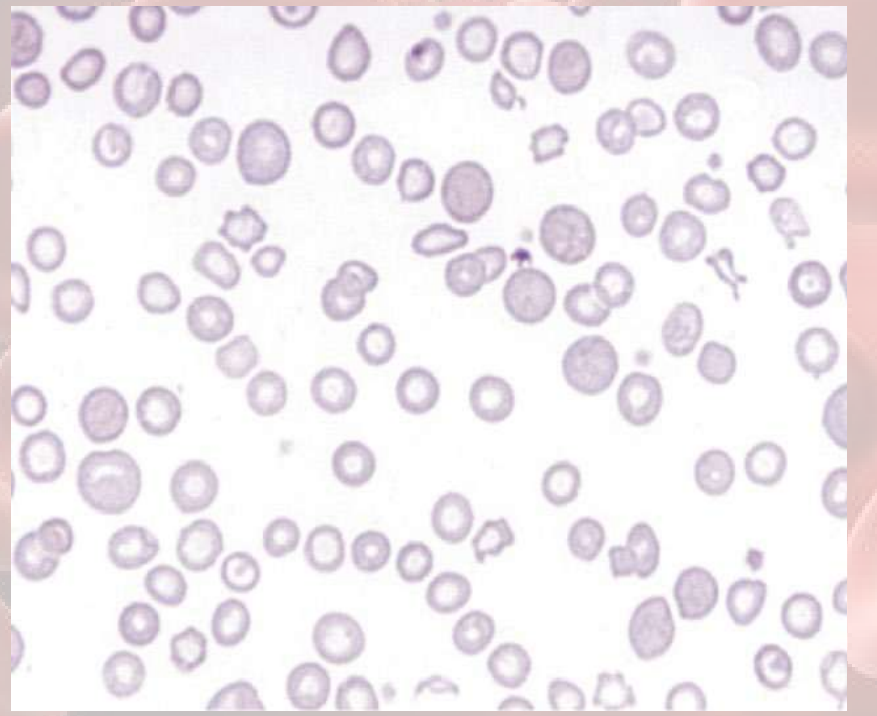
- **Dimorphic** picture (dual cell population) can be seen in;

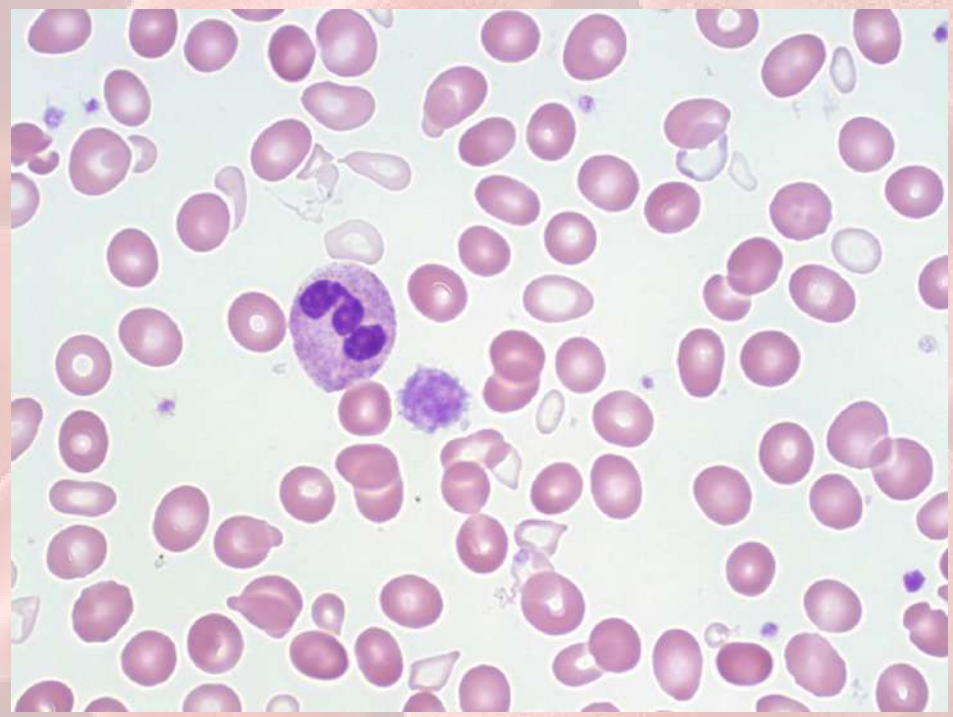
1- Cases of B_{12} and folate deficiency with the iron deficiency.

2- Partially treated IDA.

3- Sideroblastic Anemia.

4- Transfused IDA patients.

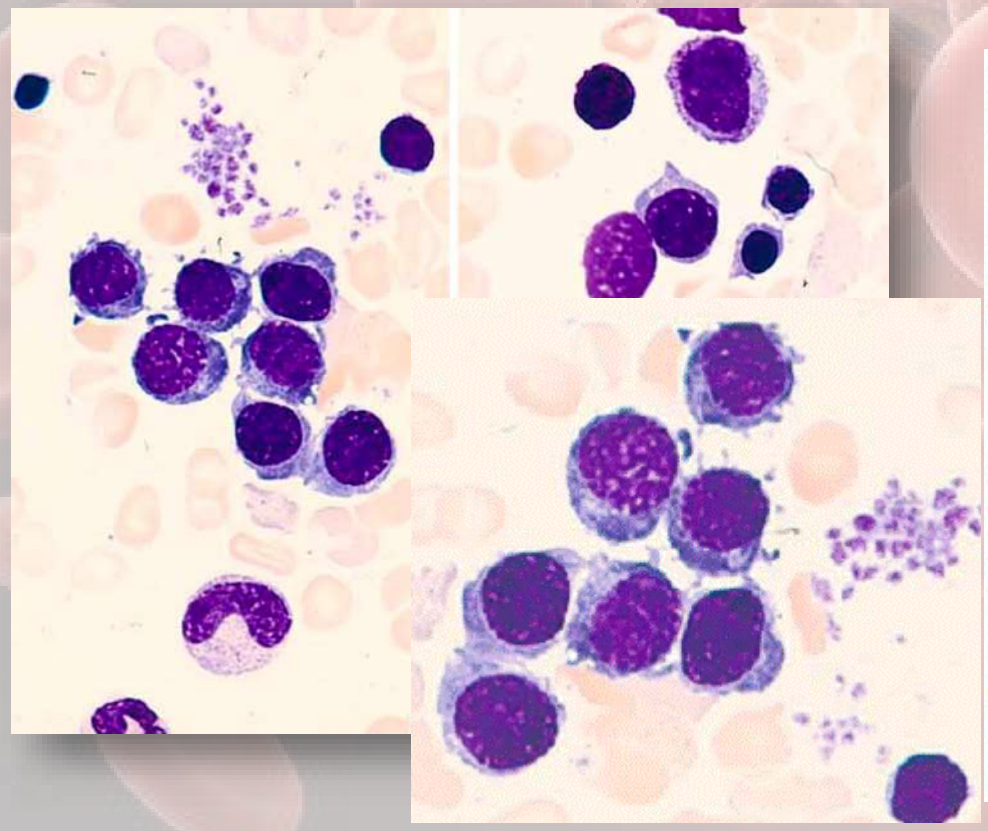


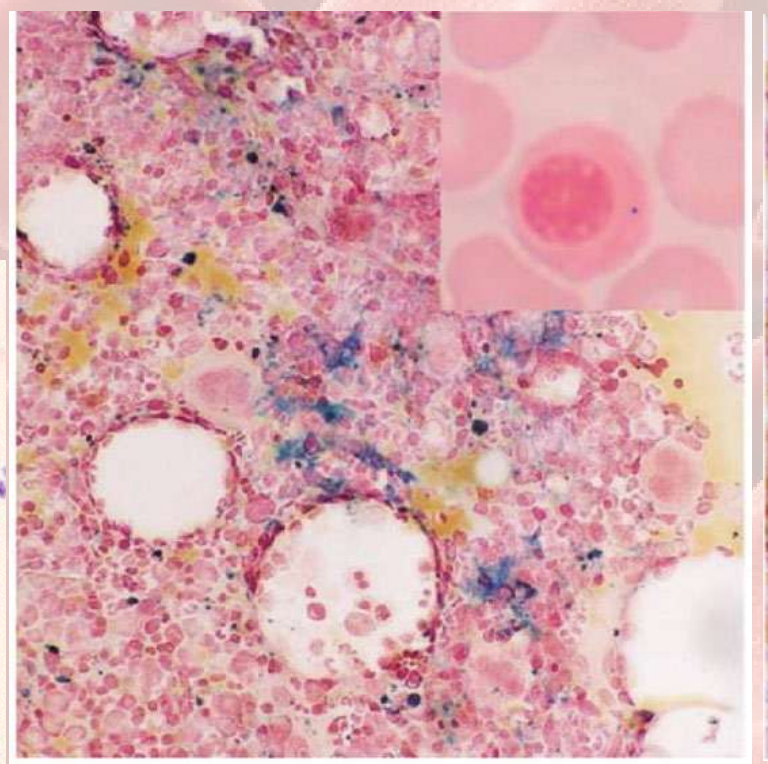


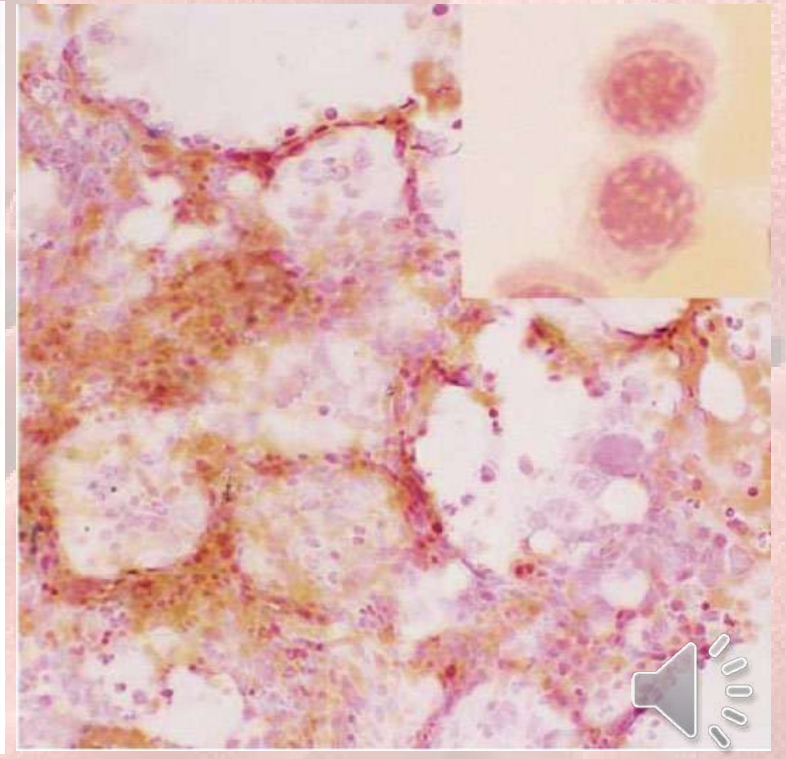
- Low serum iron (NR; 60-170μg/dL, 10-30 μmol/L).
- High total iron-binding capacity (TIBC); (NR; 250-400 μg/dL 47-75 μmol/L).
- Low transferrin saturation; usually <10% (NR; 16-50%).
- Low serum ferritin; <15μg/L (NR; 15-300μg/L for males and 15-200μg/L for females.
- Increased serum transferrin receptors.
- Increased free erythrocyte protoporphyrin (FEP).
- Low serum Hepcidin level.

- **Bone Marrow Aspirate:**

- Not indicated, but may be used for the assessment of iron store.
- Normo- or hypercellular with hyperactive erythropoiesis of different stages of maturation, showing poor hemoglobinization (show a ragged vacuolated cytoplasm)
- Depleted iron in stores and erythrones (Iron stain; Perls' stain, Prussian blue reaction

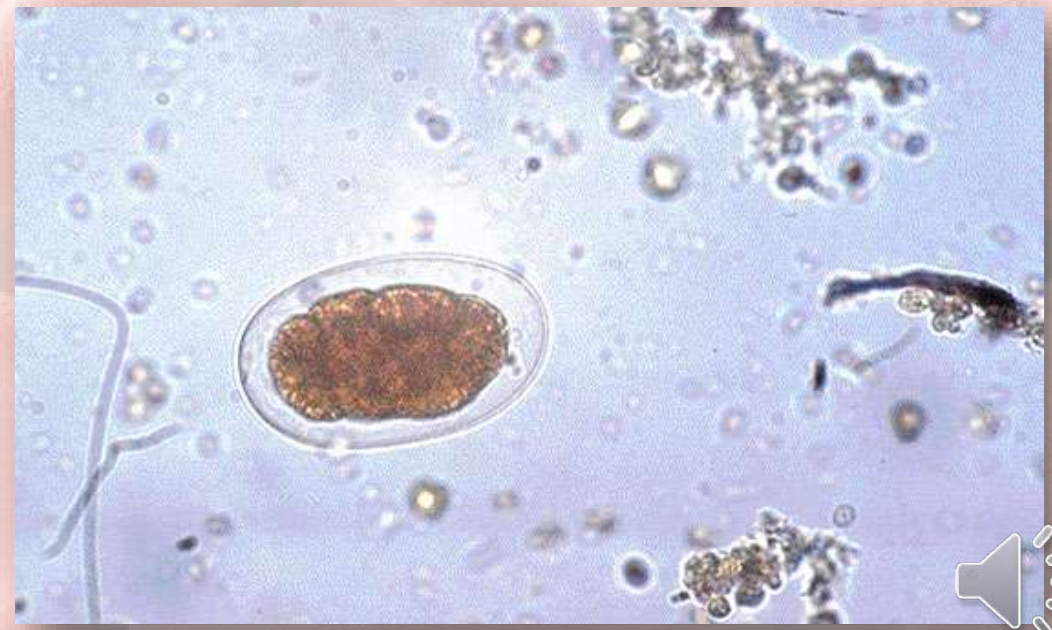






Underlying Cause:

- Dietary.
- Presence of worm infestation; by GSE.
- GIT; physical and rectal examination with searching for occult blood and endoscopic examination. *H.pylori* need to be ruled out.
- Women; uterine or multipregnancy may be the cause.



Iron-deficiency anaemia: an ovum of the hookworm Ancylostoma duodenale, a frequent cause of iron-deficiency anaemia in many parts of the world, is present. Blood loss and therefore severity of anaemia is related to the degree of parasitization.

❖ Differential Diagnosis of IDA

1. Thalassaemia Minor.
2. 25% of Chronic diseases (75% usually normocytic).
3. Lead poisoning.
4. Sideroblastic Anemias.

   * Hereditary

   * Acquired (May give macrocytic)

▪ Treatment;

➢ Oral;

- Ferrous sulphate is the best, for it's cheap price with sufficient concentration.
- Empty stomach, before meal.
- Long enough (about 6 months), to replenish stores.
- Hb response usually 2g/dL per 3 weeks.

➢Parenteral (Injection);

- Not faster than oral.
- IV slow infusion of iron-dextran, in cases with oral intolerance or need rapid storage replenishment.
- Dose depends on body weight and degree of anemia.
- Used if high amount required or GIT disease.
- Hypersensitivity or anaphylactic reaction can be a serious reaction, so a small testing dose can be used.

➢Treatment of Underling Cause.

MEGALOBLASTIC ANEMIA

A pancytopenic disorder related to reduction of DNA synthesis.

Characterized by:

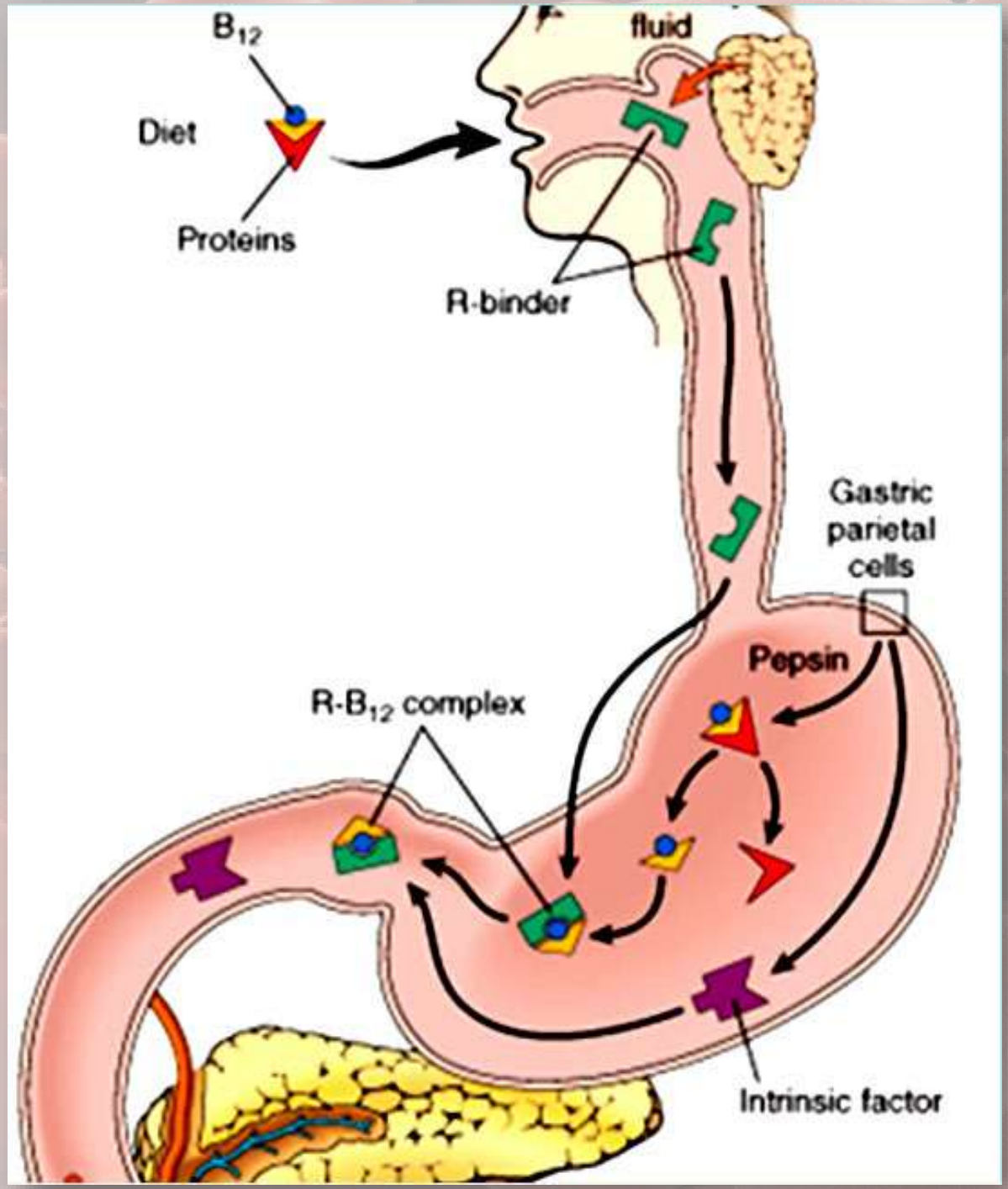
- presence of macro-ovalocytes and hypersegmented neutrophils in the peripheral blood.
- Megaloblastic maturation in the bone marrow.
- Asynchrony in nuclear/cytoplasmic maturation, with a delay of nuclear maturation in relation to the cytoplasm cells may skip one or two mitoses. Normally 4-5 divisions during erythropoiesis.
- Increased ineffective erythropoiesis (Normal 10-15%), many of the cells die in the bone marrow.
- Usually caused by folate, vitamin B12 deficiency, or its abnormal metabolism or chemotherapeutic agents that interfere with DNA synthesis.

❖Macrocytosis; MCV> 100 fL

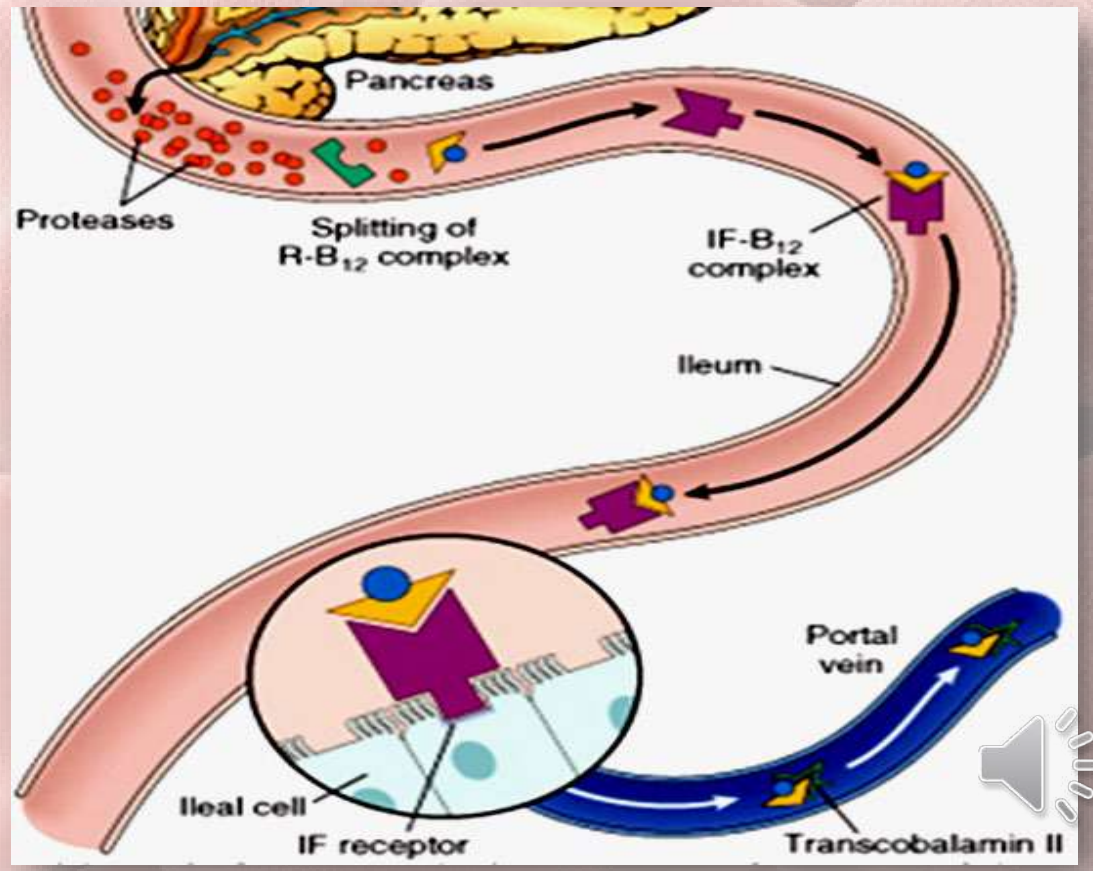
1. Megaloblastic Anemias.
2. Reticulocytosis
3. Pregnancy.
4. Aplastic Anemias.
5. Neonate.
6. Liver diseases and Alcohol consumption.
7. Hypothyroidism (Myxodema).
8. Myelodysplasias; eg; MDS, Chemotherapy.
9. Sideroblastic Anemias (Acquired).

Metabolism of Vitamin B12 and Folic acid

- Vitamin B12 is present in meat and other animal products.
- It combines with intrinsic factor (IF) which is secreted by the stomach.
- After complexing with the IF it is maximally absorbed in the distal small bowel, the ileum.
- B12 in food is released from protein binding by proteolytic enzymes and attached to a so-called R-binder .


B_{12}
Diet
Proteins
fluid
R-binder
Gastric parietal cells
Pepsin
R-B_{12} complex
Intrinsic factor

- B12 is released from this binding by pancreatic enzymes and transferred to intrinsic factor secreted by the parietal cells of the stomach.
- Intrinsic factor-bound B12 is carried to the ileum, where it attaches to specific receptors; the intrinsic factor is digested and B12 appears in the portal blood attached to a polypeptide protein, transcobalamin II.
- In peripheral blood most B12 is attached to the glycoprotein transcobalamin I, but it is transcobalamin II that is responsible for delivery of the vitamin to the tissues.



❖ B12 (Cobalamin) Deficiency

- Stored in amounts of 2–3 mg.
- Daily losses (mainly in the urine and faeces) and required by 1–3 μg, therefore it takes 2-4 years for B12 deficiency to develop from dietary lack or malabsorption.
- Vitamin B12 and folate is present in meat and other animal products especially liver, the main storage organ. A normal Western diet contains between 5 and 30μg of cobalamin daily.
- B12 occurs only in foods of animal origin. Veganism may leads to B12 deficiency, while FA presents in most foods, including fruit, vegetables and cereals as well as animal products .
- It serves as the cofactor for the enzyme methionine synthase.

Causes of vitamin B12 Deficiency

Malabsorption	**1. Pancreatic insufficiency** **2. Small intestine absorption defect** **3. Crohn's disease** **4. Sprue (nontropical and tropical)** **5. Lymphoma** **6. Diverticulosis or blind loop** **7. Fish tapeworm** **8. Ileal resection**
Intrinsic factor deficiency	Autoimmune: antiparietal cell / IF antibody (pernicious anemia) Gastric surgery
Poor vitamin B12 intake (vegetarians)	
Congenital defects (TCII deficiency)	

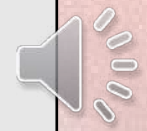
❖Folate (pteroylglutamic acid) Deficiency

- Total body folate (FA) in the adult is about 10-15mg, the liver containing the largest store.
- Most foods contain some folate. The highest concentrations are found in liver and yeast , spinach, other greens and nuts.
- The total FA content of an average Western diet is about 250μg daily, but the amount varies widely according to the type of food eaten and the method of cooking. It is easily destroyed by cooking.
- Daily adult requirements are about 100μg. Up to 13μg is lost in the urine each day, and its breakdown products are also lost in urine. Losses of folate also occur in sweat and skin.
- Faecal folate is largely derived from colonic bacteria.

- Dietary folate is deconjugated to the monoglutamate form, fully reduced and methylated in the upper intestinal epithelial cells, so that it is all absorbed in the form of methyl-THF.
- Folate is easily destroyed by cooking.
- Stores are only sufficient for about 4 months in normal adults, so severe folate deficiency may develop rapidly.
- The most common cause of deficiency is pregnancy, when folate requirements rise from the normal 100–200mg daily to about 350mg daily.
- Other causes of increased folate utilization include diseases with increased bone marrow or other cell turnover. The excessive demands in these conditions, combined with poor dietary intake, may lead to megaloblastic anemia.

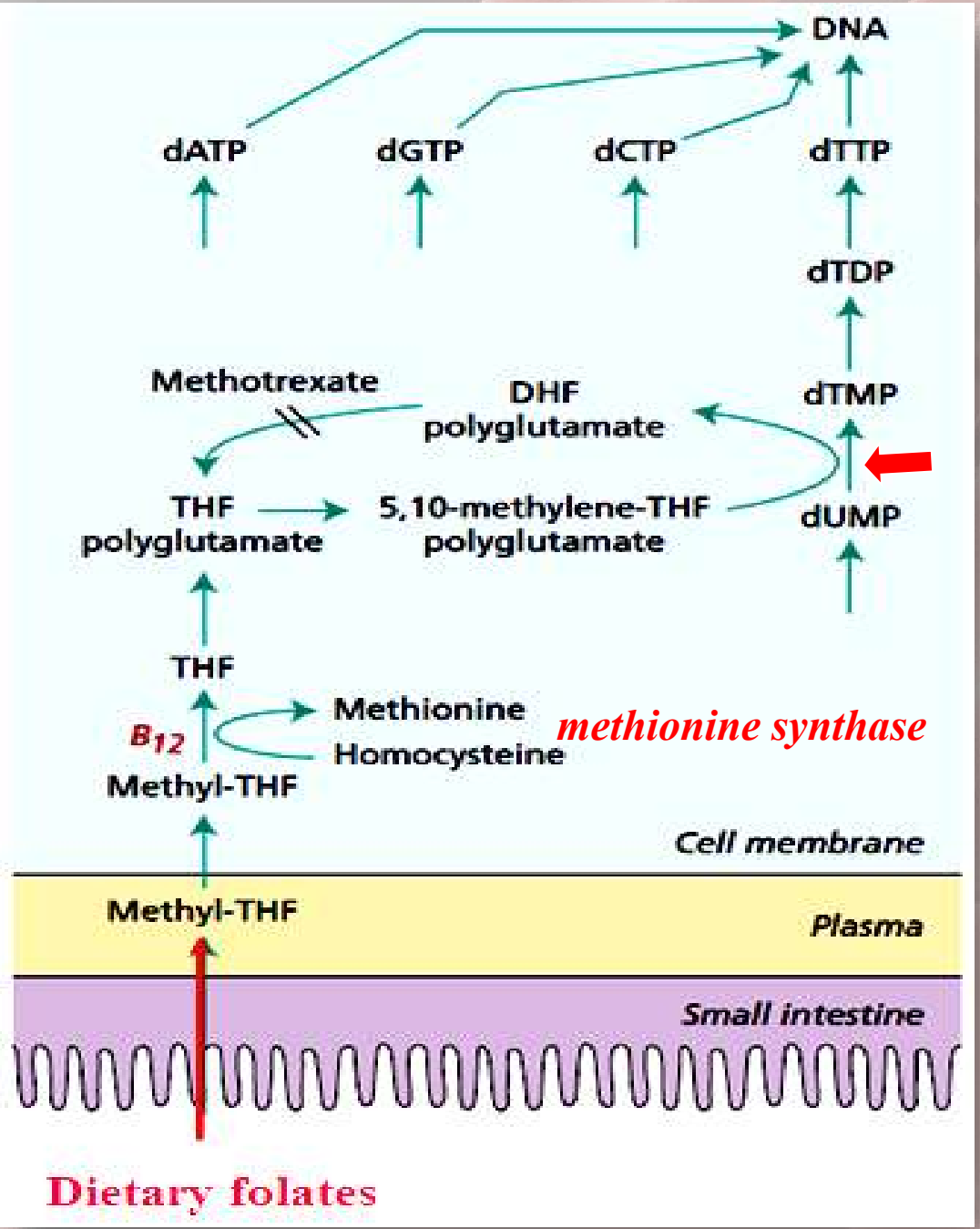
Causes of folate deficiency

Poor folic acid intake	Dietary lack Alcoholism
Increased requirement	Hemolytic anemias Exfoliative dermatitis/psoriasis Pregnancy Hyperthyroidism
Drugs	Oral contraceptive and anticonvulsants lead to increase FA consumption. Dihydrofolate reductase inhibitors (methotrexate, trimethoprim) Vitamin C deficiency
Loss	Hemodialysis
Malabsorption	Sprue (non-tropical and tropical) Lymphoma Small bowel resection Crohn's disease



❖ Pathogenesis of Megaloblastic Anemia

- The defect in DNA synthesis is the main effect of FA and B12 deficiency in megaloblastic anemia, by the defect in thymine synthesis. The interaction of both of them is important for this synthesis.
- Folate affects thymidylate synthesis, a rate-limiting step in pyrimidine synthesis, since a folate coenzyme, 5,10-methylene tetrahydrofolate-polyglutamate, is necessary for this reaction.
- B12 is not required directly for DNA synthesis. It involves as a coenzyme in the methionine synthase reaction in which homocysteine is methylated to methionine, is needed to convert 5-methyltetrahydrofolate (methyl-THF), which enters cells from plasma, into other folate coenzyme forms (including all the polyglutamate derivatives).
- polyglutamate derivatives are sharing in thymine synthesis.

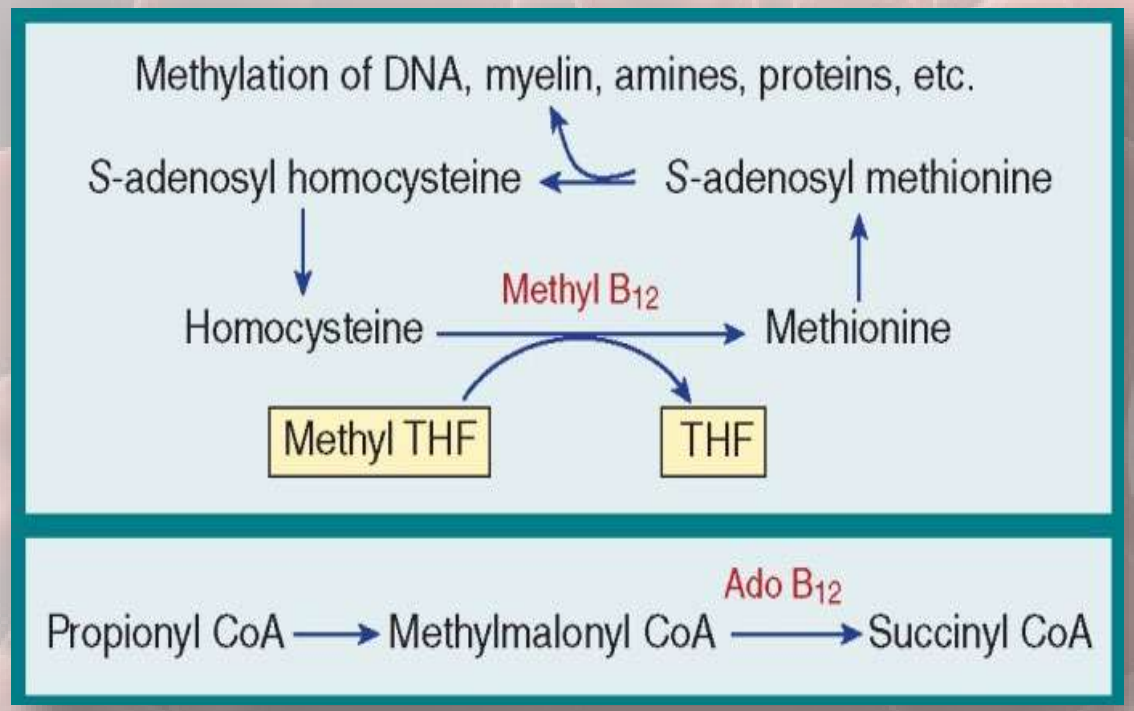


Role of folate (as 5,10 - methylene - THF polyglutamate and methylcobalamin) in DNA synthesis.

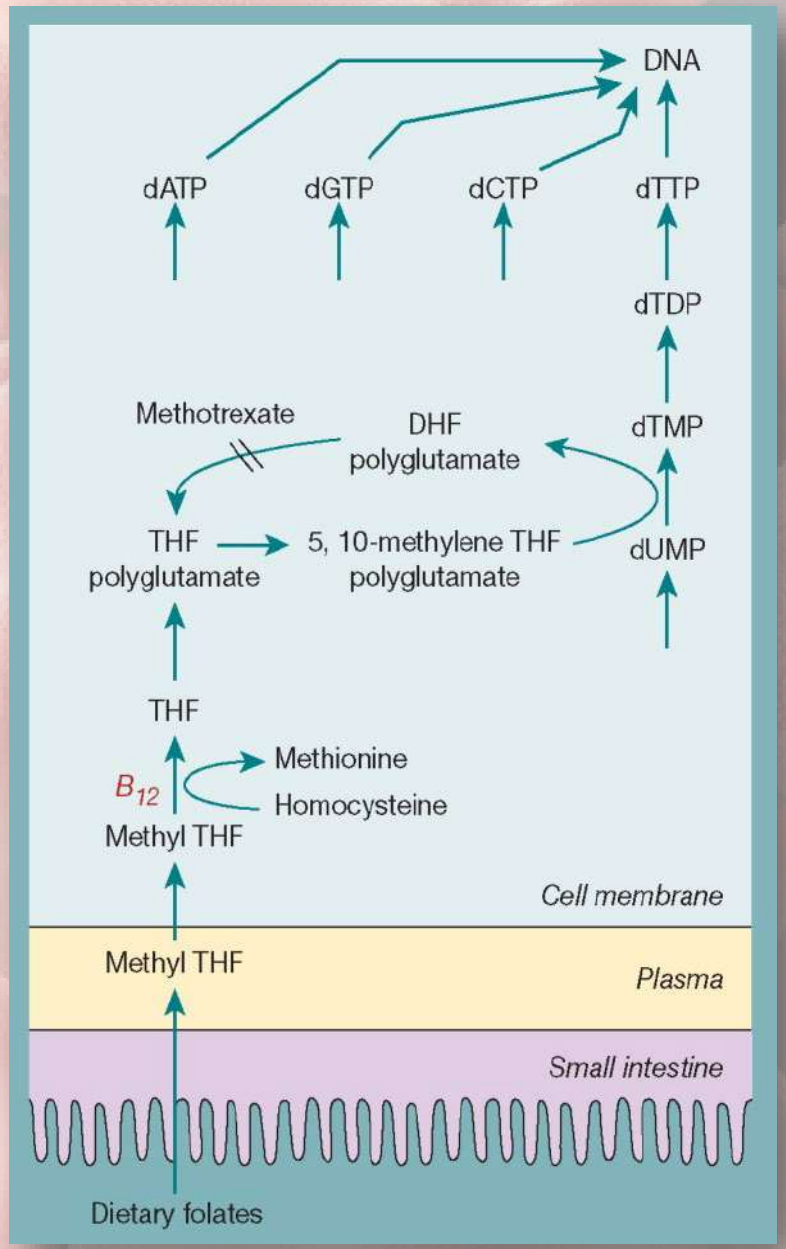
THF; tetrahydrofolate
MP; monophosphate
TP; triphosphate
d; deoxyribose
A; adenine
T; thymidine
C; cytosine
G; guanine
U; uridine

❖Mechanism of Actions:

B_{12}



Folate

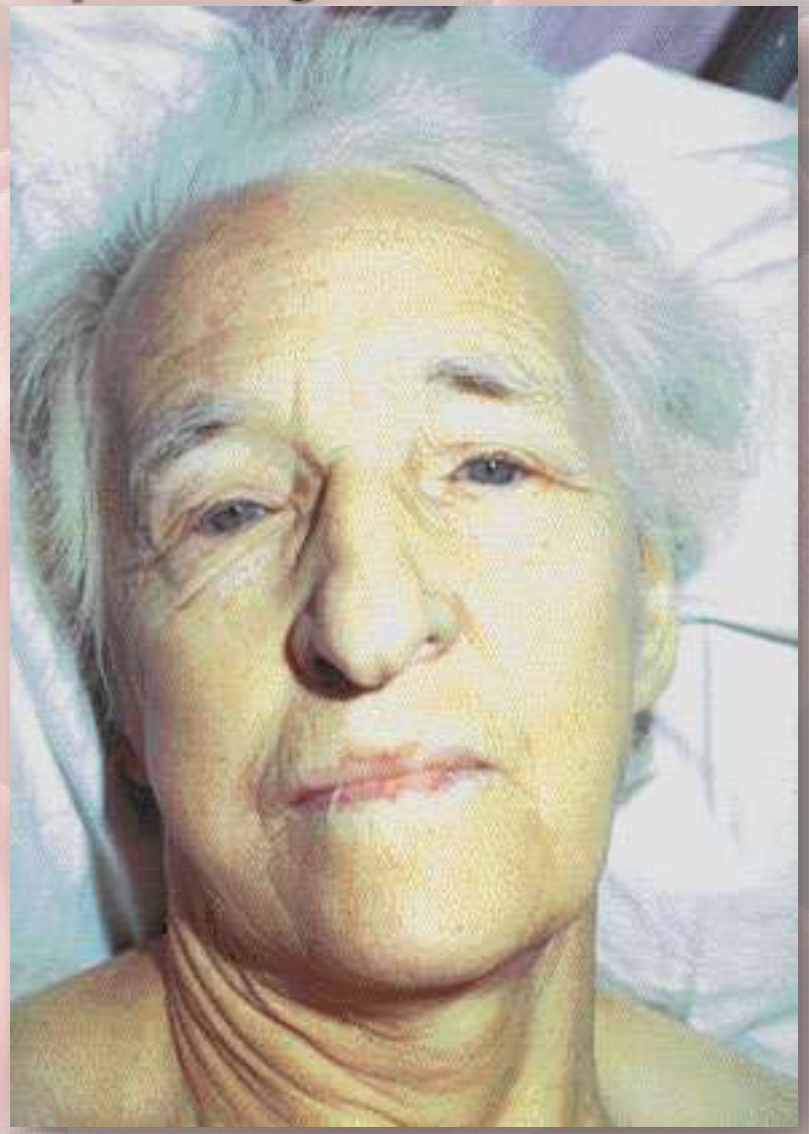


❑ Causes of Megaloblastic Anemia:

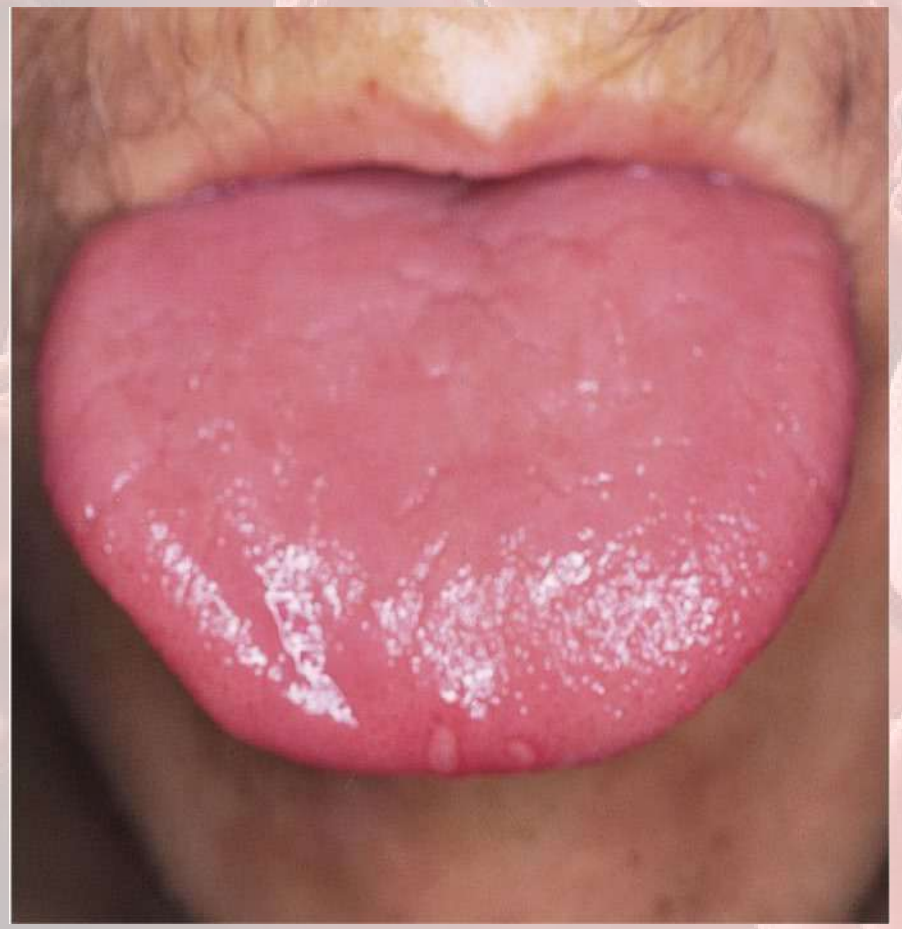
Vitamin B_{12} deficiency
Folate deficiency
Abnormalities of vitamin B_{12} or folate metabolism (e.g. transcobalamin deficiency, nitrous oxide, antifolate drugs)
Other defects of DNA synthesis Congenital enzyme deficiencies (e.g. orotic aciduria) Acquired enzyme deficiencies (e.g. alcohol, therapy with hydroxyurea, cytosine arabinoside)

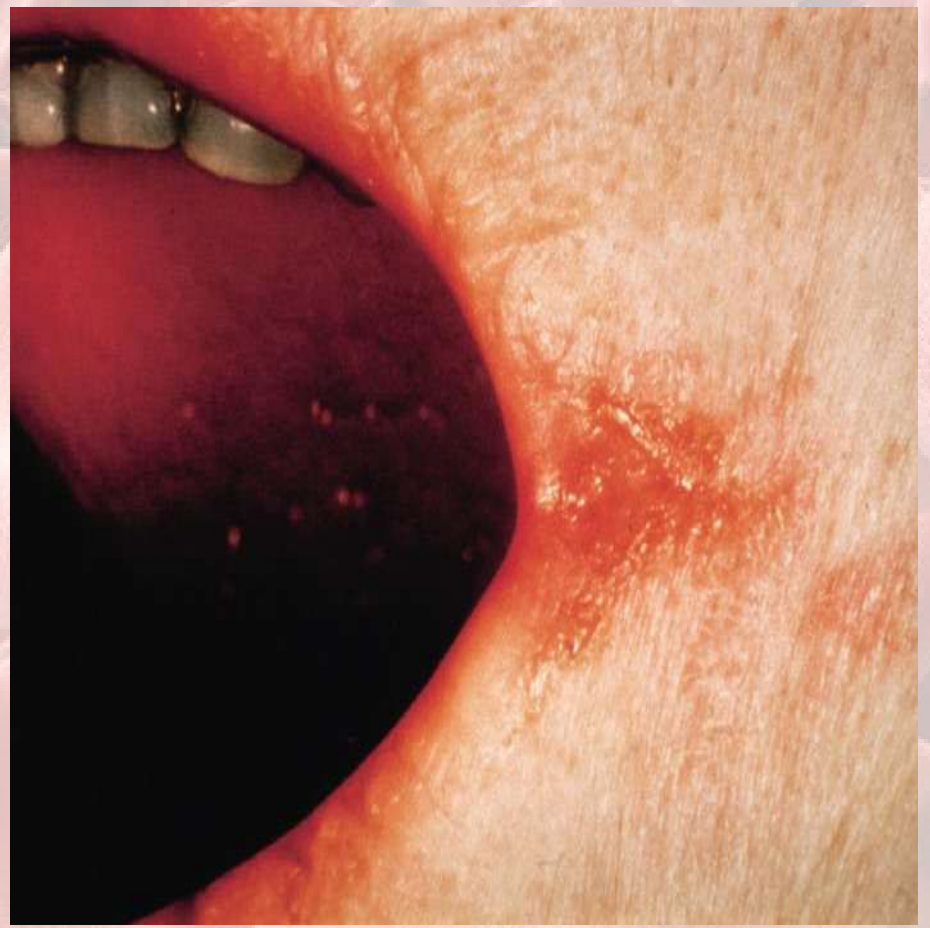
❑Clinical Features:

- Asymptomatic (mostly). unless diagnosed early through an incidental blood examination for other reasons.
- Insidious onset with gradually developing features of anemia. The patient may therefore not present until the anemia is quite severe.
- Jaundice (mild degree) of unconjugated type, due to ineffective erythropoiesis. Its combination with anemia, giving the patient a lemon-yellow tint.

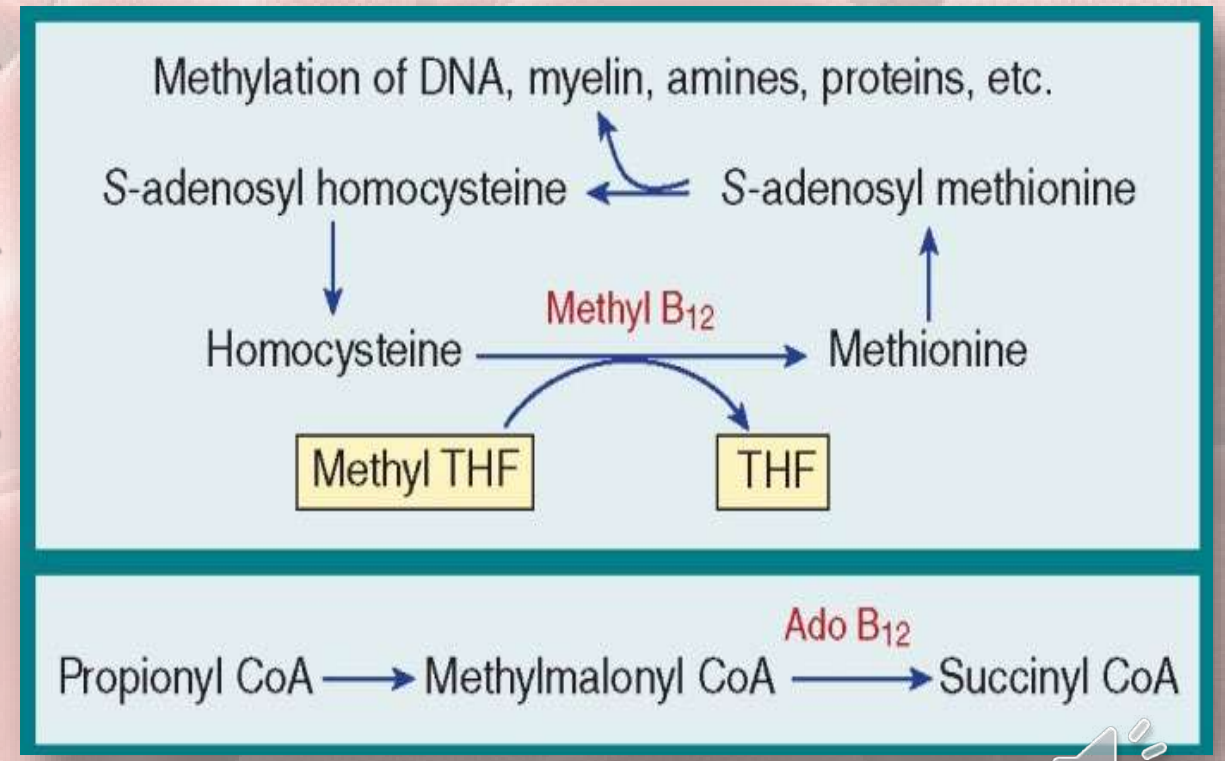


- Beefy red tongue (Glossitis) and angular stomatitis.





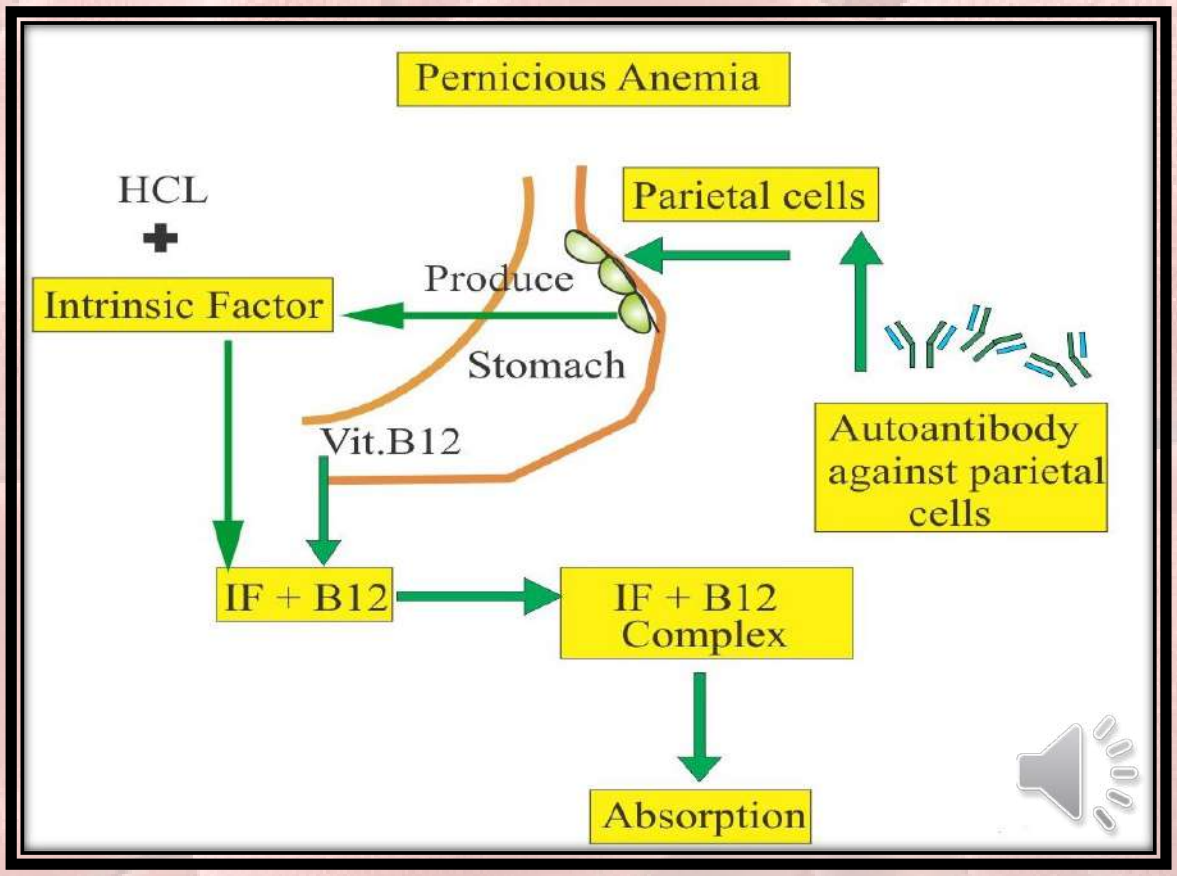
- Weight loss (Malabsorption).
- Purpura (thrombocytopenia).
- Abnormal melanin pigmentations.
- Infertility (gonads can affected in both male and female).
- B_{12} neuropathy (subacute combined degeneration of the cord); a progressive neuropathy affecting the sensory and motor mostly of the lower leg, due to demyelination of the spinal cord. This due to defective methylation process and subsequent change in SAM to SAH.



- The incidence of neural tube defects in the fetus is reduced by folic acid supplements at the time of conception and in early pregnancy.
- Visual and psychiatric disturbances are less frequent.
- Vitamin B12 deficiency can cause neuropsychiatric disorders without evidence of hematological abnormalities.

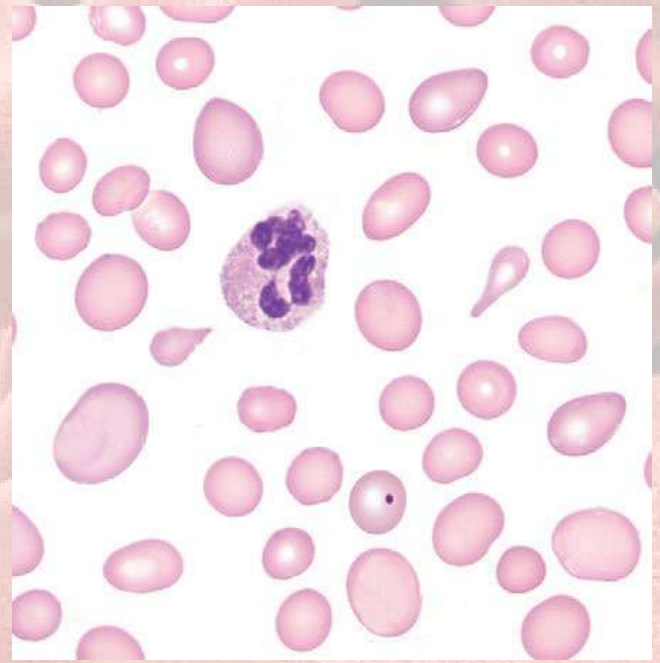
❖Pernicious Anemia

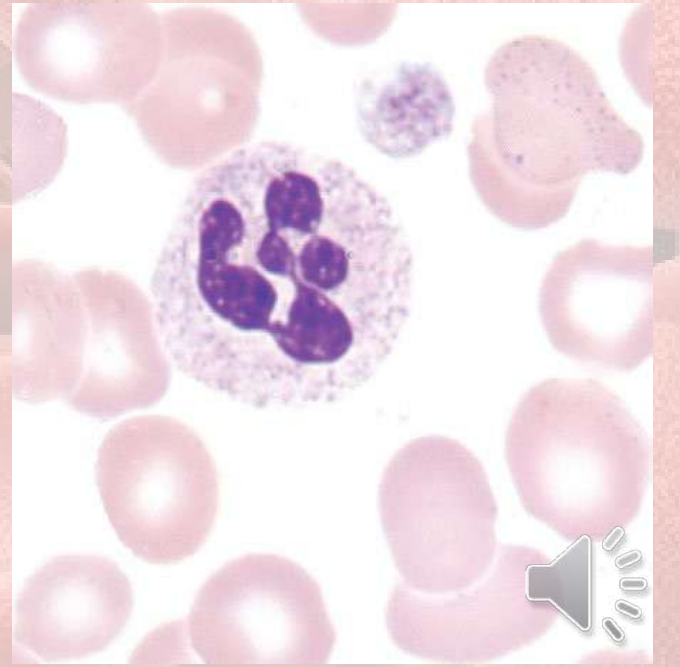
- Not uncommon cause of vitamin B_{12} deficiency.
- It is an autoimmune condition that affects stomach parietal cells with lack of IF secretion, with subsequent of vit B_{12} absorption.
- The exact cause of pernicious anemia is unknown, but it's more common in women around 60 years of age, people with a family history of the condition and those with another autoimmune condition, such as Addison's disease and vitiligo.



❑ Laboratory Findings:

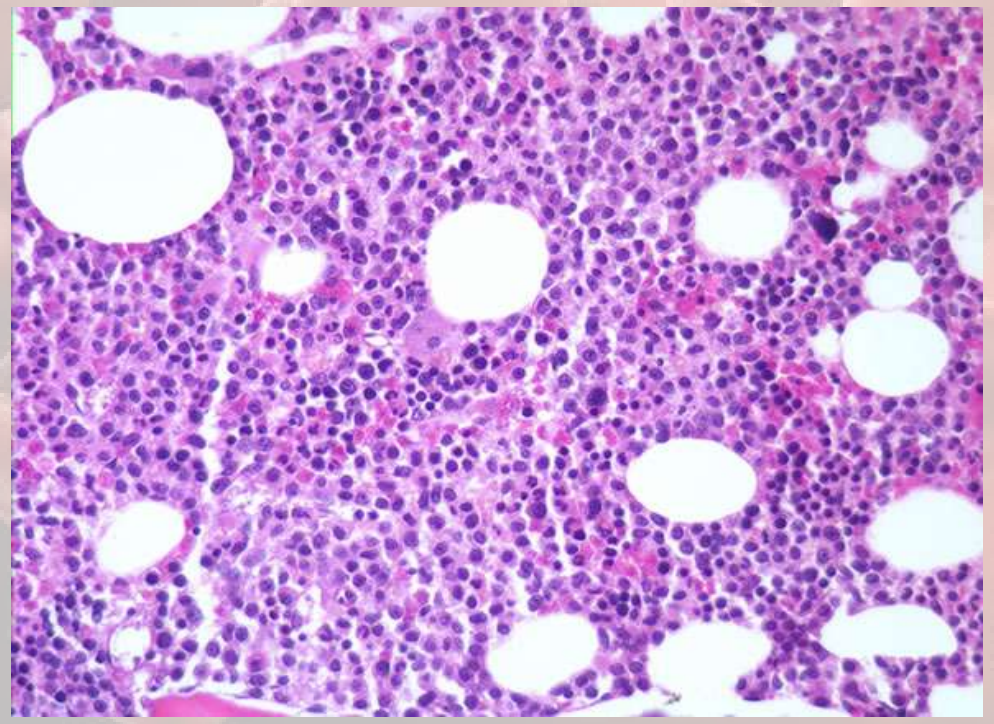
- Variable degrees of anemia with high MCV.
- Macrocytosis, mostly of oval shape.
- Reticulocytes; low.
- WBCs and platelets; reduced according to the severity.
- Hypersegmented neutrophils (6 or more lobes).
- Leukoerythroblastic picture (±); presence of nucleated RBC (erythroblast), and left shift of granulocyte (myelocyte).

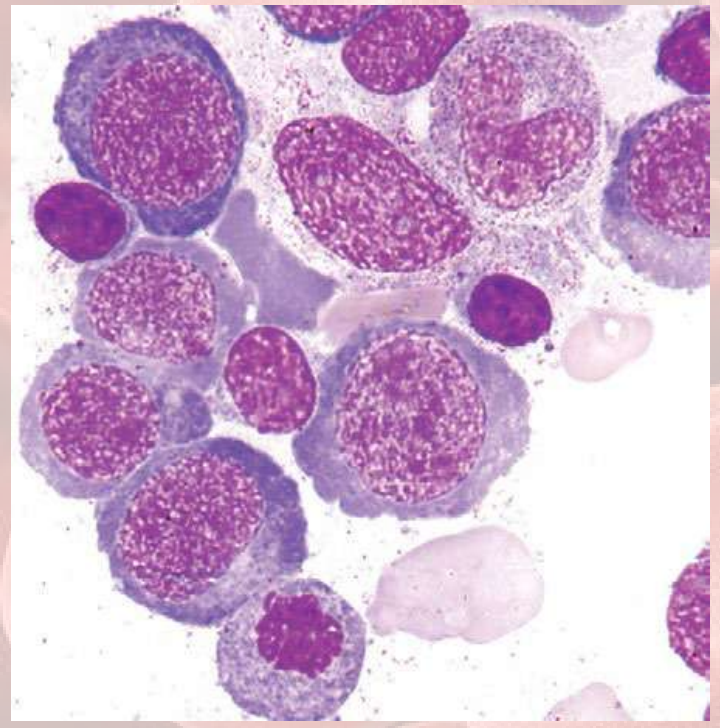


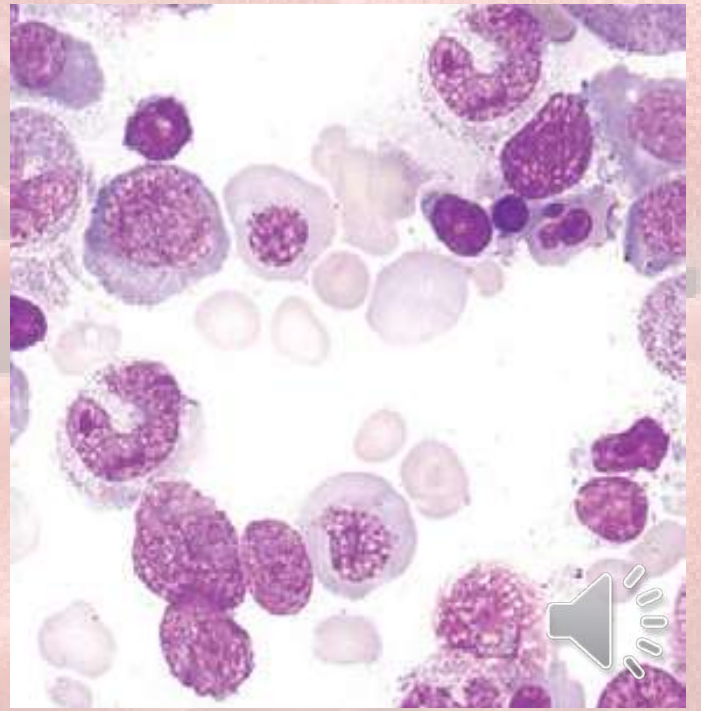


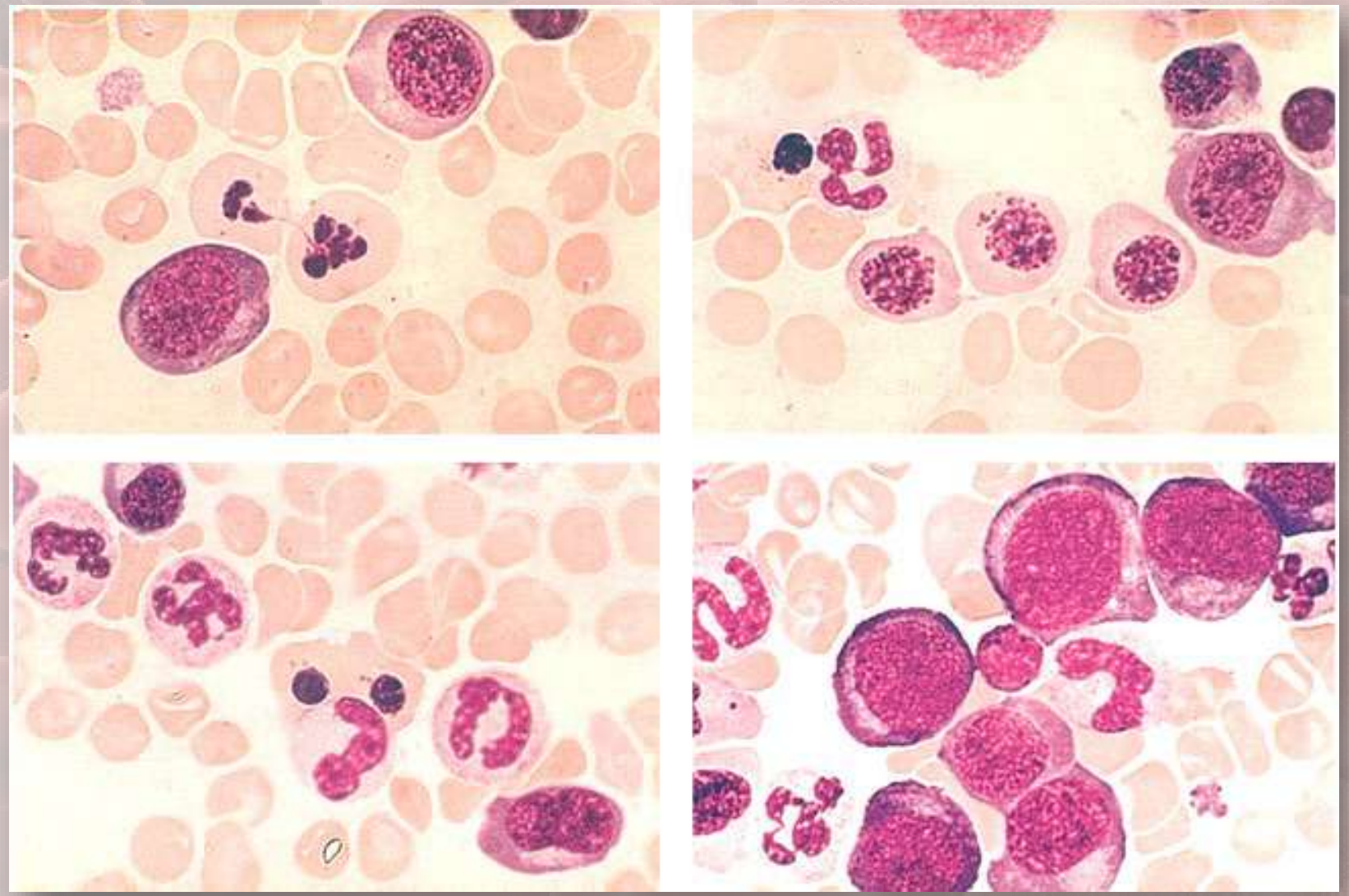
❑ BMA:

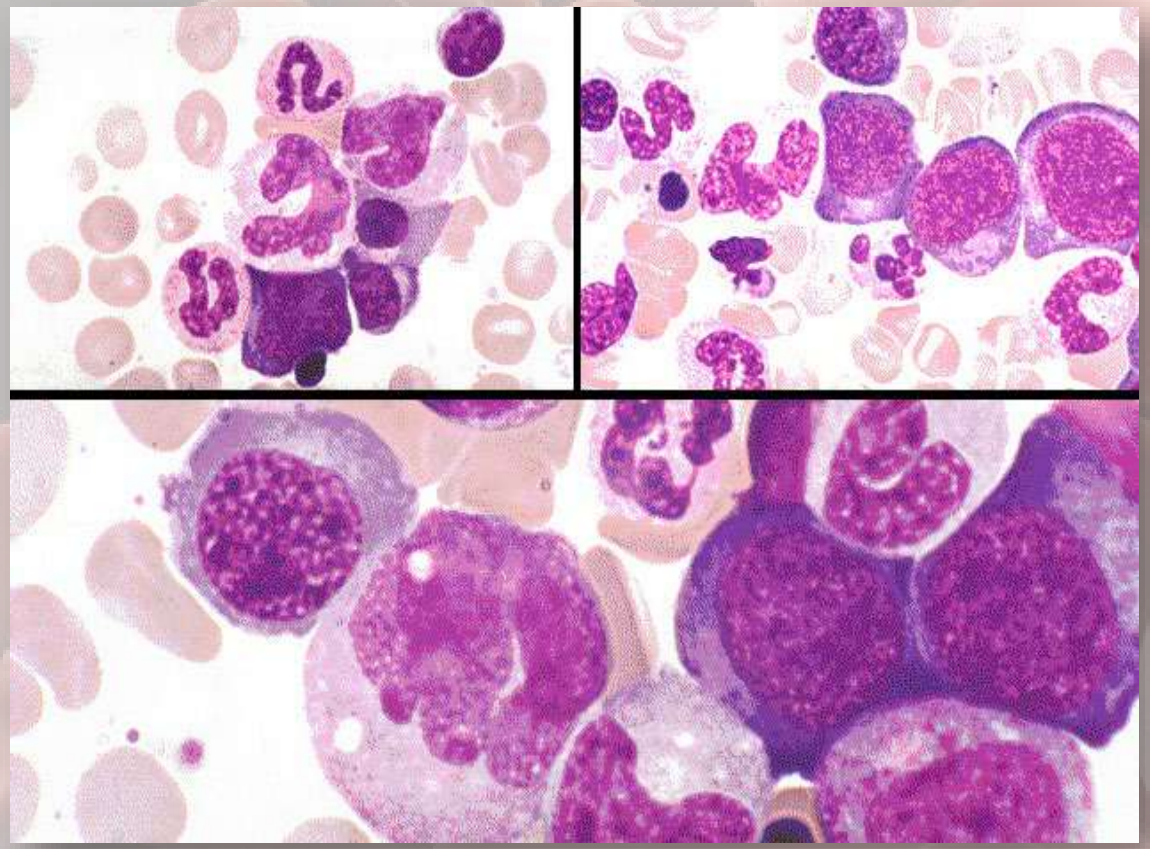
- Hypercellular, with increased erythropoiesis, mainly of the early forms.
- Erythroblast of megaloblastic maturation (asynchronization of nuclear and cytoplasmic maturation).
- Giant metamyelocytes.

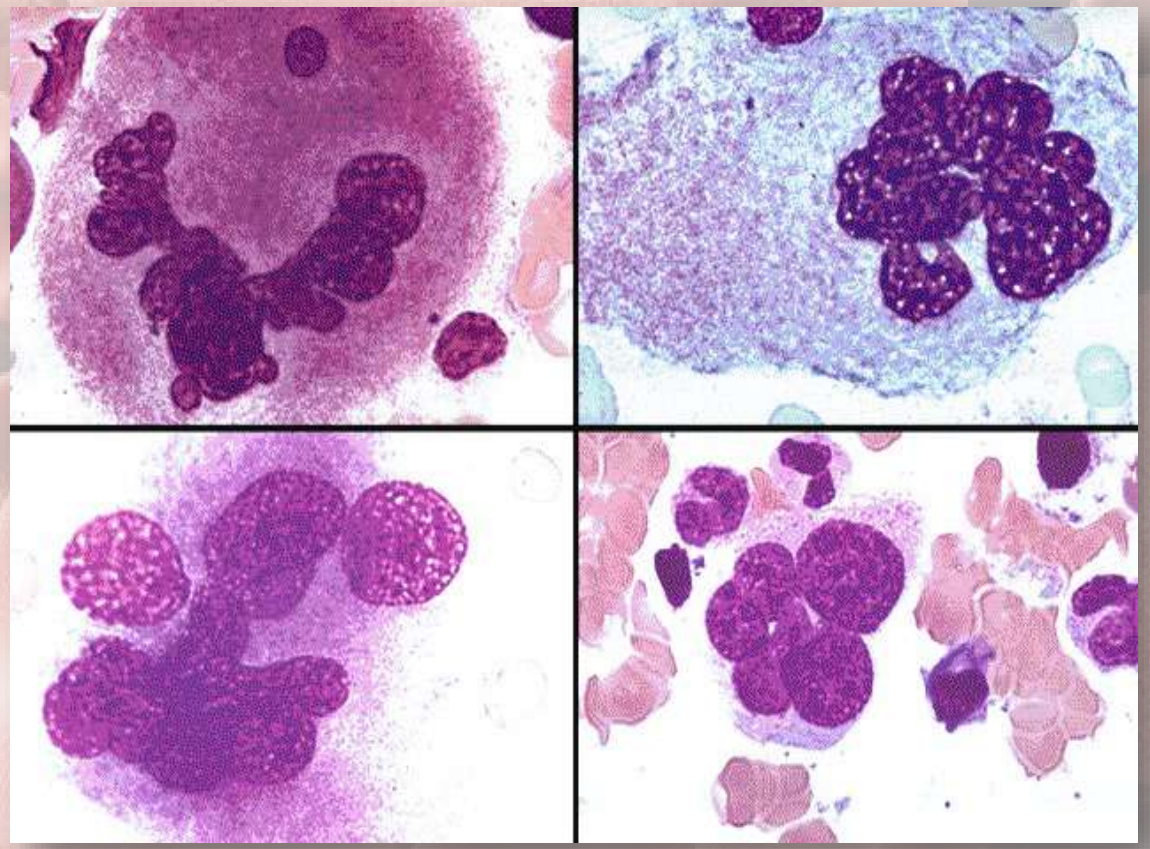












- Very high LDH levels due to excessive cell breakdown.
- Most useful laboratory tests are assays of serum vitamin B_{12} and red cell folate.
- Red cell folate is more informative than serum folate. Red cell folate reflects the body's stores of folate when the red cells were produced whereas serum folate reflects only recent folate ntake and absorption.

- Serum bilirubin (indirect, unconjugated) and LDH.
- Low serum B_{12} and/or Folate.

➢Search for underlying cause.

- **In Pernicious Anemia;**
- ***Schilling test*** (to differentiate between gastric and intestinal causes); shows reduced absorption of orally administered vitamin B_{12} that is corrected if the test is repeated with the addition of oral intrinsic factor. In small bowel B12 malabsorption there is no correction.
- Testing for antibodies to gastric parietal cells is a fairly sensitive test for pernicious anemia but is lacking in specificity.
- The presence of intrinsic factor antibodies has much better specificity although sensitivity is considerably less.

❑ Treatment:

- B_{12} ; 6 injections (im or sc) of hydroxocobalamin (1mg inj. twice a week for 3 wks. and maintenance every 3 m.) with FA (5 mg orally for 4 m).
- Given together, to avoid the possibility of increase neuropathy.
- Treat the underlying cause, and in elderly and cases of cardiac diseases must be more cautious.


thank you
danke
謝謝
ngiyabonga
شكراً جزيلاً
рахмат
teşekkür ederim
Баярлалаа
спасибо
faafetai lava
dank je
gracias
tapadh leat
хвала
asante
manana
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obrigada
mochchakkeram
bedankt
dziękuję
hvala
mauruuru
obrigado
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