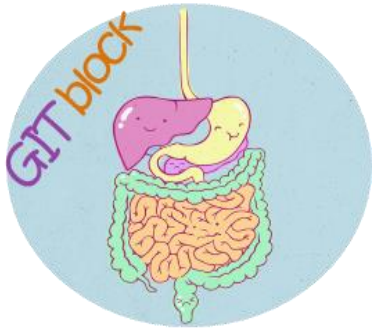


Megaloblastic anemia

NOTE : THIS TEAMWORK DON'T VIEW EVERYTHING IN THE SLIDES ONLY
THE IMPORANT THINGS NOTED BY THE DOCTORS

Color coding

- **important**
- **Extra info**
- **Notes from lecturer**

دعاء فبل المذاكرة :

(اللهم أني أسالك فهم النبين و حفظ الملرسلين و الملائكة المقربين اللهم اجعل السنتنا عامرة بذكرك و قلوبنا بخشيتك، أنك على كل شيئا قدير و حسبنا الله نعم الوكيل)

Please don't hesitate to contact us on:Haematology434@gmail.com

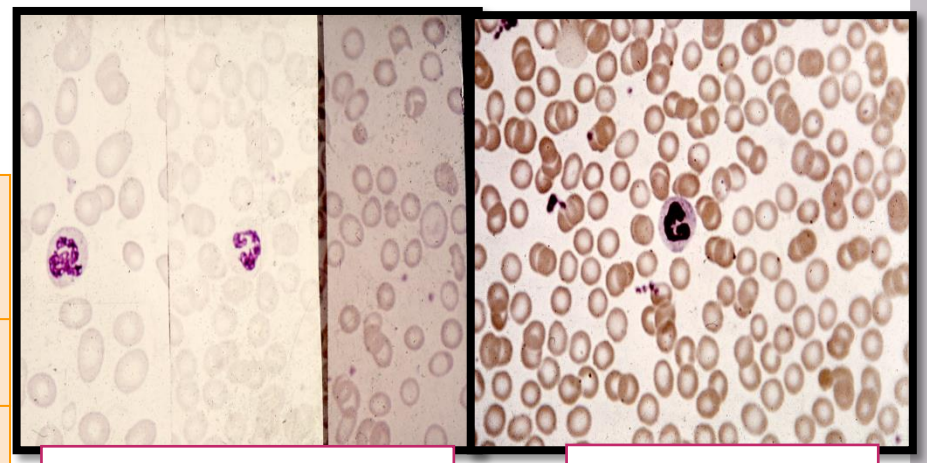
	Male	Female
Hemoglobin(g/dL)	13.5-17.5	11.5-15.5
Hematocrit (PCV) (%)	40-52	36-48
Red Cell Count ($\times 10^{12}$)	4.5-6.5	3.9-5.6
Mean Cell Volume (MCV) (fL)	80-95	
Mean Cell Hemoglobin (MCH) (pg)	30-35	
MCHC %	31 - 37	
Platelet count	140-450x109/L	
NORMAL PLATELET SIZE MPV	7.2-11.1 fl	
NORMAL PLATELET DIAMETER	1-2.5 µ	
WBC	4000-11,000 /L	
Segmented (neutrophils)	1.8-7.8	
Eos	0-0.45	
Baso	0-0.20	
Lymphs	1.0-4.8	
Monos	0-0.80	

- **In children normal haemoglobin values are: newborn:150 –210g/L, 3 months: 95 – 125g/L, 1 year to puberty:110 – 135g/L**
- **Children have higher lymphocytes count**

A Good Doctor Knows CBC

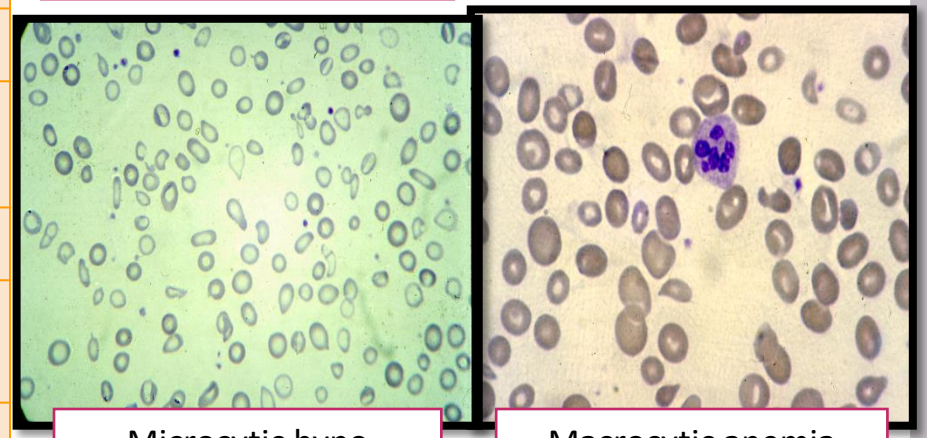
Normocytic normochromic anemia & Microcytic hypochromic anemia

Microcytic Hypochromic Anaemia	Normocytic Normochromic Anaemia
MCV< 80 FL	MCV 80 - 95 FL
MCH< 27 pg	MCH> 26 pg
Iron deficiency	Many haemolytic Anaemia
Thalassaemia	Anaemia of chronic disease (some cases)
Anaemia of chronic disease (some cases)	Bone marrow failure, e.g. post-chemotherapy
Lead poisoning	Renal disease
Sideroblastic anaemia (some cases)	Mixed deficiencies
	After acute blood loss



Normocytic normochromic

Microcytic hypo chromic

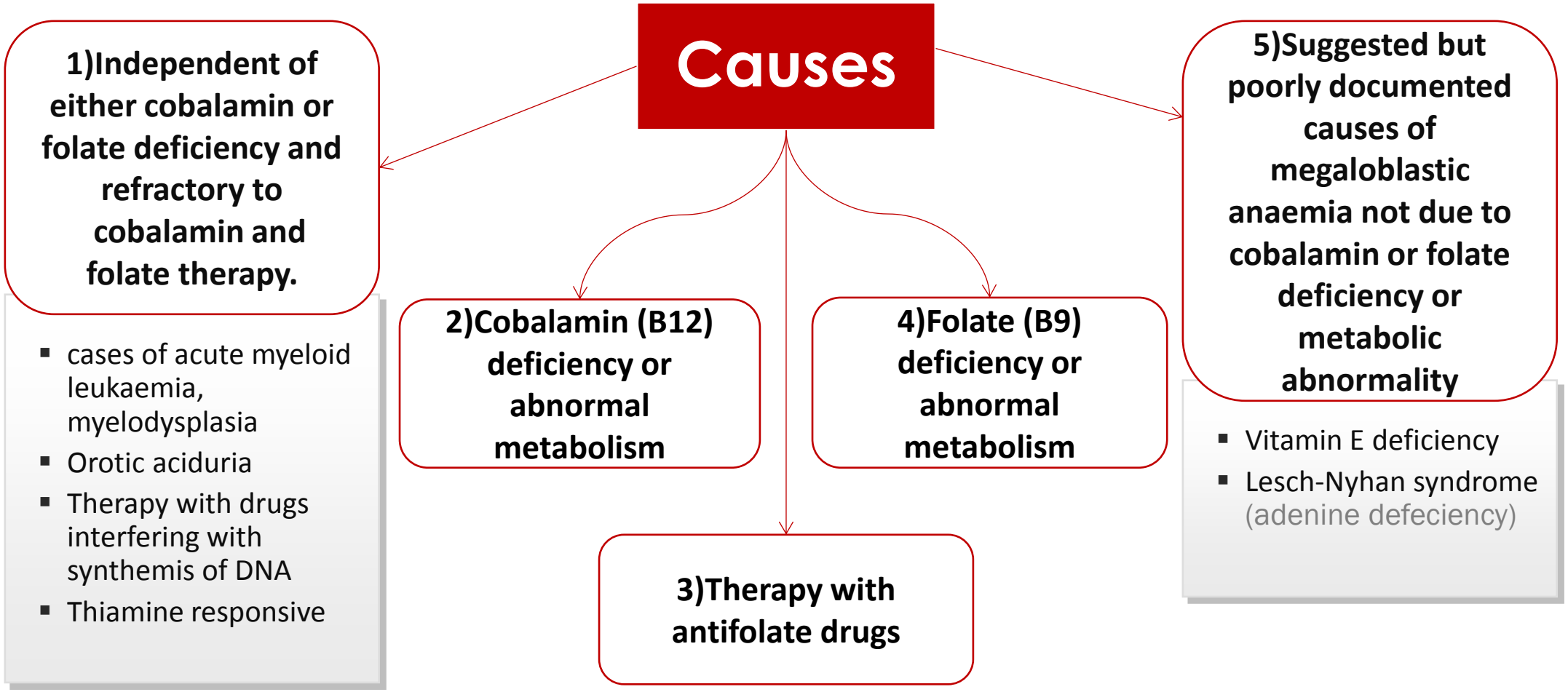


Microcytic hypo chromic
Sever iron deficiency anemia

Macrocytic anemia

Megaloblastic anemia

It is an anemia of **macrocytic classification** that results from inhibition of DNA synthesis during RBCs production



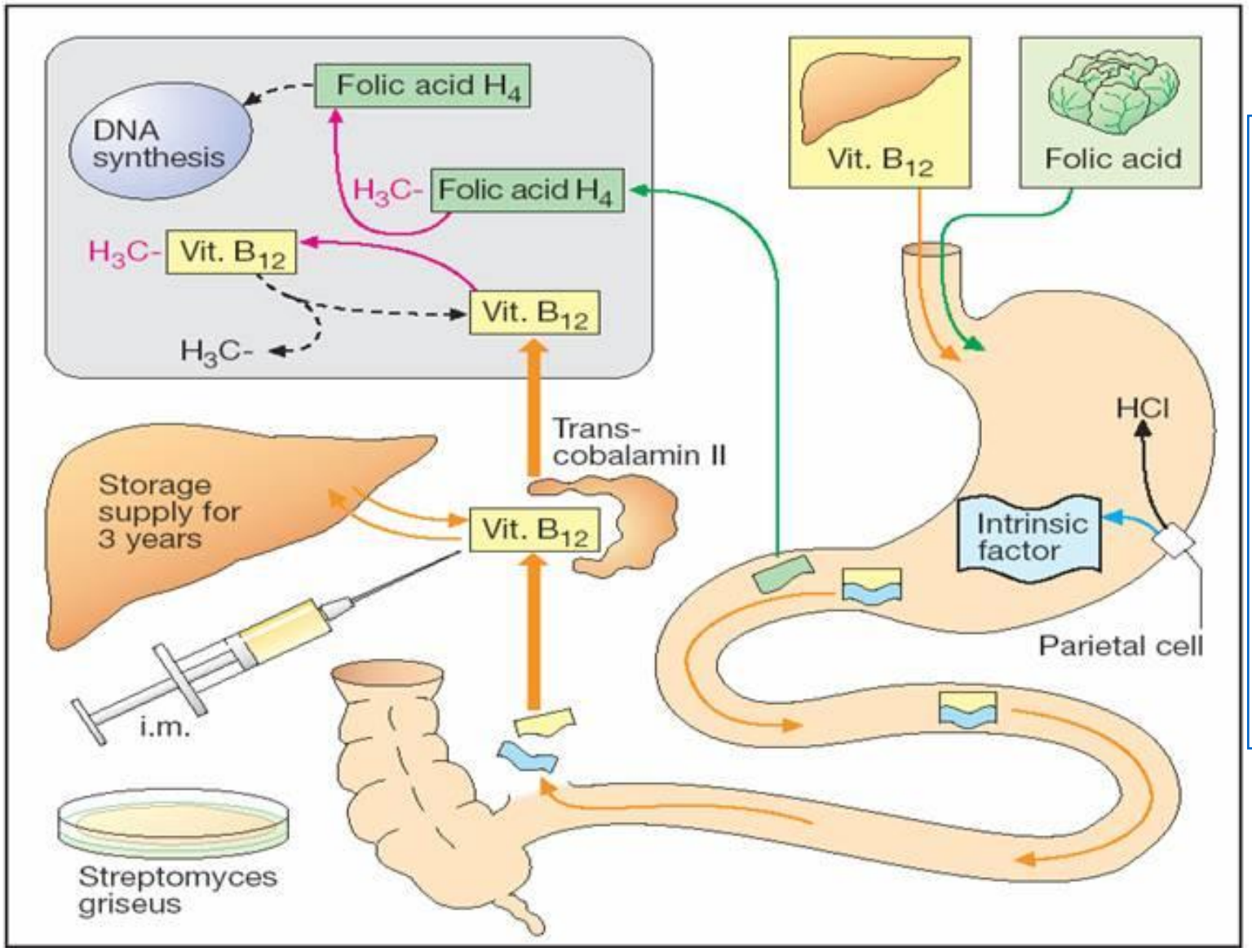
Vitamin B12 and folate nutrition and absorption

	Vitamin B12	Folate
Dietary source	Only food of animal origin, especially liver	Most foods, especially liver, green vegetable and yeast; destroyed by cooking
Average daily intake*	7 - 30 µg	200-250 µg
Minimum daily requirement*	1-3 µg	100-200 µg†
Body stores*	3-5 mg, mainly in the liver	8-20 mg, mainly in the liver
Time to develop deficiency in the absence of intake or absorption*	Anaemia in 2-10 years	Macrocytosis in 5 months.
Requirements for absorption	Intrinsic factor secreted by gastric parietal cells	Conversiion of polyglutamates to monoglutamates by intestinal folate conjugase
Site of absorption	Terminal ileum	Duodenum and jejunum

* In adults.

† Higher during pregnancy and lactation.

Vitamin B12 & B9 absorption



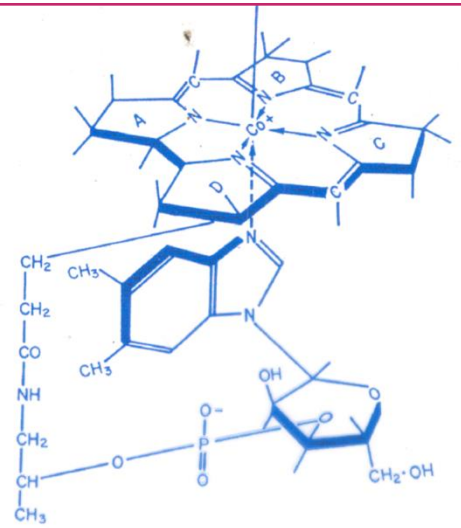
- Absorption of dietary **vit B12** after combination **with intrinsic factor** which is released from the stomach**, through terminal ileum.**

- **Folate** absorption occurs **through the duodenum and jejunum** after conversion of all dietary forms to **methyltetrahydrofolate (THF).**

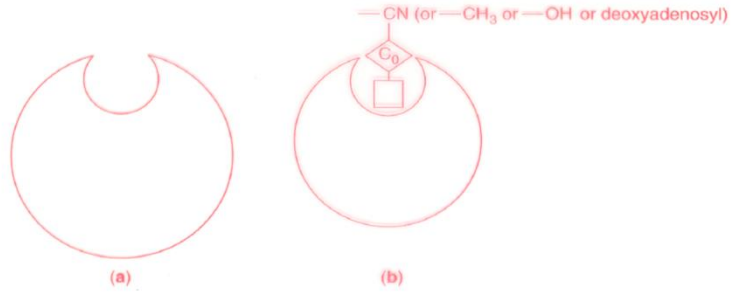
Causes vitamin B12 deficiency

- **Inadequate intake:** Veganism, lactovegetarianism (some cases) strict diet.
- **Inadequate secretion of intrinsic factor:** Pernicious anaemia antibody of intrinsic factors, Total or partial gastrectomy.
- **Congenital intrinsic factor deficiency (rare).**
- **Inadequate release of B12 from food:** Partial gastrectomy, vagotomy, gastritis, acid-suppressing drugs, alcohol abuse.
- **Diversion of dietary B12:** Abnormal intestinal bacterial flora multiple jejunal diverticula, small intestinal strictures, stagnant intestinal loops. Normaly small intstine has no bacteria.
- **Diphyllobothrium latum** flat tape worm.
- **Malabsorption:** Crohn's disease, ileal resection, chronic tropical sprue, congenital selective B12 malabsorption with proteinuria (Imerslund-Grasbeck syndrome).

Structure of cobalamin(not important)



The structure of vitamin B_{12} (cyanocobalamin).



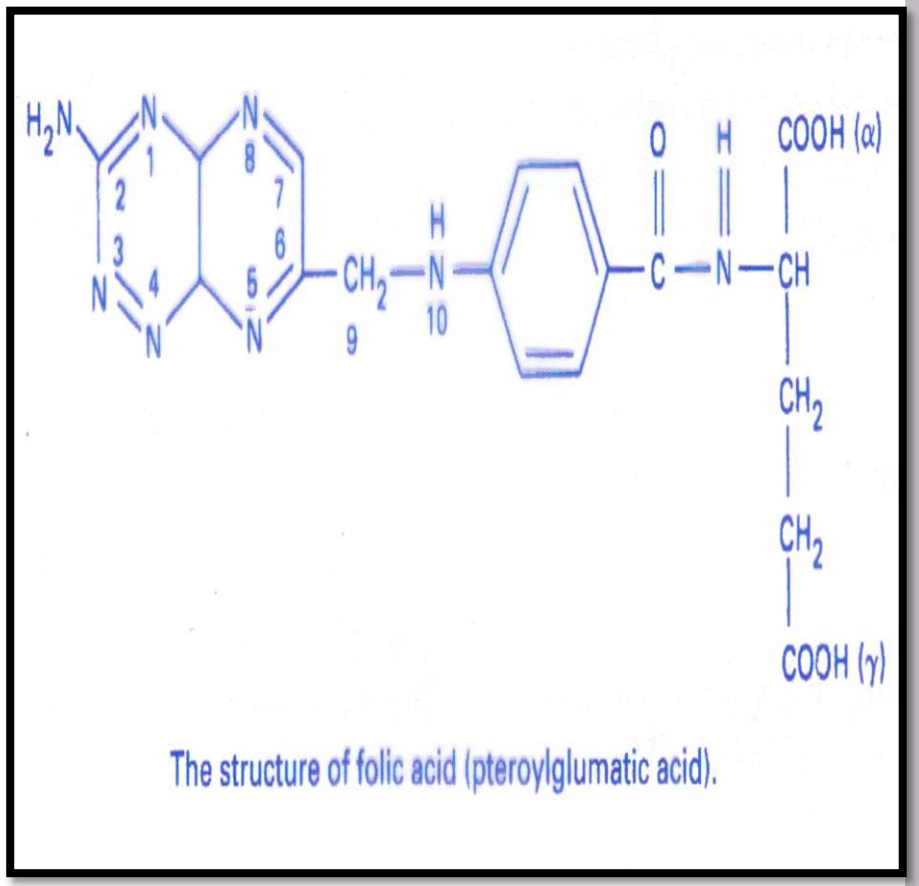
(a) Intrinsic factor and **(b)** intrinsic factor–cobalamin complex. Intrinsic factor has been estimated to have a molecular radius of 3.6 nm, vitamin B_{12} 0.8 nm, and the complex 3.2 nm.

Folate deficiency

It is called folic acid or folate (vitamin B9).

- **Causes of deficiency:**
- **Inadequate dietary intake**
- **Malabsorption:** Coeliac disease, jejunal resection, tropical sprue.
- **Increased requirement:** Pregnancy, premature infants, chronic haemolytic anaemias, myelofibrosis, various malignant diseases.
- **Increased loss:** Long-term dialysis, congestive heart failure, acute liver disease.
- **Complex mechanism:** Anticonvulsant therapy, ethanol abuse Only some cases with macrocytosis are folate deficient.

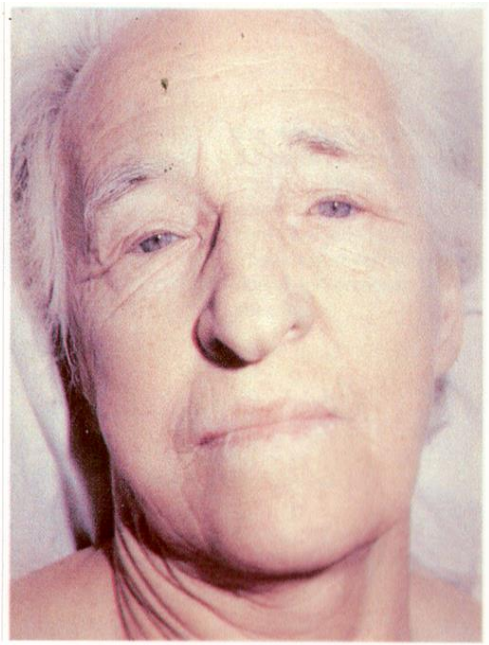
Structure of folate(not important)

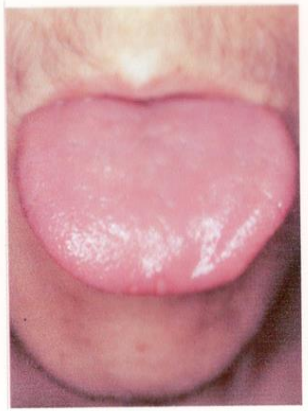


The structure of folic acid (pteroylglumatic acid).

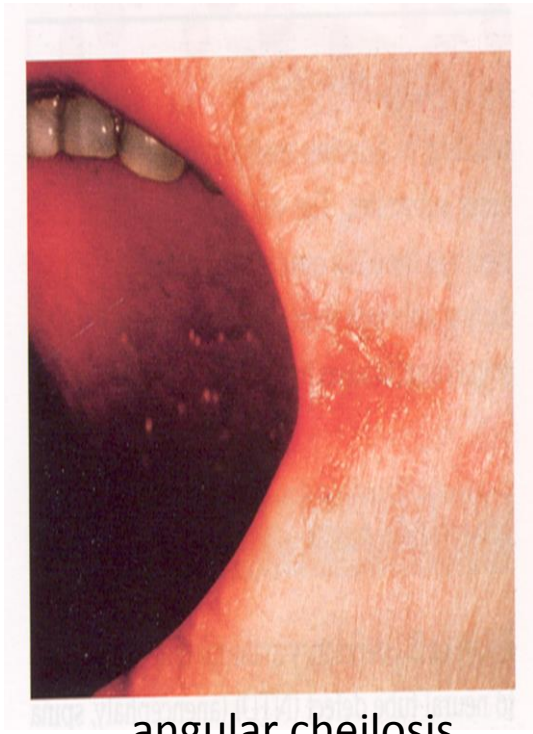
Clinical presentation

Clinical Features of Megaloblastic Anaemia – Progressive symptoms and signs of anaemia
Weakness, anorexia, weight loss, diarrhea or constipation, tiredness, shortness of breath, angina of effort, heart failure
Mild jaundice, glossitis (hypertrophy/every inflammation) ,stomatitis, angular cheilosis many lips splits
Purpura, melanin pigmentations
Infections





glossitis



angular cheilosis

Neuropathy due to Vit B12 and folate deficiency

Neuropathy due to Vit B12 and folate deficiency

- Progressive neuropathy affecting:

- The peripheral sensory nerves
- Posterior and lateral columns of the spinal cord (subacute combined degeneration of the cord)
- Optic atrophy
- Psychiatric symptoms

-The neuropathy is likely due to accumulation of S-adenosyl homocysteine and reduced level of S-adenosyl methionine in nervous tissue resulting in defective methylation of myelin and other substrates.

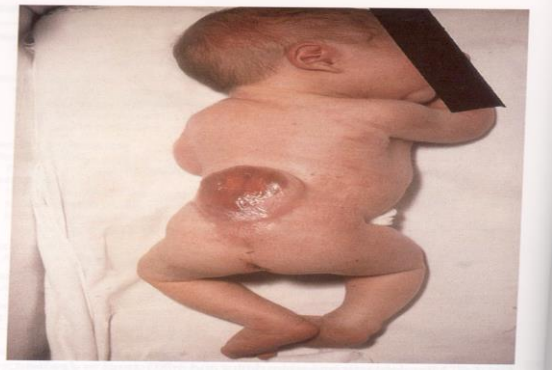
- Neuropathy is mostly due to vitamin B12 deficiency.

Neural tube defect (NTD):

- (**Anencephaly, spina bifida or encephalocoele**) **in the fetus due to folate or Vit B12 deficiency in the mother**. This result in build-up of homocysteine and S-adenosyl homocysteine in the fetus which impair methylation of various proteins and lipids.

- **Polymorphism in the enzyme 5,10 methylene tetrahydrofolate reductase (5,10-MTHFR). This mutation** (677 C T) in the MTHFR gene **results in low serum and red cell folate and high serum homocysteine in the parents and fetus with NTD.**

- **Cleft palate and hair lip.**



Haematological findings in Megaloblastic Anaemia

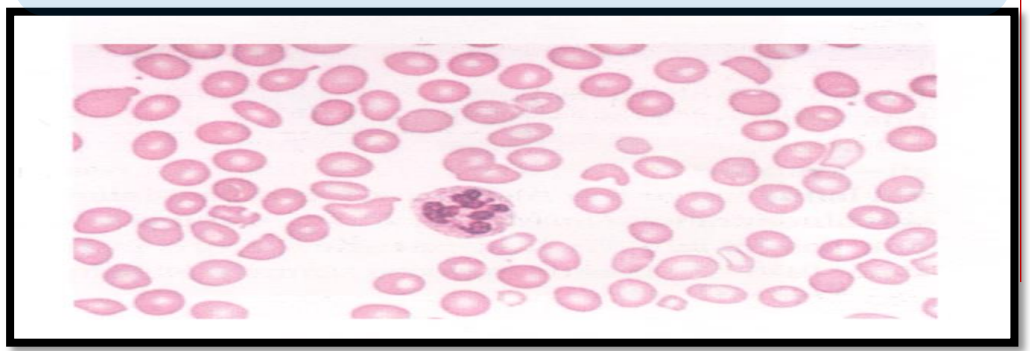
Peripheral blood

Macrocytic anaemia, oval macrocytes, anisocytosis, poikilocytosis high MCV.

Dimorphic anaemia when it is associated with iron deficiency or with thalassaemia trait.

Hypersegmented neutrophils.

Leucopenia and thrombocytopenia



Bone marrow

❖**Hypercellular marrow** with M:E ratio in normal or reduced.

❖**Accumulation of primitive cells** due to selective death of more mature cells.

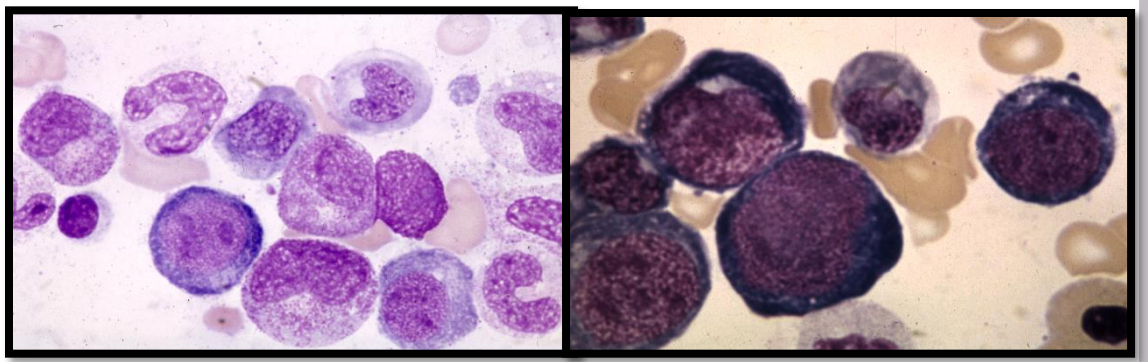
❖**Megaloblast** (large erythroblast which has a nucleus of open, fine, lacy chromatin).

❖**Dissociation between the nuclear and cytoplasmic development in the erythroblasts.**

❖Mitosis and dying cells are **more frequent than normal.**

❖**Giant and abnormally shaped**, metamyelocytes, polypoid megakaryocytes.

❖**Increased stainable iron** in the macrophage and in the erythroblasts**.**



Other laboratory abnormalities:

Chromosomal abnormalities
Ineffective haemopoiesis (Intramedullary cell death by apoptosis) associated with increased serum indirect bilirubin
↑ urobillinogen and faecal stercobillinogen
↑ LDH ↑ serum iron ↑ blood carbon monoxide
↑ serum lysozyme
↓ reduced haptoglobins
Positive schumm's test
Positive urine haemosiderin

Treatment (not important)

Vitamin B12 deficiency	Folate deficiency
Intra masculare hydroxocobalamin	Oral folic acid
6 days (for 2-3 weeks) then once every 3 months	Daily for 4 months
In some cases we give treatment as prophylactic: 1- total gastrectomy 2- illegal resection	In some cases we give treatment as prophylactic: 1- pregnancy 2- severe hemolytic anemia 3- dialysis 4- prematurity

Causes of macrocytic of hypersegmented neutrophil other than megaloblastic anemia

macrocytosis
Alcohol
Liver diseases
Myxoedema
Myelodysplastic syndrome
Cytotoxic drugs
Aplastic anemia
Pregnancy
Reticulocytosis
Myeloma and paraprotienemia
Neonatal

Hyper segmented neutrophil
Renal failure
Congenital familial abnormalities

1-Which one of these lead to microcytic hypochromic anemia:

A. renal failure
B. MCH> 26 pg
C. thalassemia
D. non of the above

2- which one is not a cause of megaloblastic anemia:

A. high folic acid intake
B. cobalamin defeciency
C. folate deficiency
D. abnormal metabolism

3- time in developing folate deficiency in absence of intake or absorption:

A. anemia 2-3 years
B. anemia in 5 months
C. macrocytosis in 2-3 years
D. macrocytosis in 5 months

4- which one is the cause of vit B12 deficiency:

A. Inadequate release of B12 from food
B. diversion of diatry B12
C. malabsorption
D. all of the above

5-clinical presentation of megaloblastic anemia:

A. mild jaundice
B. purpura
C. A &B
D. none of them

6-other laboratory abnormalities in megaloblstic anemia:

A. ↓ urobillinogen
B. ↓ reduced haptoglobins
C. ↓ serum iron
D. ↓ blood carbon

1- C
2- A
3- D
4- D
5- C
6- B

Q1 what are the heamatological findings in peripheral blood?

Perepheral blood : Macrocytic anaemia, oval macrocytes, anisocytosis, poikilocytosis high MCV, Dimorphic anaemia when it is associated with iron deficiency or with thalassaemia trait , Hypersegmented neutrophils, Leucopenia and thrombocytopenia.

Q2 how does hypersegmented neutrophil be happen other than megaloblastic anemia?

-Renal failure

-Congenital familial abnormalities

Q3 what are the site of vit B12 & B9 absorption?

-B12 : terminal ileum

-B9 : duodenum and jejunum

Thank you for checking our work

Now you can check a lecture out :D

Done by:

Khalil alhindas

Salih albnyan

Abdulrahman alnoaem

Mohammed albadrany

Reviewed by:

Hadeel B.Alsulami

Abdullah M.albasha

If you donate money,

you give food!

But if you

donate blood,

you give Life!!

دعاء بعد المذاكرة :

(اللهم اني أستودعتك ما قرأت وما حفظت وما تعلمت، فرده لي عند حاجتي اليه أنك على كل شيء قدير، وحسبنا الله ونعم الوكيل)