Anemia

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4/11/18

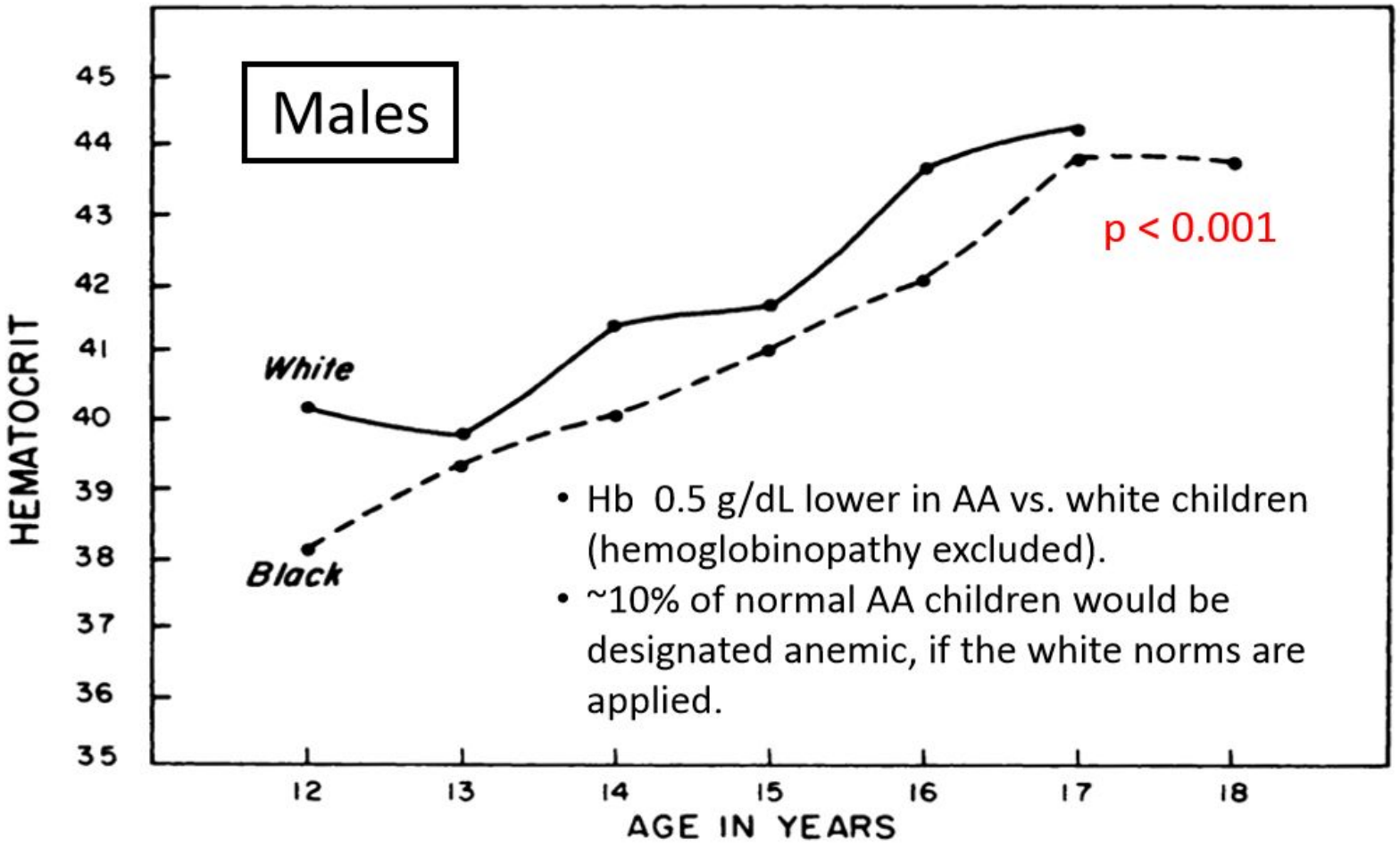
Definition

- Statistical
- Physiologic

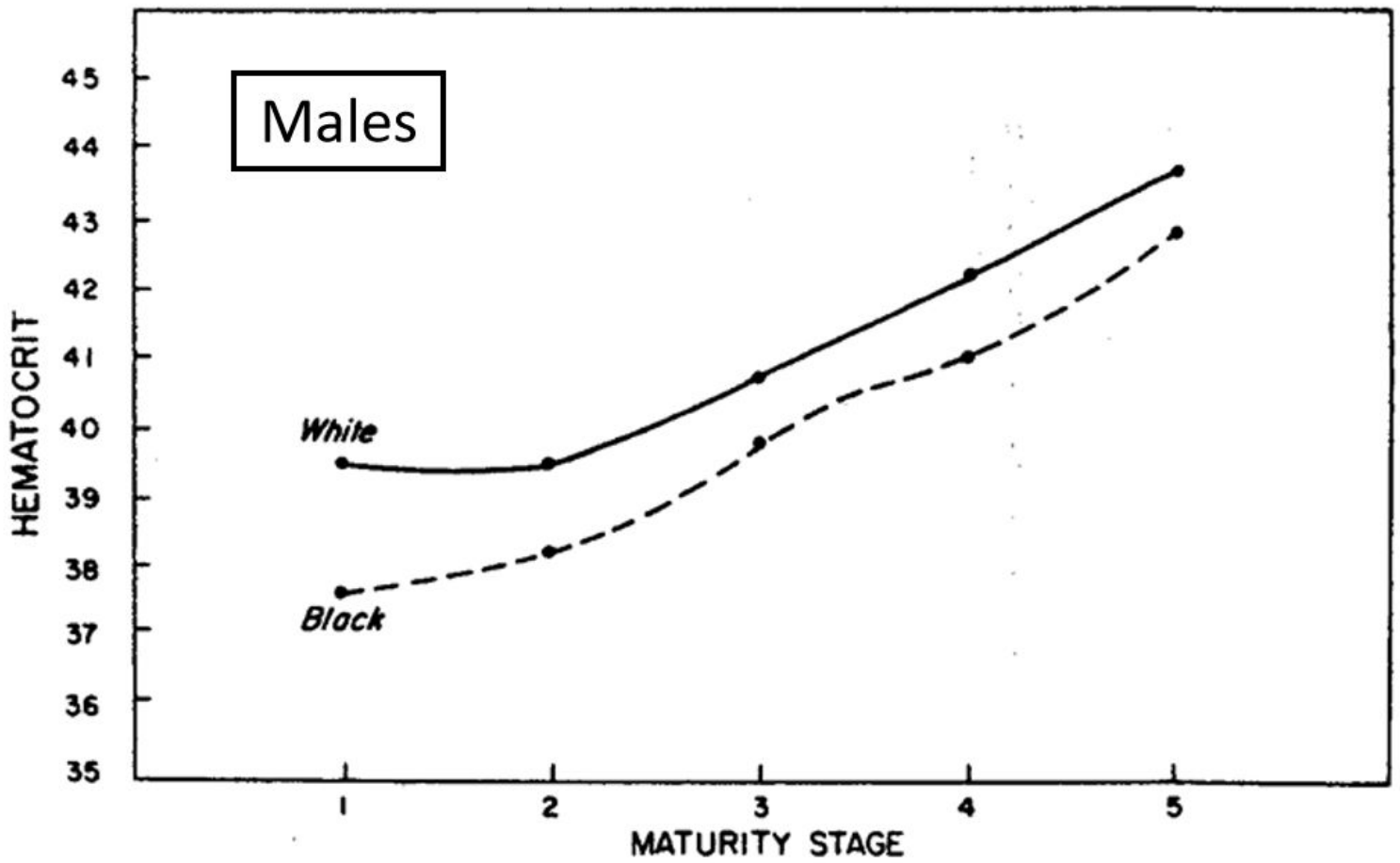
Factors deciding normal hemoglobin values.

- Age.
- Gender.
- Race.
- Altitude.
- Hereditary factors
- Hormonal factor.

Racial differences in Hemoglobin



Tanner Stage and Hematocrit



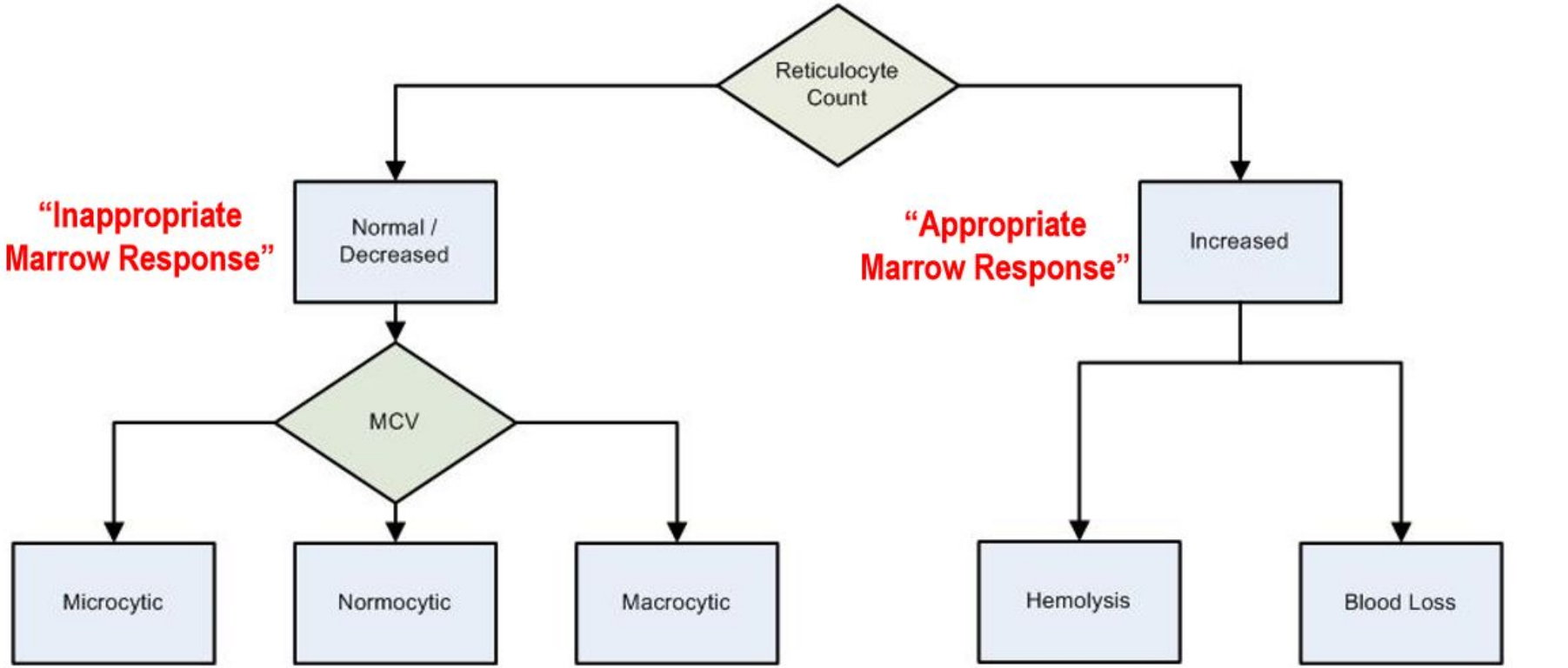
Daniel WA, Pediatrics 1973;52:388-94

Classification of anemia

- By morphology: helps diagnose cause.
- By pathophysiology: helps diagnose cause

- By cause: helps guide treatment.

Pathophysiologic Approach to Anemia



Fe deficiency
Thalassemia
Lead
ACD ('late')
Sideroblastic

Myelophthisic
BM invasion
Non Myelophthisic
Low Epo / Renal
ACD ('early')
BM Hypo/Aplasia

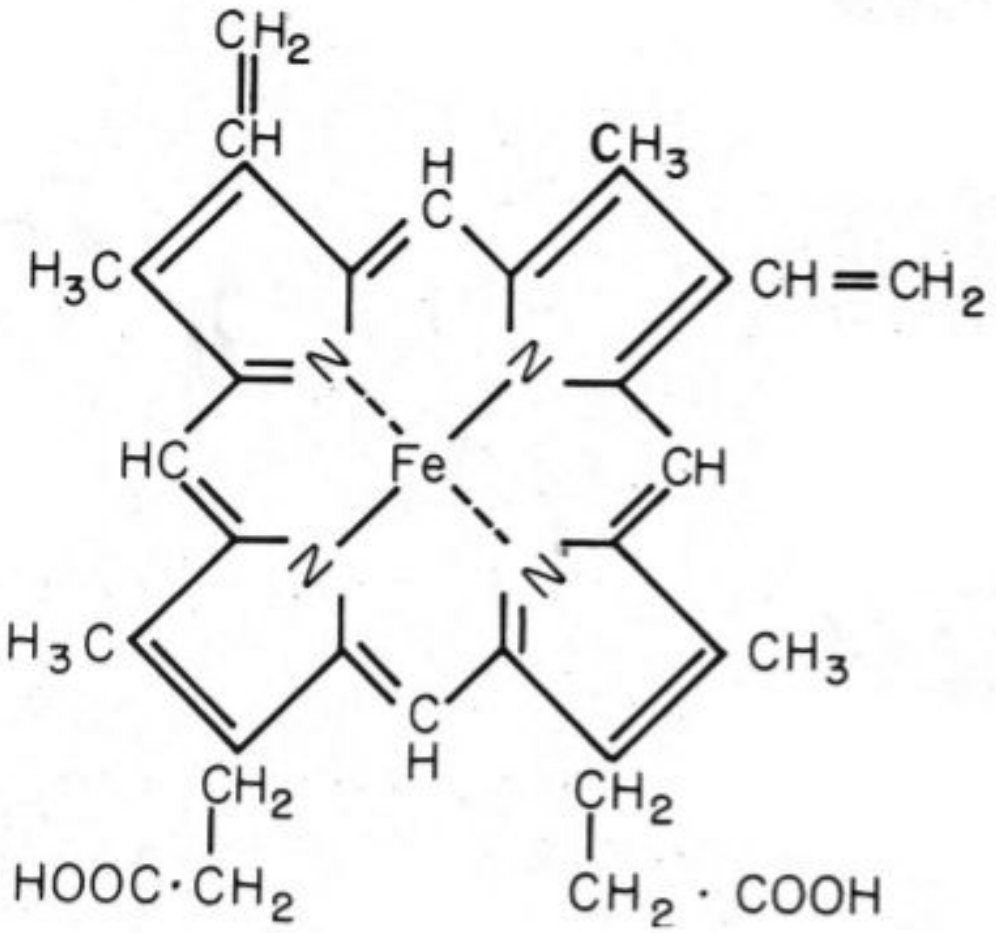
Megaloblastic
B12 / Folate
Medication
Non-Megaloblastic
BM Hypo/Aplasia

Extrinsic to RBC
Immune (direct Coombs +)
Non-Immune (mechanical, microangiopathic)
Intrinsic to RBC
Membrane, Hb
Enzyme

Nutritional Anemias:

Iron deficiency anemia.

- Most common anemia worldwide.
- For better understanding, we need to review iron absorption and metabolism.


CH2
CH
CH3
H
C
H3C
CH=CH2
N
N
HC
Fe
CH
N
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H3C
CH3
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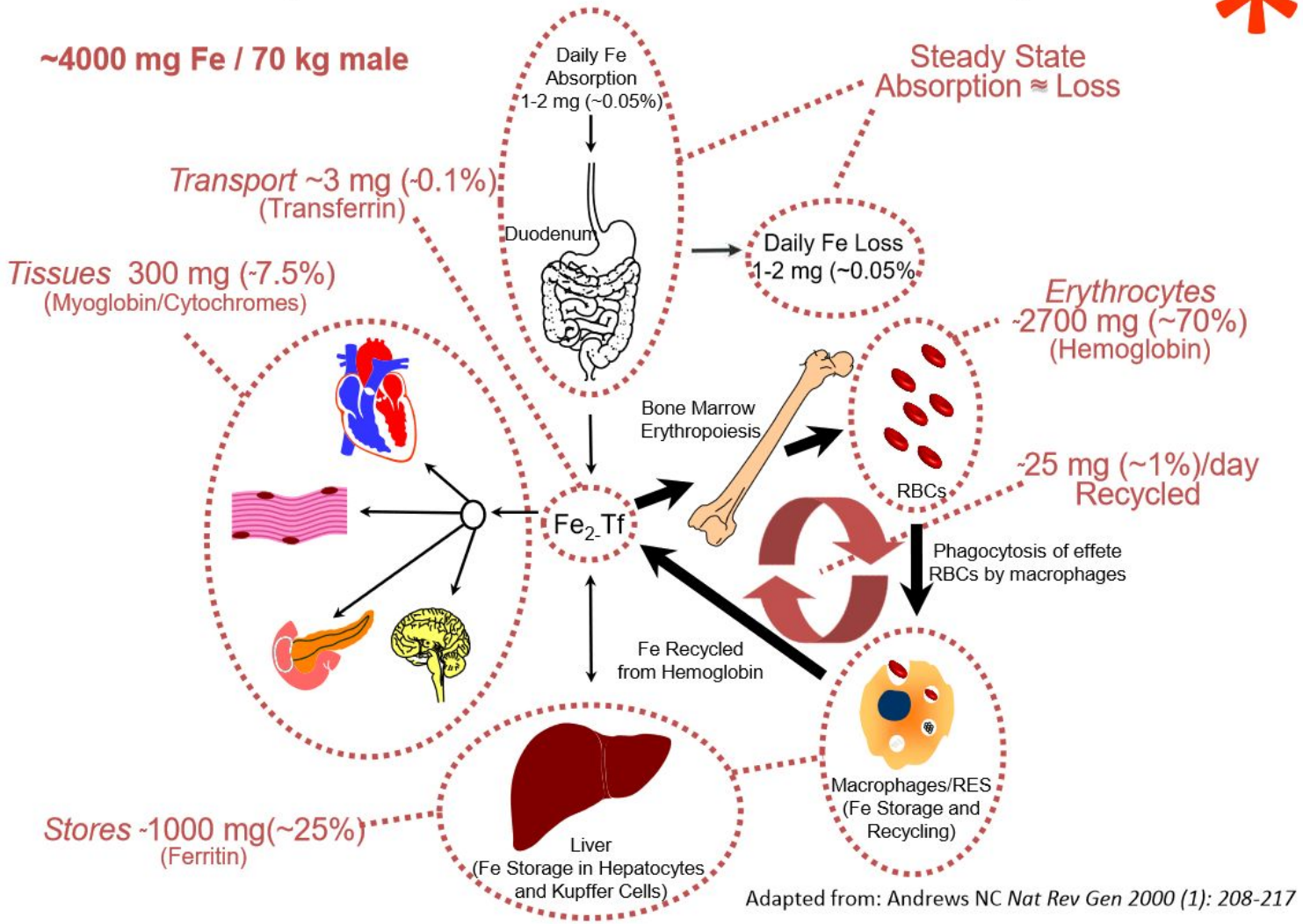
H
CH2
CH2
HOOC·CH2
CH2·COOH

Systemic iron economy

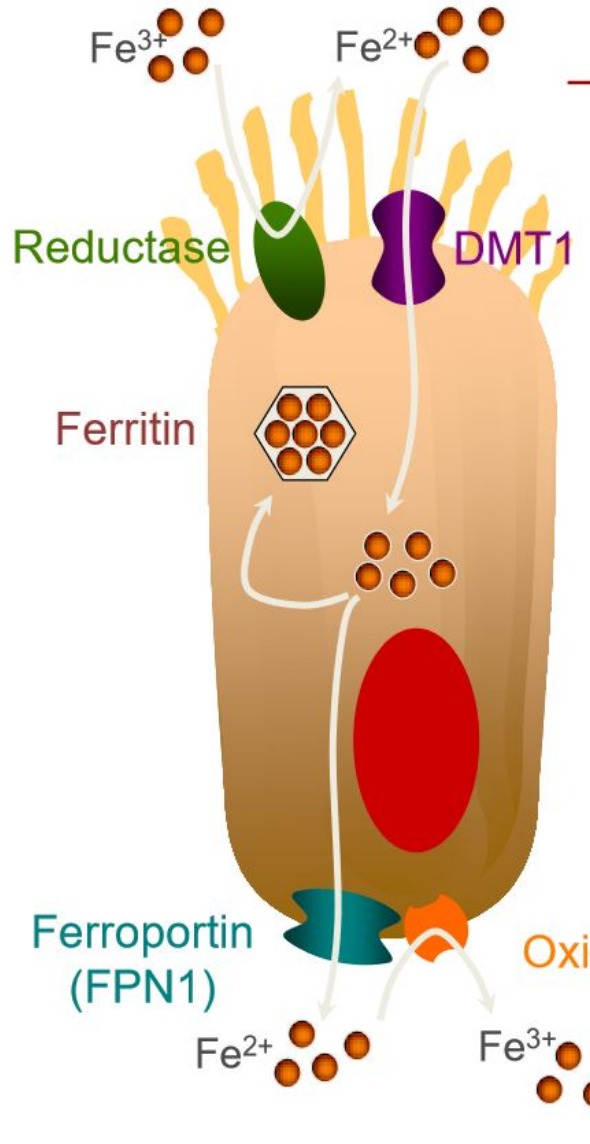


Dietary iron comes in 2 forms

Heme iron

Non – heme iron

Intestinal iron absorption



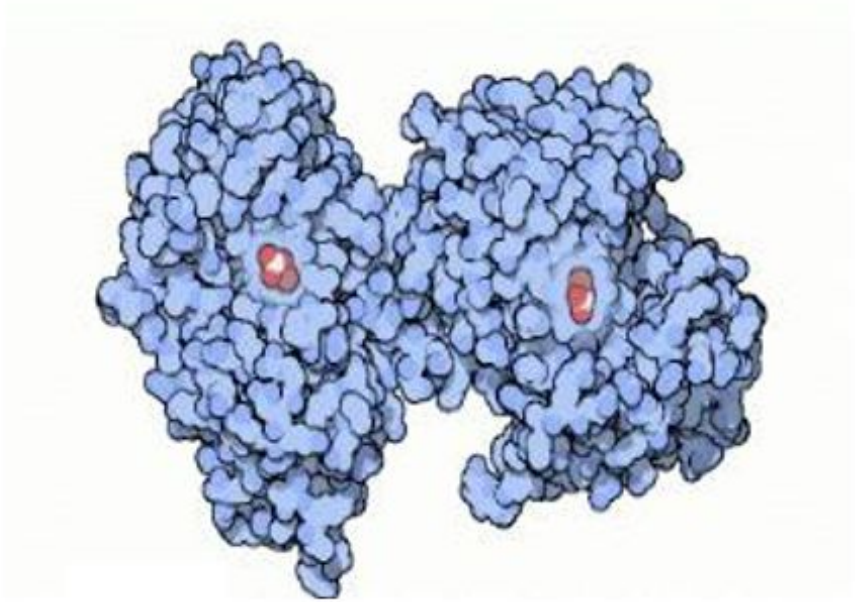
- Elemental iron absorption occurs in enterocytes in the duodenum
  - Heme iron >> elemental iron
  - Mechanism of heme iron absorption unknown
- Elemental iron is largely in the form of iron oxy-hydroxides (*rust*)
  - Fe^{3+} must be solublized and reduced to Fe^{2+}
  - The identity of the reductase is uncertain.
- DMT1 transports Fe^{2+} at the apical side.
  - Dependent upon acidic pH
- Iron can be stored as ferritin and eventually sloughed into the waste stream.
- FPN1 exports Fe^{2+} at the basolateral side.
- Fe^{2+} is oxidized to Fe^{3+} to bind to transferrin (Tf) to circulate in the body.
  - The oxidase is likely ceruloplasmin or hephaestin.

Transferrin

Mark D. Fleming, MD, DPhil

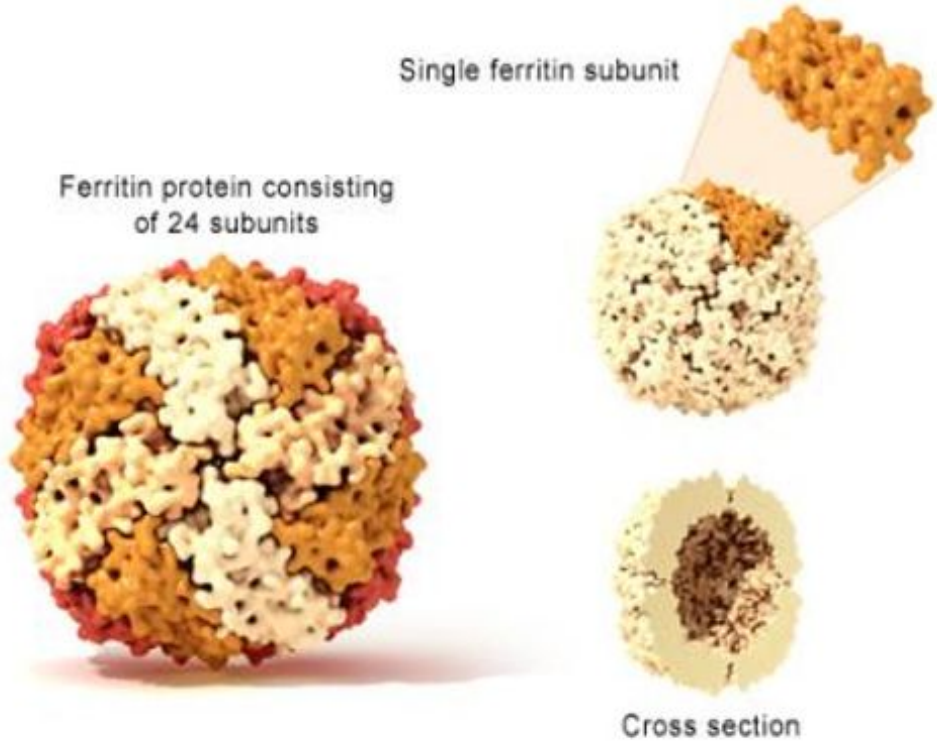
Transferrin and Ferritin

- Solublize iron in aqueous environments
- Minimize irons reactivity – ‘chaperones’



David S. Goodell, RCSB Protein Data Bank (http://www.rcsb.org/pdb/)

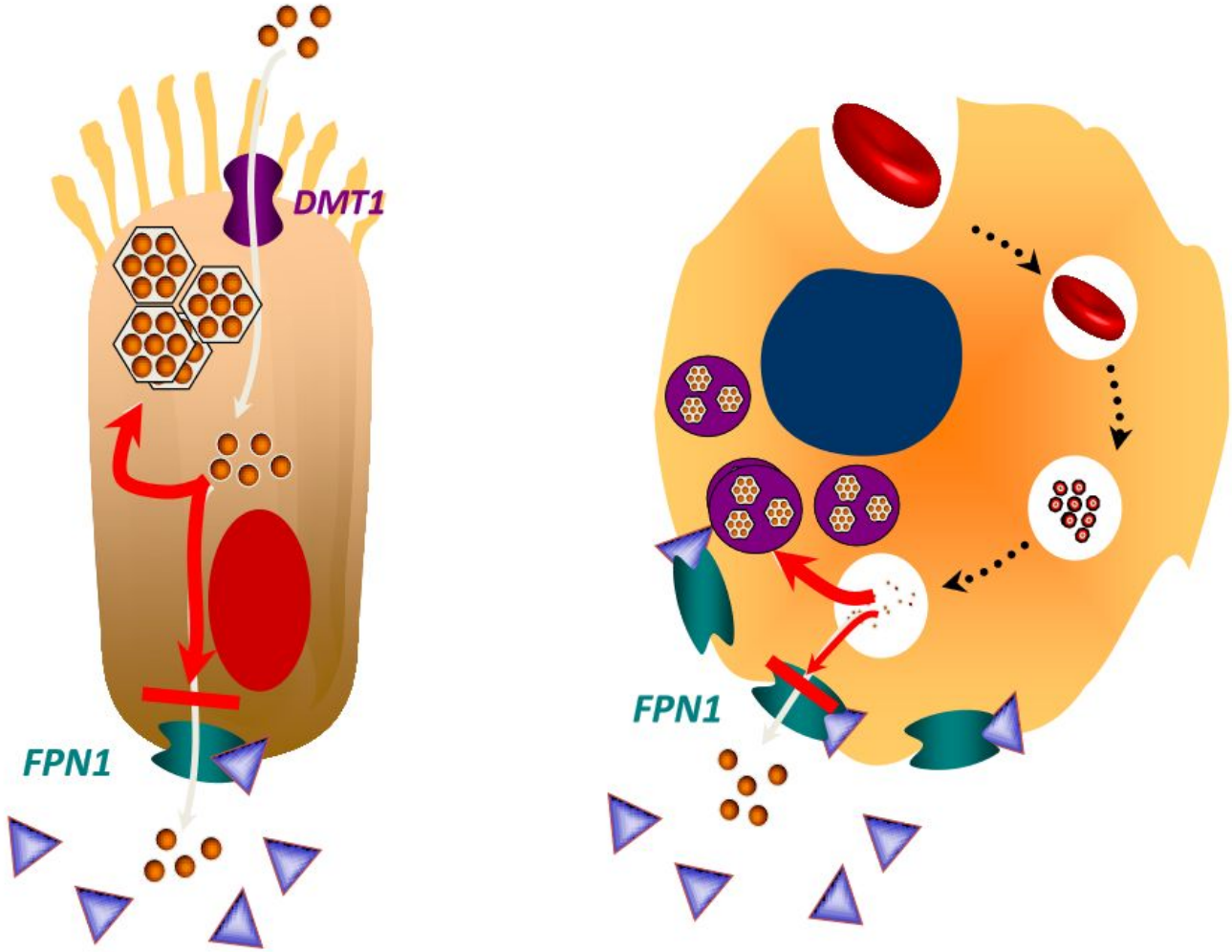
Transferrin



U.S. National Library of Medicine (http://ghr.nlm.nih.gov/handbook/illustrations/ferritin)

Ferritin

Hepcidin down-regulates ferroportin



Differentiate between iron deficiency and iron deficiency anemia

Most common cause is poor dietary intake

Less frequent causes include malabsorption, GU bleeding, GI bleeding and others.

Before you treat iron deficiency anemia , know the underlying cause!!!

- Iron replacement therapy.
- Transfusion.
- Treat the underlying cause!!!

Be aware!

Early during treatment of iron deficiency, RDW will increase !

Follow response

- Corrected parameters.
- Replenish iron stores.
- Neurodevelopmental changes may be irreversible.

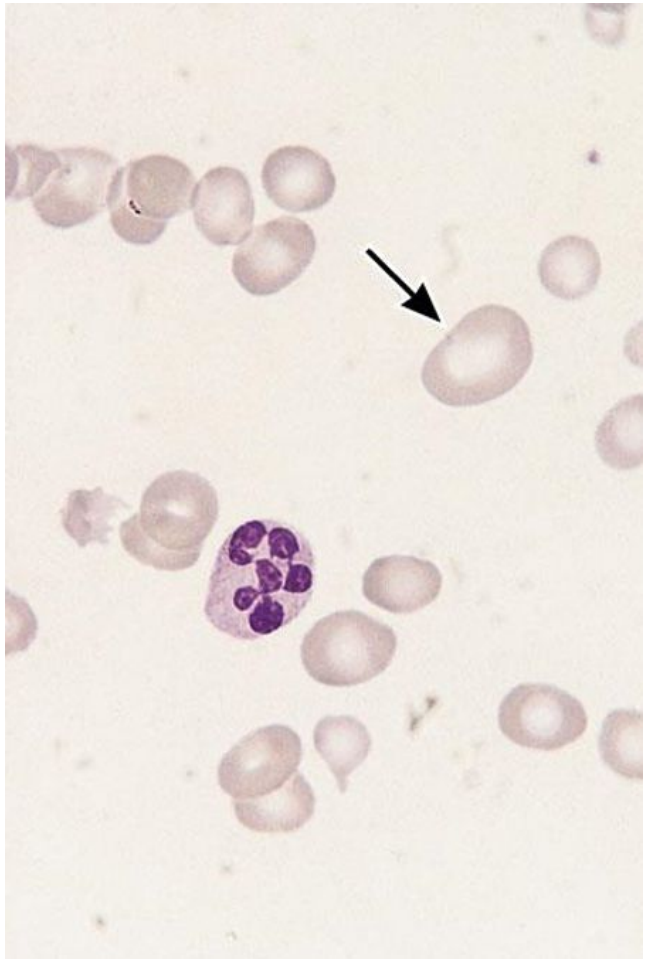
No response to treatment?

Relationship between PICA, iron deficiency anemia and Lead poisoning.

Mechanism of anemia of inflammation and chronic disease.

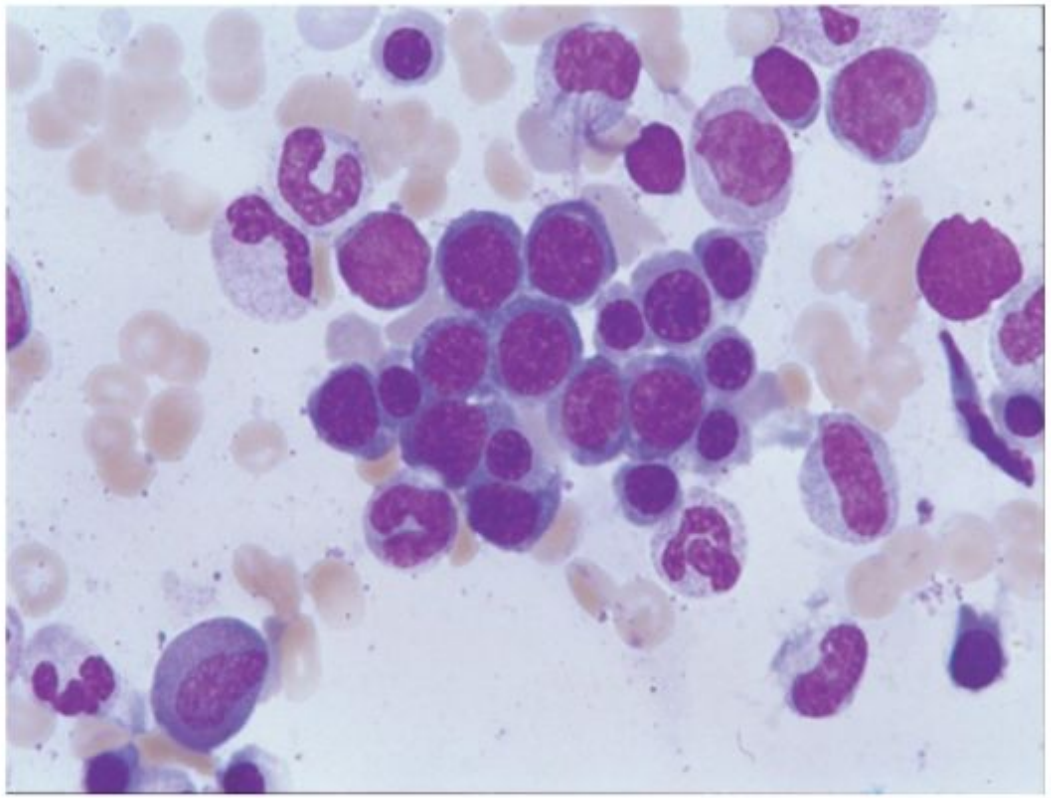
Folate and vitamin B12 deficiency

- Causes.
- Mechanism.
- Presentation.
- Treatment and response.

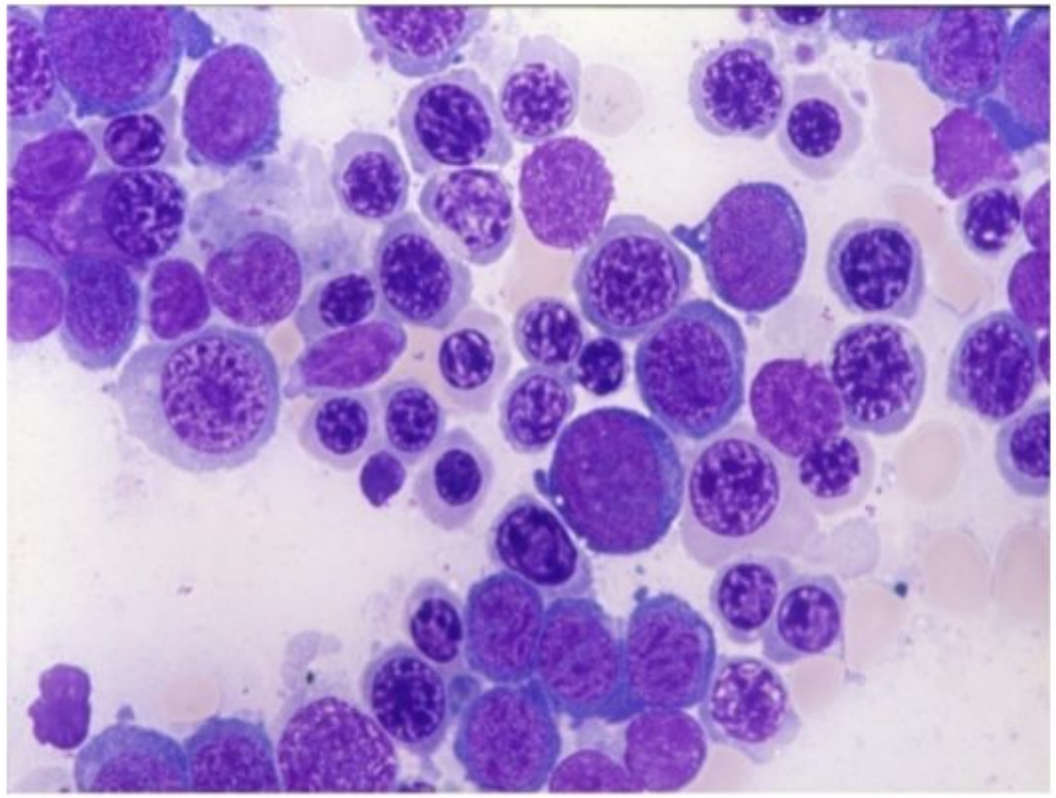


Megaloblastic bone marrow

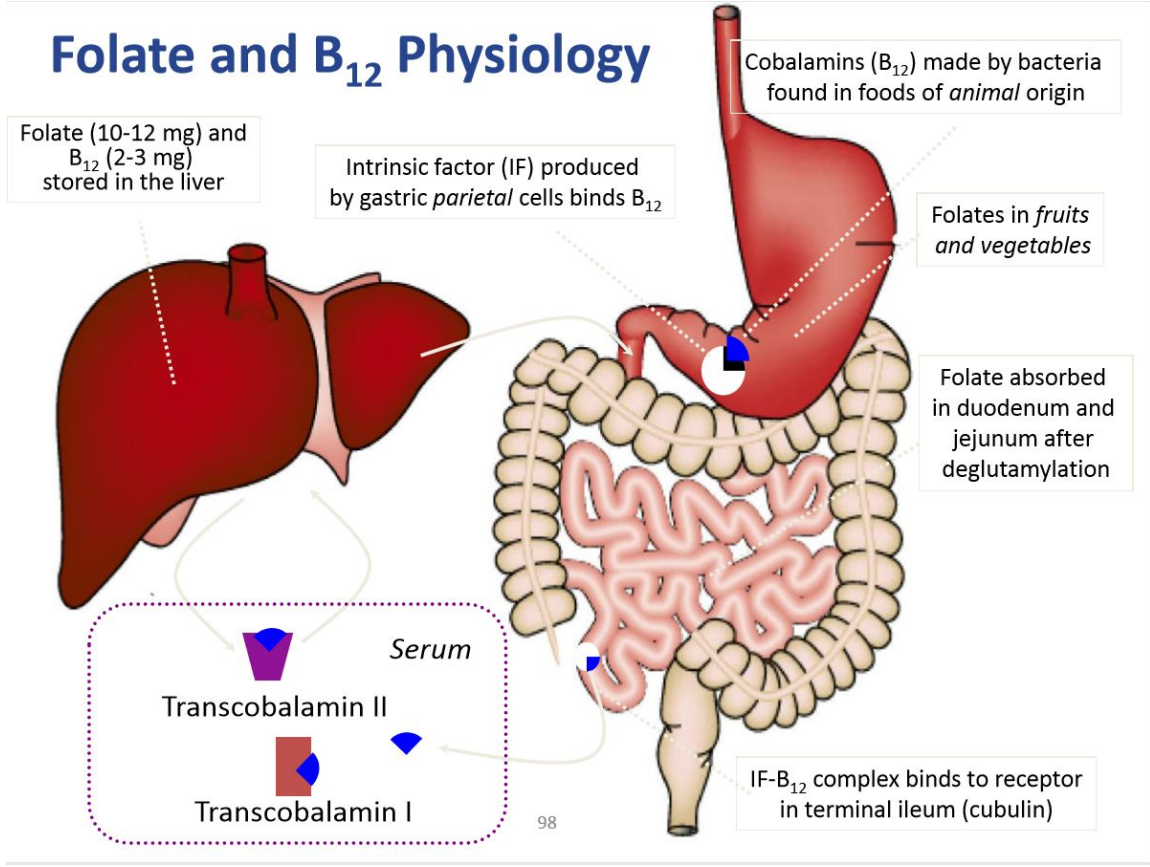
Normoblastic



Megaloblastic



Folate and B_{12} Physiology



B_{12} deficiency

Nutritional (1 mg)
- Strict vegetarians

"IF deficiency"
- Gastrectomy
- Autoimmune gastritis (*Pernicious anemia*)

Competition
- Fish tapeworm
- Intestinal blind loop

"Receptor deficiency"
- Ileal resection
- Crohn's disease
- Imerslund-Gräsbeck syndrome

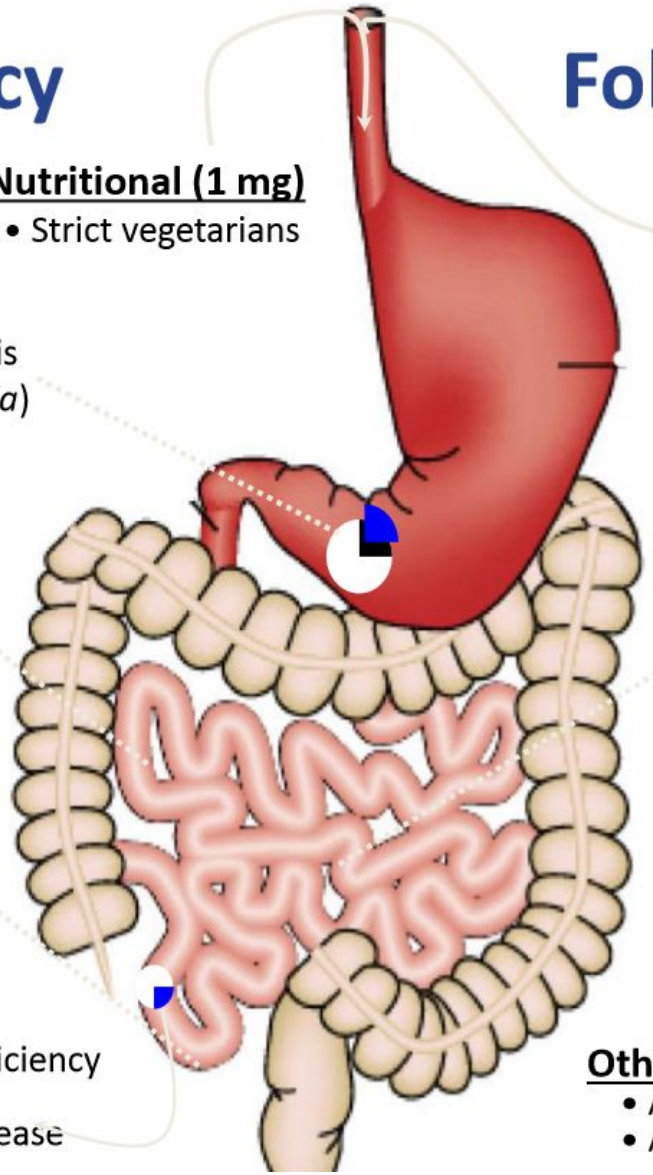
Other
- Transcobalamin II deficiency
- Nitric oxide
- Severe pancreatic disease

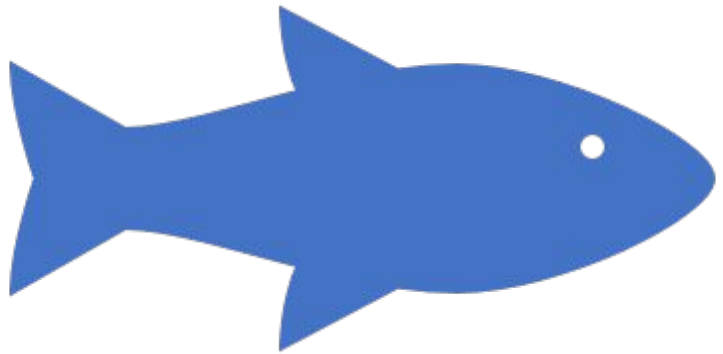
Folate deficiency

Nutritional (100 mg)
- Malnutrition
- Increased demand
  - pregnancy
  - hemolytic anemias

Malabsorption
- Gluten-sensitive enteropathy
- Tropical sprue
- Jejunal resection
- Severe Crohn's disease
- Short gut syndrome
- Sulfasalazine

Other
- Anti-folate drugs (methotrexate)
- Alcohol

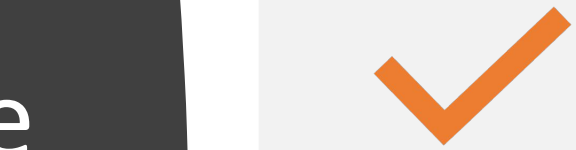




2 types of pernicious anemia

- Adult and Juvenile

Beware of the big difference between these 2!



Both present with megaloblastic changes and a smooth tongue

Only Cobalamin deficiency has neurologic manifestations.

Rare disorders

Imerslund-Grasbeck syndrome

Transcobalamin II deficiency

Response to treatment

RETICULOCYTOTIC WITHIN A WEEK

CORRECTION OF ANEMIA WITHIN A MONTH

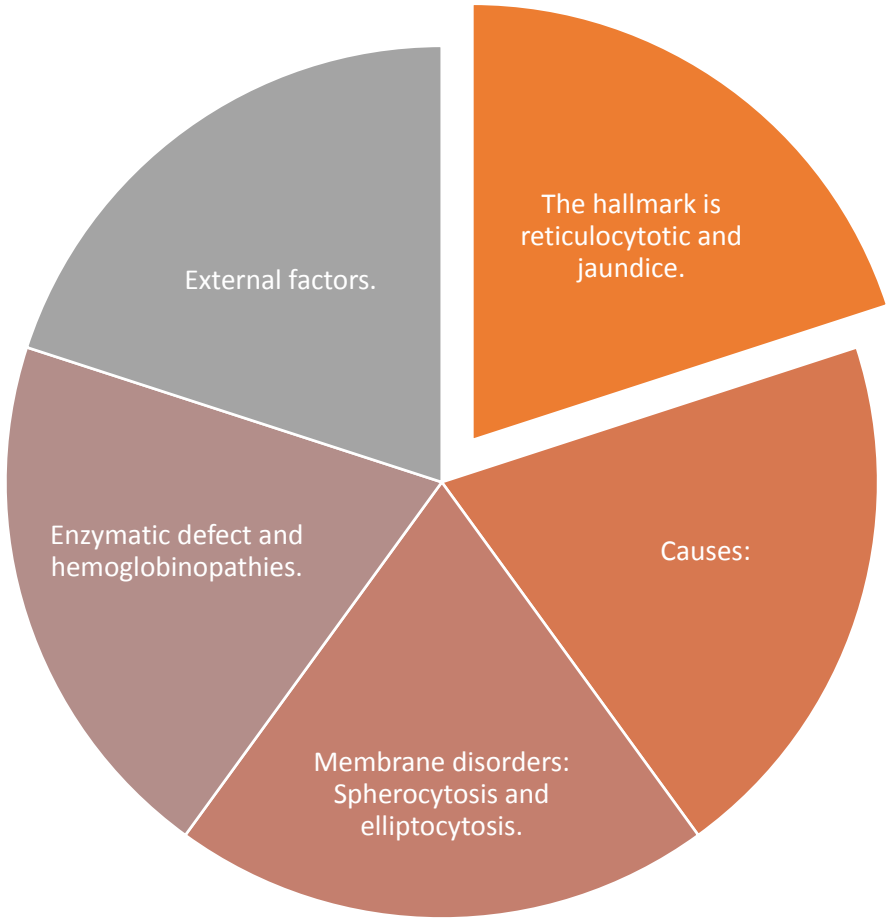
NORMALIZATION OF MCV WITHIN 2 MONTHS.

NEUROLOGIC DAMAGE MAY BE IRREVERSIBLE.

Never treat Vit B12 deficiency with folic acid!

It won’t end up well at all!

Hemolytic anemias (Shortened RBC life span)



External causes

MECHANICAL.

DRUGS.

IMMUNE BASED AND COMPLEMENT MEDIATED.

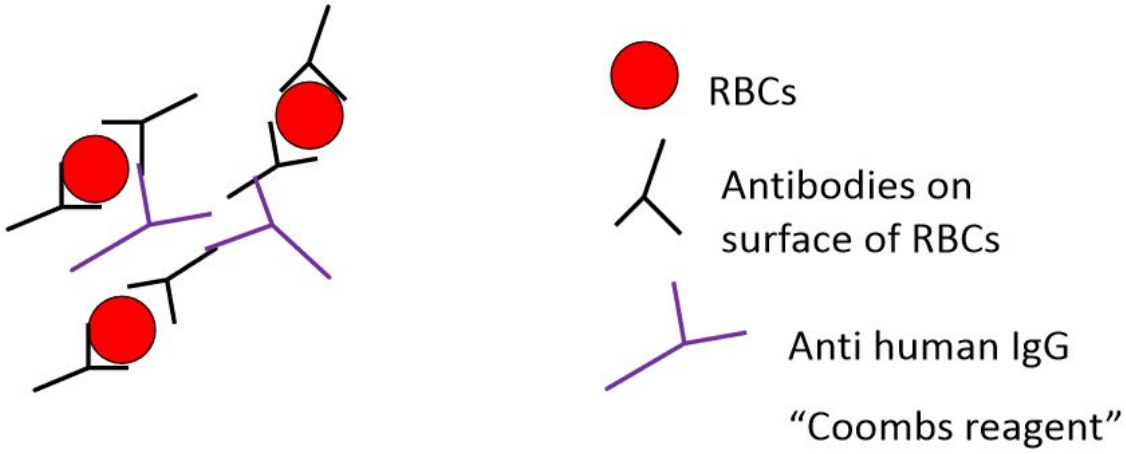
Immune can be alloimmune or autoimmune.

- Neonatal alloimmune hemolytic anemia.
- Warm autoimmune hemolytic anemia.
- Cold autoimmune hemolytic anemia.
- Paroxysmal cold hemoglobinuria (Donath Landsteiner antibody).
- PNH.
- TTP

Extravascular vs Intravascular Hemolysis

	Intravascular	Extravascular
Location of RBC Clearance	Inside vessels	In spleen and/or liver (RES)
Antibody Type (if immune)*	IgM (occ. IgG)	IgGs which don't fix complement
Mechanism of Hemolysis	Complement or shear mediated	Macrophages digest RBCs
Lab Findings	Hgbin*emia* & Hgbin*uria* , ↑ LDH Haptoglobin↓	↑ Bilirubin ↑LDH Haptoglobin ↓
Example	PCH*, PNH, valves	Warm AIHA*, HDN*, HS

Direct Antiglobulin Test



- Detects antibodies present on the surface of RBCs in vivo
- Addition of anti human IgG leads to agglutination of RBCs in vitro

IgG vs IgM mediated hemolysis

	IgM	Warm IgG
Fixes Complement	Yes	Usually not
Mechanism of Hemolysis*	Complement	Macrophages digest Ab-coated RBCs
Steroid response*	Poor	Fair to good
Pheresis response	Good (intravascular)	Fair or poor (tissue distribution)

Distinguishing AIHA from HS*: DAT, family history, acquired vs congenital;
NON-distinguishing features: spherocytes, Osmotic fragility, and the confusing Situation of negative standard DAT requiring super-sensitive methods.