
IRON DEFICIENCY ANEMIA
&THALASSEMIA

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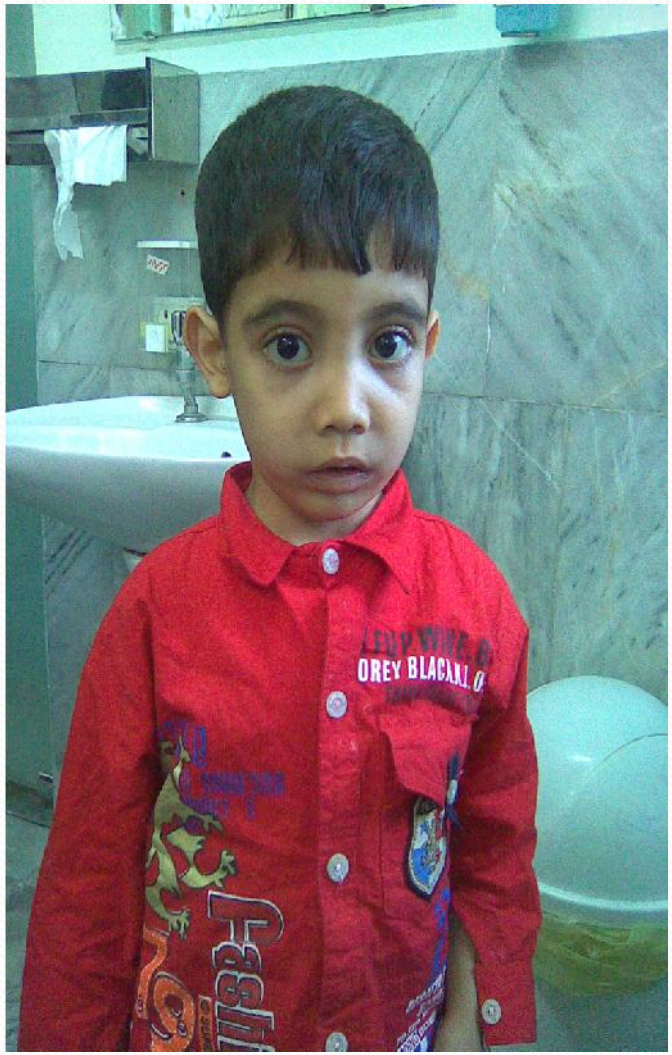
مرکزتحقیقات بیماری های خونی مادرزادی کودکان

B Major Thalassemia



Anemia

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It is a reduction
of the red cell volume or hemoglobin concentration below -2SD for age, sex.

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Normal Range,Hb

Birth:16/6 gr/dl

2 Mo:11/5

3-6 Mo 11/5

6-24 M :12

2-6 Y:12/5

6-12 Y:13/5

12-18 Y: F =12-14 M=14-16

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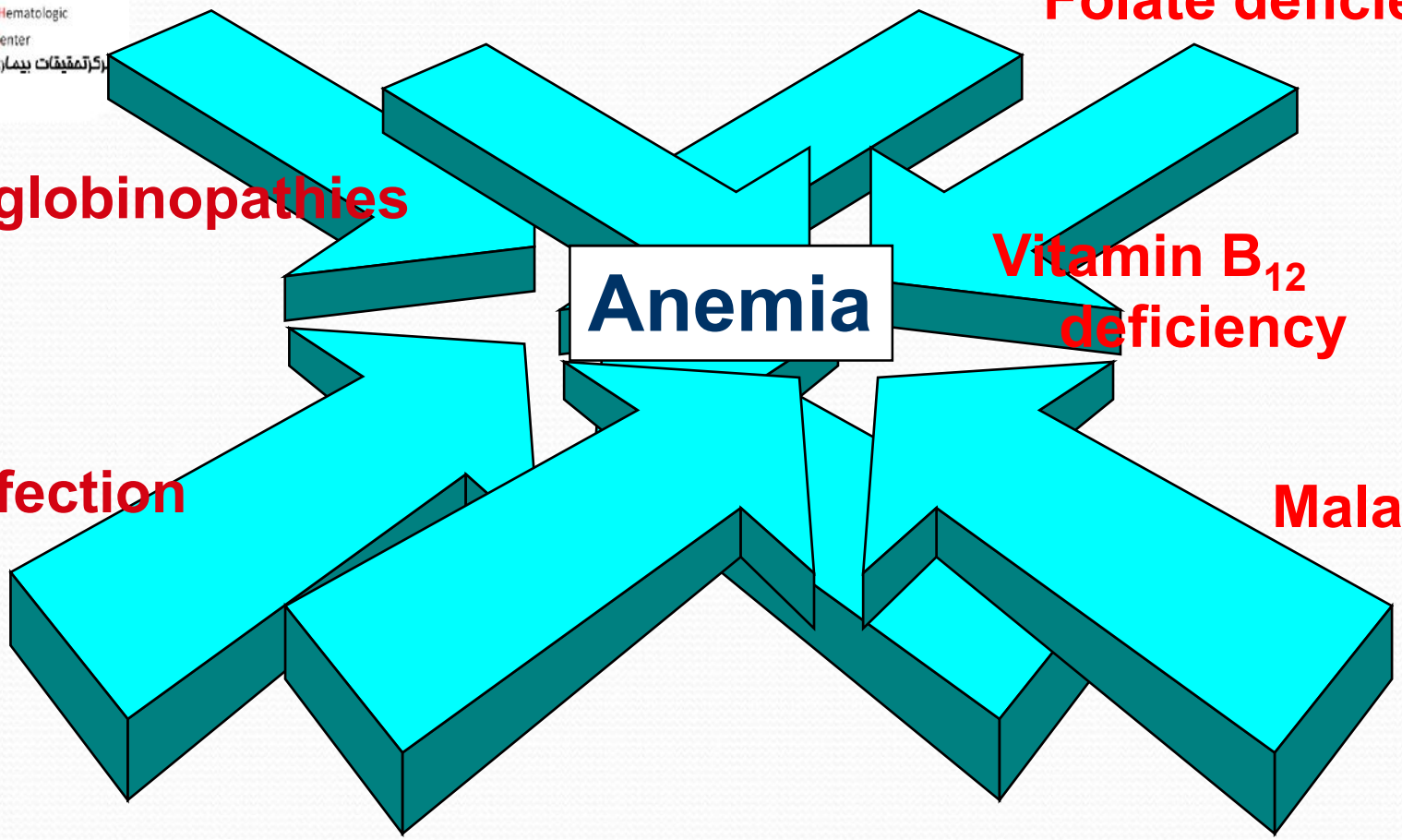
Normal Range,MCV

- Birth:108FL
- 2 Mo:96
- 3-6 Mo:91
- 6-24 M :78
- 2-6 Y:81
- 6-12 Y:86
- 12-18 Y: F =90 M=88

Iron deficiency



Infectious/inflammatory disorders — Helminth infection

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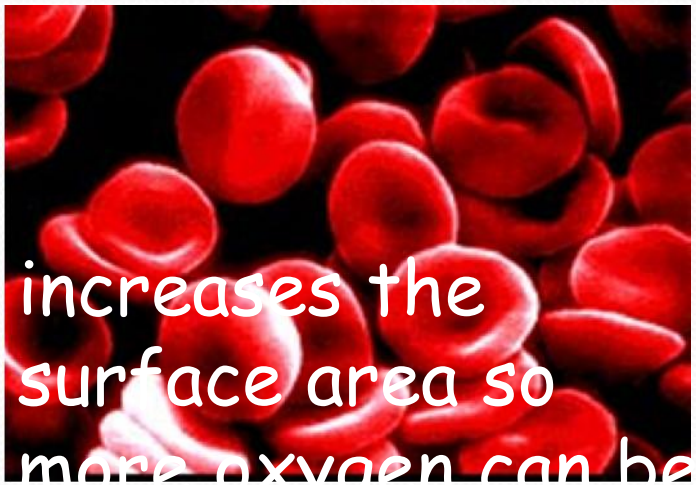
Iron is vital for all living organisms; oxygen Transport

Red blood cells specialisations

biconcave shape

no nucleus

→ extra space inside



contain **haemoglobin**

→ the oxygen carrying molecule

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- Iron deficiency is a major health problem worldwide and especially in developing countries.
- Iron-deficiency is the most prevalent nutritional deficiency worldwide
- Iron deficiency is the most common single cause of anemia worldwide

Review Of Articles 1

- Prevalence of iron deficiency anemia in 6mo-5 years old children in Fars , southern IRAN
  - **Kadivar MR & Collegues. Med Sci Monit,2003;9(2);CR 100-104**

- **541 patients:**
- **110 p(%19.7): Serum Ferritin level < 12ng/ml**
- **101 P(%18.7): low serum Hb**
- **Developing Countries: IDA%25-%35**
- **Industerialized Country: IDA %5-%8**
- **Iron supplements by Health care centers , Free of charge**

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Iron status

The concentration of Iron in:

Infant: 75-80 mg/kg(BW)

50mg/kg: Hb Mass

25mg/kg: Storage Iron

5mg/kg: Myoglobin & tissue Iron

Iron status

The concentration of Iron in:

Adult: 40-50 mg/kg(BW)

30mg/kg: Hb Mass

6-7mg/kg: Myoglobin, Heme enzymes

& non heme enzymes

* 6-7mg/kg (F) storage Iron

* 10-12 mg/kg (M)

< 0/5%: Transport Iron

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Iron Metabolism

Cellular sequestration & Metabolism of Iron is mediated by 3 proteins:

- ***Transferrin***
- ***Transferrin receptor***
- ***Ferritin***

Ferritin

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Ferritin is the major storage protein with 24 subunit:

*** Light chain (L), 19 kD**

*** Heavy chain (H) 21 kD**

H gene locus: ch 11: Heart, Iron – Metabolism

L gene locus: ch 19: Liver & spleen- Iron storage function

Ferritin is found in virtually all cells especially:

Erythroied precursors

Macrophages

Hepatocytes

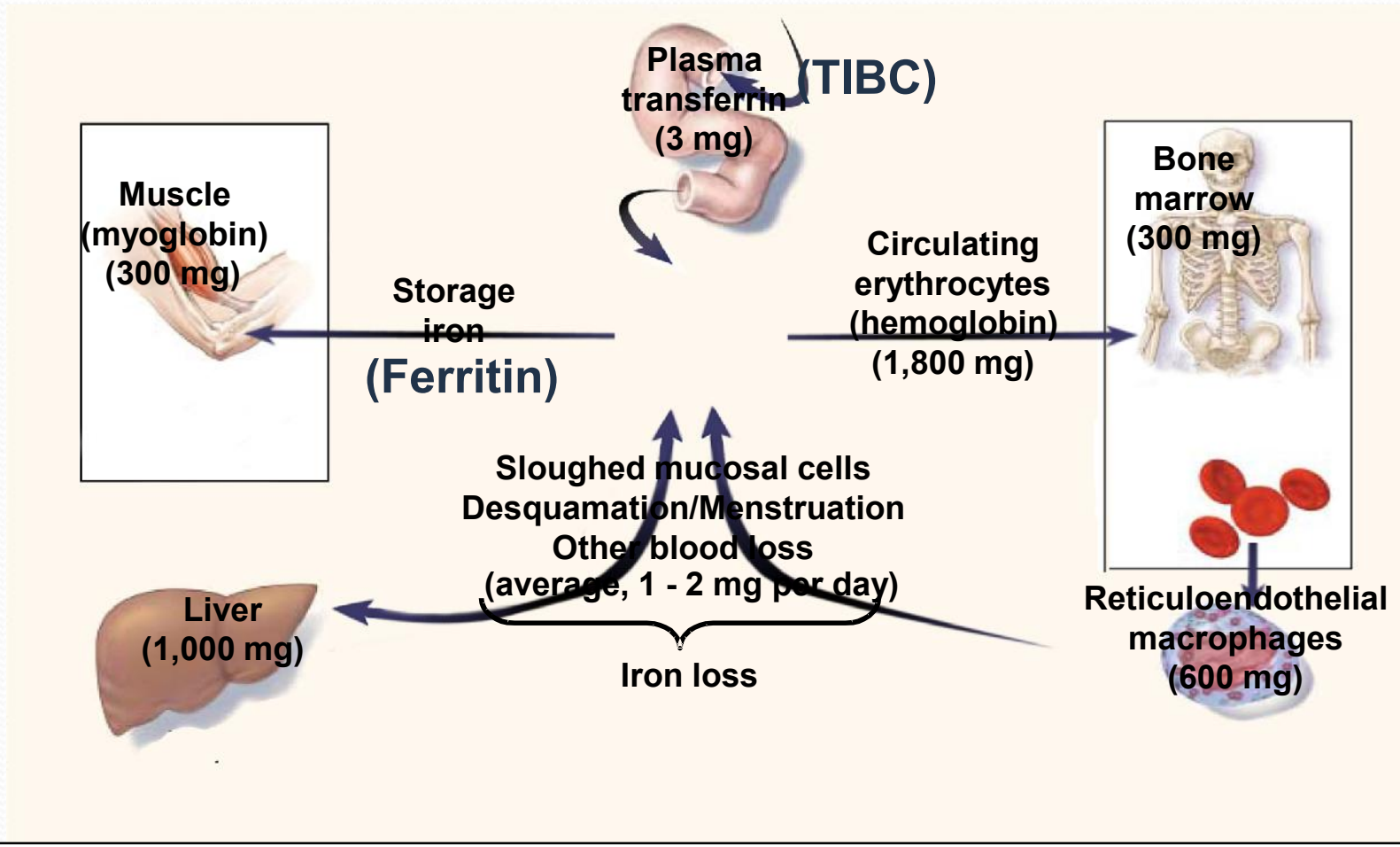
F.molecule: 4500 Iron atoms

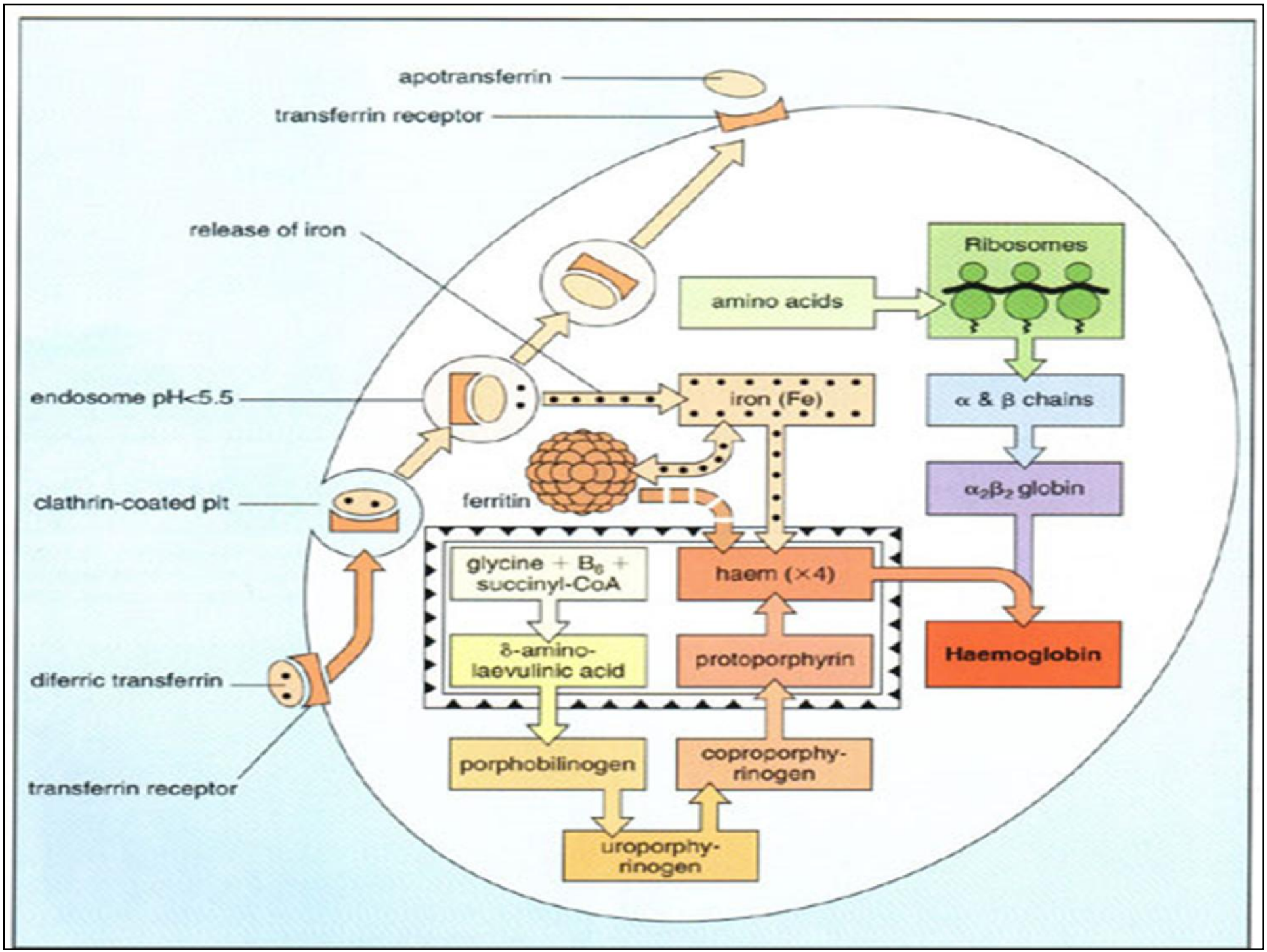
Half life: 60 hour

Catabolism of, F: Reutilization of Iron core

Hemosiderin conversion

Body Iron Distribution and Storage




apotransferrin
transferrin receptor
release of iron
endosome pH<5.5
clathrin-coated pit
diferric transferrin
transferrin receptor
Ribosomes
amino acids
iron (Fe)
α & β chains
ferritin
$\alpha_2\beta_2$ globin
glycine + B_6 + succinyl-CoA
haem (×4)
δ-amino-laevulinic acid
protoporphyrin
Haemoglobin
porphobilinogen
coproporphy-rinogen
uroporphy-rinogen

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Iron balance

Iron balance is physiologically regulated by controlling Iron absorption.

The availability of dietry Iron for absorption is dependent to:

- ***The amount of Iron***
- ***Form of Iron***
- ***Composition of the diet***
- ***GI factors***

CBC

Hb, HCT → -Anemia

WBC → -leukocytosis
-leukopenia
-Abnormal cells

Platelet → -Thrombocytosis
-Thrombocytopenia

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peripheral Blood,CBC

- R BC
- Hb (is not specific)
- MCV
- MCH
- Reticulocyte
- Peripheral blood smear, Morphology

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Indirect: 1- plasma ferritin:

(the most useful) in the absence of:

* *Tissue necrosis*
* *Inflammation*
* *Neoplasm*
* *liver disorder*
* *↑ turn over of RBC*

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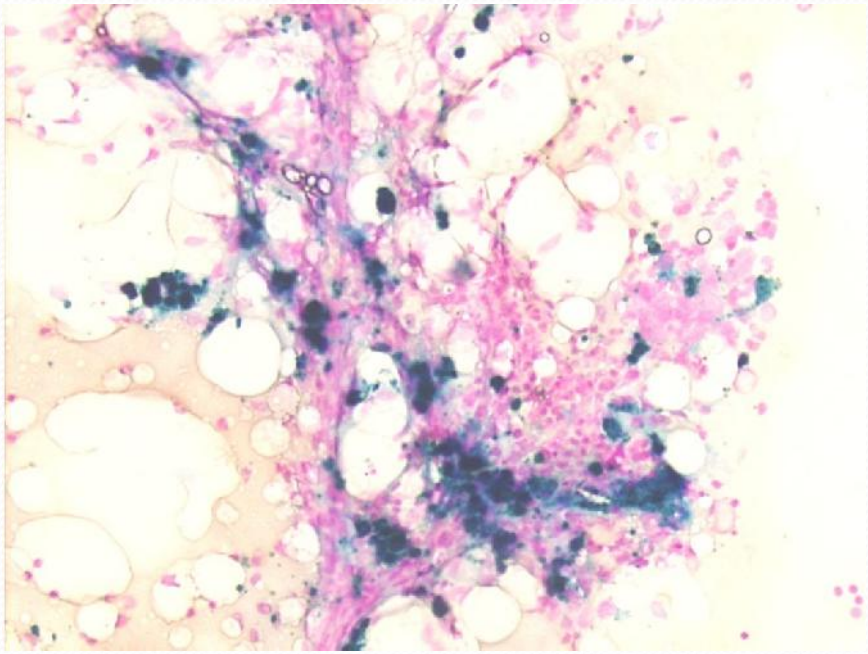
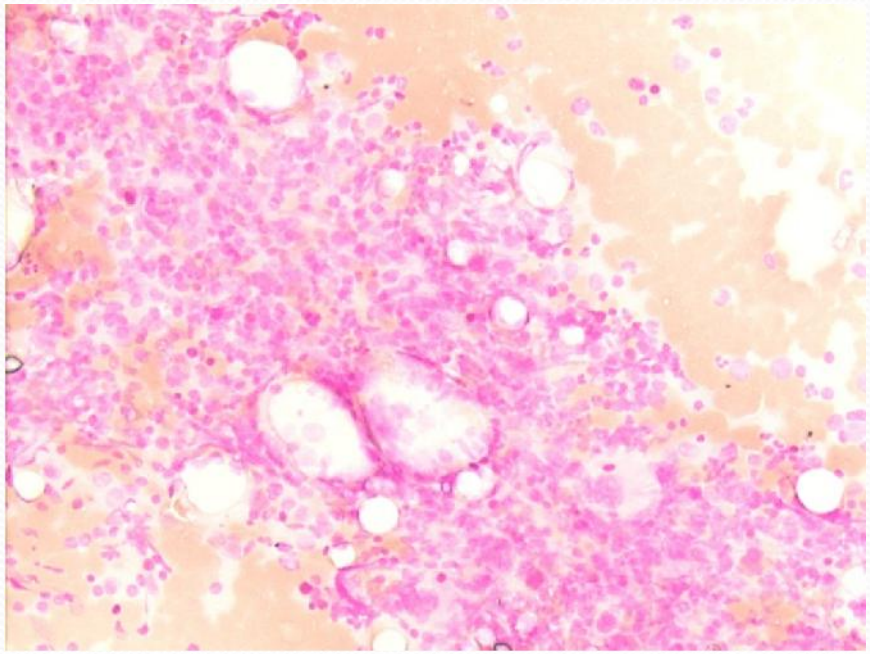
Prussian Blue Stain of Bone Marrow





Iron Present

No Iron Present

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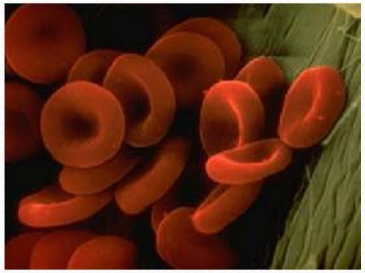
Iron deficiency anemia

Iron deficiency anemia is the most common cause of anemia.

Growth & diet are almost always contributing factors in childhood

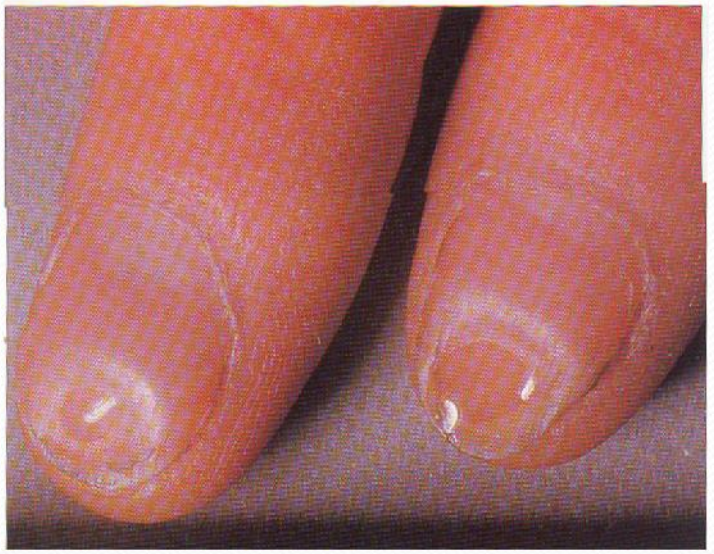
Etiology / IDA

- Blood Loss
- Gastrointestinal Tract:
  - Milk -induced Enthropathy
    - Peptic ulcer
    - Inflamatory Bowel Diseaes
    - Meckel Diverticuculm &Polips
    - Drugs: Salicylates
    - Hookworm Infestation
    - Pulmonary Hemosiderosis
    - Iatrogenic
    - Menstural Blood Loss
    - Urinary Blood Loss(rare)



Etiology/IDA

- Increased Physiologic Requirement
  - -Pregnancy
  - -Infancy
  - -Adolescence
- Malabsorption
  - - Inflamatory Bowel Diseaes
  - -Tropical Sprue
    - Gastrectomy
    - Pica
- Dietary inadequacy: Iron Poor Diet
- Combinations of above

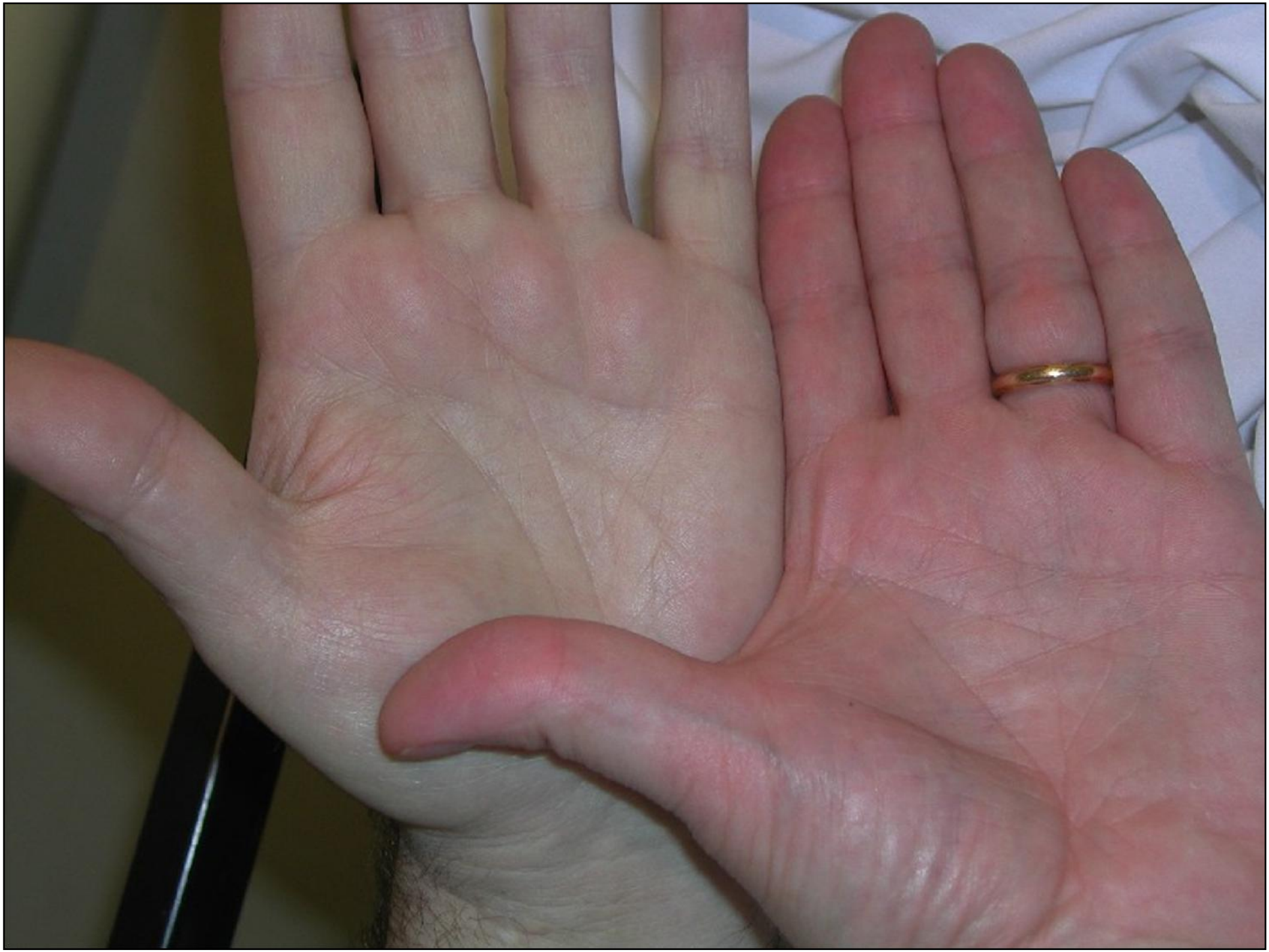


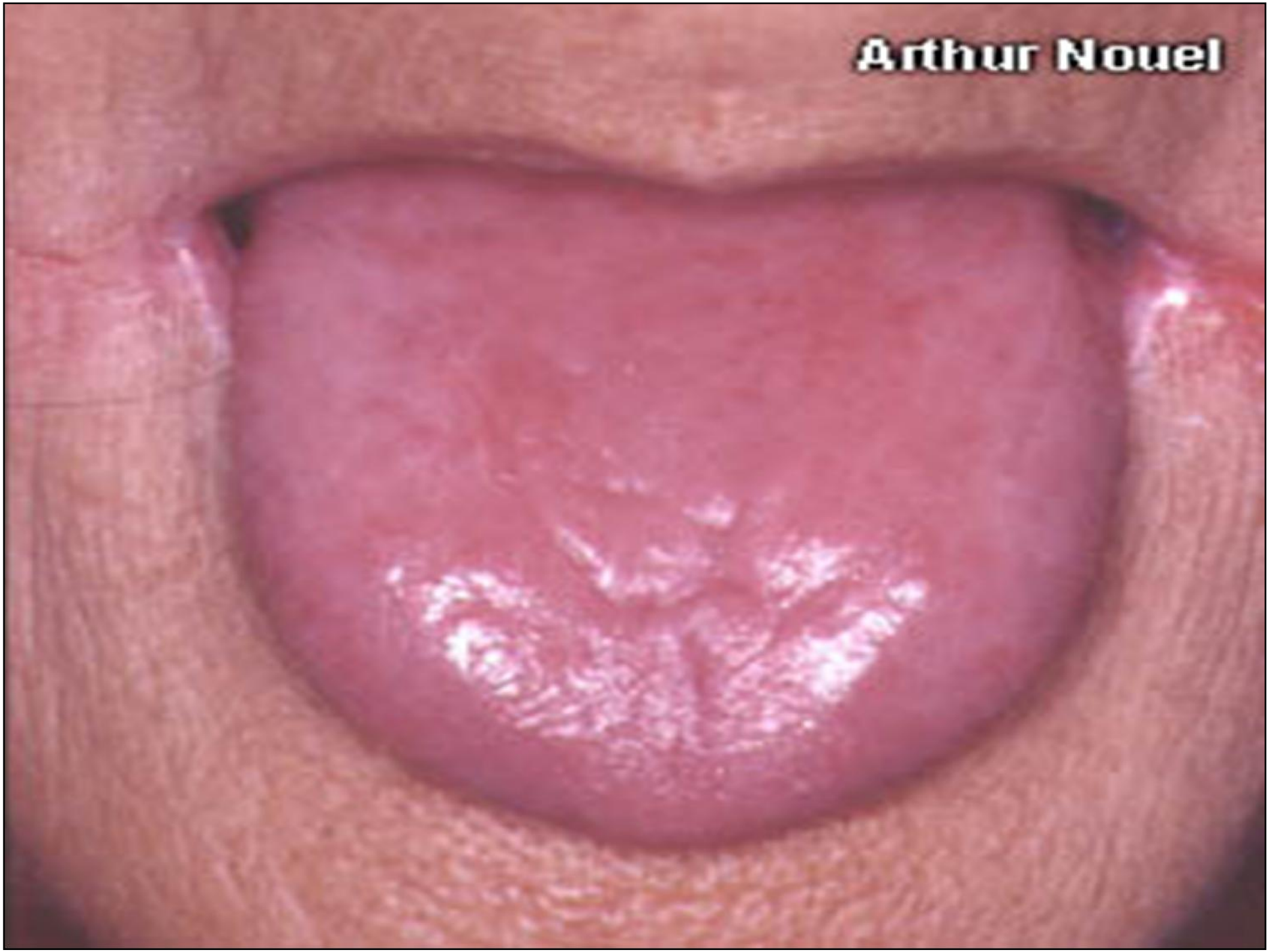
Clinical manifestations

*Hematologic

* Non Hematologic

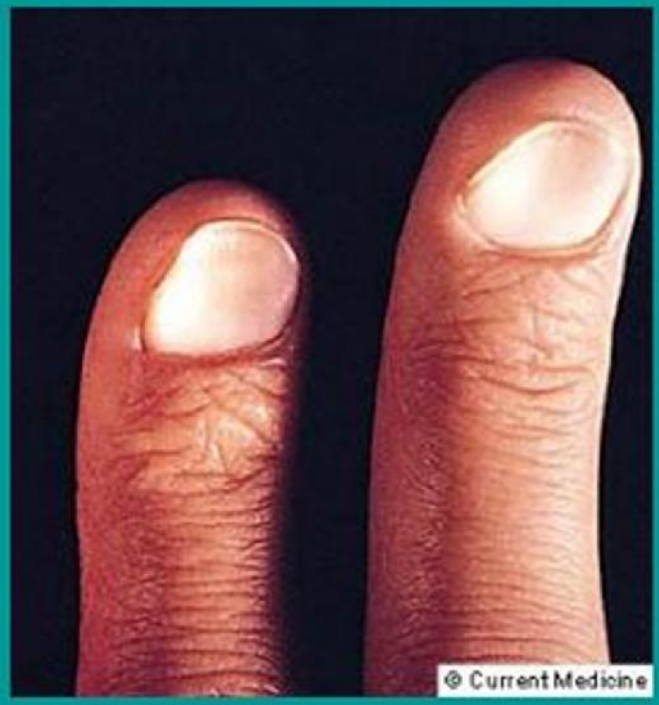
- Pallor
- Weakness, fatigue, Irritability
- Anorexia
- Pica
- Blue sclera
- Koilonychias (spoon- shaped nails)
- Glossitis
- Angular stomatatis
- Post cricoid esophageal web (plummer winson syndrome)
- Impair of intellectual & learning
- Impaired of immunity
- Slightly enlarged spleen
- Cardiopulmonary failure & death.

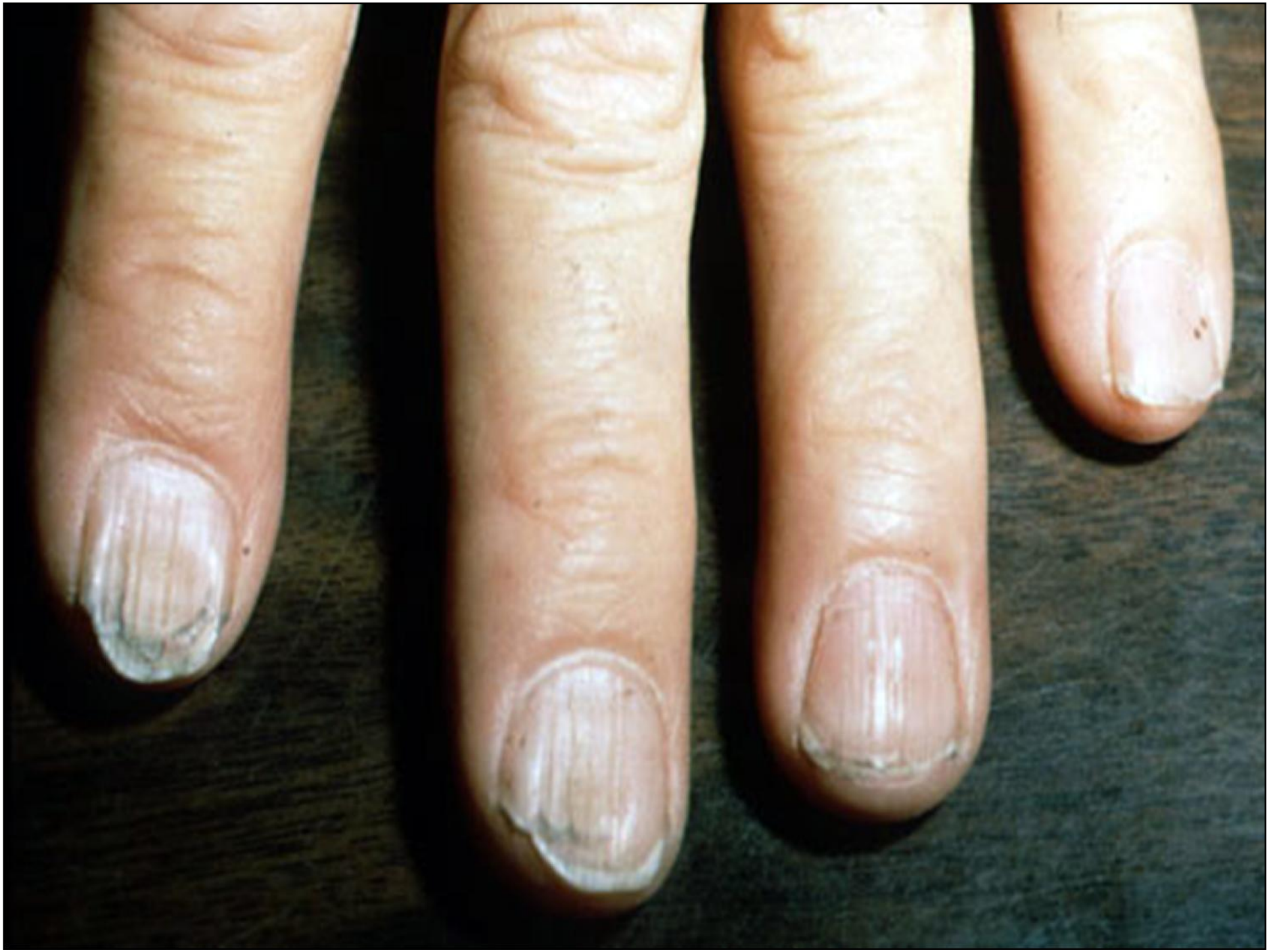


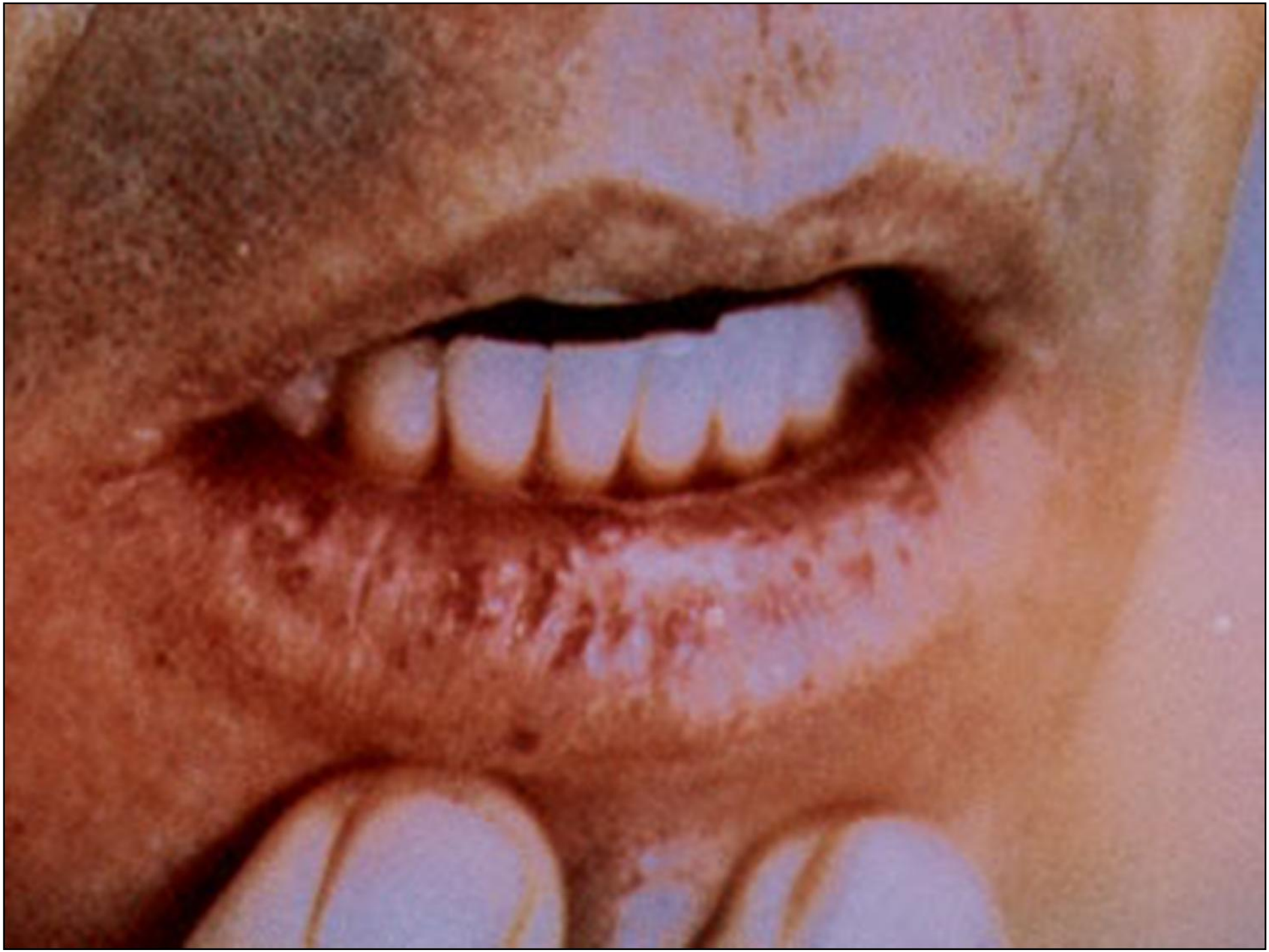

Arthur Nouel

Iron Deficiency Anemia

- Additional signs/symptoms
  - spoon-shaped nails (koilonychia)
  - cheilosis
  - glossitis
- Laboratory findings
  - hypochromic, microcytic
  - ↓ ferritin
  - ↓ serum iron
  - ↑ TIBC
  - ↑ transferrin







Laboratory test:

1-Serum Ferritin: < 10-12 ug/l

2- Serum Iron(Decrease)

3-Total iron binding capacity TIBC ↑

4- peripheral blood : RBC, Hb- HCT↓

MCV, MCH ↓

(RDW(Red blood cell distributaion width)↑

Reticulocyte , Mild↑

4- Serum Soluble Transferrin Receptor ↑

5-FEP ↑

6- BMA & BM Biopsy (Prussian Blue Staining)

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Reticulocyte count

Normal = 0.2-2 %

$$\text{Corrected reticulocyte} = \frac{\text{Pt HCT X Reti.}}{\text{Normal HCT}}$$

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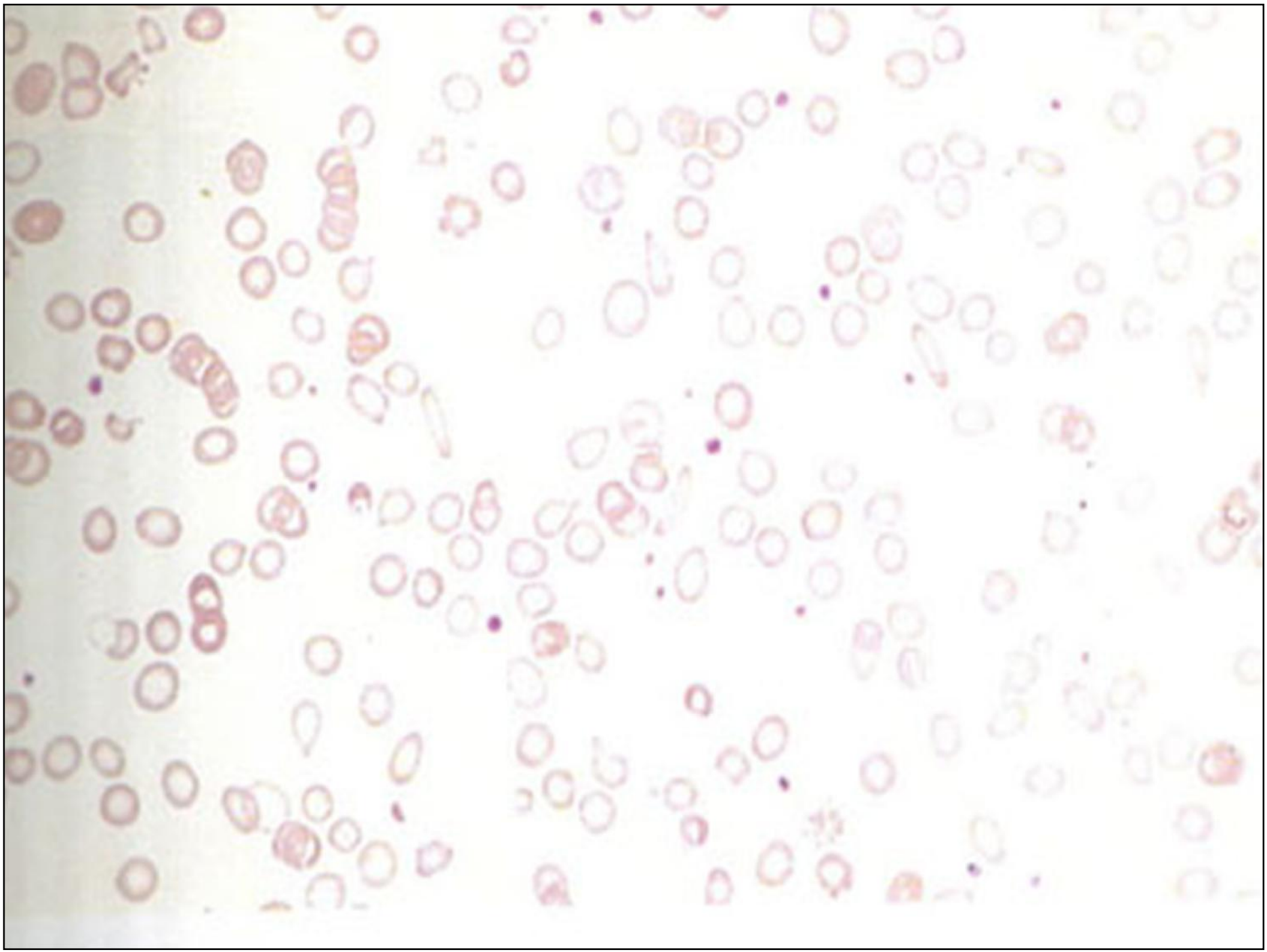
Hb, HCT ⇒ -Anemia

CBC

WBC ⇒ -leukocytosis
-leukopenia
-Abnormal cells

Platelet ⇒ -Thrombocytosis
-Thrombocytopenia



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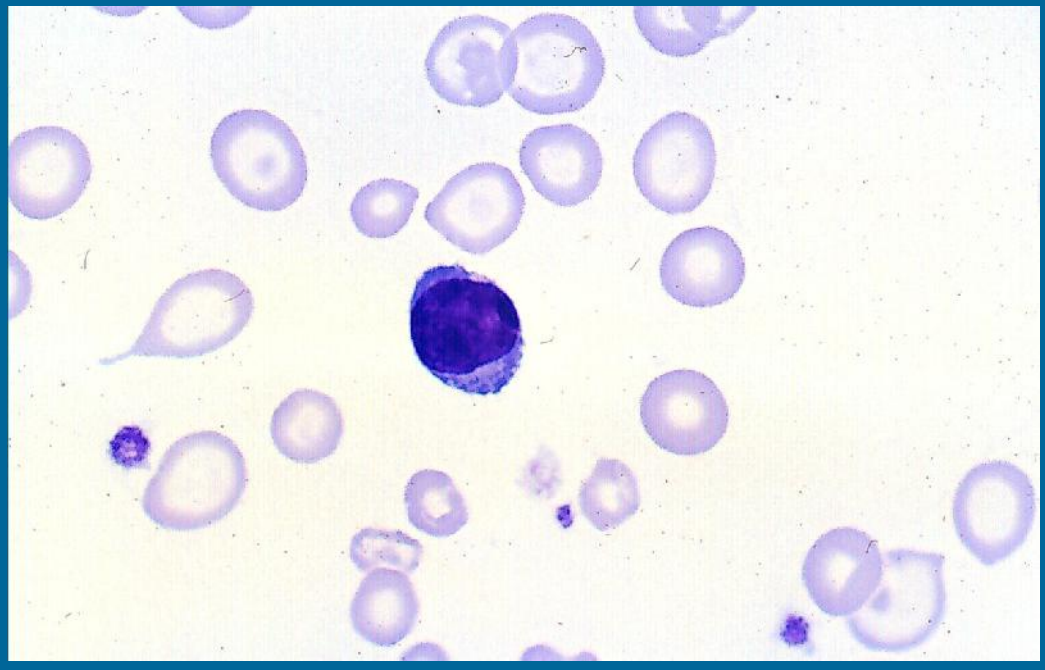
IDA



Differential Diagnosis of I.D.Anemia

1- β. Thalassemia minor

2- β. Thalassemia major

3- Chronic disorders

4- lead poisining

5- α. Thalassemia

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B Thalassemia trait (Heterozygous)

- Expression of one β gene is impaired by mutation where as the other gene is normal.
- Slight ineffective erythropoiesis & modestly decrease of RBC survival
- **Mild erythrocytosis**
- **Marked microcytosis**
- Peripheral Blood: microcytosis, hypochromia & targeting

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Differntial Diagnosis
B Thalassemia trait / Iron Deficiency Anemia

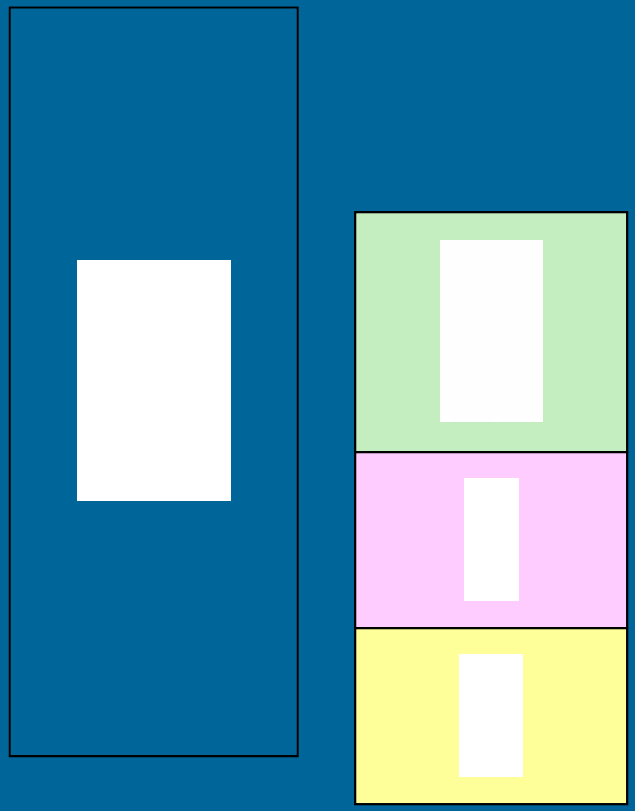
B. **Th. Trait:**

- **Increase of RBC- Mild Erythrocytosis,**
- **Marked microcytosis**
- **IDA : RBC count decreased, MCV is rarely as low as B. Th .Trait**
- RDW (Red Cell Disrtribution Width by Automated cell counter) : Increased in IDA
- Mentzer Index(MCV/RBC):
- B .Th .Trait <13
- IDA > 13

CBC
B. TH .Trait &I. D.A

WBC=10000/mm3	WBC=6000/mm3
RBC=6/000/000/mm3	RBC=3/200/000/mm3
Hb=10 gr/d	Hb=7gr/dl
HCT=%30	HCT=%21
MCV=60 FL	MCV=74FL
MCH=23 pg	MCH=25Pg
Platelet=180000/mm3	Platelet=600000/mm3

thalassemia



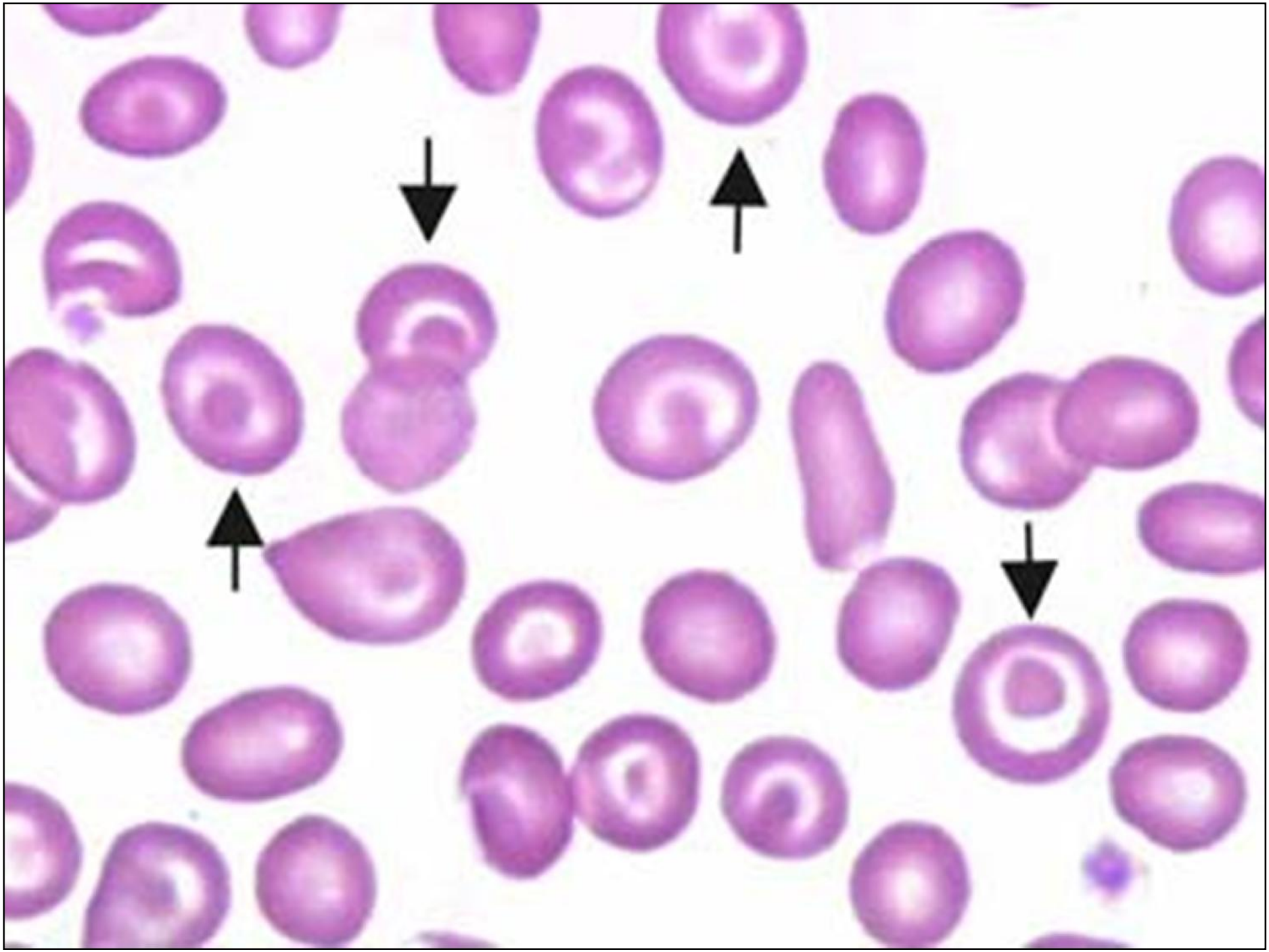
Hb A ↓

Hb A_2 ↑

Hb F ↑

B Thalassemia trait (Heterozygous)

- **Hb Electrophorasis:**
  - **High A2 Hb (3.5- 8%)**
  - **High A2 & High F Hb(5%-20%)**
  - **Low A2 Hb (Hb F 5%-15%,δβ Thalassemia)**
  - **Normal A2 Hb**



IRON DEFICIENCY *versus* ACD

	Serum Iron	Transferrin	Ferritin
Iron Deficiency	↓	↑	↓
ACD	↓	↓	↑

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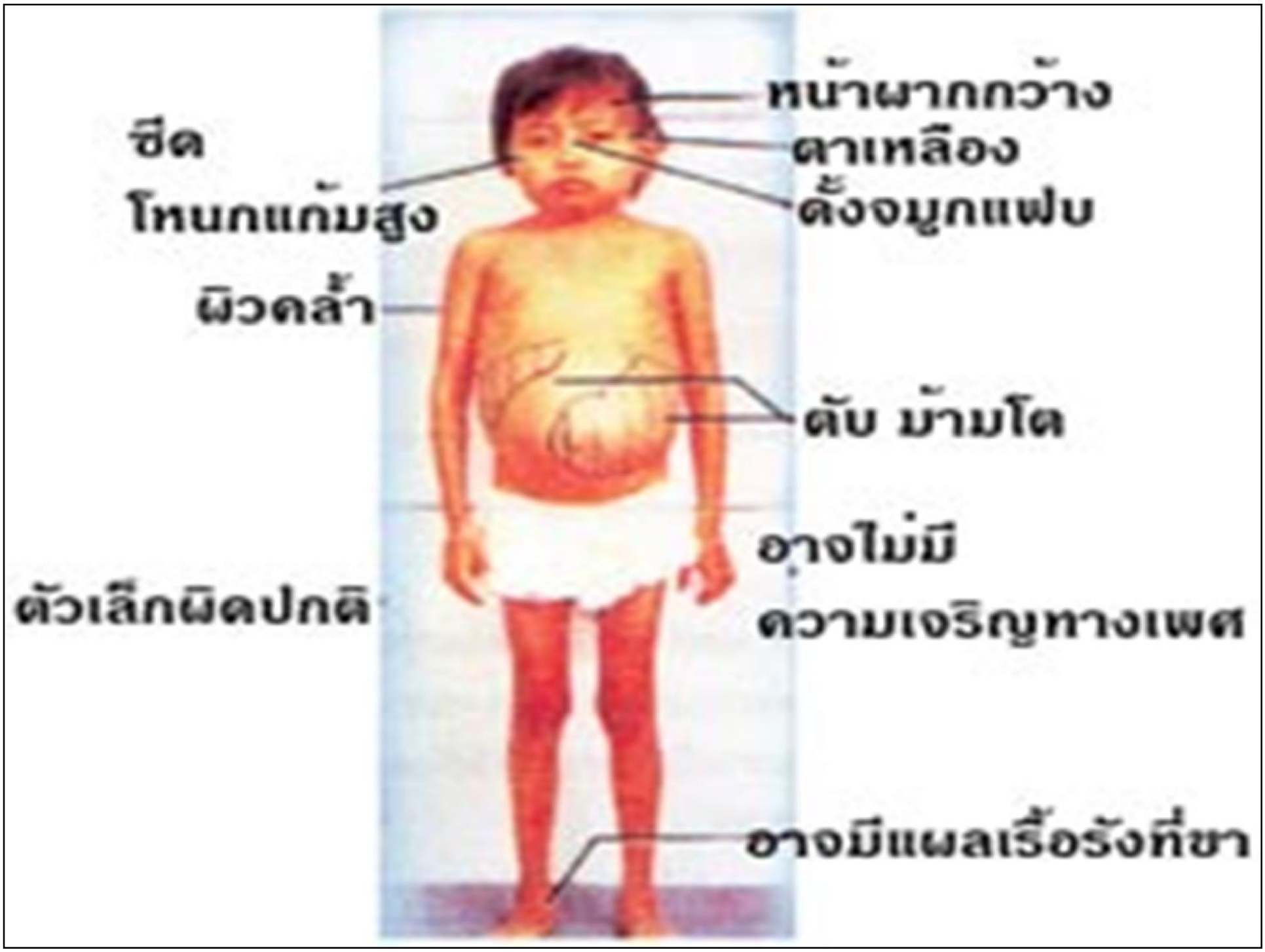
Major Thalassemia /Cooley Anemia

- Compound heterozygous state for two different β-globin gene mutations
- Homozygous state for the same mutation
- Age of diagnosis: 6-12 months
  - 60% of: first year
  - 30% of: second year
  - 9% of: later

Clinical manifestations

- Pallor
- Failure to thrive
- Irritability
- Icterus
- Hepatosplenomegaly
- Skeletal changes
- Prone to infection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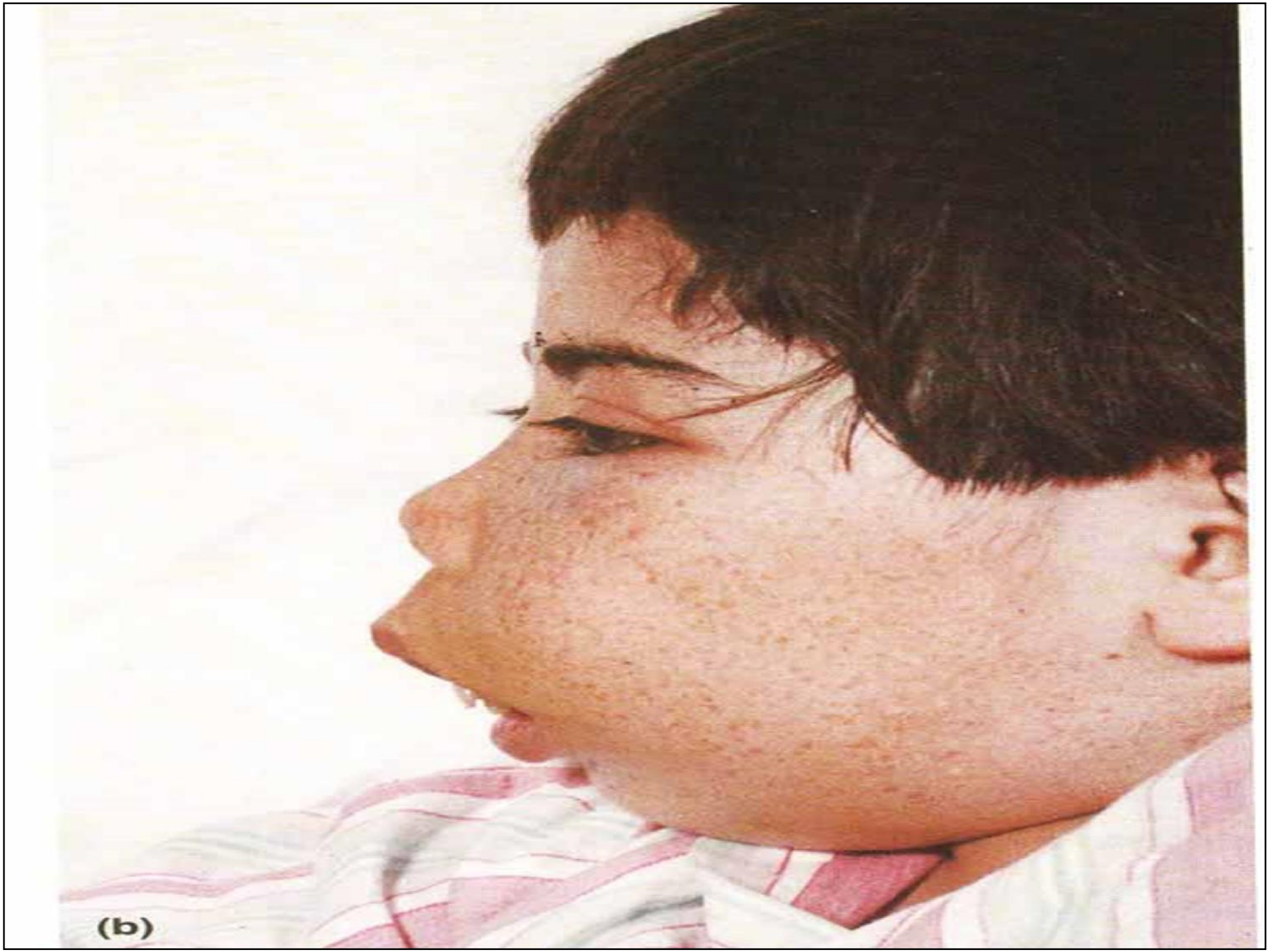
ตาเหลือง
ตั้งจมูกแฟบ
ซีด
โหนกแก้มสูง
ผิวคล้ำ
ดับ ม้ามโต
อาจไม่มี
ความเจริญทางเพศ
ตัวเล็กผิดปกติ
อาจมีแผลเรื้อรังที่ขา


(b)

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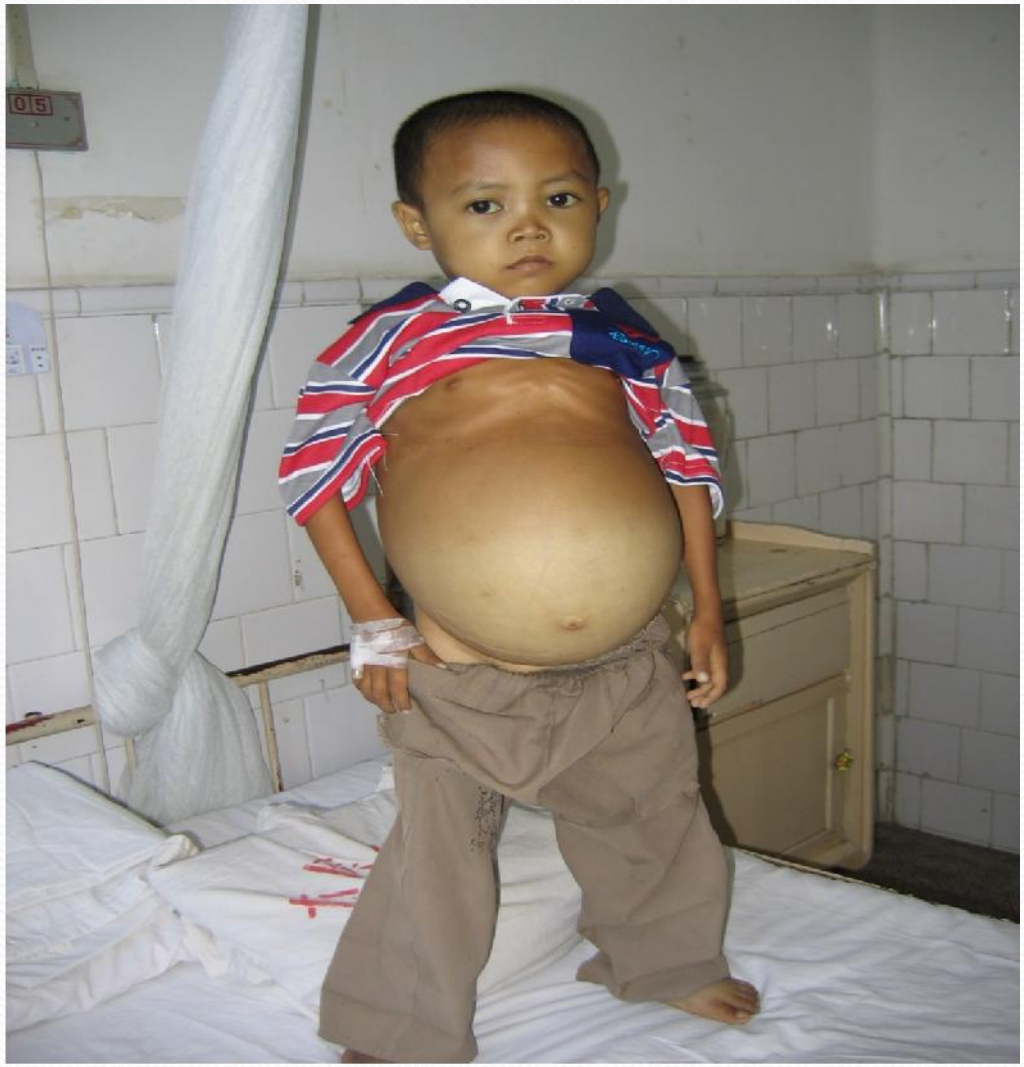
B MAJOR THALASSEMIA



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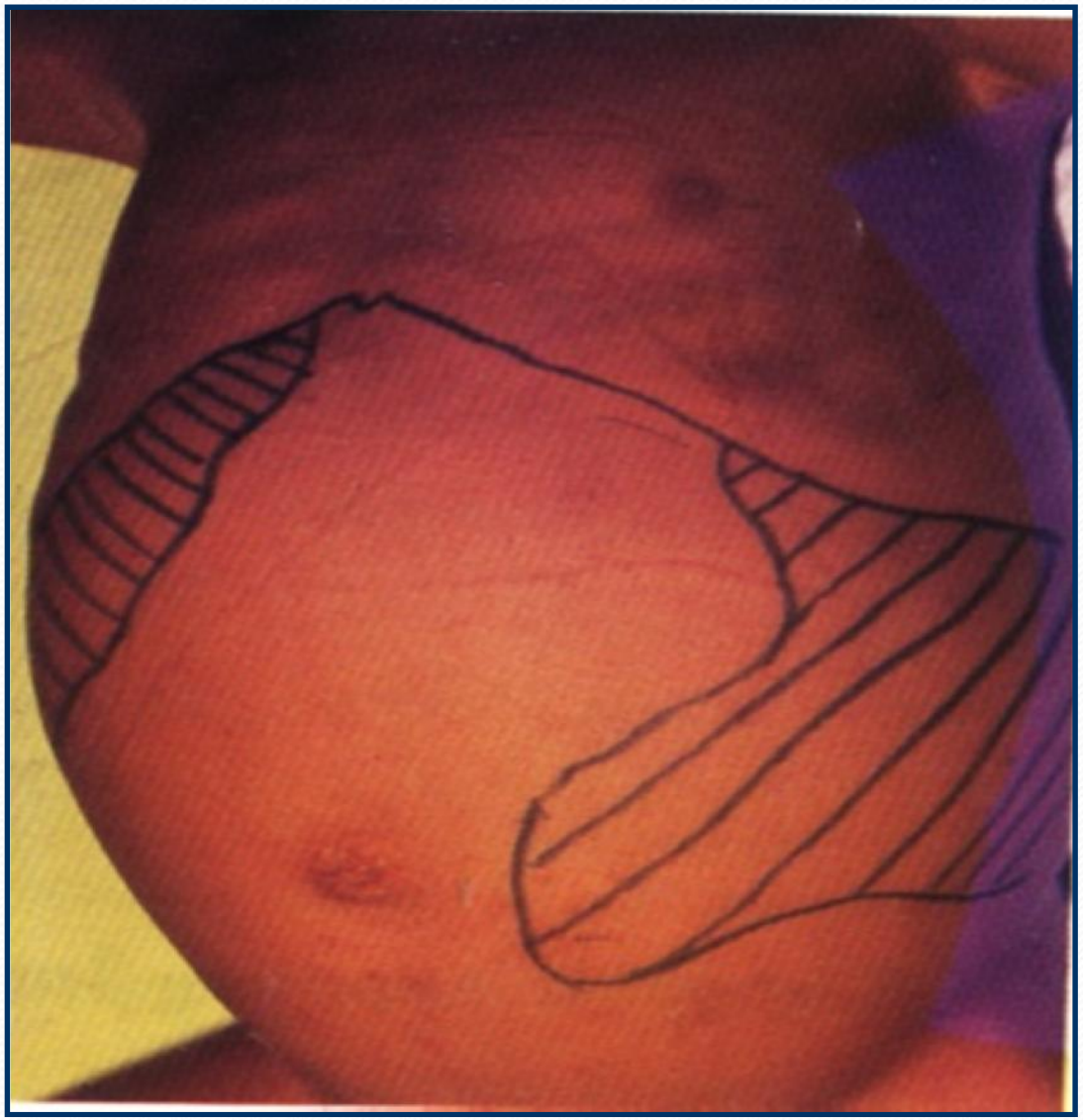
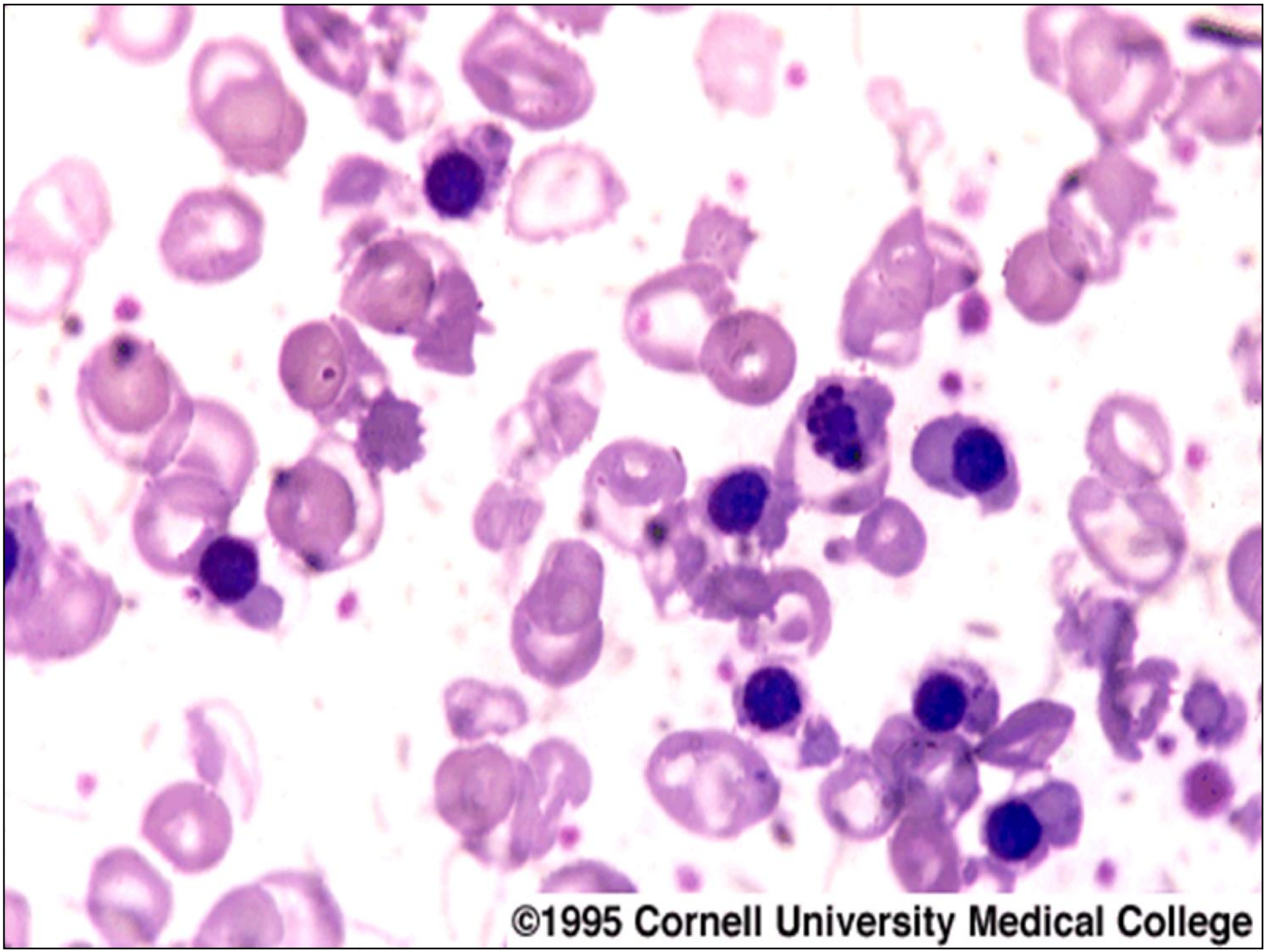
Hepatosplenmegaly



Laboratory Test

- ***Hypochromic & microcytic anemia***
- ***NRBC ↑***
- ***Serum Iron & Ferritin ↑***
- ***BMA: marked E hyperplasia***
- ***E/M: 20/1***
- ***Hb electrophoresis:***
- ***Hb F ↑***
- *Hb A2: variable levels*
- *Hb A: reduced or absent*
- *Th. Trait in both parents*
- *Globin biosynthetic ratio: diagnostic*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Treatment of β Thalassemia Major

- Gene therapy
- Stem cell transplantation
- Blood transfusion


2006 4 12

Blood Transfusion in β.Th. Major

- Determine the blood type & minor Red Cell Antigen :
- ABO, RH ,Kell, Kidd, Duffy

Guidelines For Blood Transfusion

- Patients should not receive PRBC more than two weeks old
- Hb level:9/5-11/5 gr/dl
- Volume of PRC:10-20 Ml/kg of leukocyte-poor and filterd RBC
- Transfusion interval:3-5 weeks
- pretransfusion laboratory tests:CBC
- cross match,RBC antibody screen

Treatment of I.D.A

Replenishment of body Iron

Correction of factor responsible for Iron deficiency

Iron administration:

***Oral: safe, cheap & effective**

***Parenteral: IM, IV**

Parentrarl Indication :

*** poor tolerance**

*** GI Iron absorption is compromised**

*** has Iron needs that can not be met oral therapy because of chronic uncontrollable bleeding**

Oral Iron therapy

Ferrus sulphate is the preferred, salt.

The Iron element: 20%

Dose: 3-6mg/kg/day divided dose

Administration: between meals

Side effects ,10-20%: Nausea

Vomiting

Diarrhea, constipation

Abdominal pain

Plan for side effects : 1- Administration immediately after meal

2- ↓ dose

Parenteral Iron therapy

Dextran :

Side effects

1- Anaphylaxia

2- Serum sickness- like reaction

3- Skin staining (IM)

4- Muscle necrosis

5- Phlebitis

6- Persistent pain

7- Artralgia

Because of anaphylaxia: Test dose 0/5cc

1 hour before.

Parenrtral iron Therapy

- Iron Dextran
- Iron Gluconate
- Iron Sucrose
- Total Dose of Iron dextran (mg): Weight (kg) ×desired increament Hb (g/dl) ×2.5
- 10mg/kg: Additional for Iron Stores

Not more than 2cc/day

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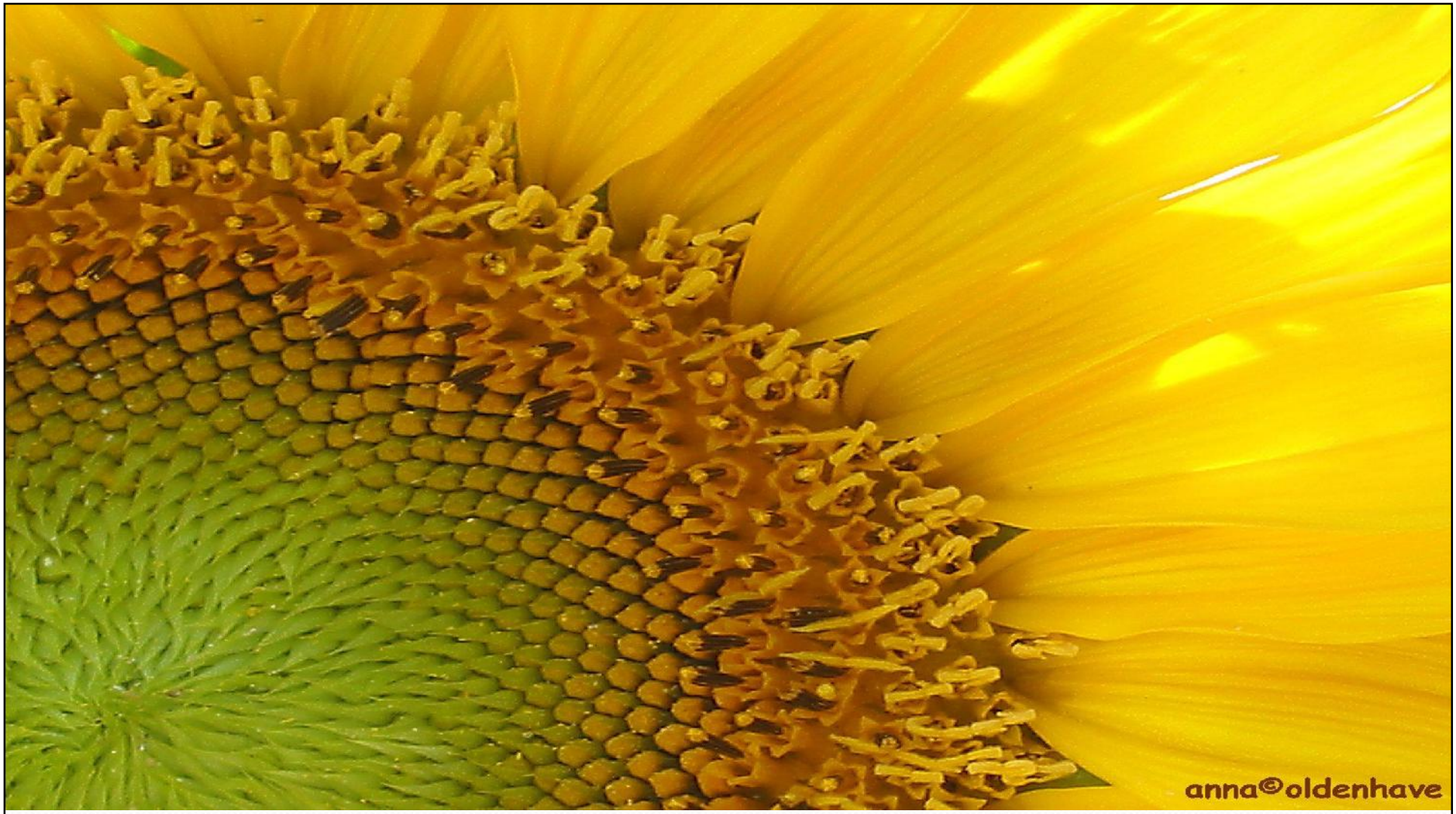
Timing for Iron replacement in infant

1- Breast milk infant: 1mg/kg/day Iron supplementation beyond 6 months

2- Infant with Iron supplemented formula: 12mg/lit Iron

3- Cow's milk should be avoided during the first year.

4- premature infants should receive Iron supplements immediately.



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