Anemia

MARCH ,12,2019

Definition of anemia

- Anemia: A reduction in
  - red cell mass
  - O_2-carrying capacity
- It is expressed in terms of reduction in the concentration of Hb (or RBC or Hct%) compared to values obtained from a reference population.

  (2 SD below normal)

Definition of anemia

- Hb level of a patient which is below the normal ranges of that age and sex.

  For adults:

- WHO criteria define anemia as hemoglobin level lower than 12 g/dL in women and 13 g/dL in men
- But: **The reference values for red cells ,Hb or Hct may difer according to**
  - sex/age
  - Race
  - Altitude
  - Socioeconomical changes
  - Study/reference etc

Reference values (I)

Parameter	Female	Male
RBC ($x10^{12}$/L)	4.8±0.6	5.4±0.9
Hb (g/dL)	14±2	16±2
Htc (%)	42±5	47±5

Reticulocyte

Normal Ranges

- Male: % 0.8 - 2.5
- Female: % 0.8 - 4.1

Corrected Rtc: Patient Hb/Normal Hb x Rtc %

Reticulocytosis: > 100.000 /mm^3

Lower limits of normal of hemoglobin concentration of the blood of adult men and women, as assessed by various sources

Source	Men, g/dL	Women, g/dL	Percent normal below cutoff	Effect of race
WHO (Blanc et al[1])	13	12	Not provided	Not provided
Jandl[3]	14.2	12.2	2.5	Discussed
Williams (Beutler et al[4])	14.0	12.3	2.5	Not provided
Wintrobe (Lee et al[5])	13.2	11.6	Not provided	Not provided
Rapaport[6]	14	12	Not provided	Not provided
Goyette[7]	13.2	11.7	5	Blacks' hemoglobin 0.5 g/dL lower
Tietz[8]	13.2	11.7	Not provided	Not provided
Hoffman et al[9]	13.5	12.0	2.5	Not provided

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- Anemia is rarely a disease by itself,
- It is mostly a manifestation or consequence of an underlying (genetic or acquired) disease.
- The finding of anemia has to start attempts to disclose an underlying disease .

  - What is the cause of anemia ?

Anemia leads to two symptom complexes;

- Tissue hypoxia
  - Fatigue,dyspnea on exertion etc
- Compensatory attempts
  - Tachycardia,hyperventilation etc

- Reduced levels of Hb results with reduced oxygen delivery to tissues , leading to tissue hypoxia.
- The symptoms and findings of anemia concern many different systems/organs due to the widespread nature of hypoxia.

Symptoms of Anemia

- Nonspecific and reflect tissue hypoxia:
  - Fatigue
  - Dyspnea on exertion
  - Palpatations
  - Headache
  - Confusion, decreased mental acuity
  - Skin pallor

Clinical symptoms and findings of anemia (2)

- Fatigue, weakness
  - Tiredness, lassitude, reduced exercise tolerence
  - Generalized muscular weakness
- Pallor /skin or mucous membranes
  - Skin color may change due to other reasons;

    eg :Blood flow of skin, subcutaneous fluid , pigment changes

- Some other skin/mucosal changes
  - Premature graying of hair:pern.anemia
  - Hair loss and fragility + spooning of the nails:iron deficiency
  - Chronic leg ulcers:Sickle cell or other hemolytic anemia
  - Glossitis/burning sense :Pern. anemia, iron deficiency(rare)
  - Chelitis(angular stomatitis):iron def.
  - Siideropenic dysphagia: iron def.
  - Painful ulcerative mouth lesions: aplastic anemia/leukemia

Clinical symptoms and findings of anemia

Cardiovascular System

- High output state: Collapsing pulse, high pulse pressure
- Cardiomegaly
- Congestive failure
- Ischemic ECG changes

Clinical symptoms and findings of anemia

Reproductive system

- Menstrual changes:
  - Amenorrhea ,
  - Menorrhagia(mostly a cause of anemia)
- Loss of libido

Clinical symptoms and findings of anemia .

Gastrointestinal system

(these symptoms may indicate underlying disorder that might indeed be a cause of anemia)

- Anorexia
- Flatulence
- Nausea
- Constipation
- Weight loss

These should remind GIS disease as a cause of anemia

(eg:a bleeding lesion-ulcer/malignancy etc)

Clinical symptoms and findings of anemia .

- Renal Changes
  - Slight proteinuria
  - Concentrating defects
  - Further reduction of renal function in patients with previous renal impairment

  (Renal failure itself is a cause of anemia!!!!)

History and Physical in Anemia

- Duration and onset of symptoms
- Change in stool habits: Stool Guaiacs in all
- Splenomegaly?
- Jaundiced?

Classification of anemia

- Morphologic
  - Normocytic: MCV= 80-100fL
  - Macrocytic: MCV > 100 fL
  - Microcytic : MCV < 80 fL
- Pathogenic (underlying mechanism)
  - Blood loss (bleeding)
  - Decreased RBC production
  - Increased RBC destruction/pooling

Normocytic Anemias

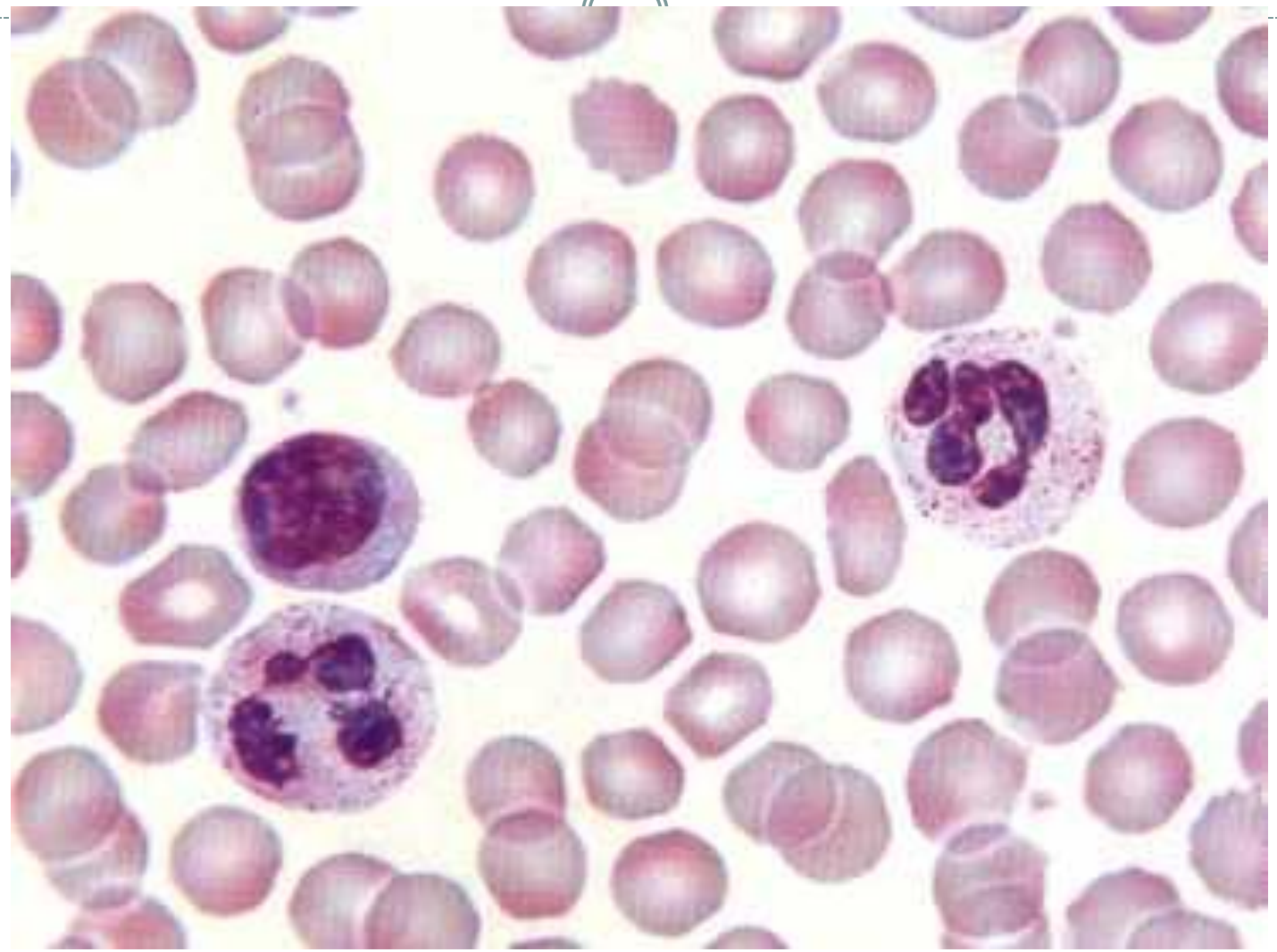
- Acute post-hemorrhagic anemia
- Hemolytic anemia (except thalassemia and some other Hb disorders)
- Aplastic anemia
- Pure red cell aplasia
- Bone marrow infiltration

- Endocrin diseases
- Renal failure
- Liver disease
- Chronic disease anemia
- Protein malnutrition
- Hypovitaminosis C

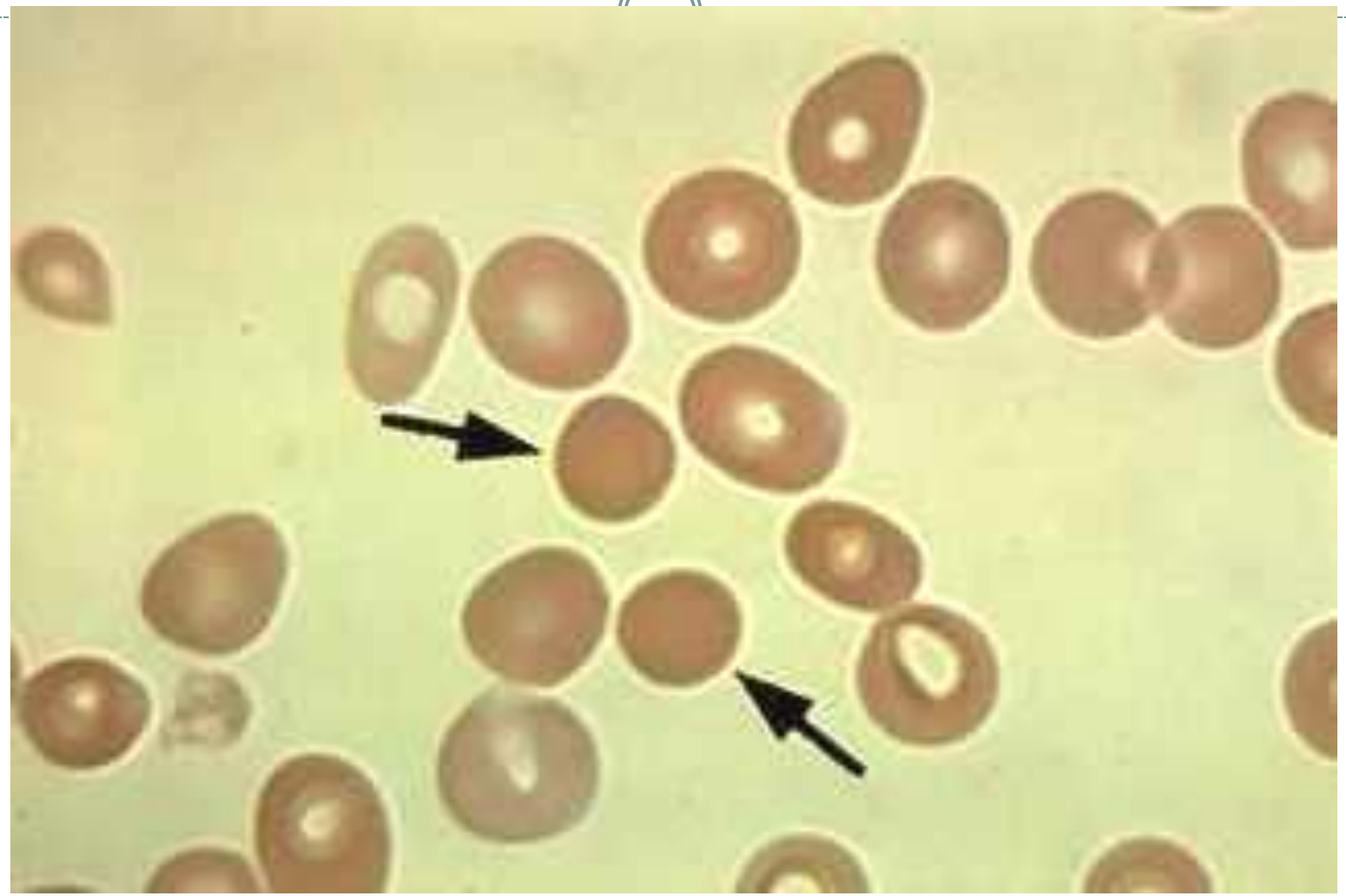
Microcytic anemias

- Iron deficiency anemia
- Thalassemia
- Sideroblastic anemia
- Lead poisoning
- Anemia of chronic diseases (some cases)

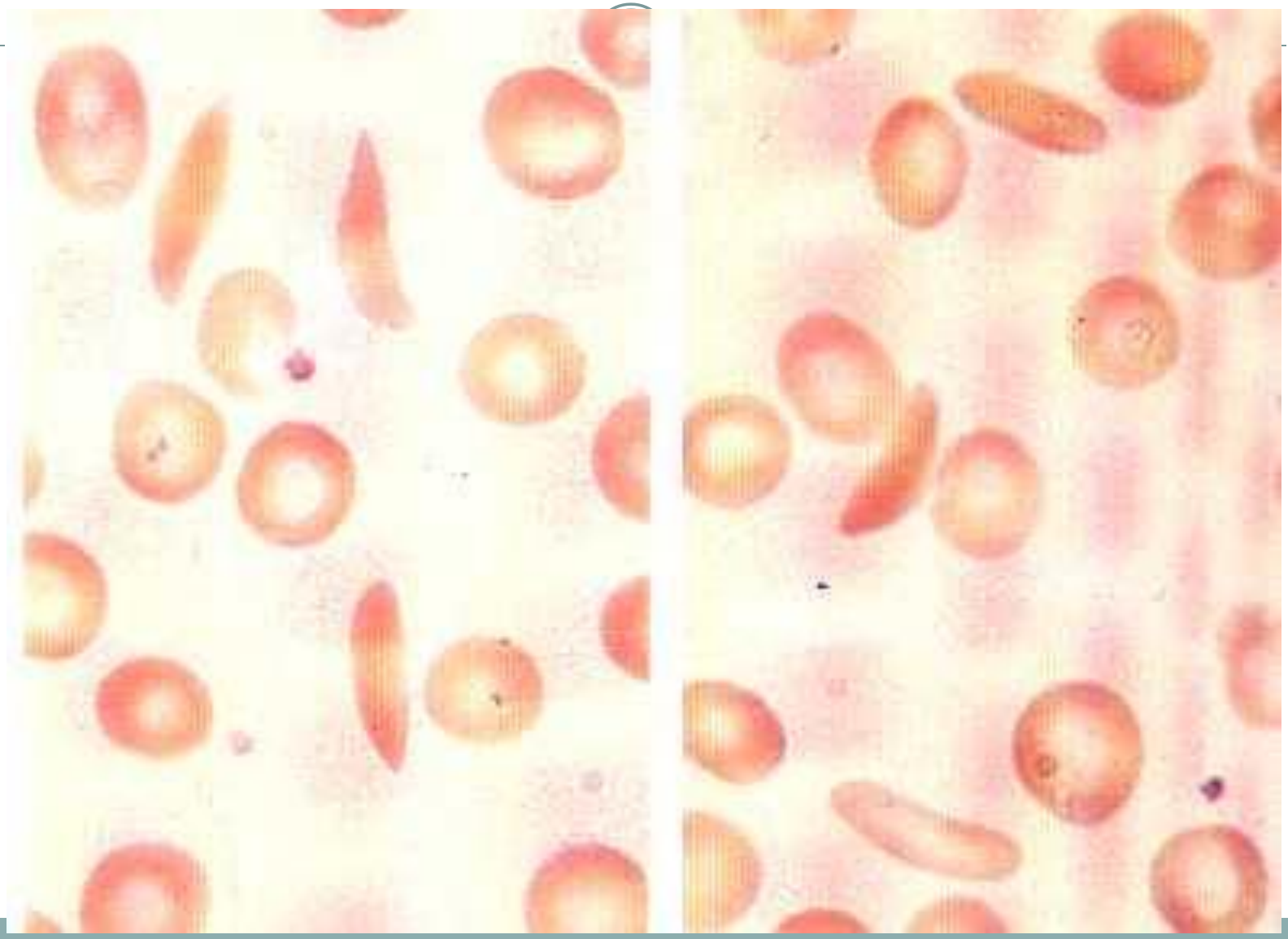
Blood Smear - Normal



Her. Spherocytosis:



Sickle Cells



Macrocytic anemias

- Megaloblastic
- Non-megaloblastic

Megaloblastic Macrocytic Anemias

- Vit B12 deficiency
- Folic acid deficiency
- Other.

Non-megaloblastic Macrocytic Anemias

- Anemia of acute bleeding
- Hemolytic anemias
- Leukemias

(esp: acute)

- Myelodysplastic syndromes
- Liver disease
- Aplastic anemia
- Diseases infiltrative to the bone marrow
- Alcoholism
- Hypothyroidism
- Scurvy

Pathogenic classification (Causes of anemia)

- Relative (increased plasma volume)
- Decreased RBC production
- Blood loss
  - Anemia due to acute bleeding
- Increased RBC destruction

Pathogenic classification (Causes of anemia)

- Decreased RBC production
  - Decreased Hb production
  - Defective DNA synthesis
  - Stem cell defects
    - Pluripotent stem cell
    - Erythroid stem cell(progenitors)
  - Other less defined reasons
- Blood loss
  - Anemia due to acute bleeding
- Increased RBC destruction
- Relative(increased plasma volume)

Decreased Hb production

- Iron deficiency anemia
- Thalassemia
- Sideroblastic anemia
- Lead poisoning

Defective DNA synthesis

- Vit B12 deficiency
- Folic acid deficiency
- Other.

Decreased RBC production due to multipl or undefined mechanisms

- Anemia of chronic diseases
- Bone marrow infiltration
- Anemia due to nutritional defects

Anemias caused by increased RBC destruction (hemolytic anemias)

Can be classified as;

- Hemolysis due to intracorpuscular defects
- Hemolysis due to extracorpuscular defects

Or

- Hereditary hemolytic diseases
- Acquired hem. diseases

Or

- Intravascular hemolysis
- Extravascular hemolysis etc.

A Very Simple Classification of Hemolytic Anemias

Intracorpuscular

1- Abnormalities of RBC interior

- **a. Enzyme defects**
- **b. Hemoglobinopathies & Thalassemia M**

2-RBC membrane abnormalities

- **a. Hereditary spherocytosis, elliptocytosis etc**
- **b. Paroxysmal nocturnal hemoglobinuria**

Extracorpuscular

- **c. Spur cell anemia**

3- Extrinsic factors

- **a. Hypersplenism**
- **b. Antibody : immune hemolysis**
- **c. Traumatic & Microangiopathic hemolysis**
- **d. Infections , toxins , etc**

Hereditary

Acquired

Diagnosis and investigation:

- Is the patient anemic?
- What is the type of anemia?
- What is the cause of anemia?

Is the patient anemic ?

- RBC count
- HB level
- Hct level
- Volume status

What is the type of anemia?

- History and physical exam.
- RBC,HB,Hct ,
- MCV, MCH,RDW
- Red cell morphology (peripheral smear)
- Reticulocyte count
  - Incresed ?
- Other Lab. investigations

Lab. investigation of anemia(1)

- WBC count and differential
- Platelet count and morphology
- ESR
- Biochemistry, special tests and others
- Bone marrow exam.(only when indicated)

Lab. investigation of anemia(2)

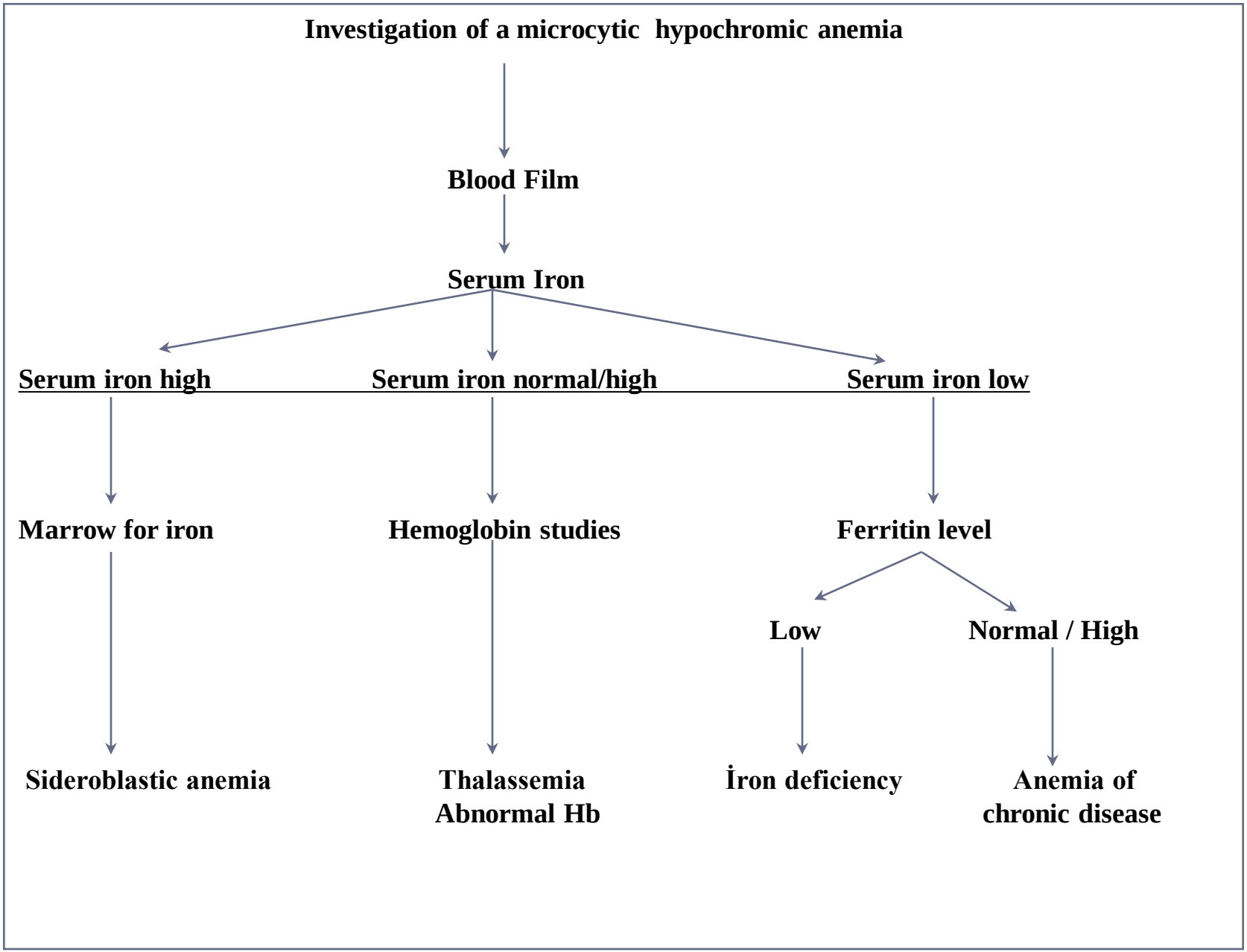
- Serum values of
  - Iron
  - TIBC
  - Ferritin
  - Bilirubins
  - Proteins / electrophoresis
  - LDH
  - Vit B12 and /or Folic acid

  (*None of these tests are routine screening tests*)

Lab. Investigation of Anemia(3)

- Red cell enzymes
- Hb F,A2,Hb electrophoresis
- Coombs tests
- Liver, renal, endocrin functional tests
- Urinalysis
  - Hemosiderin
- Occult GIS bleeding / parasites etc

(*tests should be chosen individually-do not order routinly*)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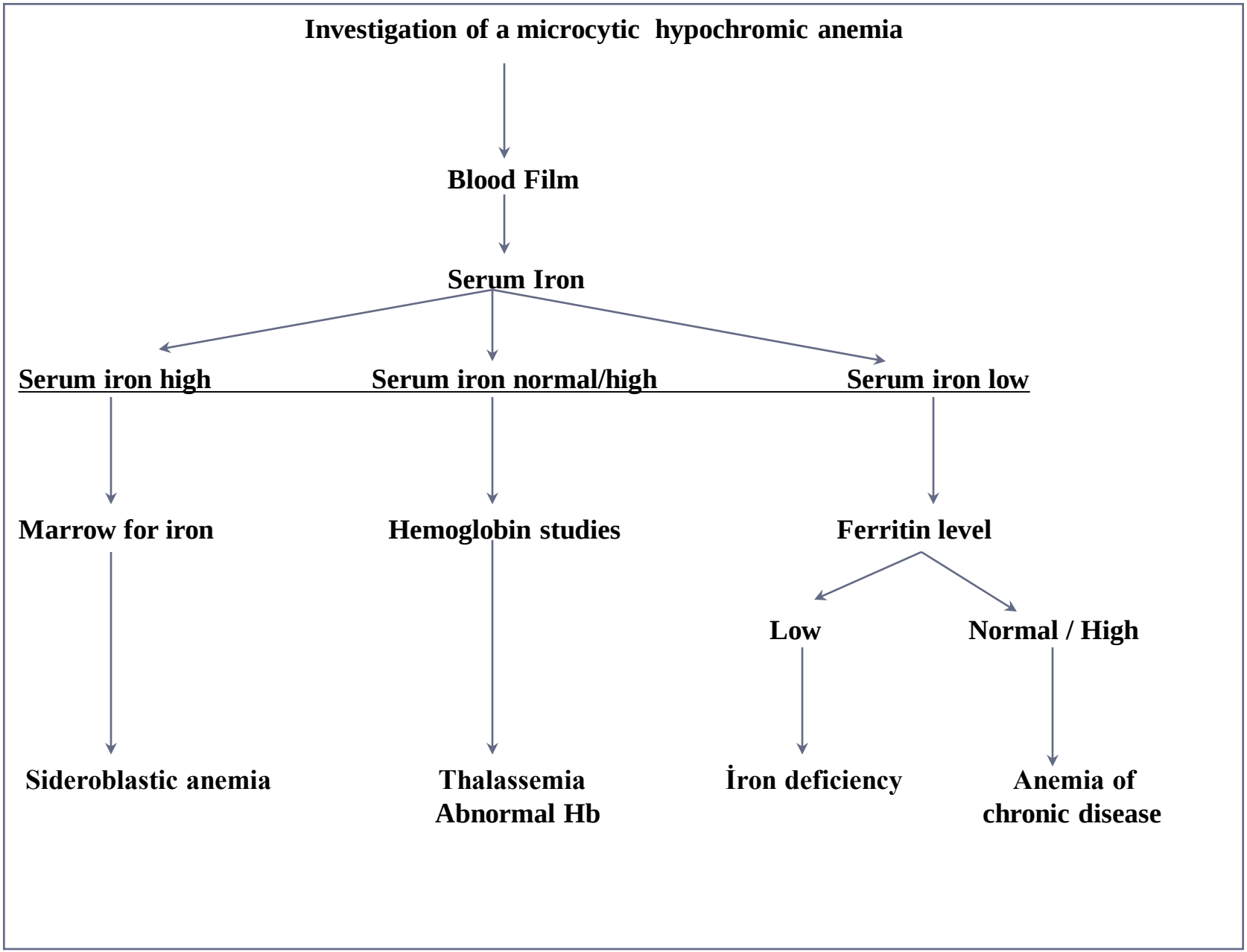
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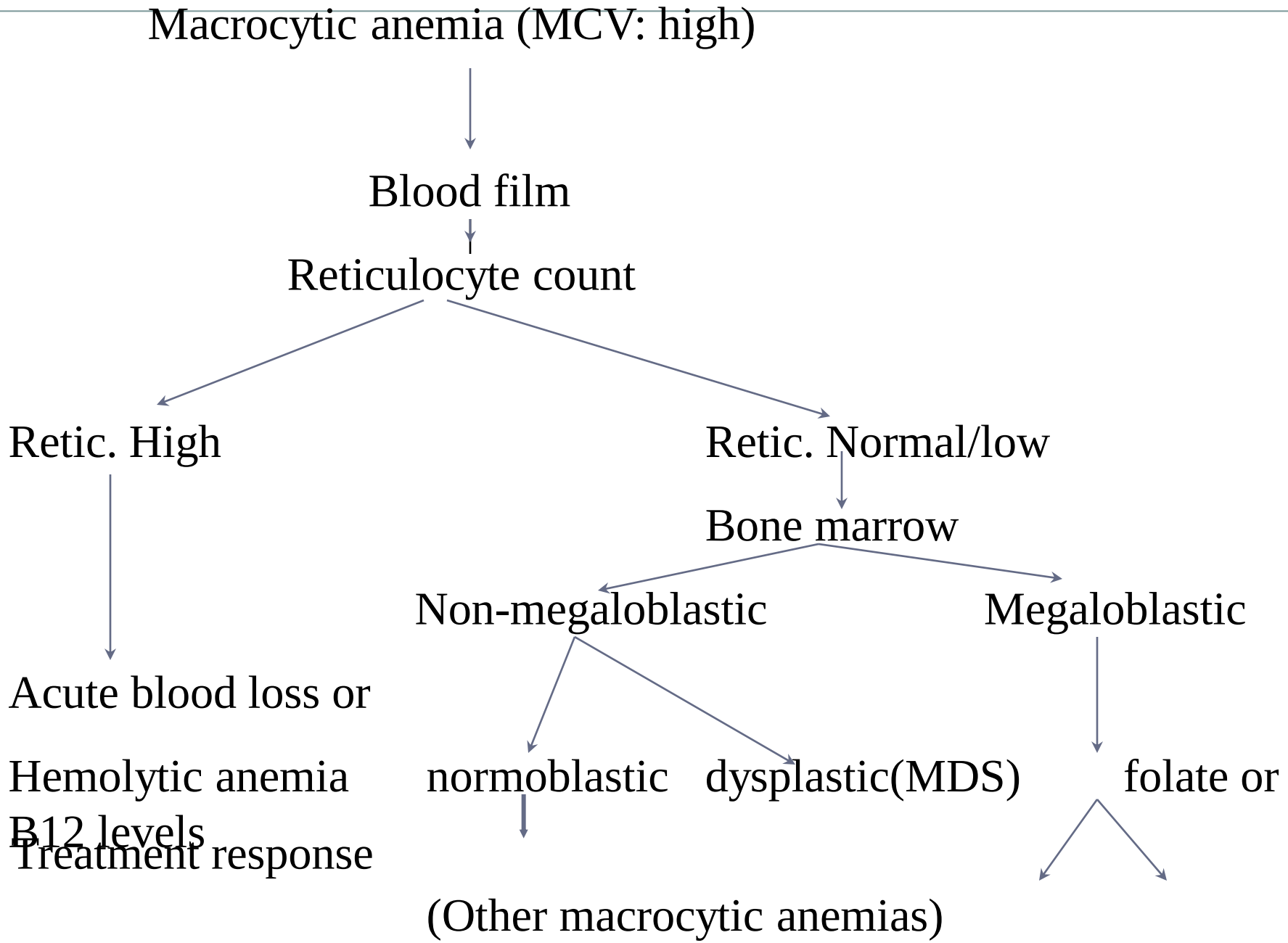

folate , Vit B12

Anemia

Low Retic count & Normal Bili/LDH **Hypoproliferative Anemia**	*High Retic count & High Bili/LDH* **Hemolytic Anemia**
Low Retic count & High Bili/LDH **Ineffective Erythropoiesis**	*High Retic count & normal Bili/LDH* **Blood Loss**

Treatment

- Depends on underlying etiology (Blood loss ,Nutritional causes, …)
- Treat Iron deficiency by tablets or IV Iron.
- B12 , Folate deficiency by replacement
- Thalassemia Blood Transfusion.
- SCD by medication and analgesia and Blood transfusion .