Mechanisms of anemia due to defects in erythrocyte production

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Term-III, Committee-II

Reference values

Parameter	Female	Male
• RBC (x10^{12}/L)	4.8±0.6	5.4±0.9
• Hb (g/dL)	12-16	13-16.5
• Htc (%)	35.5-44.9	38.3-48.9

Reference values

- **Ret (% / n)** **0.5-2.5 / 50-100x10^9/L**
- **MCV (fl)** **90±10**
- **MCH (pg)** **29±2**
- **MCHC (g/dL)** **34±2**
- **RDW (%)** **11.5-14.5**

Anemia

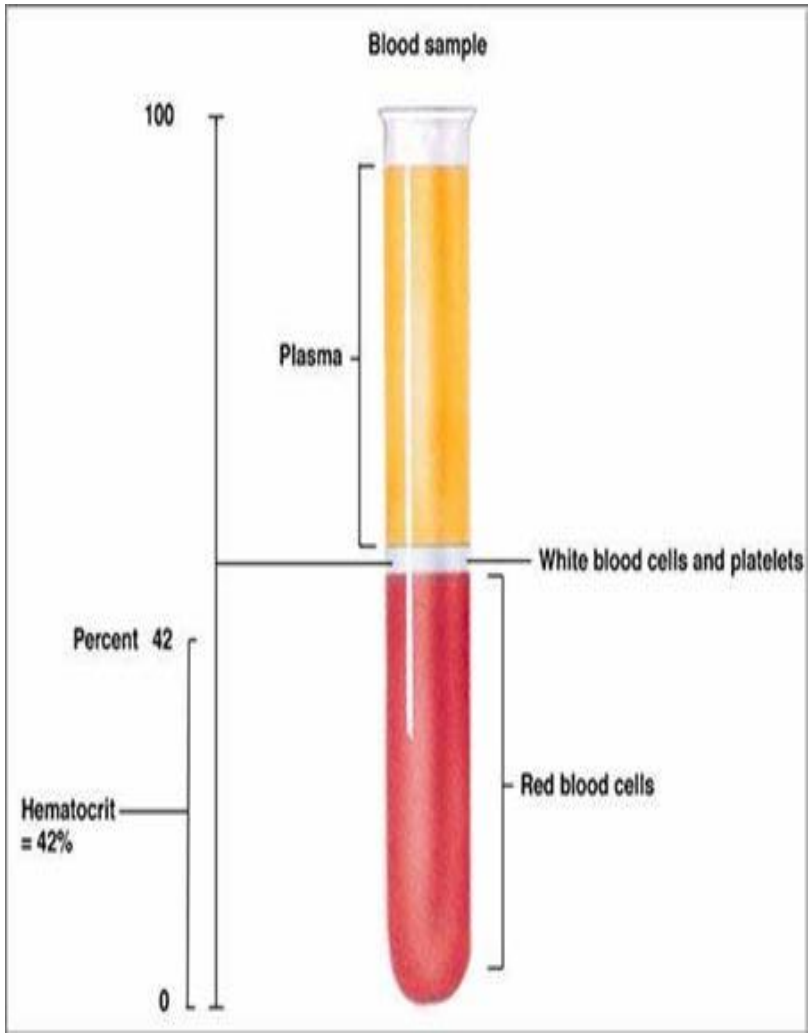
- defined as a reduction in:
  - red cell mass
  - O_2-carrying capacity
- expressed in terms of reduction in the concentration of Hb (or RBC or Hct%) compared to values obtained from a reference population which is 2 SD below normal.

Anemia

- Hb level of a patient which is below the normal ranges of that age and sex.
- WHO criteria define anemia as hemoglobin level lower than **12 g/dL** in women and **13 g/dL** in men for adults.
- **The reference values for red cells, Hb or Hct may differ according to**
  - Sex/Age
  - Race
  - Altitude
  - Socio-economical changes, etc.

Plasma Volume & Anemia

- Plasma volume changes have to be considered before determining a diagnosis of anemia.
  - **Volume contraction**: Underestimation of anemia
  - **Volume overload:** Underestimation of Hb level



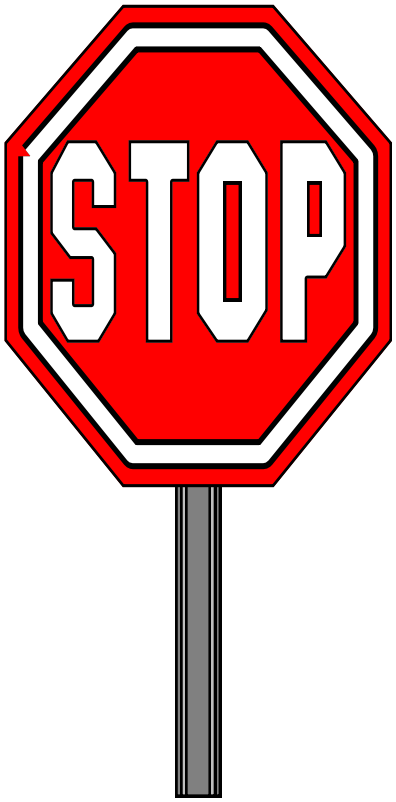
Hct= RBC Volume/Total Blood Volume

Expected Hb level & Anemia

- A normal Hb in a patient in whom an elevated Hb level is expected may represent anemia
  - e.g.: Chronic Obstructive Pulmonary Disease (COPD) + Normal Hb level

RBC level & Anemia

- Different red cell measures of the same patient may give discordant values in special conditions. (e.g.: Thalassemia trait).
- Patient with low Hb, high RBC, low MCV
  - Hb: 10 g/dL (anemia)
  - MCV : 70 fL
  - RBC: 6.5 million/mm3 (erythrocytosis)



Anemia

is **never** a diagnosis of disease.

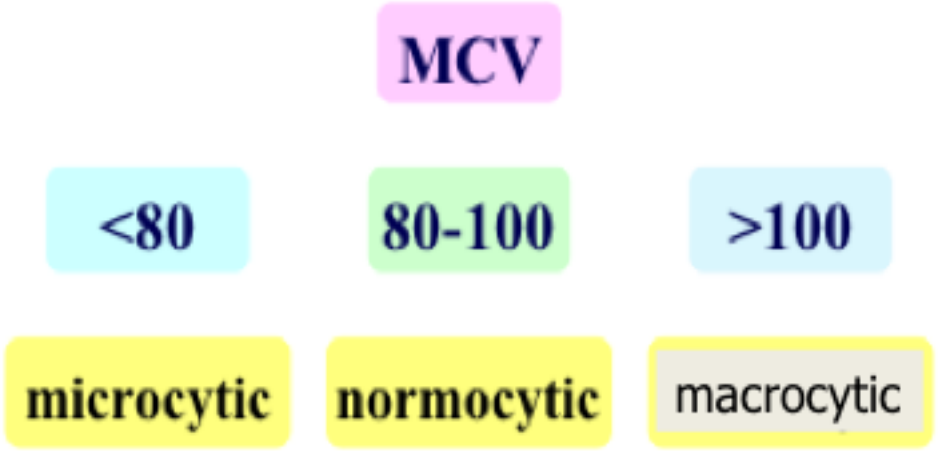
It is only a **finding**.

Underlying disease

- 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.

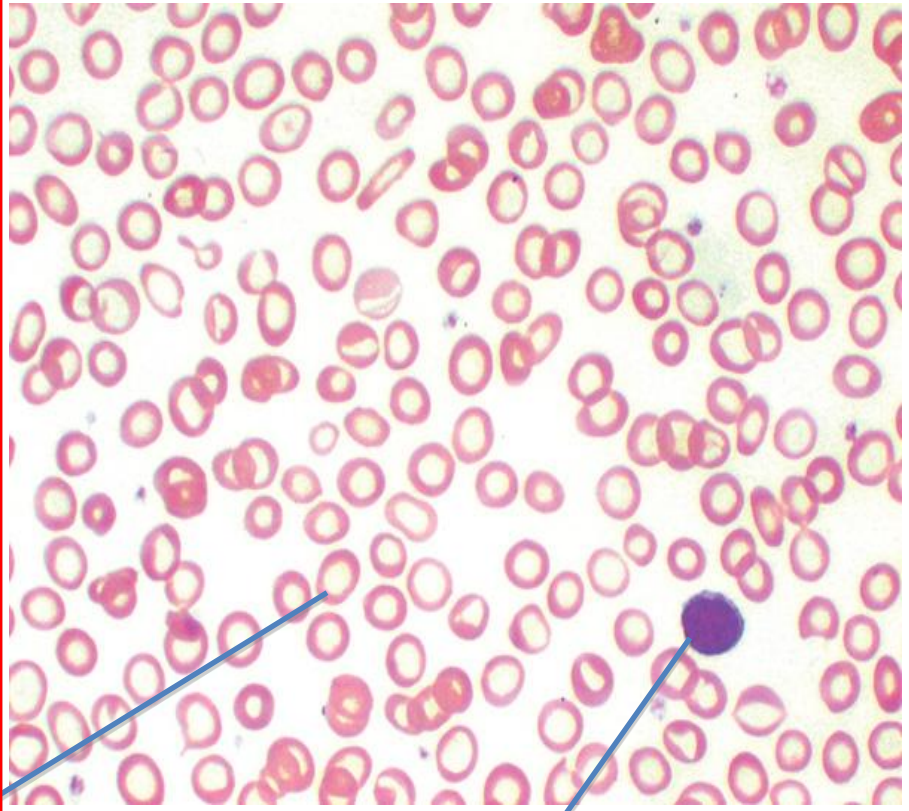
Classification of anemia-I

- I) Morphologic
- II)Pathologic
- **I) Morphologic**
  - Normocytic: MCV= 80-100 fL
  - Macrocytic: MCV > 100 fL
  - Microcytic : MCV < 80 fL



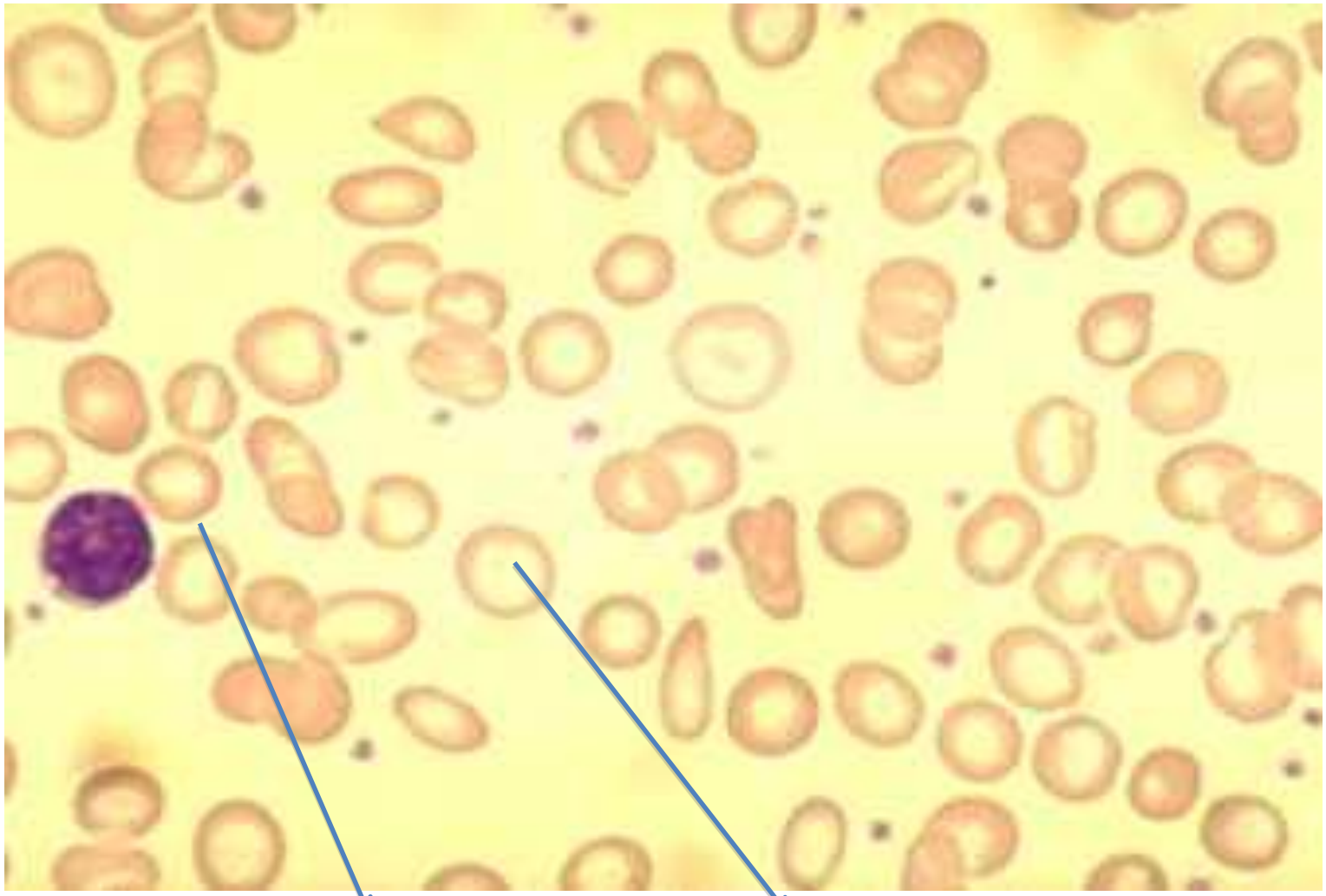
Microcytic anemias

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



RBC is smaller than lymphocyte (MCV<80 fL)

Iron deficiency anemia



Microcytosis & hypochromia

Macrocytic anemias

- **Megaloblastic**
  - Vit B12 deficiency (most common)
    - **Pernicious Anemia** (most common)
  - Folic acid deficiency
- **Non-megaloblastic**
  - Acute bleeding
  - Hemolytic anemias
  - Leukemias (esp: acute leukemia)
  - Myelodysplastic syndromes
  - Liver disease
  - Aplastic anemia
  - Bone marrow infiltration
  - Alcoholism
  - Hypothyroidism

Normocytic Anemias

- Acute Bleeding
- Hemolytic anemia (except thalassemia and some other Hb disorders)
- Aplastic anemia
- Pure red cell aplasia
- Bone marrow infiltration
- Endocrine diseases
- Renal failure
- Liver disease
- Chronic disease anemia
- Protein malnutrition
- Hypovitaminosis C

Classification of anemia-II

- II) Pathogenic (underlying mechanism)
  1) Decreased RBC production
  2) Increased RBC destruction/pooling
  3) Blood loss (bleeding)
  4) Relative (increased plasma volume)

Pathogenic classification

1. **Decreased RBC production**
   a) **Decreased Hb production**
   b) **Defective DNA synthesis**
   c) **Stem cell defects**
      I. Pluripotent stem cell
      II. Erythroid stem cell (progenitors)
   d) **Other less defined reasons**

Decreased RBC production-I

a) Decreased Hb production

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

Decreased RBC production-II

b) Defective DNA synthesis

- Vit B_{12} deficiency
  - Pernicious anemia (autoimmune disease)
- Folic acid deficiency
- Other

Decreased RBC production-III

c) Stem cell defect

- **Pluripotent stem cell defects**
  - Aplastic anemia
  - Leukemia or myelodysplastic syndromes (MDS)
- **Erythroid stem cell defects**
  - Pure red cell aplasia
  - Anemia of chronic renal failure
  - Endocrine disease anemia
  - Congenital dyserythropoietic anemias

Decreased RBC production-IV

d) Multiple or undefined mechanisms

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

Increased RBC destruction (hemolytic anemias)

2. Increased RBC destruction/pooling

- Can be classified as:
  - Intracorpuscular / extracorpuscular defects
  - Hereditary / Acquired
  - Intravascular / Extravascular

Simple Classification of Hemolytic Anemias

Intracorpuscular

1- Abnormalities of RBC interior

a. Enzyme defects (G6PD)

b. Hemoglobinopathies

2-RBC membrane abnormalities

a. Hereditary spherocytosis, elliptocytosis etc

b. Paroxysmal nocturnal hemoglobinuria (PNH)

Hereditary

Extracorpuscular

c. Spur cell anemia

3- Extrinsic factors

a. Hypersplenism

b. Antibody : immune hemolysis

c. Traumatic & Microangiopathic hemolysis

d. Infections , toxins , etc.

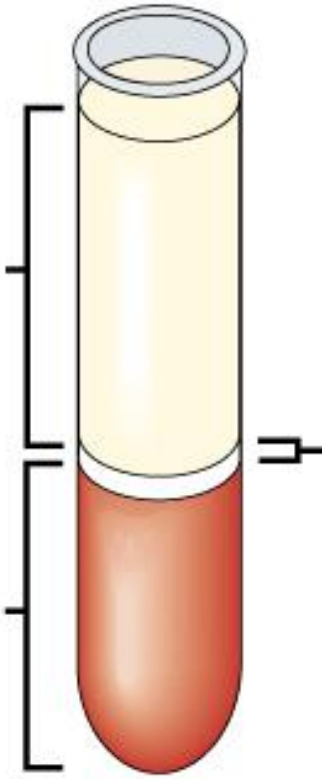
Acquired

Questions taken into consideration

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

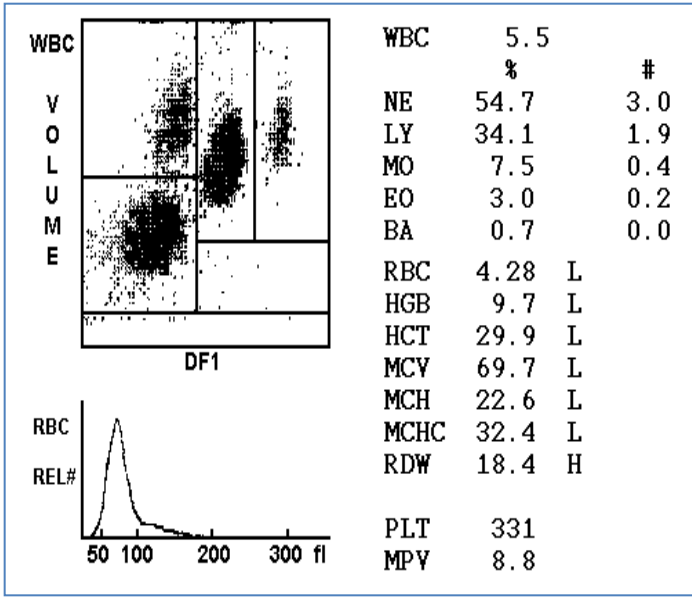
Is the patient anemic ?

- Check:
  - RBC count →
  - Hb level →
  - Hct level →
  - Volume status → N

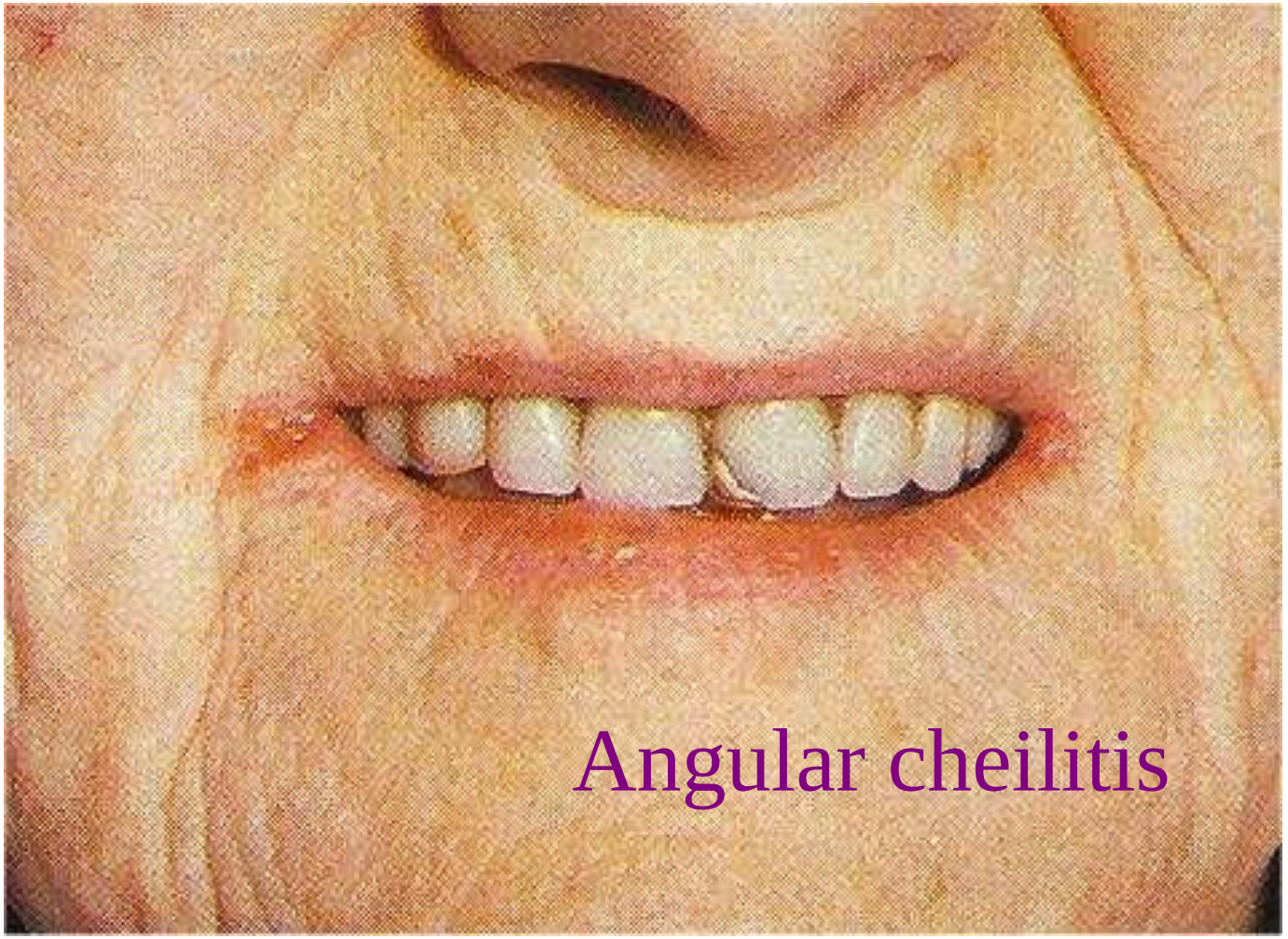


What is the type of anemia?

- History and physical exam
- CBC
  - RBC, Hb, Hct
  - MCV, MCH, RDW
  - Reticulocyte count
    - Increased ?
- Peripheral blood smear
  - Red cell morphology



What is the type of anemia?
History and physical exam



What is the type of anemia?
History and physical exam

What is the type of anemia?
History and physical exam

- Bossing of the skull
- Hypertrophy of the maxilla
- Exposing the upper teeth
- Depression of nasal bridge
- Perorbital puffiness
- Pallor
- Massive Hepatosplenomegaly

Beta thalessemia major

What is the type of anemia?

History and physical exam

DIZZINESS

Ataxia

Neurological findings

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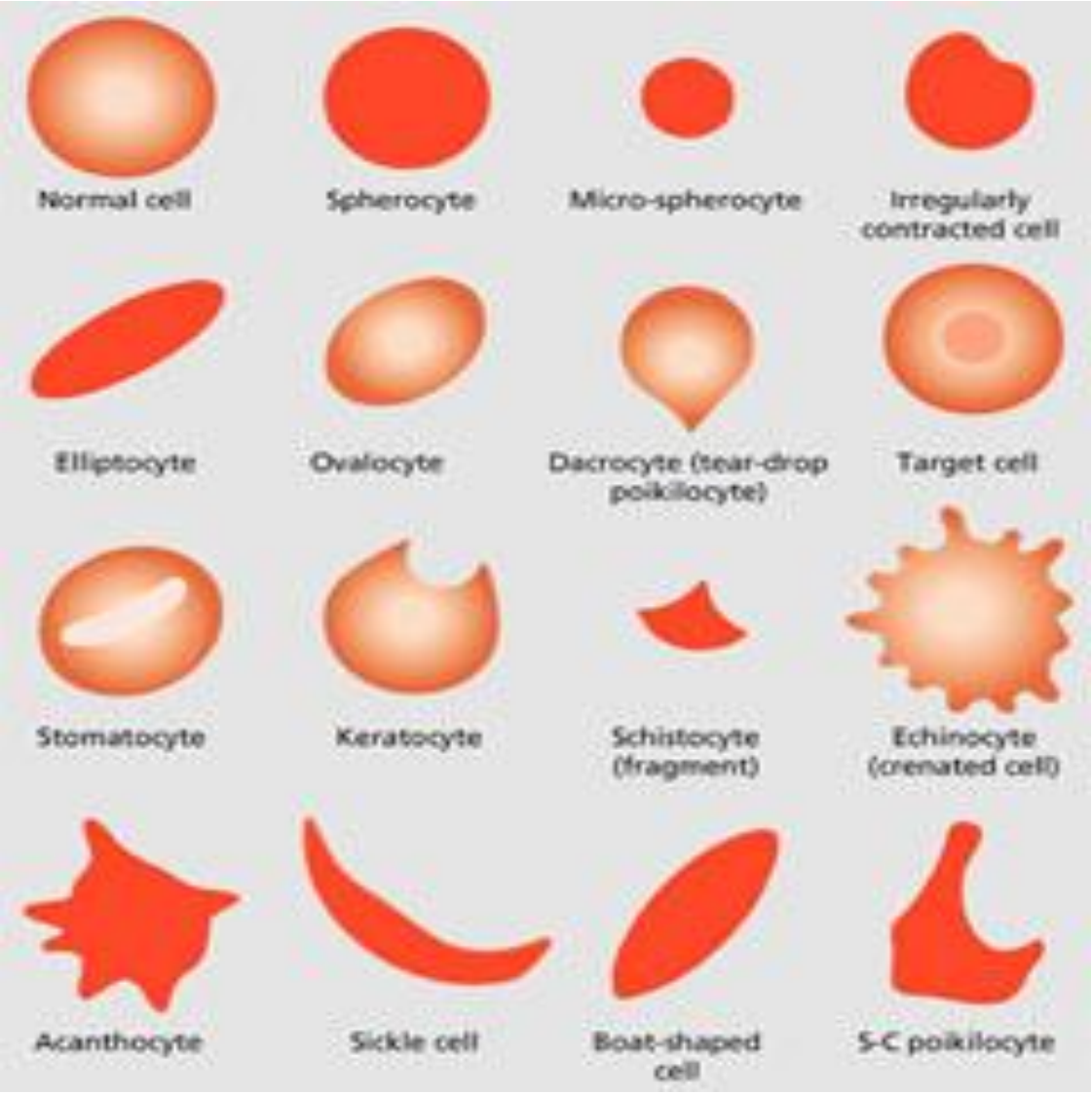
What is the type of anemia?

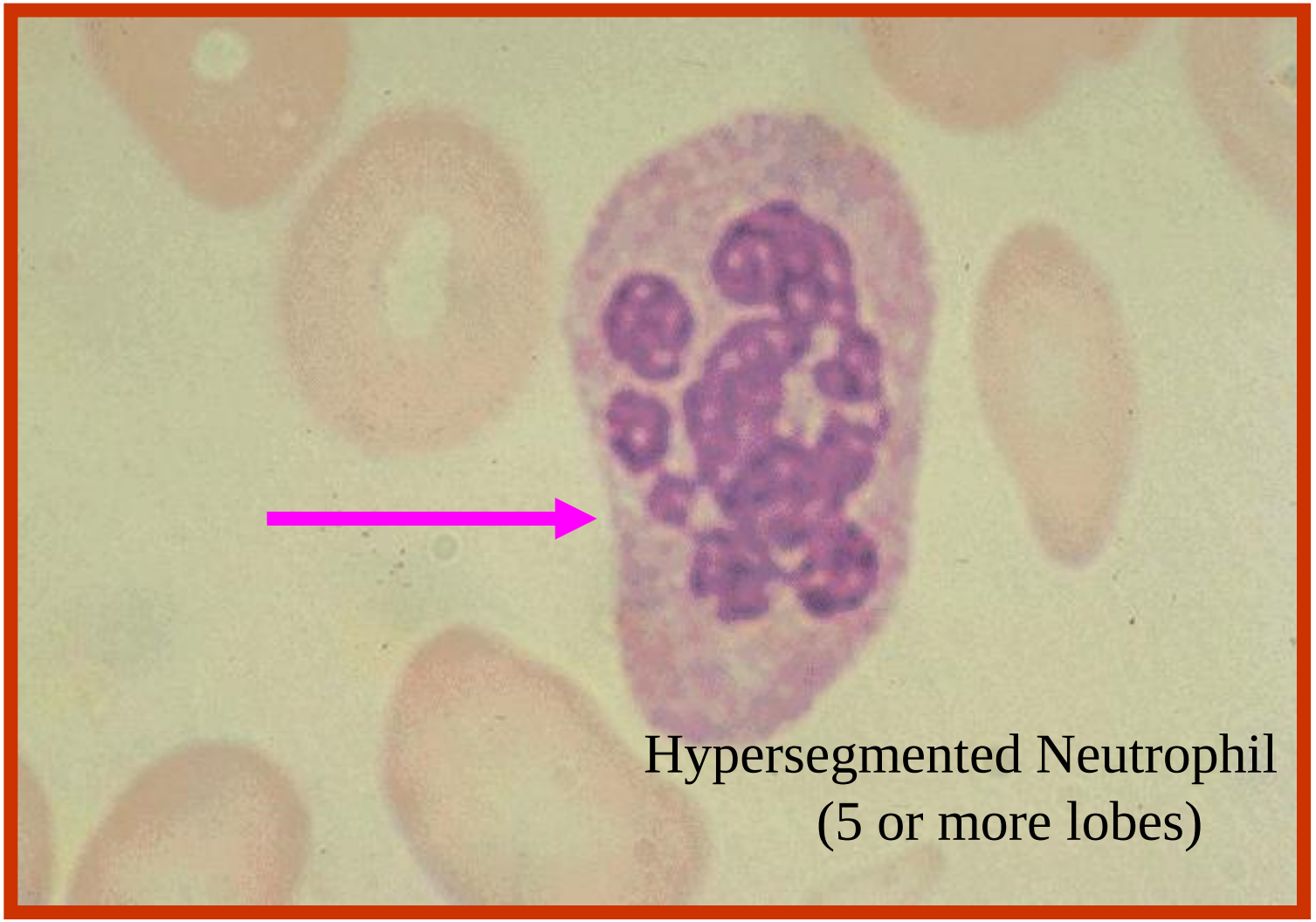
History and physical exam

Glossitis Moeller-Hunter

What is the type of anemia?
Peripheral blood smear



What is the type of anemia?
Peripheral blood smear



What is the cause of anemia?

- Lab investigation of anemia
  - WBC count and differential
  - Platelet count and morphology
  - Erythrocyte Sedimentation Rate
  - Biochemistry
  - Bone marrow exam (only when indicated)

What is the cause of anemia?

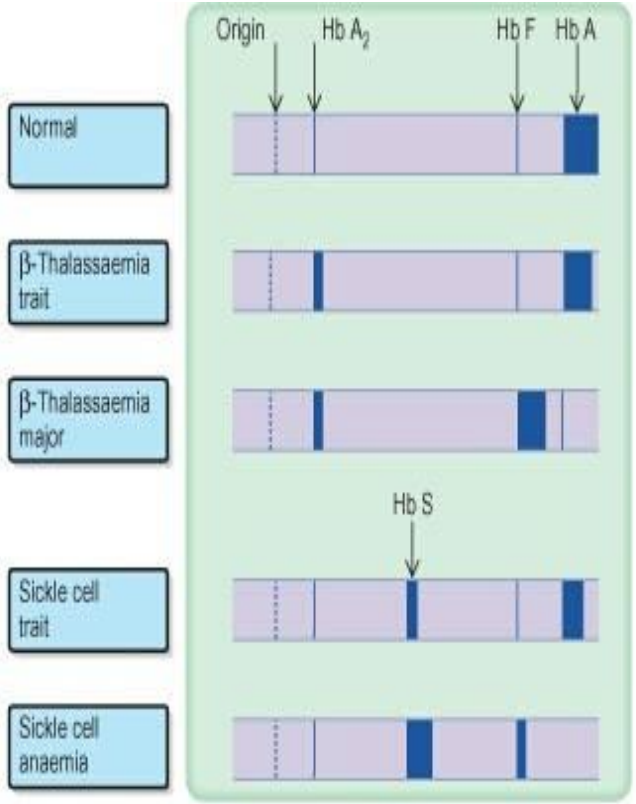
- Lab investigation of anemia
  - Serum values of
    - Iron
    - Total Iron Binding Capacity (TIBC)
    - **Ferritin**
    - Ind. Bilirubin
    - Hemoglobin electrophoresis
    - Lactate dehydrogenase (LDH)
    - Vit B12 and/or Folic acid
  - *None of these tests are routine screening tests*.

What is the cause of anemia?

- Lab investigation of anemia
  - Red cell enzymes (G6PD, PK)
  - Hb electrophoresis (HbF, HbA2,S,C,etc)
  - Direct Coombs tests (DAT)
  - Liver, renal, endocrine functional tests
  - Urinalysis
    - Hemosiderin
  - Occult GIS bleeding / parasites, etc

✓ *tests should be chosen individually.*

  ✓ *Do not order routinely*.



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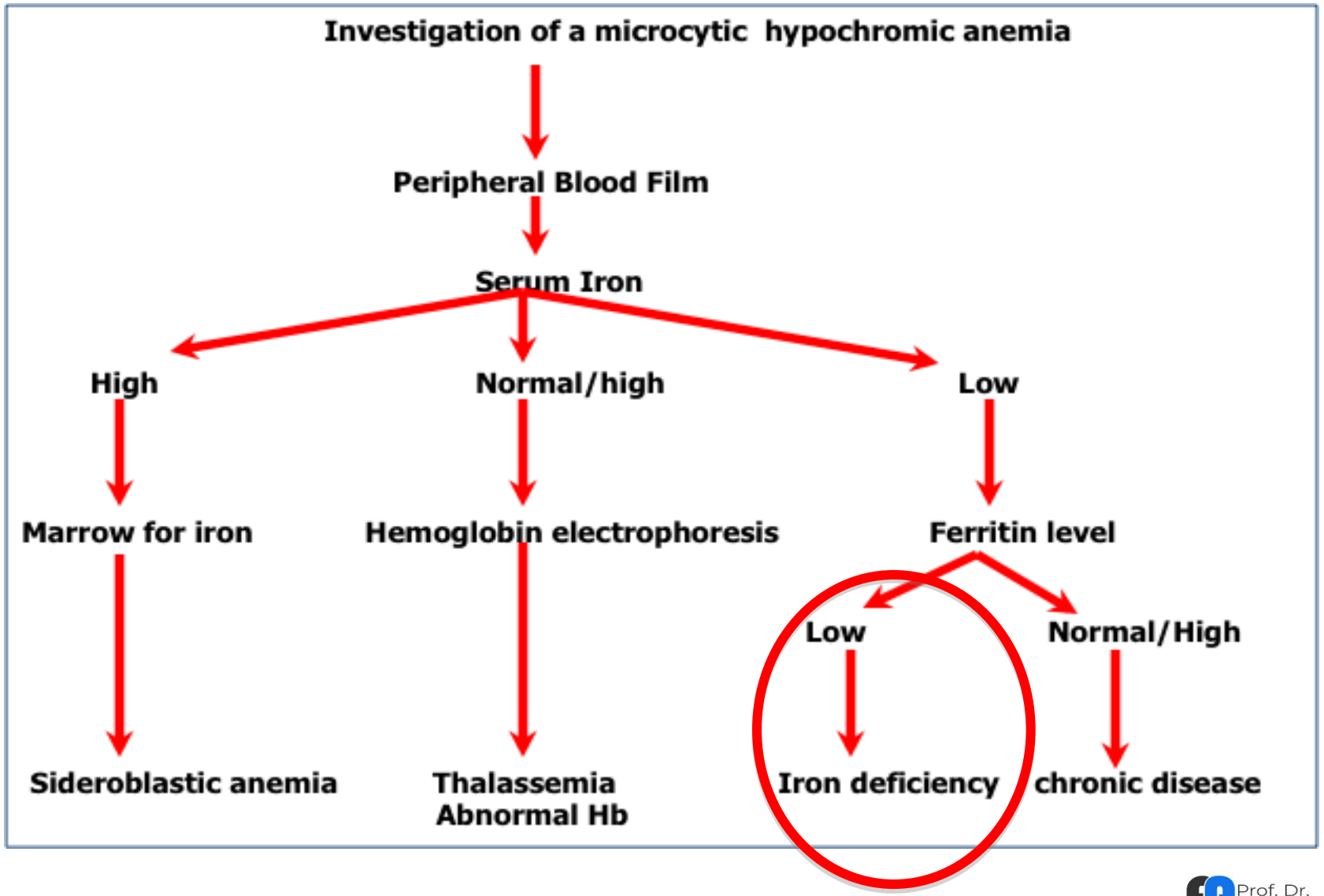

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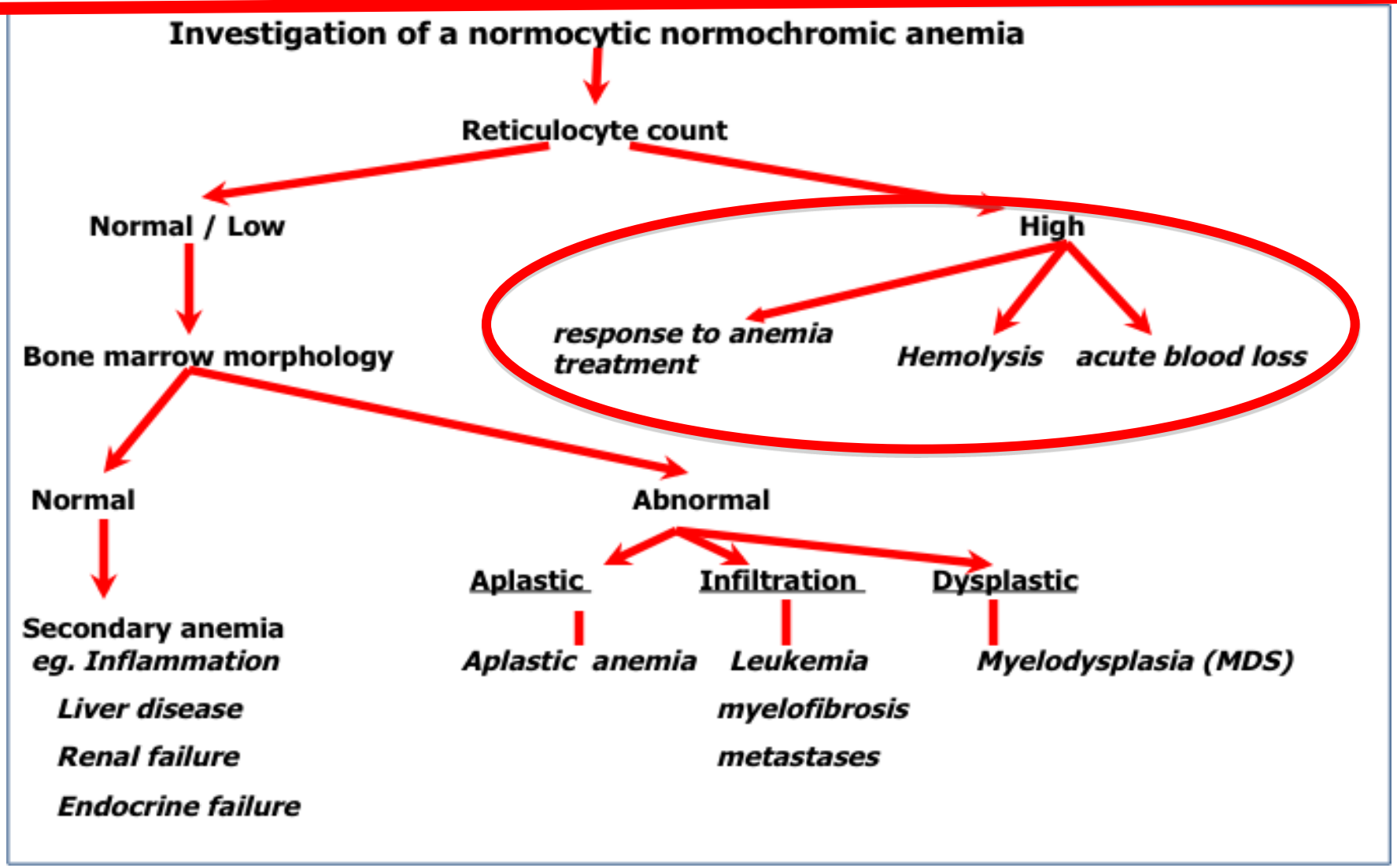

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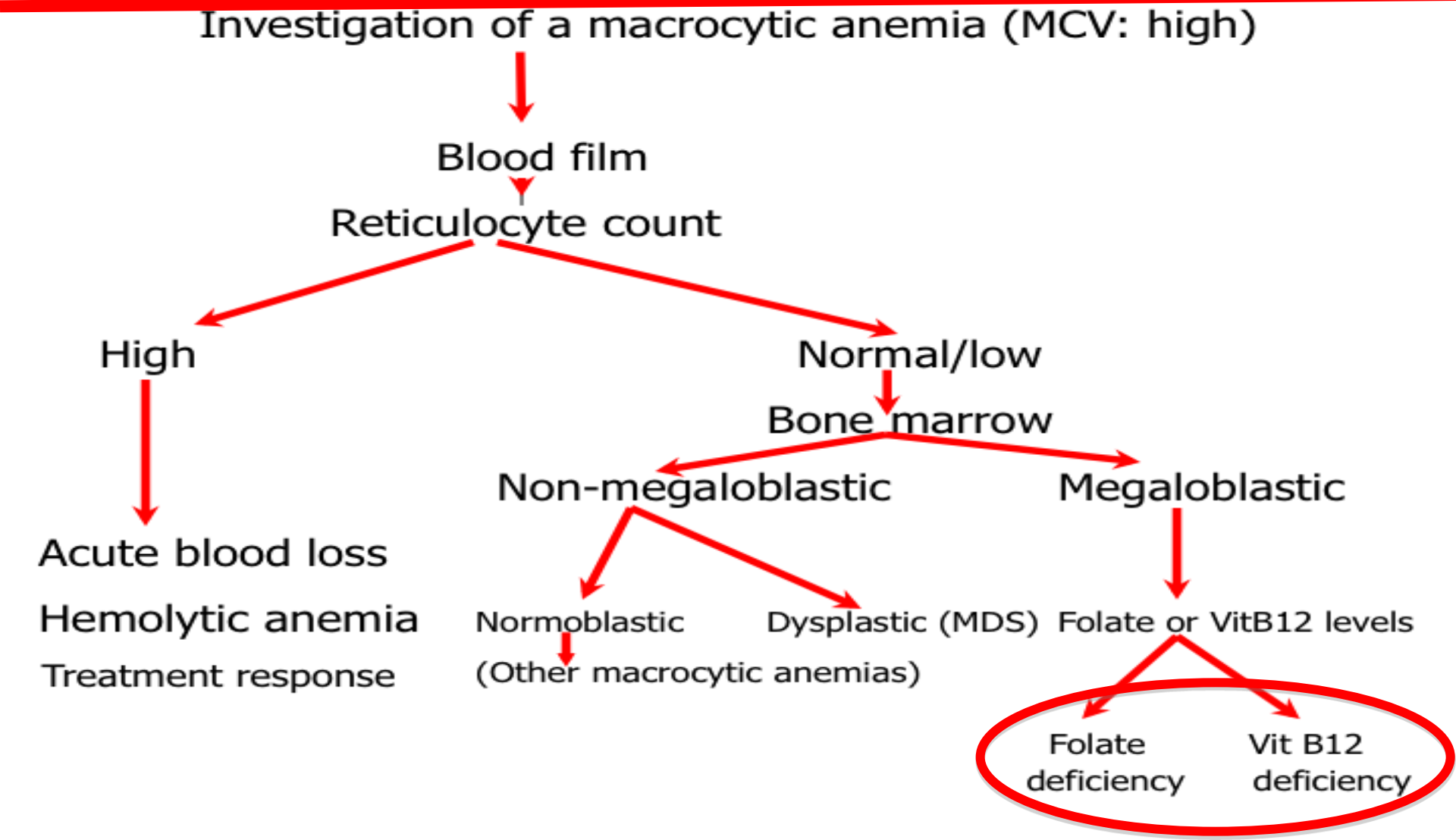

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