Approach to anemia

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What is anemia?

Pediatric anemia refers to a hemoglobin or hemocrit level lower than age adjusted reference range for healthy children.

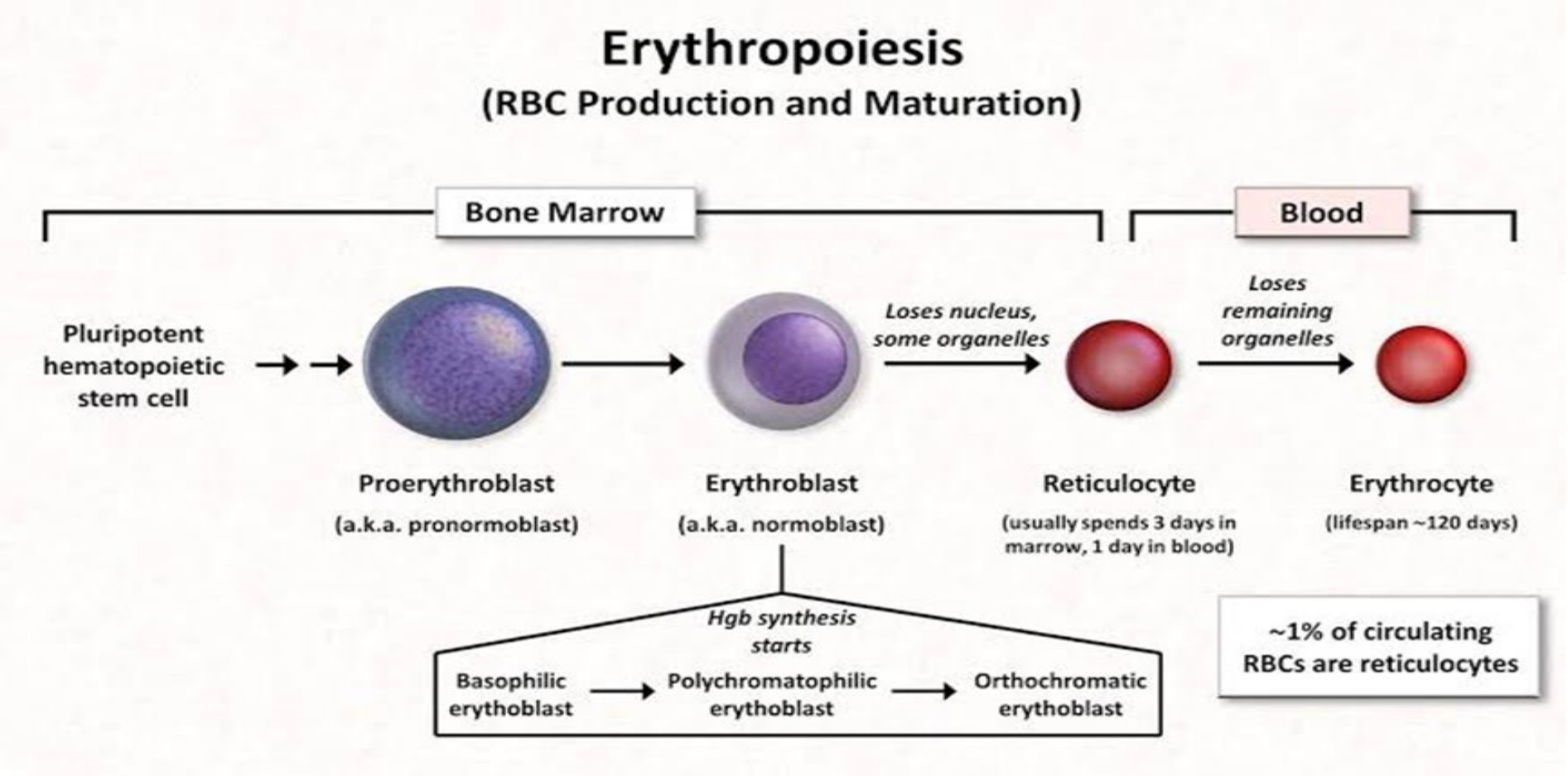
Decrease in RBC mass or Hb level to < 2SD below the mean for the population

A hemoglobin concentration below a specific cut off for age, gender, physiologic status, smoking habits and attitude at which the population being assessed lives **WHO 2023.**

Changes in Normal Hemoglobin/Hematocrit Values with Age and Pregnancy

Age/Sex	Hemoglobin g/dl	Hematocrit %
At birth	17	52
Childhood	12	36
Adolescence	13	40
Adult man	16(±2)	47(±6)
Adult woman (menstruating)	13(±2)	40(±6)
Adult woman (postmenopausal)	14(±2)	42(±6)
During pregnancy	12(±2)	37(±6)

Erythropoiesis



Primary regulator of erythropoiesis: Erythropoietin(EPO)

- Produced by monocytes and macrophages in the fetal liver (1st and 2nd trimesters), after birth (kidney)
- Role: Erythrocyte production from the CFU-E cells by inducing survival and proliferation of erythroblasts

Daily circulating RBC replacement: 0.8 -1%

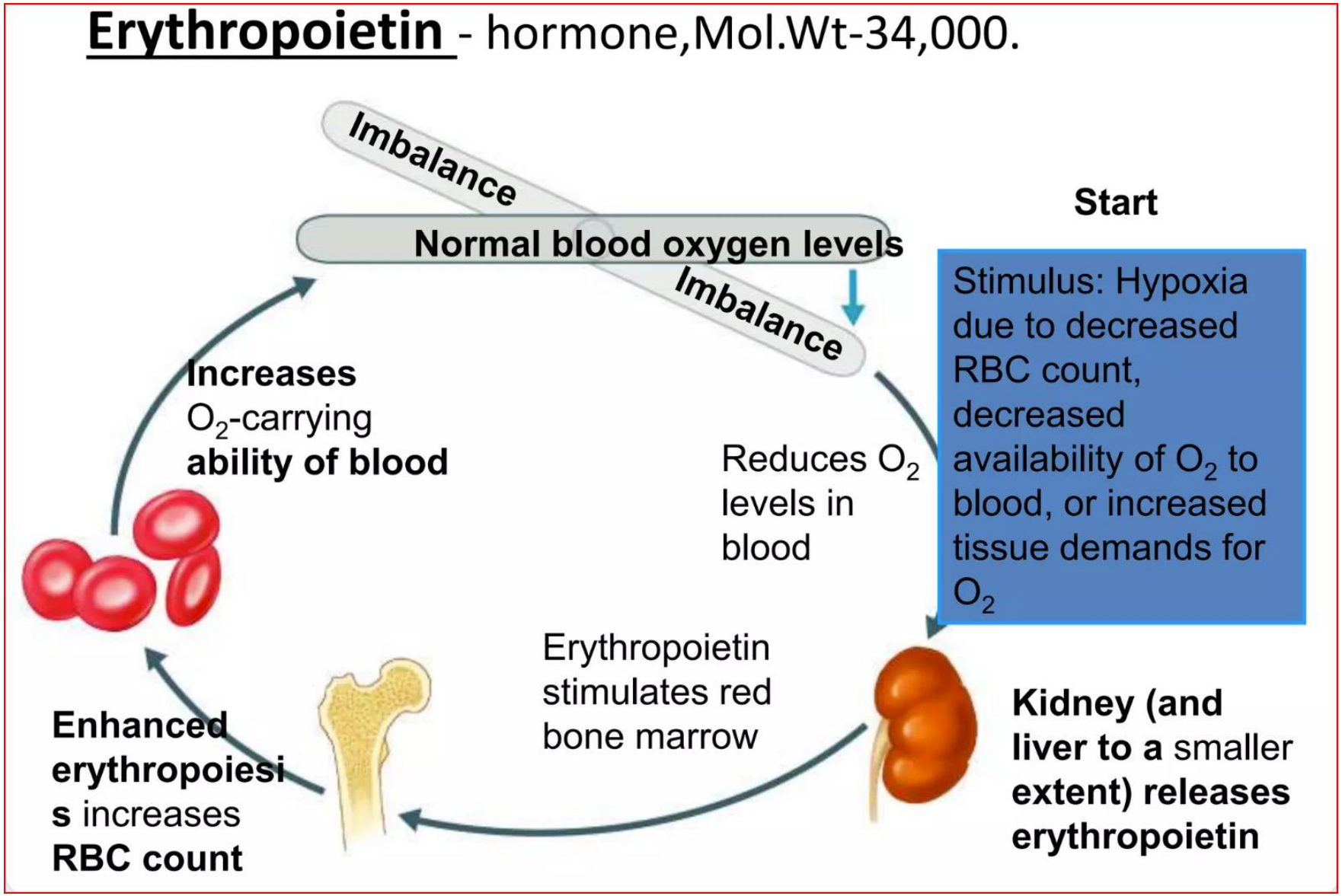
Average lifespan of RBC: 100-120 days

After 100 to 120 days RBC is destroyed in RES (for both neonates/fetal/adults)

Normal physiology = Balance between red cell production and destruction

An imbalance between production and destruction results into anemia

Erythropoietin mechanism for regulating the rate of erythropoiesis



Epidemiology

Anemia is a global problem affecting all countries appro 2billion people **(WH0 Global health observatory, 2013)**

Highest burden: Resource limited countries/regions (47% in children aged 6-59mo in Africa). Anemia affects 62% of children under age 5.

Why high: High prevalence of infectious diseases (Malaria, HIV/AIDs, Hook worm infestations, Schistosomiasis, Tuberculosis etc)

In Uganda (UDHS; 2019)

Overall prevalence of anemia in Uganda

Children 0-59mo

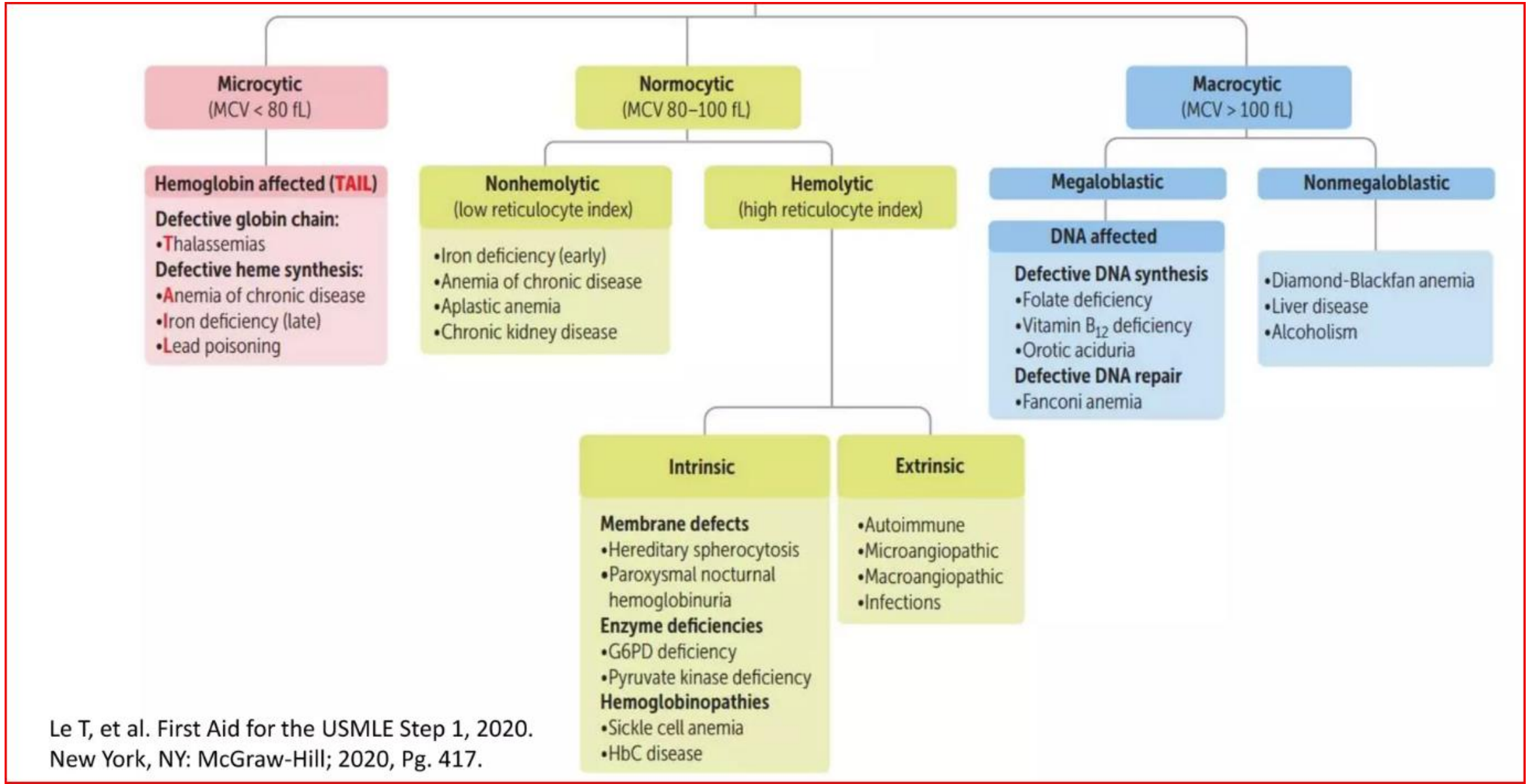
73% in 2006, 50% in 2011, and 53% in 2016 Most affected are

< 24 months prevalence of >70%

Women

In 2011, the prevalence in women (reproductive age) was 23%, 2016 32%. Higher risk: Pregnant women.

Morphological classification



Le T, et al. First Aid for the USMLE Step 1, 2020. New York, NY: McGraw-Hill; 2020, Pg. 417.

Classification/grading (Severity)

Grades of Anaemia	WHO
Normal	12gm/dl and above 12 gm/dl
Mild	10-11.9 gm/dl
Moderate	7-9.9 gm/dl
Severe	Below 7gm/dl

Grade	Severity	Hemoglobin (g/dl)
0	Normal	12.0–16.0 (women) 14.0–18.0 (men)
1	Mild	10.0–lower limit of normal
2	Moderate	8.0–<10.0
3	Severe	6.5–<8
4	Life threatening	Life threatening
5	Death	Death

Mechanism of anemia

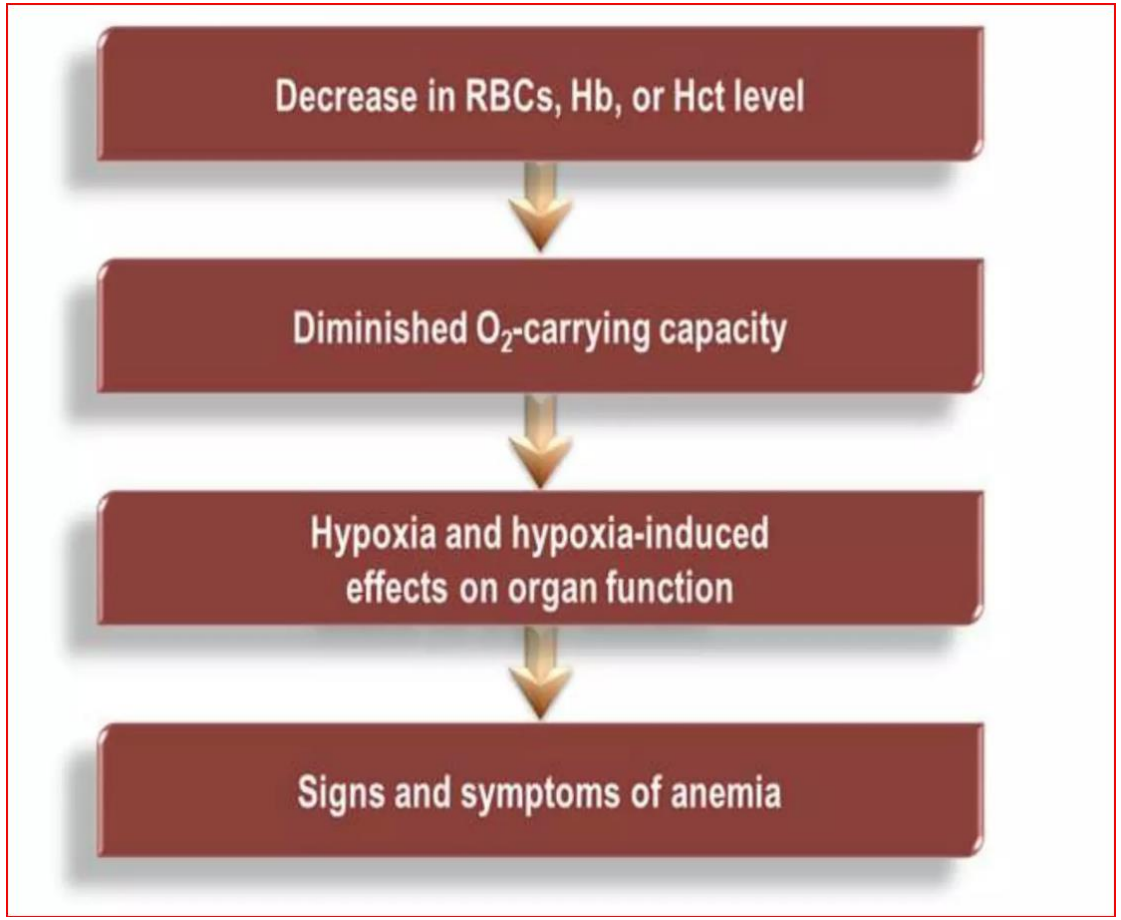
- Conceptually reflects an imbalance between RBC production and destruction and may be due to one of three mechanisms.

  – Excess RBC loss, as occurs with hemorrhage, may create anemia as RBCs are depleted in addition to loss of intravascular volume.

  – Excess or premature RBC destruction, such as from hemolysis, may create anemia as RBCs are lost from circulation prior to their normal turnover

  – Insufficient RBC production, may create anemia either from lack of stimulation of production or lack of RBC precursor availability

Pathophysiology of anemia



APPROACH

(Clinical and laboratory evaluation of anemia)

4 questions

- Is the onset slow or fast (history and examination)?: (Type of onset)
- Are red cells normal, small or large? (MCV): (Size)
- Is the red cell production decreased or increased?: (Source)
- What do the red cells look like (blood smear)?: (Morphology)

Clinical Evaluation (History/examination)

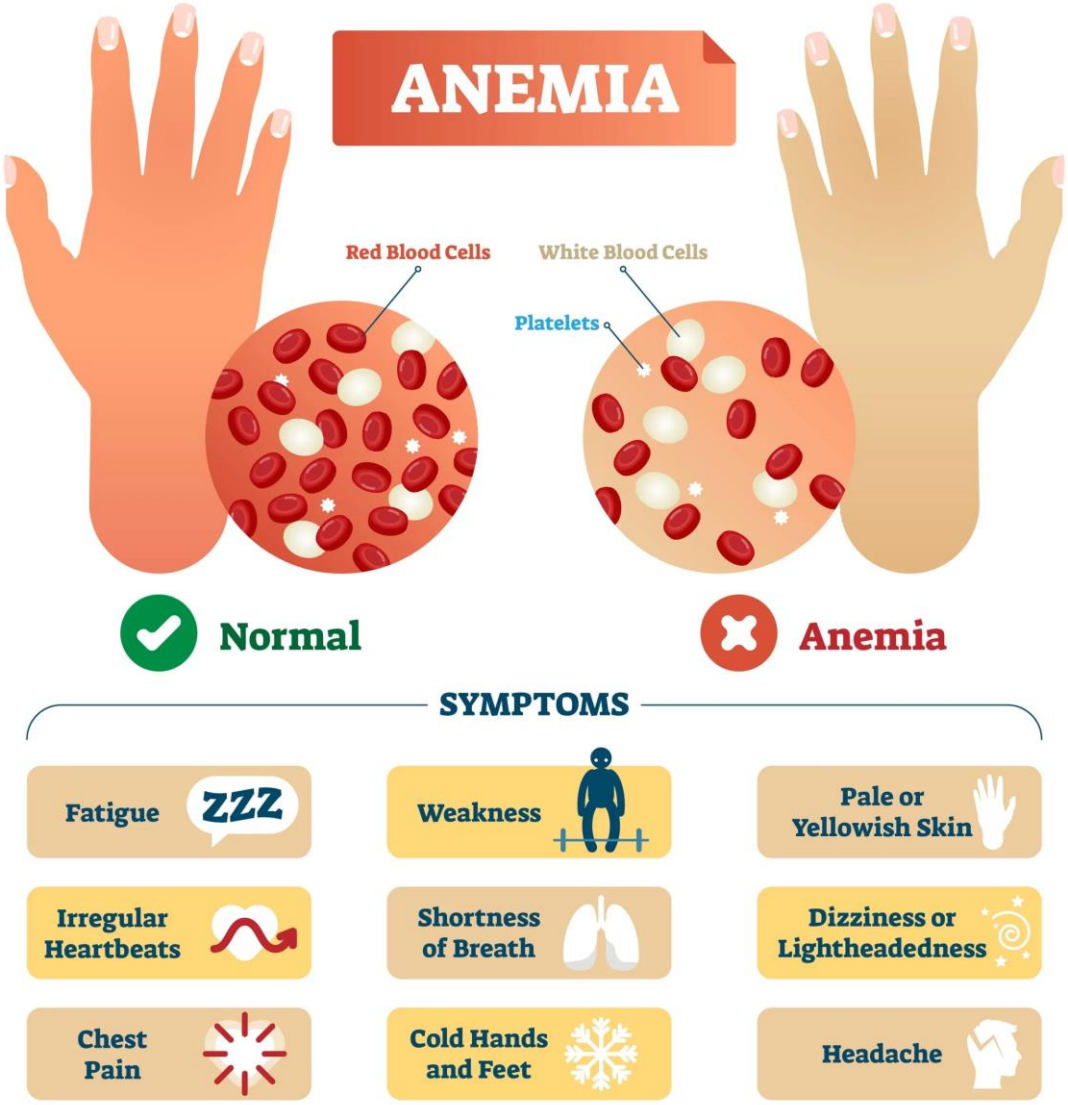
History

Focus:

- Presence of anemia complications
- Any clues as to the likely underlying cause

Asymptomatic: If anemia develops over a long time.

- **Presenting complaints**



Evidence to suggest underlying cause

Age, Sex, Race

Pre-existing illness: rheumatoid arthritis, previous abdominal surgery, dialysis

Drug history: salicylates (iron deficiency), anticonvulsants (folate deficiency), Chemotherapy, Radiotherapy (BM suppression) etc

Family history: Congenital and hemolytic anemia

Diet: Vegans (vitamin B12 deficiency), Alcoholics (folate deficiency)

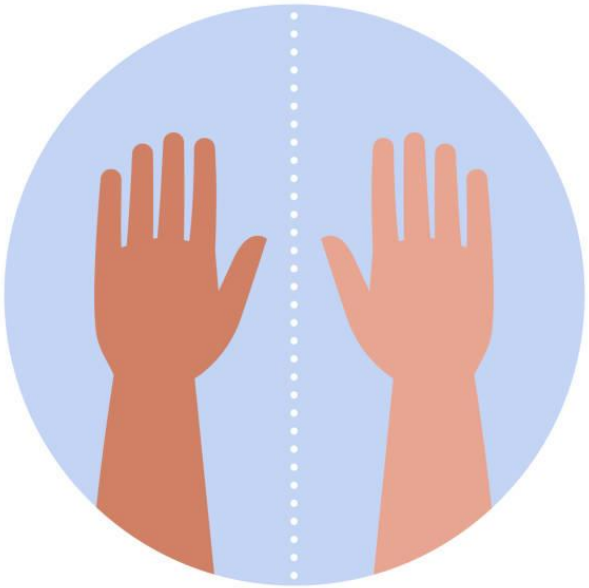
Pica (craving for specific and often bizarre foods): Iron deficiency

Pregnancy: Folate deficiency

Physical examination

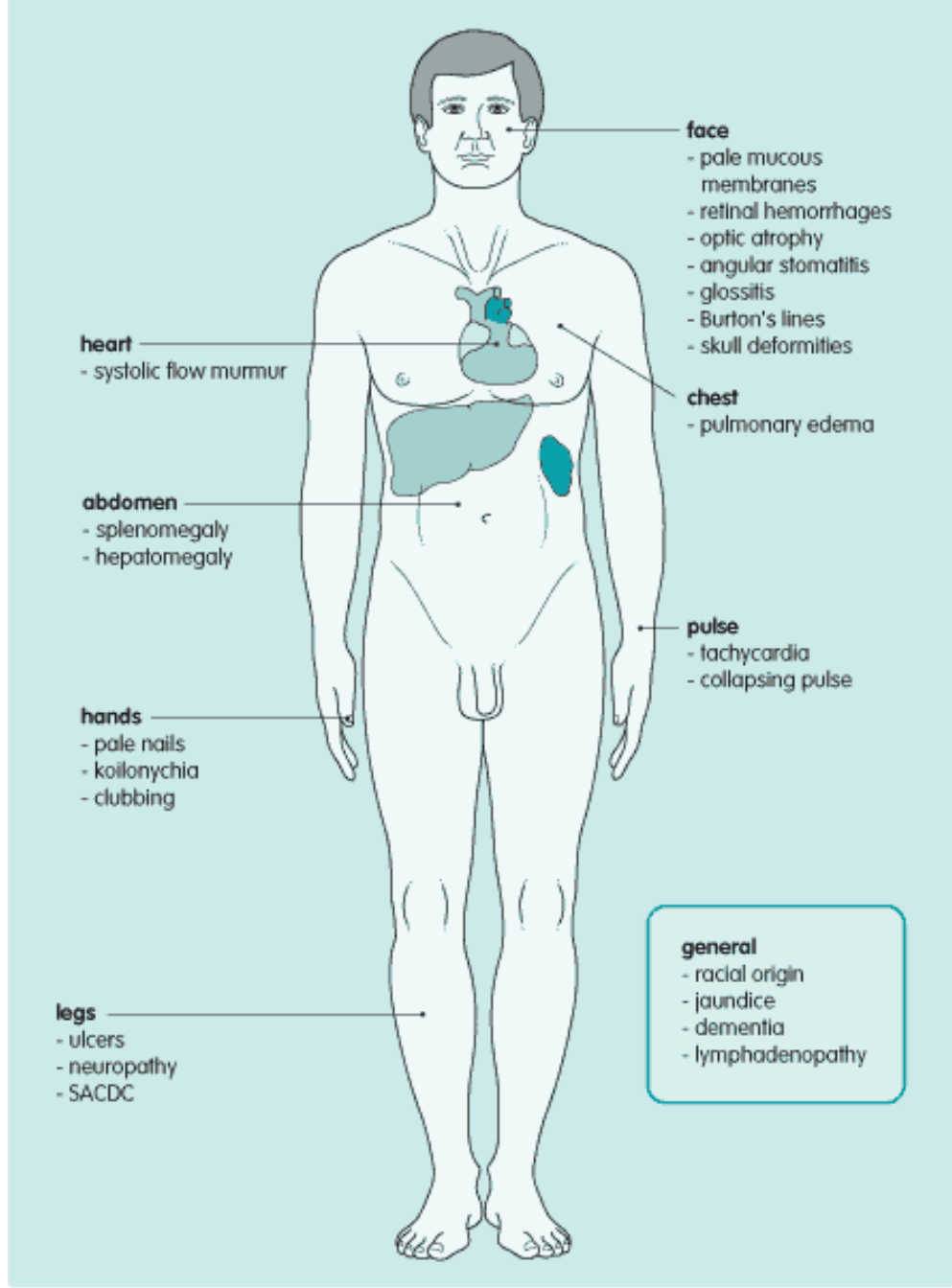
Signs of anemia and its consequences

- Pallor: Mucous membranes (mouth and conjunctivae), nails, skin creases
- Hyperdynamic circulation: Tachycardia, collapsing pulse, systolic flow murmur
- Cardiac failure
- Retinal hemorrhages



Signs of underlying disease

- **Glossitis:** Megaloblastic anemia, Iron deficiency
- **Angular stomatitis, koilonychia:** Iron deficiency
- **Jaundice:** Hemolysis, megaloblastic anemia (mild)
- **Splenomegaly:** Hemolysis, megaloblastic anemia
- **Leg ulcers:** Sickle cell disease
- **Bone deformities:** Thalassemia, Malignancy, Vit D def, SCD
- **Neurologic sequelae of vitamin B12 deficiency:** Peripheral neuropathy, optic atrophy, subacute combined degeneration of the cord, dementia
- Blue line on the gums (Burton's line), peripheral motor neuropathy, encephalopathy: Lead poisoning



Examining the anemic patient

Laboratory evaluation (General investigations)

Complete blood count (CBC/FBC)

- **Hemoglobin:** Anemia

- **Mean corpuscular volume (MCV)**: Underlying pathologies

- **White cell count (WBC):**
  - Low, consider general bone marrow failure
  - High, consider infection, inflammation, or malignancy

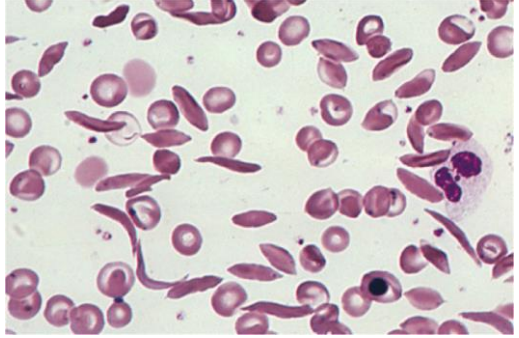
- **Platelet count:**
  - Low, consider general bone marrow failure
  - High, consider infection, inflammation, or malignancy

Reticulocyte count

- Increased if RBC production is increased and red cells are prematurely released into the circulation
  - Hemorrhage, Hemolysis, vitamin B12/folate/iron replacement, when there has been a deficiency
- Decreased in inadequate RBC production (BM involvement)
  - Infections, malignancy, drugs, red cell aplasia etc

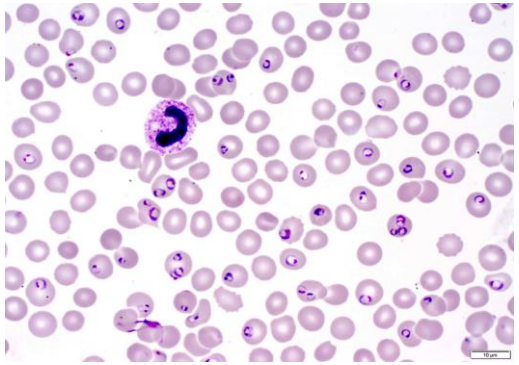
Erythrocyte sedimentation rate (ESR)

- Raised in infection, inflammation or malignancy



Peripheral blood smear (PBF)

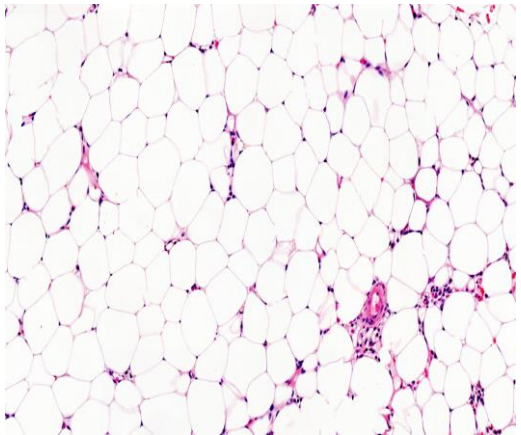
- Morphology (sizs, shape, form, structure of the cells)



Bone marrow

- Not necessary when the diagnosis is obvious (e.g., iron deficiency, SCD etc).

- **Bone marrow aspirate**
  - Gives information the different cell lines, infiltration by abnormal cells (e.g., infiltration with metastatic carcinoma)
- **Bone marrow trephine (core biopsy)**
  - Provides structural information regarding architecture and infiltration.



Abnormalities on the blood film in anemia	
Abnormality	**Changes on blood film**
iron deficiency	hypochromic, microcytic RBCs, target cells, pencil cells, poikilocytosis (variation in RBC shape), anisocytosis (variation in RBC size), often thrombocytosis
vitamin B_{12}/folate deficiency	oval-shaped macrocytosis, neutrophil nuclei hypersegmented (greater than five lobes), poikilocytosis; white blood cell and platelet count may be low
hemolysis	reticulocytosis, microspherocytes, erythroblasts many spherocytes in hereditary spherocytosis elliptocytes in hereditary elliptocytosis
thalassemia	hypochromic, microcytic RBCs, basophilic stippling, target cells, reticulocytosis
sickle cell disease	sickle cells, target cells features of hyposplenism in adults (Howell–Jolly bodies, Pappenheimer bodies, target cells)
anemia of chronic disease	normochromic, normocytic RBCs neutrophilia and thrombocytosis may be present
liver disease	macrocytic RBCs, target cells features of iron deficiency and folate deficiency may also be present

Specific investigations

Iron deficiency: Serum ferritin, serum iron, total iron-binding capacity

Vitamin B12 deficiency: Serum vitamin B12, gastric parietal antibodies, intrinsic factor antibodies, schilling test etc

Folate deficiency: RBC folate (more reliable), serum folate

Hemolysis: Serum bilirubin/haptoglobins, urinary urobilinogen, reticulocyte count, Hb electrophoresis, coombs' test, osmotic fragility, enzyme assay etc

Others: ESR, CRP, sepsis screen, malignancy test, antibody screens, imaging etc

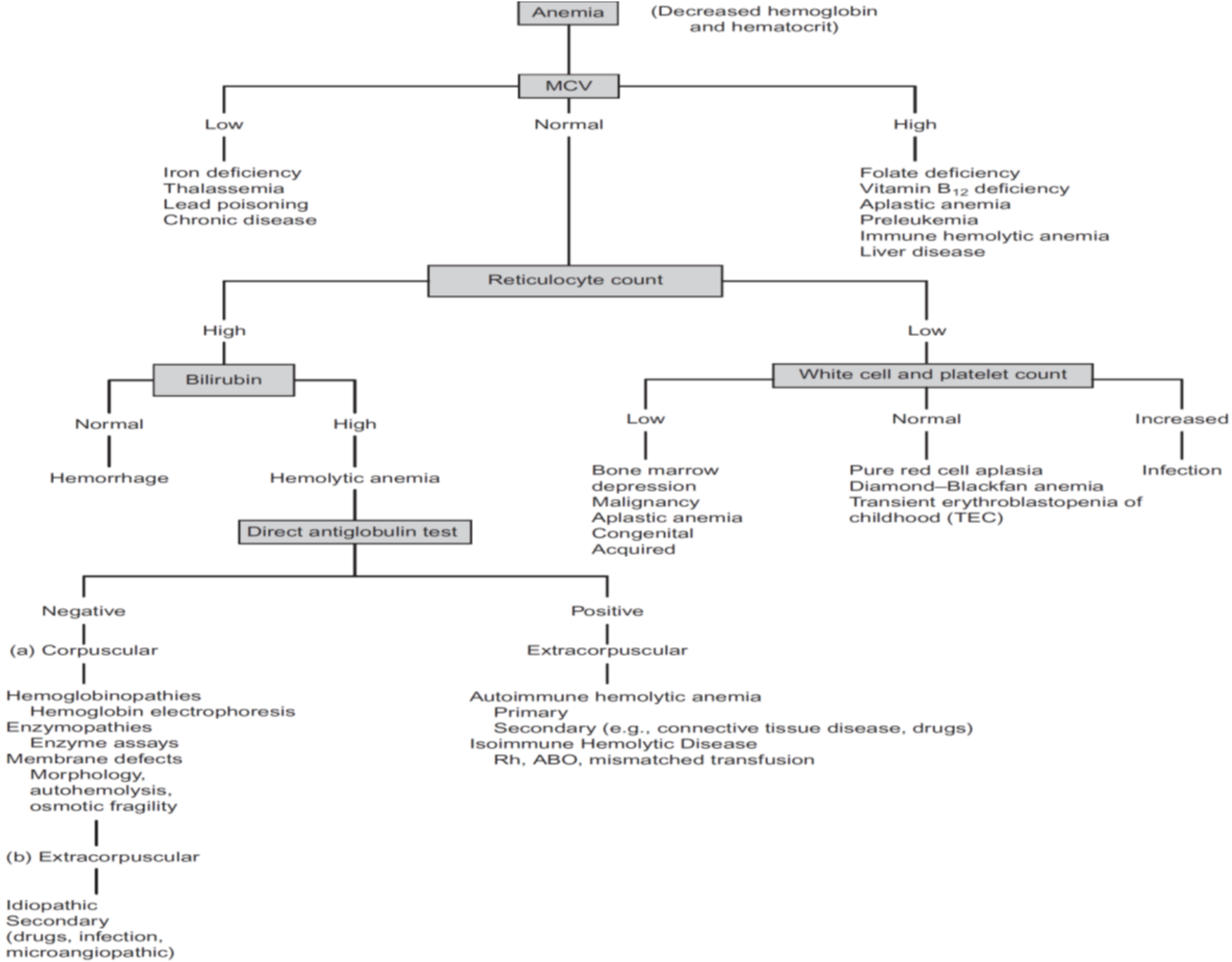


FIGURE 3.2 Approach to the diagnosis of anemia by MCV and reticulocyte count.

Management of anemia

Goal: Restore the hemodynamics of the vascular system and replace lost red blood cells

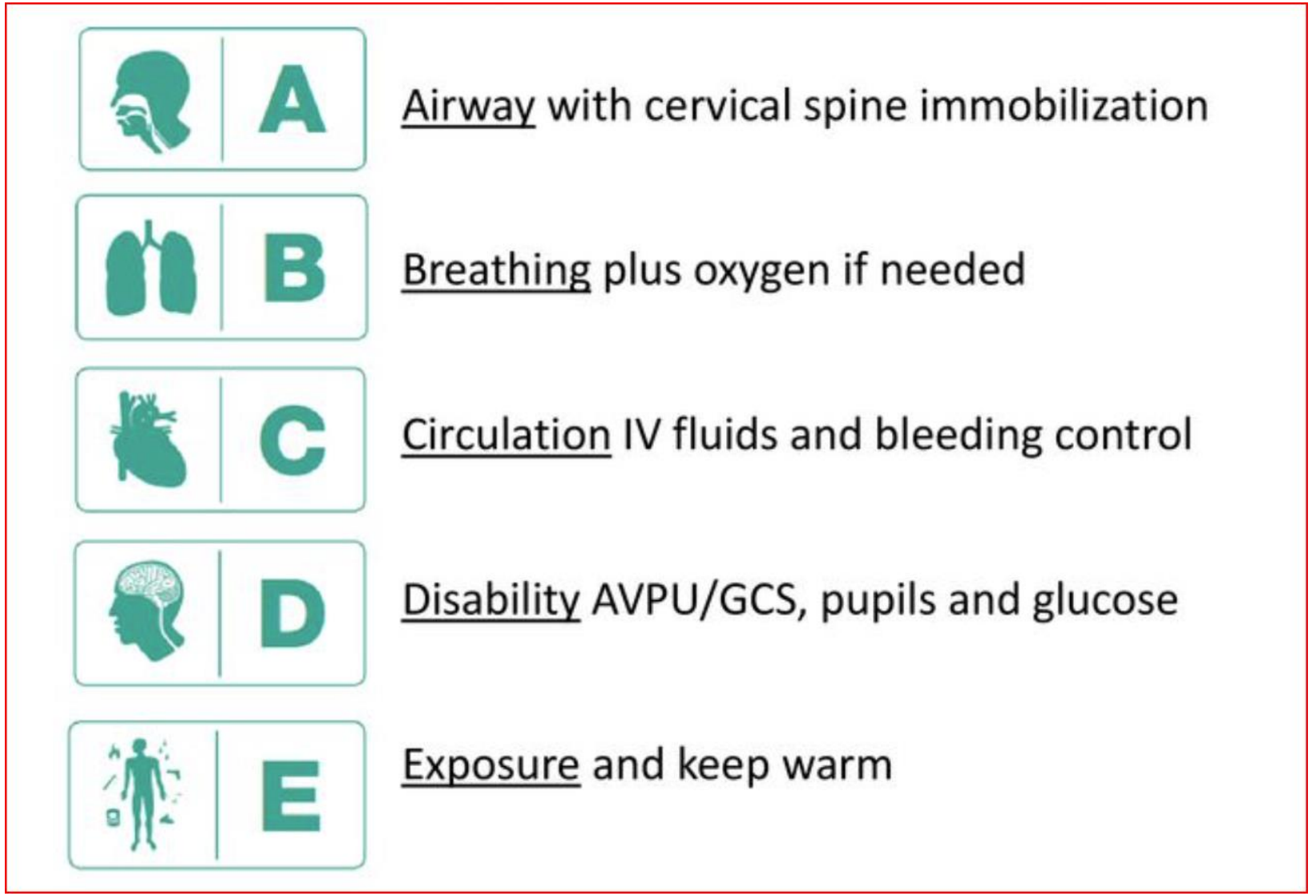
Dependent on: Patients condition and underlying cause

- Blood transfusion
- Iron supplements
- Zinc tablets
- Kidney monitoring chart
- Volume expanders
- Hydroxyurea
- Etc

Emergency management of severe anemia

Acute management those who are hemodynamically unstable

ABCDE approach



General Management of Anemia

Definitive treatment is possible for some conditions

- Nutritional supplementation to correct iron; vitamin B12 or folate deficiency
- Removal of toxin/trigger: Drug discontinuation for drug-induced IHA, Lead abatement or chelation for lead poisoning
- Hormone replacement therapy: Anemia due to endocrine dysfunction
- Corticosteroids: AIHA
- Antibiotics/antiviral medications: Infection-related anemia;
- Hematopoietic stem cell transplantation (HSCT): 1° myelofibrosis; aplastic anemia etc
- Consultations (Surgical, hematology, oncology, transfusion medicine etc)

Supportive Rx for non definitive

Anemia is a public health concern in Uganda

Timely screening coupled with appropriate diagnostic testing will afford the most optimal identification and management of patients with anemia