Department of Anesthesia Techniques
Title of the lecture:- Anemia
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Lecture two \ 2ND course

Anemia:

- Introduction,
- Manifestations,
- Classification,
- and Investigation

I. Introduction

Hemoglobin:

- Hemoglobin is the iron-containing oxygen-transporting protein in the red blood cells of vertebrates. The deficiency of hemoglobin in the red blood cells decreases blood oxygen-carrying capacity leading to symptoms of anemia.
- Hemoglobin consists of heme and globin; each complete hemoglobin unit is a tetramer or globular unit made up of four subunits; each subunit contains hem conjugated to a polypeptide chain of the globin. The globin chains are identical pairs (dimers), designated as α-chains or β-chains.
  - **Hem:** is an iron containing porphyrin derivatives (ferrous iron Fe^{+2}), there are four hem units in each (Hb) molecule.
  - **Globin:** Are polypeptides, two pairs of polypeptides in each hemoglobin molecule, they are of special amino acid sequences.

Major Hemoglobin Types by Developmental Stage:

1. Embryonic hemoglobin (Weeks 3–8 of gestation): These are transient and not detectable after birth.

2. Fetal Hemoglobin (HbF)

- Structure: $\alpha_2\gamma_2$
- Onset: ~6 weeks gestation
- Dominant: From 10 weeks gestation to birth (~70–90% at birth)
- Function:
    - ✓ Higher oxygen affinity than HbA → facilitates oxygen transfer from maternal to fetal circulation.
    - ✓ Resists sickling → therapeutic target in sickle cell disease.
    - ✓ Decline: Rapidly decreases after birth; <1% by 6–12 months.

3. Adult Hemoglobins

- HbA ($\alpha_2\beta_2$):
    - ✓ >95% of adult hemoglobin
    - ✓ Begins production at ~6 weeks gestation, becomes dominant by 6 months of age.
- **HbA_2 ($\alpha_2\delta_2$):**
    - ✓ 2–3% in healthy adults
    - ✓ Elevated in β-thalassemia trait (diagnostic clue).
- **HbF ($\alpha_2\gamma_2$):**
    - ✓ Normally <1%, but may persist or reactivate in certain conditions.

Abnormal hemoglobin's (hemoglobin variants) are structurally altered forms of hemoglobin caused by mutations in globin genes, most commonly point mutations in the β-globin gene (HBB) on chromosome 11. These variants can lead to:

- Hemoglobinopathies (e.g., sickle cell disease)

- Thalassemia syndromes (reduced globin chain production)
- Unstable hemoglobin
- High- or low-oxygen-affinity variants

Packed Cell Volume (PCV), also known as hematocrit (Hct), is a simple, widely used laboratory test that measures the proportion of blood volume occupied by red blood cells (RBCs). It provides critical insight into a patient's oxygen-carrying capacity and is essential in evaluating anemia, polycythemia, hydration status, and response to therapy. Adult males 40–50% and Adult females 36–48%.

Clinical Interpretation:

A. Low PCV (Anemia)

Indicates reduced RBC mass. Causes include:

- Blood loss (acute or chronic)
- Hemolysis (e.g., sickle cell, G6PD deficiency)
- Decreased production (e.g., iron/B12 deficiency, aplastic anemia, CKD)
- Hemodilution (e.g., pregnancy, overhydration)

Caution: In acute hemorrhage, PCV may be normal initially (equal loss of RBCs and plasma)—drops over 24–72 hours as interstitial fluid shifts in.

B. High PCV (Polycythemia)

- Relative polycythemia:
  - ✓ Due to dehydration or plasma loss (e.g., burns, diarrhea) → hemoconcentration.
  - ✓ RBC mass is normal; corrects with rehydration.

- **Absolute polycythemia:**
  - ✓ Primary: Polycythemia vera (JAK2 mutation)
  - ✓ Secondary: Chronic hypoxia (COPD, cyanotic heart disease), EPO-secreting tumors, high altitude

Red blood cell (RBC) indices are quantitative parameters derived from the complete blood count (CBC) that describe the size, hemoglobin content, and concentration of red blood cells. They are essential for classifying anemia and guiding further diagnostic workup.

Index	Full Name	Formula	Normal Range	What it tells You
MCV	Mean Corpuscular Volume	Hematocrit (L/L) ÷ RBC count (x10^{12}/L)	80–100 fL	Average RBC size
MCH	Mean Corpuscular Hemoglobin	Hemoglobin (g/L) ÷ RBC count (x10^{12}/L)	27–31 pg	Average hemoglobin mass per RBC
MCHC	Mean Corpuscular Hemoglobin Concentration	Hemoglobin (g/dL) ÷ Hematocrit (dL/dL)	32–36 g/dL	Hemoglobin concentration within the RBC

Note: fL = femtoliters (10^{-15} L), pg = picograms (10^{-12} g), MCHC is the only concentration (not total amount)

Anemia is defined as a reduction in the total circulating red blood cell (RBC) mass or hemoglobin (Hb) concentration below normal for age and sex. The World Health Organization (WHO) defines anemia as:

- Hb <13 g/dL in men
- Hb <12 g/dL in non-pregnant women
- Hb <11 g/dL in pregnant women and elderly

Anemia is not a diagnosis but a clinical sign of an underlying disorder. It results from:

1. Decreased RBC production (e.g., iron deficiency, bone marrow failure)
2. Increased RBC destruction (hemolysis)
3. Blood loss (acute or chronic)

Because oxygen delivery to tissues is impaired, anemia can significantly affect quality of life and, if severe or acute, lead to cardiovascular compromise.

II. Major Clinical Manifestations:

Symptoms of anemia depend on severity, onset (acute vs. chronic), and patient comorbidities (e.g., cardiac disease).

General Symptoms (due to tissue hypoxia):

- ✓ Fatigue, weakness
- ✓ Pallor (conjunctiva, nail beds)
- ✓ Dyspnea on exertion
- ✓ Tachycardia, palpitations
- ✓ Dizziness, headache

Symptoms Specific to Etiology:

- ✓ Iron deficiency: Pica (craving for ice, clay), koilonychia (spoon nails), glossitis
- ✓ Vitamin B12/folate deficiency: Neurological symptoms (numbness, paresthesia, ataxia – B12 only), smooth red tongue
- ✓ Hemolytic anemias: Jaundice, dark urine (hemoglobinuria), splenomegaly
- ✓ Chronic disease: Often asymptomatic beyond underlying illness

Note: Patients with chronic anemia may tolerate very low Hb levels due to compensatory mechanisms (e.g., increased cardiac output, 2,3-DPG shift).

III. Classification of Anemia

Anemia can be classified morphologically (by RBC size) or etiologically (by mechanism). Both approaches are complementary.

A.Morphological Classification (Based on MCV – Mean Corpuscular Volume)

Type	MCV (fL)	Common Causes
Microcytic	<80	Iron deficiency, thalassemia, anemia of chronic disease (sometimes), sideroblastic anemia
Normocytic	80–100	Acute blood loss, hemolysis, anemia of chronic disease, bone marrow failure (e.g., aplastic anemia), early iron/B12/folate deficiency
Macrocytic	>100	Megaloblastic: B12/folate deficiency, drugs (methotrexate) Non-megaloblastic: alcohol, liver disease, hypothyroidism, myelodysplastic syndromes

B. Etiological Classification (Pathophysiologic)

1. Impaired RBC Production

- Nutritional deficiencies (iron, B12, folate)
- Bone marrow disorders (aplasia, infiltration, myelodysplasia)
- Anemia of inflammation/chronic disease (AI/ACD)

2. Increased RBC Loss

- Acute hemorrhage (trauma, surgery)
- Chronic blood loss (GI bleed, menorrhagia → often leads to iron deficiency)

3. Increased RBC Destruction (Hemolytic Anemias)

- Intrinsic RBC defects:

- ✓ Membrane (hereditary spherocytosis)
- ✓ Enzyme (G6PD deficiency)
- ✓ Hemoglobinopathies (sickle cell, thalassemia)

- Extrinsic causes:

- ✓ Immune (AIHA), mechanical (prosthetic valves), infections (malaria), toxins

IV. Diagnostic Approach & Key Investigations

A stepwise evaluation guides accurate diagnosis.

Step 1: Confirm Anemia & Assess Severity

- CBC: Hb, Hct, MCV, RDW, reticulocyte count
- Peripheral blood smear: RBC morphology (e.g., spherocytes, schistocytes, target cells)

Step 2: Determine RBC Production Status

- Reticulocyte count (corrected or index):

  - High → hemolysis or blood loss
  - Low/normal → underproduction

✓ Corrected reticulocyte count = % reticulocytes × (patient Hct / 45)

✓ Reticulocyte production index (RPI) <2 = inadequate response

Step 3: Classify by MCV and Target Testing

A. Microcytic Anemia (MCV <80 fL)

- Serum ferritin (best initial test for iron deficiency; low = deficient)
- Iron, TIBC, transferrin saturation
- Hb electrophoresis if thalassemia suspected (↑ RBC count, normal/high ferritin, elevated HbA2 in β-thalassemia trait)
- CRP or ESR: to assess inflammation in anemia of chronic disease

B. Macrocytic Anemia (MCV >100 fL)

- Check for megaloblastic features on smear (hypersegmented neutrophils)
- Serum B12 and folate levels

- Methylmalonic acid (MMA) & homocysteine:

✓ ↑ MMA + ↑ homocysteine → B12 deficiency

✓ Normal MMA + ↑ homocysteine → folate deficiency

✓ Consider liver function tests, TSH, alcohol history if non-megaloblastic

C. Normocytic Anemia (MCV 80–100 fL)

- Reticulocyte count is key:

High: Think hemolysis or bleeding → check LDH, haptoglobin, indirect bilirubin, Coombs test

Low: Think underproduction →

- ✓ Anemia of chronic disease: normal/high ferritin, low serum iron, low TIBC
- ✓ Bone marrow failure: pancytopenia, consider marrow biopsy
- ✓ Endocrine causes: hypothyroidism, hypogonadism

Additional Tests (as indicated):

- ✓ Haptoglobin, LDH, indirect bilirubin → hemolysis
- ✓ Direct Antiglobulin Test (DAT/Coombs) → autoimmune hemolytic anemia
- ✓ G6PD assay (during hemolytic episode or after recovery)
- ✓ Stool for occult blood → chronic GI blood loss
- ✓ Bone marrow biopsy → unexplained cytopenias, suspected malignancy