ANEMIA

TERM DEFINITION

A condition in which the blood has reduced ability to carry oxygen owing to a reduction in the amount of hemoglobin (Hb).

ANEMIA DEFINED AS

♀ **Hb < 12 g/dL** | ♂ **Hb < 13 g/dL**

CAUSES

According to red cell kinetics:

- Decreased production
- Increased destruction
- Sequestration
- Blood loss

According to red cell size and degree of hemoglobinization:

- Microcytic
  - Hypochromic
  - Normochromic
- Normocytic
- Macrocytic

CLINICAL PEARLS

Affects ~2 billion people worldwide and ~6% of Americans.

Order a reticulocyte count (separate from the CBC) as it will streamline your work-up.

The Hct can be normal & the Hb in the anemic range if the MCHC is low; focus on the Hb, not the Hct.

If the mean cell volume (MCV) is normal, check the RDW; if it is increased, there is likely a subpopulation of microcytic cells in the blood.

MCHC, mean corpuscular hemoglobin concentration

PRESENTATION

CBC, complete blood count; MCHC, mean corpuscular hemoglobin concentration; MCV, mean cell volume

SIGNS & SYMPTOMS

Patients with anemia may present with **symptoms** of weakness, fatigue, headache, shortness of breath and palpitations on exertion, chest pain and symptoms specific to the underlying cause such as pica and restless legs in iron deficiency, jaundice and neurological symptoms in pernicious anemia, or red colored urine in paroxysmal nocturnal hemoglobinuria (PNH).

Signs of anemia include paleness of skin and mucous membranes, resting tachycardia, and hypotension. Signs associated with specific causes include glossitis, angular cheilitis and nail changes in iron deficiency; jaundice and scleral icterus in hemolytic anemia, and gait changes in pernicious anemia.

LABS*

HEMATOLOGICAL FINDINGS

By definition, the Hb is low

Other hematological findings associated with anemia may include decreased/increased:

- White cell count
- Platelet count

NUTRITION, INFLAMMATION & ORGAN FUNCTION

- Iron indices
- Vitamin B12, folate
- C-reactive protein
- Liver function tests
- Urea and creatinine
- Thyroid function tests

HEMOLYTIC MARKERS

- Lactate dehydrogenase
- Haptoglobin
- AST
- Bilirubin (indirect)

** What you order will depend on where your patient is on the algorithm below.*

CLASSIFICATION

Hb < 12 (women) or < 13 g/dL (men)

Reticulocyte count elevated (> 0.12 x 10^{12}/L)

Reticulocyte count low

Bleeding Hemolysis, Hypersplenism*

** Can be associated with low reticulocyte count if there is another process inhibiting erythropoiesis, for example inflammation or iron deficiency*

MCV low

MCV high

MICROCYTIC ANEMIA

NORMOCYTIC ANEMIA

- Inflammation
- Chronic kidney disease
- Liver disease
- Hypothyroidism
- Hypogonadism
- Hypoadrenalism
- Myelodysplasia
- Aplastic anemia
- Multiple myeloma

MACROCYTIC ANEMIA

- B12 deficiency
- Folate deficiency
- Drugs
- Alcohol
- Liver disease
- Hypothyroidism
- Elevated retics *(which should have been ruled out by now)*

MCHC low

MCHC high

MICROCYTIC HYPOCHROMIC ANEMIA

- Iron deficiency
- Thalassemia major

MICROCYTIC NORMOCHROMIC ANEMIA

- Iron deficiency
- Thalassemia
- Hb C, Hb E
- anemia of inflammation
- Lead poisoning
- Sideroblastic anemia
- Hyperthyroidism

MICROCYTIC HYPERCHROMIC ANEMIA

- Spherocytosis
- Hb C

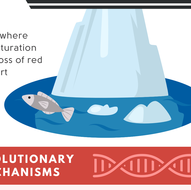
MCV, mean cell volume; MCHC, mean corpuscular hemoglobin concentration

THERAPEUTIC PRINCIPLES

The goal is to **treat the underlying cause** of anemia, for example with iron supplementation in iron deficiency anemia, or steroids in autoimmune hemolytic anemia. Red cell transfusion is generally reserved for cases of severe, symptomatic anemia. In patients who are hemodynamically stable, the threshold for transfusion is 6-10 g/dL, depending on the clinical situation. Patients whose oxygen dissociation curve is shifted to the right (chronic kidney disease, pyruvate kinase deficiency) tolerate lower levels of Hb.

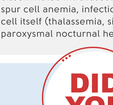
COMPARATIVE PHYSIOLOGY

All vertebrates have red cells with the exception of the **Antarctic ice fish**. These creatures are not just anemic, they have no red cells whatsoever! All of their oxygen is dissolved in plasma. They evolved in the cold waters of the Antarctic, where the oxygen is dissolved in high amounts and where niche competition is minimal. Somewhere along the way, they developed a mutation that led to maturation arrest of the erythropoietic series. They weathered the loss of red cells by acquiring several adaptations: an enormous heart with high cardiac outputs, low peripheral resistance, and dense capillary networks under the skin that can take up oxygen to name a few.



PROXIMATE MECHANISMS

As we have seen, anemia may result from reduced production, increased destruction or sequestration. The **production** side may involve lack of essential nutrients, toxic effects of kidney or liver disease, alcohol or drugs, hormonal imbalance or congenital or acquired defects in red cell precursors including those found in aplastic anemia or myelodysplasia.



Hemolytic anemia is caused by changes in the cell's environment (for example, thrombotic thrombocytopenia purpura, disseminated intravascular coagulation, spur cell anemia, infection) or within the cell itself (thalassemia, sickle cell disease, paroxysmal nocturnal hemoglobinuria).

EVOLUTIONARY MECHANISMS

Iron sequestration in **anemia of inflammation** (AI) may have evolved as a means of protecting the host against iron-dependent microbes.

AI may represent an evolutionary trade off in which the benefits of starving microbes of iron outweighed the risks associated with a mild anemia.

Many of the mutations associated with **hemoglobinopathies and red cell membrane disorders** provided a survival advantage in malaria-endemic regions of the world, and have therefore been selected for over evolutionary time.

DID YOU KNOW?

HISTORY OF MEDICINE

In the 1800s, anemia was divided into primary types and secondary types. **Primary anemias** (those whose cause was felt to be known) included pernicious anemia and chlorosis. **Secondary anemias** included all other types of anemia, for which the etiology was poorly understood. Many of these patients with secondary anemia probably had anemia of inflammation because chronic infections (including tuberculosis, osteomyelitis, endocarditis, and empyema) and cancer were highly prevalent at the time.

NOTES

ATTRIBUTIONS

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ENCYCLOPEDIA OF BLOOD