NOTES
MICROCYTIC ANEMIA

GENERALLY, WHAT IS IT?

PATHOLOGY & CAUSES

- Inherited/acquired anemias, small erythrocytes, varying hemoglobin content

SIGNS & SYMPTOMS

- Decreased oxygen to tissues → fatigue, pallor, dyspnea, activity intolerance

MNEMONIC: Find Those Small Cells Last

Microcytic anemias

Fe deficiency
Thalassemia
Sideroblastic
Chronic disease
Lead poisoning

DIAGNOSIS

LAB RESULTS

- Complete blood count (CBC), peripheral blood smear analysis, blood chemistry, iron studies

TREATMENT

OTHER INTERVENTIONS

- Nutrient replacement, packed red blood cell transfusions

IRON STUDIES IN MICROCYTIC ANEMIA

	IRON DEFICIENCY	LEAD POISONING	THALASSEMIA
IRON (SERUM)	↓	↓	Normal or ↑
FERRITIN (SERUM)	↓	↓	Normal or ↑
IRON BINDING CAPACITY	↑	↑	Normal

IRON-DEFICIENCY ANEMIA

osms.it/iron-deficiency-anemia

PATHOLOGY & CAUSES

- Microcytic, hypochromic anemia, small erythrocytes, decreased hemoglobin
- Insufficient iron → decreased iron for hemoglobin synthesis → impaired erythropoiesis → production of microcytic, hypochromic erythrocytes
  - Insufficient iron to synthesize hemoglobin during erythropoiesis (most common cause of anemia worldwide)

CAUSES

Insufficient intake/absorption

- Decreased intake
  - Eating disorders (e.g. pica, anorexia, bulimia); self-imposed dietary restrictions (e.g. vegan diet); food insecurity
- Decreased absorption
  - Celiac disease, surgical resection of gastrointestinal (GI) tract, bariatric surgery, excessive dietary calcium, tannates, oxalates

Increased need

- Increased need
  - Pregnancy, lactation
- Increased growth
  - Infants, children, adolescents

Increased loss

- Overt blood loss
  - Hematemesis, trauma-related hemorrhage, heavy menses, hematuria, multiple blood donations
- Occult
  - GI bleed (e.g. peptic ulcer, tumor); vascular lesions (e.g. hemorrhoids); hookworm/other helminthic infections

COMPLICATIONS

- High-output heart failure, angina, cardiorespiratory failure
- Infants, young children
  - Impaired growth, development

SIGNS & SYMPTOMS

Decreased oxygen to tissues

- Pallor
- Fatigue, activity intolerance, exertional dyspnea, angina
- Compensatory mechanisms
  - Palpitations, increased pulse, increased cardiac output, tachypnea, selective shunting of blood to vital organs (e.g. skin to kidneys)

Effects on epithelial tissues

- Glossitis
  - Smooth, "beefy red" tongue
- Cheilosis
  - Scaling, fissuring; dryness; lip scaling
- Koilonychia
  - Spoon-shaped, concave nails
- Esophageal stricture
- Gastric atrophy
- Blue sclerae
- Pagophagia
  - Obsessive consumption of ice

DIAGNOSIS

LAB RESULTS

- ↓ red blood cell count
- Low/normal reticulocytes
- ↓ hemoglobin, hematocrit
- Hypochromic-microcytic erythrocytes
  - *Decreased:* mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC)

- *Blood smear analysis:* erythrocytes with increased central pallor (> ⅓ diameter, anisocytosis (anisto = unequal), poikilocytosis (poikilo = irregular), target cells (resemble target; center stain with pallor ring, outside stain ring)
- Iron studies
  - Decreased serum iron, ferritin (stores cellular iron)
  - Decreased transferrin saturation (major iron transport protein)
  - Increased total iron binding capacity

OTHER DIAGNOSTICS

- History, physical examination (e.g. colonoscopy for GI bleed)

TREATMENT

MEDICATIONS

- PO iron supplements (e.g. ferrous sulfate)
- Parenteral iron
  - Severe, persistent anemia
  - Intolerance of PO iron
  - Nonadherence to PO supplements/ dietary changes

OTHER INTERVENTIONS

- Increase dietary iron
  - Heme iron (e.g. meat) absorbed better than non-heme iron (e.g. eggs, legumes, nuts)
  - Vitamin C increases absorption; calcium decreases absorption
- Blood transfusion

LEAD POISONING-RELATED ANEMIA

osms.it/lead-poisoning

PATHOLOGY & CAUSES

- Lead exposure, toxicity → anemia
- Lead absorbed through lungs/skin/GI tract
  - Interferes with enzymatic steps in heme pathway → decreased hemoglobin synthesis, microcytosis
  - Impairs sodium/potassium ATPase in erythrocyte cell membrane → hemolysis

RISK FACTORS

- Water contaminated with industrial waste/ from pipes made of lead/that contain lead solder
- Exposure to leaded paint/paint dust/chips (esp. children); increased risk in older homes (built before 1978, lead in paint since banned)
- Exposure to soil/dust contaminated with lead
- Breathing industrial emissions containing lead (e.g. smelters, refineries, battery manufacturing, recycling)
- Food/ beverages from lead-glazed ceramics

SIGNS & SYMPTOMS

- Small, hypochromic red blood cells → hypoxemia → decreased oxygen to tissues → tissue hypoxia → fatigue, dyspnea, activity intolerance
- Lead toxicity
  - Abdominal pain, headache, difficulty concentrating, muscle/joint pain, confusion, ataxia

DIAGNOSIS

LAB RESULTS

- ↑ serum blood lead level (BLL)
- Basophilic stippling
- ↓ or normal MCV
- ↓ mean MCH
- Hemolysis
  - ↑ indirect bilirubin, LDH
  - ↓ haptoglobin

TREATMENT

OTHER INTERVENTIONS

- Eliminate exposure
- Chelation therapy
  - Dimercaptosuccinic acid (DMSA, AKA succimer), $CaNa_2EDTA$

THALASSEMIA

osms.it/thalassemia

PATHOLOGY & CAUSES

- Thallas = sea; emia = blood
- Inherited hemoglobinopathies; most common in individuals with Mediterranean, Middle Eastern, Southeast Asian, African genetic descent
- Hemoglobin synthesis with insufficient globin chains → impaired erythropoiesis, malfunctioning erythrocytes
- Autosomal recessive inheritance; wide range of phenotypes, clinical syndromes
- Deficient alpha/beta chains → imbalanced beta chain to alpha chain ratio → globin chains aggregate, precipitate in erythroid precursors → unstable hemoglobin tetramer
  - Impaired erythropoiesis
  - Intramedullary hemolysis and apoptosis
  - Small, hypochromic cells → decreased oxygen to tissues
  - Production of few microcytic, hypochromic erythrocytes with rigid, less deformable membranes → extravascular hemolysis, phagocytosis by reticuloendothelial macrophages

TYPES

Alpha-thalassemia

- Deletion of ≥ one gene(s) encoding alpha globin chains → absent/ reduced chains
- *One gene missing:* alpha-thalassemia minima
  - Benign carrier state
- *Two genes missing:* alpha-thalassemia minor, alpha thalassemia trait
  - Mild anemia
- *Three genes missing:* hemoglobin H (HbH) disease
  - Mild anemia/may require periodic transfusions (variable presentation)
- *Four genes missing:* alpha-thalassemia major, hydrops fetalis, hemoglobin Barts
  - Incompatible with extrauterine life due to inability to form normal hemoglobin; death occurs before/shortly after birth
  - Only hemoglobin Barts (Hb Barts) is produced; tetramers of gamma globulin, oxygen not delivered to fetal tissues
  - Severe anemia during fetal development → hydrops fetalis → heart failure, hepatomegaly, ascites, death

Beta-thalassemia

- Genetic mutations of one/both genes → absent/reduced beta chains
- *Mutation in one beta globin chain:* beta-thalassemia minor, thalassemia trait
  - Asymptomatic carrier state/mild anemia
- *Mutation in two beta globin chains:* reduced beta globin production → beta-thalassemia intermedia

- Heterogeneous presentation
- May become transfusion-dependent later in life

- *No beta globin chains produced:* beta-thalassemia major
  - Transfusion dependent

COMPLICATIONS

- Hemolytic, microcytic, hypochromic anemia
  - Chronic tissue hypoxia
  - Leg ulcers
  - High output heart failure
  - Hypermetabolic state → nutritional deficiencies (children: growth impairment)
- Extrameduallary hematopoiesis → bone marrow hyperplasia, bone marrow widens, structural malformations (e.g. facial irregularity, osteoporosis, premature fusion of epiphysis in children)
- Hemolysis → increased bilirubin → gallstones
- Iron overload, deposition in tissue
  - Myocardium → arrhythmias, restrictive cardiomyopathy, heart failure
  - Pancreas, other endocrine glands → endocrinopathies (e.g. diabetes, thyroid dysfunction)
  - Liver → cirrhosis, hepatocellular cancer
  - Kidneys → renal insufficiency (metabolic load from high hematopoietic cell turnover)
- Hydrops fetalis
  - Alpha thalassemia major only
- Treatment-related complications
  - Transfusions, chelation therapy

SIGNS & SYMPTOMS

- With exception of alpha-thalassemia major, mild compared to beta-thalassemia
- Decreased oxygen to tissues
  - *Systemic:* pallor, fatigue, activity intolerance
  - *Cardiac:* altered hemodynamics, e.g. tachycardia, low blood pressure, arrhythmias
- Chronic hemolysis
  - Jaundice, dark urine, hepatosplenomegaly

DIAGNOSIS

LAB RESULTS

- ↓ serum hemoglobin
- Decreased/normal/increased reticulocyte count → degree of impaired erythropoiesis
- White blood cells, platelets normal
- Red blood cell indices
  - Hypochromic-microcytic erythrocytes
  - MCHC increased related to erythrocyte dehydration
  - Decreased MCV
  - High red cell distribution width (RDW)
- Blood smear analysis
  - Poikilocytosis (dacrocytes, i.e. teardrop-shaped cells)
  - Anisocytosis
  - Erythroblasts (nucleated red blood cells)
  - Target cells
  - Inclusions (precipitated globin chains)
- Blood chemistry indicative of hemolysis
  - Increased lactate dehydrogenase (LDH)
  - Increased indirect (unconjugated) bilirubin
  - Decreased haptoglobin
- Iron studies
  - Increased serum iron, transferrin saturation (TSAT), serum ferritin
- Diagnostics to determine organ involvement (e.g. cardiac MRI, thyroid hormone, glucose levels, bone mineral density)
- Hemoglobin analysis using high-performance liquid chromatography (HPLC)/hemoglobin electrophoresis, genetic testing (confirmation)

TREATMENT

- According to phenotype

MEDICATIONS

- *Folic acid supplements:* support erythropoiesis

SURGERY

- Splenectomy

OTHER INTERVENTIONS

- Blood transfusions
- Chelation therapy
- Allogeneic hematopoietic cell transplantation (beta-thalassemia major)
- *Consultation with cardiology, other specialties:* organ involvement
- *Ongoing monitoring:* individuals with high impairment (e.g. blood, iron studies; liver studies; growth, development in children)