NOTES
NORMOCYTIC ANEMIA (DECREASED PRODUCTION)

GENERALLY, WHAT IS IT?

PATHOLOGY & CAUSES

- Insufficient production of erythrocytes AKA red blood cells (RBCs)

CAUSES

- Chronic diseases most common cause (e.g. kidney disease, cancer, rheumatoid arthritis)

SIGNS & SYMPTOMS

- Variable depending on degree of hypoxia, pallor; fatigue; dyspnea; activity intolerance; cardiorespiratory compromise

DIAGNOSIS

LAB RESULTS

- Complete blood count (CBC)
- Peripheral blood smear analysis
- Blood chemistry
- Iron studies
- Genetic testing (rarely)

TREATMENT

MEDICATIONS

- Dietary changes

OTHER INTERVENTIONS

- Supplementation (address iron deficiency)

ANEMIA OF CHRONIC DISEASE (ACD)

osms.it/anemia-of-chronic-disease

PATHOLOGY & CAUSES

- Deficient RBC production due to chronic diseases (e.g. infection, inflammation, malignancy)
- AKA anemia of chronic inflammation

CAUSES

- Inflammatory processes in iron homeostasis
- Systemic inflammation → ↑ circulation cytokines, interleukin 1 (IL1), interleukin 6 (IL6), tumor necrosis factor alpha (TNF alpha), interferon beta (IFN beta), interferon gamma (IFN gamma)
  - ↑ hepcidin secretion by liver → ↓ iron absorption from gastrointestinal (GI) tract, ↓ iron sequestration in reticuloendothelial system → ↓ iron available for erythropoiesis
  - ↓ secretion of erythropoietin
  - Direct inhibition of erythropoiesis
  - ↓ erythrocyte lifespan

RISK FACTORS

- Advanced age, physical trauma

SIGNS & SYMPTOMS

- Hypoxia, pallor; fatigue; dyspnea; activity intolerance; cardiorespiratory compromise
- Variable depending on degree of hypoxia

DIAGNOSIS

LAB RESULTS

- RBCs normochromic, normocytic
- Microcytic, hypochromic RBCs (rarely)
- Leukocytosis
  - Underlying disorder
- Normal/low mean corpuscular hemoglobin (MHC), mean corpuscular volume (MCV)
- Normal mean corpuscular hemoglobin concentration (MCHC)
- Normal/increased red cell distribution width (RDW) normal/increased
- Erythrocyte hypoproliferation
  - Decreased RBC count
  - Mild to moderate decrease in hemoglobin
- Elevated erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), IL6
- Decreased serum iron levels
- High ferritin
- Decreased serum transferrin saturation
- Decreased total iron binding capacity
- Low serum erythropoietin concentration
- Decreased reticulocyte count
- Bone marrow examination
  - Increased iron in macrophages (related to actions of hepcidin), erythroid precursors

TREATMENT

MEDICATIONS

- Supplemental iron
  - IV more effective than oral iron for systemic inflammation
- Erythropoiesis-stimulating agents (e.g. epoetin alfa, darbepoetin alpha)
  - For severe anemia

OTHER INTERVENTIONS

- Transfusion of packed RBCs
  - For severe anemia

APLASTIC ANEMIA

osms.it/aplastic-anemia

PATHOLOGY & CAUSES

- Pancytopenia due to bone marrow hypoplasia/aplasia
- Idiopathic/inherited/acquired

CAUSES

- Inherited
  - Fanconi anemia; Shwachman–Diamond syndrome; familial aplastic anemias; reticular dysgenesis
- Acquired
  - Immune processes (e.g. systemic lupus erythematosus, graft-versus-host disease, paroxysmal nocturnal hemoglobinuria)
  - Drugs (e.g. cytotoxic cancer chemotherapy, carbamazepine, phenytoin, indomethacin, sulfonamides, chloramphenicol)
  - Viruses (e.g. Epstein–Barr, HIV, hepatitis, herpes)
  - Toxic chemicals (e.g., solvents, benzene, pesticides)
  - Ionizing radiation
- Acquired or idiopathic
  - Insidious onset of bone marrow hypoplasia/aplasia, hematopoietic cell loss → ↓ production of cell lineages (thrombocytes, leukocytes, erythrocytes) → peripheral pancytopenia

COMPLICATIONS

- Impairment of blood's immunity, hemostasis, oxygen-carrying capacities

SIGNS & SYMPTOMS

- Deficient thrombocytes, leukocytes
  - Shorter lifespan
- Neutropenia
  - Increased frequency/severity of infections
  - Neutropenia-related sepsis common cause of death
- Thrombocytopenia
  - Mucosal hemorrhage (e.g. gingival, nares, ecchymosis, petechiae, heavy menstrual flow, occult blood in stool, intracranial hemorrhage)
- Anemia
  - Pallor, fatigue, dyspnea, activity intolerance, cardiorespiratory compromise

DIAGNOSIS

LAB RESULTS

- Prolonged bleeding time
- Decreased hemoglobin, hematocrit
- Absolute neutrophil count decreased
- Platelet count decreased
- Reticulocyte count decreased
  - Normal erythrocyte morphology
- Bone marrow biopsy
  - Some lymphocytes, plasma cells, stromal elements (e.g. blastoid cells)
  - No increase in blasts/dysplasia

TREATMENT

- Treat underlying cause
  - Discontinue offending drug treatment
- Varies by age, severity of symptoms, likelihood of finding donor match

MEDICATIONS

- Manage cytopenias
- Antimicrobials for infections
  - *Medical emergency:* fever + low absolute neutrophil count
- Growth factors
  - *Granulocyte colony-stimulating factor*

(G-CSF): frequent/severe infections
    - Thrombopoietin (TPO) receptor agonists with immunosuppressive therapy
    - Hematopoietic growth factors (rarely)
- Immunosuppressive therapy (IST)
    - Consists of antithymocyte globulin (ATG) + cyclosporin A
    - *Administer glucocorticoid with ATG:* steroid reduces risk of serum sickness; immunosuppressive properties
    - *Cyclosporin A:* immunosuppressive
    - Eltrombopag (thrombopoietic agent) to increase platelet count

OTHER INTERVENTIONS

- Hematopoietic stem cell transplant
    - Curative if effective
- Transfusions
    - Platelets, packed red blood cells
    - Increased risk of alloimmunization, graft rejection after bone marrow transplant

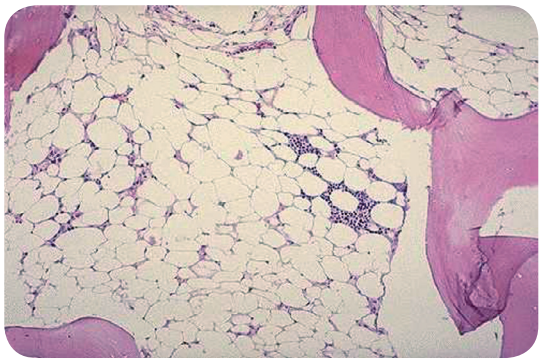

Figure 53.1 A bone marrow biopsy from an individual with aplastic anemia. The bone marrow spaces contain large amounts of fat and minimal hematopoietic tissue is present.