Blood and Lymphatic Disorders

Bio 375

Pathophysiology

Blood Dyscrasias

- The anemias:
  - Cause a reduction in oxygen transport in the blood due to:
    - Decrease in hemoglobin production
    - Decrease in erythrocytes
    - Combination of these two
  - Oxygen deficit results:
    - Less energy is produced in cells
    - Cell metabolism is decreased
    - Cell reproduction is decreased

Results of Anemia

- Compensatory mechanisms include tachycardia and peripheral vasoconstriction
- This leads to fatigue, pallor, dyspnea and tachycardia
- Decreased regeneration of epithelial cells causes the digestive tract to become inflamed and ulcerated; cracked lips; dysphagia; hair and skin may show degenerative changes
Severe anemia may lead to angina during stressful situations if oxygen supply to the heart is sufficiently reduced.

Chronic severe anemia may cause congestive heart failure.

Anemia may occur when:
- There is a deficiency of a nutrient
- When bone marrow function is impaired
- When blood loss is excessive
- When there is excessive destruction of RBC's

Iron Deficiency Anemia
- Very common
- Ranges from mild to severe
- Occurs in all age groups
- Lack of iron impedes synthesis of Hb
- Produces microcytic, hypochromic RBC's
- Decrease in stored iron with:
  - Decreased serum ferritin
  - Decreased hemosiderin
  - Decreased iron containing histiocytes in bone marrow

Etiology of Iron Def Anemia
- Iron deficit can occur for several reasons:
  - Inadequate iron containing vegetables or meat in diet
  - Chronic blood loss from ulcers, hemorrhoids, cancer or excessive menstrual flow
  - Malabsorption syndromes, e.g. achlorhydria
  - Severe liver disease
  - In some infections and cancer, iron is absorbed but not well utilized; leads to low hemoglobin counts but high iron storage levels
**Signs and Symptoms**

- Mild anemias are often asymptomatic
- As hemoglobin levels drop, signs appear:
  - Pallor of the skin
  - Fatigue, lethargy and cold intolerance
  - Irritability, a CNS response to hypoxia
  - Degenerative changes like brittle hair, concave and ridged nails
  - Inflammation of tongue and oral mucosa
  - Menstrual irregularities
  - Delayed healing
  - Tachycardia, heart palpitations, dyspnea, fainting

**Tests and Treatment**

- Lab tests for hemoglobin, hematocrit, mean corpuscular volume and mean corpuscular hemoglobin, serum ferritin, serum iron and transferrin saturation
- Underlying cause must be identified and resolved if possible
- Iron-rich foods and iron supplements may be given
- Iron supplements usually cause constipation

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**Iron Deficiency due to blood loss**
Pernicious Anemia (B₁₂ Def)
- Characterized by very large, immature, nucleated erythrocytes (megaloblastic anemia)
- Usually results from deficits of either folic acid (vitamin B₉) or vitamin B₁₂
  - Folic acid deficits usually diet related
  - B₁₂ deficit may have multiple causes

Vitamin B₁₂ Deficiency
- Often caused by the malabsorption of B₁₂ due to a lack of intrinsic factor (IF) from the gastric glands of the stomach
- Lack of IF usually due to:
  - Formation of autoantibodies against IF or the parietal cells that produce it; results in atrophy of the gastric mucosa
  - Any condition that reduces the gastric mucosa

The gastric mucosa atrophy not only causes IF deficiency but also achlorhydria which interferes with:
- Early protein digestion
- Absorption of iron
- Iron deficiency may coexist with pernicious anemia
- Vitamin B₁₂ must bind to IF to enable absorption of the vitamin in the lower ileum.
Deficiency of vitamin B12 leads to impaired maturation of erythrocytes (it interferes with DNA synthesis)
- The RBC's are very large and many have nuclei
- They are destroyed prematurely leading to low hemoglobin count or anemia
- Often granulocytes are also affected with hypersegmented nuclei

Additional Problems
- Thrombocyte (platelet) levels may be low
- Lack of B₁₂ is also a direct cause of demyelination of nerve fibers of peripheral nerves and eventually the spinal cord; first sensory nerves are affected and later motor nerves are involved
- Demyelination interferes with nerve conduction

Etiology and Treatment
- Dietary deficiency not typically a cause
- Most common cause is malabsorption:
  - Autoimmune reaction
  - Chronic gastritis
  - Inflammatory conditions like regional ileitis
- Oral supplements for pregnant women and vegetarians
- B₁₂ injections for people with pernicious anemia
Normal Erythropoiesis

Vitamin B12 Deficiency

Aplastic Anemia

- Results from impairment or failure of bone marrow function resulting in loss of stem cells
- Pancytopenia leads to many complications
- Bone marrow is hypocellular with increased fatty tissue
### Signs and Symptoms
- Anemia (pallor, weakness and dyspnea)
- Leukopenia with recurrent or multiple infections
- Thrombocytopenia with small pinpoint hemorrhages and a tendency to bleed excessively especially in the mouth

### Etiology
- About half the cases are middle aged and cause is unknown or ideopathic
- In others, damage may be caused by myelotoxins, such as:
  - Radiation
  - Industrial chemicals (e.g. benzene)
  - Drugs (e.g. chloramphenicol, gold salts, phenylbutazone, phenytoin, antineoplastic drugs)
- Also viruses, particularly hepatitis C may cause aplastic anemia
- If the risk is from cancer treatment, a patient's stem cells may be harvested prior to drug treatment and then transfused later when needed
Other Blood Disorders Include

- Hemolytic anemias
  - Sickle cell anemia
  - Thalassemia

Other Blood Disorders Include

- Polycythemia vera
- Blood clotting disorders
  - Hemophilia A
  - Disseminated Intravascular Coagulation
The Leukemias

- The leukemias are a group of neoplastic disorders involving white blood cells
- One or more of the leukocyte types are present as undifferentiated, immature, nonfunctional cells that multiply uncontrollably and large numbers are released into the general circulation
- They infiltrate the liver, spleen, brain and other organs

Acute leukemias are characterized by:

- High proportion of very immature, nonfunctional cells in the bone marrow and peripheral circulation
- Onset is usually abrupt
- Signs are obvious
- Complications are common
- Chronic types have a higher proportion of mature cells, an insidious onset, with mild signs and a better prognosis

Types of Leukemias

<table>
<thead>
<tr>
<th>Types of Leukemias</th>
<th>Malignant Cells</th>
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<tbody>
<tr>
<td>Acute lymphocytic leukemia (ALL)</td>
<td>Lymphocytes</td>
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<tr>
<td>Acute myelogenous or myelocytic leukemia (AML)</td>
<td>Granulocytes (neutrophils, eosinophils, and basophils)</td>
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<tr>
<td>Acute monocyctic leukemia</td>
<td>Monocytes</td>
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<tr>
<td>Chronic lymphocytic leukemia (CLL)</td>
<td>B lymphocytes</td>
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<tr>
<td>Chronic myelogenous leukemia (CML)</td>
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<td>Hairy cell leukemia</td>
<td>B lymphocytes</td>
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Lymphatic Disorders

- These are malignant neoplasms involving lymphocyte proliferation in the lymph nodes
- Two types are distinguished on the basis of lymph node biopsy:
  - Hodgkin's Lymphoma
  - Non- Hodgkin's Lymphoma
- No specific etiology is known

Hodgkin's Lymphoma

- Primarily occurs in adults 20-40 years old
- Initially involves a single lymph node but progresses to adjacent lymph nodes and finally to other organs via the lymphatic system
- T lymphocytes appear to be defective
- Lymphocyte count is depressed
- Reed-Sternberg cell, found in lymph nodes, is used as marker in diagnosis
Typical spread of Hodgkin's lymphoma

Reed-Sternberg Cell (large cell with irregular nucleus)

Staging is based on number of nodes and organs involved and whether they are located on one or both sides of the diaphragm.

Treatment involves:
- Radiation
- Chemotherapy
- Surgery

Prognosis in early stages is excellent.
Non-Hodgkin’s Lymphoma

- Increasing in incidence (cause unknown)
- Similar to Hodgkin’s in many ways
- Clinical signs, staging and treatment are similar
- Distinguished by multiple node involvement scattered throughout the body and a widespread pattern of metastases, often present at diagnosis
- Intestinal nodes and organs often involved in early stages

Multiple Myeloma or Plasma Cell Myeloma

- This is a neoplastic disease of unknown etiology occurring in older adults
- It involves plasma cells (mature B cells)
- Malignant plasma cells replace bone marrow and erode the osseous tissue
- Blood cell production is impaired
- Antibody production is impaired
- Multiple tumors with bone destruction develop in vertebrae, ribs, pelvis, skull

- Spontaneous fractures at weakened sites in the bone are common
- Hypercalcemia develops as osseous tissue is broken down
- The tumor cells can spread throughout the body into lymph nodes and many organs
- Treatment involves chemotherapy
- Median survival is three years