Anemias

Anemia is an absolute or relative deficiency in the concentration of circulating red blood cells. Anemias can be classified as nutritional, hemolytic, and genetic (hemoglobinopathies, thalassemias). In a healthy person, symptoms do not develop until the hemoglobin level decreases below 7 g/dL. Symptoms are variable and depend on concurrent disease processes.

ANESTHETIC CONSIDERATIONS:

- Etiology, duration and stability of anemia
- Comorbid conditions, especially cardiorespiratory, may influence need for blood transfusion
- No evidence for benefit of pre-operative optimization of Hb above any certain "transfusion trigger" number (decision to transfuse is patient and case specific)
- Patients with chronic anemias are usually compensated

ANESTHETIC GOALS:

- Diagnose and treat underlying cause of anemia
- Ensure T&S and X-match, availability of blood if transfusion may be required
- Minimize interfering with oxygen delivery to tissues:
    - Avoid drugs that decrease cardiac output and myocardial depressants
    - Avoid hyperventilation
    - Keep the patient warm, avoid hypothermia
    - Optimize oxygenation and ventilation

HISTORY

- Etiology, duration and stability of the anemia, any treatments including transfusions?
- Related symptoms – headache, weakness, exertional dyspnea, loss of endurance, palpitations, fatigue, chest pain, weight loss, pallor
- History of colon cancer, gastrointestinal or genitourinary bleeding, menorrhagia, chronic infections, inflammatory diseases, nutritional deficiencies (including gastric bypass recipients)
- Comorbid conditions that may influence oxygenation or be affected by hypoxia, such as pulmonary, cerebrovascular, or cardiovascular disease
- Vitamin B12 deficiency is associated with bilateral peripheral neuropathy due to degeneration of the lateral and posterior columns of the spinal cord
    - Symmetrical paresthesias with loss of proprioceptive and vibratory sensations, especially in the lower extremities
    - Unsteady gait
    - Diminished deep tendon reflexes
    - Memory impairment and mental depression may be prominent
- Hereditary spherocytosis: hemolytic crises? viral or bacterial infections, abdominal pain, vomiting, cholelithiasis, jaundice

PHYSICAL

- Cardiorespiratory exam – murmurs
- Hepatospenomegaly or lymphadenopathy

INVESTIGATIONS

- Search for and treatment of the underlying cause
- The World Health Organization defines anemia as a hemoglobin level lower than 13 g/dL in adult men and less than 12 g/dL in adult women
- CBC, peripheral smear, determination of mean corpuscular volume (MCV), a reticulocyte count, and further testing such as iron studies, vitamin B_{12}, or folate levels depending on the findings on the smear and the MCV, LDH and bili for hemolysis
    - MCV, iron, and ferritin are low and total iron-binding capacity (TIBC) is high in iron deficiency anemia
    - MCV and TIBC are low or normal and iron and ferritin are normal or high in anemia associated with chronic disease
    - MCV is high and vitamin B_{12} or folate levels are low in macrocytic anemia associated with these deficiencies
- Type and screening and preoperative transfusion may be necessary, depending on the level of anemia and anticipated surgical blood loss

OPTIMIZATION

- Minimum acceptable Hb concentrations that should be present before proceeding with elective surgery in patients with chronic anemia cannot be recommended
    - Hb concentrations of 10 g/dL are commonly cited as a reference point, but there is no evidence that Hb values below this level mandates the need for perioperative RBC transfusions
    - Ultimately, the decision to administer RBCs during the perioperative period is influenced by the risks of anemia (decreased oxygen-carrying capacity) and the risks of transfusions (transmissible diseases, hemolytic and nonhemolytic transfusion reactions, immunosuppression)
    - The risks of anemia in addition to decreased tissue oxygen delivery vary among individuals, depending on co-existing medical diseases, age, and the magnitude of the blood loss
    - For patients at risk for current ischemic heart disease, data indicate that transfusion to a hematocrit level of 29% to 34% may be appropriate
- The minimum hematocrit necessary to ensure adequate oxygen transport in children has not been well established
    - Preoperative hemoglobin testing, however, is of limited value in healthy children undergoing elective surgery when minimal blood loss is expected
    - Children with chronic anemia, such as those with renal failure, do not require preoperative transfusion because of compensatory mechanisms, such as increased 2,3-diphosphoglycerate, increased oxygen extraction, and cardiac output
    - Elective surgery for children who are anemic should take into consideration the medical history, underlying diseases (hemoglobinopathies, von Willebrand, sickle cell, other factor deficiency), the nature of the surgery, and its urgency
    - Most pediatric anesthesiologists would recommend a hematocrit greater than 25% before elective surgery in the absence of chronic disease
    - If significant blood loss is anticipated and the surgery is elective, then the cause of anemia should be investigated and treated and the surgery postponed until the hematocrit is restored to the normal range
    - *Healthy children scheduled for elective surgery that is not expected to cause substantive bleeding should not routinely receive a blood transfusion just to bring their hematocrit to 30%.*
- In special circumstances, such as a patient's refusal of perioperative blood transfusion or elective procedures with expected significant blood loss in anemic patients, postponement of surgery to treat with recombinant human erythropoietin and iron may be warranted
- Treatment of iron deficiency anemia is with ferrous iron salts, such as ferrous sulfate administered orally for at least 1 year after the source of blood loss that caused the iron deficiency anemia is corrected
- For Vitamin B12 deficiency anemia, administration of parenteral vitamin $_{B12}$ reverses both the hematologic and neurologic changes in adults
- Hereditary spherocytosis is treated by splenectomy that is usually delayed until the patient is age 6 years or older

- For patients with cold autoimmune hemolytic anemia, plasmapheresis to reduce the titer of cold antibody is recommended before hypothermic procedures such as cardiopulmonary bypass
- Treatment of immune hemolytic anemias is with corticosteroids and immunosuppressants; Splenectomy may be beneficial in some patients

ANESTHETIC OPTIONS

- The coexisting neuropathy of vitamin B_{12} deficiency must be considered when regional or peripheral nerve blocks might be used

ANESTHETIC SETUP

- Standard emergency drugs and set-up
- Consider having cross-matched blood readily available for major surgery or where considerable blood is expected
- For cold autoimmune hemolytic anemia maintaining a warm environment is essential for prevention of hemolysis

MANAGEMENT OF ANESTHESIA

- Minimize the likelihood of significant changes that could further interfere with oxygen delivery to tissues
    - For example, drug-induced decreases in cardiac output or a leftward shift of the oxyhemoglobin dissociation curve owing to respiratory alkalosis from iatrogenic hyperventilation of the patient's lungs could interfere with tissue oxygen delivery
    - Decreased body temperature also shifts the oxyhemoglobin dissociation curves to the left
    - Efforts to offset the impact of surgical blood loss by such measures as normovolemic hemodilution and intraoperative blood salvage are considerations in selected patients
- Although supporting evidence is not available, it is likely that a decision to replace intraoperative blood loss with whole blood or packed RBCs will be made when Hb concentrations decrease acutely to less than 7 g/dL, especially if there is co-existing anemia or cardiovascular or cerebrovascular disease
- For megaloblastic anemia due to vitamin B12 deficiency, avoid nitrous oxide
    - Nitrous oxide inactivates the vitamin B_{12} component of methionine synthetase and prolonged exposure to nitrous oxide produces megaloblastic anemia and neurologic changes similar to those that occur with pernicious anemia
    - In susceptible patients (those with chronic illness, the elderly) there is also evidence that short-term exposure to nitrous oxide can cause megaloblastic red blood cell changes
    - The issue of nitrous oxide causing postoperative neurologic dysfunction is also controversial and case reports of neuropathy linked to intraoperative nitrous oxide exposure have increased

DISPOSITION & MONITORING

- The time of most danger to the patient may be the early recovery room period, during which time oxygen delivery to the lungs is perhaps at its worst

COMPLICATIONS

- No controlled studies have documented the Hb concentrations at which RBC transfusions prevent myocardial ischemia or infarction and improve clinical outcome
- No evidence that postoperative morbidity (wound healing, infection) is adversely affected when surgery is performed in the presence of mild to moderate anemia

PATHOPHYSIOLOGY

- The most important adverse effects of anemia are decreased tissue oxygen delivery owing to associated decreases in arterial content of oxygen (CaO2)
    - Compensation for decreased CaO2 is accomplished by a rightward shift of the oxyhemoglobin dissociation curve (facilitates release of oxygen from Hb to tissues) and increased cardiac output as a reflection of decreased blood viscosity
    - When oxygen delivery to tissues is inadequate, the kidneys release erythropoietin, which subsequently stimulates erythroid precursors in the bone marrow to produce additional RBCs
    - Fatigue and decreased exercise tolerance reflect the inability of the cardiac output to increase further and maintain tissue oxygenation, especially in anemic patients who become physically active
- There are many causes and forms of anemia, with the most common causes of chronic anemia being iron deficiency, the presence of chronic diseases, thalassemia, and anemia due to acute blood loss
- Nutritional deficiency anemia:
    - Iron deficiency - microcytic, hypochromic red blood cells
        - May be an absolute deficiency secondary to decreased oral intake or a relative deficiency caused by a rapid turnover of RBCs (e.g., chronic blood loss, hemolysis)
    - Vitamin B_{12} (cobalmin) deficiency – macrocytic, megaloblastic anemia
        - Absorption of vitamin B_{12} by the GI tract depends on release of intrinsic factor (produced by gastric parietal cells)
        - Chronic gastritis and gastric atrophy may be caused by autoantibodies to gastric parietal cells
        - In addition to anemia, vitamin B_{12} deficiency can interfere with myelination and cause nervous system dysfunction (peripheral neuropathy, symmetric loss of proprioception and vibratory sensation in the lower extremities secondary to degeneration of the lateral and posterior spinal cord columns)
    - Folic acid deficiency – macrocytic, megaloblastic anemia
        - Although peripheral neuropathy may occur, it is not as common as with vitamin B_{12} deficiency
        - Causes of folic acid deficiency include alcoholism, pregnancy, and malabsorption syndromes
        - Methotrexate, phenytoin, and ethanol are among the drugs known to interfere with folic acid absorption
    - Refractory bone marrow disease – megaloblastic anemia
    - Chronic illness, cancer, and poor dietary intake
- Hemolytic anemias:
    - The normal life span of an erythrocyte is 120 days
    - Abnormalities in the erythrocyte may result in premature destruction of the cell (hemolysis)
    - Structural erythrocyte abnormalities
        - *Spherocytosis* is the most common of the red cell membrane defects producing hemolysis (abnormal proteins in the skeleton of the RBC membrane cause it to be rounded, fragile, and more susceptible to hemolysis than the normal biconcave RBC)
        - The spleen destroys the abnormal RBCs and chronic anemia ensues
    - Enzyme deficiencies
        - *G6PD Deficiency* – see separate G6PD seminar
        - *Pyruvate Kinase Deficiency* - Pyruvate kinase is a glycolytic enzyme of the Embden-Meyerhof pathway (which converts glucose to lactate and is the primary pathway for ATP synthesis in the RBC); A deficiency of pyruvate kinase results in a potassium leak from

the red blood cell, increasing their rigidity and accelerating destruction in the spleen

- Immune hemolytic anemias
  - Alloimmune hemolysis (erythrocyte sensitization) - warm and cold antibody hemolytic anemia
    - Cold hemagglutinin disease is caused by IgM autoantibodies that react with I antigens of RBCs
    - Collagen vascular diseases, solid organ transplant, blood transfusion, neoplasia, and infections can produce immune hemolytic anemia by a variety of mechanisms including warm and cold antibody-mediated hemolysis
  - Drug-induced immune hemolysis: autoantibody type, hapten-induced type, and immune complex type
    - IgG antibody mediated hemolysis that doesn't fix complement: induced by α-methyldopa
    - The hapten-induced type is characteristic of the response to penicillin
    - The immune type of reaction can occur after the administration of quinidine, quinine, sulfonamides, isoniazid, phenacetin, acetaminophen, cephalosporins, tetracyclines, hydralazine, and hydrochlorothiazide

PHYSIOLOGIC ANEMIA IN INFANTS

- Physiologic anemia of infancy occurs between 2 and 4 months of age
- At this time there is an increased production of hemoglobin A and an increase in red cell 2,3-diphosphoglycerate, which contribute to a right shift of the oxygen-hemoglobin dissociation curve
- Therefore, in infants 2 to 4 months of age, a reduced hemoglobin value is acceptable
- Anemia, with a hematocrit of less than 30%, in former preterm infants represents a special category of patients who may have an increased incidence of postoperative apnea, but transfusion is still not recommended

PHYSIOLOGIC ANEMIA IN PREGNANCY

- During normal pregnancy, plasma volume increases by approximately 50%, but red blood cell (RBC) mass increases by only 30%, resulting in a dilutional anemia
- RBC mass increases linearly after the first trimester until delivery, and plasma volume plateaus or falls slightly near term
- Therefore hemoglobin concentrations are lowest between 28 and 34 weeks' gestation
- If the hemoglobin concentration falls below 10.5 g/dL, the physician should consider causes other than the dilutional anemia of pregnancy

REFERENCES

- Barash P. 633-634
- Miller Chpt 34 and 35
- Coexisting Chpt 17
- Cote Chpt. 4
- Chestnut Chpt 43