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Acute Anemia

click here for types

click here for exam

treatment options

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Continuing Education Activity

Acute anemia occurs when there is an abrupt drop in red blood cells, usually due to acute hemorrhage or hemolysis. This activity reviews the presentation, etiology, evaluation and management of this condition and highlights the role of interprofessional teams in caring for patients with this condition.

Objectives:

- Describe the signs and symptoms of acute anemia that are likely to be present when a patient has lost greater than twenty percent of their blood volume.
- Identify the most critical steps that should be taken immediately when a patient presents with acute anemia.
- Review the threshold at which a patient should receive a red blood cell transfusion.
- Explain why an interprofessional care team is critical to improving outcomes for patients with acute blood loss anemia.

Access free multiple choice questions on this topic.

Introduction

The definition of anemia is either a decreased amount of circulating red blood cells (RBCs), the amount of hemoglobin (Hgb), or volume of packed RBCs (hematocrit).[1] The World Health Organization defines anemia as a hemoglobin level less than 13 g/dL in men and less than 12 g/dL in women.[2]

Anemia classifies as either acute or chronic:

- Acute anemia occurs when there is an abrupt drop in RBCs, most often by hemolysis or acute hemorrhage.
- Chronic anemia, on the other hand, is generally a gradual decline in RBCs, and causes include iron or other nutritional deficiencies, chronic diseases, drug-induced, and other causes.

Etiology

Anemia can result from many events.

- Blood loss is the most prevalent cause of anemia, causing a direct loss of RBCs. It is the most common cause of acute anemia seen in the ER.
    - Emergent conditions include traumatic injury resulting in arterial bleeding, ruptured aneurysm, massive upper or lower gastrointestinal (GI) hemorrhage, ruptured ectopic pregnancy, and disseminated

intravascular coagulation.

- Hemolytic anemias can also cause either acute or chronic anemia. There are numerous causes, which result in reduced survival of RBCs.

One way to classify hemolytic anemias is intracorpuscular (the defect is within the RBC itself) versus extracorpuscular (the problem is external to the RBC).

- **Intracorpuscular**:
    - Affecting the hemoglobin (hemoglobinopathies): Sickle cell disease (caused by a point mutation on the DNA of the beta-globin chain resulting in Hgb S) which causes the Hgb S to polymerize and sickle in response to oxidative stress, alpha and beta thalassemias
    - Enzymopathies: RBC enzyme abnormalities including the following:
        - Glucose-6-phosphate dehydrogenase (a deficiency which affects the pentose pathway)
        - Hemophilia A (caused by factor VIII deficiency) in which severe bleeding is common
        - Glucose-6-phosphate dehydrogenase (G6PD) and pyruvate kinase (PK) deficiencies
        - Phosphofructokinase deficiency
        - Phosphoglycerate kinase deficiency
        - Aldolase deficiency
        - Triosephosphate isomerase deficiency
        - Membrane-cytoskeletal defects - Hereditary spherocytosis or hereditary elliptocytosis
        - Paroxysmal nocturnal hemoglobinuria (PNH)
- **Extracorpuscular:**
    - Familial (atypical) hemolytic-uremic syndrome - Familial (atypical) hemolytic-uremic syndrome (HUS) caused due to mutations in any one of several genes encoding complement regulatory proteins.
    - Mechanical destruction (microangiopathic)[3][4][5][6][7]:
        - Thrombotic thrombocytopenic purpura (TTP) is a trio of microangiopathic hemolytic anemia, severe thrombocytopenia, and organ ischemia, all of which are caused by platelet-rich thrombi; the cause of TTP is a deficiency in ADAMTS13 (a metalloprotease)
        - HUS: characteristic presentation is by microangiopathic hemolytic anemia, thrombocytopenia, and renal failure. It is similar to TTP, but lesions are limited to the kidney
            - In children, the pathology may present after diarrheal illness caused by *Escherichia coli*, *Salmonella, and Shigella* species, or viral gastroenteritis.
            - In adults, it may be precipitated by pregnancy or estrogen use; uremia may also lead to bleeding resulting from abnormal platelet function
        - complement-mediated Thrombotic microangiopathy
    - Immune thrombocytopenic purpura (ITP): caused by IgG autoantibodies binding to platelets, which subsequently get destroyed in the spleen; when platelet counts get very low, bleeding occurs

- Disseminated intravascular coagulation (DIC}: a condition in which systemic activation of coagulation occurs, resulting in the formation of intravascular fibrin, which initially causes thrombosis then is followed by bleeding due to consumption of coagulation factors.
- Toxic agents and Drugs: hyperbaric oxygen (or 100% oxygen), methyldopa, nitrates, chlorates, methylene blue, dapsone, cisplatin, and numerous aromatic (cyclic) compounds; other chemicals include arsine, stibine, copper, and lead
- Infectious: malaria is the most common cause of hemolytic anemia. In other parts of the world, Shiga toxin–producing E. coli O157:H7 causing hemolytic uremic syndrome; in patients with open wounds, septic abortion, or who received contaminant blood, *Clostridium perfringens* sepsis can induce life-threatening hemolysis due to the action of a toxin with lecithinase activity
- Autoimmune hemolytic anemia: can be associated with autoimmune diseases (e.g., lupus, certain types of lymphomas and leukemias), is drug-induced, or, most times there is no identifiable cause. Hemolysis is caused by immunoglobulin G (IgG) autoantibody binding to the RBCs, resulting in macrophages attacking the RBCs' membrane, changing their shape to spherocytes, which undergo destruction more rapidly
- Hypersplenism

Epidemiology

Anemia is common, affecting one-fourth of the population overall, approximately 50% of hospitalized patients, and up to 75% of elderly hospitalized patients. Data collected during the year 2000 on over 81000 health plan members show that the highest rates of anemia are in patients with chronic kidney disease (34.5%), cancer (21%), chronic heart disease (18%), inflammatory bowel disease (13%), rheumatoid arthritis (10%), and infection with human immunodeficiency virus (10%).[8]

Pathophysiology

The common causes in acute anemia are hemolysis or hemorrhage, which results in a sudden reduction in RBCs. When the drop is quick, hemoglobin of 7 to 8 g/dL is usually symptomatic since the body has inadequate time to compensate and replace the volume lost. Healthy individuals can tolerate 20% loss of their blood volume without significant symptoms, due to reflex vasospasm and redistribution of blood flow. With greater losses, patients develop the signs and symptoms of hypovolemia. Compensatory mechanisms such as redistribution of blood flow are no longer sufficient to maintain blood pressure, and clinical signs include postural hypotension, altered mental status, cool and/or clammy skin, tachycardia, and hyperventilation. In acute hemorrhage, hemoglobin and hematocrit levels can be normal, owing to concomitant loss of both red cells and plasma, which becomes apparent after patient’s plasma volume is restored, either spontaneously or with intravenous fluids.

Histopathology

Viewing the peripheral blood smear under a microscope

- Helmet cells, schistocytes, RBC fragments, and spherocytes can present in microangiopathic hemolysis (TTP, ITP, HUS, and DIC)
- Sickle-shaped cells and Howell-Jolly bodies present in sickle cell disease

History and Physical

History

Get a thorough but focused history if possible, but priority assessment should include the ABCs (*A*irway, *B*reathing, *C*irculation) and if necessary, initiating resuscitation.

If patients are unable to communicate, obtain as much history as possible from EMS or those at the bedside.

History should also focus on the possible source of bleeding, such as a more complete gastrointestinal (GI) history if there is a concern for GI hemorrhage, and likewise a focused menstrual and/or pregnancy history if concern for gynecological causes.

Physical Exam

Vital signs should undergo frequent monitoring. As above, the initial exam should focus on the organ thought to be the cause of the patient's bleeding. If trauma is suspected, then the chest, abdomen, pelvis, and extremities must be both physically examined and imaged, as clinically indicated.

Below are the various stages of presentation of hemorrhagic shock:

- Class I (<15% blood loss):
  - Mild tachycardia is usually the first sign
  - Blood pressure is normal
  - Skin may start to feel cool to the touch
- Class II (15-30% blood loss):
  - Tachycardia continues
  - Tachypnea begins
  - Decreased pulse pressure
- Class III (30-40% blood loss):
  - Tachycardia worsens
  - Decrease in blood pressure as well
  - Skin becomes cold and appears pale and mottled
  - Urine output decreases significantly
- Class IV (=40% blood loss):
  - Extremely dangerous with high mortality
  - Tachycardia and decreased blood pressure continue to worsen and can lead to loss of consciousness
  - If there is more than 50% loss of blood, the pulse can disappear

Other useful skin examination findings include:

- Flank ecchymosis (Grey-Turner sign): suggests retroperitoneal hemorrhage
- Umbilical ecchymosis (Cullen sign): suggestive of intraperitoneal or retroperitoneal bleeding
- Jaundiced, yellow skin may suggest liver disease, hemoglobinopathies, or other forms of hemolysis
- Purpura and petechiae suggest platelet disorders

- Hemarthrosis suggests hemophilia
- Diffuse bleeding from intravenous (IV) sites and mucous membranes may be due to disseminated intravascular coagulation (DIC)

Evaluation

Further workup is essential in learning the etiology and acuity.

- Send a blood sample immediately to be typed and cross-matched - so blood can be readied
- Complete blood count (CBC): to assess the hemoglobin and hematocrit
    - It is important to note that in an actively bleeding patient, the hematocrit level on initial presentation could be normal
        - Follow serial CBCs with suspicion of acute bleeding
- Mean corpuscular volume (MCV) classifies the anemia as microcytic, normocytic, or macrocytic:
    - Microcytic anemias (usually defined as MCV less than 80 fL) include the mnemonic TAILS: thalassemia, anemia of chronic disease, iron deficiency, and sideroblastic/sickle cell disease
    - Normocytic anemias (MCV 80 to 100 fL) include anemias due to active bleeding, hemolysis, or malignancy
    - Macrocytic anemias (usually defined as MCV greater than 100 fL): anemias related to alcohol, folate and vitamin B-12 deficiencies (pernicious anemia), and some preleukemic conditions
- LDH, haptoglobin, bilirubin, and blood urea nitrogen (BUN) levels
    - in hemolytic anemia, LDH and indirect bilirubin are elevated, and haptoglobin is low
    - an elevated BUN is common in patients with upper GI bleeds, due to undigested blood
- Reticulocyte count: erythropoietic response by the bone marrow assessment is via the reticulocytes; there will be an increase in both percentage of reticulocytes and the absolute reticulocyte count (the more definitive parameter).
    - Reticulocytosis correlates with an increased mean corpuscular volume (MCV) in the blood count
    - A low value may suggest an inadequate bone marrow response: this occurs with aplastic anemia, hematologic cancers, drugs, or toxins
- Screening labs for DIC: prothrombin time (PT), activated partial thromboplastin time (aPTT), fibrinogen, fibrin split products, and platelets
    - Findings associated with DIC include increased coagulation times, decreased platelets and fibrinogen, and fibrin split products
    - DIC should be a diagnostic consideration in patients with severe sepsis, complications with giving birth, burns, malignancies, or uncontrolled hemorrhage

Other tests that merit consideration include:

- Iron studies
- Folate and vitamin B-12 levels

- Lead levels
- Hemoglobin electrophoresis
- Factor deficiency tests
- Bleeding time
- Bone marrow aspiration
- Coombs test

Imaging:

- Ultrasound: a quick and noninvasive way for diagnosing intraperitoneal bleeding. The focused abdominal sonography for trauma (FAST) examination is commonly performed to diagnose intra-abdominal hemorrhage in unstable trauma patients
- Chest x-ray: useful in trauma patients. Can look for hemothorax, pulmonary contusions, aortic rupture, or free air under the diaphragm with suspected GI bleeding
- CT: useful for a patient with GI trauma causing bleeds
- Esophagogastroduodenoscopy (EGD): for diagnostic and treatment an upper GI bleed
- Sigmoidoscopy or colonoscopy for diagnosis a lower GI bleed

Treatment / Management

Initial Management

- Evaluate the ABCs (*A*irway, *B*reathing, and *C*irculation)
- Treat any life-threatening conditions immediately
- Supplemental oxygen
- Obtaining two large-bore intravenous (IV) lines
- IV fluid resuscitation (crystalloid is the initial fluid of choice)
- Apply direct pressure to any hemorrhage if possible

Treatment

- Packed red blood cells (pRBCs) are the primary treatment used in acute anemia to restore the blood lost. Each unit of pRBCs is expected to increase the hematocrit by 3 points
    - For hospitalized hemodynamically stable adult patients, including critically ill patients, transfusion is not recommended until the hemoglobin concentration is 7 g/dLF[9]
    - However, in patients with acute coronary syndrome, transfusion should be considered when Hgb is equal or less than 8[10]
    - EXCEPTION: if the patient is actively bleeding, then transfuse as clinically indicated
        - In cases of active hemorrhage, massive transfusion protocol should initiate immediately, and the patient is transfused more liberally to maintain hemodynamic stability until control of the source of bleeding

- Other treatment options include other components of blood: platelets, fresh frozen plasma (FFP), and cryoprecipitate
    - Each unit of platelets has normal amounts of fibrinogen and coagulation factors and raises the platelet count by approximately 10,000/microliters.
    - Fresh frozen plasma (FFP) contains all the coagulation factors.
    - Blood products (i.e., red blood cells, plasma [clotting factors], and platelets) should be given in equivalent amounts (1:1:1 ratio)
    - Cryoprecipitate contains fibrinogen, factor VIII, von Willebrand factor (vWF), and factor XIII, and is used to treat hemophilia
- Pharmacological options:
    - Vasopressors: causes vasoconstriction by decreasing blood flow. Used for hypovolemic shock, variceal bleeding
    - Gastric acid inhibitors (H2-receptor antagonists): aids healing of gastric and duodenal ulcers
    - Glucocorticoids (e.g., prednisone): treats idiopathic and acquired autoimmune hemolytic anemias
    - Vitamin K: used in patients with liver disease to correct prolonged PT and factors VII, IX, and X

Specific treatments:

Sickle cell anemia

The decision to begin transfusion depends on the rate of fall of the hemoglobin and the patient's clinical condition. Blood transfusion is necessary for aplastic crisis indicated by low reticulocyte counts. In the case of vaso-occlusive crisis, exchange transfusion is warranted to reduce the number of sickle cells and to lower the viscosity of the blood. Hydroxyurea can be used to reduce the incidence of sickle cell crisis.

Platelet disorders

Patients with thrombocytopenia with clinical evidence of bleeding should receive a platelet transfusion. Patients with platelet count lower than 10,000/microliter are at risk for spontaneous cerebral hemorrhage and thus require a prophylactic transfusion. Large-volume plasmapheresis with FFP replacement is the preferred treatment for HUS and TTP. Many patients will require daily plasmapheresis. Goals include increasing platelet count, decreasing lactate dehydrogenase (LDH), and decreasing red blood cell (RBC) fragments, which will indicate a positive response to treatment. Many patients also receive high-dose glucocorticoids in addition to antiplatelet agents (e.g., aspirin). Patients with a poor response to plasmapheresis can receive with splenectomy or immunosuppression.

In atypical HUS (aHUS), the initial management is supportive and similar to the approach used for STEC-HUS. However, in patients with severe complement-mediated HUS who are at risk for death or ESRD, use of eculizumab, a humanized monoclonal antibody to C5 is recommended. Evidence suggests that early initiation can improve renal and nonrenal recovery.

The goal in ITP is to provide a safe platelet count to prevent clinically significant bleeding rather than normalizing the platelet counts. Bleeding risk is highest when the platelet counts are less than 10,000/microL. For all patients with severe bleeding (e.g., intracranial, gastrointestinal) and a platelet count less than 30,000/microL, immediate platelet transfusion along with ITP-specific therapy including intravenous immune globulin (IVIG), glucocorticoids, and romiplostim is recommended.

Congenital bleeding disordersTreatment of von Willebrand disease is with desmopressin (DDAVP), recombinant von Willebrand factor (rVWF), or von Willebrand factor/factor VIII (vWF/FVIII) concentrates; Factor VIII and IX concentrates are used for the treatment of hemophilia A and B respectively, and the dosage is based on the site of the bleeding.

Disseminated intravascular coagulation (DIC)

A primary principle in the management of DIC is the treatment of the underlying cause to eliminate the stimulus for ongoing coagulation and thrombosis; as long as the platelet count is greater than or equal to 10,000/microL, prophylactic transfusion of platelets and coagulation factors are not recommended. Treatment is justified in patients with severe bleeding, are at high risk for bleeding, or require invasive procedures. Antifibrinolytic agents, such as tranexamic acid (TXA), epsilon-aminocaproic acid (EACA), or aprotinin are generally contraindicated.

Differential Diagnosis

Do Not Miss

- Trauma: history of trauma or blood loss
- GI bleed: history of GI bleeding, nonsteroidal anti-inflammatory drug (NSAID) or corticosteroid use, alcohol use, cirrhosis, anticoagulant use
- Rupture of a vascular aneurysm: may be sudden tearing pain, loss of consciousness possible

Other Causes

- Surgery: recent surgery with at least moderate blood loss; history of bleeding disorders or excessive bruising; use of antibiotics
- Menorrhagia: excessive menstrual bleeding lasting greater than 7 days
- Nutritional deficiencies/malnutrition: iron deficiency, B12, or folate deficiency
- Myelodysplastic syndrome: macrocytic anemia with leukopenia, macro-ovalocytes
- Leukemia: Acute leukemias with pancytopenia, with 20% blasts on peripheral smear; chronic leukemias with normocytic anemia
- Infiltration of bone marrow by malignancy: weight loss, malaise, fevers, fatigue
- Drug toxicity: known or suspected ingestion of causative drug prior to the onset
- Anemia of chronic disease: history of known chronic inflammatory, autoimmune, or infectious states
- Chronic kidney disease or chronic liver disease
- Pregnancy, especially in the third semester

Complications

The most severe complication occurs from hypovolemic shock from hemorrhage. Tissue hypoxia can occur, resulting in end-organ damage, including a heart attack, heart failure, renal failure, acute hypoxic respiratory failure, or other end-organ damage.

Consultations

- Hematology Oncology - for challenging to manage anemias, leukemia patients, or in cases of severe ITP, TTP, or HUS
- Gastroenterology - in cases of GI bleeding
- Surgery - for trauma or aneurysmal rupture

Pearls and Other Issues

- Acute anemia occurs when there is an abrupt drop in RBCs; hemolysis or acute hemorrhage are the most common causes.
- Prioritize the ABCs (*A*irway, *B*reathing, *C*irculation) and starting resuscitation
- Immediately send a blood sample to be typed and cross-matched; obtain serial CBCs to assess the hemoglobin and hematocrit
- Initial management: supplemental oxygen, obtaining large bore IV access, intravenous (IV) fluid resuscitation (crystalloid is the initial fluid of choice), and applying direct pressure to a hemorrhage
- Packed red blood cells (pRBCs): transfuse when hemoglobin is less than 7 or clinically indicated
    - Each unit of pRBCs is expected to raise the hematocrit by 3 points

Enhancing Healthcare Team Outcomes

interprofessional care in acute anemia results in improved outcomes. Education should focus on compliance with any medications (such as iron, steroids, etc.), avoiding triggers (such as alcohol, NSAID use) and a solid understanding of what caused the anemia and how best to avoid another episode. The prognosis of acute anemia largely depends on the etiology and is highly variable — rapid stabilization and treatment results in a better prognosis.

Review Questions

- Access free multiple choice questions on this topic.
- Comment on this article.

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