Anemia is among the most common medical problems and clinical and laboratory evaluation need to be approached logically. The complete blood count with red cell indices offers clues to diagnosis. Many anemias have characteristic red cell morphology. The reticulocyte count serves as a useful screen for hemolysis or blood loss. Testing for specific causes of the anemia is performed. Occasionally, examination of the bone marrow is required for diagnosis. Molecular testing is increasingly being use to aid the diagnostic process. This article reviews diagnostic tests for anemia and suggests a rational approach to determining the etiology of a patient’s anemia.

Impaired iron homeostasis and the suppressive effects of proinflammatory cytokines on erythropoiesis, together with alterations of the erythrocyte membrane that impair its survival, cause anemia of inflammation. Recent epidemiologic studies have connected inflammatory anemia with critical illness, obesity, aging, kidney failure, cancer, chronic infection, and autoimmune disease. The proinflammatory cytokine, interleukin-6, the iron regulatory hormone, hepcidin, and the iron exporter, ferroportin, interact to cause iron sequestration in the setting of inflammation. Although severe anemia is associated with adverse outcomes in critical illness, experimental models suggest that iron sequestration is part of a natural defense against pathogens.

Vitamin B₁₂ and folate deficiencies are major causes of megaloblastic anemia. Causes of B₁₂ deficiency include pernicious anemia, gastric surgery, intestinal disorders, dietary deficiency, and inherited disorders of B₁₂ transport or absorption. The prevalence of folate deficiency has decreased because of folate fortification, but deficiency still occurs from malabsorption and increased demand. Other causes include drugs and inborn metabolic errors. Clinical features of megaloblastic anemia include anemia,
cytopenias, jaundice, and megaloblastic marrow morphology. Neurologic symptoms occur in B₁₂ deficiency, but not in folate deficiency. Management includes identifying any deficiency, establishing its cause, and replenishing B₁₂ or folate parenterally or orally.

Iron Deficiency Anemia 319

Thomas G. DeLoughery

Iron deficiency is one of the most common causes of anemia. The 2 main etiologies of iron deficiency are blood loss due to menstrual periods and blood loss due to gastrointestinal bleeding. Beyond anemia, lack of iron has protean manifestations, including fatigue, hair loss, and restless legs. The most efficient test for the diagnosis of iron deficiency is the serum ferritin. Iron replacement can be done orally, or in patients in whom oral iron is not effective or contraindicated, with intravenous iron.

Myelodysplastic Syndromes: Updates and Nuances 333

Kim-Hien T. Dao

Myelodysplastic syndrome (MDS) is a heterogeneous, clonal stem cell disorder of the blood and marrow typically diagnosed based on the presence of persistent cytopenia(s), dysplastic cells, and genetic markers. Common issues that arise in the clinical management include difficulty confirming MDS diagnosis, lack of a standard approach with novel agents in MDS, and few prospective long-term, randomized controlled MDS clinical studies to guide allogeneic blood and marrow transplant. With the recent genetic characterization of MDS, certain aspects of these issues will be better addressed by integrating genetic data into clinical study design and clinical practice.

Autoimmune Hemolytic Anemia 351

Howard A. Liebman and Ilene C. Weitz

Autoimmune hemolytic anemia is an acquired autoimmune disorder resulting in the production of antibodies directed against red blood cell antigens causing shortened erythrocyte survival. The disorders can present as a primary disorder (idiopathic) or secondary to other autoimmune disorders, malignancies, or infections. Treatment involves immune modulation with corticosteroids and other agents.

Congenital Hemolytic Anemia 361

Kristina Haley

Red blood cell (RBC) destruction can be secondary to intrinsic disorders of the RBC or to extrinsic causes. In the congenital hemolytic anemias, intrinsic RBC enzyme, RBC membrane, and hemoglobin disorders result in hemolysis. The typical clinical presentation is a patient with pallor, anemia, jaundice, and often splenomegaly. The laboratory features include anemia, hyperbilirubinemia, and reticulocytosis. For some congenital hemolytic anemias, splenectomy is curative. However, in other diseases, avoidance of drugs and toxins is the best therapy. Supportive care with
transfusions are also mainstays of therapy. Chronic hemolysis often results in the formation of gallstones, and cholecystectomy is often indicated.

Sickle Cell Disease: A Brief Update

Sharl Azar and Trisha E. Wong

Sickle cell disease (SCD) is an inherited monogenic disease characterized by misshapen red blood cells that causes vaso-occlusive disease, vasculopathy, and systemic inflammation. Approximately 300,000 infants are born per year with SCD globally. Acute, chronic, and acute-on-chronic complications contribute to end-organ damage and adversely affect quantity and quality of life. Hematopoietic stem cell transplantation is the only cure available today, but is not feasible for the vast majority of people suffering from SCD. Fortunately, new therapies are in late clinical trials and more are in the pipeline, offering hope for this unfortunate disease, which has increasing global burden.

 Syndromes of Thrombotic Microangiopathy

Joseph J. Shatzel and Jason A. Taylor

Thrombotic thrombocytopenia purpura (TTP) and the hemolytic uremic syndrome (HUS) are rare thrombotic microangiopathies that can be rapidly fatal. Although the acquired versions of TTP and HUS are generally highest on this broad differential, multiple rarer entities can produce a clinical picture similar to TTP/HUS, including microangiopathic hemolysis, renal failure, and neurologic compromise. More recent analysis has discovered a host of genetic factors that can produce microangiopathic hemolytic syndromes. This article discusses the current understanding of thrombotic microangiopathy and outlines the pathophysiology and causative agents associated with each distinct syndrome as well as the most accepted treatments.

Unusual Anemias

Molly Maddock Daughety and Thomas G. DeLoughery

Many processes lead to anemia. This review covers anemias that are less commonly encountered in the United States. These anemias include hemoglobin defects like thalassemia, bone marrow failure syndromes like aplastic anemia and pure red cell aplasia, and hemolytic processes such as paroxysmal nocturnal hemoglobinuria. The pathogenesis, diagnostic workup, and treatment of these rare anemias are reviewed.

Blood Transfusion Therapy

Lawrence Tim Goodnough and Anil K. Panigrahi

Transfusion of red blood cells (RBCs) is a balance between providing benefit for patients while avoiding risks of transfusion. Randomized, controlled trials of restrictive RBC transfusion practices have shown equivalent patient outcomes compared with liberal transfusion practices, and meta-analyses have shown improved in-hospital mortality, reduced cardiac events, and reduced bacterial infections. This body of level 1
evidence has led to substantial, improved blood utilization and reduction of inappropriate blood transfusions with implementation of clinical decision support via electronic medical records, along with accompanying educational initiatives.