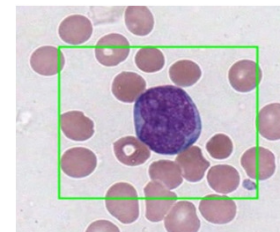
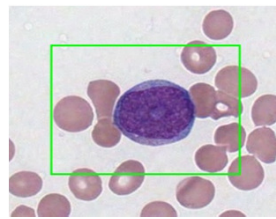
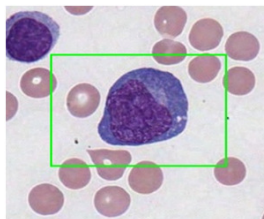




## EDUCATIONAL CHALLENGES

Specimen 1	No.
Blast, undifferentiated	178
Myeloblast	61
Immature WBC, would refer	12
Abnormal Lymphocyte, would refer	10
Promyelocyte	9
Abnormal, would refer	6
Lymphocyte, reactive (atypical, Downey, variant)	5
Plasma Cell, any stage	5
Myelocyte	3
Monocyte, any stage	3
Metamyelocyte	2
PMN or Band with Dohle Bodies	1
Abnormal Granulocyte, would refer	1
Total Population:	305



\*To see the original full-sized images, please refer to the original CD or sign on to your data entry sheet at <http://www.aab-pts.org/>

Educational Challenge 1Q2011 Slide 1 - **Acute Myeloid Leukemia:** *A 73-year-old man presents to his family physician complaining of fatigue, bruising on his legs, and recurrent nosebleeds. He worked until retirement in a refinery where he was exposed to numerous chemical agents, including benzene. Although he has been active since retirement, in the last six months he gets out of breath when climbing stairs, feels like he has no energy or appetite, and has lost 20 lbs. Physical examination is remarkable for numerous petechiae on his abdomen, chest, and back, and there are recent and resolving bruises on his lower legs. The spleen is enlarged. CBC results: WBC 52,000/ $\mu$ L, Hgb 7.6 g/dL, Hct 22.8%, Plts 41,000/ $\mu$ L. Identify the indicated cells.*

The automated CBC results show a marked elevation of the WBC count, accompanied by anemia and thrombocytopenia. This is confirmed upon review of the peripheral blood smear. The red cells are primarily spherocytic, often without an area of central pallor. The increase in WBCs is quite noticeable with the majority being immature; several basket cells or disintegrated cells are present. The cells to be identified are all **blasts**.

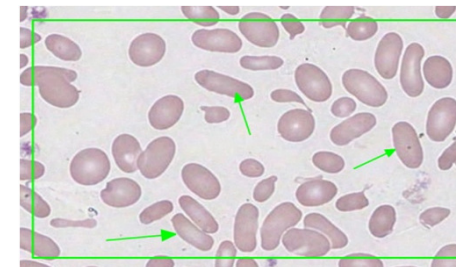
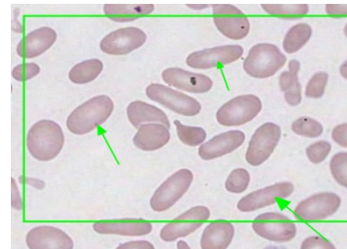
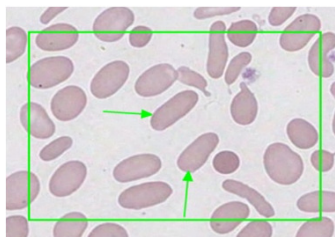
This patient was diagnosed with **acute myeloid leukemia (AML)**. AML is one of the most common types of adult leukemia and is more common in men than in women. The disease is due to an abnormal proliferation of myeloid stem cells within the bone marrow. The neoplastic cells slowly replace the normal cells in the bone marrow, leading to pancytopenia (decreased platelets, RBCs, and WBCs). The signs and symptoms of AML include easy bruising, bleeding from the nose and gums, petechiae, infection, fatigue, pallor, bone pain, shortness of breath, and weight loss.

The majority of patients with AML have circulating blast cells, easily seen on the peripheral blood smear. There may be a slight progression towards more mature myeloid cells, however the patient is typically neutropenic. Most patients have a normocytic, normochromic anemia. Based on clinical and laboratory findings, a bone marrow aspirate and biopsy are typically performed for further studies and cytogenetic analysis. In this patient, the circulating blast count is high enough to perform many of these studies; nonetheless, most physicians also prefer to obtain a bone marrow biopsy to assess the degree of marrow involvement.

The etiology of most cases of AML is unknown, however, it has been shown to be associated with exposure to radiation, certain chemotherapy agents, and certain chemicals, such as benzene. A genetic predisposition has also been identified. An individual with Down Syndrome has a 10- to 18-fold increase in risk for developing AML.

There are several subtypes of AML and treatment and prognosis varies depending on the subtype. Since AML is an acute process, death occurs within weeks to months if left untreated. With treatment, five-year survival varies from 15–70%, and relapse rate varies from 78–33%, depending on subtype. Initial treatment is with chemotherapy with the aim of inducing remission. Bone marrow and peripheral blood stem cell transplants have been used for individuals with AML who relapse or do not respond to chemotherapy.

Specimen 2	No.
Elliptocyte/Ovalocyte	293
Poikilocytosis	2
Howell-Jolly Bodies	1
S/C crystasis	1
Stomatocyte	1
Blast, undifferentiated	1
Lymphocyte, reactive (atypical, Downey, variant)	1
Abnormal RBC, would refer	1
Total Population:	305



\*To see the original full-sized images, please refer to the original CD or sign on to your data entry sheet at <http://www.aab-pts.org/>

Educational Challenge 1Q2011 Slide 1 - **Hereditary Elliptocytosis:** A 14-month-old boy is brought to the pediatric clinic when his mother becomes concerned about his skin "turning yellow". He and his family recently immigrated to the United States from Greece. His two older siblings are in good health. He appears ill with jaundiced skin. On physical examination, he is small for his age and found to have scleral icterus, splenomegaly, and tachycardia. CBC results: WBC 4.3, Hgb 7.3 g/dL, Hct 21.9%, RDW 18.1, Plts 624,000/ $\mu$ L. Identify the indicated cells.

The CBC values indicate this child is anemic with an elevated platelet count. Review of the peripheral smear confirms elevation of the platelet count. A few of the lymphocytes are relatively large and contain prominent granules in the cytoplasm. Most significant, however, are the abnormalities seen in the red blood cells. There is marked anisocytosis and poikilocytosis, with the presence of elliptocytes, schistocytes, bizarre forms, and occasional polychromasia and basophilic stippling. The cells to be identified are all **elliptocytes**.

Based on the peripheral blood smear and clinical presentation, it likely this child has the more severe form of **hereditary elliptocytosis (HE)**. This is an inherited autosomal dominant abnormality of spectrin, a protein in the red cell cytoskeleton. Members of the same family can be affected and yet show very different manifestations, if any. Red cell precursors begin as normal discoid RBCs, but progressively become more elliptical in shape as they age. Typically, to be classified as hereditary elliptocytosis, at least 25% of the red cells must be elliptocytes, although the number may be much higher. HE affects about 3 to 5 per 10,000 individuals in the United States and is more common in individuals of African and Mediterranean descent (this child is from Greece). The majority of patients with HE are completely asymptomatic and, due to a compensated hemolysis, have normal hemoglobin values and red cell indices. The diagnosis in these individuals is made incidentally when a routine blood smear is examined. However, about 5-10% of individuals with HE suffer from moderate to severe hemolysis, such as seen with this child. In children, the chronic anemia can lead to a failure-to-thrive and slow growth. A hemolytic episode may be triggered by infection, particularly a viral infection. Note that several of this child's lymphocytes were large with scalloped borders and large cytoplasmic granules, all of which may be seen in association with a viral infection. As the abnormal RBCs are destroyed in the spleen, levels of unconjugated bilirubin increase, leading to jaundice.

There is no cure for hereditary elliptocytosis and, fortunately, most individuals with HE need no treatment. Due to the low level of compensated hemolysis, they are at an increased risk for development of gallstones. Individuals with more severe hemolysis may require a splenectomy. This allows the RBCs to circulate longer and bypass destruction in the spleen. However, once a splenectomy has been performed, the individual is at increased risk for bacterial infections and must be closely monitored. Oftentimes, when hemolysis begins during infancy, it will decrease as the infant becomes older and a splenectomy may not be necessary.