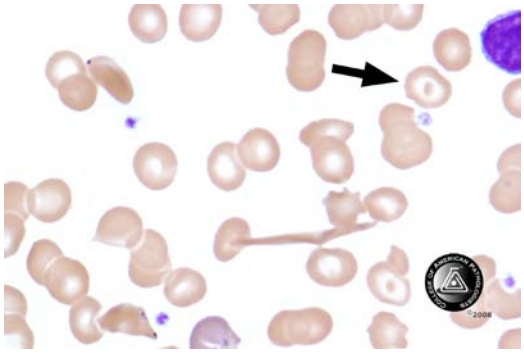
Blood Cell Identification – Graded

Case History

The patient is a 20-year-old female with sickle cell disease who presents with bilateral leg pain for 3 days. She is scheduled to have bilateral hip and leg surgery. Laboratory data include: WBC = 20.9 x 10^9/L; RBC = 2.67 x 10^{12}/L; HGB = 7.8 g/dL; HCT = 23.7%; MCV = 88.7 fL; MCHC = 33.0 g/dL; RDW = 18.5; and PLT = 394 x 10^9/L.

BCP-11

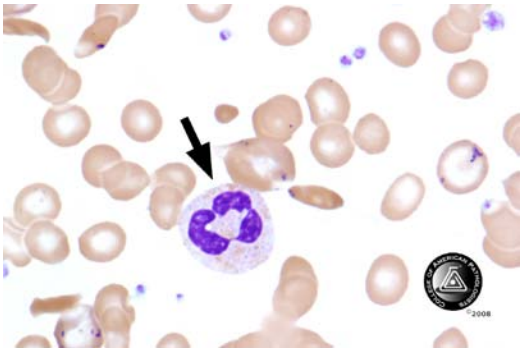


Identification	Referees No.	Referees %	BCP Participants No.	BCP Participants %	Evaluation
Target cell (codocyte)	33	100.0	5440	99.7	Good

The red blood cell identified by the arrow is a target cell (codocyte), as correctly identified by 100.0% of the referees and 99.7% of the participants. Target cell formation is due to a greater-than-normal surface membrane to volume ratio that results in a central hemoglobinized area within a surrounding area of pallor, which in turn is surrounded by a peripheral hemoglobinized zone. These features give target cells the appearance of a bull's-eye. Target cells are seen in conditions that result in increased surface membrane, such as liver disease and in conditions that result in decreased intracellular contents including thalassemia and some hemoglobinopathies. In this smear, target cells are accompanied by a sickle cell.

Blood Cell Identification – Graded

BCP-12

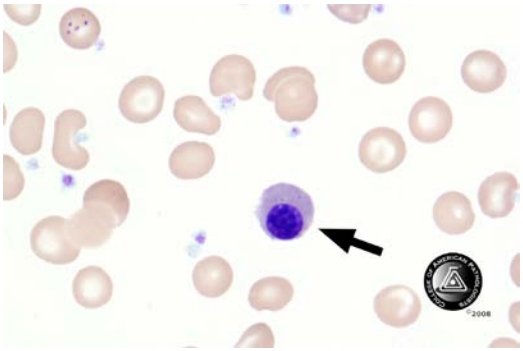


Identification	Referees No.	Referees %	BCP Participants No.	BCP Participants %	Performance Evaluation
Neutrophil, segmented or band	32	97.0	5318	97.5	Good
Neutrophil w/dysplastic nucleus and/or agranular cytoplasm	1	3.0	10	0.2	Unacceptable
Neutrophil, toxic (to include toxic granulation and/or Döhle bodies, and/or toxic vacuolization)	-	-	102	1.9	Unacceptable

The white blood cell identified by the arrow is a normal segmented neutrophil, as correctly identified by 97.0% of the referees and 97.5% of the participants. Neutrophils have a segmented nucleus with condensed nuclear chromatin. The nuclear segments are connected by thin filaments with no internal chromatin structure. The cytoplasm is pale pink with specific granules.

Blood Cell Identification – Graded

BCP-13

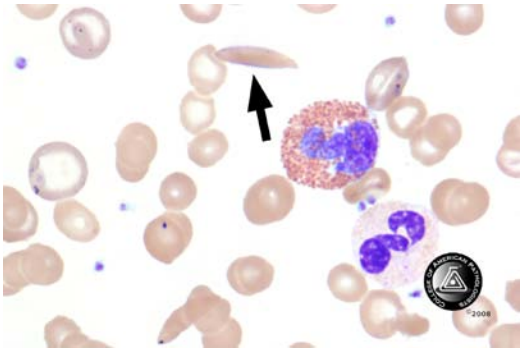


Identification	Referees No.	Referees %	BCP Participants No.	BCP Participants %	Performance Evaluation
Nucleated red cell, normal or abnormal morphology	33	100.0	5292	97.0	Good
Normoblast, any stage	-	-	145	2.7	Acceptable

The cell identified by the arrow is a nucleated red cell, as correctly identified by 100.0% of the referees and 97.0% of the participants. The nucleated red cell contains an eccentrically placed nucleus with condensed nuclear chromatin. The nucleus may be pyknotic.

Blood Cell Identification – Graded

BCP-14

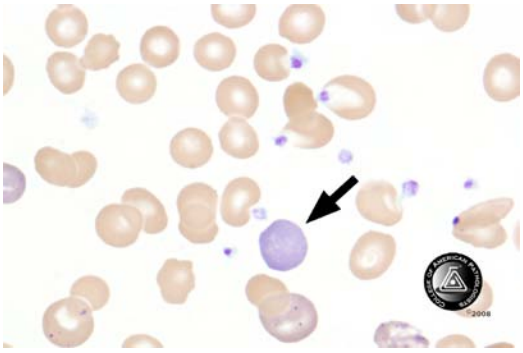


Identification	Referees No.	Referees %	BCP Participants No.	BCP Participants %	Performance Evaluation
Sickle cell (drepanocyte)	32	97.0	5340	97.9	Good
Fragmented red cell (schistocyte, helmet cell, keratocyte)	1	3.0	12	0.2	Unacceptable
Ovalocyte (elliptocyte)	-	-	89	1.6	Unacceptable

The red blood cell identified by the arrow is a sickle cell or drepanocyte, as correctly identified by 97.0% of the referees and 97.9% of the participants. Classic sickle cells are crescent shaped with two pointed ends. The cells lack central pallor. Sickle cells are due to deformity of the red blood cell membrane by polymerized deoxygenated hemoglobin S. Sickle cells can be seen in sickle cell anemia, hemoglobin SC disease, hemoglobin SD disease and S-beta-thalassemia.

Blood Cell Identification – Graded

BCP-15



Identification	Referees No.	Referees %	BCP Participants No.	BCP Participants %	Performance Evaluation
Polychromatophilic (non-nucleated) red cell	33	100.0	5382	98.7	Good

The cell identified by the arrow is a polychromatophilic red blood cell, as correctly identified by 100.0% of the referees and 98.7% of the participants. The polychromatophilic cell is non-nucleated and represents the final stage of red cell maturation after exiting the bone marrow. It is slightly larger than a mature erythrocyte and lacks central pallor. The cell contains hemoglobin and a small amount of RNA, which imparts the gray or pale purple color.

Discussion

This case illustrates an example of a patient with sickle cell anemia. Sickle cell anemia results from the homozygous state for the hemoglobin S (ß6Val) mutation. Sickle cell anemia is common in individuals of African descent. In the United States, sickle cell anemia occurs in approximately 1 in 500 African-American births.

Hemoglobin S has a single amino acid substitution, valine for glutamic acid, at position 6 of the beta chain (ß6Val). Hemoglobin S has decreased solubility in the deoxygenated state. Decreased solubility can lead to polymerization of hemoglobin S molecules, which distorts the membrane of the red blood cell. Distorted red blood cells or sickle cells have decreased membrane deformability impairing passage through small blood vessels. Sickle cells also have increased adhesion to the endothelial lining of blood vessels. The changes in red blood cell dynamics are responsible for the symptoms and morbidity associated with sickle cell anemia.

Sickle cell trait results from inheriting one copy of the sickle cell gene (ß6Val) and one normal beta chain gene and occurs in approximately 8% of African-Americans. Sickle cell trait is largely asymptomatic and sickle cells are not seen in the peripheral blood, except in rare instances. Sickle cell anemia results from inheriting two copies of the sickle cell gene. Homozygosity for hemoglobin S causes a serious anemia that often first manifests in childhood. Many of the complications from sickle cell anemia involve the decreased ability of sickled cells to navigate through small blood vessels. The spleen is subject to repeated bouts of sequestration of blood causing repeated splenic infarcts and autosplenectomy by adulthood. The spleen also has a decreased ability to phagocytize certain types of bacteria. Vaso-occlusive crises are painful episodes resulting from plugging of small blood vessels by sickled red blood cells. Vaso-occlusive crises cause abdominal or bone pain and may lead to bone infarcts with subsequent bacterial osteomyelitis. Sickle cell anemia patients are at increased risk of cerebrovascular accident (stroke). Patients with sickle cell anemia have decreased life expectancy due to infections and complications of vaso-occlusive crises. Homozygosity for hemoglobin S also causes a profound anemia with morphologic features that can be readily identified by examination of the peripheral blood smear.

The peripheral blood smear in patients with sickle cell anemia is striking due to the presence of abnormal crescent or boat shaped sickle cells. Other sickled forms including splinter shapes, holly leaf and envelope forms may be seen. The background red blood cells include target cells, polychromatophilic cells, apparently hypochromic cells and nucleated red blood cells. Howell Jolly bodies and Pappenheimer bodies may be seen due to asplenia. There may also be leukocytosis and thrombocytosis.

References:

1. Glassy EF. *Color Atlas of Hematology. An illustrated Field Guide Based on Proficiency Testing.* Northfield: College of American Pathologists, 1998.
2. Greer JP, Forester J, Lukens JN, Rodgers GM, Paraskevas F, Glader B. In 1263-1294 Wintrobe's Clinical Hematology. Philadelphia: Lippincott Williams and Wilkins, 2004.
3. Hoyer JD, Kroft SH. *Color Atlas of Hemoglobin Disorders. A Compendium Based on Proficiency Testing*. Northfield: College of American Pathologists, 2003.
4. Platt OS, Brambilla DJ, Rosse WF, et al. Mortality in sickle cell disease. Life expectancy and risk factors for early death. *N Engl J Med* 1994;330:1639-44.

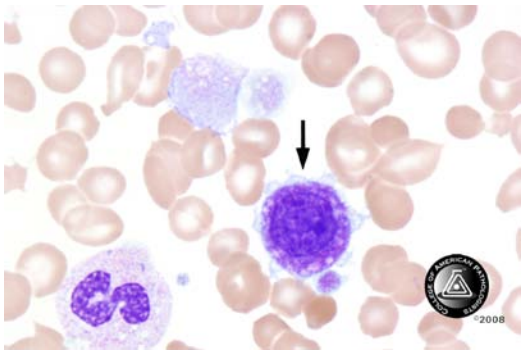
Joel F. Gradowski, MD
Hematology and Clinical Microscopy Resource Committee

Blood Cell Identification – Ungraded

Case History

This blood film is from a 64-year-old male with history of chronic idiopathic myelofibrosis and rising WBC. Laboratory data include: WBC = 96.2 x 10^9/L; RBC = 4.73 x 10^{12}/L; HGB = 13.8 g/dL; HCT = 48%; MCV = 100 fL; and PLT = 138 x 10^9/L.

BCP-16

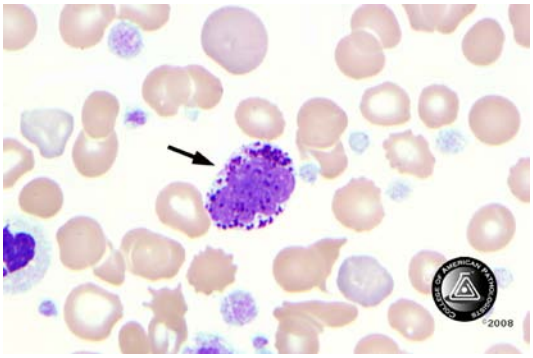


Identification	Referees No.	Referees %	BCP Participants No.	BCP Participants %	Evaluation
Megakaryocyte or precursor, abnormal	21	77.8	2945	55.4	Educational
Megakaryocyte or precursor, normal	3	11.1	964	18.1	Educational
Neutrophil, myelocyte	1	3.7	119	2.2	Educational
Nucleated red cell, normal or abnormal morphology	1	3.7	5	0.1	Educational
Megakaryocyte nucleus	1	3.7	343	6.5	Educational
Lymphoma cell (malignant), includes Hairy cell and Sezary cell	-	-	344	6.5	Educational
Platelet, giant	-	-	160	3.0	Educational

The cell identified by the arrow is an abnormal megakaryocyte as correctly identified by 77.8% of referees and 55.4% of participants. This cell may also be referred to as a micromegakaryocyte or dwarf megakaryocyte. It can be recognized as a megakaryocyte by its characteristic fine purple-red cytoplasmic granules that transition to a shaggy peripheral rim of pale blue-grey cytoplasm. The cytoplasm is similar to the appearance of a normal platelet, an example of which is immediately below the arrowed cell. In contrast to a normal megakaryocyte, which is a very large cell (25 to 50 μm in diameter, or about 2 to 5 times the size of a mature neutrophil) with abundant cytoplasm and numerous nuclear lobes, the abnormal megakaryocyte in the image is small, has an N:C ratio of approximately 1:1, and has a single round nucleus. The presence of several giant and hypogranular platelets in the background is another clue to the origin of the arrowed cell. Megakaryocytes (normal or abnormal), megakaryocyte nuclei, and megakaryocyte nuclear fragments may suggest a bone marrow process such as a myeloproliferative neoplasm, or possible recent cardiac surgery/ cardiopulmonary bypass.

Blood Cell Identification – Ungraded

BCP-17

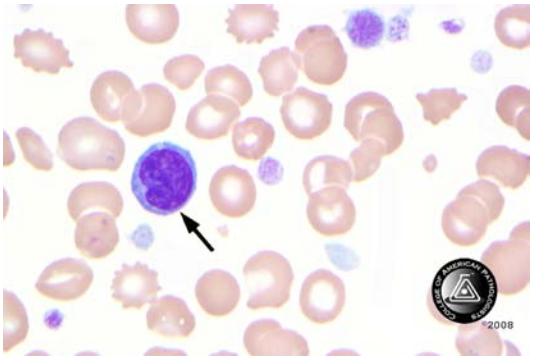


Identification	Referees No.	Referees %	BCP Participants No.	BCP Participants %	Performance Evaluation
Basophil, any stage	26	100.0	5291	99.2	Educational

The cell indicated by the arrow is a basophil as correctly identified by 100.0% of referees and 99.2% of participants. Basophils are characterized by large coarse cytoplasmic granules that are typically blue-black, but occasionally may be purple to red. The granules vary in size, are roughly spherical, and frequently overlay or even obscure the nucleus. The nucleus is lobated. The maturation sequence of basophils is similar to that of neutrophils, with the characteristic granules becoming evident at the basophilic myelocyte stage of maturation. In the background numerous abnormal platelets are shown as well as red cell abnormalities.

Blood Cell Identification – Ungraded

BCP-18

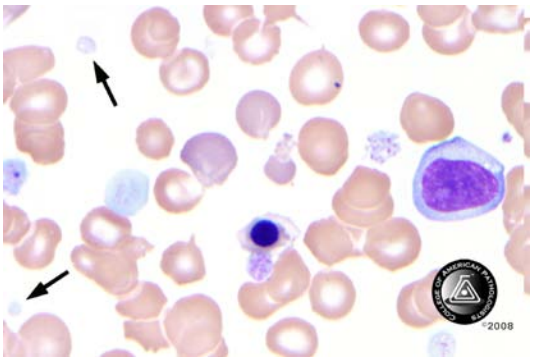


Identification	Referees No.	Referees %	BCP Participants No.	BCP Participants %	Performance Evaluation
Lymphocyte	25	96.1	4377	82.1	Educational
Monocyte, immature (promonocyte, monoblast)	1	3.9	47	0.9	Educational
Lymphocyte, reactive (to include plasmacytoid and immunoblastic forms)	-	-	444	8.3	Educational
Monocyte	-	-	132	2.5	Educational
Lymphoma cell (malignant), includes Hairy cell and Sezary cell	-	-	139	2.6	Educational

The cell identified by the arrow is a normal lymphocyte as correctly identified by 96.1% of referees and 82.1% of participants. Lymphocytes are small, round to ovoid cells with scant pale blue to moderately basophilic, agranular cytoplasm. The arrowed cell has a slightly increased amount of cytoplasm, but the N:C ratio is within the 5:1 to 2:1 range seen in normal lymphocytes. The nucleus is round to oval and, as seen in this image, may be slightly indented or notched. The nuclear chromatin is diffusely dense and clumped.

Blood Cell Identification – Ungraded

BCP-19

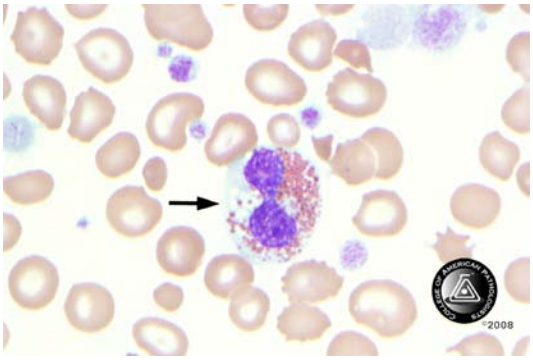


Identification	Referees No.	Referees %	BCP Participants No.	BCP Participants %	Performance Evaluation
Platelet, hypogranular	26	96.3	3641	68.3	Educational
Platelet, normal	1	3.7	1636	30.7	Educational

The objects identified by the arrows are hypogranular platelets, as correctly identified by 96.3% of referees and 68.3% of participants. They are the same size as normal platelets (1.5 to 3 μm in diameter), but lack the fine purple-red granules typical of normal platelets. They can be identified as platelets by their cytoplasmic zoning, which refers to the alternating lighter and darker areas within the blue-gray cytoplasm. Hypogranular and other dysplastic platelet forms are often seen in myeloproliferative and myelodysplastic disorders. A large hypogranular platelet is also present in this image. In addition to the abnormal platelets, the red cells are abnormal as evidenced by the nucleated red cell in the center of the field, several polychromatophilic red cells, and anisocytosis.

Blood Cell Identification – Ungraded

BCP-20



Identification	Referees No.	Referees %	BCP Participants No.	BCP Participants %	Performance Evaluation
Eosinophil, any stage	27	100.0	5307	99.5	Educational

The cell indicated by the arrow is an eosinophil as correctly identified by 100.0% of referees and 99.5% of participants. The cell displays the typical coarse, orange-red cytoplasmic granules characteristic of eosinophils, with some degranulation present on the left side. The nucleus has two lobes of equal size with dense, compact chromatin. In this example, the filament connecting the two lobes is slightly thicker than usual suggesting that the cell may not be fully mature. Eosinophils exhibit the same nuclear characteristics and the same stages of development as neutrophils. In the background of this image, numerous abnormal platelets are evident including some hypogranular forms. The red cells show marked anisocytosis and poikilocytosis.

Kyle T. Bradley, MD
Hematology and Clinical Microscopy Resource Committee