**Answers of part 1 slides “blood cell Identification”:**

**HS#1: (microcyte with central pallor)**
The cell indicated by the arrow is microcyte with central pallor. The cell is smaller than a normal red cell, measuring <6.5 μm in diameter and less than 80fL in volume. It has an increased amount of central pallor (more than one third the cell diameter). The combination of small size (microcytosis) and apparently decreased amount of hemoglobin (hypochromia) indicate a disorder of hemoglobin synthesis. Other types of small red cells such as fragmented cells and spherocytes are small but lack any pallor. Note in this case that not all cells are microcytes; there is a dimorphic appearance, with a microcytic population existing side by side with normal cells.

**HS#2 : (ovalocyte)**
The cell indicated by the arrow is an ovalocyte. Ovalocytes are elongated along one axis, ends are blunt, and for some distance along the long axis, the sides of the cell are parallel. A small number of ovalocytes may be developmental abnormality is present.

**HS#3 : (normal platelet)**
The arrow is pointing at a normal platelet. It is a typical example of a normal platelet, a 2-3 μm in diameter fragment of blue-gray megakaryocyte cytoplasm containing fine purple-red granules.

**HS#4 : (target cell)**
The cell indicated by the arrow is target cell. Target cells are thin red cells with a greater than normal surface membrane to hemoglobin volume content ratio. They are characterized by the central hemoglobinized area within a surrounding area of pallor, which in turn is surrounded by a peripheral hemoglobinized zone. They are most commonly observed in patients with hemoglobinopathies or liver disease, but are also observed in conditions with decreased synthesis of normal hemoglobin.

**HS#5: (microcyte with central pallor)**
The cell indicated by the arrow is microcyte with central pallor. The central arrowed cell is quite small and may be reason some of you chose Fragmented Cells. It should be noted, however, that fragmented cell usually any lack of central pallor and that the second, more peripheral arrowed cell is clearly not a fragmented cell.
**Case # 1 (Discussion)**

The child in this case has X-linked hereditary sideroblastic anemia. Additional studies in this patient that assisted in the diagnosis included: a reticulocyte count of 1.5%; a transferrin saturation of 95%; a serum ferritin of 222 ng/mL (normal 6-60 ng/mL); a free erythrocyte protoporphyrin of 15 μg/dL (normal <70 μg/dL); a bone marrow aspirate which demonstrated erythroid hyperplasia with ringed sideroblasts present on the iron stain; and a review of his mother’s blood smear that demonstrated a population of microcytic cells. The findings of a low to normal reticulocyte count, increased serum transferrin saturation and ferritin, low protoporphyrin levels and ringed sideroblasts in the bone marrow are constant features of hereditary sideroblastic anemias. A characteristic dimorphic red blood cell distribution is evident on a hematology analyzer generated RBC count vs. RBC size plots.

X-linked hereditary sideroblastic anemia is usually a result of decreased production of 5-aminolevulinate (ALA) due to defective ALA synthetase. ALA synthesis is the first unique step in heme synthesis. The erythroid ALA synthetase gene is on the X chromosome and studies of families with X-linked hereditary sideroblastic anemia have in most cases demonstrated heterogeneous point mutations in the catalytic domain of the enzyme. Precise correlation between the location of the mutations and severity of anemia or responsiveness of the anemia to pyridoxine (a cofactor of ALA synthetase) have not been made.

Approximately one third of patients with hereditary sideroblastic anemia will respond to large doses of pyridoxine (vitamin B6). Among those that respond to pyridoxine, the quality of response is variable. An optimal response is characterized by reticulocytosis and normalization of hemoglobin within months. Free erythrocyte protoporphyrin levels increase but morphologic abnormalities do not disappear. Patients that fail to respond can be managed with transfusion. Total body iron status must be carefully monitored and managed with phlebotomies in pyridoxine response cases and use of iron chelating agents in those that are transfusion dependent. Treatment of anemia allows normal growth and development. Splenectomy in hereditary sideroblastic anemia appears to invariably be complicated by thromboembolic complications. In contrast to idiopathic acquired sideroblastic anemia, evolution to leukemia has not been observed in heritable forms.

**References**


Updated on August 28, 2013 Los Angeles
Answers of part 2 slides “blood cell Identification”:

**HS#6: (Sezary cells or Lymphoma cells)**
The cell indicated by the arrow represents **Sezary cells or Lymphoma cells**. Note the slightly larger nuclear size and prominent nuclear convolutions, resulting in a cerebriform appearance.

**HS#7: (Sezary cells or Lymphoma cells)**
The cell indicated by the arrow represents **Sezary cells or Lymphoma cells**.

**HS#8: (Monocyte)**
The arrow is pointing at a **Monocyte**.

**HS#9: (Normal Platelet)**
The cell indicated by the arrow is **Normal Platelet**.

**HS#10: (Reactive Lymphocyte)**
The cell indicated by the arrow is a **Reactive Lymphocyte**. Contrast this cell to the two malignant cells in HS#6 and HS#7, which demonstrate prominent abnormal nuclear convolutions.

**Case # 2 (Discussion)**

The Sezary Syndrome (SS) was described in 1938 by Sezary and Bouvrain as a "generalized exfoliative erythroderma with intense pruritis and a cutaneous infiltrate" composed of atypical mononuclear cells, which also involved peripheral blood and lymph nodes, but not the bone marrow.

Mycosis fungoides (MF) is a related disorder, that typically presents with "cutaneous patches and plaques that may progress to erythrodermic or nodular stages". The skin changes are caused by abnormal lymphoid cells that infiltrate the dermis and epidermis. There is considerable clinical overlap between the two diseases, and both are caused by a malignant lymphoid proliferation, typically with a helper T-cell phenotype (CD4+).

The diagnosis of SS/MF can be difficult, especially in the setting of idiopathic erythroderma. In one study 28 patients with idiopathic erythroderma were followed with a median follow-up of 33 months: 35% of these patients went into complete remission, and 52% showed partial remission. Only three patients had persistent chronic erythroderma, and of these three, one developed SS and one
developed MF. No evidence of T-cell lymphoma was found in any of the patients with complete or partial remission.

However, in patients with proven circulating clonal T-cell proliferations (detected by T-cell receptor beta gene rearrangement on Southern blot analysis of peripheral blood mononuclear cells) biopsies of erythrodermic skin often show a non-specific histologic appearance such as chronic dermatitis (33% of skin biopsies or 11/41 patients). Therefore, when SS is strongly suspected, skin biopsies of erythrodermic skin should be taken, but a negative result should not dissuade the physician from further studies, such as peripheral blood analysis, biopsy of abnormal lymphadenopathy, or scans of chest, abdomen, and pelvis, looking for hepatosplenomegaly or adenopathy.

Peripheral blood analysis includes examination of a Wright-Giemsa stained smear, in which Sezary cells have a characteristic cerebriform nucleus. These cells are typically slightly larger than normal lymphocytes, and have sparse to moderate amounts of cytoplasm. Occasionally, larger cells can be found with similar morphology, or with more vesicular nuclei. FACS (flow activated cellsorter) analysis of peripheral blood lymphocytes with a variety of lymphoid antibodies typically shows an elevated CD4/CD8 ratio, with an expanded population of CD4 + CD7- cells in many patients with SS (25% of cases will be CD4+CD7+).

The prognosis of SS has not been as well studied as other lymphomas, but in general, patients who are older (> 60 years) with higher stage disease, or evidence of large cell transformation (defined as > 25% large cells) do the worst. Therapy options are diverse, usually including a combination of systemic and topical treatment

References
Answers of part 3 slides “blood cell Identification”:

**HS#11: (Neutrophil with Pelger-Huet nucleus)**

The arrowed cell is several times the diameter of a red cell and has a low nuclear to cytoplasmic ratio. The segmented nucleus and the pale pink/orange granulation identify it as a granulocyte. However, in contrast to the usual segmented neutrophil which has 3-5 nuclear lobes that tend to be elongate and irregular in shape, the two nuclear lobes in this cell are strikingly round. They are closely approximated and are connected by a thin, short filament. In addition, the chromatin is slightly more condensed than a typical mature neutrophil. These features allow its identification as a Pelger-Huet neutrophil.

**HS# 12: (Erythrocyte, normal)**

The arrowed cell in this photomicrograph is an anucleate cell with a bright red color, indicating that it is an erythrocyte. It is the same size as other red cells in the field, is round in contour, and has an area of central pallor which occupies about one third of the diameter of the cell. These features are those of a normal erythrocyte. Because of the lack of a nucleus, this cell should be easily distinguished from a nucleated red blood cell.

Also present in the field is a granulocyte. This cell has a single nuclear lobe shaped like a peanut. While this cell resembles a metamyelocyte, the nucleus is smaller and has more clumped chromatin than in a normal metamyelocyte, and is bilaterally rather than unilaterally indented. This in fact represents a mature Pelger-Huet neutrophil. In contrast to the previous example (see HS#16, above), the nucleus has failed to segment completely.

**HS#13: (Platelet, normal)**

The arrowed objects in this slide are anucleate, round cells which are about one fourth the diameter of a red blood cell. They appear purple due to the presence of closely packed azurophilic granules occupying the majority of the cytoplasm. These findings are typical of normal platelets.

Also present in the slide is another variety of Pelger-Huet cell. This mononuclear variant has a lopsided, slightly indented nucleus. Again, the relatively small size of the nucleus and degree of chromatin clumping help to distinguish it from a normal metamyelocyte.
**HS#14: (Stain precipitate)**

The arrowed material on the slide represents a loose, irregular, extracellular aggregation of dark blue particles. While this aggregate is superimposed on the red cells, there is no suggestion of specific cellular association or localization, and it has no apparent limiting membrane. Smaller amounts of this material are also scattered throughout the field. These findings are typical of **stain precipitate**, which may arise as a result of a variety of technical factors.

**HS#15: (Monocyte)**

The arrowed cell is a large cell with a single irregular nucleus with somewhat condensed chromatin and several small, indistinct nuclei. The cytoplasm is moderately abundant and has a pink-gray appearance with vacuolization and indistinct, evenly distributed azurophilic granulation. These findings are consistent with its identification as a **monocyte**. Also present is a granulocyte with pale pink-orange granulation and a single oval, unsegmented nucleus. This represents another mononuclear variety of a Pelqer-Huet cell, this time lacking in even nuclear indentation. It is distinguished from a myelocyte by the smaller size of the nucleus and the highly condensed chromatin.

**Case # 3 (Discussion)**

This case is an illustration of the true Pelqer-Huet anomaly, a dominantly inherited neutrophil disorder that results in abnormal nuclear segmentation. The neutrophils are functionally normal, and the condition is completely benign. The incidence has ranged from 1/1000 to 1/10000 in various studies.

The hallmark of the Pelqer-Huet anomaly is the abnormal nuclear segmentation present in the large majority of the cells. In normal blood smears, the majority of neutrophils have three or more lobes, whereas only a minority (up to 27%) have two lobes. In the heterozygous form of the Pelqer-Huet abnormality, few cells (<10%) have three lobes, and virtually none have more than three.

Furthermore, the neutrophils that are segmented in this condition have regular, round nuclear lobes, rather than the often elongate, irregular lobes of normal neutrophils, and have abnormally condensed chromatin. In the very rare homozygous state, 100% of the neutrophils have round or oval nuclei without any segmentation.
The classic Pelger-Huet cell seen in the heterozygous state is the "pince-nez" cell exemplified in photomicrograph HS-11. The two round lobes are connected by a short filament, producing a resemblance to spectacles. The spectrum of forms that may be seen is further illustrated in photomicrographs HS-12, HS-13, and HS-15. Mononuclear forms may have rod-like, dumbbell or peanut-shaped, lopsided, or round nuclei. All have in common hypercondensed chromatin.

Similar or identical nuclear abnormalities may be seen in a variety of acquired disorders, in which case they are referred to as pseudo-Pelger-Huet or Pelgeroid cells. Most important in the differential diagnosis are myelodysplastic syndromes and related disorders. Other settings in which Pelgeroid cells may be seen include sulfonamide administration, *Mycoplasma* infections, and AIDS. Important distinguishing features are that in the true Pelger-Huet anomaly, essentially all of the neutrophils in the blood are abnormal, whereas only a subset show these changes in most other settings. In addition, in myelodysplastic states, other dysplastic features may be present in the neutrophils (hypogranulation) or other cell lines, and cytopenias will be present.

References
Answers of part 4 slides “blood cell Identification”:

**HS# 16: (Neutrophil Necrobiosis)**

The arrowed cell is a **necrobiotic neutrophil**. Degenerating neutrophils are most easily identified by their granular cytoplasm. The nucleus has become pyknotic and very dense. The chromatin strand that once separated the nuclear lobes is no longer visible. This cell is most commonly confused with a nucleated red cell. A circulating red cell of the orthochromatophilic type would have homogeneous agranular pink-orange cytoplasm and a single, often eccentric nucleus. The presence of cytoplasmic granularity is the best clue that this cell is a neutrophil and so careful inspection of the cytoplasm is necessary to not misclassify a necrobiotic neutrophil as a nucleated red cell. This cell is still recognizable as a neutrophil and so should not be termed a basket or smear cell.

**HS#17: (Target Cell)**

The arrowed cell is a **target cell**. Target cells have increased surface membrane relative to their cellular contents resulting in central hemoglobin concentration and their characteristic appearance. Target cells may be seen in many disease states including inherited hemoglobinopathies. Between the two target cells is an elongated cell with blunt ends, lack of central pallor and condensed hemoglobin which is rod-like in shape, most consistent with a hemoglobin C crystal.

**HS# 18: (Hemoglobin C Crystal)**

The arrowed cell demonstrates a **Hemoglobin C crystal**. Hemoglobin C crystals have a variable appearance. The classic form is that of the "Washington monument" as is seen here. Typically, the crystal distorts the cell shape and causes the rest of the cell to appear colorless. This finding is typically seen in homozygous C disease, although it may rarely be present with C trait and SC disease.

**HS# 19: (Epithelial/Endothelial Cell)**

The arrowed cell is an **epithelial cell**. Epithelial cells are present on blood films as a result of contamination from the skin during phlebotomy. Epithelial cells are extremely large when compared to hematologic cells. They are often polyhedral shaped with a low nuclear
to cytoplasmic ratio. The nucleus is often dense and pyknotic without atypia. The cytoplasm is lightly basophilic and often contains kerato-hyaline granules. The more pyknotic the nucleus and lower the nuclear to cytoplasmic ratio, more likely the cell originated from the superficial skin layer. At times, these granules can be so numerous and plentiful to resemble stain precipitate. Appreciation that the granules are localized with the pale blue cytoplasm of a large cell is helpful in recognizing that they are kerato-hyaline granules contained within an epithelial cell and not stain precipitate.

**HS# 20 : ( Monocyte):**

The arrowed cell is a *monocyte*. It has an indented and lobulated nucleus with mildly clumped chromatin and no nucleolus. The cytoplasm is abundant, gray-pink, and contains several small vacuoles and fine pink azurophilic granules.

**Case # 4 ( Discussion)**

This case illustrates the red cell abnormalities typically found in individuals homozygous for hemoglobin C. Hemoglobin C is a qualitative hemoglobinopathy resulting from a point mutation substituting lysine for the glutamic acid normally present at position 6 on the beta hemoglobin chain. This is the same position that is affected by hemoglobin S, but with a different amino acid substitution. Heterozygotes for hemoglobin C are designated as AC and are said to have hemoglobin C trait. Heterozygotes for hemoglobin C are designated as CC and are said to have hemoglobin C disease. In the United States, 2% of African-Americans are heterozygous for hemoglobin C and 0.02% are homozygous for hemoglobin C. Hemoglobin C is also found in individuals of Mediterranean descent.

Hemoglobin electrophoretic evaluation in individuals with Hemoglobin C trait will have 30-40% hemoglobin C, 50-60% hemoglobin A, and a small amount of hemoglobin A2. Hemoglobin F will not be increased. They will generally be asymptomatic. A mild anemia may be present and review of a blood smear will demonstrate moderate numbers of target cells. Hemoglobin C crystals are not present in individuals with hemoglobin C trait.

Homozygotes for hemoglobin C will have almost all of their hemoglobin as hemoglobin C on electrophoresis. A small amount of hemoglobin A2 and hemoglobin F may be present. Hemoglobin A will be absent. They will demonstrate a mild to moderate hemolytic anemia with a mild
reticulocytosis. Review of a blood smear will show a marked increase in target cells, dense spherocytes, and hemoglobin C crystals.

Hemoglobin C crystals most characteristically appear as a "Washington monument" (octahedral) shape. When the classic form is present, the remainder of the red cell is often palelcolorless with empty cytoplasm. The dense spherocytes present on the blood smears most likely also contain crystallized hemoglobin C. The crystals may be difficult to find in patients with functional spleens. In splenectomized patients, up to 10% of the red cells may contain hemoglobin C crystals. In the laboratory, crystallization can be encouraged by exposure to hyperosmolar solutions such as sodium chloride. Physical examination will reveal splenomegaly as a result of the chronic extravascular hemolysis present in these individuals. The primary mechanism responsible for the erythrosenesence in these patients is an overzealous potassium efflux pump which rids the red cell of surplus water, dessicatinq the cells and encouraging hemoglobin C crystallization. It is these shrunken, pyknotic spherocytes that are trapped in the splenic cords and removed from the circulation resulting in an extravascular hemolytic anemia.

Unlike patients with sickle cell disease, these patients do not undergo autosplenectomy with time. This is due to the fact that hemoglobin C crystals are composed of oxyhemoglobin which "melt" or become less pronounced in low oxygen environments. Despite the anemia and mild splenomegaly, individuals homozygous for Hb C are relatively symptom free and have normal growth and development without increased infectious complications. As with any chronic hemolytic process, they are at increased risk of cholelithiasis. The presence of splenomegaly places them at an increased risk of splenic rupture.

References
Answers of part 5 slides “blood cell Identification

**HS #21 : (Neutrophil, segmented or band)**

The arrowed cell is a **segmented neutrophil**. The nucleus is divided into three discrete lobes by a thin filament of nuclear material. The cytoplasm is pale pink and contains fine lilac (secondary or specific) granules. The presence of a clearly segmented nucleus distinguishes the cell from other leukocytes and the fine pink granules from other granulocytes (eosinophils and basophils). There are multiple red cell fragments and occasional spherocytes in the background. The platelets are markedly decreased in number.

**HS #22 : (Spherocyte)**

The arrowed cell is a **spherocyte**. A spherocyte appears microcytic, with absent central pallor and may appear hyperchromic. Although most spherocytes look smaller and completely spherical compared to normal red cells on blood films, scanning electron microscopy studies have demonstrated them to have a normal MCV and actually be cup shaped. The spherocyte has lost part of its membrane resulting in a decreased ratio of cell surface area to volume. As a result, the normal biconcaved disc form is not favored and a smaller, spherical cell is formed. This new shape is rigid and is more readily removed from the circulation by the spleen. Spherocytes are seen in cases of hereditary spherocytosis, Coombs' positive hemolytic anemias and in much fewer numbers in cases of microangiopathic hemolytic anemias.

**HS #23 : (Fragmented cell)**

The arrowed cell is a **fragmented red cell**. Five percent of participants identified the arrowed cells as acanthocytes. Red cell fragments include triangulocytes, helmet cells and horn cells. The fragments may be composed of various sizes and shapes. The keratocyte (horn cell) may maintain an area of central pallor, but the smaller fragments lack central pallor. It is important to differentiate them from red cell abnormalities such as spherocytes, bite cells, acanthocytes and sickle cells that are associated with a different differential diagnosis. While there are "points" present on the arrowed cell on the left, they do not reflect true projections of the red cell membrane emerging from a round center. Rather, this cell is a fragment that is triangular in shape. Red cell fragments are most commonly associated with traumatic intravascular hemolysis, microangiopathic hemolytic anemias, and severe burns.
**HS #24 : (Basophil, any stage)**

The arrowed cell is a **basophil**. Basophils are most easily identified by the presence of small to moderate sized densely stained cytoplasmic granules. The granules range in color from red purple to dark purple are usually slightly larger than those found in neutrophils and about the same size as the cytoplasmic granules found in eosinophils. The nucleus is segmented but is often obscured by granules. The other cell in the field is an eosinophil. It has a classic bilobed nucleus. Eosinophilic granules rarely overlie the nucleus.

**HS #25 : (NRBC, blood)**

The arrowed cell is a **nucleated red cell**. The cell has a dense round nucleus and pink cytoplasm without granulation. This nucleated red cell corresponds to the orthochromatophilic stage of red cell maturation.

**Case # 5 (Discussion)**

Red cell fragmentation can be seen in a variety of pathologic processes. The laboratory triad of red cell fragments, anemia, and thrombocytopenia is consistent with a microangiopathic hemolytic process. In this patient, the underlying process responsible for the production of the red cell fragments is disseminated intravascular coagulation (DIC) secondary to the patient’s wide spread metastatic carcinoma (carcinomatosis).

DIC is a thrombohemorrhagic process that occurs in many clinical scenarios. The triggers are varied and most commonly include exposure or release of tissue factor into the circulation followed by widespread endothelial cell damage, immune complex deposition and proteolytic enzyme release. The "thrombotic" part of this disorder is the result of activation of the coagulation cascade (intrinsic and extrinsic) with formation of multiple, small fibrin or platelet thrombi throughout the circulatory system. This uncontrolled consumption of fibrin and other procoagulants coupled with the elaboration of plasmin ironically results in a hemorrhagic stage. Platelets and red cells are entrapped in the fibrin meshwork. This results in anemia, thrombocytopenia and red cell fragmentation (schistocytes). The thrombocytopenia also contributes to the "hemorrhagic" complications seen in this disorder.
As the red cells traverse the small vessel lumina that have been narrowed by the deposition of fibrin several things happen. The red cells can be entrapped in the fibrin mesh network, contributing to the anemia. Fragmented red cells are formed as some of the erythrocytes traverse the fibrin meshwork and are damaged. The abnormal red cell shapes that are formed occur in several ways. If the red cell crossing the fibrin breaks in two, the larger piece often forms a helmet cell and the small piece(s) form triangulocytes and microspherocytes. If the red cell experiences membrane damage but remains intact, keratocytes (horn cells) can be formed. A portion of the membrane seals on itself producing a clear area lacking hemoglobin (a blister cell). The blister cell (prekeratocyte) can rupture at the point of the fused membrane, forming a horn cell (keratocyte).

In addition to activation of the coagulation cascade, the fibrinolytic pathway is simultaneously activated with plasminogen being converted to plasmin to break down the fibrin clots. This activation of the fibrinolytic system contributes to the hemorrhagic complications seen with DIC. Degradation of cross-linked fibrin results in increased D-dimer production. All of this results in a constellation of clinical and laboratory findings seen in the group of disorders termed microangiopathic hemolytic anemia. Entities in this group share the cliiopathologic features of a hemolytic anemia coupled with thrombocytopenia and red cell fragments seen on the blood smear.

Some of the more common clinical scenarios associated with ole are sepsis, trauma/massive tissue necrosis, pregnancy/post partum, carcinomatosis and hemolytic transfusion reactions. The microthrombi in the brain, heart, lungs, kidney, spleen and liver result in a variety of clinical signs resulting from microinfections located in the affected organ. The consumption of coagulation factors is associated with a variety of clinical signs associated with a bleeding diathesis including petechial hemorrhages, ecchymoses, intracranial bleeding and oozing from surgical and IV sites.

Laboratory testing for DIC demonstrates a prolonged PT and aPTT, thrombocytopenia, decreased fibrinogen and increased fibrin split products such as D-dimers. Haptoglobin will be decreased and LDH increased. Review of the blood smear is necessary to demonstrate the presence of schistocytes. Treatment of DIC rests primarily in controlling/removing the underlying cause. This may not always be possible and the treatment is thus predicated on controlling the prevailing clinical symptom. When bleeding predominates, the use of fresh frozen plasma and anti-thrombin III concentrates as well as
platelet transfusion may be considered. Platelet transfusion is performed realizing that any increase in platelet count will be short lived, as they will continue to be removed from the circulation and that the use of fresh frozen plasma may help "fuel the fire" as it provides a source of clotting factors. The use of heparin in treating DIC is controversial.

References:

HS #26 :(Myelocyte)

The arrowed cell is a neutrophil myelocyte. In this example, the nucleus is eccentrically located. The nuclear chromatin is moderately clumped and there is no discernable nucleolus. The nucleus is not indented. The abundant cytoplasm contains both primary (azure) granules and secondary granules. Although it is sometimes difficult to discern the presence of secondary granules in early myelocytes, the nuclear features and nuclear/cytoplasmic ratio should also be considered in classifying these early granulocyte precursors. This myelocyte also contains a cytoplasmic vacuole that probably represents toxic vacuolization in this patient with bacterial sepsis.

HS # 27 :(Hypersegmented neutrophil)

The cell is a hypersegmented neutrophil. To be defined as a truly hypersegmented neutrophil, there should be at least six discrete nuclear lobes. This neutrophil appears to have seven nuclear lobes. Although characteristic of megaloblastic anemia, hypersegmented neutrophils may be seen in blood smears from septic patients in association with toxic neutrophil changes.
**HS #28 : (Echinocyte)**

The arrowed erythrocyte is an echinocyte. There are several other echinocytes in the same field. Echinocytes are a type of spiculated red cell that are characterized by preservation of central pallor and the presence of numerous, short, evenly spaced surface projections. The number of surface spicules can be quite variable, and should not be used as the sole criteria for identifying echinocytes. Echinocytes are most likely to be confused with acanthocytes. The most reliable distinguishing feature is that acanthocytes lack central pallor, while echinocytes retain central pallor. There are also several extra-cellular bacteria in the field, some of which are overlying a monocyte.

**HS #29 : (Lukocyte with phogocytized bacteria)**

The arrowed cell is a leukocyte (neutrophil) containing bacteria. In this example, it is difficult to discern discrete vacuoles surrounding the engulfed bacteria. However, it is still possible to conclude that the bacteria are intra-cellular because they are entirely contained within the limits of the neutrophil cytoplasm. In addition, some of the bacteria are paler-staining, which suggests degradation.

**HS #30 : (Bacteria, extracellular)**

The arrowed objects are extra-cellular bacteria. The organisms are small and uniformly rod shaped. Fungal organisms are generally larger than bacteria. A common problem is distinguishing bacterial organisms from stain precipitate. The presence of a uniform size and shape among microorganisms helps to distinguish them from the more amorphous stain precipitate.

**Case # 6 (Discussion)**

This case represents bacterial sepsis due to urinary tract infection involving the kidney(s), also known as pyelonephritis. The history of paralysis and neurogenic bladder implies that this patient probably had an indwelling urinary catheter, a situation that predisposes to infection of the bladder. Bacterial infection of the bladder can spread retrograde up the ureters to involve the kidneys. The infection may disseminate through the blood stream, as happened in this patient.
The patient's blood smear demonstrates many of the features that are characteristic of disseminated bacterial infection. There is a marked leukocytosis of greater than $50 \times 10^9$/L. The presence of myelocytes indicates that there is a left shift. A hypersegmented neutrophil is also demonstrated. Hypersegmented neutrophils may be seen in septic conditions, and do not necessarily indicate folate or Vitamin B12 deficiency. Toxic granulation is characterized by the presence of large purple or blue granules in the cytoplasm of more mature granulocyte forms. The so-called "toxic" granules probably represent persistent primary granules beyond the myelocyte stage. Toxic granulation is not well-demonstrated in the few granulocytes selected for this exercise. Some of the granulocytes do, however, contain cytoplasmic vacuoles. The vacuoles are round clear spaces in the cytoplasm that represent the sites of digestion of phagocytosed material. The presence of vacuoles may be clinically important, because they occur frequently in cases of sepsis. Vacuolization of leukocytes may also occur as an artifact of EDTA, and therefore, it is important to correlate the presence of cytoplasmic vacuoles with the presence of other toxic changes.

Another type of toxic change is the presence of Dahle bodies. Dahle bodies are pale, blue-gray inclusions of variable size and shape in the cytoplasm of neutrophils. They represent parallel strands of rough endoplasmic reticulum (RER). Dahle bodies may also have been present in the patient's blood smear. It is important to note the presence of toxic changes, such as toxic granulation, vacuolization, and Dahle bodies in the morphology comments of the leukocyte differential count, because these findings have clinical significance in the diagnosis of microbial infection.

The patient's anemia is not explained by the bacterial sepsis, and we can draw no conclusions about the etiology of the anemia. The presence of echinocytes may be due to metabolic imbalances due to the overwhelming infection, or possibly, renal failure.

References