Approach to the child with anemia

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INTRODUCTION — The approach to anemia in the pediatric patient is reviewed here. Included are pertinent issues related to the history and physical examination, the initial laboratory workup, methods for classifying anemia, and algorithms designed to help guide diagnosis. A systematic approach to the examination of the peripheral blood smear and bone marrow also is discussed separately. (See "Evaluation of the peripheral blood smear" and "Evaluation of bone marrow aspirate smears".)

DEFINITION OF ANEMIA — Anemia may be defined as a reduction in red blood cell mass or blood hemoglobin concentration. In practice, anemia most commonly is defined by reductions in one or both of the following:

- Hematocrit (HCT) — The hematocrit is the fractional volume of a whole blood sample occupied by red blood cells (RBCs); it is expressed as a percentage. As an example, the normal HCT in a child age 6 to 12 years is approximately 40 percent.

- Hemoglobin (HGB) — This is a measure of the concentration of the RBC pigment hemoglobin in whole blood, expressed as grams per 100 mL (dL) of whole blood. The normal value for HGB in a child age 6 to 12 years is approximately 13.5 g/dL.

The age variation for HGB and HCT is pronounced in the pediatric population; thus, it is particularly important to use age and sex adjusted norms when evaluating a pediatric patient for anemia (table 1). In addition, there is racial variation with healthy black children having average hemoglobin values 0.5 g/dL below that of white children of the same age and sex [1].

OVERVIEW OF ERYTHROPOIESIS — Fetal erythropoiesis begins with primitive megaloblastic erythropoiesis; these cells can be identified at approximately four to five weeks gestation [2]. A transition is made to normoblastic erythropoiesis at approximately six weeks gestation. At this time, blood formation begins in the liver, which is the primary organ of hematopoiesis from the third to sixth month of gestation [2]. At approximately the third month of gestation, hematopoiesis begins in the spleen, thymus, and lymph nodes. The liver and spleen continue to produce blood cells into the first week of postnatal life [2].

Bone marrow hematopoiesis begins around the fourth month of gestation and increases throughout intrauterine development. After birth, further marrow volume expansion occurs. Throughout development, hematopoiesis is primarily under fetal control and is only partially influenced by maternal factors [2]. (See "Structure and function of normal human hemoglobins".)

Erythropoiesis decreases dramatically after birth. Red cell production decreases by a factor of 2 to 3 in the first few days of life and by a factor of 10 in the week following birth [2]. This decrease is initiated by the increase in tissue oxygen level that occurs at birth and is accompanied by a decrease in

erythropoietin production resulting in the "physiologic anemia of infancy" [2,3]. Red cell production is at a minimum during the second week after birth and subsequently rises to maximum values at approximately three months. The net result of these changes is an anemia that typically nadirs at 6 to 9 weeks of age [4,5]. Erythropoietin levels correspond with these findings and in term infants are lowest at month 1 and highest at month 2 of age [3].

Anemia in preterm infants may be more pronounced because of the shorter life span of preterm red cells. The mean half-life of RBCs, as measured by the Cr-51 method, for term infants is 23.3 days, versus 16.6 days in preterm infants and 26 to 35 days in adults [2]. (See "Red blood cell survival: Normal values and measurement", section on 'Red blood cell half-time'.) and (see "Anemia of prematurity").

Infants presenting with RBC membrane abnormalities, such as hereditary spherocytosis, may in the neonatal period have anemia that is exacerbated both by the decrease in erythropoiesis that follows birth and the concomitant increase (normalization) in splenic filtration and phagocytosis [6]. (See "Hereditary spherocytosis: Clinical features; diagnosis; and treatment", section on 'Symptoms according to age'.)

CLASSIFICATIONS OF ANEMIA — Anemias may be classified on either a physiologic or a morphologic basis. Approaching the workup of an anemic patient using one of these algorithms aids in defining the necessary diagnostic workup.

Physiologic classification — Physiologic etiologies for anemia may be classified in two broad categories:

- Disorders resulting in an inability to adequately produce red blood cells (ie, bone marrow depression).
- Disorders resulting in rapid RBC destruction (hemolysis) or RBC losses from the body (bleeding).

An evaluation of the reticulocyte count aids in defining the etiology of the anemia. An increased reticulocyte count generally is seen as a normal bone marrow response to ongoing hemolysis or nonchronic blood loss. On the other hand, a low reticulocyte count, which reflects decreased production of red blood cells, is more consistent with bone marrow depression. Table 2 outlines etiologies for anemia in the pediatric population as defined by these physiologic categories (algorithm 1). (See 'Reticulocyte count' below.)

These two categories are not mutually exclusive, however, and although patients generally have one major etiology for their anemia, hemolysis or blood loss may co-exist with bone marrow suppression. As an example, a child with sickle cell disease will have life-long hemolysis, anemia, and a brisk reticulocyte response. However, during times of infection, the bone marrow may be suppressed, as evidenced by a reduction in the reticulocyte response and a consequent worsening of the anemia.

Morphologic classification — Anemias may be classified also according to RBC size (mean corpuscular volume, MCV), hemoglobin content (mean corpuscular hemoglobin, MCH), or hemoglobin concentration (mean corpuscular hemoglobin concentration, MCHC), (table 1). The etiology of the anemia may be elucidated by using these indices, the white blood cell (WBC) and platelet counts (PLT), and the reticulocyte count.

Mean corpuscular volume — The mean corpuscular volume (MCV) is perhaps the most useful RBC parameter used in the workup of anemia. It is measured directly by automated blood cell counters and represents the mean value (in femtoliters, fL) of the volume of individual RBCs in the blood sample. Values may be low (microcytic), normal (normocytic), or large (macrocytic). As with the HGB and HCT, normal values for MCV vary based upon age. In particular, infants have an increased MCV compared to older children. MCV values also increase with decreasing gestational age so that a

preterm infant with a gestational age of 25 weeks will have a MCV of 119 fL compared to a value of 106 fL in a term infant [7]. Because reticulocytes have a greater MCV than do mature cells (picture 1), patients with significant degrees of reticulocytosis may have elevated MCV values in the face of otherwise normocytic RBCs [8]. (See "Macrocytosis".)

Mean corpuscular hemoglobin concentration — The MCHC is a calculated index (MCHC= HGB/HCT), yielding a value of grams of HGB per 100 mL of RBC. Values in the normal range (33 to 34 g/dL), indicate that cells are normochromic, whereas values lower than normal indicate the presence of hypochromia. MCHC values vary depending upon the age of the child (table 1) with infants having a higher value than older children. MCHC also increases with decreasing gestational age [7].

When the red cell loses membrane and/or water, as may be seen with congenital or acquired spherocytosis or during cellular dehydration, an increased MCHC may be present along with hyperchromia that can be appreciated on the peripheral smear (picture 2) [9].

HISTORY AND PHYSICAL EXAMINATION — The clinical signs and symptoms of anemia vary based on the age of the child and the etiology and chronicity of the anemia. As with most other disorders in medicine, a thorough history and physical examination are important factors in evaluating the child with anemia.

History — Patients with inherited etiologies often present in childhood. Thus, when evaluating the history of an anemic patient, one must not only review the symptoms of the patient, but also ask pointed questions regarding family history. In addition, the birth history and neonatal course may provide important etiologic clues. Common symptoms of anemia include lethargy, tachycardia, and pallor. Anemic infants may present with irritability and poor oral intake. In contrast, patients with chronic anemia may be well compensated and may not have significant complaints.

In addition to the age and sex of the child, the following components should be part of the history when evaluating an anemic child:

- Severity and initiation of symptoms — Because of the body's compensatory abilities, patients with chronic anemia may not be as symptomatic as patients with acute anemia with similar hemoglobin values. Prior episodes of anemia may indicate inherited forms, whereas anemia in a patient with previously documented normal blood counts suggests an acquired etiology.

- Questions relating to hemolytic episodes — Specific questions regarding changes in urine color, scleral icterus, or jaundice associated with the symptoms of anemia should be asked. Hemolytic episodes that occur only in male family members may indicate the presence of a sex-linked disorder, such as glucose-6-phosphate dehydrogenase deficiency. (See "Diagnostic approach to the patient with jaundice or asymptomatic hyperbilirubinemia" and "Genetics and pathophysiology of glucose-6-phosphate dehydrogenase deficiency".)

- Prior therapy or anemic episodes — Prior anemic episodes, duration, etiology, and resolution, as well as all prior therapy for anemia, should be reviewed. Patients with hemoglobinopathies resulting in the production of small (microcytic) and pale (hypochromic) RBCs, such as Hb E or the various thalassemias, may have a history of treatment on multiple occasions for an erroneous diagnosis of iron deficiency anemia, in which the RBCs are also hypochromic and microcytic. (See 'Blood smear' below and "Clinical manifestations and diagnosis of the thalassemias".)

- Questions about possible blood loss — Specific questions related to bleeding from the gastrointestinal tract, including changes in stool color, the identification of blood in stools, and history of bowel symptoms, should be reviewed. Teenagers may have excessive menstrual losses without

realizing it, and, therefore, information regarding the menstrual history including duration of periods, flow, quantitation and saturation of tampons or pads, should be obtained.

A very common cause of anemia in children living in low and middle income countries is the presence of intestinal nematode infection (eg, hookworm, whipworm). (See "Enterobiasis and trichuriasis" and "Hookworm infection".)

- Underlying medical conditions — A careful past medical history and review of symptoms should be obtained to elucidate chronic underlying infectious or inflammatory conditions that may result in anemia. Travel to/from areas of endemic infection (eg, malaria, hepatitis, tuberculosis) should be noted. Recent illnesses should be reviewed, and possible infectious etiologies for the anemia should be explored. As an example, a mild drop in hemoglobin concentration of 1 to 1.5 g/dL is not uncommon in the presence of active infection.

- Prior drug or toxin exposure — Prior medications as well as environmental toxin exposure, including the use of well water containing nitrates, should be reviewed. Any history of oxidant-induced hemolysis should be obtained. Inquiries regarding type and duration of homeopathic or herbal medications should be undertaken because children receiving these preparations may be at risk for exposure to lead and other toxins. In addition, when evaluating a child with microcytic anemia, one should ask specific questions regarding environment, housing, paint exposure, cooking materials, and use of poorly glazed ceramic pots in order to evaluate for possible lead exposure. (See "Screening tests in children and adolescents", section on 'Lead poisoning'.)

- Questions relating to diet — Questions should be primarily aimed at determining iron content in the diet and, to a lesser degree, folate and B12 content. The type of diet, type of formula (if iron fortified), and age of infant at the time of discontinuation of formula or breast milk should be documented. In addition, the amount and type of milk the patient is drinking should be determined. Specific questions as to whether the child has symptoms consistent with pica may aid with the diagnosis of lead poisoning and/or iron deficiency (see "Childhood lead poisoning: Clinical manifestations and diagnosis" and "Iron deficiency in infants and young children" and "Iron requirements and iron deficiency in adolescents").

- Birth history — A birth and neonatal history including infant and mother's blood type, any history of exchange or intrauterine transfusion, and a history of anemia in the early neonatal period should be obtained. Gestational age at birth is important, as premature infants may have iron or vitamin E deficiencies resulting in anemia. The presence of jaundice or need for phototherapy may signify the presence of an inherited hemolytic anemia.

- Developmental milestones — Parents should be asked questions to determine if the child has reached age-appropriate developmental milestones. Loss of milestones or developmental delay in infants with megaloblastic anemia may signify abnormalities in the cobalamin pathway.

- Family history, race, and ethnicity — Any family history of anemia should be pursued in depth. Family members with jaundice, gallstones, or splenomegaly should be identified. Asking if family members have undergone cholecystectomy or splenectomy may aid in the identification of additional individuals with inherited hemolytic anemias. Race and ethnic background are helpful in guiding the workup for hemoglobinopathies and enzymopathies. For example, thalassemia syndromes are more common in individuals of Mediterranean and Southeast Asian descent; Hemoglobin S and C are most commonly seen in Black populations.

Physical examination — The physical exam also may provide important clues as to the etiology of the anemia. Areas of particular importance on the physical examination include: the skin, eyes, mouth, facies, chest, hands, and abdomen (table 2).

Pallor should be assessed by examining sites where capillary beds are visible through the mucosa (eg, conjunctiva, palm, and nail beds). Pallor in these locations is predictive of severe anemia, but mild and even severe anemia may be overlooked when relying solely on this physical finding [10,11]. As an example, in a field study of 535 preschool children, clinical pallor in the conjunctiva, palm, and nail beds was detected in only 20 percent of those with HGB <11.0 g/dL and 61 percent of those with severe anemia (HGB <7.0 g/dL) [12].

Patients with hemolytic processes resulting in anemia may present with signs of jaundice and hepatosplenomegaly resulting from increased red cell destruction. However, as with the clinical detection of anemia through evaluation of pallor, clinical detection of jaundice often is poor. For example, in an emergency department setting, the clinical detection of jaundice was found to have sensitivity and specificity of only approximately 70 percent, with an average difference between estimated and measured serum bilirubin concentrations of 3.4 ± 5.3 mg/dL [13].

LABORATORY EXAMINATION — The laboratory examination should begin with a complete blood count including red blood cell indices, a reticulocyte count, and a review of the peripheral blood smear. These components will allow for morphologic evaluation of the cells, classification of the anemia based on red blood cell size, and aid in the identification of the physiologic basis for the anemia [14]. After the evaluation of these parameters, precise laboratory tests may be obtained to identify and confirm the etiology of the anemia.

In the pediatric population, many blood samples obtained for anemia screening are capillary samples such as finger or heel "sticks." Although these means of sampling are acceptable, one must keep in mind that HGB and HCT values may be slightly elevated in such samples as compared to venous samples when using automated counting methods [15,16]. This difference may be more pronounced when using microhematocrit measurements from capillary samples [17]. Although the likelihood of masking significant anemia is low, borderline low values may be "normalized" using the capillary collection and processing method.

Blood smear — A review of the peripheral smear is an essential part of any anemia evaluation. The diameter of a normal RBC should be the same as the diameter of the nucleus of a small lymphocyte (picture 3). This comparison will help the investigator identify the patient with microcytosis (picture 4) or macrocytosis (picture 5). The normal mature RBC is a biconcave disc (picture 6), as a result, RBCs on the peripheral smear demonstrate an area of central pallor, which, in normochromic RBCs, is approximately one-third the diameter of the cell (picture 3). Increased central pallor indicates hypochromic cells, which most often are seen in iron deficiency (picture 4) and thalassemia (picture 7) . On the other hand, spherocytes (picture 2) and reticulocytes (picture 1), not being biconcave discs, do not show central pallor. (See "Evaluation of the peripheral blood smear".)

Although the patient's overall RBC indices may be normal, review of the blood smear may reveal the presence of small numbers of fragmented cells, indicating a microangiopathic process (picture 8). (See "Extrinsic nonimmune hemolytic anemia due to mechanical damage: Fragmentation hemolysis and hypersplenism".) Other anemias may be characterized by typical morphologic abnormalities such as:

- Sickle cells, as seen in sickle cell disease (picture 9). (See "Diagnosis of sickle cell syndromes".)

- Elliptocytes, as seen in congenital elliptocytosis (picture 10). (See "Hereditary elliptocytosis: Clinical features and diagnosis".)

- Stomatocytes, as seen in hereditary or acquired stomatocytosis (picture 11). (See "Stomatocytosis".)

- Target cells, as seen in the various hemoglobinopathies, in liver disease, and post-splenectomy

(picture 12). (See "Spiculated cells (echinocytes and acanthocytes) and target cells".)

- Bite cells, as seen in Heinz body hemolytic anemia (picture 13). (See "Extrinsic nonautoimmune hemolytic anemia due to drugs and toxins".)

The presence of numerous nucleated red blood cells indicates rapid bone marrow turnover and is seen with hemolytic processes (picture 9 and picture 14). These findings may go undetected without inspection of the peripheral smear.

Red blood cell indices — The red blood cell indices MCV, MCH, and MCHC have been discussed already and are an integral part of the evaluation of the anemic child.

Red cell distribution width — The red cell distribution width (RDW) is a quantitative measure of the variability of RBC sizes in the sample (anisocytosis). The RDW is a function of MCV and, therefore, normal values vary slightly with age. However, normal values generally fall between 12 and 14 percent [17]. The RDW is especially helpful in differentiating iron deficiency from thalassemia in the pediatric patient with microcytic anemia. Patients with a RDW greater than 20 are more likely to have iron deficiency, whereas patients with normal RDW values are more likely to have thalassemia or the anemia of chronic disease [18].

Reticulocyte count — Reticulocytes are the youngest red cells in the circulation, and are identified via the presence of residual RNA, which gives them a blue tint on standard Wright-Giemsa stains (picture 1). They are quantitated via staining with vital dyes, such as new methylene blue or thiazole orange, and are reported as a percentage (picture 15). After the first few months of life, the mean reticulocyte percentage is the same as that of the adult, approximately 1.5 percent [19].

The reticulocyte count is an indication of bone marrow erythropoietic activity. Thus, anemia with an elevated reticulocyte count suggests active erythropoiesis in response to hemolysis, acute blood loss, or recent institution of replacement therapy (eg, successful treatment of iron or folic acid deficiency). On the other hand, anemia with a low reticulocyte count indicates a suboptimal bone marrow response and is suggestive of marrow aplasia, infiltration with malignant cells, depression caused by infection or other toxic agents, or suboptimal production of erythropoietin [11]. (See "Approach to the adult patient with anemia", section on 'Reticulocyte count'.)

White blood count and platelet count — The presence of leukopenia (low total white blood cell count) and/or neutropenia (low total number of neutrophils) and/or thrombocytopenia (low platelet count) may signify abnormal bone marrow function in the patient with anemia and may indicate the presence of bone marrow hypoplasia caused by drugs or toxins, deficiency of folic acid or vitamin B12, or the presence of splenic hyperfunction ("hypersplenism"). Increases in circulating neutrophils (neutrophilia), especially in the presence of a "left shift" or toxic changes (picture 16), or the presence of atypical lymphocytes (picture 17) may lead one to suspect the presence of infectious or inflammatory conditions. The presence of early white blood cell forms (eg, blasts, (picture 18) along with anemia may lead one to consider the diagnosis of leukemia or lymphoma. (See "Approach to the patient with neutrophilia" and "Approach to the patient with lymphocytosis" and "Overview of the presentation and classification of acute lymphoblastic leukemia in children".)

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GRAPHICS

Hemoglobin, hematocrit, red blood cells, and white blood cells in children 1-14 years of age, by age group and sex: the Third National Health and Nutrition Examination Survey (1988-91)

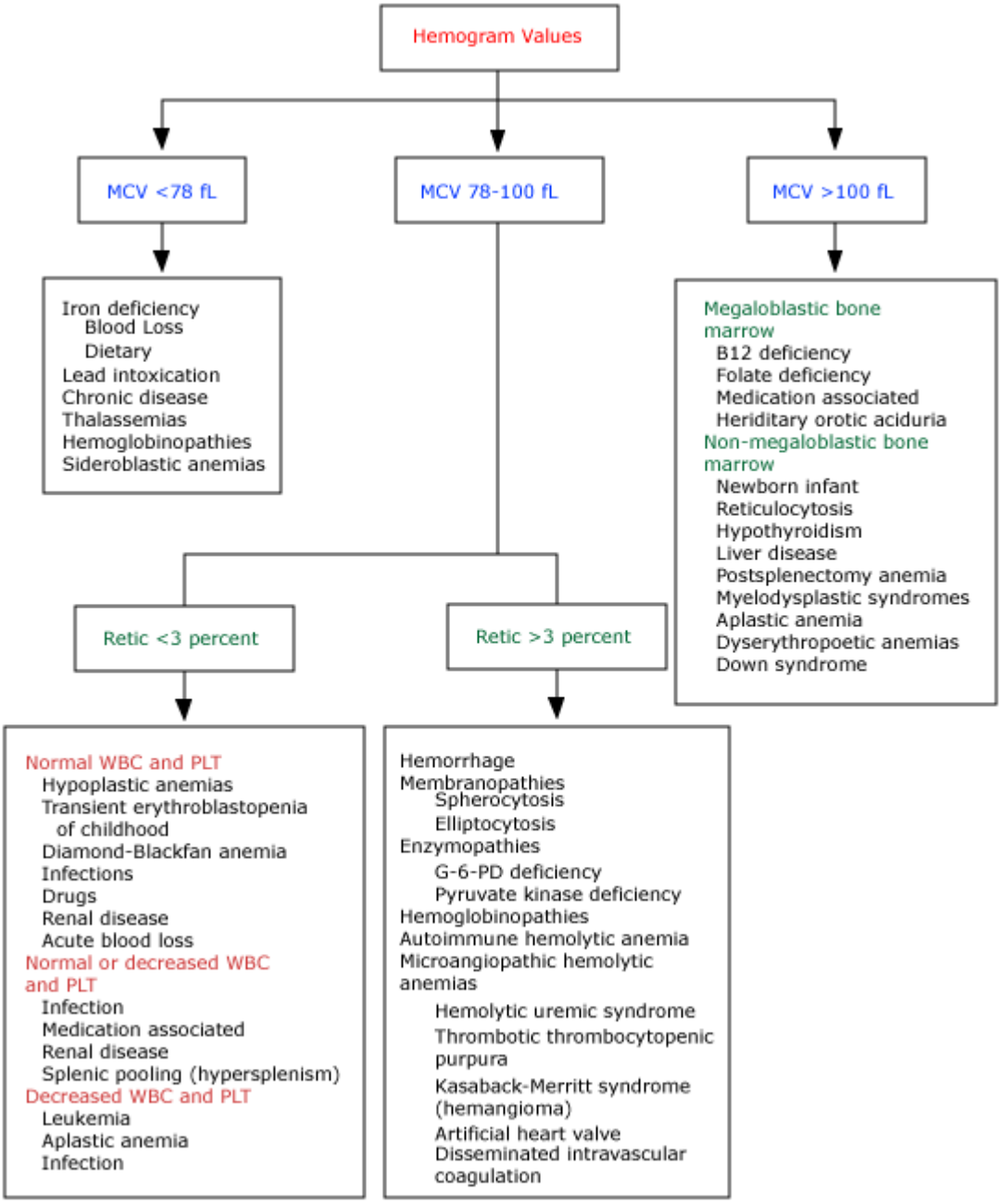
Characteristic	Male*			Female*		
	NHANES III			NHANES III		
	Number	Mean	SD•	Number	Mean	SD•
Hemoglobin, g/dL						
1-2 years	931	12.0	0.08	858	11.8	0.09
3-5 years	1281	12.4	0.08	1337	12.0	0.08
6-8 years	709	12.9	0.08	675	12.4	0.08
9-11 years	773	13.3	0.08	734	12.7	0.08
12-14 years	540	14.1	0.11	621	12.5	0.09
Hematocrit, percent						
1-2 years	931	36	2	858	36	2
3-5 years	1281	37	2	1337	37	2
6-8 years	709	38	2	675	38	2
9-11 years	773	39	2	734	39	2
12-14 years	540	42	3	621	40	3
Red blood cells, 10^{12} cells per liter						
1-2 years	931	4.55	0.34	858	4.50	0.34
3-5 years	1281	4.51	0.34	1337	4.49	0.32
6-8 years	709	4.60	0.29	675	4.56	0.31
9-11 years	773	4.71	0.32	734	4.62	0.30
12-14 years	540	4.93	0.39	621	4.59	0.32
White blood cells, 10^{9} cells per liter						
1-2 years	931	8.74	2.53	858	8.66	2.41
3-5 years	1281	7.68	2.26	1337	7.90	2.12
6-8 years	709	7.45	2.02	675	7.63	2.10
9-11 years	773	7.01	2.07	734	7.20	1.98
12-14 years	540	7.02	2.07	621	7.30	2.06

* Includes all race/ethnic groups.

• SD is standard deviation.

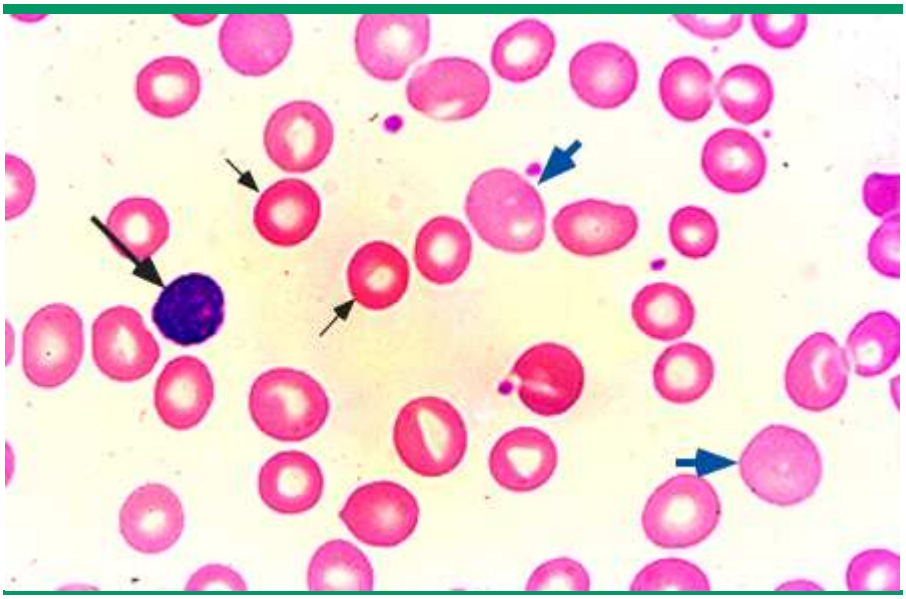
Adapted from: Hollowell, JG, van Assendelft, OW, Gunter, EW, et al. Hematological and iron-related analytes-reference data for persons aged 1 year and over: United States, 1988-94. Vital Health Stat 2005; 11:1.

Anemia algorithm



Adapted from Nathan, DG, Oski, FA. Hematology of Infancy and Childhood, 4th ed, WB Saunders, Philadelphia, PA 1993. p. 352.

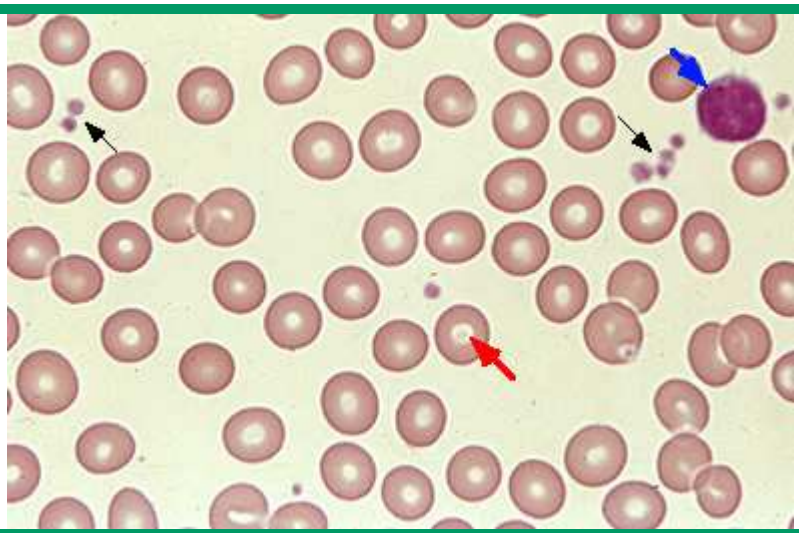
Polychromatophilia



Peripheral blood smear taken from a patient with increased reticulocytes. Unlike mature red cells (thin black arrows), which have central pallor and are the same size as the nucleus of a small lymphocyte (thick arrow), reticulocytes (blue arrows) are larger, have a blue tint, and lack central pallor because they are not biconcave discs. (Wright-Giemsa stain).

Courtesy of Stanley Schrier, MD.

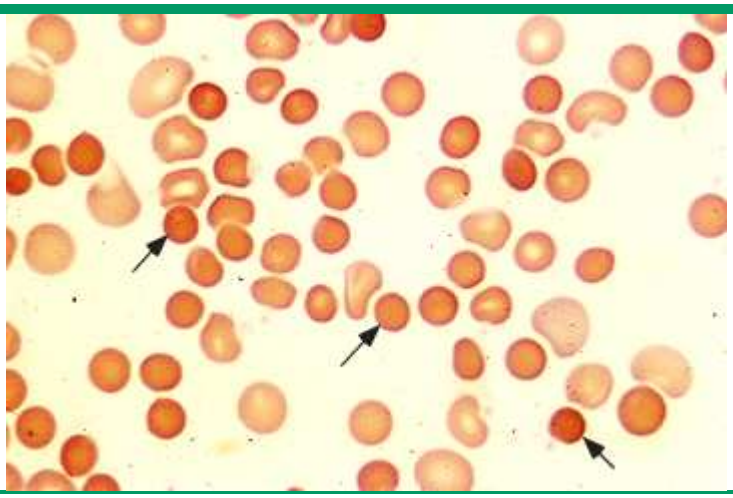
Normal peripheral blood smear



High power view of a normal peripheral blood smear. Several platelets (black arrows) and a normal lymphocyte (blue arrow) can also be seen. The red cells are of relatively uniform size and shape. The diameter of the normal red cell should approximate that of the nucleus of the small lymphocyte; central pallor (red arrow) should equal one-third of its diameter.

Courtesy of Carola von Kapff, SH (ASCP).

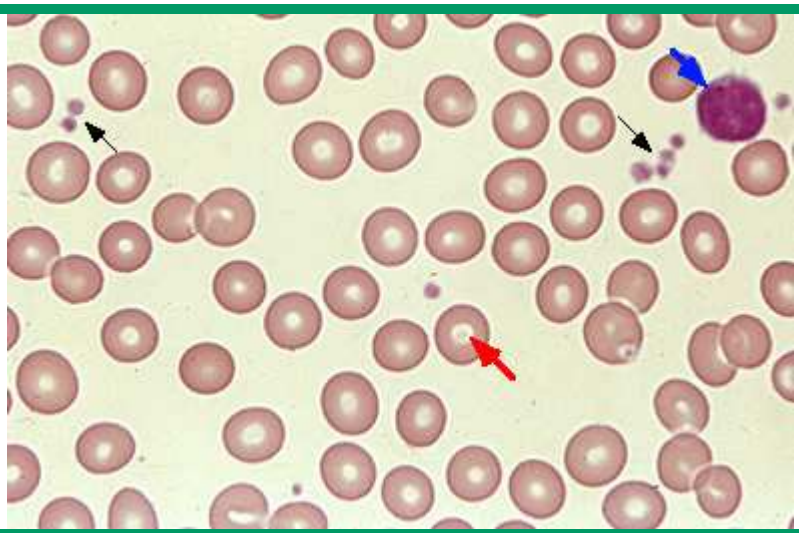
Spherocytes



Peripheral blood smear shows multiple spherocytes which are small, dark, dense hyperchromic red cells without central pallor (arrows). These findings are compatible with hereditary spherocytosis or autoimmune hemolytic anemia.

Courtesy of Carola von Kapff, SH (ASCP).

Normal peripheral blood smear



High power view of a normal peripheral blood smear. Several platelets (black arrows) and a normal lymphocyte (blue arrow) can also be seen. The red cells are of relatively uniform size and shape. The diameter of the normal red cell should approximate that of the nucleus of the small lymphocyte; central pallor (red arrow) should equal one-third of its diameter.

Courtesy of Carola von Kapff, SH (ASCP).

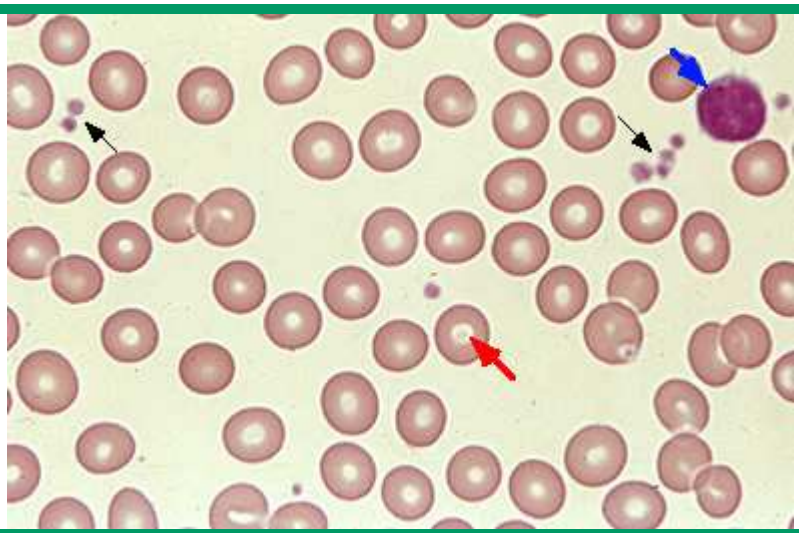
Physical findings as clues to the etiology of anemia

Finding	Possible etiology
Skin	
Hyperpigmentation	Fanconi's aplastic anemia
Petechiae, purpura	Autoimmune hemolytic anemia with Thrombocytopenia, hemolytic-uremic syndrome, bone marrow aplasia, bone marrow infiltration
Carotenemia	Suspect iron deficiency in infants
Jaundice	Hemolytic anemia, hepatitis, and aplastic anemia
Cavernous hemangioma	Microangiopathic hemolytic anemia
Ulcers on lower extremities	S and C hemoglobinopathies, thalassemia
Facies	
Frontal bossing, prominence of the malar and maxillary bones	Congenital hemolytic anemias, thalassemia major, severe iron deficiency
Eyes	
Microcornea	Fanconi's aplastic anemia
Tortuosity of the conjunctival and retinal vessels	S and C hemoglobinopathies
Microaneurysms of retinal vessels	S and C hemoglobinopathies
Cataracts	Glucose-6-phosphate dehydrogenase deficiency, galactosemia with hemolytic anemia in newborn period
Vitreous hemorrhages	S hemoglobinopathy
Retinal hemorrhages	Chronic, severe anemia
Edema of the eyelids	Infectious mononucleosis, exudative enteropathy with iron deficiency, renal failure
Blindness	Osteopetrosis
Mouth	
Glossitis	Vitamin B12, deficiency, iron deficiency
Angular stomatitus	
Chest	
Unilateral absence of the pectoral muscles	Poland's syndrome (increased incidence of leukemia)
Shield chest	Diamond-Blackfan syndrome
Hands	
Triphalangeal thumbs	Red cell aplasia
Hypoplasia of the thenar eminence	Fanconi's aplastic anemia

Spoon nails	Iron deficiency
Spleen	
Enlargement	Congenital hemolytic anemia, leukemia, lymphoma acute infection, portal hypertension

Reproduced with permission from: Oski, FA, Brugnara, G, Nathan DG. A diagnostic approach to the anemia patient. In: Nathan and Oski's Hematology of Infancy and Childhood. WB Sauders, Philadelphia. 1998. p 378.

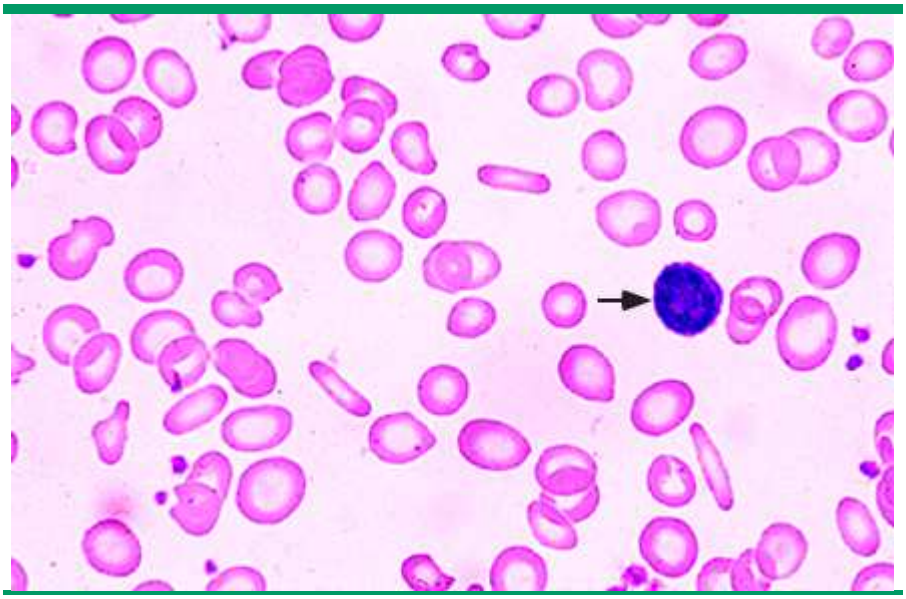
Normal peripheral blood smear



High power view of a normal peripheral blood smear. Several platelets (black arrows) and a normal lymphocyte (blue arrow) can also be seen. The red cells are of relatively uniform size and shape. The diameter of the normal red cell should approximate that of the nucleus of the small lymphocyte; central pallor (red arrow) should equal one-third of its diameter.

Courtesy of Carola von Kapff, SH (ASCP).

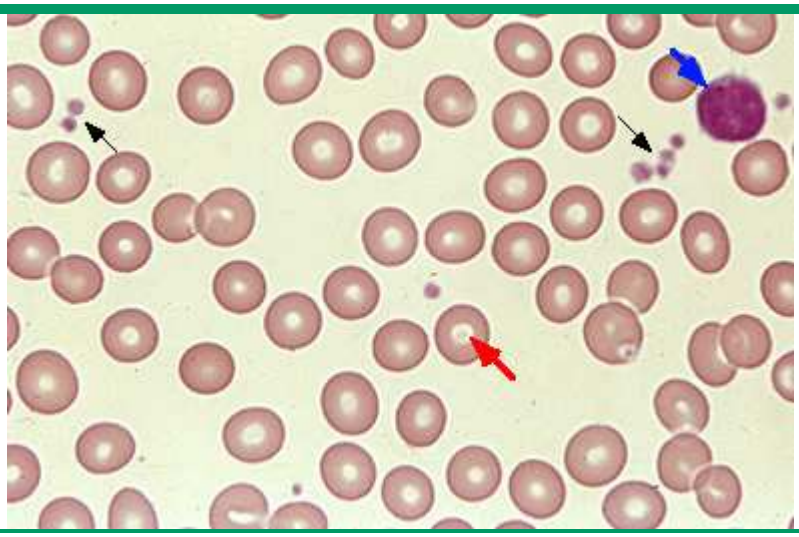
Microcytic hypochromic red cells



Peripheral smear from a patient with iron deficiency shows pale small red cells with just a scant rim of pink hemoglobin; occasional "pencil" shaped cells are also present. Normal red cells are similar in size to the nucleus of a small lymphocyte (arrow); thus, many microcytic cells are present in this smear. Thalassemia can produce similar findings.

Courtesy of Carola von Kapff, SH (ASCP).

Normal peripheral blood smear



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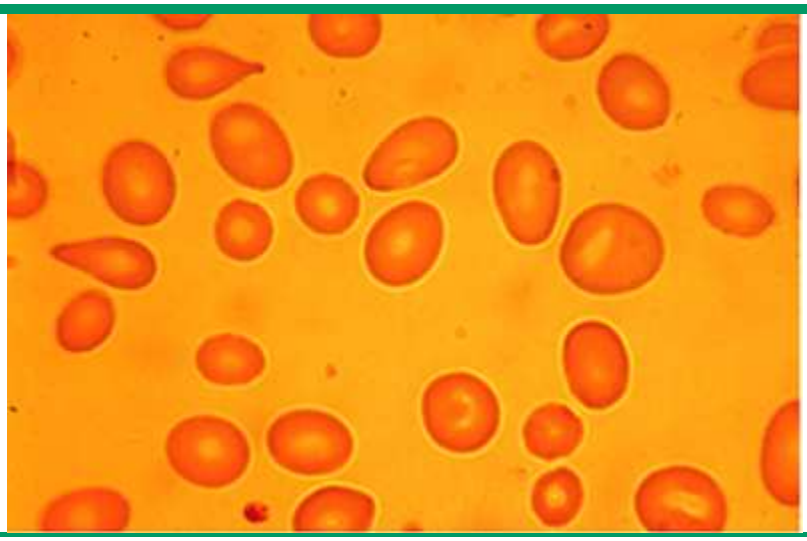
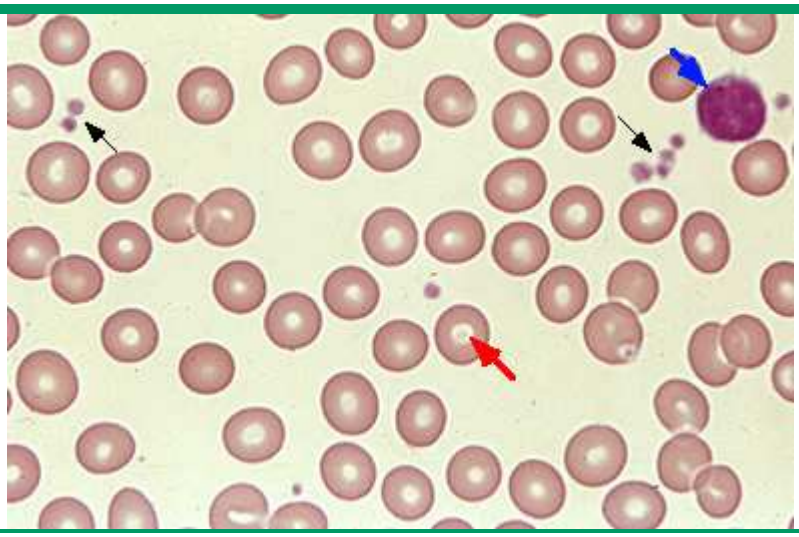
Macroovalocytosis



Peripheral smear shows marked macroovalocytosis in a patient with vitamin B12 deficiency.
Courtesy of Stanley L Schrier, MD.

Normal peripheral blood smear



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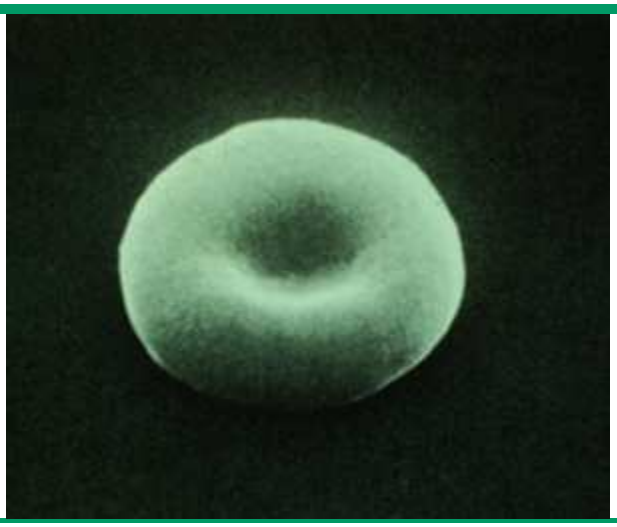
Courtesy of Carola von Kapff, SH (ASCP).

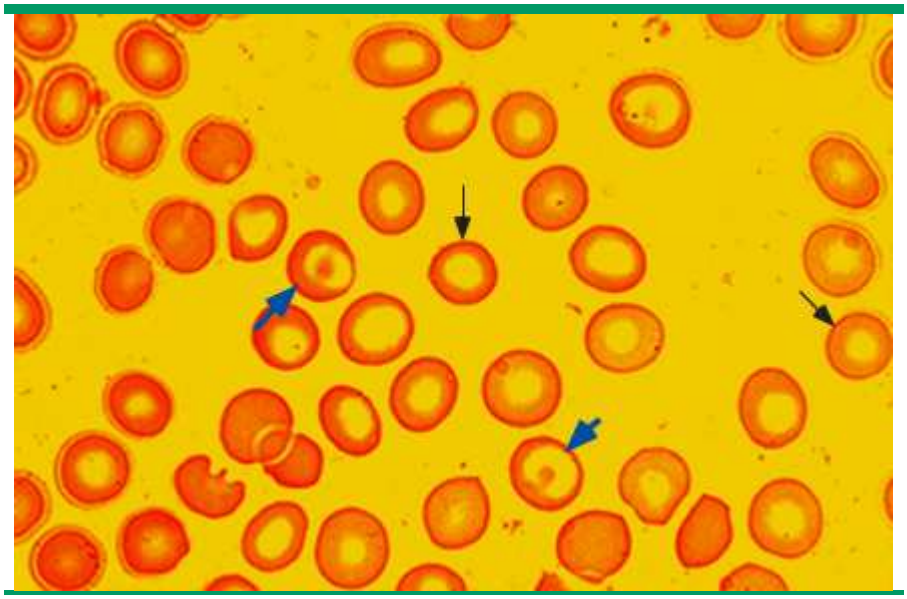
Normal red blood cell



Scanning electron microphotograph of a normal adult human red blood cell. Note the biconcave disc shape, which gives the cell more surface area than a sphere of identical volume. The normal red cell is thinnest in the center, resulting in the central pallor seen on the peripheral smear.

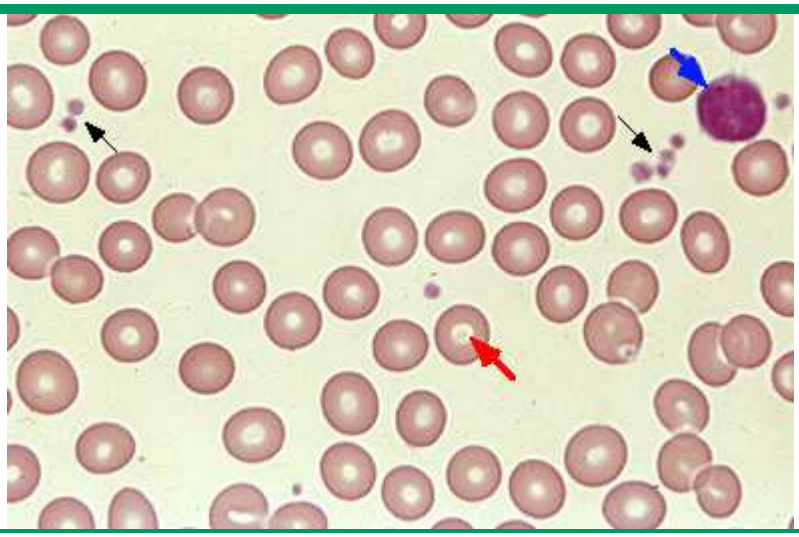
Courtesy of Stanley L Schrier, MD.

Beta thalassemia trait



Peripheral smear from a patient with beta thalassemia trait. The field shows numerous hypochromic and microcytic red cells (thin arrows), some of which are also target cells (blue arrows).
Courtesy of Stanley Schrier, MD

Normal peripheral blood smear



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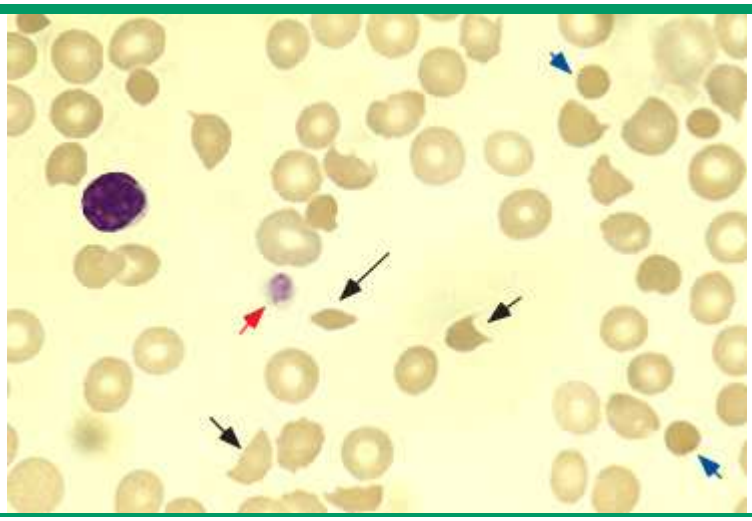
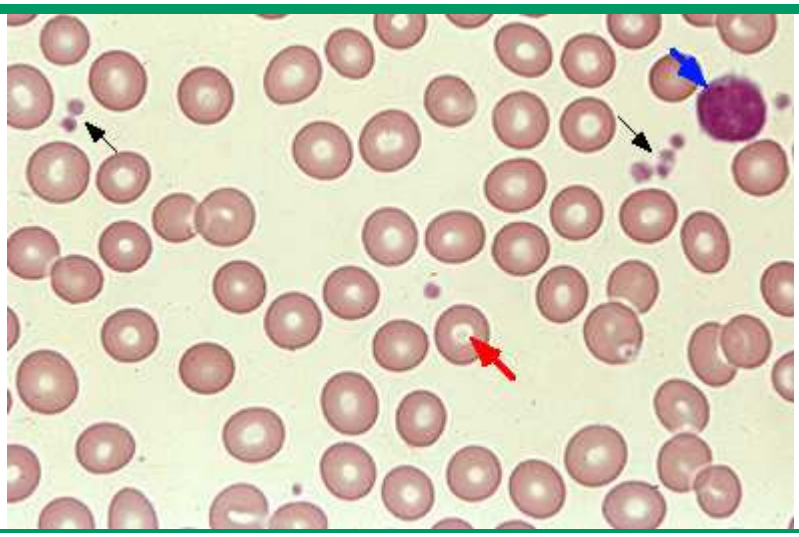
Courtesy of Carola von Kapff, SH (ASCP).

Microangiopathic smear



Peripheral blood smear from a patient with a microangiopathic hemolytic anemia with marked red cell fragmentation. The smear shows multiple helmet cells (small black arrows), other fragmented red cells (large black arrow); microspherocytes are also seen (blue arrows). The platelet number is reduced; the large platelet in the center (red arrow) suggests that the thrombocytopenia is due to enhanced destruction.
Courtesy of Carola von Kapff, SH (ASCP).

Normal peripheral blood smear



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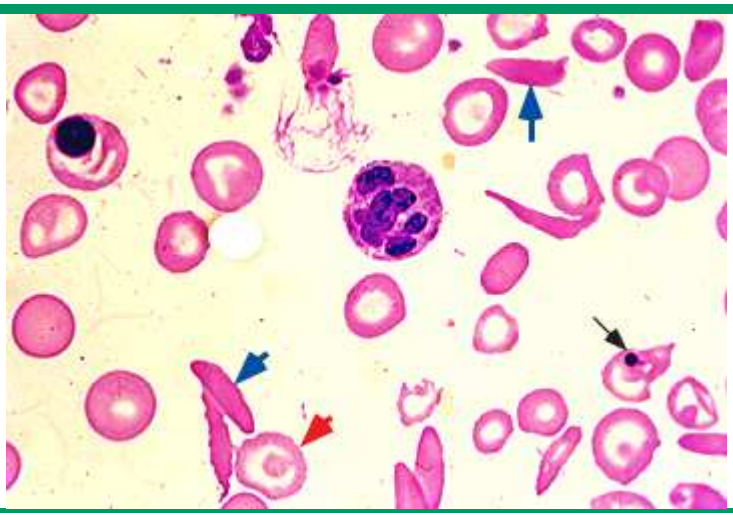
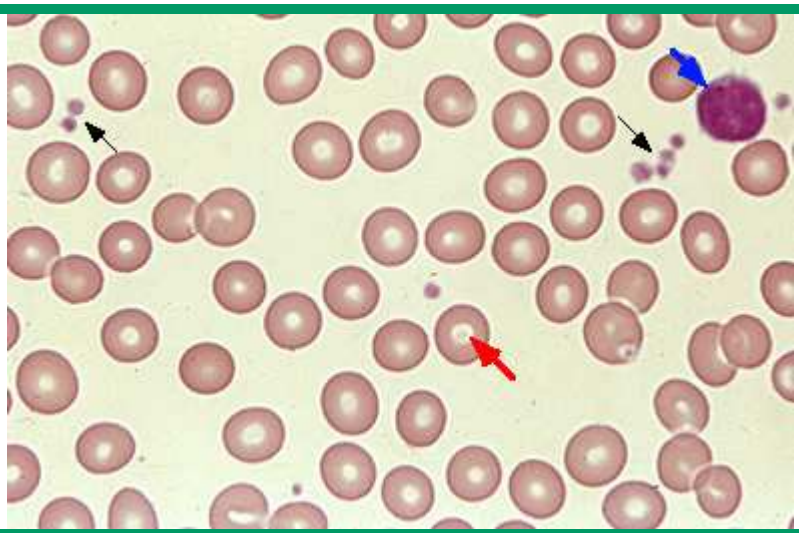
Courtesy of Carola von Kapff, SH (ASCP).

Sickle cell anemia



Peripheral smear from a patient with sickle cell anemia shows multiple spindly sickle cells (blue arrows), a nucleated red blood cell in the upper left, and a Howell-Jolly body (black arrow), which is a nuclear fragment normally removed by the spleen. Target cells are also present (red arrow). This patient has functional asplenia because of repeated splenic infarctions.
Courtesy of Carola von Kapff, SH (ASCP).

Normal peripheral blood smear



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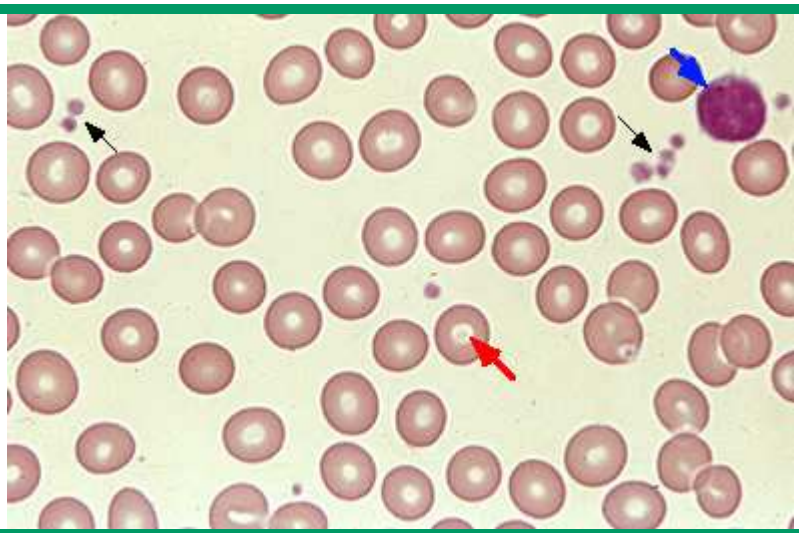
Courtesy of Carola von Kapff, SH (ASCP).

Elliptocytosis

Peripheral blood smear from a patient with hereditary elliptocytosis shows multiple elliptocytes.
Courtesy of Carola von Kapff, SH (ASCP).

Normal peripheral blood smear



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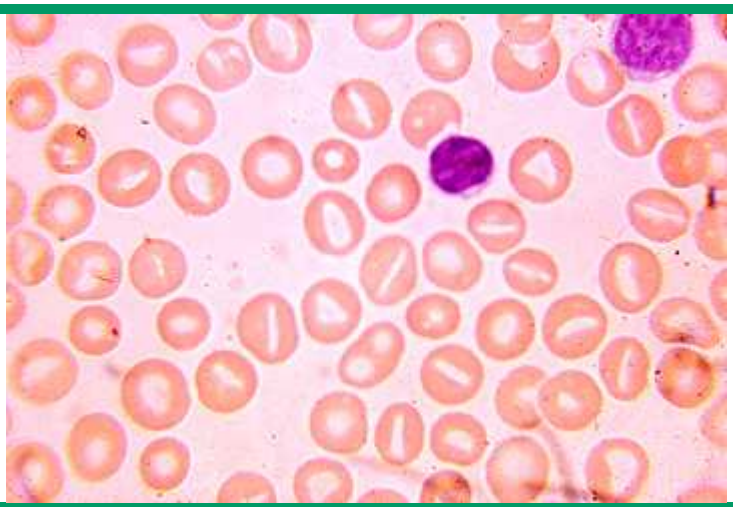
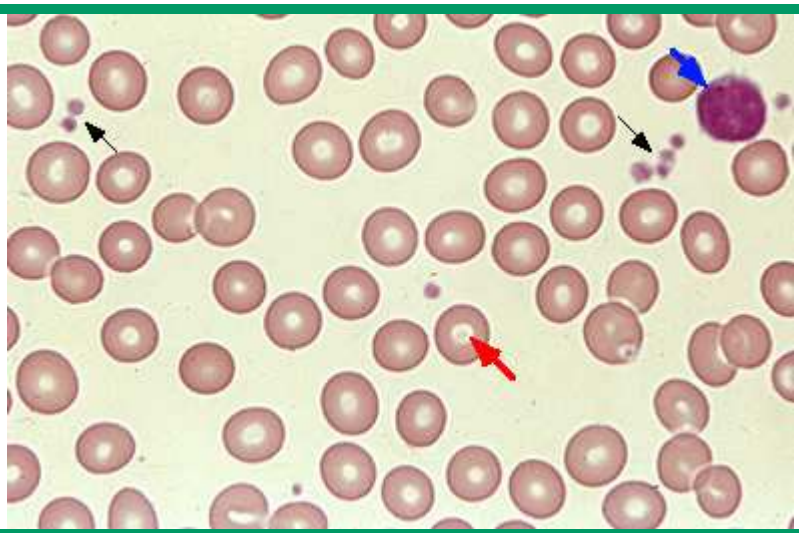
Stomatocytosis



Peripheral blood smear showing multiple stomatocytes characterized by a mouth-shaped area of central pallor.
Courtesy of Carola von Kapff, SH (ASCP).

Normal peripheral blood smear



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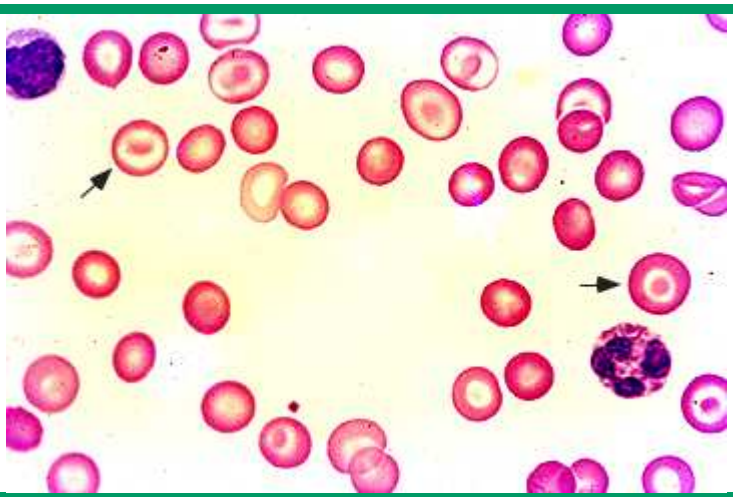
Courtesy of Carola von Kapff, SH (ASCP).

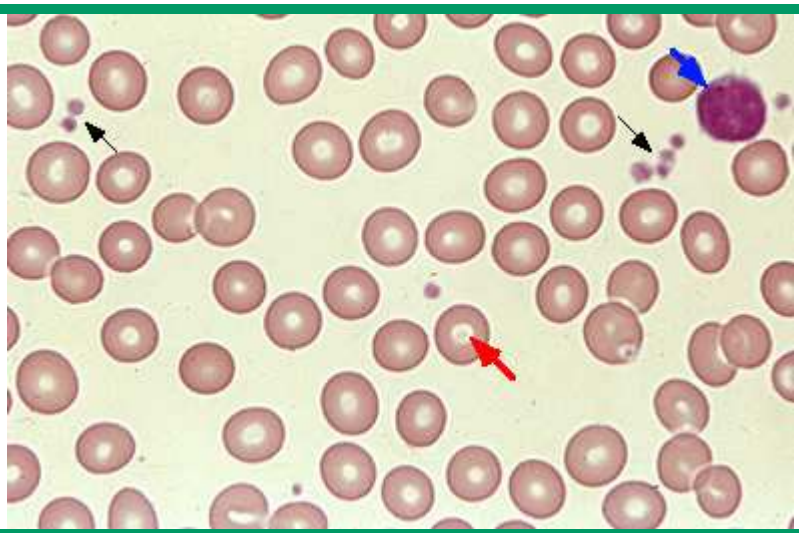
Target cells



Peripheral smear shows multiple target cells which have an area of central density surrounded by a halo of pallor (arrows). These cells are characteristic of liver disease and certain hemoglobinopathies (most notably hemoglobin C disease).

Courtesy of Carola von Kapff, SH (ASCP).

Normal peripheral blood smear



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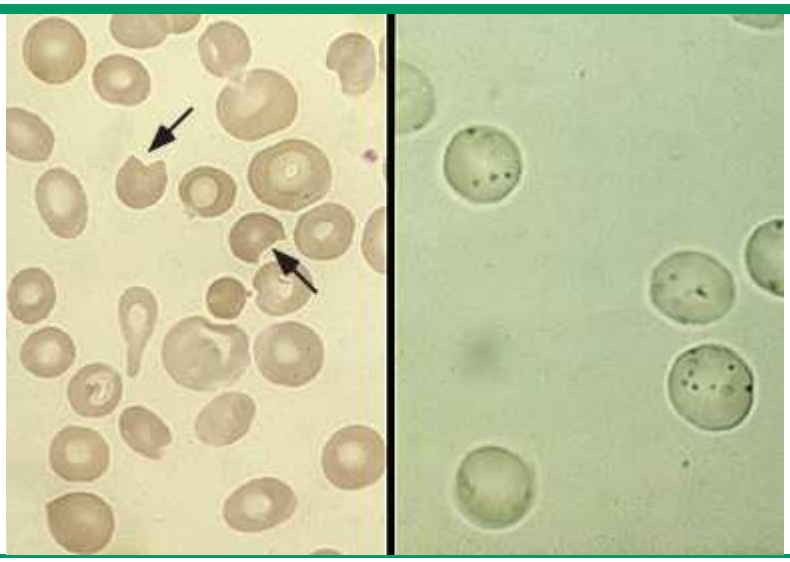
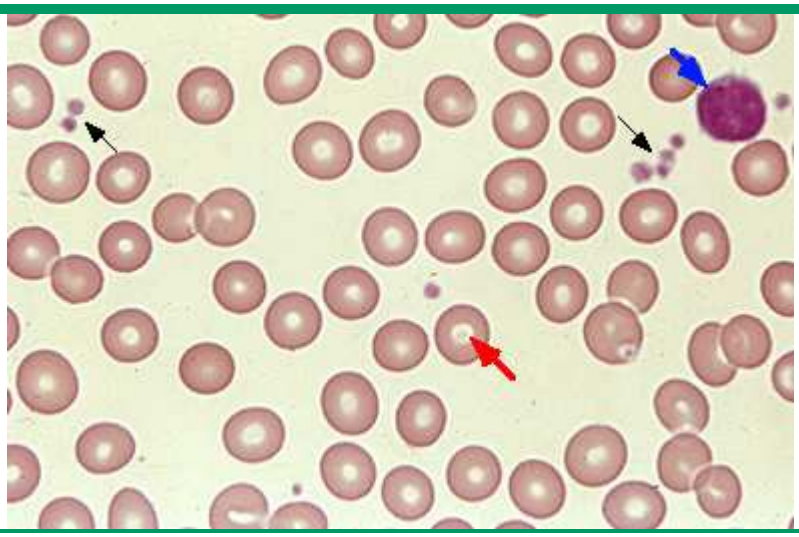
Courtesy of Carola von Kapff, SH (ASCP).

Heinz body hemolytic anemia



Split screen view of a peripheral smear from a patient with Heinz body hemolytic anemia. Left panel: red cells with characteristic bite-like deformity (arrows). Right panel: Heinz body preparation which reveals the denatured hemoglobin precipitates.
Courtesy of Carola von Kapff, SH (ASCP).

Normal peripheral blood smear



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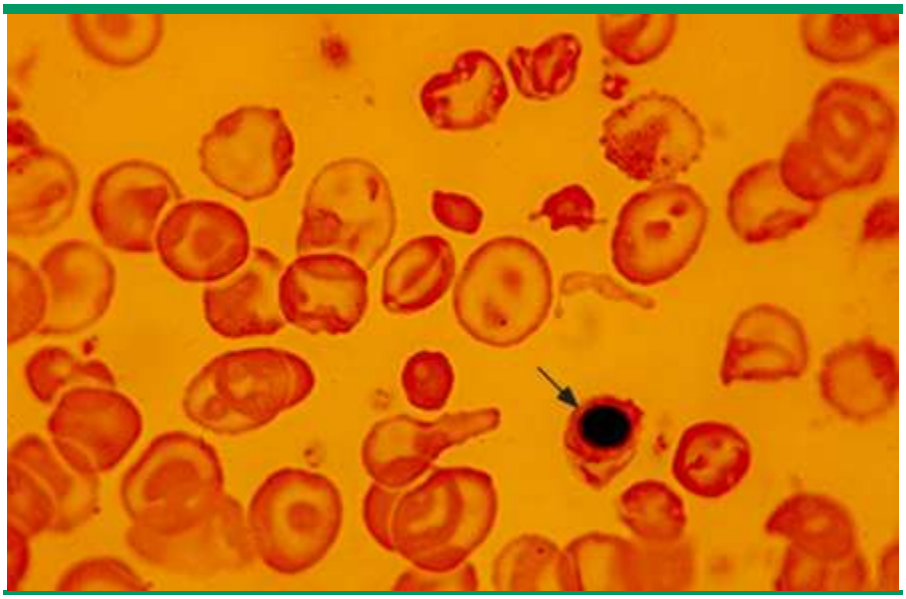
Courtesy of Carola von Kapff, SH (ASCP).

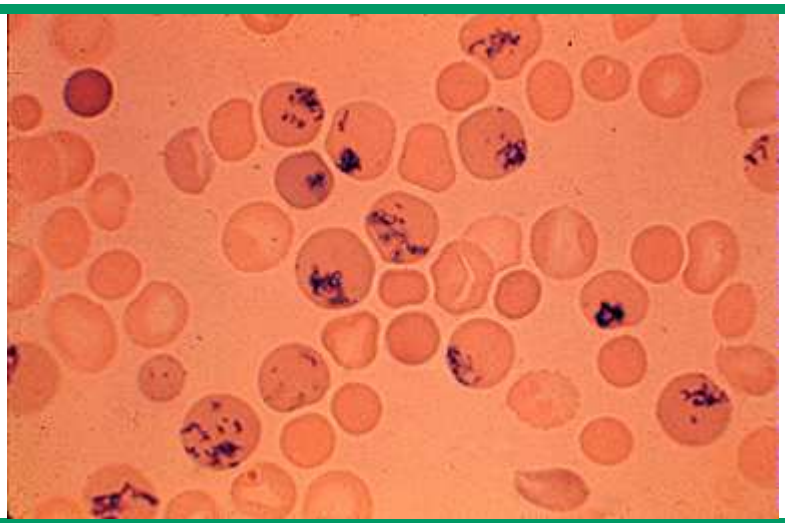
Beta thalassemia intermedia



Peripheral smear from a patient with beta thalassemia intermedia post-splenectomy. This field shows target cells, hypochromic cells, microcytic cells, red cell fragments, red cells with bizarre shapes, and a single nucleated red cell (arrow).

Courtesy of Stanley Schrier, MD.

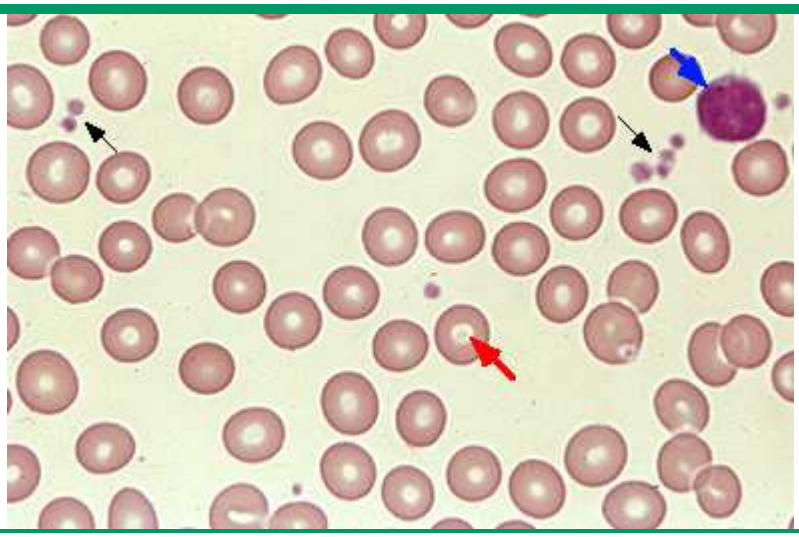
Reticulocytosis in peripheral blood



Supravital stain of a peripheral blood smear shows blue-stained residual reticulin (ribosomal RNA) in reticulocytes.

Courtesy of Stanley L Schrier, MD.

Normal peripheral blood smear



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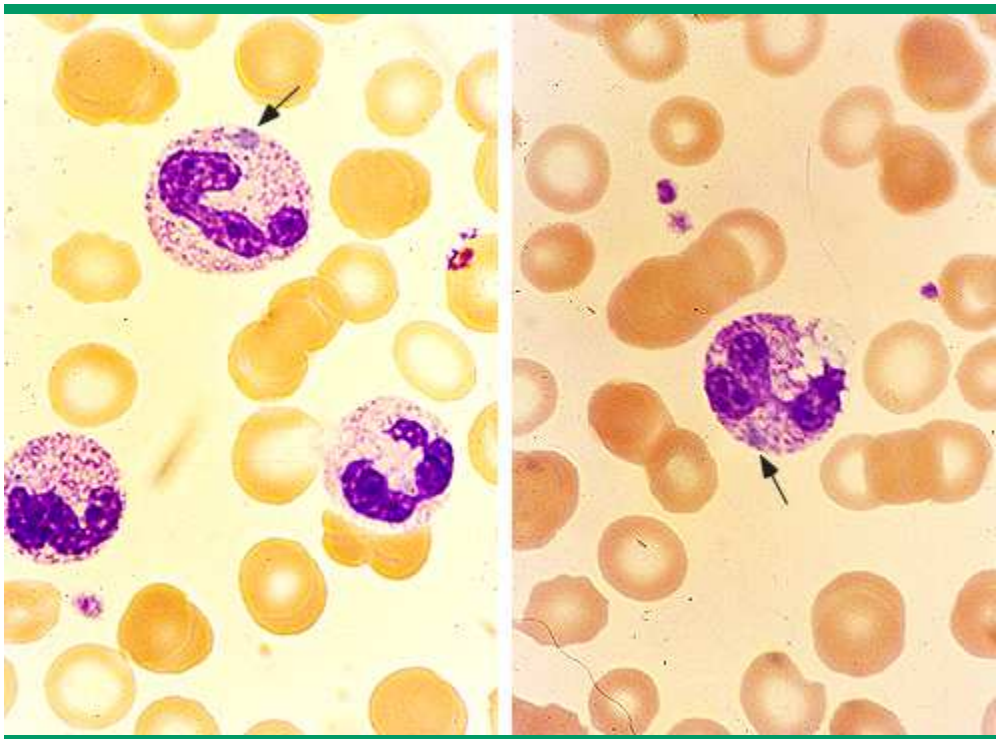
Courtesy of Carola von Kapff, SH (ASCP).

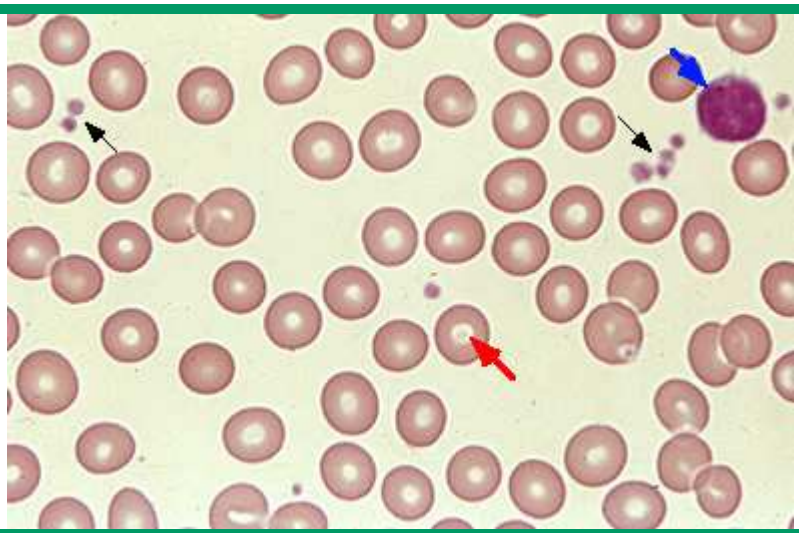
Toxic granulations and Döhle bodies



Left panel: Peripheral blood smear shows neutrophils with toxic granulations, which are dark coarse granules. A Döhle body is also seen (arrow). Right panel: A neutrophil with toxic granulations, vacuoles (another toxic change), and a Döhle body (arrow). These abnormalities are characteristic of toxic systemic illnesses.

Courtesy of Carola von Kapff, SH (ASCP).

Normal peripheral blood smear



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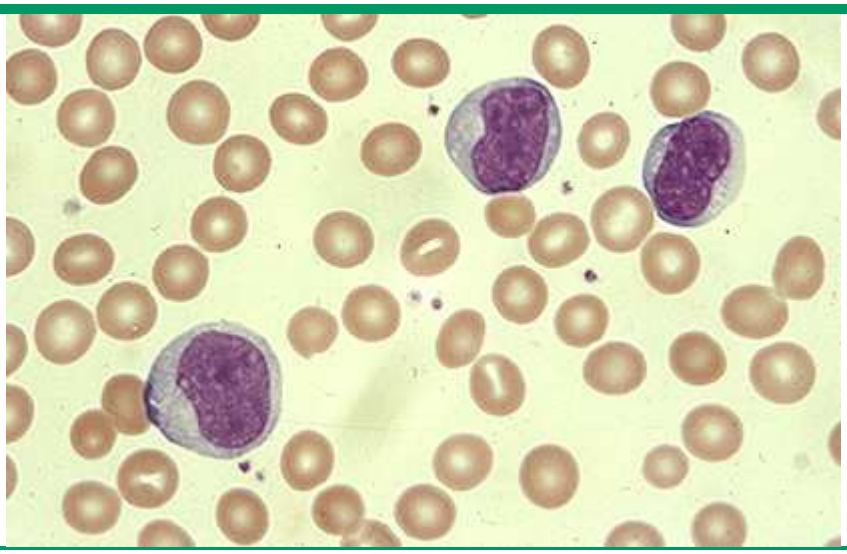
Courtesy of Carola von Kapff, SH (ASCP).

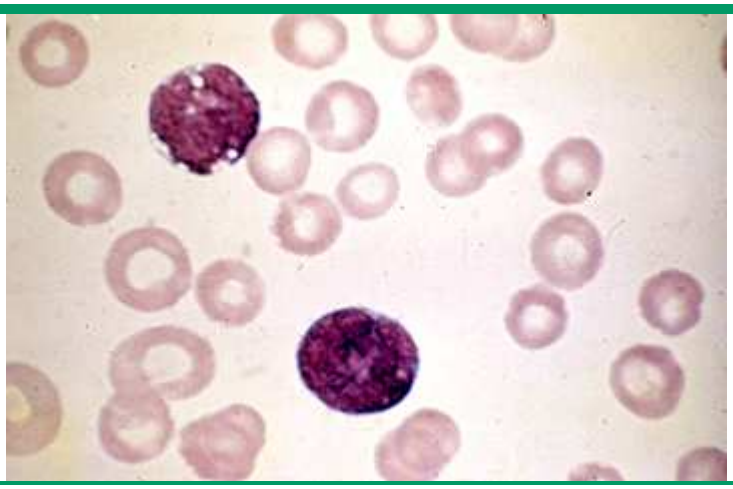
Atypical lymphocytes



Peripheral smear from a patient with infectious mononucleosis shows three atypical lymphocytes with generous cytoplasm.

Courtesy of Carola von Kapff, SH (ASCP).

Lymphoblasts in ALL L-1



Blood smear showing small lymphoblasts with rare nucleoli and vacuoles, as seen in acute lymphocytic leukemia (ALL) of the L-1 morphologic type.

Courtesy of Robert Baehner, MD.