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SEVENTEENTH EDITION

THE MERCK MANUAL OF

DIAGNOSIS AND THERAPY

Editors

MARK H. BEERS, M.D., and ROBERT BERKOW, M.D.

Senior Assistant Editors

ROBERT M. BOGIN, M.D., and
ANDREW J. FLETCHER, M.B., B.Chir.

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FOREWORD

With this edition, *The Merck Manual* celebrates its 100th birthday. When the editors of the 1st Edition produced their 192-page compendium, they could not have realized the extent to which medical knowledge would explode over the next century. *The Merck Manual* now fills 2,655 pages and covers countless diseases that were not known 100 years ago. A brief review of medical practice as reflected in *The Merck Manual* during the past century follows on page vii.

Although the knowledge of medicine has grown, the goal of *The Merck Manual* has not changed—To provide useful clinical information to practicing physicians, medical students, interns, residents, nurses, pharmacists, and other health care professionals in a concise, complete, and accurate manner. *The Merck Manual* continues to cover all the subjects expected in a textbook of internal medicine as well as detailed information on pediatrics, psychiatry, obstetrics, gynecology, dermatology, pharmacology, ophthalmology, otolaryngology, and a number of special subjects. *The Merck Manual* quickly provides information that helps practitioners achieve optimal care. The more specialized the practice of medicine becomes, the more important such information becomes. Specialists as well as generalists must at some time quickly access information about other specialties.

The 17th edition of *The Merck Manual* is the culmination of an arduous but rewarding 7-year enterprise. Every topic has been updated, and many have been completely rewritten. Topics new to this edition include hand disorders, prion diseases, death and dying, probabilities in clinical medicine, multiple chemical sensitivity, chronic fatigue syndrome, rehabilitation, smoking cessation, and drug therapy in the elderly, among others. The members of the Editorial Board, special consultants, and contributing authors are listed on the following pages with their affiliations. They deserve a degree of gratitude that cannot be adequately expressed here, but we know they will feel sufficiently rewarded if their efforts serve your needs.

Because of the extensive subject matter covered and a successful tradition developed through trials of successes and failures, *The Merck Manual* has some unique characteristics. We urge readers to spend a few minutes reviewing the Guide for Readers (p. xii), the Table of Contents at the beginning of each section (indicated by a thumb tab), and the Index (p. 2657). Subject headings within each section, internal headings within a subject discussion, and boldfaced terms in the text form an outline intended to help with use of the text.

We hope this edition of *The Merck Manual* will serve as an aid to you, our readers, compatible with your needs and worthy of frequent use. Suggestions for improvements will be warmly welcomed and carefully considered.

MARK H. BEERS, M.D., and ROBERT BERKOW, M.D., Editors

KAPOSI'S SARCOMA

(Multiple Idiopathic Hemorrhagic Sarcoma)

A multicentric vascular neoplasm caused by herpesvirus type 8 that has three forms: indolent, lymphadenopathic, and AIDS-related.

Lesions of Kaposi's sarcoma (KS) originate from multifocal sites in the mid-dermis and extend to the epidermis. Histopathology shows spindle cells and vascular spaces admixed to various degrees. The cell of origin is the endothelial cell, shown by specific staining for factor VIII; tumor cells resemble smooth muscle cells, fibroblasts, and myofibroblasts. The **indolent form of KS** manifests nodular or plaque-like dermal lesions. The **lymphadenopathic form** is disseminated and aggressive, involving lymph nodes, viscera, and occasionally the GI tract. In the **AIDS-related form** (see also Chs. 145 and 163), there may be few lesions or lesions may be widely disseminated in skin, mucous membrane, lymph nodes, and viscera.

Incidence

KS used to occur most often in Eastern Europe, Italy and the USA, mainly in the indolent form in men of Italian or Jewish ancestry > 60 yr old. Now, because of AIDS, KS is endemic in equatorial Africa, where it is more aggressive, occurs commonly in children and young men, and accounts for nearly 10% of all malignancies in Zaire and Uganda. Since 1981, aggressive KS has occurred in at least 1/3 of patients with AIDS and has assumed epidemic proportions in the USA and many other countries.

Symptoms and Signs

In older men without AIDS, KS generally appears on the toes or legs as purple or dark brown plaques or nodules that may fungate or penetrate soft tissue and invade bone; disseminated lymph node and visceral involvement follow in 5 to 10%.

In patients with AIDS, KS may be the first notable manifestation. Barely elevated purple, pink, or red papules or round or oval brown or purple plaques appear first primarily on the upper body or mucosa. They may become widely disseminated on the skin and are associated with visceral lesions and disseminated lymph node involvement. Bleeding, including from internal organs, may be extensive.

Treatment

For indolent superficial lesions, cryotherapy, electrocoagulation, or electron beam radiotherapy flattens and fades most lesions. Unresponsive dermal or lymph node disease with lymphedema is treated locally with 10 to 20 Gy of x-ray therapy.

AIDS-related KS has been treated with single agent or combination chemotherapy (eg, with etoposide, vincristine, vinblastine, bleomycin, and doxorubicin). Interferon- α effectively slows progression of early lesions and cures others. Intravesicular vinblastine is also very useful.

The course of KS in HIV infection is dictated by the level of immunosuppression, which determines the likelihood of opportunistic infections. Treatment of KS does not prolong life in most patients because infections dominate the clinical course.

SECTION 11 HEMATOLOGY AND ONCOLOGY

127 / ANEMIAS	849
Anemias Caused by Blood Loss	849
Acute Posthemorrhagic Anemia	855
Chronic Blood Loss Anemia	855
Anemias Caused by Deficient Erythropoiesis	856
Microcytic Anemias	856
Iron-Deficiency Anemia	858
Iron-Transport-Deficiency Anemia	860
Iron-Utilization Anemias	860
Anemia of Chronic Disease	861
Normochromic-Normocytic Anemias	861
Hypoproliferative Anemias	862
Aplastic Anemia	862
Myelodysplasia	864
Myelodysplasia	865
Nonmegaloblastic Macrocytic Anemia	865
Megaloblastic Macrocytic Anemias	865
Anemia Caused by Vitamin B ₁₂ Deficiency	865
Anemia Caused by Folate Deficiency	869
Anemia Caused by Vitamin C Deficiency	870
Anemias Caused by Excessive Hemolysis	870
Hemolysis Caused by Defects Extrinsic to the Red Cell	871
Anemia Caused by Reticuloendothelial Hyperactivity	872
Anemias Caused by Immunologic Abnormalities	872
Anemias Caused by Mechanical Injury	875
Hemolysis Caused by Intrinsic Red Cell Defects	875
Anemias Caused by Alterations of Red Cell Membrane	875
Anemias Caused by Disorders of Red Cell Metabolism	877
Anemias Caused by Defective Hemoglobin Synthesis	877
Sickle Cell Diseases	878
Hemoglobin C Disease	880
Hemoglobin S-C Disease	880
Hemoglobin E Disease	881
Thalassemias	881
Hemoglobin S- β -Thalassemia Disease	882
128 / IRON OVERLOAD	883

129 / TRANSFUSION MEDICINE	885
Blood Collection	885
Pretransfusion Testing	886
Blood Products	888
Technique	889
Complications	889
Therapeutic Hemapheresis	893
130 / MYELOPROLIFERATIVE DISORDERS	895
Polycythemia Vera	896
Secondary Erythrocytosis	900
Myelofibrosis	900
Primary Thrombocythemia	901
Secondary Thrombocythemia	902
131 / HEMOSTASIS AND COAGULATION DISORDERS	902
Hereditary Coagulation Disorders	911
Hemophilia	911
Uncommon Hereditary Coagulation Disorders	913
Acquired Coagulation Disorders	915
Liver Disease-Related Coagulation Disorders	915
Disseminated Intravascular Coagulation	915
Coagulation Disorders Caused by Circulating Anticoagulants	917
132 / THROMBOTIC DISORDERS	918
133 / PLATELET DISORDERS	920
Thrombocytopenia	920
Platelet Dysfunction	925
134 / VASCULAR BLEEDING DISORDERS	928
Purpura Simplex	928
Senile Purpura	928
Hereditary Hemorrhagic Telangiectasia	929
Hemoch-Schönlein Purpura	930
Vascular Purpura Caused by Dysproteinemias	930
Leukocytoclastic Vasculitis	930
Autoerythrocyte Sensitization	930
135 / LEUKOPENIA AND LYMPHOCYTOPENIA	931
136 / EOSINOPHILIC DISORDERS	938
137 / HISTIOCYTIC SYNDROMES	941
138 / LEUKEMIAS	944
Acute Leukemia	946
Chronic Leukemia	949
Myelodysplastic Syndrome	953
139 / LYMPHOMAS	955
Hodgkin's Disease	955
Non-Hodgkin's Lymphomas	958
Burkitt's Lymphoma	962
Mycosis Fungoides	962
140 / PLASMA CELL DYSCRASIAS	963
Monoclonal Gammopathy of Undetermined Significance	963
Macroglobulinemia	964
Multiple Myeloma	965
Heavy Chain Diseases	968

141 / DISORDERS OF THE SPLEEN	969
Hypersplenism	970
Splenic Rupture	973
142 / OVERVIEW OF CANCER	973
143 / TUMOR IMMUNOLOGY	981
Tumor Antigens	981
Host Response to Tumors	982
Tumor Immunodiagnosis	983
Immunotherapy	984
144 / PRINCIPLES OF CANCER THERAPY	986
145 / AIDS-ASSOCIATED HEMATOLOGIC DISORDERS AND MALIGNANCIES	996

127 / ANEMIAS

Decreases in numbers of RBCs or Hb content caused by blood loss, deficient erythropoiesis, excessive hemolysis, or a combination of these changes.

Abbreviations Used in This Chapter

AdoCbl	Adenosylcobalamin	Hct	Hematocrit
ag	Allotrans	MCH	Mean corpuscular Hb
AIHA	Autoimmune hemolytic anemia	MCHC	Mean corpuscular Hb concentration
ATG	Equine antithymocyte globulin	MCV	Mean corpuscular volume
C3	Complement	MeCbl	Methylcobalamin
CBC	Complete blood count	NaCl	Sodium chloride
EDTA	Ethylenediaminetetraacetic acid	O ₂	Oxygen
ELISA	Enzyme-linked immunosorbent assay	PCH	Paroxysmal cold hemoglobinuria
EPO	Erythropoietin	PNH	Paroxysmal nocturnal hemoglobinuria
Fe	Iron	Po ₂	Partial pressure of oxygen
G6PD	Glucose-6-phosphate dehydrogenase	RBC	Red blood cell
Hb	Hemoglobin	RDW	RBC volume distribution width
		WBC	White blood cell

The term anemia has been used incorrectly as a diagnosis; more properly, it denotes a complex of signs and symptoms. The type of anemia defines its pathophysiologic mechanism and its essential nature, allowing for appropriate therapy. Not investigating mild anemia is a serious error; its presence

indicates an underlying disorder, and its severity reveals little about its genesis or true clinical significance.

The symptoms and signs of anemia represent cardiovascular-pulmonary compensatory responses to the severity and duration of tissue hypoxia. Severe anemia (eg, Hb <

7 g/dL) can be associated with weakness, vertigo, headache, tinnitus, spots before the eyes, fatigability, drowsiness, irritability, and even bizarre behavior. Amenorrhea, loss of libido, GI complaints, and sometimes jaundice and splenomegaly can occur. Finally, heart failure or shock can result.

General diagnostic patterns can expedite the differential diagnosis (see TABLE 127-1). Anemia results from one or more of three basic mechanisms: **blood loss**, **deficient erythropoiesis** (RBC production), and **excessive hemolysis** (RBC destruction). Blood loss should be the first consideration. Once it is ruled out, only the other two mechanisms need to be considered. Because RBC survival is 120 days, maintenance of a steady RBC population requires daily renewal of 1/120 of the cells. Complete cessation of erythropoiesis results in a decline of about 10%/wk (1%/day) of RBCs. Deficient erythropoiesis results in relative or absolute reticulocytopenia. When RBC values fall > 10%/wk (ie, 500,000 RBCs/ μ L) without blood loss, hemolysis is a causative factor.

A convenient approach to most anemias that result from deficient erythropoiesis is to examine changes in RBC size and shape. Thus, microcytic anemias (see Laboratory Tests, below) suggest altered heme or globin synthesis (eg, iron [Fe] deficiency, thalassemia and related Hb-synthesis defects, anemia of chronic disease). In contrast, normochromic-normocytic anemias suggest a hypoproliferative or hypoplastic mechanism. Some anemias are characterized by macrocytes (large RBCs), which suggest a defect in DNA synthesis. These anemias are usually caused by defective vitamin B₁₂ or folic acid metabolism or by an interference with DNA synthesis by chemotherapeutic cytoreductive drugs. Adequate marrow response to anemia is evidenced by peripheral blood reticulocytosis or polychromatophilia.

TABLE 127-1. CHARACTERISTICS OF COMMON ANEMIAS

Etiology or Type	Morphologic Changes	Special Features
Acute blood loss	Normochromic-normocytic, with polychromatophilia; hyperplastic marrow	If severe, possible nucleated RBCs and left shift of WBCs; leukocytosis and thrombocytosis
Chronic blood loss	Same as iron deficiency, may show severe hemorrhage has supervened	Possible features of acute blood loss if recent
Iron deficiency	Microcytic, with anisocytosis and poikilocytosis; reticulocytopenia; hyperplastic marrow, with delayed hemoglobinization	Possible achlorhydria, smooth tongue, and spoon nails; absent stainable marrow Fe; low serum Fe; increased total Fe-binding capacity; low serum ferritin; low RBC ferritin
Vitamin B ₁₂ deficiency	Oval macrocytes; anisocytosis; reticulocytopenia; hypersegmented WBCs; megaloblastic marrow	Serum B ₁₂ < 180 pg/mL (< 130 pmol/L); frequent GI and CNS involvement; positive Schilling test, elevated serum bilirubin; increased LDH; antibodies to intrinsic factor in serum (common), absent gastric intrinsic factor secretion
Folate deficiency	Same as vitamin B ₁₂ deficiency	Serum folate < 5 ng/mL (< 11 nmol/L); RBC folate < 225 ng/mL RBCs (< 510 nmol/L); nutritional deficiency and malabsorption (sprue, pregnancy, infancy, alcoholism)
Marrow failure	Normochromic-normocytic; reticulocytopenia; failed marrow aspiration (often) or evident hypoplasia of erythroid series or of all elements	Idiopathic (> 50%) or secondary to exposure to toxic drugs or chemicals (eg, chloramphenicol, quinine, hydantoins, insecticides)

Fe = iron.

TABLE 127-1. Continued

Etiology or Type	Morphologic Changes	Special Features
Sideroblastic anemia	Usually hypochromic but dimorphic with normocytes and macrocytes; hyperplastic marrow, with delayed hemoglobinization; ringed sideroblasts	Inborn or acquired metabolic defect; stainable marrow Fe (plentiful); response to B ₆ (rare); commonly part of myelodysplastic syndrome
Acute hemolysis	Normochromic-normocytic; reticulocytosis; marrow erythroid hyperplasia	Increased serum bilirubin and LDH; increased stool and urine urobilinogen; hemoglobinuria in fulminating cases; hemosiderinuria
Chronic hemolysis	Normochromic-normocytic; reticulocytosis; marrow erythroid hyperplasia; basophilic stippling (especially in lead poisoning)	Increased serum bilirubin and LDH; shortened RBC life span; increased radio-Fe turnover; hemosiderinuria
Hereditary spherocytosis	Spheroidal microcytes; normochromic-normocytic; hyperplasia	Increased mean RBC Hb concentration; increased RBC fragility; shortened survival of labeled RBCs; increased radioactivity of spleen (exceeds that of liver)
Paroxysmal nocturnal hemoglobinuria	Normocytic (may be hypochromic) because of Fe deficiency; marrow may be hypercellular or hypocellular	Dark morning urine; hemosiderin; positive acid hemolysis (Ham's) and sugar-water tests
Paroxysmal cold hemoglobinuria	Normochromic-normocytic	Follows exposure to cold; results from a cold agglutinin or hemolysin; often associated with syphilis or other infections
Sickle cell anemia	Anisocytosis and poikilocytosis; some sickle cells in smear; all RBCs sickle in preparation with hypoxia or hyperosmolar exposure	Largely limited to blacks; urinary isos-themuria; Hb S on electrophoresis; possibly painful vaso-occlusive crises and leg ulcers; bony changes on x-ray
Thalassemia	Microcytic; thin cells; target cells; basophilic stippling; anisocytosis and poikilocytosis; nucleated RBCs in homozygotes	Decreased RBC fragility; elevated Hb A ₂ and Hb F (often); Mediterranean ancestry (common); anemic homozygotes from infancy; splenomegaly; bony changes on x-ray
Infection or chronic inflammation	Normochromic-normocytic early, then microcytic; normoblastic marrow; normal Fe stores	Decreased serum Fe; decreased total Fe-binding capacity; normal serum ferritin, RBC ferritin, and marrow Fe content
Marrow replacement (myelophthisis)	Anisocytosis and poikilocytosis; nucleated RBCs; early granulocyte precursors; marrow aspiration may fail or may show leukemia, myeloma, or metastatic cells	Marrow infiltration with infectious granulomas, tumors, fibrosis, or lipid histiocytosis; possible hepatomegaly and splenomegaly; possible bony changes; radio-Fe uptake greater over spleen and liver than over sacrum

Similarly, a few common mechanisms of increased destruction (eg, sequestration by the spleen, antibody-mediated hemolysis, defective RBC membrane function, abnormal Hb) greatly aid in the differential diagnosis of hemolytic anemias.

A critical tenet in managing anemias is to give specific therapy, which implies that a specific diagnosis is necessary. The response to therapy corroborates the diagnosis. Although multidrug (or "shotgun") therapy may provide transient repair of the anemia, such therapy is not justifiable because it risks serious sequelae. RBC transfusion provides a form of instant repair that should be reserved for patients with cardiopulmonary symptoms, signs of active uncontrollable blood loss, or some form of hypoxicemic end-organ failure. Transfusion procedures and blood components are discussed in Ch. 129.

TABLE 127-2 classifies anemias according to cause.

TABLE 127-2. ANEMIAS CLASSIFIED BY CAUSE

Blood loss	
Acute	
Chronic	
Deficient erythropoiesis	
Microcytic	
Iron deficiency	
Iron-transferrin deficiency	
Iron utilization	
Thalassemias (see intrinsic RBC defects, below)	
Normochromic-normocytic	
Hypoproliferation	
In kidney disease	
In endocrine failure (thyroid, pituitary)	
In protein depletion	
Aplastic anemia	
Myelophthisis	
Myelodysplasia (see Ch. 138)	
Macrocytic	
Vitamin B ₁₂ deficiency	
Folate deficiency	
Copper deficiency (see Ch. 4)	
Vitamin C deficiency	
Excessive hemolysis	
Extrinsic RBC defects	
Reticuloendothelial hyperactivity with splenomegaly	
Extrinsic RBC defects (continued)	
Immunologic abnormalities	
Isoimmune (isoagglutinin) hemolysis	
Autoimmune hemolysis	
Warm antibody hemolysis	
Cold antibody hemolysis	
Paroxysmal nocturnal hemoglobinuria	
Mechanical injury	
Trauma	
Infection	
Intrinsic RBC defects	
Membrane alterations	
Congenital	
Congenital erythropoietic porphyria (see Ch. 14)	
Hereditary elliptocytosis	
Hereditary spherocytosis	
Acquired	
Stomatocytosis	
Hypophosphatemia	
Metabolic disorders (inherited enzyme deficiencies)	
Emden-Meyerhof pathway defects	
Hexose monophosphate shunt defects	
G6PD deficiency	
Hemoglobinopathies	
Sickle cell anemia (Hb S)	
Hb C, S-C, and E diseases	
Thalassemias (β , β -6, and α)	
Hb S- β -thalassemia disease	

sure should be exerted on the stopper end of the tube. Whenever possible, sterile tubes or needle and tube arrangements that have a check valve should be used.

Ethylenediaminetetraacetic acid (EDTA) is the preferred anticoagulant for blood collection because the morphology is less distorted and platelets are better preserved. It can be added to clean test tubes, or vacuum tubes containing EDTA may be obtained commercially. Slides should be prepared within 3 to 4 h after obtaining blood, or within 1 to 2 h for platelet counts.

For small amounts of blood or when venipuncture is infeasible, the finger, the earlobe, or, in infants, the plantar surface of the heel is punctured quickly with a sterile disposable lancet, piercing deeply enough to ensure spontaneous flow of blood. Undue pressure that might cause tissue fluids to dilute the blood should be avoided during collection.

In some circumstances, EDTA tubes are used for coagulation testing. Regardless of the anticoagulant used, because significant anemia (Hct < 20%) or polycythemia (Hct > 50%) may affect coagulation results, the sample volume must be adjusted after CBC data are known. For significant anemia, less blood can be added to the fixed amount of anticoagulant by drawing the blood in a syringe; for polycythemia, the amount of anticoagulant must be reduced (see TABLE 127-3).

Complete blood count: The CBC is a basic evaluation that usually includes Hb, Hct, WBC count, WBC differential count, platelet count, a description of the blood smear relative to RBC morphology and degree of polychromatophilia, and platelet spread and architecture. An RBC count is often included, especially when calculation of RBC indices is desired.

Indications for a CBC include suspected hematologic, inflammatory, neoplastic, or infectious disease and screening of infants < 1 yr, pregnant women, the institutionalized elderly, and patients with nutritional abnormalities. Its value during routine patient evaluation on hospital admission is controversial.

Anemia, erythrocytosis, leukemias, bone marrow failure, infection, inflammation, or adverse drug reactions may be detected. Blood smear examination can help detect other abnormalities (eg, thrombocytopenia, malarial and other parasites, significant for-

TABLE 127-3. ADJUSTING SAMPLE VOLUME FOR HEMATOCRIT IN COAGULATION TESTING

Hct (vol %)	Blood Volume for 0.5 ml Anticoagulant	
	IN ADULTS	IN CHILDREN
10	3.0	1.8
12	3.0	1.8
14	3.1	1.9
16	3.2	1.9
18	3.3	2.0
20	3.4	2.0
> 20, < 50	4.5*	2.7*
> 50	Use specially prepared tube with reduced anticoagulant volume	

*When the tube is allowed to fill passively, the vacuum in the tube should automatically draw this volume.

mation of rouleaux, nucleated RBCs or immature granulocytes, inclusions in RBCs or granulocytes) that may occur despite normal counts. Evaluation of the blood smear is important to assess RBC morphology and abnormal WBCs.

Through automated technology, the RBC count, Hb, Hct, and platelet count are available in about 30 sec. In rare cases, blood counts can also be measured by mixing a measured volume of blood with an appropriate diluent or lysing agent and counting in a chamber under the microscope. Hb can be measured colorimetrically after treatment with dilute hydrochloric acid, which permits colorimetric or spectrophotometric comparison with standards of hematin or cyanmethemoglobin, respectively. Hct can be measured by centrifuging a volume of blood and determining the percentage of RBCs relative to total blood volume. The WBC differential count is measured by staining a drop of blood on a glass slide with a metachromatic stain (eg, Wright's) and examining it with oil immersion microscopy. A minimum of 100 WBCs are counted; each type is reported as a percentage. Some automated instruments also measure differential counts by pattern recognition. The platelet number can be

estimated on the blood smear (using 20,000/ μ L for each platelet seen in a given [90 $\times$] oil immersion field).

Normal values for the total WBC count range between 4,300 and 10,800/ μ L; normal values for the differential WBC count are as follows: segmented neutrophils, 34 to 75%; band neutrophils, $\leq$ 8%; lymphocytes, 12 to 50%; monocytes, 3 to 15%; eosinophils, $\leq$ 5%; and basophils, $\leq$ 3%.

RBC counts: The normal range at sea level is 5.4 $\pm$ 0.8 million/ μ L for men and 4.8 $\pm$ 0.6 million/ μ L for women. At birth, this count is slightly higher; by the 3rd month, it falls to about 4.5 $\pm$ 0.7 million/ μ L and slowly increases after age 4 through puberty.

Normal Hb is 16 $\pm$ 2 g/dL for men and 14 $\pm$ 2 g/dL for women. Hct (ie, the volume of packed RBCs) is 47 $\pm$ 5% for men and 42 $\pm$ 5% for women. The diagnostic criterion for anemia in men is RBC $<$ 4.5 million/ μ L, Hb $<$ 14 g/dL, or Hct $<$ 42%; for women this criterion is RBC $<$ 4 million/ μ L, Hb $<$ 12 g/dL, or Hct $<$ 37%.

Reticulocyte count: Daily RBC replacement (40,000 to 50,000/ μ L) represents 0.5 to 1.5% of the total RBC count. These cells can be identified as polychromatophilic cells on routine staining (eg, Wright's or Giemsa stain colors remnants of RNA) or as reticulocytes on supravital staining, which recognizes endoplasmic reticular material within the cells. The reticulocyte count is done by taking a few drops of blood initially stained with fresh methylene blue, then counterstained with Wright's stain. Under oil immersion, the number of 1000 consecutive RBCs having a blue-staining reticulum are counted and expressed as a percentage (normally 0.5 to 1.5%). Reticulocytes may be enumerated using automated differential counters.

Because reticulocytes represent a young cell population, reticulocyte count is an important criterion of marrow activity that can be considered a response to a need for RBC renewal. An increased reticulocyte count (reticulocytosis) suggests a restoration response after acute blood loss or specific therapy for anemias caused by deficient erythropoiesis (ie, vitamin B₁₂, folic acid, and Fe-deficiency anemias). Reticulocytosis is particularly prominent in hemolytic anemias and in acute and severe bleeding. A normal reticulocyte count in anemia indicates failure of the bone marrow to respond appropriately. Such a reticulocytopenia is usually

caused by a nutrient or hormonal deficiency resulting in deficient erythropoiesis; one dramatic mechanism is the presence of viral infections (especially human parvovirus B19) as a cause for severe, but transient, decreased RBC production.

RBC indices: The type of anemia may be indicated by the RBC indices: mean corpuscular volume (MCV), mean corpuscular Hb (MCH), and mean corpuscular Hb concentration (MCHC). RBC populations are termed **microcytic** (MCV $<$ 80 fL) or **macrocytic** (MCV $>$ 95 fL). The term **hypochromia** refers to RBC populations with MCH $<$ 27 pg/RBC or MCHC $<$ 30%. These quantitative relationships can usually be recognized on a peripheral blood smear and, together with the indices, permit a classification of anemias that correlates with etiologic classification (see TABLE 127-1) and greatly aids diagnosis.

Automated electronic techniques directly measure Hb, RBC count, and MCV, whereas Hct, MCH, and MCHC are derived from these data. Thus, the MCV has become the most important RBC index in the differential diagnosis of anemias, and confidence in the derived figures (especially Hct) has declined. Automated-flow cytometry provides a new parameter in differential diagnosis: A histogram of anisocytosis (variation in cell size) can be automatically expressed as the coefficient of variation of the RBC volume distribution width (RDW).

Poikilocytosis (variation in shape) may also occur. RBC injury may be identified by finding RBC fragments, portions of disrupted cells (schistocytes), or evidence of significant membrane alterations from oval-shaped cells (ovalocytes) or spherocytic cells. Target cells (thin RBCs with a central dot of Hb) are RBCs with insufficient Hb or excess membrane.

Bone marrow aspiration and biopsy: These studies provide direct observation of erythroid activity and maturation of the RBC precursors; abnormal maturity (dyspoiesis) of the cells; and semiquantitation of the amount, distribution, and cellular pattern of Fe content. These are helpful in anemias, other cytopenias, unexplained leukocytosis, and thrombocytosis and when leukemia or myelophthisis is suspected. Simultaneous culture of the bone marrow aspirate is an excellent diagnostic tool in patients with FUO. Cytogenetic and molecular analyses

can be performed on aspirate material in hemopoietic or other neoplasms or in suspected congenital lesions. Flow cytometry can be performed in suspected lymphoproliferative or myeloproliferative states to define the immunophenotype.

Because bone marrow aspiration and biopsy are not difficult nor do they pose significant invasive risk, they should be performed early in suspected hematologic diseases. In general, both can be performed as a single procedure. Because biopsy requires adequate bone depth, usually the posterior (or less commonly, anterior) iliac crest is used. After the biopsy needle is inserted, a small amount of marrow (preferably $<$ 0.5 mL) is aspirated into a syringe. A few drops are smeared directly onto slides, stained with metachromatic stains (eg, May-Grünwald, Giemsa, Wright's), and examined under a microscope. The remaining aspirate can be placed in heparin for subsequent study or cytogenetic analysis; a portion can be permitted to clot and is handled as a surgical tissue. If bone marrow culture is desired, 1 mL is aspirated through the same implanted needle after the histologic material has been obtained. The core biopsy can be obtained by advancing the same needle 1 cm and performing rotary cutting. The core must be decalcified and handled as surgical tissue. If only aspiration is sought, the sternum or dorsal lumbar vertebral spine marrow should be avoided because dilution with peripheral blood makes interpretation difficult.

RBC fragility (osmotic fragility): Twelve small test tubes containing sodium chloride (NaCl) solutions varying from 0.28 to 0.5% in 0.02% increments are prepared. A drop of the patient's blood is placed in each tube, and the blood of a normal control is added to another series of tubes. The percentage of NaCl at which hemolysis begins (normally $\approx$ 0.44 $\pm$ 0.04%) and the percentage at which the first tube shows complete hemolysis (usually about 0.32 $\pm$ 0.04%) are noted. If many spherocytes are present, as in familial hemolytic jaundice (eg, congenital spherocytosis), hemolysis appears at higher concentrations because of the increased fragility. If the predominating cell is abnormally thin, as in β -thalassemia major, hemolysis first appears at lower concentrations and may never be complete.

Other tests are discussed below under specific anemias and bleeding disorders. For tests of hemostasis (eg, bleeding time, clot retraction and observation, fibrin and fibrinogen degradation products, partial thromboplastin time and prothrombin time), see TABLE 131-2.

ANEMIAS CAUSED BY BLOOD LOSS

ACUTE POSTHEMORRHAGIC ANEMIA

Anemia caused by rapid massive hemorrhage.

Etiology and Pathogenesis

Because marrow reserve is limited, anemia may result from massive hemorrhage associated with spontaneous or traumatic rupture or incision of a large blood vessel, erosion of an artery by lesions (eg, peptic ulcer, neoplasm), or failure of normal hemostasis. Immediate effects depend on the duration and volume of hemorrhage. Sudden loss of 1/3 of blood volume may be fatal, but as much as 2/3 may be lost slowly over 24 h without such risk. Symptoms are caused by a sudden decrease in blood volume and by subsequent hemodilution with a decrease in the O₂-carrying capacity of the blood.

Symptoms and Signs

The pace of the hemorrhage determines the degree of symptoms. Faintness, dizziness, thirst, sweating, weak and rapid pulse, and rapid respiration (at first deep, then shallow) may occur. Orthostatic hypotension is common. BP may at first rise slightly because of reflex arteriolar constriction, then gradually fall. If bleeding continues, BP may fall and death may ensue (see also Ch. 204).

Laboratory Findings

During and immediately after hemorrhage, the RBC count, Hb, and Hct may be deceptively high because of vasoconstriction. Within a few hours, tissue fluid enters the circulation, resulting in hemodilution and a drop in the RBC count and Hb proportional to the severity of bleeding. The resultant anemia is normocytic. Polymorphonuclear granulocytosis and a rise in platelet count may occur within the first few hours.