SEVENTH EDITION

Clinical Hematology

- MAXWELL M. WINTROBE, B.A., M.D., B.Sc. (Med.), Ph.D., D.Sc. (Hon., Manitoba), D.Sc. (Hon., Utah), Distinguished Professor of Internal Medicine, University of Utah
- G. RICHARD LEE, M.D., Professor of Medicine, and Associate Dean, University of Utah
- DANE R. BOGGS, M.D., Professor of Medicine and Chief, Hematology Section, Department of Medicine, University of Pittsburgh
- THOMAS C. BITHELL, M.D., Associate Professor, Clinical Pathology and Internal Medicine, University of Virginia
- JOHN W. ATHENS, M.D., Professor of Medicine and Chief, Hematology Division, Department of Internal Medicine, University of Utah
- JOHN FOERSTER, M.D., Assistant Professor, Department of Internal Medicine, University of Manitoba

SEVENTH EDITION

LEA & FEBIGER



PHILADELPHIA

First Edition, 1942. Reprinted, 1943, 1944 (Twice)

Second Edition, 1946. Reprinted, 1946 (Twice), 1947 (Twice), 1949

Third Edition, 1951. Reprinted, 1952 (Twice), 1953

Fourth Edition, 1956. Reprinted, 1956, 1957, 1958

Fifth Edition, 1961. Reprinted 1962 (Twice), 1964, 1965

Sixth Edition, 1967. Reprinted 1968.

Seventh Edition, 1974

First Spanish Edition, 1948 Second Spanish Edition, 1960 First Italian Edition, 1958 First Greek Edition, 1965

Library of Congress Cataloging in Publication Data

Main entry under title: Clinical hematology.

First-6th ed., by M. M Wintrobe.

1. Hematology I. Wintrobe, Maxwell Myer, 1901- II. Wintrobe, Maxwell Myer, 1901- Clinical hematology. [DNLM: 1. Blood.

2. Hematologic diseases. WH100 W794c 1974]

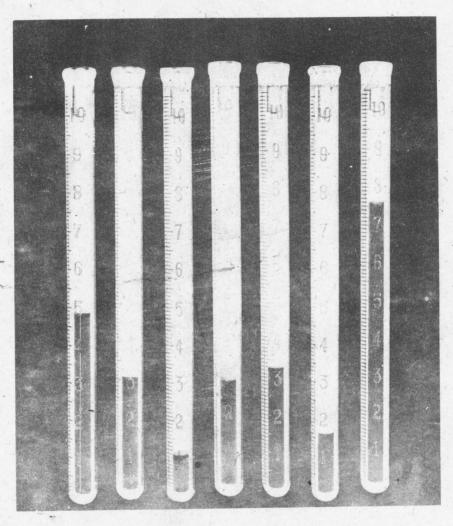
RB145.C54 1974 616.1'5 73-23029

ISBN 0-8121-0414-5

Copyright © 1974 by Lea & Febiger. Copyright under the International Copyright Union All Rights Reserved. This book is protected by copyright. No part of it may be reproduced in any manner or by any means without written permission of the publisher.

Published in Great Britain by Henry Kimpton Publishers, London
PRINTED IN THE UNITED STATES OF AMERICA

PLATE I



A B C D E F G

The appearance of centrifuged blood in various conditions.

- A, Normal blood.
- B, Anemia associated with chronic infection.
- C, Iron-deficiency anemia. The blood plasma is very pale.
- D. Chronic myelocytic leukemia. There are distinct layers of white corpuscles and of platelets above the red corpuscles.
- E, Post-hepatic jaundice and moderate anemia. In this case the coloring of the blood plasma is due to biliary obstruction rather than to increased blood destruction.
- F, Pernicious anemia. Note the small amount of packed red corpuscles, the very narrow layer of leukocytes and platelets, and the coloring of the blood plasma due to hyperbilirubinemia.
 - G. Polycythemia.

(The blood was collected and treated as described on page 1110.)

SBW39 /05 OL

Preface

More than three decades have passed since I first began the task of assembling what was known about hematology in book form. Even then, the undertaking was not easy. Since that time, hematology has developed to a degree unmatched by any other field of medicine, in scope as well as in the depth of our understanding. Hematology now encompasses broad aspects of cytology, biochemistry, molecular biology, biophysics and immunology, not to speak of the various ramifications of clinical medicine.

The first six editions of Clinical Hematology were written entirely by me. With each edition the task has become more challenging and it has been more and more difficult to do justice to all dimensions of this remarkable field.

In planning the Seventh Edition, therefore, I enlisted the collaboration of some of my present and former associates. Their names are given on the title page. They were chosen because of their special interest in certain aspects of hematology, in addition to their thorough understanding of the whole field of hematology and their proved qualifications.

The organization of the book has been revised in keeping with present-day needs. In Part I, the approach to hematologic problems is considered from the viewpoint of the clinician. The principles of hematologic examinations are discussed and the simpler methods are outlined for the physician's own use. In addition, the principles and pitfalls of modern machines are presented. These discussions are presented so that the person who carries the ultimate responsibility for the patient will have enough understanding to do so with

confidence. This book, however, is not intended to be a laboratory manual.

In Part II a thorough account is given of the essentials of cytology, physiology, and biochemistry as they apply to the hematopoietic system. Such an understanding is essential for the intelligent and effective application of modern-day knowledge to medical practice. To attempt to practice hematology without an understanding of the normal hematopoietic system, as described in Part II, and without a physiologically basic concept regarding the approach to a hematologic problem would be like trying to sail in the open sea without landmarks or instruments and under a sky without stars.

To aid in the approach to the different varieties of hematologic problems, chapters and subsections which introduce the various areas or types of problems have been prepared; eg, the approach to the patient with anemia (Chapter 13), a kinetic approach to normocytic anemias (Chapter 19), an approach to hemolytic anemias (Chapter 20), a diagnostic approach to the bleeding disorders (Chapter 33), and the approach to the patient with disorders of the phagocytic and lymphatic systems (Chapter 40). In regard to treatment, the approaches are as diverse as hematologic conditions are varied.

In order to bring together in a single volume the ever-expanding body of information pertaining to clinical hematology, we have condensed some of the material found in earlier editions. Methodology, for example, has been given less space because advanced technology has produced sophisticated machines that have rendered it unnecessary for the physician to carry out as many procedures as he used to perform. Yet he must understand these procedures—their purpose, their degree of reliability, and their pitfalls—and he must continue to be at home with elementary morphology, such as that required for examination of the blood smear and the bone marrow. Consequently, discussions of the latter topics have not been abbreviated. In hematology, morphologic examinations hold importance equal to the medical interview and the physical examination and should never be neglected. The morphologic descriptions are supported by 24 plates in color, most of which are new.

We have attempted to control the size of the book, but not at the expense of thoroughness and excellence. Furthermore, our original policy of providing, insofar as possible, careful and complete documentation, still obtains. As in past editions, reference lists are selective, as are citations in the text. When necessary, preference has been given to the latest report on a subject, in which the interested reader may find additional references to earlier literature. Whenever possible, comprehensive reviews and monographs have been listed. In citing the literature when a study has been carried out by more than two authors only the name of the first is given. Our apology is offered to those whose names are not listed.

In keeping with the decisions of the editorial boards of *Blood* and of the *British Journal of Haematology*, as well as other publications, we have adopted most of the units of the system recommended by the International Committee for Standardization in Hematology. These and their former equivalents appear inside the back cover of this book, as does our system of abbreviations. The style adopted for bibliographic material is that recommended by the Index Medicus of 1973.

Although each co-author, including the senior author, has assumed primary responsibility for certain chapters, no chapter is solely the work of one person, and all the material in this book has been thoroughly reviewed and edited by the senior author. Each member of the team has contributed in

some degree to chapters written by others, and all have utilized the material of earlier editions when this was appropriate.

As always, the preparation of a new edition of this book has been a rewarding though arduous task. Todav's young hematologist probably has no conception of the rate at which his specialty has developed, especially since the mid-twenties. Clinical hematology exemplifies the ways in which clinical medicine has fed the basic sciences with questions and with clues, and the basic sciences in turn have illuminated human disease. The science of nutrition, for example, was enormously stimulated by the investigations that established the role of vitamin B₁₂ in pernicious anemia and those demonstrating the role of other vitamins in hematopoiesis. Exploration into the phenomenon of sickling opened the whole field of molecular biology and brought to light the many hemoglobinopathies of which we are now aware. These remarkable advances in turn prompted investigation of the pathogenesis of thalassemia, which revealed pathogenetic mechanisms hitherto unknown. Basic investigations of carbohydrate metabolism and of the metabolism of the red cell resulted in the recognition of enzyme deficiencies of the red cell, some of which have serious consequences. Many other examples of the interplay of basic science and clinical medicine could be cited.

We should like to express our gratitude to Dr. Arthur Haut of the University of Arkansas for two chapters; Dr. Wallace N. Jensen of George Washington University for one chapter; Dr. A. S. Wiener for reviewing the chapter on blood groups and blood transfusion and making valuable suggestions; Dr. Phaedon Fessas for valuable comments regarding the chapter on thalassemia; Dr. George Stamatovannopoulos for his advice regarding hereditary polycythemias; Dr. W. A. Schroeder for his comments on hemoglobinopathies; and, for their comments and criticisms of various other chapters, Doctors E. J. Hershgold, Gerald Rothstein, R. E. Lynch, James Kushner, Dana Wilson and Joseph Sannella of the University of Utah, Phillip M. Allen, Byrd S. Leavell and Oliver B. Babbit of the University of Virginia, Alan Winkelstein and Sallie Boggs of the University of Pittsburgh, and Frixos Paraskevas of the University of Manitoba.

We are especially indebted to Dr. Albert Clarysse, formerly Assistant Professor of Medicine, University of Utah, for his skillful preparation of photomicrographs, as well as to Miss Anne Sasyniuk of the University of Manitoba; to those who generously furnished illustrations from their publications or personal collection; and to their publishers. These include Dr. Dorothea Zucker-Franklin, Dr. Walter Seegers, Dr. C. L. Conley, and Dr. William McDivitt.

Secretarial assistance has been provided by Vreni Bithell, Carolyn Bailes, Franklin White

Barnes, Mary Welch, and Pearl Emery, but it is with very special appreciation that the many long hours of hard work and the extraordinary efficiency of the senior author's secretary, Mrs. Katharyn Rees, are acknowledged. Without such unstinting effort his task would have been much more difficult.

It is a special pleasure, also, to acknowledge the skill and whole-hearted cooperation of the publishers, Lea & Febiger and their staff, especially Mr. T. J. Colaiezzi and Miss Emily Anderson.

As in the past, I must express my sincere appreciation of the understanding and unselfish support of my wife. With this edition, the support of the wives of my collaborators also is gratefully acknowledged.

MAXWELL M. WINTROBE

Salt Lake City, Utah

Contents

Part I. Introduction	
1. The Approach to Hematologic Problems	3
General considerations 3 Principles of hematologic examination 6	
Part II. The Normal Hematopoietic System	
Section 1. Basic Cytology	41
2. Origin and Development of the Blood and Blood-Forming Tissues	41
Proliferation and differentiation of cells 42 Hematopoietic stem cells 49 Blood formation in the embryo and fetus 53 Blood of newborn infants and children 56 Extramedullary hematopoiesis 57 Medullary hematopoiesis 59 Methods of obtaining bone marrow specimens 63 Preparations of bone marrow specimens 66 Examination of bone marrow specimens 67 Indications for marrow aspiration 73 Indications for bone marrow biopsy 75	
Section 2. The Erythrocyte	80
3. Morphology, Intrinsic Metabolism, Function, Laboratory Evaluation	80
Discovery of the erythrocyte and early studies 80 Normal development of the erythrocyte 81 The mature erythrocyte 91 Laboratory evaluation of erythrocytes 109	

•	4. Production of Erythrocytes	135
	Nutritional requirements for red cell production 135 Iron metabolism 154	
	Hemoglobin structure and synthesis 167 Control of erythropoiesis 179	
	5. Destruction of Erythrocytes	195
	The life span of the erythrocyte 195 Erythrocyte aging 200	
	Mechanisms of red cell destruction 201 Sites of erythrocyte destruction 204	
	Hemoglobin catabolism 208	
Sectio	n 3. Leukocytes, Spleen, and the Reticuloendothelial System	221
(6. Granulocytes and Monocytes	221
	Morphology and chemical properties 221 Leukocyte kinetics 243	
	Neutrophil series—Kinetics, properties, and function 244	
	Eosinophil series—Kinetics, properties, and function 262	
**	Basophil series—Kinetics, properties, and function 265 Monocyte series—The mononuclear phagocyte system—Kinetics, properties, and function 267	
	7. Lymphocytes and Lymphatic Tissues and Their Relation to Humoral and Cellular Immunity	286
	The lymphatic system 287	
	Development of the immune system 293 Lymphokinetics 298	
	Lymphocyte function 305	
	Complement 333 Methods of examination 337	
8	3. The Reticuloendothelial (Mononuclear Phagocyte) System and the Spleen	351
	The reticuloendothelial (mononuclear phagocyte) system (RES, MPS) 351 The spleen 354	
€ 2 • ₅	Structure 354 Changes in the blood following splenectomy 358 Functions 360	
Sectio	n 4. Platelets, Hemostasis, and Coagulation	371
<u> </u>	D. Platelets and Megakaryocytes: The Physiology of Primary Hemostasis	372

	The blood platelet 372	
	The megakaryocyte 380	
•	Kinetics of thrombopoiesis 383	
	The vascular phase of hemostasis 389	
	The platelet phase of hemostasis 390	
	Homeostatic control mechanisms 399	
	Miscellaneous platelet functions 399	r
10.	Blood Coagulation	409
	The coagulation factors 409	
	The physiology of coagulation 421	
	Homeostatic control mechanisms 430	
	The fibrinolytic enzyme system 432	•
•	Homeostatic significance of coagulation 438	
Section	5. Blood Groups and Blood Transfusion	451
11.	Transfusion of Red Cells	451
	Blood groups 451	
	Methods of blood typing 469	
	Collection and preservation of blood 472	
	Blood transfusion 474	
	Clinical use of plasma and plasma derivatives 488	
12	Leukocyte and Platelet Antigens and Transfusions	400
12.	Ecukocyte and Flatelet Antigens and Flansiusions	498
4	Leukocyte antigens 498	
	Leukocyte transfusions 508	
	Platelet antigens 511	
	Platelet transfusion 515	
Part II	I. Disorders of the Red Cells	
Section	1. Introduction	529
13.	The Approach to the Patient with Anemia	529
	The approach to the diagnosis 530	
	Manifestations of anemia 532	
	Evaluation and diagnosis 538	
	Classification of anemia 546	
	Treatment of anemia 550	
	Anemia in pregnancy 555	
	Features of anemia unique to infants and children 558	
	Nutritional considerations in anemia in infants and children 561	

Section	2. Macrocytic Anemias	566
14.	Macrocytosis and Macrocytic Anemias	566
	Significance of macrocytosis 566	
	Non-megaloblastic, macrocytic anemia 567	
	Megaloblastic anemia 568	
15	Dominious Anomio	600
15;	Pernicious Anemia	602
,	History 602	
	Incidence 603	
	Etiology and pathogenesis 604	
*	Clinical manifestations 610	
	Laboratory findings 614	•
	Course, prognosis, and complications 615	
	Pathology 616	
	•	
Section	3. Anemias Characterized by Impaired Iron Metabolism	621
16.	Anemias Characterized by Deficient Hemoglobin Synthesis and Im-	
•	paired Iron Metabolism	621
	D C '' 11 (' CO)	
	Definition and detection 621	
	Etiology and pathogenesis 622	
	Laboratory tests useful in detection and differential diagnosis 626	
	Diagnostic approach 633	
17.	Iron Deficiency and Iron-Deficiency Anemia	635
	History 635	
	Iron-deficiency states 636	
	Prevalence 638	
	Etiology 638	
-	Clinical manifestations of iron deficiency 649	
	Laboratory findings 656	
	Management 660	
18.	The Anemia of Chronic Disorders and the Sideroblastic Anemias	671
	Anemia of chronic disorders 671	
	Sideroblastic anemias 678	
Section	4. Normocytic Anemias Other than Hemolytic Anemias	693
10	The Names and Names almost A	693
19.	The Normocytic, Normochromic Anemias	UYS
	Classification and diagnostic approach 693	
	Acute posthemorrhagic anemia 695	

Congenital dyserythropoietic anemias 699	
The anemia of chronic renal insufficiency	700
Anemia in cirrhosis and other liver diseases	706
Anemias associated with endocrine disorders	709

Section	5. Hemolytic Anemias	717
20.	The Hemolytic Disorders: General Considerations	717
	Definitions 717	
	Pathogenesis and classification 719	
	Clinical manifestations 722	
	Laboratory manifestations 725	
	Diagnostic approach 737	
	Therapy 739	
	Acquired hemolytic anemia resulting from infections, from chemical agents, and from physical agents 740	
	Acquired hemolytic anemia associated with hypophosphatemia 746	
21.	Hereditary Spherocytosis and Other Hemolytic Anemias Associated	
	with Abnormalities of the Red Cell Membrane	751
	Hereditary spherocytosis 751	
	Hereditary elliptocytosis 759	
	Acanthocytosis 762	
	Other disorders involving the red cell membrane 764	
22.	Hereditary Hemolytic Anemias Associated Mainly with Abnormalities in the Glycolytic Metabolic Pathway of Erythrocytes	769
	Pyruvate kinase deficiency 769 Other en syme deficiencies 774	
23.	Glucose-6-Phosphate Dehydrogenase Deficiency and Related Deficiencies Involving the Pentose Phosphate Pathway and Glutathione Metab-	
	olism	779
	G6PD deficiency 779 Other deficiencies involving the PP(HMP) pathway and GSH metabolism 789	٠,
24.	The Hemoglobinopathies: Structural Abnormalities in Globin. General Principles. Unstable Hemoglobin Disease	794
	Introduction 794	
	Etiology and pathogenesis. Genetics and molecular pathology 796 Laboratory approach to abnormal hemoglobin identification 805 Prevalence 810	
	Unstable hemoglobin disease 813	

25.	Hemoglobinopathies S, C, D, E, and Q, and Associated Diseases	822
	Sickle cell trait and sickle cell anemia 823 Hemoglobin C disorders 843 Hemoglobin D 846 Hemoglobin E 847 Hb S-O Arabia 847	
26.	The Thalassemias and Related Disorders—Quantitative Disorders of Hemoglobin Synthesis	855
	Introduction 855 The β - and $(\delta\beta)$ -thalassemias 862 The α -thalassemias 876 Geographic and racial distribution of thalassemia 882 Diagnosis and differential diagnosis of thalassemia 883	
27.	Immunohemolytic Anemias	891
	Incompatible transfusion reactions 891 Hemolytic disease of the newborn 895 Hemolytic disease of the newborn due to ABO incompatibility 908 Immunohemolytic anemias due to warm reactive antibodies 910 Drug-induced immunohemolytic anemias *916 Immunohemolytic anemias due to cold reactive antibodies 921	
28.	The Red Cell Fragmentation Syndromes	934
	Red cell fragmentation due to cardiac abnormalities 934 Red cell fragmentation in association with small vessel disease (microangiopathic anemia) 938 March hemoglobinuria 947	
29.	Paroxysmal Nocturnal Hemoglobinuria (PNH)	953
X	Etiology and pathogenesis 954 Clinical manifestations 958 Laboratory findings 960 Differential diagnosis 963 Treatment 963 Course and prognosis 964	
	, and the second	
Section	6. Other Red Cell Disorders	968
30.	Polycythemia	968
	General considerations. Pathologic physiology 968 Classification 974 Relative erythrocytosis 975 Absolute erythrocytosis 977	

Abnormal hemoglobins 982 Polycythemia vera 988

31. Methemoglobinemia and Other Disorders Usually Accompanied by Cyanosis

1009

Cyanosis 1009
Oxidation of hemoglobin *1010
Methemoglobinemia 1011
Sulfhemoglobinemia 1016
Carboxyhemoglobin. CO poisoning 1016
Detection of abnormal hemoglobin pigments 1017

32. The Porphyrias

1021

Congenital erythropoietic porphyria 1025
Acute intermittent porphyria 1025
Variegate porphyria 1029
Hereditary coproporphyria 1032
Protoporphyria 1032
Acquired porphyria 1034

Part IV. Disorders of Platelets and Hemostasis

Section 1. Approach to Problems of Hemostasis and Coagulation

1043

33. The Diagnostic Approach to the Bleeding Disorders

1043

Clinical evaluation of the bleeding patient 1043

Laboratory methods for the study of hemostasis and blood coagulation 1049

Tests of the vascular and platelet phases 1049

Tests of the coagulation phase 1056

Initial laboratory approach 1062

Laboratory evaluation in the newborn 1067

Section 2. Disorders of Platelets

1071

1071

34. Quantitative Variations of Platelets in Disease; Thrombocytopenia and Thrombocytosis

Thrombocytopenia 1071
Immunologic platelet destruction 1075
Idiopathic thrombocytopenic purpura 1075
Other forms of immunologic platelet destruction 1090
Deficient platelet production 1095
Thrombocytopenia due to abnormal platelet pooling 1098

	Miscellaneous forms of thrombocytopenia 1099 Thrombocytosis 1103 Thrombocythemia 1103 Reactive thrombocytosis 1107	
	Reactive infomovityisis 1107	
35.	Qualitative Disorders of Platelet Function	·1119
	Hereditary disorders of platelet function 1119 Acquired disorders of platelet function 1128	
36.	Bleeding Disorders Caused by Vascular Abnormalities	1136
	Autoimmune vascular purpuras 1136 Purpura associated with infections 1143 Structural malformations of vessels and perivascular tissues 1144 Miscellaneous vascular purpuras 1151	
Section	3. Coagulation Disorders	1158
37.	The Hereditary Coagulation Disorders	1158
	Nomenclature 1158 Principles of pathophysiology 1159 Hemophilia A (Factor VIII deficiency) 1161 Hemophilia B (Factor IX deficiency) 1172 Factor XI deficiency 1173 Disorders of fibrinogen 1174 Factor XIII deficiency 1176 Deficiency of prothrombin 1177 Factor V deficiency 1177 Factor VII deficiency 1178 Factor X deficiency 1178 Factor XII deficiency 1179 Von Willebrand's disease 1179 Miscellaneous hereditary coagulation disorders 1183 Treatment 1183 Replacement therapy 1184	
38.	Acquired Coagulation Disorders	1201
	Deficiencies of vitamin K-dependent factors 1201 Hemorrhagic disease of the newborn 1201 Hepatic disease 1205 Pathologic inhibitors of coagulation 1208 Diffuse intravascular coagulation 1211 Fibrinogenolysis 1224 Miscellaneous disorders 1226	

1233

Pathophysiology of thrombosis 1233 Hematologic methods for the detection of thromboembolic disease 1238 Anticoagulant therapy 1238 Miscellaneous antithrombotic agents 1246	
Part V. Disorders Characterized by Adenopathy, Splenomegaly, and/or Abnormalities of Leukocytes or Immunoglobulins	
Section 1. Approach to Disorders of the Phagocytic and/or Lymphatic Systems	1255
40. Diagnostic Steps in the Evaluation of the Patient with Abnormalities of Leukocytes or Immunoglobulins, or Lymphadenopathy, Splenomegaly, Fever of Unknown Origin, or Recurrent Infection	1255
Examination of the blood 1256 Bone marrow examination 1258 Lymph node examination 1259 Examination of the spleen 1262 Fever of unknown origin 1263 Recurrent infections 1263	
Section 2. Non-neoplastic Disorders of Leukocytes and RES	1266
41. Variations of Leukocytes in Disease	1266
Leukocytes in inflammation 1266 The neutrophil series 1268 The eosinophil series 1282 The basophil series 1286 The monocyte-macrophage series 1286 The lymphocyte series 1288 Plasma cells 1290 Agranulocytosis and drug-induced neutropenia 1290 Leukemoid blood pictures 1301	
42. Quantitative, Morphologic, and Functional Disorders of the Granulo-cyte and Monocyte-Macrophage Systems	1313
Quantitative disorders of granulocytes 1313 Disorders of phagocytic leukocytes characterized by morphologic changes 1319 Functional disorders of leukocytes not characterized by morphologic changes 1326	•

39. Thrombosis and Antithrombotic Therapy

•	Disorders involving the monocyte-macrophage system—the "storage diseases" 1330 Histocytosis X 1343	
43.	Infectious Mononucleosis	1356
	History and terminology 1356 Etiology 1357	
	Epidemiology 1358	
	Clinical manifestations 1359	
	Laboratory findings 1364	
	Differential diagnosis 1369	
	Treatment 1371	
	Prognosis 1371	
	Pathology 1371	
44.	Immune Deficiency Diseases	1377
	Definition and terminology 1377	
	Infantile sex-linked agammaglobulinemia 1378	
	Selective immunoglobulin deficiency (IgA) 1381	
	Transient hypogammaglobulinemia of infancy 1383	·
	Immunodeficiency with hyper IgM 1384	
	Thymic hypoplasia 1384	
	Immunodeficiency with ataxia telangiectasia 1385	
	Immunodeficiency with thrombocytopenia and eczema 1387	
	Severe combined immunodeficiency 1389	
	Immunodeficiency with short-limbed dwarfism 1390	
	Variable immunodeficiency 1391	
	Other congenital disorders of host defense against infections 1392 Acquired immune deficiency syndromes 1392	
45.	Disorders Primarily Involving the Spleen	1405
	Causes of splenomegaly 1405	
	Chronic congestive splenomegaly. 1412	
•	Concept of "hypersplenism" 1417	
	Methods of evaluating suspected splenomegaly 1419	
	Indications for splenectomy 1426	
Section	3. Neoplastic Diseases of the Hematopoietic System	1431
46.	Classification, Pathogenesis, and Etiology of Neoplastic Diseases of the	
,	Hematopoietic System	1432
	Classification and historic development 1432	
	Interrelations of the diseases 1434	
	Incidence 1435	
	Pathogenesis 1440	
	Etiology 1450 Familial disease 1460	
	Familial disease 1460	