MANUAL OF HEMATOLOGY

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PREFACE

Manual of Hematology is designed in outline form to provide a concise and clear overview of the subject of hematology. Both laboratory and clinical aspects of hematologic disorders are covered, but the primary emphasis is on the pathophysiology of hematologic disorders. The book is aimed at the medical student and resident in medicine, pathology, or other discipline who wishes a concise review of the subject. It should also be a helpful quick reference source for the general pathologist.

The book is divided into six sections. Part 1 provides a concise review of the structure and function of the normal cell components of the hemic system as well as the major plasma components, such as iron, vitamin B_{12}, and folate, that are of special interest in hematologic disease. The methods of study of these components are also reviewed. Part 2 deals with the major disease groups and presents the important basic features of the disorders, such as frequency, genetic factors, symptomatology, diagnostic features, appropriate laboratory studies, course, and treatment. Part 3 deals with hemostasis and coagulation. The components of the hemostatic mechanisms are described, and the normal and abnormal physiology of these factors is emphasized. The pathophysiology, clinical and laboratory features, and diagnostic approach to both the hereditary and acquired coagulation disorders are discussed. The use of anticoagulants in management of thrombotic disorders is summarized. Part 4 covers immunohematology, with special attention to the blood group antigens, HLA antigens, use of blood components in therapy, and transfusion reactions. Various morphologic terms are described and the classification systems of the acute and chronic leukemias and the lymphomas are presented in the Appendix.

The last section of the book is unique; it consists of a series of diagnostic problems in which pertinent clinical and laboratory data are provided. These cases are selected to teach interpretation of laboratory data in a logical manner and should prove a valuable and interesting aspect of the book.

The contents of this book are based on teaching material and principles developed by Professor Sultan and his colleagues at the Henri Mondor Hospital and Créteil University in Paris. This program has demonstrated its excellence for many years.

When I encountered the first edition of this textbook in French, I was greatly impressed by its succinct but lucid style. The illustrations, tables, and flow charts were well thought out and effective teaching devices. I told Professor Sultan that I was not aware of a comparable book in English and that I had frequently recommended it to students, residents, and pathologists who were seeking a concise, up-to-date text for review of hematology, but always had to point out that, unfortunately, it was only available in French. Professor Sultan

suggested that I translate the text into English. I accepted this task since I believed that the book would be a valuable addition to the English language hematology literature.

French hematologists of the past several decades have made major contributions to the field of hematology, such as describing clinical and laboratory entities, in providing an understanding of basic pathogenetic mechanisms of disease, and in classifying leukemias, but many of these significant achievements are not well known or recognized in the United States because of the language barrier. We have also frequently misunderstood some differences in basic concepts that exist between French and other European hematologists and ourselves because of the difficulty in communication. I hope that the readers of this book will gain a new respect for the knowledge and excellence of our European colleagues in the field of hematology.

Robert V. Pierre

CONTENTS

PART 1

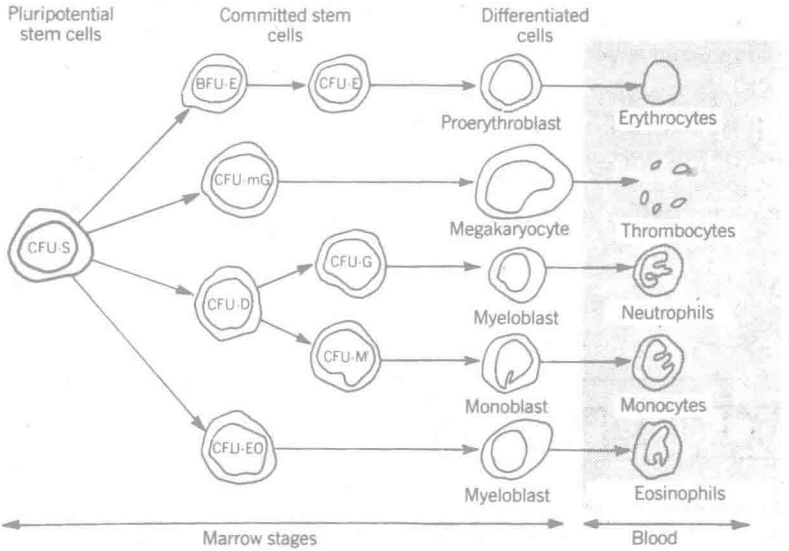
GENERAL HEMATOLOGY: PHYSIOLOGY AND METHODS OF STUDY

1 MYELOPOIESIS

Myelopoiesis is the production and release into the circulation of red blood cells, granulocytes, monocytes, and platelets. The precursors of these cells are found in the bone marrow.

STAGES OF MYELOPOIESIS

In vitro cell culture studies have defined the interrelations of the marrow precursor cells.



Pluripotential Myeloid Stem Cell

The pluripotential stem cell of the marrow is called CFU-S (colony forming unit—spleen). The bone marrow function of lethally irradiated animals may be restored by transfusion of blood or bone marrow of an isologous animal containing CFU-S. The different myeloid cell lines form colonies in the spleen of the irradiated mouse in a few days. The pool of CFU-S remains constant and is self-renewing.

Committed Stem Cells

Cells at this stage are committed to differentiation along a particular cell lineage under the influence of humoral control factors.

Erythropoiesis (Red Cell Line)

Two types of committed stem cells are recognized: the BFU-E (burst forming unit), which appear first in culture and show little response to erythropoietin stimulation, and the CFU-E, which appear later in culture and are very sensitive to the action of erythropoietin.

Granulopoiesis (Granulocyte and Monocyte Cell Lines)

A committed stem cell called CFU-D appears to be common to neutrophil and monocyte production. It gives rise to two cells: the CFU-G and the CFU-M. A precursor cell for the eosinophil cell line must exist; therefore, the term CFU-EO is proposed for the eosinophil precursor. The humoral factor "granulopoietin" has not been fully characterized. It appears to be a glycoprotein substance secreted partly by monocytes, and has been called "colony stimulating factor," or CSF. It is thought to play an essential role in the regulation of granulocyte and monocyte differentiation.

Thrombocytopoiesis (Megakaryocyte Cell Line)

The committed stem cell is called the CFU-MG. This cell differentiates to megakaryocytic precursors under the influence of a humoral factor called *thrombopoietin*.

The mature, differentiated cells are described in the following chapters.

2 ERYTHROPOIESIS

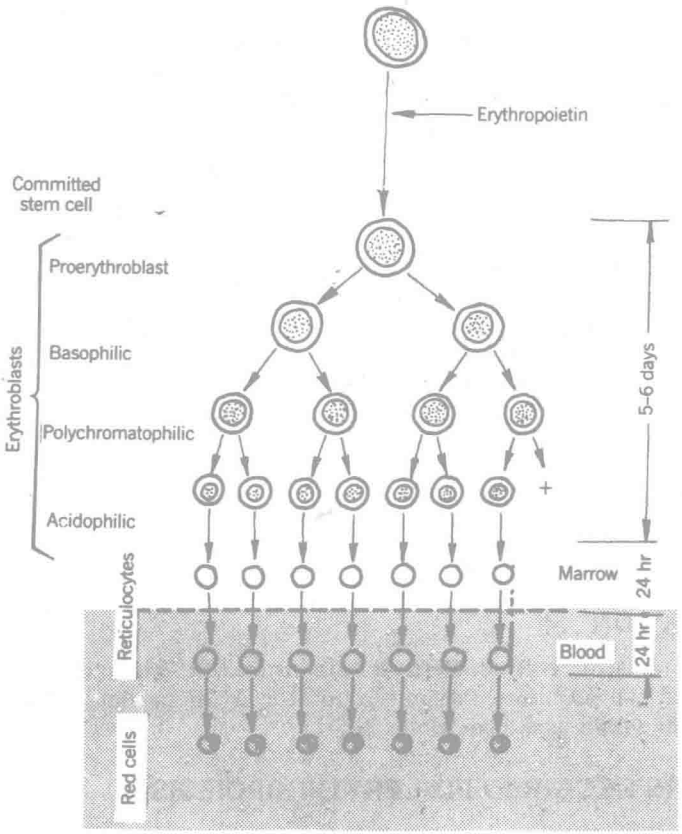
Erythropoiesis consists of a well-regulated mechanism that maintains the number of red blood cells and the level of hemoglobin within narrow physiologic limits.

The life span of the normal red blood cell is 120 days; 1/120th (0.83%) of the red cell mass is destroyed each day. The bone marrow production compensates for this loss of red cells and hemoglobin by production of the same quantities.

Normal erythropoiesis consists of

- Progressive decrease in size of erythroblasts
- Reduction in nuclear/cytoplasmic ratio
- Progressive increase in hemoglobin content
- Expulsion of the nucleus

- Intramedullary death of 5 to 10% of erythrocytic precursors (i.e., ineffective physiologic erythropoiesis)



STAGES OF ERYTHROPOIESIS

ERYTHROPOIESIS (MORPHOLOGIC CHARACTERISTICS OF CELL STAGES)

Cell Type (Size in μm)	*Nucleus*		*Cytoplasm*	
	Chromatin	*Nucleolus*	*Color*	
Proerythroblast (15 to 20)	Very fine	Visible	Basophilic	
Basophilic erythroblast (12 to 18)	Fine	Absent	Basophilic	
Polychromatophilic erythroblast (12 to 15)	Clumped	Absent	Polychromatophilic	
Acidophilic erythroblast (8 to 12)	Very dense	Absent	Red to purple	
Reticulocyte (8 to 10)	No nucleus		Red, + reticulin	
Erythrocyte (7 to 8)			Red	

REGULATION

The humoral factor, **erythropoietin,** transforms the CFU-E into the first recognizable red cell precursor, the proerythroblast. Erythropoietin also partially controls the synthesis of hemoglobin.

FACTORS REQUIRED FOR ERYTHROPOIESIS

- Metals: iron, copper, and cobalt primarily
- Vitamins:
  - **Folic acid** and **vitamin B_{12}** are required for normal cell division (DNA synthesis)
  - Vitamins E, B_6, B_1, C
- Amino acids: Required for globin chain synthesis
- Hormones: **Erythropoietin,** androgens, thyroxine

LABORATORY ASSESSMENT OF ERYTHROPOIESIS

Initial studies:

- Hemoglobin value
- Absolute reticulocyte value