FOREWORD TO THE I-st EDITION

This work was undertaken by us on the incentive of our Teacher, the Head of the II Medicinal Clinic of the Medical Academy in Gdańsk, Professor M. Semerau-Siemianowski, who being aware of the difficulties of learning haematology without adequate illustrative material, spurned us on to prepare the first Polish atlas of the cells of the blood and bone marrow.

This work took four years. Often we met with difficulties — lack of adequate material for the preparation of drawings, lack of time for the time-consuming execution of tables, the stress of the everyday duties of hard-working physicians. In all such moments Professor Semerau-Siemianowski was ready to help and to encourage us.

Therefore we are happy to express here our deep gratitude to Him, for He enabled us to bring our task to end.

The tables, with the exception of a few, represent the smears from our personal cases, which have been followed by us in the Medicinal Clinic of the Medical Academy in Gdańsk and afterwards in the II Medicinal Clinic of the Medical Academy in Warsaw. Several blood smears as well as bone-marrow smears from the cases of tropical diseases or of diseases not occurring in Poland were obtained by us during a scholarship journey abroad, in the year 1948. All originals of colour-tables were executed by associate professor I. Krzemińska-Ławkowicz with watercolours.

Our work does not represent the whole scope of haematology, it is rather an attempt to depict the basic morphological features of the blood and bone-marrow cells. We omitted splenograms, because these as well as a detailed description of tumour cells will be subjects of a separate work. On the other hand, in several cases the lymph-node biopsy was taken into account.

The present work represents rather an introduction to morphologic haematology and it may be useful in teaching students or in routine work in haematological laboratories.

It could be said that the scope of the text is broader than it is usual in an atlas. In giving, however, such extensive interpretations of the tables we were moved by following considerations:

1) there are only few textbooks of haematology;

2) the descriptions of the drawings could be made more interesting and more readily understandable when supplemented by physiopathologic remarks;

3) the usefulness of such a work to the clinicist, by supplementing additionally other diagnostic points besides the morphology of blood or bone-marrow cells;

4) we endeavoured also to inform the reader of some new acquisitions in diagnostic methods.

During the execution of this work we were moved also by an additional aim, which is readily understood by anybody, who would see haematology developing and progressing. This aim is the awakening of interest for haematology in a greater number of workers and an increase of the number of haematologists. The importance of haematology becomes greater every day, it surpasses mere laboratory considerations, it reaches into the field of prophylactics. Haematological ambulatories and periodic examinations of blood morphology of the populace are of greater and greater importance. As an example the rôle of haematological examinations in early diagnosis cancer may be cited, when discrete signs of anaemia lead the clinicist to the diagnosis of the causative disease.

There follows the importance of clinical haematology, which grows because of the growing frequency of disorders of the blood. The training of haematologists is among the pressing exigencies of the present moment, because their number in Poland is far too scarce in proportion to the needs.

We should consider our aim fulfilled, if this work could at least partially induce a wider interest in haematology.

THE AUTHORS

FOREWORD TO THE II-nd EDITION

The first edition of the "Atlas of Haematology" was out of press in 1952, in the following year — the Czech translation. The first issue was sold out in a short time. The friendly reception it received and many letters from various countries induced us to the preparation of a second edition.

An additional incentive to the revision and extending of the text was the proposal to translate this book into Russian, English and German with a view of facilitating the study of haematology to students and young physicians in their own language.

During the preparation of the second edition the work was equal to that of the preparation of a new book. In printing the first edition and the Czech translation in Prague the delicate original watercolours became so used up, that all tables were painted anew from the preparations remaining in our collection.

We began this time-consuming task with pleasure. Now our work was given to Polish polygraphist and Polish printers. Their work was so excellent that we had difficulties in finding differences between the copies and the originals of our drawings.

We obtained also new technical aids — in the Institute of Haematology in Warsaw we were able, due to excellent modern microscopes, to draw the cells in a more detailed and true manner.

As in the first edition, all tables were painted in watercolours by associate prof. I. Krzemińska-Ławkowicz. In view of the progress made by haematology the text was thoroughly revised. We endeavoured to take into account new acquisitions as well as our personal experience gained during the time elapsed. The second edition contains moreover selected references to the literature. It was necessary to omit many basic publications from our literature as well as from the world's literature. To atone for this, a special division of literature has been adopted and works with an extensive bibliography (textbooks, atlases, monographs etc.) have been grouped separately. The remaining references are the works cited in the chapters of the "Atlas of Haematology", these are in the first place new publications not cited elsewhere.

In spite of many additions to the text the present work remains an attempt to represent only basic traits of haematological morphology and does not

cover the ever growing field of this science. The comparatively extensive text (in comparison to other atlases) should serve the clinicist, as it contains the basic diagnostic points.

A continuation of the present work will be instituted by the "Textbook of Haematological Diagnostics" which is now in preparation. This textbook will contain chapters on haematological cytology, cytochemistry, blood coagulation, immunohaematology and related subjects.

In presenting to the reader the second, revised edition of the "Atlas of Haematology" we should like to express our sincere thanks to the Polish State Medical Publishers for technical help and careful edition of this book as well as to all those, whose nameless work enabled the second edition and the translations into English, Russian and German to appear.

We are also indebted to dr. Przemysław Czerski for his aid in the tedious task of selecting and searching under the microscope for cells, which served as models for the drawings, for his help in the preparation of the list of references, as well as for his meticulous English translation.

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Note. All drawings were made from original preparations using objective 90 x. imm. and ocular 15 x. Under such magnification all details are readily discerned, using lower magnifications and less perfect optical equipment the cellular structures may be blurred, the images obtained being less distinct.

INTRODUCTION

Recent years have brought many advances in haematology, both as regards diagnostic procedures and such special laboratory techniques as cytochemistry, biochemistry, electron- and phasemicroscopy. Among the numerous new microscopic techniques, fluorescence microscopy has lately been successfully applied in haematologic investigations. These advances, have made possible a better understanding of vital processes of normal and pathological blood cells, and have contributed towards explaining a number of intricate and obscure phenomena in cell metabolism.

It might be thought that such progress would reduce the importance of the time-honoured morphological methods of blood examination, hitherto considered essential in the diagnosis of blood disorders. Morphologic haematology is, however, far from being in decline. On the contrary, the introduction of cytochemical methods is causing it to gain new ground. This is reflected in the constantly increasing number of haematological publications devoted to morphologic diagnostic methods, nor is this trend limited to haematology only; a new branch of medical sciences — clinical cytology — is acquiring greater and greater importance in the diagnosis of various diseases.

The times are not remote, in which the diagnosis of blood diseases was based entirely on peripheral blood examination. Joint biopsies of several organs has enabled us today to acquire direct insight into the blood-forming system.

Although blood examination is essential in diagnosis, nevertheless the supplementary information derived from direct examination of the blood-forming tissue — the bone marrow — is of great value; even if it does not contribute any new positive diagnostic findings indicating a definite disease, it can be helpful in ruling out certain syndromes.

When examining a bone marrow or lymph node aspiration smear pictures strictly specific for a definite blood disorder should not be expected. Rather should we endeavour to evaluate the functional efficiency of the bone marrow on the basis of the morphological pattern.

There are but few haematological syndromes, which are accompanied by a pathognomonic bone-marrow picture, making it possible to identify the

disorder at first glance. Among these are Addison-Biermer's disease and allied megaloblastic anaemias, multiple myeloma, acute aleukaemic myeloses, Gaucher's disease, kala-azar and certain parasitic diseases.

This explains why increasing attention is being devoted to joint biopsies, which, supplemented if necessary, by lymph node, spleen, liver or tumour puncture, enable us to correlate the findings in peripheral blood and bone marrow. Although the clinician intrudes in such cases upon the alien domain of histopathology, he is compensated by numerous advantages, the smears of bioptic specimens bringing out such details of cell structure as become obscured or totally lost in histological sections of fixed tissue.

Therefore oligobiopsy (puncture procedures) should be regarded as an independent diagnostic method. Smears prepared from aspirated material or imprints from excision biopsy specimens are to be seen as a valuable addition to classical histopathological techniques. What are needed, are further investigations by both these techniques (confronted by microphotography) with a view to forming a scientific basis for haematological cytodiagnostics.

This should be extended as regards oncological research. Such a work is planned by the present authors, in view of the keen interest of haematologists in the problems of neoplastic proliferation.

Bone-marrow biopsy has, since Arinkin introduced sternal puncture in 1929, been adopted as a routine clinical examination. This technique has been generally accepted and is in common use throughout the world.

Nowadays, bone-marrow examination is performed daily by the clinical haematologist in all cases of blood diseases. The interpretation of the morphology of bone-marrow cells is not always easy. Not only is profound knowledge of characteristic cell types necessary, but also long experience and constant study of atypical cells. It may be said that the clinician's personal haematological knowledge depends on the number of cases followed. There are, however, cases in which even an eminent haematologist of long experience cannot recognise an individual cell or diagnose a syndrome. One of the gravest difficulties in precise diagnosis, is the frequent occurrence of intermediate conditions between individual haematological syndromes. A single examination may be compared to a snapshot of an object in motion — that is the findings pertain only to the given moment. The morphological picture represents the state of the blood-forming system at the moment of aspiration of the specimen. It may change in the near future, and it is often impossible to predict, with any degree of certainty, in what direction. Generally known are the difficulties encountered in differential diagnosis of granulocytopenia or bone-marrow aplasia, which may correspond to an initial period of acute

myelosis. Typical "textbook" bone marrow, lymph node or spleen aspiration smear pictures are, unfortunately, encountered somewhat infrequently in clinical practice. Conclusions from the examination of haematological preparations must be drawn with the utmost prudence, and confronted with the entire clinical picture. Diagnosis based solely upon microscopical findings often proves incorrect. A hasty diagnosis may lead to serious errors and cause loss of the patient's confidence. The cytological diagnosis should be rather descriptive, the diagnosis of a syndrome only tentative. For example, the presence of megaloblasts does not always indicate Addison-Biermer's disease or some related syndrome of the "acastlose" group; it may be caused by other, hitherto incompletely understood pathogenetic mechanisms.

Only when the cytological picture is confronted with the remaining symptoms, and often after a prolonged period of clinical observation can diagnosis be established. It is these reservations which have caused us to supplement with short clinical notes the plates representing morphological pictures.

The present work has been divided into chapters according to the generally adopted classification of cellular elements of the blood-forming system. Disorders characterised by hyperplasia of the leucocytic and reticulo-endothelial systems, parasitic diseases and tumours are discussed in separate chapters. Such an arrangement of the contents was felt to be best suited to the aim of this book, which is to provide basic haematologic information in an orderly and systematic form. On the other hand, this division was imposed upon the authors by the limited scope of their work as well as by the necessity to cover not only the pathology but also normal haematologic morphology and the development of the cellular elements of the blood.

The authors are conscious of the shortcomings of the morphologic criteria upon which haematologic diagnosis has hitherto been based. It may well be that advances in cytochemistry and cytoimmunology will cast on the chemical structure and antigenic properties of the cell such new light as to bring out the individual nature of the elements of the blood-forming system.

Although research work of this kind has made great progress, nevertheless it has not as yet achieved application in routine practice. It may be presumed that when, in future, new methods are included in routine clinical examinations, classical morphology will acquire a new and wider meaning.

It is not so long ago that haematology was a discipline cultivated only by a small group of initiated investigators. In our day, it has entered the ranks of the most universal sciences covering almost all fields of modern

clinical and experimental medicine. The blood, being an ubiquitous tissue instituting the "internal environment" of the human body, reflects the life processes of all the organs and systems. Biology interests itself in the rôle and interrelationship of the various systems in the functions of the organism considered as a whole. It is evident, therefore, that the phenomena occurring in the blood and blood-forming tissues also cannot be regarded as a strictly individual separate problem, not connected with the remaining organs and tissues.

The discovery of the nervous regulation of the course of haematopoiesis opens up a vast field for haematologic investigations. Pavlov's theory concerning the rôle of the nervous system, his concept of the integrity of the organism, the idea of nervism and of the evolution of functions, has prepared the way for new ideas about the onset, development and the final outcome of diseases.

New opportunities thus arise for the elaboration of modern methods of prevention, diagnosis and treatment of blood diseases.

A better understanding of the laws which govern haematopoiesis will clarify the mechanism of the responses and diseases of blood-forming organs, and will probably enable us to influence their course.

OUTLINES OF BONE MARROW EXAMINATION TECHNIQUE

Aspiration biopsy has been found, among the various methods proposed for obtaining bone-marrow samples for examination, to be the most convenient procedure. In the case of adults, sternal puncture according to Arinkin's technique is generally performed. It should, however, be borne in mind that other bones may be punctured in cases, where the presence of localised lesions (*e.g. tumor metastases*) or of a generalised disease of the blood-forming system are suspected. In addition to the sternum, the iliac crest, the ribs or spinal processes of lumbar vertebrae are commonly selected for diagnostic puncture. There are instances in which the sternal pulp remains normal in the course of a blood disorder, while the biopsy of another bone (*e.g.* of the iliac crest) yields pathological findings. A "dry" sternal marrow also constitutes an indication of the desirability of effecting puncture of another bone.

Sternal puncture is in children under three years hazardous, since the needle may easily penetrate the posterior lamina and enter the mediastinum. The large vessels are in such cases usually injured with fatal consequences. In children under three years, therefore, the tibia is the bone of choice, the upper third of the diaphysis, medially from the tuberosity, being selected as the site for puncture. This procedure is known to be quite safe and easy.

The needle for bone puncture should be of hard steel, with a sharp belevelled point and stylet. On the needle should be placed a movable guard to prevent unnecessary (and dangerous) deep penetration. Different types of needles are advocated by various authors. The needle devised by M. Kubiczek is among the more convenient instruments. The present authors used successfully for a long time Strauss' vene puncture needles, for sternal puncture. Lumbar or pleural puncture needles may be also adapted for this purpose and particularly for bone puncture in children.

In adults, the manubrium of the sternum is selected as the site for puncture, at a point approximately 2 cm. below the sternal incisure. A thin needle is inserted and the skin and subcutaneous tissue, as well as the periosteum are infiltrated with 2% sterile solution of novocaine. An amount

equal to 2 ml. of the solution is usually sufficient to spare the patient all pain.[1] Following anaesthesia, the puncture needle, held vertically, is inserted. The bone cortex is penetrated with slight pressure and a gentle, rotary motion, to and fro twist. When the needle enters the bone-marrow cavity, a sudden "give" is usually felt. The stylet is then withdrawn, a syringe promptly attached and a small amount of bone marrow aspirated. Usually from 0.25 to 0.3 ml. of the bone marrow is sufficient for all purposes (intravital staining, phase-contrast microscopy, tissue culture, etc.). For the preparation of smears for routine staining, the contents of the lumen of the needle are more than ample.

The aspirate is placed on a watch glass, liquid blood being poured off. Bone-marrow particles are selected, using a small forceps or bacteriological loop, posed upon an object or cover glass for the execution of smears. In addition to May-Grünwald-Giemsa stain, supravital stains (brilliant-cresil blue or Nile-blue sulphate) should be used.

The iliac crest is punctured approximately 5 cm. posterior to the spina iliaca anterior. The patient lies on his back, or, in cases of ascites, on his side. Following local anaesthesia the needle is inserted at right angles to the frontal plane. The skin and subcutaneous tissue are penetrated, the needle being at an angle of 45 degrees to the iliac crest. When the outer cortex is reached, the needle is posed at right angles to the iliac crest and bored into the bone by rotary motion, its tip pointing in the direction of the lower extremities. On entering the marrow cavity, a distinct "give" is felt. A 20 ml. syringe is best suited for aspiration. This procedure is completely safe. A word of warning must, however, be given against entering the bone from the lateral aspect in the direction of the abdominal cavity.

If a spinal process of the lumbar vertebra is to be punctured, the patient takes a sitting position, inclined forward. Broad processes, such as those of the third or fourth lumbar vertebra, are selected. Adipose subjects are not suited for this procedure. Following local anaesthesia, the puncture needle is inserted at right angles to the surface of the spinal process. Penetration to a depth of from 1.5 to 2 cm. is usually quite sufficient. The puncture is usually almost painless and more tolerable for sensitive patients than sternal puncture. The ribs are best punctured at a point several centimeters laterally to the vertebral column.

The technique of biopsy of the remaining organs lies beyond the scope of the present work. Detailed descriptions are to be found in standard textbooks of haematology or in specialised monographs.

[1] Rigid sterile precautions must, of course, be ensured throughout the entire procedure, the skin of patient and the operators' hands sterilised with antiseptic solutions etc.

CHAPTER I

THE RED-CELL SERIES

The course of human erythropoietic activity may be divided into two different periods: the foetal (megaloblastic) generation and the normoblastic generation. Each of them is characterised by the presence of morphologically distinct red-cell types — the megaloblast and the normoblast.

In physiological conditions, the megaloblastic phase is of short duration, comprising only the first two months of foetal life. As development proceeds, the temporary oxygen carriers — megalocytes — are replaced by normal red cells — normocytes — and the normoblastic trend of erythropoiesis prevails.

Although both red-cell types have similar functions in common, they are morphologically different. Precise knowledge of their characteristic traits is of fundamental importance in the identification of pathological states of the haematopoietic system.

It should be emphasised, that the megalocytes are a red-cell species possessing full functional efficiency, and that they participate in the physiological development of the human foetus and its haematopoietic system during intrauterine life. The appearance of megaloblasts during extrauterine life is considered as an abnormal condition suggesting a pathological phenomenon.

NORMOBLASTIC ERYTHROPOIESIS

The stem-cell of the normocytic red-cell series is termed proerythroblast. It is a cell measuring 14—20 μ in diameter. This cell possesses a large oval or round nucleus. Its chromatin is arranged in fine interwoven strands and filaments. Parachromatin (oxychromatin) is, as in most immature cells, abundant. It is generally held, that with progressing differentiation, parachromatin is converted into basochromatin, which intensively takes basic stains. Several faint nucleoli may often be observed. These are usually darker than the rest of the nuclear structure. This trait is helpful in differentiation between proerythroblasts and myeloblasts. The nucleoli