

# LEUKEMIA

THIRD EDITION—REVISED AND ENLARGED

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WILLIAM DAMESHEK and FREDERICK GUNZ'S

# LEUKEMIA

THIRD EDITION—REVISED AND ENLARGED

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## Preface to the Third Edition

This edition appears 10 years after its predecessor, a wide gap in an area where new developments are taking place with great rapidity. Unhappily, much of the delay was occasioned by the sudden death in 1969 of Dr. William Dameshek, the senior author of the first two editions, and a medical writer of such distinction that his loss was almost irreplaceable. In the preparation of this revision, we have attempted to adhere to the purpose set forth in the preface to the first edition, to present an account of those features of the leukemias in which practitioners such as internists, pediatricians, or clinical pathologists may be interested; an account which, without being encyclopedic, contains the most important information now available on human leukemia and related diseases. We have also tried to follow William Dameshek in making this a book to be read, rather than a catalog of facts and opinions. Since knowledge is still patchy in many areas of our subject, we have felt it important to pinpoint and to discuss deficiencies, as well as achievements, and, as in previous editions, to speculate on reasons for shortcomings and on likely lines of progress. No doubt some of our views will be found controversial by a number of readers.

Although the general structure of the work has been retained, we have rearranged some of the chapters in a more logical order, subdivided two of them, and, in place of the former Epilogue, added a brief account of very recent developments. To avoid duplications, the chapter on laboratory diagnosis has been amalgamated with that on the clinical features of the leukemias. Overall, a radical revision was found to be necessary, and much of the contents of the first two editions had to go, in order to make room for new material. Most importantly, we were fortunate in enlisting the help of a number of our colleagues who took over the rewriting of essential parts in their own specialized fields. We thank in this place Drs. M. A. McGrath, R. Penny, A. S. D. Spiers, P. C. Vincent, J. B. Ziegler, and the late Dr. Y. Rabinowitz for their most valuable contributions, without which we could not have completed our task. We are also grateful to many friends and their publishers for allowing us to reproduce illustrations or tables from their published work or for supplying us with original material for illustrations. Their generosity is acknowledged in the legends to the relevant figures.



In looking back over the years since the appearance of the second edition, we can discern solid progress on a wide front. The most spectacular advances have probably occurred in the therapy of the acute leukemias, with acute lymphocytic leukemia of childhood in the van. The extraordinary extension of survival of many such children is the first tangible reward for the enormous effort that has been made in so many fields of research, and gives hope for similar advances in the therapy of other forms of the disease. Yet it is sobering that, in spite of the steady widening and deepening of insights into the life history, the physical and chemical constitution, the kinetics, and immunology of normal hematopoietic cells and their pathologic counterparts; and despite the great improvements in pharmacology and therapeutic methods, we still lack basic information on the reasons why some leukemias—or certain patients with leukemia—respond to treatment, while others remain resistant. Nor are we as yet treating diseases whose causation is clearly understood. Much knowledge has been gained from the study of animal leukemias, their etiology and pathogenesis, but its application to the human disease still faces major obstacles. Progress here, as elsewhere in the leukemia field, is likely to come by means of multiple small steps, rather than by great breakthroughs which are so ardently hoped for by patients and their friends.

In completing this work, we should like to express our indebtedness to our publisher, Grune & Stratton, and to our wives and families for their tolerance and support over very many busy months.

F.G.

A.G.B.

## **Preface to the Second Edition**

In the more than five years since this book was first published, enormous efforts by many different groups of workers have been made to advance the knowledge of leukemia and its treatment. In sifting through the great mass of publications, one may wonder if the progress that has been made can be equated with the quantity of work done. To be sure, neither the fundamental causative factors, nor the cure of the various disorders classified under the heading of leukemia have been elucidated, but perhaps a much clearer picture of a many-sided problem seems to be emerging. It is not too much to say that with the present logarithmic proliferation of basic knowledge, we may be on the verge of at least partial solutions.

Many of the advances have come from basic work on blood cells and their normal functions. In particular, the hitherto enigmatic lymphocyte has at length begun to shed some of its veils and something is now known of the history and purpose of its life. Connections between the recently "rediscovered" thymus, the growth of lymphocytes and immunologic phenomena have been found and the many analogies and relationships between immunologic and neoplastic lymphocytic and plasmocytic proliferations have emerged. Some forms of leukemia may, indeed, be perversions of normal reactions to foreign proteins, a possibility which constitutes a challenge to experimental investigation. Among other important advances is the unravelling of the minute structure of chromosomes from normal and leukemic blood cells. The Philadelphia chromosome, as noted in chronic granulocytic leukemia, the finding of trisomy for the G21 chromosome in Down's syndrome, the almost twenty-fold increase of acute leukemia in this condition—these correlations are fascinating developments. Information is very rapidly accumulating on the place of viruses in the causation of animal, but not yet of human, leukemias, although even here, there are hints of possibly important things to come. The Burkitt "lymphoma" with its relation to leukemia, the occurrence of acute leukemia in "clusters," the contention by some workers that immune bodies against leukemic tissue presumed to contain virus may be found in leukemic contacts—these are bits of evidence that must be seriously considered, especially in the light of future developments. The role in leukemogenesis of extraneous agents such as ionizing radiations has been more



clearly assessed. Methods of therapy in both acute and chronic leukemia have been refined and several new and useful drugs have been introduced. The place of the corticosteroids in therapy, particularly with the use of large, "pharmacologic" doses of these materials in acute leukemia of adults and in the lymphoproliferative disorders has been a revelation.

In revising this monograph, we have tried to integrate an account of the newer knowledge with already established material and to present a balanced picture where this was possible. It must be confessed that not infrequently, we have resorted to speculation, particularly in relation to such things as abnormal or "forbidden" clones, matters of ecology and the closeness of autoimmune and certain leukemic disorders. This has seemed to us desirable in a field where so many uncertainties remain and where new work may conceivably be stimulated by, perhaps, unorthodox approaches. It has been our aim to include all relevant work, although omissions—some deliberate, others accidental—have been unavoidable. Some 1000 new references appear in this edition; a number of those previously cited have been deleted.

We have made more or less extensive additions and alterations in every chapter. The most complete reorganization has occurred in the clinical chapters, one of which has been subdivided. There is also a new chapter on lymphoproliferative diseases to balance that on the myeloproliferative disorders. Some illustrations have been changed and many new ones added. The index is new.

Without our many co-workers, and these include our Senior Associates: Drs. Mario Baldini, W. J. Mitus, Robert S. Schwartz and Joseph Sherman; our Clinical and Research Fellows in Hematology, our Trainees in Hematology, our technicians and our secretarial force, this book could not have got off the ground. We are particularly grateful to Dr. Brian MacMahon, Professor of Epidemiology, Harvard School of Public Health for his critique of the chapters devoted to Incidence and Etiology; to Dr. W. J. Mitus for his collaboration on the chapters devoted to the pathology of the leukemic cell and to the course and special pathology as related to symptomatology; to Dr. Anna Mitus for her help in writing the section on the treatment of childhood leukemia; to Lt. Commander Ross Moquin, USN, MC, for his close collaboration on the section devoted to the various chemotherapeutic agents; to Dr. Kosmas Kiossoglou for his studies on the chromosomes; to Mrs. Joan Gunz for her new index; and to Mrs. Virginia McKinney for her extraordinary secretarial efforts. To our friend, the publisher—Dr. Henry M. Stratton—we are, as ever, indebted for his excellent advice and sound judgment. To our patients with leukemia and particularly to parents of leukemic children, we extend the hope that some of the enormous research experience of today and tomorrow will be quickly channeled into practical accomplishment.

William Dameshek  
Frederick Gunz

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