

*FORMATION & DESTRUCTION OF
BLOOD CELLS*



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THE AMERICAN NATIONAL RED CROSS THIRD ANNUAL
SCIENTIFIC SYMPOSIUM, WASHINGTON, DC, APRIL 1970

IN MEMORIAM ERIC PONDER, DSC, MD

FORMATION & DESTRUCTION OF
BLOOD CELLS

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J. B. LIPPINCOTT COMPANY
Philadelphia & Toronto

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Distributed in Great Britain by
BLACKWELL SCIENTIFIC PUBLICATIONS
OXFORD AND EDINBURGH

Library of Congress Catalog Card No. 77-118343

PRINTED IN THE UNITED STATES OF AMERICA
SP-B

Eric Ponder, DSc, MD

ERIC PONDER was born 23 May, 1898, in Darjeeling, India, of Scotch parents, his father a medical missionary of the Church of Scotland. The family returned to Britain, to live in England then in Edinburgh, where his early schooling was the usual strong classics and mathematics. At 16, he passed the entrance examinations, entered the Medical School of Edinburgh University, with a brief interruption for naval duty, and received the degrees MB and ChB (the Edinburgh medical qualifying degrees, equivalent to the American MD) in 1919. The next year he was a junior medical officer in an asylum in Wales, and becoming interested in W. E. Cooke's work on the polymorphonuclear leukocytes, he studied the cells of patients suffering from various types of insanity. Together, they published a small monograph *The Polynuclear Count* (1927).

In 1920 he became a member of the Department of Physiology at Edinburgh under Professor Sir Edward Sharpey-Schafer. He studied the process of hemolysis; his first publication apparently was "A method for investigating the haemolytic activity of chemical substances," *Proceedings of the Royal Society B*, volume 92, 1921. In 1925 he received the DSc and in 1926 the postgraduate medical MD, both from Edinburgh University. He had published his first monograph in 1924, *The Erythrocyte and the Action of Simple Haemolysins*.

In 1927 he went to New York University to become Professor of General Physiology. No suitable textbook being available, he typed out the first (and final) draft of his *Textbook of General Physiology*. He continued his work on hemolysis, and studied comparative hematology at the Bronx Zoo.

He joined the staff of the Biological Laboratory at Cold Spring Harbor in 1933, as Investigator in General Physiology, and later became Director. The Laboratory was forming an all-year staff of investigators in fundamental biological research, Hugo Fricke being the other full-time researcher then in residence. Unfortunately, with the approach of the war, financial difficulties brought an end to the Lab-

oratory's research program in the form it was then developing. During 1933 to 1934, Ponder completed his second monograph *The Mammalian Red Cell and the Properties of Hemolytic Systems*.

In 1940, he began a somewhat different research program at Nassau Hospital in Mineola, New York. This was the beginning period of intravenous therapy, and clinical problems of a basic physiological nature were numerous. He studied fluid balance, traumatic and surgical shock, the use of plasma and whole blood transfusions. Since receiving his medical degrees, he had not practiced medicine except for the year in Wales. But in 1942 he passed the New York State medical examinations, and thus was able to practice medicine. He was appointed to the Department of Internal Medicine at Nassau Hospital; his interests were inevitably in clinical hematology, but he continued the "shock" program. After the end of the war, he spent most of his time on his own research program of red cell studies. The hospital began to provide a more adequate program of instruction for the house staff. Ponder was largely responsible for the development of this teaching program, which led to approved residencies in most of the clinical specialties. As a "guest" at the Brookhaven National Laboratory, he did some research using isotopes; later he was able to add a small isotope unit to the research laboratory at Nassau Hospital, for studying hemolysis and fragmentation using labeled reagents. He received a grant from the Eli Lilly Special Research Grants Committee, was also named a Certified Clinical Chemist by the American Chemical Society, and became a member of the National Research Council Subcommittee on Blood. The American Cancer Society supported investigations on hemolytic phenomena observed in tumor-bearing mice (1951-1958). This work was continued with the support of the National Cancer Institute (National Institutes of Health) from 1959 to 1966. Between 1955 and 1962, the Department of the Army awarded him contracts to study some aspects of red cell structure and changes occurring during the storage of blood; later contracts were concerned with problems in connection with open-heart surgery. From 1955 until his death, Ponder received research grants from the National Heart Institute for the in-depth study of the structure of red cells, ghosts, and myelin forms, using a wide variety of physicochemical and optical techniques. In 1948, he published his third monograph, *Hemolysis and Related Phenomena*.

In 1951 he went abroad for a six-weeks lecture trip in England and a short visit to Paris, where he met two investigators whom he then knew only by their work—M. Bessis and D. G. Dervichian. Thenceforth he made annual trips to Paris and worked with both of them in their laboratories. When he decided to leave Nassau Hospital in 1962,

it was not to retire, but to continue his research in their laboratories (Dervichian at l'Institut Pasteur, Service de Biophysique; Bessis at his newly formed Institut de Pathologie Cellulaire). He continued thus until shortly before his death. A small monograph on ghosts and myelin forms was completed but so far has not been published. Dr. Ponder died on 6 February, 1970, at the American Hospital of Paris, of heart insufficiency.

Ponder was not a great "joiner;" nor did he like to have technicians do his work, preferring to do the bulk of his research himself. He had much technical skill and a strong imagination. He was a great teacher. One of his most useful tools was the mathematics, which he had pursued since his early research days in Edinburgh.

His extrascientific interests were many. He was an incessant reader, of all kinds of books from the classics to the ultramodern, history, biography, fiction, poetry, theatre. He was interested in "the legal mind at work" and studied many famous published trials. He had a reading knowledge of several languages. All kinds of art were part of his life; he had many friends among contemporary artists and a small collection of Klee paintings and Guyot drawings and sculptures. He seemed to be drawn to sculpture, particularly church sculpture. Parallel to these interests went his interest in music.

Ponder was a Member of the Physiological Society (London) and of the American Physiological Society, a Founder of the Society of General Physiologists, a "Godfather" of the Red Cell Club, a Fellow of the New York Zoological Society, a Member of the New York Academy of Sciences, a Fellow of the International Society of Hematology, a Member of the American Society of Hematology, and an honorary Member of the Société Française d'Hématologie.

Ponder's scientific publications include over 300 papers and contributions to symposia, and sections in various more inclusive volumes such as *The Cell* (ed. Brachet & Mirsky) and *Protoplasmatologia Handbuch der Protoplasmaforschung* (ed. Heilbrunn & Weber). He translated from the French M. Bessis' *Traité de Cytologie Sanguine*.

We are most grateful to Mrs. Ponder for this fine terse biography of Dr. Ponder.

THE EDITORS

Introductory Remarks

TIBOR J. GREENWALT, MD

GENERAL COLLINS, President of the American National Red Cross, is attending the Red Cross International Conference in Cannes, France, and has requested me to extend to you his official welcome to this Third Red Cross sponsored Scientific Symposium. The previous symposium on the Structure and Function of the Red Cell Membrane was published in December 1969 by the J. B. Lippincott Company seven months after it was held.

Last year I mentioned the important contributions of Dr. Eric Ponder, and Dr. Weed suggested that we invite Dr. Ponder to this conference. The intention was to honor him in person and to have him present a paper. Dr. Ponder readily agreed to prepare a manuscript but indicated that poor health precluded his attendance. Unfortunately, death has thwarted us and instead we dedicate this Symposium and book to him in memoriam. Later this morning, Dr. Weed will present a resumé of Dr. Ponder's achievements, and a number of Dr. Ponder's colleagues and students will add their words of tribute.

Dr. Graham Jamieson, Director of the Red Cross Blood Research Laboratory in Bethesda, served as chairman of the Planning Committee for this Symposium. His task was made immeasurably lighter by the help of Drs. Shirley A. Johnson, Clement A. Finch, Seymour Perry, Frederick A. Stohlman and Robert I. Weed. Mr. Robert Earl, Director of the Red Cross Convention Office, Mr. Jack Pokras, Administrative Director of the Red Cross Blood Research Laboratory, Mrs. Jan Brannock, Mrs. Betty Swanson and Mrs. Alice Scipio have contributed much to the organization of the facilities. We again express our gratitude to Dr. Abraham Horwitz, Director, and Mr. Earl Brooks, Chief, Management and Personnel Branch of the Pan American Health Organization, for their kindness in permitting us to use these excellent facilities.

Before concluding, I am obliged to give you a brief progress report on the Red Cross Blood Program, which now has 59 Regional Blood Centers in the States, the District of Columbia, Puerto Rico and the

Virgin Islands, collecting over three million units of blood exclusively from volunteer donors. Each Blood Center is equipped to prepare whatever blood components are needed for the management of patients. Eighteen centers will be operating frozen red cell programs by early 1971—seven are already equipped. Twenty-five Centers will have automated blood typing within the next 12 months. The Rare Blood Donor Registry is well on the way to be the largest and most active in existence. The plasma fractionation program supplies gamma globulin, plasma protein fraction, albumin and fibrinogen prepared from 120,000 liters of plasma annually. The volume of plasma processed is expected to reach 300,000 liters by 1974. A high potency anti-hemophilic factor concentrate will shortly be released and a prothrombin complex concentrate is ready for clinical trials. Future plans include the addition of intravenous gamma globulin, IgM and IgA concentrates.

The goal is to deliver complete, patient-oriented service and to keep abreast of developments in hemotherapy. This can best be accomplished by attracting scientifically oriented medical leadership to our Red Cross Blood Centers. Affiliation with medical schools has already been achieved in Rochester, NY, Boston, Birmingham, Atlanta, Tucson, Portland, Oregon, Los Angeles, and Lansing, and is imminent in Philadelphia, Nashville, and Omaha.

These Symposia are only part of the evidence that we are interested in blood and not just in collection and distribution. Your attendance and participation in these programs is greatly appreciated. We hope that you will enjoy this conference.

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I

Eric Ponder

Prophet and Explorer of Research on the Red Cell

I

ROBERT I. WEED, MD *

MOST REGRETTABLE it is that Dr. Ponder did not live to see the Proceedings of this Red Cross Symposium published in his honor. Although they will now become a memorial volume, nevertheless we can be thankful that he was aware that he was to be so honored.

Although my acquaintance with Dr. Ponder was limited and others can relate personal anecdotes about him better than I, I would share with you a remark that he made when he visited us in Rochester in 1960, because it provides a glimpse of his wisdom and keen insight. We were talking to him about red cell membrane proteins and one of us asked him if he had any comment regarding a controversial report recently presented in a short paper at Atlantic City. He responded in a considered fashion: "I don't go to meetings. I feel that anything presented there that is worthwhile will be published and then I can read it carefully." Whether honesty or perception or both, his comment should prick each of us whose name at one time or other may have appeared on a title or abstract submitted or even presented but not followed by a publication. It can surely be said that Eric Ponder himself was responsible for a truly amazing number of worthwhile publications.

The major contributions that he made to the study of the red cell are unfortunately often overlooked, especially by those whose literature search as preparation for writing a paper seldom goes back further than five years. Between 1921 and 1966, Eric Ponder averaged three or more publications a year. He was the senior and often sole author of a great majority of these publications, often having personally designed the equipment and done the experiments himself or with Mrs. Ponder. Recently, as I looked back through his bibliography, I

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was reminded that his papers are models, which we all might well emulate. He brought important and significant results home to the reader by virtue of the simplicity of the experimental design, his clarity of expression, his conciseness and absolute minimum of speculation. The length of the discussion section of his papers seldom exceeded the results section.

Dr. Ponder's monograph entitled *The Mammalian Red Cell and the Properties of Hemolytic Systems* (1934), his book entitled *Hemolysis and Related Phenomena* (1948), his monograph on *Red Cell Structure and Its Breakdown* (1955), and his chapter on "The Cell Membrane and Its Properties" in the book entitled *The Cell* (edited by Brachet and Mirsky, 1961) are true classics for students of red cell physiology and pathophysiology. In fact, they should be required reading for anyone who wishes to do research on the red cell. We have a cardinal rule at Rochester, which at times, to my chagrin, I have been guilty of breaking myself, that whenever one thinks he has thought of a new idea for studying the red cell, he should read Ponder first, particularly the "green bible" (*Hemolysis and Related Phenomena*, 1948) because the chances are that he has already published the results of the experiment that you are about to devise.

Since this is a Symposium dealing with formation and destruction of all blood cells, we should recall some of Dr. Ponder's contributions to our understanding of white blood cells before we turn to the erythrocyte. He wrote several papers dealing with Arneth counts (Ponder 1927, 1942a, 1942b) which led to a simplified classification, and he also made a clear distinction between the large macropoly with hypersegmentation and the "polycyte," a cell with increased segmentation but of normal size seen in infection or inflammatory conditions. His review of the physical factors involved in phagocytosis (Ponder 1928) was a remarkable discussion, much of which remains valid today. He also studied the volume and relative protein concentration in normal and leukemic white cells by interference microscopy (Ponder 1959), and demonstrated that the more malignant cells appeared to have higher water content. In recent years, his interests in white cells and in erythrocytes merged in studies dealing with the fatty acid nature of red cell hemolysins found in animal leukemias and lymphomas and their relationship to erythrophagocytosis by the tumor cells (Ponder 1962).

Turning now to the red cell, let me quote from the introduction to *Hemolysis and Related Phenomena* (Ponder 1948b):

"I have been told that I tend to speak of the red cell as if it were a microcosm and as if understanding of its nature and properties would