NEWS AND VIEWS

Boston Hematology

American hematology is of relatively recent vintage, as compared with that of Central Europe. The many investigators in Germany and the Austro-Hungarian Empire, working eagerly in the field of the blood cells, writing at length and often polemically of their minor variations, for a long time had no counterpart in the United States. However, here in Boston a great student of medicine, Richard C. Cabot, versed in the European literature and anxious to acquaint American workers with the importance and practical value of hematology, wrote the first American textbook in the field: "A Guide to the Clinical Examination of the Blood for Diagnostic Purposes." This work, which was published in 1897, went through several editions. Cabot, fundamentally an internist and diagnostician, later developed the now famous Clinico-Pathologic Conferences and the concept of Social Service. Eventually he became a Social Scientist. Cabot's book, which was based in large measure on 4,000 blood counts done at the Massachusetts General Hospital, stressed the practical value of the blood for diagnostic purposes, and contained a few colored lithographs (made in Germany). Cabot was a good microscopist and gave excellent discussions on red cell abnormalities, one of them being known to this day as Cabot ring bodies. Cabot's interest in hematology as a sub-specialty of internal medicine was to set the pattern for the development of Boston hematology as a segment of the larger field of diagnostic and physiologic medicine, and thus not simply a study dealing with the morphologic aspects of the blood cell.

Cabot, as did most others with an interest in hematology, took Hayem's book, "Du Sang," 1889, as his Bible. In many ways Hayem was far ahead of his time and had a clear, almost startlingly modern conception of many hematologic disorders. This was particularly true of the purpuras, in which he had a particular interest because of his previous work on the "Hematoblast," or blood platelet as it came to be known. In Boston, a then osbcure pathologist, J. Homer Wright, also working at the Massachusetts General Hospital, believed he could see a rather striking resemblance between the platelets of the blood and the cytoplasm of the megakaryocytes of the bone marrow. Wright's careful studies indicated strongly that the megakaryocytes of the bone marrow produced the platelets of the blood. This was startling news to the Central European workers, and for a number of years Wright's conclusions were shrugged off, eventually being accepted only with considerable reluctance. By now they are commonplace, and have recently received confirmation at the hands of those working with time-lapse cinematography, bone marrow culture, etc. Wright's stain, a modification of the Giemsa Romanowsky stain, is still used extensively in staining blood smears.

One of Wright's students was George R. Minot, who even as a medical student had developed an interest in the blood. When he returned from post-graduate study at Johns Hopkins, Minot was given a tiny laboratory at the Massachusetts General Hospital next to Wright's area. Here began an active collaboration, from which several excellent articles, notably on platelets and purpura, arose.

Despite this collaboration, Minot believed firmly that hematology was a branch of the developing field of internal medicine rather than of pathology. With James H. Means he inaugurated a novel course in the second year curriculum of Harvard Medical School. This dealt with the pathophysiology of various diseases. As a medical student in 1921, the writer was privileged to hear Minot expound the principles of the disturbed physiology of pernicious anemia, hemolytic anemia, polycythemia, etc. To be sure, the morphology of the cells was described, but emphasis was placed on the "dynamic" approach, rather than on the more static morphologic details of the various disease states. Thus, in pernicious anemia, Minot's emphasis was on the gastro-intestinal tract and the diet, rather than on the minutiae of the red cell morphology.

Francis H. Peabody taught the course in "Clinical Pathology" also during the second

year of Harvard Medical School, and like Minot was a "clinical investigator," a man who believed that problems in the laboratory should be derived from the clinic, and when solved, brought back to the clinic. Peabody's studies of the bone marrow in pernicious anemia were outstanding, but his chief work was to organize and head (until his untimely death) the Thorndike Memorial Laboratory at the Boston City Hospital. This was to become a famous training center for many future distinguished men of medicine: Soma Weiss, Chester Keefer, William B. Castle, and Charles A. Doan, to mention but a few.

At the Boston City Hospital, some years before the Thorndike Laboratory was organized, Dr. Ralph C. Larrabee had inaugurated one of the first (perhaps the first) "Blood Laboratory" in the country. Here hematologic studies of the various "blood" cases on the wards and blood grouping tests prior to the increasing numbers of blood transfusions that were being given, were made.

Kimpton, who had developed a paraffin tube for collecting and giving blood, worked in close collaboration with the laboratory. The writer began his career in hematology under Dr. Larrabee in 1923, and as his first work studied the "reticulated red cells." It soon became apparent (1925) that a striking increase in these cells took place just prior to a remission in pernicious anemia. Minot and Murphy later used the reticulocyte percentage as a "yardstick" indicating a response to liver and other products in pernicious anemia.

Dr. Minot moved from the Massachusetts General Hospital to the C. P. Huntington Memorial Hospital, which was concerned with the care of malignant disease, including leukemia. There was no waning of his interest in pernicious anemia, however, nor in his belief that a nutritious diet of animal protein might be helpful. This was bolstered by Whipple's work in the hemorrhagic anemia of dogs, in which liver therapy seemed highly beneficial. The story of the use of liver in pernicious anemia, in which Minot and William P. Murphy of the Peter Bent Brigham Hospital collaborated, is one of the most exciting ones in all of medicine, transforming as it did a previously fatal disease to one with an invariably happy ending. With this epochal event, the center of gravity of hematology may be said to have shifted from Europe to the United States, and notably Boston.

William B. Castle, an investigator with a profound physiologic bent, was determined to solve the riddle of the pathogenesis of pernicious anemia. He too had developed the belief that the disorder was connected with an improper functioning of the stomach. In a series of now classic experiments, Castle demonstrated that the gastric juice of the patient with pernicious anemia was a "conditioned deficiency" state, in which, although the diet could be considered adequate, the lack of intrinsic factor *conditioned* the development of pernicious anemia. Castle's absorption with the ever-expanding problem of what is now no longer "*pernicious*" anemia has resulted in much of the enormous wealth of knowledge centering about this and related conditions. With Peabody's death, Minot became Director of the Thorndike Memorial Laboratory, with Castle his Associate.

Minot turned to his friend Edwin H. Cohn, in charge of Physical Chemistry at the Harvard Medical School, for help in preparing an extract of liver to thus make more liveable the life of the pernicious anemia patient, in whom eating ½ to 1 pound of liver daily had become a great chore. Cohn developed the first liver extract powders, and in later years, worked on highly purified fractions. It was possibly this interest in blood which led Cohn to do his epoch-making work in blood fractionation and to develop our now every-day knowledge of the various plasma fractions. His plasma fractionating machine, his use of ion exchange resins—continued in recent years by Surgenor, Oncley and Tullis—have done much to advance modern hematology.

Between 1930 to 1940, Boston was a veritable beehive of hematologic activity, with several active foci at various hospitals and medical schools. At the Boston City Hospital, there were Minot and Castle; at the Children's Hospital Louis K. Diamond, who did much to advance pediatric hematology; at the Beth Israel, the writer. At the latter hospital, some of the first bone marrow biopsies in the country were performed and studies made in leukemia, thrombocytopenia, and polycythemia. The finding of hemolysins in cases of acute hemolytic anemia led to a series of experimental and clinical studies in the field of immunohemolytic anemia and to the development of concepts of auto-immune disorders. These have broadened out since 1940, at the Blood Research Laboratory of the New Eng-

land Center Hospital, to include thrombocytopenia, generalized vascular disturbances (e.g., Henoch-Schonlein purpura) etc. In 1942, during the war, collaboration was effected with Goodman and Gilman of New Haven in using the "poison gas" nitrogen mustard for the treatment of Hodgkin's disease and lymphosarcoma. This represented a revival of interest in the use of chemotherapy for neoplastic disorders of the white cells.

Discovery of the Rh factor in 1942 and its relationship to hemolytic disease of the newborn, led to a rapid expansion in the field of immunohematology. Diamond at the Children's Hospital was in the forefront of this advance, and developed technics for detecting the often elusive anti-Rh antibody, and for treating erythroblastosis fetalis by exchange transfusion. Soon a Blood Grouping Laboratory was established, and here several "new" blood groups have been found. Also at the Children's Hospital, Sidney Farber, fundamentally a pathologist, became interested in the properties of pteroylglutamic acid (folic acid) and in its analogue aminopterin, just synthesized by Subbarow at Lederle Laboratories in Pearl River, New York. Experimental work indicated that folic acid antagonist might suppress leukocyte growth, and after preliminary trials in leukemic mice, it was used in children with acute leukemia. Striking remissions were obtained with sufficient consistency to rule out coincidence, and the life span of many children was significantly prolonged. This was a major breakthrough in what one hopes is the eventual control of leukemia. At the Massachusetts Memorial Hospital another hematologic focus became established under Joseph Ross, whose work with radioactive isotopes, chiefly in iron metabolism, became well known. At the Beth Israel Hospital, Benjamin Alexander discovered a "new" blood-clotting factor which he called SPCA (serum prothrombin conversion accelerator).

With all these various foci and leaders of their laboratories of hematology in the various hospitals, it goes without saying that many young men received at least part of their training in hematology in Boston. Many of them have since become famous in their own right and have developed "metastatic" departments of their own in hospitals and universities throughout the world.

Boston hematology, like others throughout the world, has gone through both the descriptive and physio-pathologic stages and is now in a chemical and isotope phase of its development. Unlike some cities, notably in the Midwest, hematology has continued to be the province largely of the internist rather than of the pathologist. Furthermore, in contrast with New York, where transfusion therapy was developed to a high peak under Nathan Rosenthal, Boston's hematologists did little with transfusions until recently.

Thus, as the result of the pioneer efforts of Cabot, Wright, and Minot, Boston became preeminent in the field of hematology and interest in that field has continued unabated. The Boston Congress of the International Society of Hematology, in association with the Sixth Congress of the International Transfusion Society and the Ninth Annual Meeting of the American Association of Blood Banks, may well have proven a milestone in the continuing advance of the ever-expanding field of the Blood.—*William Dameshek, M.D.*

Inter-American Medical Convention

The Second Inter-American Medical Convention will convene at the Hotel El Panama, Panama City, Republic of Panama, April 3, 4 and 5, 1957, under the sponsorship of the Medical Society of the Isthmian Canal Zone, a chapter of the American Medical Association since 1906. Colonel Charles O. Bruce, MC, USA, Chief Health Officer of the Panama Canal Company and President of the Medical Society, will act as keynote speaker at the invocation ceremonies, which will include addresses by the President of the Republic of Panama and by the Governor of the Panama Canal Zone.

Registration will take place at the Hotel El Panama at 9:00 A.M. April 2, the registration fee being $5.00. The program will be wide in scope, and on the order of a state medical convention in the United States. Speakers will be from North and South America, and all papers will be translated into both English and Spanish. For further information write to Dr. William T. Bailey, Chairman of the Convention Executive Committee.

Eleventh Annual Symposium on Fundamental Cancer Research

March 7, 8 and 9, 1957

at the University of Texas M. D. Anderson Hospital and Tumor Institute, Texas Medical Center, Houston 25, Texas

Thursday, March 7

The program will consist of open house to all symposium members, and presentation of annual progress reports on certain current research projects will be made by principal investigators of M. D. Anderson Hospital.

Friday, March 8

Morning Session Chairman: Albert B. Sabin, The Children's Hospital Research Foundation, Department of Pediatrics, College of Medicine, University of Cincinnati, Cincinnati, Ohio.

Introduction: R. Lee Clark Jr., Director and Surgeon-in-Chief, The University of Texas M. D. Anderson Hospital and Tumor Institute, Houston.

Pathology of Virus Neoplasia: Ernest W. Goodpasture, Department of Pathology, Armed Forces Institute of Pathology, Washington, D. C.

Genetic, Hormonal and Age Factors in Susceptibility and Resistance to Tumor-Inducing Viruses: Howard B. Andervont, National Cancer Institute, National Institutes of Health, Bethesda, Maryland.

Immunological Factors in Viral Infections: Edwin H. Lennette, Viral and Rickettsial Disease Laboratory, California State Department of Public Health, Berkeley, California.

Factors Influencing Proliferation of Viruses: Joseph L. Melnick, Section of Preventive Medicine, School of Medicine, Yale University, New Haven, Connecticut.

Factors Influencing Proliferation of Tumor-Inducing Viruses: George O. Gey, Finney-Howell Cancer Research Laboratory, Department of Surgery, The Johns Hopkins Hospital, Baltimore, Maryland.

Transmission of Tumor-Inducing Avian Viruses Under Natural Conditions: Ben R. Burmester, United States Department of Agriculture, Agricultural Research Service, Animal and Poultry Husbandry Research Branch, East Lansing, Michigan.

Friday Afternoon–First Session Chairman: Edwin H. Lennette.

Enhancement of Susceptibility to Viruses in Neoplastic Tissues: Hilary Koprowski, Viral and Rickettsial Research, Lederle Laboratories Division, American Cyanamid Company, Pearl River, New York.

Virus Range of Stable and Pure-Line Cell Strains: Jerome T. Syverton and Leroy C. McLaren, Department of Bacteriology and Immunology, The Medical School, The University of Minnesota, Minneapolis, Minnesota.

Oncolytic Properties of Viruses: Alice E. Moore, Sloan-Kettering Institute for Cancer Research, New York, N. Y.

Friday Afternoon–Second Session Chairman: Jerome T. Syverton.

Cell-Free Transmissions of Leukemia: Ludwik Gross, Cancer Research Unit, Veterans Administration Hospital, Bronx, New York.
(Discussants) George W. Woolley, Division of Steroid Biology, Sloan-Kettering Institute for Cancer Research, New York, N. Y.; Noriaki Ida, and H. Grant Taylor, Section of Pediatrics, The University of Texas M. D. Anderson Hospital and Tumor Institute, Houston, Texas; Arthur Kirschbaum, Department of Anatomy, Baylor University College of Medicine, Houston, Texas.

Isolation and Identification of Tumor-Inducing Viruses: Joseph W. Beard, Department of Surgery, School of Medicine, Duke University, Durham, North Carolina.

Saturday, March 9

Session Chairman: Joseph W. Beard.

Host-Virus Relationship in Tumor-Inducing Viruses: W. Ray Bryan, National Cancer Institute, National Institutes of Health, Bethesda, Maryland.

Electron Microscopy of Tumor-Inducing Viruses: Leon Dmochowski, Section of Virology and Electron Microscopy, The University of Texas M. D. Anderson Hospital and Tumor Institute, and Department of Microbiology, Baylor University College of Medicine, Houston, Texas.

Carcinogens and Viral Infections: Francisco Duran-Reynals, Department of Microbiology, Yale University, New Haven, Connecticut.

The Action of Viruses on Cells: Earl A. Evans, Jr., Department of Biochemistry, University of Chicago, Chicago, Illinois.

The Potential Significance of Nucleic Acids and Nucleoproteins of Specific Composition in Malignancy: Wendell M. Stanley, Virus Laboratory, University of California, Berkeley, California.

Viruses as Transducing Agents and Their Potential Significance in Cancer: Joshua Lederberg, Department of Genetics, University of Wisconsin, College of Agriculture, Madison, Wisconsin.

The presentation of the Seventh Annual Bertner Foundation Award and Bertner Lecture will be made Friday evening. Established in 1950, the award in honor of the late Dr. E. W. Bertner, first acting director of the M. D. Anderson Hospital and the first president of the Texas Medical Center, is presented annually for outstanding contribution in the field of cancer research. Previous recipients of the Bertner Award have been: Dr. Fred Stewart, the late Dr. George Milton Smith, Dr. Charles B. Huggins, Dr. Francis P. Rous, Dr. George Nicolas Papanicolaou, and Dr. Joseph C. Aub.

General Chairman of the Symposium is Dr. Leon Dmochowski, Section of Virology and Electron Microscopy at M. D. Anderson Hospital. Members of the advisory committee for the program were Drs. Beard, Lennette, Sabin and Syverton.

Erratum

In the article "Further Observations on the Effect of Cortisone and Thyroxin on the Blood Picture of Hypophysectomized Rats" by Howard A. Meineke and Roger C. Crafts, appearing in the January 1957 issue of BLOOD, the amount *5 ml.* (page 12, line 17) should read *0.5 ml.*

Organizations wishing to publish announcements of interest to the readers of BLOOD in the Journal should have such announcements in the hands of the Editor-in-Chief at least seven weeks prior to the first day of the month of the issue which is most appropriate to the announcement.