



Maxwell M. Wintrobe

THIS ISSUE OF BLOOD is published in honor of Dr. Maxwell Myer Wintrobe. The diversity of Dr. Wintrobe's major contributions to the field of medicine is such that it would be impossible to catalogue them adequately unless the entire issue were devoted to his biography. Certainly one of his major accomplishments is the hematology training program which he and Dr. George E. Cartwright built and continue to supervise. Approximately 110 of us have graduated from this program during the past 25 years. Eighty-five per cent of the graduates are associated with medical schools or research institutes, distributed among 26 U.S. medical schools, 8 Canadian or British schools, and 14 schools in other countries. At least

one author of each paper published in this issue is a graduate of the Utah program. Many other authors can be considered members of the first or even second generation of the program since most of us have tried to carry much of the philosophy and structure of the Utah program into our own training endeavors.

Dr. Wintrobe was born in Halifax, Nova Scotia, Canada on October 27, 1901. He received his B.A. degree from the University of Manitoba in 1921 and his diverse talents and interests of later years may have been predicted by receipt of gold medals in French and Political Economy. He received an M.D. from that University in 1926 and a B. Sci. in Medicine in 1927. He interned at the Winnipeg General Hospital in 1925–1926 and was a fellow at the University of Manitoba in 1926–1927. In 1927 he joined the faculty of Tulane University as an instructor of medicine and received a Ph.D. from that University in 1929. He joined the faculty at Johns Hopkins in 1930 as an instructor, was promoted to Associate in Medicine in 1935, and was later named Physician-in-Charge of the clinic for nutritional, gastrointestinal, and hemopoietic disorders.

An adventuresome move to Salt Lake City was undertaken in 1943. He joined the University of Utah as Professor of Internal Medicine and Head of the Department of Medicine in order to build the school from 2-yr to a 4-yr program. In addition he has served as director of the Laboratory for Hereditary and Metabolic Diseases since 1945. The grant which still supports that laboratory was among the first few to be awarded by NIH (AM-00-002). The “statutory senility” clause led to his retirement as chairman of Medicine in 1967, but failed to influence the pace of his activities. He has continued his teaching activities, was named Chief Consultant in Medicine to the V.A. Hospital in Salt Lake City in 1967 and has served first as Planning Coordinator and then as Director of the Cardiovascular Research and Training Institute of the University of Utah since 1967. In 1970 he was honored by the University of Utah by being named Distinguished Professor of Internal Medicine. This honor to Dr. Wintrobe also benefited the University since otherwise he would have been required to retire.

One of his strengths as a teacher is his insistence on and attention to doing a complete and detailed clinical job, as is illustrated by the following. Bob Edmundson, a clinical fellow in 1960–1961, had worked up a patient without seeing the blood and bone marrow smears which had been forwarded to Dr. Wintrobe. Bob indicated he had little idea as to what might be wrong with the patient since the only complaint was easy fatigability and no abnormalities were found on physical examination except for palor. Dr. Wintrobe queried Bob repeatedly about the presence of bony tenderness, noting that it must be present since the marrow smears indicated multiple myeloma to be the correct diagnosis. He then proceeded to do an exceedingly thorough exam of the skeletal system. Failing to find tender areas in the skull, sternum, spine, clavicles, or humeri, he moved to the ribs. A tender area was detected in the lateral rib cage and Dr. Wintrobe turned to Bob and inquired why he had missed bony tenderness as a physical sign. Bob authored “Edmundson’s Law” by replying, “The completeness of a

physical examination is certainly facilitated by prior knowledge of the diagnosis." Dr. Wintrobe thought for a moment and acknowledged the "Law's" accuracy by sharing our laughter.

Rebecca Zanzhir and Dr. Wintrobe were married in Winnipeg in 1928. Becky has played a very positive role in all stages of Dr. Wintrobe's career, with duties ranging from helping with "the book" to carefully guarding his working time. Many of us have had some difficulty convincing Becky that our telephone call was important enough to interrupt Dr. Wintrobe when he was working at home. Their daughter, Susan, and their four grandsons are a continuing source of pleasure. The tragic death of the Wintrobes' son, Paul, is still mourned.

A few examples of Dr. Wintrobe's scientific contributions should be mentioned. While at Tulane he developed an instrument, the Wintrobe hematocrit, which allowed him to provide the first careful definition of normal values for red blood cells. Hematocrit is commonly used as an expression of results of any method of determining volume of packed red cells (VPRC), but those of us who have been in Utah are regularly reminded by Dr. Wintrobe that we are using poor terminology. The hematocrit was the instrument, the VPRC was the result. Utilizing data from the VPRC, as well as the red blood cell count and hemoglobin determination, Dr. Wintrobe derived the red cell indices which form the basis of the morphologic classification of anemia which he derived.

He became interested in the basophilic stippling observed in the red cells of several patients in an outpatient clinic at Hopkins. These patients had no evidence of any hematologic disorders, were not lead intoxicated, but were of Italian ancestry. Some months later he examined a 16-year-old boy, also of Italian ancestry, with splenomegaly and an unexplained microcytic, hypochromic anemia which had failed to respond to iron therapy. Dr. Wintrobe wondered about a relationship to Cooley's anemia, but the disease was much milder than that described by Cooley and Lee. Shortly thereafter he had the opportunity to study a child with Cooley's anemia and he examined the blood of both parents, which Cooley and Lee had failed to do. Blood changes similar to those seen in the cells of the people he had observed in the outpatient department were present in both parents. Consequently, the first evidence for the hereditary nature of Cooley's anemia and the existence of thalassemia minor was published in the first edition of his book *Clinical Hematology* in 1942.

The discovery of cryoglobulin was a matter of serendipity. While studying the blood of a patient with hemorrhagic phenomena and retinal artery thrombosis, a centrifuged hematocrit was placed in the icebox. When he removed it from the cold, he noted a dense cloudy layer in the plasma and placed the tube in his pocket to show to colleagues. When he pulled the tube from his pocket, the cloudy layer had disappeared.

Dr. Wintrobe began work on the nutritional anemias early in his career and this interest persists to the present. He recognized that the young, rapidly growing pig was a good model system for such studies and utilized it to delineate many of the required factors for normal blood formation.

He demonstrated an effect of nonautolyzed yeast in pernicious anemia, an effect later proved to be due to folic acid.

He was among the first to demonstrate the salutary effect of nitrogen mustard in Hodgkin's disease and related conditions. Within 2 years of the clinical availability of adrenal glucocorticosteroids, he published an editorial detailing the scope and limitations of their usefulness in hematologic diseases (*Am. J. Med.* 9:715, 1950). More than 20 years of continued experience with steroid therapy has led to no major change in the therapeutic indications which he outlined.

The registry of all types of adverse drug reactions maintained by the American Medical Association is in large part the progeny of Dr. Wintrobe's clinical curiosity and practical application of medical suspicion. In 1951 he observed aplastic anemia in two patients with a history of chloramphenicol usage. Dr. Philip Sturgeon visited and said he had seen a similar patient. They wrote to their hematological colleagues and from this collected experience clearly documented a relationship of the drug to aplasia. He stimulated the AMA to support a Registry of Blood Dyscrasias and later as a member of their Council on Drugs helped establish a general registry.

Clinical Hematology appeared in the first edition in 1942 and Dr. Wintrobe has revised the "bible of hematology" five times to date and is finalizing the seventh edition at the present time. Spanish, Italian, and Greek editions have been published. This book is undoubtedly the best known textbook of hematology and is probably the most widely used single authored medical text of any type. He has been a major contributor to another well-known text, *Harrison's Principles of Internal Medicine* and is currently serving as Editor-in-Chief for the seventh edition which is nearing completion. He has authored or co-authored more than 350 journal articles on diverse aspects of hematologic problems. His editorial ability has been utilized by more than 20 journals and other publications, ranging in scope of contents from *Blood* to the *Encyclopedia Britannica*.

Dr. Wintrobe's role in the development of the University of Utah School of Medicine was crucial, but the intangibles are so great that it cannot be evaluated fully. When he arrived in 1943 the two-year school was the only medical school between the Rockies and the Sierras. He and the excellent faculty which he helped to attract developed a center which regularly serves as a consulting facility for patients in the intermountain region from the Canadian to the Mexican border and beyond. His growing reputation as a hematologist brought referrals of interesting patients from all over the world. Thus, two of the absolutely necessary ingredients for outstanding medical teaching were brought together: a good faculty and a large and varied patient population. Money and physical facilities were a different story. Utah was not a wealthy state and could furnish little "hard" money for a medical school. Dr. Wintrobe's department was located in the Salt Lake County Hospital for more than 20 years prior to the construction of the new Medical Center. The original space available for as many as a dozen people working in the combined clinical and research laboratories in hematology was approximately 500 square feet. The acquisition of the "blood

shed," a two-storey frame army surplus barracks, was a major advance in that everyone who wanted to work in the lab could do so at once rather than having to take turns. Without the enthusiasm and high standards of teaching, clinical care, and research maintained by such men as Wintrobe, George Cartwright, Frank Tyler, Hans Hecht, and their colleagues, the school would have remained third rate at best.

Dr. Wintrobe's contributions to medical education are not limited to his role at Tulane, Hopkins, and Utah nor to his writing. He has been Visiting Professor or given Special or Memorial lectures at more than half of the medical schools in this country as well as in dozens of schools in foreign countries.

He is a member or honorary member of some 34 medical and scientific societies serving as President of the Association of American Physicians (1956–1957), Association of Professors of Medicine (1965–1966), Utah Society for the History of Medicine (1971–) and the American Society of Hematology (1971–1972).

He has been generous of his time in the administrative aspects of the advancement of science by serving on committees, councils, and study sections of international, federal, and independent agencies concerned with medicine and research. For instance, he has worked with the World Health Organization in such roles as a special consultant in nutritional anemias and he has served the National Institutes of Health on seven councils or study sections, including the first hematology study section. The Leukemia Society developed as an outgrowth of his association with Mr. de Villiers. This society's policy of devoting most of its support to develop young scientists was the result of plans formulated by the original Scientific Board which Dr. Wintrobe chaired.

A listing of his numerous awards is available in references such as *Who's Who in America* or the *National Cyclopedia of American Biography*. It should be mentioned that the University of Manitoba and the University of Utah have awarded him honorary D.Sc.'s.

Much of this biography covers ongoing activities of "The Professor," so it should be evident that he is an exceedingly well organized, exceedingly busy man. He finds relaxation with his family, with music, and with outdoor activities. He plays the violin for his personal enjoyment and has served on the Board of the Utah Symphony and the Chamber Music Society of Salt Lake City. The magnificent mountains of Utah have repaid a portion of the Intermountain West's debt to Dr. Wintrobe. Shortly after arriving in Salt Lake City he formed a lasting friendship with Alf Engen, the head of the "Alta" ski school. Wednesday afternoon is still "ski day" at the University of Utah Medical School as long as the lifts are running at Alta. Dr. Wintrobe still looks a bit askance at the Hematology fellow who doesn't learn to ski and join him on "Mombo" or "Mainstreet."

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