The Blood Transfusion Service

JOEL UMLAS AND CHRISTOPHER P. STOWELL

TRANSFUSION MEDICINE probably began in 1667 when Jean Baptiste Denis reported successfully transfusing three patients in France using lamb's blood (1). A fourth patient died, apparently as a direct result of the procedure, which led to the banning of transfusions by the French Parliament (2). Blood banking, the storage of blood for future transfusion, was still more than two centuries in the future.

Interest in transfusion was revived by Dr. James Blundell, a London gynecologist, who reported successful direct human-to-human transfusions, that is, directly from a donor's artery into the recipient's vein (3), and who invented devices to accomplish this (4). Examples of this type of transfusion were well documented pictorially in the nineteenth century. A host of obstacles prevented the practice from achieving widespread acceptance, however-for example, a lack of clearly defined indications for transfusions by most of the advocates of the procedure (most did not list acute blood loss as an indication until Blundell's reports), lack of successful outcomes, and the obvious problems of donor procurement. The first recorded transfusion at the Massachusetts General Hospital (MGH) was a direct transfusion given preoperatively to an anemic woman, which was performed by Drs. C. A. Porter, Henry Marble, and Adams Leland in 1912. It was considered successful, although the donor suffered a reaction (5).

The Early Years

In 1913 Dr. Roger I. Lee, an MGH physician, working with an MGH intern, Dr. Paul Dudley White, developed a test of the coagulation system, which came to be known as the Lee-White clotting time, one of the first standardized tests of the coagulation cascade (6). This work, as well as subsequent studies related to transfusion medicine that Dr. Lee performed with Dr. Beth Vincent, an MGH surgeon, was done in the Pathology Department in the laboratory of Dr. James Homer Wright. In several publications in 1914 and 1915, Drs. Lee and Vincent outlined the coagulation system in humans, the role of calcium in clotting, the use of paraffin-coated collection tubing to delay the surface activation of the coagulation cascade, and the use of citrate to anticoagulate collected blood (7–9).

Also in 1913 Lee and Vincent were joined in the Pathology Laboratory by Oswald Hope Robertson, then a third-year Harvard Medical School (HMS) student, who also studied blood preservation problems. Following graduation, Robertson worked with Peyton Rous at the Rockefeller Institute. Rous, together with J. W. Turner, was among the first to describe anticoagulation-preservation of blood, as well as the testing of blood donors and recipients for compatibility (10–12). In 1917 Robertson joined the HMS Unit of the U.S. Army attached to the British Expeditionary Forces during World War I. Serving as a captain (under his mentor, now Major Roger I. Lee), Robertson published on the collection and storage of blood for transfusion (13–14), which led to the establishment of "blood depots," supplies of stored whole blood that could be transported to the battlefield, thereby obviating the need for direct transfusions on the battlefield. This innovation might be considered to be the beginning of blood banking.

The first civilian blood bank was established in Moscow at the Sklifosovsky Institute by Dr. Sergei Yudin (sometimes spelled Judine) in 1930 (15). Great reliance was placed on the use of cadaveric blood, with which Dr. Yudin, a prominent Russian surgeon, had extensive experience (16, 17). The use of cadaveric blood did not gain widespread acceptance outside the U.S.S.R.

In 1937 the first civilian blood bank in the United States was established in Cook County Hospital in Chicago by Dr. Bernard Fantus, who coined the term *blood bank* (18).

Lamar Soutter and the Founding of the MGH Blood Bank

Lamar Soutter (figure 22.1) was born in 1909, the son of a surgeon. He graduated from Harvard College in 1931 and HMS in 1935. After completing his surgical training in New York City, he returned to Boston as a surgeon at the MGH in 1940. Aware of the universally accepted utility of blood transfusions and of the merits of the blood bank system set up in New York City for its municipal hospitals, he set about trying to establish a blood bank at the MGH. By March 1942 "the ranks of the opponents had become seriously depleted because of defections to the armed forces," (19) so that, with the help of Dr. Tracy Mallory, then Chief of Pathology and Microbiology, Dr. Soutter's proposal for a blood bank was approved, with a budget of \$5,000 and a refrigerator in the basement of the Moseley Building. The MGH Blood Bank opened on April 1, 1942, and Dr. Soutter was its Director. In addition, Dr. Soutter was the first MGH volunteer blood



Figure 22.1 Lamar Soutter

donor. The early days were beset with numerous problems, such as clotting of the stored blood, ineffective filtration, and a high rate of febrile transfusion reactions, but, with perseverance and ingenuity, these challenges were overcome within three months. Since the hospital administration insisted that the Blood Bank be financially selfsufficient for its continued existence, money was raised from outside benefactors to acquire additional equipment for making and storing plasma. This endeavor proved prescient: nearly eight months after the opening of the MGH Blood Bank, Boston suffered one of its greatest civilian mass casualty disasters, the Cocoanut Grove nightclub fire on November 28, 1942 (chapter 15). The large store of plasma on hand was adequate to handle the needs of over 200 burn victims, and Dr. Soutter's judgment was vindicated. The utility of plasma for treating burn patients, an MGH innovation, was amply demonstrated and established as a standard therapy for many years.

In 1943 Dr. Soutter enlisted in the U.S. Army. Rising to the rank of major, he was awarded the Silver Star for conspicuous gallantry in action during the Battle of the Bulge. During his absence, the Blood Bank was managed by Dr. Carroll Miller, and much of the technically demanding and diagnostically challenging cases were outsourced to the Boston Blood Grouping Laboratory. It was apparent to Dr. Soutter upon his return that developments in blood bank serology (immunohematology) had achieved a level of such complexity, and the volume of transfusion activity, with its attendant testing and crossmatching, had increased so greatly, that the need for medical oversight vastly exceeded what could reasonably be provided by a part-time doctor whose main activity was surgery. To this end, he began to take on a series of fellows for one or more years. One of these fellows, Dr. Morten Grove-Rasmussen, who arrived in 1948, proved so satisfactory that he was made Assistant Director in 1951. Together they published five technical papers from 1950 to 1953, and Dr. Soutter published 17 papers on transfusion and blood bank issues.

In 1953 Dr. Soutter moved to Boston University School of Medicine, initially to pursue his surgical career but eventually becoming the Dean of Boston University School of Medicine in 1960. In 1963 the governor appointed Dr. Soutter to be the Dean of the University of Massachusetts Medical School project, a role that required him to start a new medical school. The school opened in 1970, a year in which he also served as President of the Massachusetts Medical Society. He retired as Dean in 1975 but continued to be active in medical matters and volunteer activities until his death in 1996.

Dr. Soutter's major contributions to the Blood Bank and Transfusion Service (as it was known until 1973) were his uncanny insights into the future needs of the MGH as medical changes unfolded, his administrative abilities, and his talent for getting his objectives implemented. These same traits characterized his successes at Boston University School of Medicine and the University of Massachusetts Medical School.

Morten Grove-Rasmussen and the MGH Blood Bank and Transfusion Service, 1952–1973

Morten Grove-Rasmussen (figure 22.2) was born in Copenhagen, Denmark, in 1911. He graduated from the University of Copenhagen Medical School in 1938 and over the next eight years pursued training in surgery at various Danish hospitals. In 1946 he joined the State Serum Institute in Copenhagen, where, over the next two years, he studied the rapidly emerging field of immunohematology. This preparation provided him with the exact credentials that Dr. Soutter was looking for in a fellow. Although Dr. Rasmussen (as he was known informally) came to the United States as a surgical fellow, he needed more money than the surgical fellowship could provide, so he accepted a fellowship with Dr. Soutter (19). The expectation was that he would provide the medical supervision of all the technical, interpretive, and administrative aspects that Dr. Soutter had come to recognize as necessary for the MGH Blood Bank and Transfusion Service.

In 1952, Dr. Rasmussen succeeded Dr. Soutter as the Director of the service and immediately put his own stamp on the position. His technical and medical skills were matched only by his personal skills and his "ability to draw divergent groups together by placing patient benefits paramount" (20). He was a warm and engaging person who, despite his international status, always made it easy for Pathology residents (and virtually anyone else) to approach him for discussions and clarification. Pathology resident rotations in the Blood Bank began under his aegis in 1953. Like his predecessor, he had a vision, not only for the needs of the MGH but for the entire field of transfusion medicine and blood banking. Already well known in blood banking circles for his work on the potential danger of using group



Figure 22.2 Morten Grove-Rasmussen

O whole blood as a "universal donor" source (21) and for his reporting of various serologic studies, he immediately became involved in national blood banking affairs, organizing the Reference Laboratories Program of the American Association of Blood Banks (AABB) in the 1950s. One of the earliest reference laboratories was established at the MGH and continues to operate today. The reference laboratories provided technical assistance in the workup of difficult cross-matching problems as well as a file of donors of rare blood types. The latter service later became the nationwide Rare Blood Donor Registry, which is now administered by the AABB and the American Red Cross (22). More than 30 reference laboratories were established nationally by 1973. Dr. Rasmussen served as the Chairman of the Reference Laboratory Committee of the AABB from 1958 until his death in 1973. He also recognized the importance of standardizing methodology across a wide variety of testing and clinical situations and, to this end, helped establish the Standards Committee of the AABB, which developed the first edition of a set of practice standards that is now used around the world and is in its twentyfifth edition. He served on this committee from 1956 until his death. It would be difficult to overestimate the importance of these committees and of the duration of his membership and leadership in these areas. Nationally, he was also on the AABB Scientific Advisory Committee and became the Vice-President of the AABB in 1956. From 1961 until his death, he was on the Editorial Board of *Transfusion*, the premier journal devoted to transfusion medicine and blood banking.

The first 10 years of Dr. Rasmussen's tenure are well summarized in his report to the General Executive Committee dated January 10, 1962. They include the "Nationwide Functions" (by which he meant the national endeavors at the AABB cited above); the "Special Functions" (an arrangement with the Ortho Pharmaceutical Corporation for the Blood Bank to provide serum from patients with valuable antibodies in return for receiving its total supply of blood-grouping antisera); the "Staff, Education and Research Functions" (which revealed that technical staff training and education were accomplished primarily on the job, that the night shifts were covered by medical students, and that physical examinations and interviews of blood donors were performed by Pathology residents). In addition, his report predicted the need for a centralized tissue typing laboratory that would be most suitably located in the Blood Bank, and the importance of having a team of nurses skilled at placing intravenous lines operating under the supervision of the Medical Director of the Blood Bank and Transfusion Service. Under his leadership, the functions of the IV team were expanded to include administration of blood transfusions, donor phlebotomy, and patient blood specimen collection.

In 1963 Dr. Charles Huggins, an MGH surgeon who had been doing research on organ cryopreservation, invented the Huggins

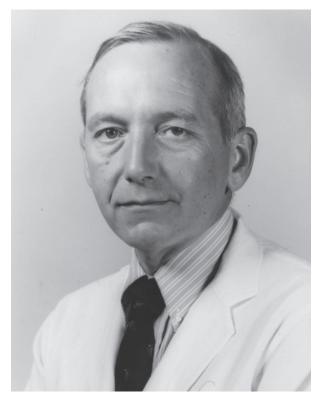


Figure 22.3 Charles Huggins

Cytoglomerator, a device that could recover large quantities of viable, previously frozen red blood cells for transfusion. Seeing the potential of this modality for inventory management as well as for storage of units of rare blood types, Dr. Rasmussen recruited Dr. Huggins to be the Clinical Director of the Blood Bank and Transfusion Service. By 1965 a repository of frozen units of rare blood was established at the MGH, as well as one at Chelsea Naval Hospital, which was supplied by the MGH. The MGH also supplied the first 150 units of frozen O-negative blood to U.S. military facilities in Vietnam and the Philippines during the Vietnam War. Although much of the technical development in this program was the result of Dr. Huggins's involvement, Dr. Rasmussen's input, besides his being the ultimate enabler, was the identification of important rare blood type donors.

Dr. Rasmussen realized that many new blood donors would be necessary to satisfy the

increasing demands of the more complicated surgery coming online, as well as the needs of patients who required transfusion for nonsurgical indications. At the time of his 1962 report to the General Executive Committee, 35 percent of MGH blood came from replacement by patients and their friends and families, 25 percent came from professional donors (a practice later discontinued when shown to be less safe), and 40 percent came from the American Red Cross. He noted, "A limited number of units of blood are obtained from volunteer donors and donor clubs." Consequently, he set up a program to recruit such donors; George Parkhurst was the first donor recruiter in 1967. A further innovative program to increase voluntary blood donations was initiated in 1969 with the formation of the Massachusetts State Employee Blood Program, a cooperative effort of the state, the American Red Cross, the University of Massachusetts Blood Bank, and the MGH.

In 1972 Dr. Rasmussen was able to act on his earlier prediction that there would be a need for a hospital tissue typing laboratory based in the Blood Bank, and he convinced a postdoctoral fellow, Thomas Fuller, to take the job of setting it up and directing it.

Morten Grove-Rasmussen died unexpectedly in 1973. His legacy was large and diverse and extends from the bench to the bedside. He was able to accomplish great expansion of the Blood Bank without encountering resistance because he was able to convince decision makers of the wisdom of his requests and because his motives were so recognizably altruistic. He inspired people and was an exemplary human being. The MGH transfusion medicine fellowship is named in his honor, and both the AABB and the Massachusetts Association of Blood Banks recognize special contributions to transfusion medicine with awards named for him. Ironically, for all his celebrity, Dr. Rasmussen was never licensed as a physician in Massachusetts, nor did he have a medical school appointment.

Charles E. Huggins and the Blood Transfusion Service, 1973–1990

Charles Huggins (figure 22.3), the son of a surgeon who was a Nobel Prize-winner in Medicine, was born in Chicago, where he attended the University of Chicago. He graduated from HMS in 1952 and completed training in surgery at the MGH. In 1958, as a Moseley Traveling Fellow, Dr. Huggins did research at the National Institute for Medical Research in London. While there, he developed an interest in cryobiology and the cryopreservation of organs, and it was during this time that he began the work that culminated in his invention of the cytoglomerator, the device to which his name became attached and which was to make him internationally famous. Until this invention, banked blood stored in the refrigerator had a shelf life of only 21 days, and freezing red blood cells caused damage resulting in their hemolysis upon thawing. By using a cryopreservation agent (glycerol or DMSO) to prevent damage during freezing, and by removing that agent (as well as most of the white blood cells) using a series of glucose solution washes, it became possible to freeze entire units of donated blood, store them in freezers for years instead of for 21 days in a refrigerator, and, when needed, thaw and wash them free of cryoprotectant before transfusing them safely and with the same therapeutic effect as conventionally stored blood. More than 90 percent of the red cells survived the freeze-thaw-wash process and had normal survival times in recipients post-transfusion. The removal of white blood cells in the processing provided an added benefit, resulting in decreased human leukocyte antigen (HLA) alloimmunization, which is responsible for some adverse transfusion reactions and some forms of organ transplant rejection.

The Huggins cytoglomerator was a large machine that allowed for the automated deglycerolization of as many as five units of blood simultaneously. Dr. Rasmussen, envisioning the effect



Figure 22.4 Charles Huggins (left) and Morten Grove-Rasmussen presenting their experience with previously frozen blood at a meeting in the early 1960s

this would have on inventory management, the storage of units of rare blood, and the support of the active kidney transplant service at the MGH, was quick to engage Dr. Huggins (figure 22.4) and to set up a room dedicated to several Huggins cytoglomerators, with its own staff of operators. Dr. Huggins joined the Blood Bank in 1963, the year he published his findings on the cytoglomerator. Clinicians at the MGH were quick to accept this modality, but dissemination of details for its proper use as well as proper use of all component therapy lagged, as it did at many hospitals in the 1960s. The transfer of information from the relatively new specialty of transfusion medicine to clinicians had not yet begun in earnest and would not receive attention from practitioners until the 1980s, when transfusion transmission of dangerous and previously unfamiliar diseases made these specialists the main source of information about transfusions. By the 1980s newer techniques for frozen red cell processing replaced cytoagglomeration, but such developments do not diminish the role that Dr. Huggins played

in the advancement of knowledge and his influence on the practice of medicine. And when the time came, he retired his cytoglomerators and acquired the new machines.

In 1973, upon Dr. Rasmussen's death, Dr. Huggins was named Director of the Blood Bank and Transfusion Service. This was a busy year for him. In addition to passing the American Board of Pathology examination in Blood Banking, he set up an outpatient transfusion service so that ambulatory patients requiring elective transfusions could be safely accommodated without the inconvenience and added expense of admission to the hospital or emergency room. At this point the Blood Bank and Transfusion Service became simply the Blood Transfusion Service, the name it bears today.

Dr. Huggins's tenure coincided with a host of vexing global medical problems and technologic advances in response to those problems. The principal problems in transfusion medicine were the identification of a number of infections shown to be transmissible by transfusion (HIV, HTLV, hepatitis C, Chagas disease, for example); the added testing of donor units required to screen out infected donors; and the need to find new donors to replace them. His efforts to deal with these problems included acquiring buses fully equipped for mobile blood drives in 1976 and 1986; initiating a service whereby patients could donate blood for themselves for elective surgery (by 1987, nearly 10 percent of all transfusions at the MGH were of autologous blood); initiating an intraoperative blood salvage program manned by the IV team under the aegis of the Blood Transfusion Service; and advising the medical staff about the conservative use of transfusions (personal communications, Dr. T. Fuller). During this period, apheresis technology became available, which allowed for selective removal of the desired components of blood; the remainder was returned to the donor. Dr. Huggins acquired several of these instruments. At first, they were used primarily to collect blood

components (granulocytes in 1976, platelets in 1978), but, beginning in 1978, he began a therapeutic apheresis program. It was now possible to treat, or at least ameliorate, several diseases by selectively removing plasma, platelets, and even parasitized red blood cells.

Throughout this period, Dr. Huggins continued his research on whole organ cryopreservation, focusing his attention on the heart with MIT collaborators (personal communication, Dr. T. Fuller, 2009). In addition, he served on several important AABB committees, including the Autologous Transfusion, the Blood Components and Cryobiology, the Reference Laboratories and Rare Donor File committees, and was a District Director for the Northeast on the AABB Board of Directors from 1976 to 1980.

Charles Huggins died in 1990 after a brief illness. Like his predecessor, Dr. Huggins inspired great admiration and loyalty among his coworkers, as evidenced during interviews with his Assistant Directors in preparation for this chapter. For example, Thomas Fuller remarked, "Charlie Huggins was a staunch supporter. His door was always open and he provided me with exceptional advice on many subjects. I eventually succeeded through the constant scientific input from Dr. Huggins."

The Entry of Pathologists: "Charlie's Angels"

By 1978, Dr. Huggins realized that the role of the Blood Bank was expanding into new areas that involved therapy and that additional medical oversight would be necessary. In that year he appointed Dr. Joan Kumar (figure 22.5) Assistant Medical Director to head the therapeutic apheresis program. This was a milestone appointment for the Department of Pathology because Dr. Kumar had just finished her Pathology residency at the MGH and become the first of a succession of pathologists to be staff members in the Blood Transfusion Service; she had appointments in the Department of Pathology at the MGH and at



Figure 22.5 Joan Kumar

HMS. It was the first time in the modern era that pathologists were so extensively involved in the bedside care of patients, which gave the imprimatur of a major hospital to the practice of utilizing pathologists in this role. Dr. Huggins's repeated choices of former MGH Pathology residents to be his assistant medical directors was also a tribute to the commitment of Dr. Robert McCluskey, then Chief of the Department of Pathology, to the revival of the Clinical Pathology Training Program, which brought so many Pathology residents into contact with Dr. Huggins. In 1989, by mutual agreement, the Blood Transfusion Service was formally transferred from the Department of Surgery to the Department of Pathology.

Dr. Kumar's responsibilities included evaluating patients for suitability for the apheresis procedure, supervising all technical aspects of the procedure with the nurse/technician operating the apparatus, providing progress notes in patient charts, and consulting with the patients' physicians. In addition, she interpreted and communicated reference laboratory results to clinicians; these usually concerned complex cross-match problems and complicated transfusion issues related to autoimmune diseases. She also initiated a program of retrospective and prospective review of transfusions. That she did all this well was attested to by the fact that, as the program expanded from one to four apheresis machines, Dr. Huggins continued to look to the graduating Pathology residents as prospective assistant medical directors. Over the next five years, Drs. Katherine Kosinski, Rita Addison, Jettie Hunt, and Robert Kenney were added to the staff of the Blood Transfusion Service as they finished their Pathology residencies. They became known in the Blood Bank as "Charlie's Angels," a reference to a popular television program of the time. During interviews, four of these pathologists praised Huggins for his support and commitment to them, describing him as "charismatic," "pragmatic," "innovative," and a "gifted administrator."

Thomas Fuller, the Blood Transfusion Service, and the Development of the HLA Laboratory

Dr. Huggins was succeeded by Dr. Thomas Fuller (figure 22.6), who was named Acting Medical Director in 1990. Dr. Fuller graduated from Niagara University and earned his Ph.D. in immunochemistry from the State University of New York, Upstate Medical Center, in 1970. He came to the MGH that year as a postdoctoral fellow in the Transplantation Unit, under Drs. Paul S. Russell and Henry J. Winn. His project was to characterize the large number of serologic reagents Dr. Winn had acquired from the National Institutes of Health and to evaluate their potential role in compatibility testing for renal transplantation. Within nine months he was placed in charge of the HLA section of the unit. These endeavors brought him in close collaboration with Drs. Rasmussen and Huggins; with the latter he performed a study on 88 renal transplant patients showing a greatly decreased incidence of HLA antibody formation and hepatitis B transmission when they were transfused with previously frozen red blood cells. In 1972, Dr. Rasmussen, convinced that there was significant overlap in the



Figure 22.6 Thomas Fuller

fields of red cell and HLA serology, invited Dr. Fuller to start a clinical histocompatibility laboratory based in the Blood Bank. With the promise of generous laboratory space, equipment, and staff, and with the access to Dr. Winn's collection of HLA typing sera, Dr. Fuller accepted this unexpected offer. This began an 18-year collaboration with Dr. Huggins that resulted in numerous coauthored publications. Upon assuming the Directorship after Dr. Rasmussen's death, Dr. Huggins appointed Dr. Fuller to the position of Assistant Director (Scientific), with the added responsibilities of overseeing all aspects of red cell serology and hepatitis testing.

During this time Dr. Fuller collaborated with Dr. Huggins to develop a practical procedure for cryopreserving viable human lymphocytes that did not require expensive controlled rate freezers and that also preserved lymphocyte function. With Dr. Rasmussen's help, Dr. Fuller refined a method for antiglobulin HLA antibody screening and donor lymphocyte cross-matching. These tests continue to be used at the MGH for renal transplant candidates. Beginning in 1976, with Dr. Huggins's approval and material support, Dr. Fuller and his staff participated in quadrennial international histocompatibility workshops. All the major HLA laboratories were involved in these workshops, which resulted in several publications from the MGH HLA Laboratory. Also in 1976 the MGH received a grant from the National Heart Lung and Blood Institute for "Studies Basic to Heart Transplantation," of which Dr. Fuller was a coinvestigator. In the 1980s, with grant support, Dr. Fuller continued his HLA research, focusing on the structure of HLA antigens, the type and specificity of lymphocyte responses in normal individuals and transplant recipients, and the effects of a variety of innovative immunosuppressive drugs on nonprimate kidney transplant recipients. The result was 37 publications related to these projects.

The onset of Dr. Huggins's fatal illness in October 1989 had a predictably marked effect on the Blood Bank. In Dr. Fuller's words, the "world began to crumble." He agreed to stay on temporarily as Interim Director until a permanent one could be identified, and he accepted a position in the Department of Pathology at the University of Utah in 1991.

THE TRAINING PROGRAM

The backbone of the training in blood banking in the 1950s through 1970s was the volunteer teaching duo of Susan Jago Britten (1933–1993) and, in coagulation, of her husband, Dr. Anthony Britten (1935–1996) (figure 22.7). Sue Britten, the daughter of a British physician, received a B.S. from the University of Sheffield in 1956. After training and working at the British National Blood Transfusion Centre, she came to the United States in 1958 "as a lark" (personal communication, Rebecca Britten Loprete) and joined the Blood Bank at the MGH as a technician, quickly working her way up to Chief Technician. Pathology residents began rotating through the Blood Bank informally in 1953, with Dr. Rasmussen's encouragement. At that time there was no time allotted in the residency program specifically for that rotation and no officially scheduled lectures or demonstrations. The latter were

provided voluntarily by Sue Britten on her own time and expanded and contracted depending on the interest and diligence of the resident. Each morning Sue would deliver an ad lib lecture on an antigen system, antibodies, blood collection, transfusions, blood bank history, and so on. Following this, she would take the resident to a bench where she had set up panels for antibody detection and identification and units for crossmatching. Her skills as a teacher and her enthusiasm for her subject made it difficult not to pay close attention. By the end of a few weeks under her tutelage, a resident could be a reasonable facsimile of a blood bank technician.

It was during this time (1962) that she met (and later married) Anthony Britten, an expert on coagulation, who had emigrated from South Africa. Dr. Britten, a severe hemophiliac, had been home-tutored for most of his childhood and adolescence. Despite serious complications from his disease, he was able to read medicine at the University of Witwatersrand and complete his medical training. After initially working at New England Medical Center, Dr. Britten came to the MGH as a Research Fellow in Hematology. His research interests centered on the treatment of hemophilia, but he was also interested in bleeding problems associated with open heart surgery, a major activity at the MGH. By 1965, in collaboration with Dr. Edwin Salzman, an MGH surgeon, he had already written a well-received manual for medical staff to manage hemorrhage and thrombosis (23). Tony Britten played the same role in teaching coagulation to Pathology residents that his wife Sue did in blood banking. Sue Britten also managed to teach enough blood banking to her husband that he was able to become the Medical Director of the American Red Cross Program in Albany, New York, for which they both departed in 1972. Tony Britten later became head of the blood program of the League of Red Cross and Red Crescent Societies in 1985, where he served until his retirement in 1989.



Figure 22.7 Anthony and Susan Britten

Joel Umlas, an author of this chapter, while in residency training at the MGH in the mid-1960s, had the privilege and good fortune to receive his blood bank training from Dr. Grove-Rasmussen and the Brittens. The instruction and inspiration they provided, especially by Sue Britten, was instrumental in mapping the course of his career for more than 30 years.

In the mid-1970s, Dr. McCluskey's commitment to providing an excellent, structured training program in clinical pathology resulted in the establishment of a formal rotation in blood banking and transfusion medicine. This rotation evolved considerably over the years. The core rotation today is for two months and includes lectures and hands-on experience in all areas of transfusion medicine, including recruitment and initial evaluation of donors, drawing blood units, blood component preparation, testing and storage, and use of the information system. Residents evaluate and manage transfusion therapy of outpatients as well as therapeutic apheresis. An additional two weeks is spent in the Histocompatibility Laboratory, and a series of lectures on transplant immunology and histocompatibility testing is offered before and during the laboratory rotation. The residents generate interpretative reports

and consultations for new apheresis patients. After an initial phase-in period, the resident has a graduated increase in patient care responsibilities, culminating in carrying an on-call beeper and taking first call for consultations.

The Transfusion Medicine Fellowship at the MGH, started by Dr. Christopher P. Stowell, first received accreditation from the Accreditation Council for Graduate Medical Education in 1992. From 1998 to 2000 it was affiliated with a similar program at Brigham and Women's Hospital (BWH), and in 2001 the Transfusion Medicine Fellowship at MGH merged with the those at Beth Israel Deaconess Medical Center (the oldest of the Harvard Transfusion Medicine Fellowships, founded in 1986 by Dr. Walter Dzik at New England Deaconess Hospital) and BWH to form the HMS Transfusion Medicine Fellowship, one of the largest accredited programs in the United States. It is approved for four clinical training positions and eight research positions, the latter supported by an NIH T32 Training Grant. Clinical fellows rotate among the three founding hospitals as well as Children's Hospital Boston and the Dana-Farber Cancer Institute. The MGH program graduated seven fellows before the merger. Since then, 23 fellows have graduated from the combined program. Many of the graduates have gone on to leadership positions in prestigious academic departments.

The Blood Transfusion Service Today

Dr. Christopher P. Stowell was named Director of the Blood Transfusion Service in 1991. Dr. Stowell graduated from Brown University and received a Ph.D. in biochemistry from Johns Hopkins University. He graduated from the University of Connecticut School of Medicine and trained in clinical pathology and transfusion medicine at the Hospital of the University of Pennsylvania. Since he became the Director of the Blood Transfusion Service at the MGH, the residency training program in transfusion medicine was restructured, and a fellowship program was initiated and accredited. With the advent of a bone marrow transplantation program, new clinical services were developed in the Blood Transfusion Service, including a bone marrow processing laboratory and peripheral blood stem cell (PBSC) collection by apheresis. The MGH became the first PBSC collection facility in New England for the National Marrow Donor Program. As a result of collaborative efforts between all the physicians in the Blood Transfusion Service and their colleagues in Pediatric and Adult Hematology and Oncology, the MGH became a member of the Clinical Trials Network in Transfusion Medicine and Hemostasis, supported by the National Heart Lung and Blood Institute.

Walter ("Sunny") Dzik joined the MGH Blood Transfusion Service as Codirector in 1998. Dr. Dzik graduated from Princeton University and from the University of Pennsylvania School of Medicine. Following training in internal medicine and hematology at Boston University, and a fellowship in transfusion medicine at the National Institutes of Health, he became Director of Transfusion Medicine at New England Deaconess Hospital. He was Associate Director of the Blood Bank when that hospital merged with Beth Israel Hospital to form Beth Israel Deaconess Medical Center in 1996. Since joining the MGH Blood Transfusion Service, Dr. Dzik has coauthored with Dr. Stowell a pivotal randomized control trial on the role of universal leukocyte reduction, and he has collaborated with others in studies defining the proper use for blood components before invasive diagnostic procedures. He has worked to improve patient identification before transfusion using radiofrequency identification (RFID) technology. Dr. Dzik is also involved in malaria research in Uganda as well as attempts to improve diagnostic laboratory services at Uganda's largest pediatric hospital.

Dr. Susan L. Saidman became Director of the Tissue Typing/Histocompatibility Laboratory



Figure 22.8 MGH Blood Transfusion Service, 2010. Left to right: Robert Makar, Walter Dzik, Christopher Stowell, Susan Saidman.

in 1993. She graduated from the University of Alberta and received her Ph.D. in pathology from the University of Pittsburgh School of Medicine. Shortly after joining MGH, she introduced polymerase chain reaction (PCR)-based HLA typing to the lab. She later added solid phase assays for HLA antibodies and collaborated in studies on the diagnosis and treatment of humoral rejection in kidney transplant recipients. A chimerism assay was added to the clinical test menu in 2001 and is utilized extensively to monitor patients after bone marrow transplantation and to support pioneering studies by the MGH Transplant Center on the induction of tolerance after kidney transplantation. Dr. Saidman is also a founding member of the New England Program for Kidney Exchange, a regional registry for matching patients and kidney donors.

Dr. Robert S. Makar joined the staff of the Blood Transfusion Service in 2006 as the Assistant

Director. He received his undergraduate education at Rice University and earned an M.D. and Ph.D. at the University of Texas, Southwestern School of Medicine. Following an internship year in internal medicine at Barnes-Jewish Hospital in St. Louis, Dr. Makar completed clinical pathology at MGH and a fellowship in transfusion medicine in the newly consolidated Harvard Medical School program. Since joining the staff, Dr. Makar has carried out an important study comparing strategies to screen and test blood donors for evidence of HLA alloimmunization, and he has written a highly valued guidebook to clinical transfusion for resident trainees. He also has been recognized by the residents for the excellence of his teaching: he received the Clinical Pathology Teacher of the Year Award the first year he was on staff.

The Blood Transfusion Service in 2011, located in the Gray-Jackson Building, includes a donor

center, two mobile collection buses, an outpatient transfusion center, an AABB-accredited reference immunohematology laboratory, an American Society for Histocompatibility and Immunogenetics-certified Tissue Typing Laboratory, and a therapeutic apheresis unit. The FDA-licensed donor center processes 15,000 blood donations annually, making packed red blood cells, fresh frozen plasma, and platelet concentrates from whole blood donations, but it also collects platelets and red blood cells by apheresis. These donated components constitute approximately half of the 75,000 blood components transfused to more than 10,000 MGH patients per year. The availability of this in-house supply of blood has protected MGH from the vagaries of the blood supply, allowing the institution to support the needs of the robust surgical, trauma, and oncology services. The Blood Transfusion Service also supplies plasma derivatives such as clotting factors, intravenous immunoglobulins, albumin, and hyperimmune globulins, and carries out a variety of modifications of blood components to meet specific patient needs. The outpatient transfusion/infusion facility receives 1,700 patient visits a year and performs 600 therapeutic phlebotomies, 250 therapeutic aphereses, and 250 peripheral blood progenitor and mononuclear cell collections annually. In addition, its professional staff of three physicians (Drs. Stowell, Dzik, and Makar) and one Ph.D. immunologist (Dr. Saidman) (figure 22.8) provides consultation services over a wide range of diagnostic and management issues, including serologic problems, massive transfusion, coagulopathy, immunomodulatory therapies, transplantation issues, and the use of specialty blood components and plasma derivatives. The services of the Blood Transfusion Service are unusually wide-ranging for a hospital-based blood bank; if the service is not unique, it is one of the foremost practitioners of transfusion medicine in the nation. This represents a truly remarkable evolution for a service that started out over 68 years ago with one physician, one nurse, one technician, a part-time maid, and a refrigerator in the basement of the Department of Pathology (24).

References

- 1. Denis JB. Lettre touchant deux expériences de la transfusion faites sur des hommes. Paris: J. Cusson, 1667.
- 2. Hadju SI. A note from history. Blood transfusion from antiquity to the discovery of the Rh factor. Ann Clin & Lab Sci 33:471–473, 2003.
- 3. Blundell J. Experimentation on the transfusion of blood by the syringe. Med Chir Trans 9:56–92, 1818.
- 4. Blundell J. Observations on transfusion of blood. Lancet 12 (orig. 2):321–324, 1829.
- 5. Porter CA et al., cited in *The Massachusetts General Hospital 1935–1955*. Faxon NW, ed. Cambridge: Harvard University Press, 1959, 295.
- 6. Lee RI, White PD. A clinical study of the coagulation time of blood. Am J Med Sci 145:495–503, 1913.
- 7. Lee RI, Vincent B. The coagulation of normal human blood, an experimental study. Arch Intern Med 13:398–425, 1914.
- 8. Lee RI, Vincent B. The relation of calcium to the delayed coagulation of blood in obstructive jaundice. Arch Intern Med 16:59–66, 1915.
- 9. Lee RI, Vincent B. A study of the effect of anaphylaxis and leech extraction on the coagulation of blood. J Med Res 32:445, 1915.
- 10. Rous P, Turner JW. The preservation of living red cells in vitro. J Exp Med 23:219–237, 1916.
- 11. Rous P, Turner JW. The transfusion of kept cells. J Exp Med 23:239–247, 1916.
- 12. Rous P, Turner JW. A rapid and simple method of testing donors for transfusion. JAMA 64:1980–1982, 1915.
- 13. Robertson OH. A method of citrated blood transfusion. Brit Med J 1:477–479, 1918.
- 14. Robertson OH. Transfusion with preserved red cells. Brit Med J 1:691–695, 1918.
- 15. Alexi-Meskishvili V, Konstantinov IE. Sergei S. Yudin. An untold story. Surgery 139:115–122, 2006.
- 16. Judine S. *La transfusion du sang de cadavre à l'homme*. Paris: Masson, 1933.

- 17. Yudin SS. Transfusion of stored cadaver blood. Practical considerations: the first thousand cases. Lancet 230:362–366, 1937.
- 18. Fantus B. The therapy of the Cook County Hospital. JAMA 109:128–131, 1937.
- 19. Huggins CE, cited in *The Massachusetts General Hospital 1955–1980.* Castleman B et al., eds. Boston: Little, Brown, 1983, 351.
- 20. Obituary of Morten Grove-Rasmussen. AABB News, October 1973.
- 21. Grove-Rasmussen M et al. The use of group O donors as "universal donors." Dangers arising from

"immune" anti-AI and anti-B in group O sera. Proceedings of the Fourth Annual Meeting of the American Association of Blood Banks, Minneapolis, October 27, 1951.

- 22. Grove-Rasmussen M. The reference laboratories program of the American Association of Blood Banks. Transfusion 2:188–193, 1962.
- 23. Salzman EW, Britten A. *Hemorrhage and Thrombosis: A Practical Clinical Guide.* Boston: Little, Brown, 1965.
- 24. Soutter L. The MGH News, 112:1–3, May 1952.