MY HISTORY IN HLA

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HOW I REMEMBER IT STARTED

In 1968 I joined the faculty of the Department of Surgery at Wayne State University with the specific charge of stimulating teaching and research in transplantation immunology in the Department of Surgery and to start a clinical renal transplant clinical program in Detroit. My qualifications for assuming these responsibilities resided in the fact that my surgical training was at the University of Minnesota where I had done some research in transplantation (Transplantation Bull., 30:531-533, 1962) and had also obtained a PhD degree (1963). I had also participated in the first renal transplantation at the University of Kentucky in 1965 and had been involved in running a dialysis unit for chronic renal patients doing vascular access while in Toledo. I was generously given a great deal of support by the Chair of the Department, Dr. Alex Walt, who provided me with a laboratory and technical help. We became quite productive and produced several publications over the next few years. (Transp., 8:152-161, 1969, Transpl., 11:151-157, 1971, J. Surg. Res., 11:173-175, 1971, J. Surg. Res., 11:492-495, 1971, Europ. Surg. Res, 4:1-9, 1972, Arch. Surg., 105:255-259, 1972, Lab Invest., 27:287-295, 1972)

Our team did its first transplant at the Detroit Receiving Hospital the first year I was in Detroit (1968). The deceased donor was declared brain dead using criteria promulgated by the Uniform Anatomical Gift Act established the previous year. Transplantation was in its infancy then and only a handful of university hospitals were doing renal transplants and fewer laboratories were in existence doing research in what was becoming known as the Major Histocompatibility Complex or HLA.

I became interested in hyperacute rejection which had been described for the first time by Kissmeyer-Nielson in 1966. It was he who coined that term. He also suspected that it was caused by presensitization and circulating antibody. Two years later Mel Williams at John Hopkins came to the same conclusion based on his experience with hyperacute rejection. Having reproduced hyperacute rejection in large experimental animals and seen its devastating effects, I developed an acute awareness of this complication and a keen desire to never see it clinically. It was at the forefront of my mind when we were about to embark on our first living related transplant in 1969, the year Paul Terasaki published his seminal paper on the crossmatch in the New England Journal of Medicine.

We immediately sent blood to his laboratory in Los Angeles to confirm the fact that there were no antibodies present in the recipient against her HLA identical sibling. (see figure 1). It was comforting to have this laboratory reassurance that we would not see hyperacute rejection. After several similar transfers of blood from Detroit to Los Angeles involving deceased donors, I realized that we needed to start HLA typing and crossmatching at our center and therefore sent one of the technologists from my laboratory to Los Angeles to spend a week with Dr. Terasaki and learn the techniques he
had developed. Paul Terasaki generously hosted legions of such visitors and his generosity and his continuing willingness to share his knowledge and experience with anyone interested in transplantation and tissue typing is exemplary of collegiality among scientists. It should be pointed out that at this time, Surgery Departments were at the forefront of transplantation immunological research and many histocompatibility laboratories, even Dr. Terasaki’s, were in Departments of Surgery. Our lab started out in Surgery but was soon moved into the Hematology Laboratory at the Detroit Receiving Hospital when Dr. Margaret Palutke became interested in HLA typing.

Figure 1: Early Crossmatch Scoring Sheet

Life in a histocompatibility laboratory was simpler in the early 70s. Very few HLA specificities were known and reagents were freely available through the NIH. We were not concerned with whether the lymphocytes were B cells or T cells and were thrilled with the cell preps we got when the ficoll-hypaque gradient technique was introduced. The most complicated instrument needed for the standard crossmatch was an inverted stage phase contrast microscope. It was the most complicated instrument in the laboratory and was treated with the reverence we sometimes now give to the flow cytometer. In the beginning, when a deceased donor (which was referred to by the currently politically incorrect term, “cadaver donor”) was identified, I would go to the hospital and draw the blood and bring it back to the lab for typing and crossmatching, along with the donor’s kidneys. Later on we learned the value of using lymph nodes as a source of lymphocytes. While typing and crossmatching were carried out, the kidneys were preserved in a sterile plastic bag which was initially developed to protect the small
intestine during abdominal operations. I was often in the lab at this time, waiting for the results and chatting with the tech while she performed the assays. I never met a histotech I didn’t like and the technologist who did all the tissue typing and crossmatching at this time was one of my many favorites. Jerry Swiderski was an enthusiastic bright young lady who, like the rest of us, was always on call when a donor became available. She mastered the complexities of the HLA system as it developed and was an invaluable member of the transplant team.

In 1971 there were three centers doing transplantation in Michigan. Dr. Jerry Turcotte at the University of Michigan was involved in the first transplant in Michigan in 1964 and was head of the program. Dr. Stan Dienst at Henry Ford Hospital in Detroit had established a program there about the same time we had done so at Detroit Receiving Hospital. The Department of Surgery at the newly formed Michigan State University Medical School was planning to establish one in East Lansing and had recruited two surgeons, Drs. Edward Coppola and John Ackerman, who had experience in transplantation. We got together and, with the help of the local Kidney Foundation, established an organ procurement organization for the State of Michigan. It was incorporated as the Transplantation Society of Michigan (TSM) in December of 1971. Our name changed several times before we settled on Gift of Life Michigan in 2000. It was one of the first state wide OPOs established in the United States and has been extremely successful in fulfilling our early expectations of providing the people of Michigan with the maximum possible benefit from deceased donor organ transplantation.

In 1973 our transplant program was moved to Hutzel Hospital in the Detroit Medical Center. The Wayne State University faculty retained the responsibility of staffing the program. I moved my laboratory to that hospital when I became Chief of Surgery. We briefly did tissue typing there but later relied on Dr. Palutke’s lab which had moved to Wayne State University’s research building. This laboratory is now part of the Detroit Medical Center and supports the transplantation program at Harper University Hospital.

Despite my heavy clinical responsibilities, I maintained a close involvement with my laboratory and continued to publish in the field of transplantation biology. Shortly after the formation of the forerunner of ASHI in 1974, (the American Association of Clinical Histocompatibility Testing) I became a member of this society and presented some of our studies on detection of antibodies in prospective transplant recipients in the meeting of 1978. (J. Immunol., 112:890-896, 1974)

HLA typing and crossmatching for the deceased donor was a constant problem during the years of our OPO. At first, each program did it for their own patients. But as the number of donors grew and additional renal transplant programs were established, it became obvious that it had to be centralized. At this juncture, there were four Histocompatibility Laboratories in Michigan, one at each of the major state Universities and one established by Dr. Richard Walker at William Beaumont Hospital. He was well known for his work with paternity testing using HLA. A complex weekly rotation system was organized by TSM for each of the aforementioned laboratories to take a turn at being the laboratory responsible for typing donors and crossmatching the patients on the waiting list using...
trays prepared by the transplant program’s histocompatibility laboratory. This function was supervised by the Histocompatibility Committee of TSM which I chaired.

In 1982, TSM had grown to the extent that they needed to move into their own building instead of renting space. In planning the move, it was decided to include a Histocompatibility Laboratory in the facility. Dr. David Steinmuller became the first Laboratory Director but left after a couple of years and I stepped in as Laboratory Director, a position I have held until recently when we enticed Dr. A. Bradley Eisenbrey to take over the direction of the laboratory. I have stayed on as co-director.

Our first laboratory Supervisor was Tim Williams who had been trained at the Cleveland Clinic laboratory by Bill Braun and Andrea Zachery. He was with us for 18 years and was an outstanding administrator and technologist who could be relied upon to do everything accurately and exactly by the book. ASHI inspectors were awed by his record keeping. Dorothy Levis took over in 2000 and shepherded the laboratory to new quarters in 2008. She had been the lead technologist in the Histocompatibility Laboratory at Henry Ford Hospital before moving to Ann Arbor. She is nationally recognized as one of the most outstanding histopathology technologists in the country and her leadership has proved invaluable in expanding our laboratory to where we now have a staff of 28 full-time members in close to 6,000 square feet of laboratory space.

REFLECTIONS

I have had the privilege of entering the field of transplantation and histocompatibility early in its history and have grown professionally as it matured. I have treasured the relationships I have had with my co-workers and those whom I have met at national and local meetings. I have learned so much from them and have been warmed and comforted by their friendship. They have become my other family. My involvement in the laboratory continued long before I was a Surgeon and has continued long after I left that arena. Involvement in histocompatibility has kept me young and my enthusiasm for getting to the lab everyday has not abated, even as I approach my 81st birthday.