Obituary

Thomas Earl Starzl
(*11 March 1926–4 March 2017*)

As Starzl himself once wrote, 'all too often, the starting point of an era is arbitrary and decided upon by someone who believes the dawn to be the moment of his own arrival'.[1] He was referring to Sir Peter Medawar's work on rejection of skin grafts but for everyone in the field of liver transplantation, the era began when a young surgeon named Thomas Earl Starzl decided to figure out how to take a liver from a donor and transplant it into a patient with liver failure.

Born in the small town of Le Mars in Iowa, Starzl went to medical school at the Northwestern University, Chicago, USA. He emerged 5 years later with an MD as well as a PhD in Neuroscience. He trained in surgery—general, vascular and thoracic—at Johns Hopkins, the University of Miami and back again at Northwestern where he joined as faculty after completing his training.

In 1958, Starzl's chairman at Northwestern nominated him for a Markle scholarship. The purpose of this award was to keep young faculty in academic medicine. Each awardee was required to focus on solving a particular problem. Starzl's proposal was the development of clinical transplantation. At that time, the immunological barrier to transplantation was considered insuperable and the only successful transplants had been kidneys between identical twins. He was awarded the fellowship in 1958.

Starzl found a mentor in William Waddell who left the Massachusetts General Hospital to become the head of surgery at the University of Colorado, Denver. Starzl joined him in 1961 and they decided that clinical liver transplantation would be their highest priority. They decided that clinical trials of kidney transplantation would be performed first, followed by liver transplantation.

The kidney transplant programme was immediately successful and by 1964, about/more than 70 kidney transplants had been done.[2] However, the liver transplant programme ran into problems. The first attempt to transplant a liver was made by Starzl and his team on 1 March 1963.[3] Seven attempts to perform liver transplants in humans were made that year, five by Starzl and his team. All were unsuccessful. In hindsight, the passive veno-venous bypass used in these patients seems to have led to fatal pulmonary embolism. The team decided to impose a voluntary moratorium until they figured out what had gone wrong.

With the use of antilymphocyte globulin and azathioprine for immunosuppression, the programme started again in July 1967 when they performed the first successful liver transplant in humans. By the end of the year, many successful liver transplants had been performed.[4]

The next revolution in the field of liver transplantation was the introduction of cyclosporine A, making immunosuppression much more reliable and less toxic. Starzl was at the forefront of this development as well. He reported more than 80% survival in patients who underwent liver transplantation, utilizing cyclosporine A and prednisone for immunosuppression.[5] This established liver transplantation as a clinical service and standard of care for management of liver failure. There was a proliferation of liver transplantation centres all over the world. This was also the year that saw Starzl move from Denver to Pittsburgh to establish the centre, which now bears his name.

The University of Pittsburgh Medical Center became best known for its institute for transplantation, later the Thomas E. Starzl Transplantation Institute. Here, more abdominal organ transplants were being done than in any other centre in the world. At its peak, more than 600 liver transplants were being performed in a year.

It was here that the next important advance in transplantation, the introduction of FK-506 as a powerful immunosuppressant was announced.[6] The success rates of liver transplantation were now more than 90%. When I was a fellow at the Starzl Institute (2004–07), tacrolimus levels were still referred to and reported as 'FK levels'. The Starzl Institute was now the 'Mecca' of liver transplantation. Surgeons trained at the institute had established liver transplant programmes all over the world. Even those who had done their primary training elsewhere and had ongoing successful liver transplant programmes felt compelled to make the 'Hajj' and visit the Starzl Institute to see what the future of transplantation was like.

Starzl also provided a broad umbrella and motivated others to develop various aspects of transplantation. The best example is the perfection of intestinal transplantation under the leadership of Kareem Abu El-Magd.[7]

Starzl stopped operating in 1992 but remained intent on overcoming the last remaining challenge in organ transplantation—the aim of achieving organ-specific tolerance. Most of the long-term consequences of organ transplantation were now the side-effects of the immunosuppression, which patients had to be subjected to for the rest of their lives. If the immunosuppression could be stopped, patients would return to a normal life. Working from his office above the Pizza-Hut across the road from the hospital, he worked out a protocol for 'tolerogenic immunosuppression'. Since the protocol required a period of treatment before the transplant, it was best suited for living donor liver transplantation. Amadeo Marcos, one of the pioneers of adult-to-adult right lobe living donor liver transplantation was recruited to head the transplant unit at the Starzl Institute and trials of the new protocol began.

I was a fellow at the institute while this study was being conducted. We saw patients completely off immunosuppression 3 months after living donor liver transplants. We also encountered Starzl at the pathology conferences in which the biopsies of these patients were discussed. He would sometimes visit the patients, and he was invariably present at the research meetings where the progress of the study was reviewed.

Unfortunately, the study was marred by a high rate of complications in the recipients, particularly biliary complications and never saw the light of day. The death of one of the first patients recruited into the study, Katy Miller, after a second liver transplant due to recurrent sclerosing cholangitis led to Starzl finally announcing his retirement from the field he built into what it is now.

Starzl quoted Medawar, 'good scientists study the most important problems they think they can solve'. He solved most of the problems in the field of solid organ transplantation. What can one say about someone who achieved so much and touched so many lives across the world? There was a theory in the 19th century that history is determined by the impact of a few 'Great Men' who have a decisive impact on human society. This is certainly true of the field of transplantation. This was a Great Man. Let us celebrate his life.

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