OBITUARY

Thomas Earl Starzl, the father of transplantation (March 11, 1926–March 4, 2017)

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On March 2016, the transplant community pompously celebrated the 90th birthday of transplantation pioneer, Th. E. Starzl. More than 400 surgeons and scientists hailing from all over the United States and from all five continents met in Pittsburgh to pay tribute to their mentor, teacher, and friend. The "Starzl family" at large experienced a once-in-a-lifetime event ending with a thoughtful, but typical "Starzl speech" about the past and the future, including a humoristic but realistic view on life and aging. After three remarkable birthday parties with the presence of medical and paramedical staffs, as well as several patients ("his heroes") and their families, everyone returned home with the content of having met "their spiritual father" reminiscing the old memories. Handshake was made and, considering his excellent status, plans (or dreams) were already made to meet again in five and, why not, in ten years since then (Fig. 1).

On March 4, 2017, one week before his 91st anniversary, the world of transplantation was shaken by the sad news about the unexpected, sudden death of Th.E.Starzl.

Without any doubt, Th. E. Starzl had been one of the most influential personalities in the field of medicine during the second half of the 20th and the beginning of the 21st centuries. His relentless search for innovation indeed changed absolutely the way surgery and medicine should be conceived. He dedicated his personal life and his career as a scientist to search continuously for the improvement of patient care, taking thereby into account the highest moral and professional standards all in the setting of a "interdisciplinary matrix." Due to its everlasting endurance and determination, the initially highly controversial field of organ transplantation became rapidly accepted as a leading discipline at university and academic levels.

Figure 1 Prof.Th.E.Starzl at the occasion of his 90th birthday party

After a promising start in neuroscience research, his brilliant career focused on research in liver pathophysiology, liver and pancreas metabolism, development of safe(r) surgical techniques to replace the damaged liver, improvement in organ preservation and procurement, improvement of definition of brain death, modulation and best use of immunosuppressive drugs (termed by him as the multiple-agent techniques of immunosuppression), reversibility of immune allograft rejection, xenografting, and finally the discovery of micro-chimerism, a finding fundamental to explain "allograft accommodation" and tolerance. All these discoveries were in the forefront of medical developments, and all became applicable to all other types of organ transplantation. The micro-chimerism paper published through Lancet became one of the most frequently cited articles in the transplantation literature. This "countercurrent" finding led to the "conceptual unification" of solid organ and bone marrow transplantation and also laid the foundation

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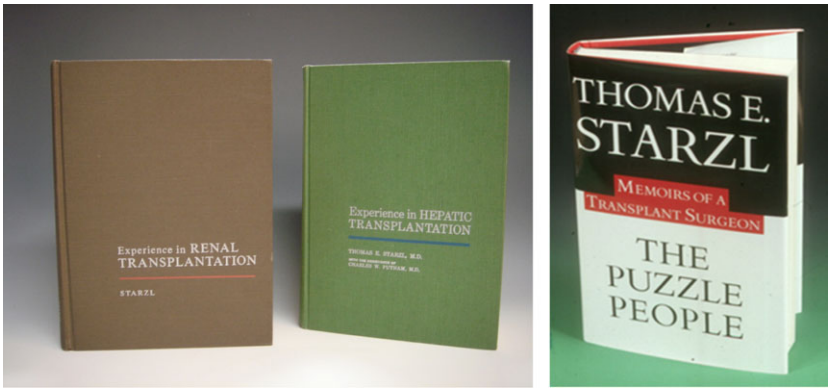

Figure 2 The 'old and new testaments' of transplantation and his legendary book 'Memoirs of a transplant surgeon'

for immunosuppression minimization and withdrawal strategies that are fundamentals to counteract the many (also lethal) side-effects of lifelong immune suppressive therapy [1,2].

His initial research and, mostly disappointing, clinical experiences intuitionally led him to rapidly understand that the road to successful liver transplantation necessarily needed to pass through the (surgically simpler) model of kidney transplantation. The detailed clinical observations of his early renal patients hospitalized in the worldwide largest renal transplant unit, at that time, made him also the real founder of renal transplantation, a merit often forgotten by the younger generations of surgeons and nephrologists! Once the surgical techniques refined, and the reason behind the immune rejection of the kidney mastered by using the "steroids plus azathioprine secret" and the antilymphocytic serum ALG, liver transplantation evolved within five years from a "wild science fiction view" to a clinical reality. Several years of round-the-clock laboratory and clinical work made the "impossible" operation possible. The first liver transplantation was performed on March 1, 1963. The first successful case was in July 1967, and the procedure was recognized finally in 1983 at the NIH Consensus Conference as a valuable therapy for patients with end-stage liver disease.

The early experiences at Denver related to renal and liver transplantations were compiled in, which I would call "the old and new testaments" of transplantation medicine. The textbooks "Experience in renal transplantation" and its companion "Experience in hepatic transplantation," edited respectively in 1964 and 1969, an era in which both types of transplantation remained highly controversial, provide a detailed, 936-pages-long information about the outcome of 74 kidney and 29 liver transplantations only, including six renal and one liver xenografts (!) [3,4] (Fig 2). These books are not only among the most frequently cited books in the history of medicine, but most of all they witness for all future generations the meaning of integrity (triumphs and defeats being equally reported) and in-depth analysis of both experimental and clinical research (all surrounding events such as coagulation disorders and de novo tumor development were also analyzed) and of excellency in translational research. The "embryonic" 1958-1990 transplantation experience at Denver rapidly became full grown one after his move to the University of Pittsburgh in December 1980. The efficacy of the calcineurin-inhibitor cyclosporine and of, its "improved version," tacrolimus (almost exclusively tested by Starzls' team), not only remarkably improved survival curves and quality of life of the recipients but also allowed to embark on the "forbidden" multivisceral and intestinal transplantations. Being criticized heavily at that time to have a monopolized use of the Japanese "million dollar drug," one has to admit that this approach still is an ideal example of how a well-conducted "investigator-driven study" is capable of reshaping the practice within a given medical field in a very short and thus efficient way, a lesson not to be forgotten in an era when clinical research is too often dominated by (paralyzing) "industry-driven studies," and "trialomania." The FK506 and other captivating stories are uniquely described in his best-selling autobiography "The puzzle people, memoirs of a transplant surgeon." Reading this book is a must for every individual involved in transplantation [5].

His unique interest in liver transplantation, an operation initially conceived to treat (nonresectable) hepatobiliary cancers, also led him to have a major change in the practice of liver surgery. The right and left trisegmentectomy eventually combined with resection of the caval vein substantially expanded the boundaries of hepatobiliary oncology.

The impact of both his ground-breaking work and his "captivating charisma and attraction" was enormous. It resulted not only in one of the most prolific scientific productions ever (with more than 2300 publications, he was one of the most cited scientist in clinical medicine; in 1991, every 1.8 days a paper was published), but even more importantly, it resulted in the training of numerous fellows coming from all over the world making Pittsburgh in no time the Mecca of the transplant world. Until the end of the 20th century, almost every liver transplant program in the world could trace "its paternal or grand-paternal lineage" to Dr. Starzl. His "extraordinary" mentorship allowed, directly or indirectly, to hundreds of thousands end-stage diseased patients to benefit from a new life!

Needless to say that numerous, national and international honorary degrees (including the ESOT honorary membership), distinctions, and awards were given to him as a token of appreciation, read admiration for his lifetime achievements. He received them all but one, the Nobel Prize. When looking back at his career and impact on the development of modern medicine and not to forget modern life (he was ranked at no. 213 of 1000 men and women who shaped the millennium), it is hard to understand that the Nobel Prize Committee omitted to recognize such an important service to humanity.

Besides being a pioneer, a medical genius and a legend, Starzl was also a great human and a great humanitarian. All who worked with him will remember his unlimited empathy, respect, and engagement for his collaborators, right from the lowest to the highest ranked level, and, even more so, for his patients, their families, and, importantly, also the donor families. His research was patient-centered, encompassing thereby all cultural, religious, gender, and racial boundaries. The core value of his medical and human behavior was not at all a business-driven but always a patient-driven medicine based on correctness, altruism, and public trust. All who worked with him will also remember his unlimited memory right from remembering the first names and even blood groups (!) of his patients via (un)usual anecdotes up to the details about every single operative event, be it a successful one or a disastrous-one. He also had a remarkable capacity to keep the track of the accomplishments, successes, and disappointments of *all* his scholars and mentees to a largest extent. It seemed to many of us that he wanted to be assured that patients could, at least indirectly, take the advantage of the right application of his wisdom, advice, and teaching as much as possible. His concern, which was already expressed as early as in 1974, not only for the real need of transplant centers and their optimal localization, the need for an adequate training of a sufficient number of transplant surgeons but also the fear for a superfluity of transplant surgeons have to be seen in this context.

When giving his presidential address at the 1974 inaugural meeting of the American Society of Transplant Surgeons, Starzl quoted these prophetic words from the distinguished scientist and historian, T.S. Kuhn: "progress consists of a series of great and small revolutions against authority. A great advance necessitates the overthrow of an established dogma, and when that occurs the advance itself becomes a new dogma to which advocates flock. It is natural for those disciplines to become protectors instead of improvers of the status quo, guardians of the past instead of seekers of the future." These prophetic words cannot simply summarize better the trailblazing input of Th. E. Starzl on today's (transplantation) medicine.

Without any doubt, Thomas Earl Starzl was an exceptional scientist, an exceptional human, a man of "hors pair" who will be missed greatly by his beloved wife Joy, by his family, as well as by the transplantation community worldwide. Let the fact that his achievements will endure in lives of countless patients and in the work of countless persons he influenced be a comfort to manage his unexpected passing away.

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