

Starzl T E, Iwatsuki S, Van Thiel D H, Gartner J C, Zitelli B J, Malatack J J, Schade R R, Shaw B W, Jr., Hakala T R, Rosenthal J T & Porter K A. Evolution of liver transplantation. *Hepatology* 2:614-36. 1982. [Transplantation Institute, University of Pittsburgh, PA]

This article demarcated the end of the experimental phase of clinical liver transplantation from the beginning of the procedure's widespread therapeutic use. [The *SCI*® indicates that this paper has been cited in more than 540 publications, making it the most-cited paper published in this journal.]

The Emergence of Liver Transplantation

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Clinical liver transplantation was first attempted at the University of Colorado (Denver) in 1963.¹ In the next 16 years, 170 patients underwent this procedure in Denver, of whom only 56 survived for one year and 22 to the present time. The results were no better in a British program begun at Cambridge in 1967 by Roy Calne. The immunosuppression used at first had been developed in kidney recipients using azathioprine combined with the highly dose-maneuverable adrenal cortical steroids² to which adjuvant antilymphocyte globulin was added in 1966.³ In 1979, Calne, the team leader two decades before in the preclinical development of azathioprine, reported the first clinical trials with the new drug cyclosporine, in 34 organ recipients, including two who were given livers.⁴ By substituting cyclosporine for azathioprine in our two- or three-drug cocktails in 1979-1980, the fuller potential was realized, first of kidney and then of liver transplantation. Eleven of the first 12 liver recipients survived for more than one year;⁵ more experience by the same team (now in Pittsburgh) in 1981-1982 was confirmatory.

In December 1981, these findings were reported to C. Everett Koop, the surgeon general, who initiated a Consensus Develop-

ment Conference for liver transplantation. Its planning took place in Washington in June 1982, to which Calne was invited as a consultant, with a side visit to Pittsburgh, where we reviewed the nearly complete evolution manuscript. The article was scheduled for oral presentation at the American Association for the Study of Liver Diseases on November 1 with publication the same month in *Hepatology*. Calne was given the data for his impending liver transplant overview to the Transplantation Society in August. It was stratified into the dramatically different pre- and post-cyclosporine eras. At the Consensus Development Conference eight months later (June 20-23, 1983), liver transplantation was certified to be a "service" procedure, beginning a stampede to start new liver transplant centers.

The events up to the evolution paper occurred before the commercialism of liver transplantation, when the purity and purpose (if not the seeming wisdom) of the crusade were palpable. By 1989, essentially all of the positions taken in the 1982 article, including the indications for liver transplantation, had been verified.^{6,7} Honors and awards resulted, but these meant little compared to the satisfaction of seeing a population of well patients grow who only one generation previously were consigned to early death, and of watching the burgeoning careers of physicians and surgeons who had trained in our programs. When I stopped clinical work, I wrote their story in a book called *The Puzzle People*.^{*} The book also described a mutually supportive professional relationship with Calne and his British team, which might be emulated by those who become so competitive that they erode the respect and affection that should come naturally between companions in a common cause.

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