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This article demarcated the end of the experimental phase of clinical liver transplantation from the beginning of the procedure's widespread therapeutic use.

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**A WATERSHED ARTICLE ON LIVER TRANSPLANTATION**

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The "evolution" article of 1982 heralded the acceptance of a procedure first attempted in 1963 (1) but not with extended patient survival until 1967 (2). Liver replacement remained an orphan operation from 1967-79, sustained by our Colorado program at the University of Colorado (Denver), which was joined in 1967 by Roy Calne's team at Cambridge University (England). In Denver, only 56 recipients survived for 1 year of 170 treated between 1963 and 1979; 22 are still living after 14-24 years. The English results were no better, but all the while technical and management advances were being made. Cocktail immunosuppression which had been developed in kidney recipients

(3) was with azathioprine combined with the highly dose maneuverable adrenal cortical steroids to which adjuvant ALG was added in 1966 (4). In 1979, Calne, the team leader 2 decades before in the preclinical development of azathioprine, reported the first cyclosporine trials in 34 patients including 2 liver recipients (5). By substituting cyclosporine for azathioprine in our 2 or 3-drug cocktails in 1979-80, the full potential of the new drug was realized in Colorado, first in kidney and then liver recipients of whom 11 of the first 12 survived for more than one year (6). More liver cases by the same team (now in Pittsburgh) in 1981-82 were confirmatory.

In December, 1981, I personally reported to C. Everett Koop, the Surgeon General, that the impending revolution in transplantation would include the liver, and Koop initiated a Consensus Development Conference for liver transplantation. Although this was not held until June 20-23, 1983, its planning in Washington took place in June 1982, where Roy Calne was invited as a consultant with a side visit to Pittsburgh. I was putting the finishing touches on the evolution manuscript which was scheduled for oral presentation at the American Association for the Study of Liver Diseases (AASLD) on November 1 with simultaneous publication in Hepatology. Calne reviewed the article and was given the data for his impending liver transplant overview to the Transplantation Society in August. The

manuscript summarized the entire Colorado-Pittsburgh experience and that elsewhere from 1963 through early 1982, and stratified this into the dramatically different pre- and post-cyclosporine eras. At the Consensus Development Conference 8 months later, liver transplantation was declared a service as opposed to an experimental procedure, beginning a stampede to start new liver transplant centers.

The events up to the evolution paper were 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 (7). Honors and awards resulted, but these meant little compared to the satisfaction of seeing a population grow of well patients 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. The achievements were theirs, and when I stopped clinical work, I wrote their story in a book called "The Puzzle People" (8). 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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