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EDITORIAL

Between Scylla and Charybdis

The ethical dilemmas of treating fulminant (or subfulminant) hepatic failure with liver replacement have been apparent since the earliest trials of this procedure. Acute hepatic failure was the indication for orthotopic liver transplantation in only 1 of our first 237 recipients[1] and accounted for only 8 of the next 300.[2] Our reluctance to proceed with more cases was that unlike candidates whose livers are chronically diseased, those with acute or subacute hepatic failure may spontaneously recover. The vast majority of patients who pass through the acute crisis are able to regenerate their own livers and return to a normal life expectancy, absent the burden of chronic immunosuppression. The incidence of a favorable outcome is strongly influenced by the cause of the hepatic failure, highest with hepatitis A (67%) and acetaminophen overdose (53%). The lowest recovery is with non-A, non-B, and non-C hepatitis and after poisoning with halothane or other hepatotoxic drugs.

No matter what the etiology, the prognosis for recovery, short of liver transplantation, currently is better than the 5% to 10% frequently cited from the literature of the 1970s, which discussed the option of conservative management. The improvement requires specialized care teams armed with protocols designed to prevent brain injury. Hopital Paul Brousse, from which the report by Bismuth et al.[3] comes, has such services. However, survival is not as good as that after liver transplantation, at least within the context of the 1- to 5-year follow-up. Consequently, liver surgeons currently are recapitulating the era preceding 1962 in kidney transplantation, when artificial kidney support was not available widely—if at all—for the treatment of acute renal failure. Then with the kidney, as currently with the liver, the first objective was to differentiate those patients who would recover from those who were doomed without draconian intervention.

In a further analogy to the history of acute renal tubular necrosis and kidney transplantation, the inherent reversibility of fulminant hepatic failure has driven research that eventually may reduce the need for liver transplantation. While the body's hepatic based metabolic machinery grinds to a halt, all of the organ systems are threatened, but the most dreaded insult is to the central nervous system. The minimal extra function provided by extra- or intracorporeal hepatic allografts or xenografts, and more recently by hepatocytes injected intravenously or lining the capillary tubes of "artificial livers," has been credited with amelioration of brain deterioration and other complications of liver failure (including renal dysfunction). Buying limited time in this way with a borrowed animal or human liver (or hepatocytes) could be a hollow gesture, but since 1975, a family of hepatic growth factors has been discovered which may speed the regeneration of the devastated native liver.[4] These molecules have not yet been successfully exploited clinically, partially because of the inability to maintain life support long enough for their effect to be evaluated. The key to success appears to be artificial liver support combined with iatrogenic promotion of hepatic regeneration.

When these technologies are developed, emergency liver transplantation for fulminant hepatic failure will become largely obsolete. Until then and even afterward, the choice of aggressive medical *versus* transplant therapy will remain. With either decision, the best results always will be with the patients who are the least ill, the ones who historically have been the most likely to recover with no specific treatment at all. Unfortunately, in such cases, a highly visible and professionally damaging error will lie in wait for the physician or surgeon who delays operation until a patient who might have been saved by transplantation has lost that chance. In contrast, the invisible error of operating on patients who would have recovered spontaneously is seldom discussed and rarely is provable. The frequency of the latter mistake and its lifetime implications for the recipient is certain to increase the earlier the timing of transplantation is decided.

The experience of Bismuth et al.[3] was acquired in this treacherous landscape, between Scylla and Charybdis. Of the 139 patients entered into their study, 23 were withdrawn–22 by death after a mean of 1.3 days and the other by spontaneous recovery. The 23 candidates who did not make it to the operating room cannot be con-

strued as a nonsurgical control series with a survival of 4.4% because the time to death was shorter than the average time required to obtain an organ. Apparently, most of these patients were not viable with either an operative or nonoperative strategy.

The overall 1-year survival of the 116 patients who came to transplantation was 68%. However, it was 83% for those with precoma (n = 6) or grade 1 and 2 coma (n = 47) compared with 55.6% for those who had reached grade 3 coma (n = 63). It was refreshing to see the French authors wade through the arcate terminology of hepatic failure stages (I–IV) and coma grades (1–4) with simplified information. Those who could still fend off abuse constituted the cohort with 83% survival, and those who could not protect themselves made up the 55.6% survival group. In another clarifying statistic, they noted that 81.1% of patients who survived could breath unaided preoperatively *versus* 63.2% when ventilator support was needed. The simplicity also should be noted of the so-called Benhamou classification of disease severity—depending essentially on the two determinants of coma grade and level of coagulation factor V—compared with more complex schemes used in many other European centers and in the United States.

Our own experience over the last decade, in which fulminant and subfulminant hepatic failure accounted for <3% of the total case load, has been similar to that of the Paris team.[5] However, for the reasons discussed by Bismuth et al.,[3] we do not use ABO incompatible, steatotic, or otherwise marginal livers for these very ill patients. The survival and avoidance of retransplantation hinges more on achieving good function promptly than on promptly receiving a graft that would not be acceptable for the average candidate with end-stage chronic disease.

The article by Bismuth et al.[3] is an important one in the narrow context of acute and subacute hepatic failure. More importantly, it exposes the philosophy of this superb team about the place of liver transplantation in the armamentarium against liver disease. The guiding principle of the French group was the prompt transplantation for, not avoidance of, those candidates thought most certain to die without such intervention. No sophistic arguments were advanced in this or their preceding publications that the life survival curve could be improved by relegating the "statistically dangerous" patients to noncandidacy. The day-to-day, hands-on practice of such professional rectitude is beyond the reach of teams possessing less skill and depth. However, an equally responsible solution for relatively inexperienced teams is prompt referral of very ill patients to specialty centers, rather than the pronouncement of these cases as hopeless when they merely are grave. If the conventional process of triage with tertiary care referral is applicable to patients with acute hepatic failure, it is difficult to comprehend the recommendation of a vociferous minority of liver transplant surgeons that profoundly ill patients with chronic liver disease should be bypassed in favor of treating less disabled elective candidates.

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