The Management of End-Stage Renal Disease (ESRD)

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End-stage renal disease (ESRD) may be defined as a state of renal insufficiency of such severity that the affected individual is unable to carry out his usual activities because of symptoms usually attributed to the uremic syndrome. This state has been reached, or is imminent, when the serum creatinine concentration rises above 10 mg/100 ml and/or the creatinine clearance falls below 5 to 10 ml/min and reversible causes of renal failure such as obstructive uropathy, bilateral renal vascular disease, severe accelerated hypertension, hypercalcemic nephropathy, uric acid nephropathy, and certain immunologic diseases such as Wegener granulomatosis have been excluded. Prospective analysis of a population of patients meeting these biochemical criteria has clearly shown that at least 80% will require dialysis within 150 days and 40% will require this method of treatment within 60 days to sustain life.[1] Thus, when ESRD is reached, weighty decisions concerning the patient's care must be made. It is the purpose of this paper to review the management of ESRD and to point out some of the problems which may complicate the several therapeutic modalities.

The alternative methods of management of the patient with ESRD are dialysis and transplantation. These two therapeutic modalities are by no means mutually exclusive and, as we shall see, should be considered complementary. However, virtually all patients must undergo a period of dialysis, even those awaiting transplantation. Therefore, dialysis is the first mode of treatment encountered by a patient entering an ESRD program.

At the present time there are few absolute contraindications to entrance into an ESRD program for dialysis and transplantation. However, patients with uncontrolled psychotic behavior, extreme old age, advanced artherosclerotic vascular disease, or disseminated malignancy are probably not candidates for therapy.

Principles of good conservative management of renal failure such as restriction of dietary protein, careful attention to fluid and electrolyte balance with tailoring of dietary sodium intake to the obligatory sodium loss, and the administration of sodium bicarbonate supplements and oral phosphate binders where appropriate may postpone the absolute need for dialysis or transplantation if introduced when the patient has moderately severe renal insufficiency. Recent studies have demonstrated that the period of conservative management can be prolonged even further by the administration of a special mixture of the keto-analogues of the essential amino acids.[2] This maneuver allows for the dietary administration of very limited quantities of nitrogen and is predicated on the assumption that some of the urea nitrogen will be recycled into the synthesis of essential as well as nonessential amino acids. Unfortunately, these keto-acids are not commercially available at present, but perhaps will be in the future.

Survival rates for patients treated by hemodialysis at home and those who have received a well-matched transplant from a living related donor are both greater than 80% at two years.[3] It is worth noting, however, that this represents patient survival

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and not graft survival which is only about 70%, thus indicating that some 10% to 15% of the transplant recipients who survive two years have suffered an undetermined amount of morbidity in association with rejection of their graft. Survival with in-center dialysis and cadaver transplantation is less good, with a two-year survival rate of approximately 70% in each case.[3] The two-year graft survival in patients with cadaver transplants is less than 50%. These statistics suggest the desirability of home dialysis and living related donor transplantation, but do not demonstrate a clear superiority of in-center dialysis or cadaver transplantation. Thus, factors other than survival must be considered in selecting a mode of therapy.

Age is a major factor which may influence therapeutic selection. Children and adolescents tend to have diminished growth and maturation while on dialysis[4] and they frequently rebel against the rigid dialysis schedule. Therefore, most authorities favor transplantation as a mode of therapy in the young.[5] On the other hand, older individuals with a well-established, stable lifestyle may prefer not to run the risk of the lost time from work and the potential complications of transplantation. The patient's psychological state also may be of importance in selecting a mode of therapy. Some older patients, like the children, may find the confining life of the dialysis patient to be more than they can tolerate and be willing to risk the uncertainties of cadaver transplantation.

The presence of complicating medical disorders may influence the type of management selected. Diabetics may fare better with transplantation because progression of atherosclerotic vascular disease and retinopathy may be less rapid than on dialysis.[5] Patients with certain enzyme defects such as Fabrey disease may also benefit from transplantation because the transplanted organ may serve as a source of the defective enzyme.[6] On the other hand, transplantation is contraindicated in patients with anti-basement membrane antibody nephritis with circulating antibodies[7] and in patients with large quantities of circulating cytotoxic antibodies[7] because of the likelihood of rapid graft destruction after transplantation. Additionally, the immunosuppressive medication given to patients may allow for enhanced tumor growth, and most surgeons will not consider performing transplantation in a patient with a history of malignancy unless there is clear evidence that the patient has been tumor-free for at least one year.[7] The presence of lower urinary tract dysfunction and an inadequate bladder are still considered relatively strong contraindications to transplantation.

Having decided that a patient's life will be sustained, a decision must be made about the form of dialysis to be instituted. Although chronic peritoneal dialysis has been an effective modality in some hands,[8] most authorities consider it to be less desirable than chronic hemodialysis, and the remainder of this discussion will be concerned with hemodialysis.

Two types of vascular access are available for connecting the patient to a dialysis machine. These are the silastic, external arteriovenous (AV) shunt[9] which protrudes through the skin and the internal AV fistula communication, using the patient's own vessels[10] or a foreign graft material.[11] The latter lies immediately under the skin and must be punctured with a needle at each dialysis. The fistula is preferred by most physicians and patients because of the freedom of movement and the safety which it provides. Where possible, it is our policy to anticipate the ultimate need for dialysis and to have the surgeon electively establish an AV fistula at about the time the serum creatinine reaches a concentration of 8 mg/100 ml. This allows time for maturation of the fistula prior to its initial use, and obviates the need for emergency surgery to establish vascular access in an ill patient.

Hemodialysis is usually initiated in the medical center, but when the patient has an acceptable helper, every effort should be made to encourage the couple to learn home dialysis. The training program can be mastered by anyone of average intelligence and takes about two months to complete. As mentioned previously, patients on home dialysis have better survival statistics and are better rehabilitated.[12]

Whether dialysis is performed at home or in a center facility, there are a number of common complications of which the physician should be aware. Bacterial infection of the shunt or fistula is a frequent problem that may lead to metastasization and requires aggressive drainage and antibiotic treatment.[13] Hepatitis B infection has been a frequent occurrence among dialysis patients.[14] It presents a particular problem in dialysis units because patients may become carriers and transmit the virus to staff and other patients. Virtually all patients on dialysis have some degree of anemia.[15] In the past, transfusion of potential transplant candidates was kept to a minimum because of possible sensitization to transplant antigens. However, recent evidence suggests that frequent transfusions may actually enhance rather than inhibit

the frequency of organ acceptance.[16] Therefore, transfusions, particularly of saline-washed red cells, are now being given with less concern than in the past. Pericarditis continues to be a frequent and poorly understood complication in the dialysis patient and it does not always appear to be a manifestation of inadequate dialysis.[17] Hypertension is seen frequently in the dialysis population and may be related either to expansion of the extracellular fluid volume or to the release of pressor substances from the residual damaged kidneys.[18] In the latter circumstance, bilateral nephrectomy may produce a dramatic return of the blood pressure to normal.[19] Neuropathy is frequently noted at the onset of dialysis but seldom progresses if dialysis is adequate.[20] Impotence is seen more frequently than not in male dialysis patients, and dialysis against a bath containing a high concentration of zinc has recently been proposed as effective therapy.[21] As more patients are sustained alive for prolonged periods of time it is becoming clear that osteodystrophy[22] and accelerated atherosclerosis[21] are problems of great magnitude. Therapy of the former includes the use of oral phosphate binders to maintain the serum phosphorus concentration levels at normal, and a supplemental vitamin D preparation to enhance intestinal calcium absorption; there does not appear to be any effective therapy for the latter.

Many of the problems mentioned above will be corrected by a functioning transplant. However, there are a number of problems which are unique to the transplant population. Most of the difficulties associated with early transplant rejection are managed by the transplant team prior to discharge from the hospital after surgery, and these will not be considered here. Chronic rejection may occur late after transplantation, is characterized by a slow deterioration in function, and is generally unresponsive to therapy. Infection remains the major cause of morbidity and mortality among transplant patients.[23] Because of the constant need for immunosuppressive medication these patients have an increased susceptibility to both common bacterial pathogens and to opportunistic viruses such as herpes hominis and cytomegalovirus; fungi such as cryptococcus and aspergillus; and protozoa such as pneumocystis and toxoplasmosis. Hypertension also is a frequent complication of transplantation and may be difficult to control. A diabetic diathesis may be brought out by the administration of steroids as immunosuppressive agents.[24] Osteoporosis may develop as a complication of long-term steroid administration.[24] The constant immunosuppression may also allow for the development of tumor growth and there is a much higher incidence of malignancy in transplant patients than in a comparable, non-immunosuppressed population.[24] Gastrointestinal bleeding is a feared complication of transplantation that is frequently fatal.[24] Consequently, many transplant surgeons perform prophylactic gastric surgery in any potential candidate who has the slightest history of ulcer disease.

It is our feeling that selection of a proper therapeutic modality in a patient with ESRD requires careful consideration of the medical, psychological, social, and economic aspects of the patient's illness. His needs may change through the course of illness and, as a consequence, the ESRD prescription may require alteration. Thus, a patient might initially be managed with home dialysis, receive a living related donor transplant after a sibling decided to become a donor, and return to home dialysis after rejection occurred.

The economic costs of ESRD treatment are staggering.[25] At present there are more than 37,000 individuals receiving some type of ESRD therapy in the United States at an annual cost of $902 million. By 1982 it is projected that the cost for 55,900 patients will be 2.3 billion. Most patients are eligible for financial coverage of the major portion of their dialysis or transplantation cost either via private insurance carrier, Medicare, or the Veterans Administration. At present the annual cost of in-center dialysis is approximately $23,400 while that of home dialysis is $12,480. The initial cost of hospitalization for transplant surgery is about $17,000. These estimates do not include the cost of hospitalization for various complications of either the dialysis or transplant state; and, as suggested earlier, these may be formidable.

In the future, dialysis equipment may be made more compact and a satisfactory portable dialyzer may be developed. The use of sorbent materials may allow dialysis with small quantities of fluid, and high potency antithymocyte globulin may improve the early survival of cadaver grafts. Techniques also may be developed for the stimulation of blocking antibodies in the recipient which will allow for improved graft survival with lower doses of immunosuppressive drugs. However, none of these innovations seem likely to dramatically change the management of ESRD in the near future.

The management of ESRD has been briefly re-

viewed; both dialysis and transplantation are useful modalities of therapy and are not mutually exclusive. Management in a given patient should be designed to best meet his medical, psychological, social, and economic needs.

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