Regular Review

Renal failure—dilemmas and developments

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Twenty years ago a patient with a blood urea concentration of 50 mmol/l (300 mg/100 ml) due to chronic renal failure was not expected to survive. The responsibility of the physician, having made the diagnosis, was to make the process of dying comfortable. Slowly progressive weakness, lethargy, nausea, vomiting, and a multitude of other symptoms usually precede the preterminal coma that has led some doctors to suggest that uraemia is a comfortable death. That renal failure is a painless death is often true, but that it is a pleasant way to die is a clinical myth. Advances in the replacement of kidney function now provide doctors with alternatives to observing a progressive deterioration. Advances in the management of dying patients ought to have helped those who do not receive treatment, whether because this is not available or because they are not "suitable." Yet the absence of pain as a symptom often seems to make doctors reluctant to give the drugs which help relieve the distress of dying. More thought should be given to making uraemia as a mode of death more acceptable when facilities or clinical circumstances rule out renal replacement.

In 1982 a patient in renal failure is, however, often given treatment, with survival the expected outcome. The prognosis is now better than in many common serious conditions (figure). As a result of progress in dialysis and in renal transplantation a young patient with renal failure and no complicating features has a better than 90% chance of living 10 years and more.¹ In most groups of patients accepted for treatment by these methods survival over five years exceeds 50%. Even in patients aged over 55 European statistics suggest that with treatment the prospects of survival may not be very different from those for slightly younger patients.¹ Such an optimistic assessment is not, however, true of the whole range of older patients, which include many marginally less suitable who are not selected for treatment and so do not enter the analyses. If more such patients were accepted into treatment programmes mortality from non-renal causes would increase. Nevertheless, the trend is for more patients to survive for more years, and this should continue as experience in old and new techniques increases and there is better selection of the right patient for the right treatment.

Survival statistics of end-stage renal failure

The specialists concerned in treating renal failure have done more than any group to audit their practice. The statistics on survival are based on all patients being treated and not just on series of patients attending the centres of excellence where analyses are done and papers are written (or are written if the

Mortality from renal failure receiving treatment, contrasted with that from three common cancers. Data from EDTA register and from Birmingham Cancer Registry and Scottish Home and Health Department (supplied by Dr S Gore, MRC Biostatistics Unit, Cambridge).

results suggest excellence). Current statistics do not, however, contain information on patients not starting treatment, and much is written of the numerical shortfall between the number of patients who might be treated and those who are.²⁻⁵ Case selection may distort national statistics—as it can distort the results published from a single unit. Analysed series may contain or omit older patients, those with systemic disorders such as diabetes mellitus, and other groups known to have a less satisfactory than average prognosis. What should be considered are not the results of a single unit or of a particular treatment but the outcome in the community under consideration of all those patients reaching end-stage renal failure.

Quality and duration of survival with treatment

Most units in Britain run an integrated approach, with most patients at some stage being given more than one of the possible modes of treatment. Despite differences in the response of patients to various types of treatment most patients feel well; irrespective of treatment, they are often in full-time employment if this is available. The proportion working is highest in patients with functioning transplants and may approach 100% in areas of full employment. The quality of life for many patients, whether having treatment with dialysis or a successful transplant, is often a surprise to those who do not regularly meet such people. In a few cases, however, some physical or psychological aspect of their state leads the patient, family, or staff to wonder whether treatment is prolonging life or prolonging dying.^{6, 7} When these circumstances may be foreseen that may be used as justification for withholding treatment. Clinical experience helps in making the assessment for treatment; but when treatment is provided for patients with an apparently poor prognosis surprisingly often those expected to fare badly may do well. There are, in fact, few objective measurements to predict the response to treatment.⁷ A trial of treatment is often the only reliable way of evaluating the physical and psychological suitability of patients, but stopping treatment once started is obvious to the patient and to the observer and is difficult for all concerned. There is no obvious answer to this dilemma.

Ideally, all patients likely to benefit from treatment should be accepted for it. Studies in various countries on the numbers of such patients show an incidence of at least 45 patients a year per million population—a figure that is not reached in Britain.²⁻⁴ In the United States acceptance rates of up to 75 patients a year per million population are recorded,⁸ but commentators there are concerned about the quality of life achieved by some patients in dialysis programmes in a setting where stopping dialysis creates legal as well as moral difficulties.⁶

Evaluation and the start of treatment

Many patients are referred to a specialist centre too late for there to be time for a carefully considered plan of investigation leading to a carefully constructed strategy for treatment; all too often treatment has to be started in a hurry. Graphical plots of plasma concentrations of creatinine and urea, using the reciprocal or logarithm, make a valuable contribution to the assessment of prognosis and can prevent undesirable delays in referral for evaluation or for starting treatment.^{9, 19} In most patients developing renal impairment deterioration follows an organised and mathematically analysable course. In the absence of active treatment to reverse or slow this deterioration it is possible to predict the likely time of onset of symptomatic renal failure in most patients. Events may move surprisingly rapidly: many physicians observing a patient with renal failure and a creatinine concentration of 300 $\mu\text{mol/l}$ (3.4 mg/100 ml) or urea concentration of 14 mmol/l (84 mg/100 ml) do not expect the crisis that often follows in a few weeks, but it is predictable by simple graphical analysis.

Treatment by regular haemodialysis

Haemodialysis is now effective and reliable and, though it is expensive, the costs have not risen to match inflation. Major advances in the details of haemodialysis procedures have reduced their morbidity and shortened the length of the treatment needed to keep patients satisfactorily well. The

introduction of ultrafiltration (the removal of plasma water and its small-molecular constituents in the absence of dialysis) makes it possible to control salt and water balance without causing unpleasant symptoms. This technique may be under-used by other specialties.¹⁰ The use of high blood flows through the dialyser, dialysers with a large surface area, and short (for example, three to five hours thrice weekly) periods of dialysis have reduced the time spent on a machine.¹¹ Newer methods of access to the circulation—some temporary, such as femoral artery and subclavian vein catheters¹²—combined with “single-needle” systems needing only one point of vascular access and vein grafts, for patients with all forearm veins damaged by earlier medical assaults, have combined to make problems of vascular access an unusual reason for death in patients accepted into dialysis programmes—though vascular access remains a common cause of a temporary crisis. Access complications may often be traced back to thoughtless damage to veins when the patient was receiving non-specialist care and to early use of an arterio-venous fistula when there has been late referral or delayed diagnosis.

A development with considerable economic implications is the reuse of dialysers after washing and sterilisation. Indeed, the cost of dialysers is now no longer the major revenue implication of starting treatment, as dialysers may now be used six times or more (though recent concern about the formaldehyde used, based on experiments of doubtful relevance in animals, is creating a lobby against reuse). Most units no longer use dialysers built by hand in the unit or in the home, but purchase commercially produced “disposables.”¹³ Unfortunately for Britain the huge world markets are not supplied from this country. No dialysers are manufactured here, despite British firms making a creditable start with early designs in the 1960s, and no British-owned companies have an important share of the large world market for dialysis machines now adapted to make the new techniques easy and safe to apply in both the unit and the home.

Yet with so much experience of haemodialysis around the world the old debates continue. Should haemodialysis be done at home or in hospital? Should small satellite units for self-dialysis or “limited-care” dialysis be developed? How can the untreated majority of patients in the older age groups be incorporated into treatment programmes already strained to the limit despite their restrictive acceptance policies and with no immediate prospects of an infusion of the necessary resources or of additional staff? The potential of new techniques in peritoneal dialysis appears to some to be one answer.

Continuous regular ambulatory peritoneal dialysis [CAPD]

Continuous ambulatory dialysis, with three or four self-administered changes of peritoneal dialysis fluid daily, was a logical extension of earlier techniques of peritoneal dialysis. In several units (though very few in Britain) automated peritoneal dialysis techniques had been developed for nocturnal dialysis with frequent fluid changes performed by machine. When appropriate calculations were made of the materials to be removed from the body and the movements of fluids required to achieve this—and it is not obvious why no one did this earlier—it became apparent that too many fluid changes were being recommended for the stable patient with absent or severely reduced kidney function. Once physicians realised that the body's biochemical balance could be kept in control with the use of only six to eight litres of dialysis fluid daily they saw the possibility of manual changes of peritoneal fluid for

very long periods, and with self-administration by the patient, possibly for years.¹⁴ Canadian groups, especially that in Toronto led by Oreopoulos, now have a large clinical experience, with some patients now completing five years of treatment.¹⁵ In Ontario around 60% of patients who develop renal failure now receive continuous ambulatory peritoneal dialysis as their initial treatment, and in many other countries there has been a rapid expansion in the use of this technique. In Britain the numbers having treatment are expected soon to reach 1000 patients, some units now having an experience of around 100 patients, some treated over several years.¹⁶ Other countries—for example, Japan, which has a very large number of patients having dialysis (around 36 000)—have not taken up this approach to treatment.¹⁷ Peritoneal infection remains the main problem, but experience has shown that a substantial proportion of patients get no infection, or very infrequent and controllable episodes. There were early concerns about whether biochemical control would be adequate. Most patients get no more and, if anything, rather fewer metabolic complications than might have been expected in the same patients having regular haemodialysis. Many patients who have experienced both modes of treatment prefer continuous ambulatory peritoneal dialysis, though this may be influenced by many of the patients who change being those with some problem with regular haemodialysis. Another alternative, “continuous cyclical dialysis” (CCPD), also with a reduced number of exchanges, but performed at night by a simple machine, is now becoming popular in some units.^{17a} Another, perhaps adverse, response is the rise in the concentration of blood lipids—but this is controllable by dietary restrictions of carbohydrate should the physician consider that these lipid disturbances might have an adverse long-term effect.^{17b} One striking change with CAPD and CCPD is the rise in haemoglobin concentrations, often to normal values.

At present the place of continuous ambulatory peritoneal dialysis is uncertain. It is a very successful mode of treatment when practised by suitable patients—suitable on account of personal attributes and perhaps also biological ones—trained and supervised by an expert team. It may well be more satisfactory for many older patients, who may suffer unpleasant symptoms from haemodynamic instability during haemodialysis, and for those with diabetes mellitus, whose glucose concentrations can be better controlled by using intraperitoneal insulin.¹⁸ Diabetics often do poorly despite the close attention they require if treated with regular haemodialysis (for which reason many units find all diabetic patients “unsuitable”). The prospect of introducing dialysis to diabetics, using continuous ambulatory peritoneal dialysis, when creatinine concentrations are only just getting outside the normal range needs careful consideration. Continuous ambulatory peritoneal dialysis with infrequent exchanges—for example, twice or thrice daily—and started early might prevent many of the complications that often develop in the months between renal failure being easily detectable and it needing dialysis using conventional assessments.

Certainly many patients will receive continuous ambulatory peritoneal dialysis for months or years while having treatment in one of the integrated programmes that have now become standard, with haemodialysis or a functioning transplant maintaining life over other periods. Can continuous ambulatory peritoneal dialysis offer the same long-term success, measured in decades, that is achieved with regular haemodialysis? The answer to that must await years of clinical experience—provided that information is being collected in an organised and analysable way.

Renal transplantation

Transplantation must be considered the treatment of choice for most patients. Operation is now sometimes performed without prior dialysis, the inevitability of a need for dialysis having been calculated by appropriate mathematical techniques—the inspection of graphed reciprocals or logarithms of plasma creatinine values.^{9 19} A transplanted kidney may pass urine on the operating table and can return plasma concentrations of urea to normal within two days and then continue to pass satisfactory urine for the next 20 years and more. Immunosuppressive treatment, even with conventional agents like prednisolone and azathioprine, may never be raised above 20 mg prednisolone daily with 100 mg of azathioprine.²⁰ Discharge from hospital at eight days is not unusual in many units, and after a few weeks of very frequent outpatient supervision this can decrease to a hospital visit every three months.

The merits of such management with the results described are obvious both in human and in economic terms. The money spent may be comparable to that for many major surgical procedures, and less than for some. This description of the course of a patient receiving a renal transplant still applies only to some patients, but the proportion is close to being the majority with a living related donor and is not small with cadaveric donors. The progressive improvements in results, especially when associated with very low dose regimens of immunosuppressives, make it possible to offer most recipients a relatively uneventful and therefore inexpensive procedure.^{20 21} With recently introduced drugs such as cyclosporin A, and more still on the horizon, results may in time be found to be even better and more easily achieved. Transplantation may end in failure and a return to dialysis, but success in some hands is now around 80% with at least three years of satisfactory kidney function.²⁰ If these results could be achieved nationwide the logistic problems of the supply of donors and of overstressed dialysis facilities would be greatly eased. The reasons for the good results and for the higher failure rate in some series are being sought diligently but without any agreement on the answers. Promising clinical developments such as the use of fine needle aspiration cytology for diagnosing rejection and other techniques that are ready for more clinical trial, need support at the expense, if necessary, of some of the basic research into immunological mechanisms and tissue typing. Publications show a heavy numerical bias to basic research with less contribution made recently to improving mortality and morbidity statistics in renal transplantation.

The problems of donor supply and demand have been repeatedly discussed. It has become my view that, excluding severe but temporary setbacks (such as were caused by the *Panorama* programme),²² the problem can be greatly eased by adequate effort in local organisation and education. The Nottingham and Leicester teams have made a major impact on kidney retrieval rates by appointing full-time supernumerary surgical registrars with responsibility for providing an information, education, and retrieval service. Other units have appointed nurses or lay persons as co-ordinators. There may still be limitations owing to the number of potential donors in a community unless policy changes, or has changed, in the proportion of patients almost certain to die who are given ventilation. The attitude to artificial ventilation in patients with head injuries and cerebrovascular accident at the time of presentation has an important influence on the number of patients considered formally using the criteria for brain death. A reluctance to initiate ventilation, often because of restricted

facilities or an irrational feeling that severely brain-damaged survivors will result, may be having a much greater influence on the logistics of the treatment of renal failure than many topics that have been more widely discussed.

Route to solving the problem of too many patients for too few facilities

The number of patients in renal failure treated is related to the nation's gross national product.²² Some countries that do better than suggested by this relation are those that have active transplantation programmes. More emphasis should be given to transplantation in Britain—but why is the success rate in the less successful units so low? Greater efforts are needed to examine the reasons and support any modifications needed in policy or facilities.²⁵ Improvements that will have an effect on units already usually successful may be more difficult to find and may come from the way they use existing drugs, or from other advances such as the correct use of preoperative blood transfusion, which is now routine in most units. In my opinion another aspect of technological advance, the computer, has greater potential than many other recent advances²³ for reducing mortality and morbidity in renal units and for allowing the same staff to look after more patients at a higher standard. This and other advances, such as continuous ambulatory peritoneal dialysis, should be enthusiastically adopted with the help of the Government and industry.

More satisfactory statistics on the number of patients accepted for treatment (and in the morbidity and mortality of those who are) will not in my opinion be achieved with present levels of trained senior staff unless some development greatly simplifies the amount of skilled and enthusiastic supervision of patients required. Many units need more consultants and many more hospitals need a general physician with specialty training in renal medicine. Those hospitals without such

experts locally and which provide a few facilities but little skill and inadequate resources of equipment and person power should delegate earlier to those that have better facilities and appropriate staff, even if also often inadequate in number. The policy of previous governments in restricting the expansion of units both in numbers and in the extent of the facilities provided was the most important single factor in limiting the number of patients successfully treated in Britain.²⁶ It resulted in a large exodus of fully trained renal physicians and transplant surgeons who saw no future for a career here. I have personal knowledge of 25 nephrologists who have emigrated, an alarming number in a specialty that had only 78 consultants in the United Kingdom when last surveyed in 1976.²⁵ Many of these now head some of the most effective renal units in the world—but in other countries. Had this pool of talent, with many of the individuals having more than an average amount of enterprise, been retained in Britain they would not have allowed the present state of affairs to develop. Those who remained or who, like myself, returned but have not persistently urged the authorities to fund an expansion of consultant numbers must share with the Government some responsibility for the current statistics. Those who control medical staffing—and it is difficult to know who this is in the Health Service—should reconsider whether there should not be more consultant appointments, and additional units would follow. Many have accepted the inertia in our system that foils such plans, but if expansion continues to be blocked it will continue to create depression and despair similar to those that in previous decades caused the defection of nephrologists who should now be sharing the problems with those of us who remain.

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