For Debate

Death after Kidney Transplantation

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British Medical Journal, 1974, 3, 736-737

Kidney transplantation has been accepted as a successful form of therapy for patients with terminal renal failure. The excitement and drama that once surrounded each operation has largely disappeared and few voices are now heard decrying the procedure as experimental and dangerous. Yet all is not well in transplantation centres, both here and abroad. Patients are still dying after a kidney transplant and there are no signs that the mortality is diminishing.¹

A patient's course after transplantation is greatly influenced by the type of kidney he receives. Kidneys obtained from living related donors fare the best, and any patient receiving such a kidney will have an 86% chance of surviving a year. A kidney from an unrelated cadaver donor is more likely to be rejected and only 70% of patients will survive a year.¹ Armed with this knowledge it might be expected that transplant centres would try to secure for their patients kidneys from living donors. This has not always been the case and in the United Kingdom it is fairly uncommon for relatives of a patient to be approached in this way. In Europe as a whole living related kidneys have accounted for only 15% of the total kidneys transplanted,² and in Australia the proportion is as low as 2%.³ In the United States, however, related living donors provide 35% of all transplants.¹

Problems and Benefits of Transplantation

The unsolved problem of transplantation is rejection. Prophylactic immunosuppressive drugs are moderately effective in suppressing the immune response but most patients will experience rejection episodes at some time. Most of these episodes can be treated successfully, but during such treatment the patient is especially liable to develop infective complications and may die as a result. Transplantation urgently requires the introduction of some new effective and safe immunosuppressive procedure. Antilymphocyte globulin has been used very widely with variable effect. In a controlled clinical trial Sheil *et al.*⁴ showed that a course of antilymphocyte globulin lasting a few weeks can improve overall graft survival by about 10-15%. Patients receiving antilymphocyte globulin are, however, very prone to develop fungal infections, and deaths from this cause have tended to cancel out the benefits from controlling rejection.^{5,6}

Even without a major change in patient management one might expect there to be some improvement in patient survival as the transplant units gain experience in managing patients on immunosuppressive drugs. Unfortunately this

has not been the case, and over the years the 12-month mortality after cadaveric renal transplantation has remained stubbornly at 30%.¹ Centres that carry out over 25 transplants a year do seem to have greater success however.¹

Despite the risks attendant on transplantation many patients have been successfully transplanted. They enjoy a normal life in most respects. Their diet is unrestricted and they gain a sense of well being which they may not have experienced for many years. Most of the men return to full time work and the women continue to raise and care for their families. Children too can grow and develop normally. These are the prizes to be won from renal transplantation, and most patients with renal failure are prepared to try their luck.

Dialysis

It falls upon the renal physician in charge of the patient to consider carefully whether transplantation is wise. In the United Kingdom home dialysis is available in most areas and most dialysis centres will undertake the necessary training. In fact 59% of all dialysis patients in this country carry out dialysis at home.² During each year of home dialysis only 9% of patients die, and this is a powerful argument for advising home dialysis rather than cadaveric renal transplantation as the treatment of choice.

The demand for chronic haemodialysis has been steadily increasing and in 1976 there will be twice as many patients on dialysis in the United Kingdom as in 1973.² Possibly dialysis units will be unable to cope with these large numbers, in which case there will be no choice but to transplant many patients. At present, however, the choice remains and home dialysis seems the safer course to take.

There are a group of patients, however, who would benefit greatly from transplantation: those who cannot be accepted for dialysis because they are too old, mentally unsuited, or incapable of home dialysis. Transplantation would give to at least half of them a useful extension to their life, since without treatment most would soon die.

Nevertheless, a problem arises whenever one of these patients rejects his transplant for haemodialysis will not be available as an alternative. The patient who may have enjoyed many months of good health while his transplant was working may wish to know why he is being discriminated against at his time of need. These patients need not die since it is often possible to perform a second transplant with or without an intervening period of peritoneal dialysis.

To reduce the mortality of patients developing chronic renal failure the following scheme might be adopted: (1) Patients accepted for chronic haemodialysis should be trained for home dialysis as soon as possible. (2) Once established at home such patients should not normally be considered for cadaveric renal transplantation. (3) Greater effort should be made to obtain kidneys from living relatives for patients requiring kidney

transplants. (4) Patients who might not be suitable for chronic haemodialysis and who would otherwise die should be offered a renal transplant.

Such a scheme may not be easy to follow in practice. Some of the patients who have been taken on for home dialysis will almost inevitably develop problems of vascular access and as a result may need to be transplanted at an early stage. Others may do badly on haemodialysis for other reasons. Despite dialysing three or more times a week a few patients can remain unwell and eventually become emaciated and bedridden. To these people a successful transplant brings a total change of health, and to witness this change is a gratifying experience to all involved. Long-term dialysis may not be the best treatment for young children and it is certainly boring and restricting for adults. After one or two years of treatment home dia-

lysis patients can become dispirited and desirous of a change. In future therefore, many home-dialysis patients may seek transplantation as a way of escape from this monotony. It is to be hoped that by then renal transplantation will have become a somewhat more predictable and safe procedure.

References

- ¹ Barnes, A. B., *et al.*, *Journal of the American Medical Association*, 1973, 226, 1197.
- ² Gurland, H. J., *et al.*, *Proceedings of the European Dialysis and Transplant Association*, 1973, 10, xvii.
- ³ Australian National Renal Transplantation Survey, *Medical Journal of Australia*, 1971, 2, 605.
- ⁴ Sheil, A. G. R., *et al.*, *Lancet*, 1971, 1, 359.
- ⁵ Sheil, A. G. R., *et al.*, *Transplant Proceedings*, 1973, 5, 561.
- ⁶ Bach, M. C., *et al.*, *Lancet*, 1973, 1, 180.

Any Questions

We publish below a selection of questions and answers of general interest

Postoperative Care after Intestinal Surgery

Several weeks after extensive surgery (ileocolic end-to-end anastomosis and right hemicolectomy) for Crohn's disease a patient is still having loose motions (with urgency) three times a day. What treatment can be used to produce a formed stool?

There are many causes, alone or in combination, for this. There may be extensive loss of small intestine and the extent of the resection is not mentioned. This must usually amount to some 50% of the total small bowel before malabsorption and diarrhoea occur. There may be macroscopic or sub-clinical Crohn's disease in the residual bowel and even if unnoticed at the time of the original resection some recurrences after surgery occur with surprising speed. The diarrhoea may be due to loss of the ileocaecal valve, and if so is quite often seen after right hemicolectomy for conditions other than Crohn's disease, such as carcinoma of the caecum. Finally, there is the possibility of a postoperative bowel infection producing an enteritis.

The stools should therefore be cultured to determine the presence of any pathogen and a barium meal and follow through examination ordered to determine the bowel transit time and give information about possible residual or recurrent Crohn's disease. Both of these possibilities may then require specific therapy. In the absence of these factors, the usual anti-diarrhoeal agents such as codeine, Lomotil, or a kaolin and morphine mixture should be tried and are often effective. Occasionally extensive loss of small intestine produces gross steatorrhoea and diarrhoea as a result of failure to reabsorb bile; this passes into the colon and there has a purgative effect which sometimes responds dramatically to cholestyramine.

Conception and the Menopause

Is there any evidence that conception can take place after the periods have ceased, and, if so, how long after is the patient at risk? Up to what age has pregnancy been proved to occur?

Conventionally the menopause is assumed to have occurred if the periods have ceased for six months in a woman aged about 50. Some authorities would extend the time of

amenorrhoea to 12 months. Cessation of periods before this age may or may not be due to the menopause and may require endocrine investigation for certain diagnosis. Raised gonadotrophin levels would suggest that the ovarian function has declined to a value normally associated with the menopause. Hot flushes are a good clinical indication that the endocrine changes of the perimenopause are occurring but may need careful interpretation. The certainty of the menopause is therefore not absolute and can only be so in retrospect. It is probably this problem of diagnosis that led to some older claims of postmenopausal pregnancy. The answer to the first half of the question is therefore that when the menopause is established then pregnancy does not occur. It is the error in diagnosis of the menopause that is responsible for apparent cases. There is presumably a risk of pregnancy if ovulation occurs, however sporadically. There is no firm evidence on this, but in the established postmenopausal period of 12 months it must be very unlikely. As a matter of clinical practice it is often recommended that contraceptive measures should be employed for 12 months after the apparent menopause. At dilatation and curettage at this time secretory endometrium is not found, nor are cyclical hormone changes demonstrated.

The *Guinness Book of Records* finds authenticated cases of women having babies when they were aged 57 years 129 days in the United States in 1956, 54 or 55 years and three days in Great Britain in 1936, and 55 years 69 days in Eire in 1931.

Control of Status Epilepticus

Is diazepam the drug of choice in controlling status epilepticus, and if so how should it be administered?

At present, diazepam is the chosen drug for controlling status epilepticus. The usual method is to give 10 mg immediately intravenously. If the fits continue then another 20 mg can be given in the next few minutes. If this is effective it is usual to give diazepam 5 mg hourly into an intravenous saline drip, until there are no more signs of abnormal excitability in the cerebral hemispheres. A new drug called chlormethiazole can also be given intravenously. It may be as good as or better than diazepam but there is great experience behind the use of diazepam in status epilepticus; this has not yet been acquired with chlormethiazole.