SYNOPSIS

## Renal replacement therapy in ESRD in children

Data extracted from the Australian and New Zealand Dialysis and Transplant Registry (ANZDATA) show that there has been an improvement in survival rates in children receiving kidney transplants over a 40-year period from April 1963 to March 2002. But while there has been an improvement in long-term survival, mortality rates among children requiring renal replacement therapy remain substantially higher than those among children without end-stage renal disease (ESRD).

A report published in the *New England Journal of Medicine* analysed the survival data in the ANZDATA database.[1] A total of 1 634 children and adolescents were followed for a median of 9.7 years. The long-term survival rate among the children undergoing transplantation was 79% at 10 years and 66% at 20 years. Mortality rates were 30 times as high as for children without end-stage renal disease. Risk factors for death were: a young age at the time the renal replacement therapy was initiated (especially for children under 1 year of age in whom the risk was 4 times as high as for children 15 - 19 years of age, and treatment with dialysis (which was associated with a risk more than 4 times as high as for renal transplantation).

The authors state that increasing the proportion of children treated with renal transplantation rather than with dialysis can improve survival even further.

In an editorial accompanying the article,[2] David S Milliner comments, 'renal failure during childhood has profound effects'. Abnormalities of skeletal growth with associated growth retardation, abnormal neurocognitive development, pubertal delay and disordered psychosocial maturation all occur. Dialysis, he continues, only provides a small fraction of normal renal clearance. It alleviates but does not eliminate uraemic symptoms such as fatigue and anorexia and does not address the nearly universal abnormalities of growth and development.

In contrast, renal transplantation can provide renal function that is 40 - 80% of the normal level. Transplantation provides improved linear growth, improved cognitive performance, enhanced psychosocial development and an improved quality of life.

Outcomes of transplantation have improved steadily since the 1960s when it was first made available to children. In 2003, the North American Paediatric Renal Transplant Cooperative Study reported that the 3-year survival rate was 96.6% for patients who received a live kidney donation and 94.8% for those receiving a cadaver kidney.

The average duration of hospitalisation for transplantation is shorter and postoperative recovery more rapid than in the past. The rate of acute rejection has been reduced with the use of newer, more effective immunosuppressive medications, and an array of antimicrobial, antihypertensive and lipid-lowering agents has reduced morbidity.

Challenges do, however, remain. Most children who receive a renal transplant require long-term corticosteroid therapy and are subject to all the attendant complications. The avoidance, replacement or discontinuation of corticosteroids, if proved safe in clinical trials, will alleviate this problem. Opportunistic infections are an increasing cause of concern as ever-more-effective immunosuppressive agents become available.

The longevity of a transplanted kidney is particularly important for paediatric transplant recipients. Calcineurin inhibitors, taken by more than 90% of children who have received transplants since 1995, lead to renal interstitial fibrosis and loss of renal allograft function over time. Virus infections, chronic rejection, allograft nephropathy, and recurrence of primary renal disease all tend to reduce renal allograft function.

Allograft survival rates are lower among adolescents who receive a kidney transplant than among younger recipients. Inconsistent adherence to medication regimens among adolescents has been implicated as one explanation for this observation.

Other sequelae of transplantation require attention: corticosteroids and tacrolimus are associated with the development of diabetes mellitus. Hyperlipidaemia is common after renal transplantation. Vascular changes, including premature coronary artery and other vascular calcification are becoming more frequently observed in kidney transplant recipients when they reach age 30 - 40.

Prospective longitudinal outcome studies are required for understanding of the factors that influence patient survival after paediatric renal replacement therapy. Because renal failure incidence is much lower in children than in adults, the number of paediatric renal transplants is much lower than in adults. As the children mature, they move away and continuity of care and follow-up information are often lost. For this reason, the article by McDonald and his co-workers is extremely valuable.

There is much work to be done as paediatric renal replacement therapy comes of age. Barriers to transplantation in children with ESRD must be removed. Greater allograft longevity must be attained. This can only be accomplished with increased knowledge of the factors that influence success or failure of paediatric renal replacement therapy.

**FNS**

1. McDonald SP *et al. N Engl J Med* 2004; **350:** 2654-2662.
2. Milliner DA. *N Engl J Med* 2004; **350:** 2637 - 2639.