

## ORIGINAL ARTICLES

## Heart-lung transplantation: all the facts

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## Abstract

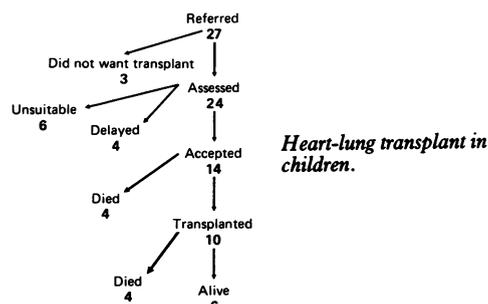
Of 27 children referred for assessment of suitability for heart-lung transplant, 10 (37%) were actually transplanted. Six are still alive from three months to three years since operation. Two thirds of the cohort have died at various stages during referral, assessment, and transplant. While the transplant has offered miraculous new life to a few children, many more have experienced increased and unnecessary suffering. Planning of transplant programmes must take all facts into account. The possibility of heart-lung transplant must not deter further efforts to control chronic lung diseases medically and must not influence appropriate terminal care.

Heart-lung transplantation is now presented as a practical treatment for children in terminal respiratory failure. Preliminary results would suggest that survival rates after transplantation are at least as good in children as in adults. A recent publication presented details of five children, alive and well, 5-17 months after heart-lung transplantation all of whom had returned to activities normal for their age. Two had primary pulmonary hypertension, two cystic fibrosis, and one Eisenmenger's syndrome. The paper presented the details of the progress of these five patients.<sup>1</sup> It did not elaborate on the fact that they came from 33 children who were initially referred to the transplant programme. Little comment was made on the problems that must inevitably have arisen among the 28 children who were either considered unsuitable for the programme, died waiting, or were still awaiting transplant.<sup>2</sup> However, this must be balanced against the inevitable demise that would have occurred in all the patients who received heart-lung transplantation, had this not been possible.

The Paediatric Respiratory Unit at the Royal Brompton and National Heart Hospital has been referred children for assessment of suitability for heart-lung transplantation and this paper details the outcome in all the patients referred over a three year period.

## Patients (figure and table)

Over a three year period, from March 1987 to March 1990, 27 children were referred to the unit for assessment. There were 15 girls and 12 boys aged between 5 and 16 years at referral. Twenty two had cystic fibrosis, two cryptogenic fibrosing alveolitis, one idiopathic pulmonary hypertension, one a combination of very severe



emphysema with pulmonary haemosiderosis, and one pulmonary fibrosis caused by cytotoxic treatment and irradiation.

## SELECTION CRITERIA

Children were considered candidates for heart-lung transplantation if their lung function was less than 30% of predicted standards for height and was continuing to deteriorate. For chronic obstructive disease, as in cystic fibrosis, forced expiratory volume in one second was taken as the key index; for restrictive disease, as in cryptogenic fibrosing alveolitis, vital capacity was used. The children were also required to have a severely impaired quality of life, and an oxygen saturation of <90% even on minimal exertion. Finally when in possession of all the facts about heart-lung transplantation, they still had to have a desperate desire to proceed. Absolute exclusion criteria were poor compliance with treatment, which was usually associated with adverse psychosocial circumstances, current high dose corticosteroid treatment, impaired renal function, and previous pleurectomy. Children with portal hypertension were excluded unless liver transplant was also contemplated. Diabetes mellitus or colonisation with *Pseudomonas cepacia* were not considered absolute contraindications and those with poor nutrition entered a rehabilitation programme including the use of gastrostomy nocturnal drip feeding to make them suitable for heart-lung transplantation.

## Results

Of the 27 children referred, remarkably there were three, all with cystic fibrosis, where neither parents nor child had any idea that they were being considered for transplant. Of the 24 children assessed six, all of whom have since died, were considered unsuitable for heart-lung transplantation and were not referred on to the surgeons, and four had their inclusion on the

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## Outcome of assessment for heart-lung transplantation

Decision	No of children	Disease	Detail	Dead/alive
Did not want transplant	3	Cystic fibrosis	Preterminal: died at home within one month of referral Increased medical treatment: alive one year later	Dead
		Cystic fibrosis		Dead
		Cystic fibrosis		Alive
Unsuitable	6	Pulmonary fibrosis after bone marrow transplant	Bilateral pneumothoraces, underweight Tuberculosis of spine Portal hypertension Too ill: died within one week of referral	Dead
		Cystic fibrosis		Dead
		Cystic fibrosis		Dead
		Cystic fibrosis		Dead
		Cystic fibrosis		Dead
		Cystic fibrosis		Dead
Delayed	4	Cystic fibrosis	Lung function >50% predicted High dose steroids being reduced Responded unexpectedly to methotrexate	Alive
		Cystic fibrosis		Alive
		Cryptogenic fibrosing alveolitis		Dead
		Cystic fibrosis		Alive
Died on waiting list	4	Cystic fibrosis	Delayed palliation Hid medication to avoid transplant After steroid withdrawal	Dead
		Cystic fibrosis		Dead
		Cystic fibrosis		Dead
		Cryptogenic fibrosing alveolitis		Dead
Died after transplant	4	Cystic fibrosis	Acute rejection and infection within one week Poor heart function: died in three days Obliterative bronchiolitis 20 months after transplant	Dead
		Idiopathic pulmonary hypertension		Dead
		Cystic fibrosis		Dead
		Cystic fibrosis		Dead
Alive after transplant	5	Cystic fibrosis	3 months-18 months	Alive
		Emphysema and pulmonary haemosiderosis		3 years

programme delayed. One delayed patient, a boy of 14 with cystic fibrosis, had developed a very rapid onset of small airway obstruction in the previous 12 months. This could not be attributed to either chronic pseudomonas infection or indeed any other obvious immunopathology. The disease was partially responsive to very high dose oral corticosteroids. He was started on oral methotrexate as a means of facilitating steroid withdrawal before being put on the waiting list for heart-lung transplantation. However, his improvement on the methotrexate was so dramatic that two years later he has returned to full normal activities with lung function well over 50% of predicted and is now too healthy to be considered for transplant.

Thus 14 patients were considered suitable to be referred on for heart-lung transplantation and were placed on the waiting list. Four children have died on the waiting list two of whom, both with cystic fibrosis, had a significant delay in institution of palliative treatments, and as a result suffered a great deal more discomfort and distress than would be considered acceptable in the terminal phase of any illness. The third girl with cystic fibrosis who died on the waiting list indicated to her parents, shortly before death, that she did not wish to have a transplant and had, in fact, failed to take any of her medical treatment for the previous two weeks. She had stored this in a polythene bag and hidden it in her locker. She presented the bag full of medications to her mother. Subsequently it transpired that she had talked to another of the patients on the ward, indicating very vehemently that the only reason she had agreed to be put on the waiting list was for her parents' sake. They were, at the time, in the process of separating and divorcing. The fourth patient who died waiting had cryptogenic fibrosing alveolitis, and deteriorated rapidly after withdrawal of steroids as a prelude to transplantation.

Ten patients have received transplants: eight with cystic fibrosis and one each with emphy-

sema combined with pulmonary haemosiderosis and idiopathic pulmonary hypertension. Four children have died after heart-lung transplantation; one boy with cystic fibrosis lasted only three days. His new heart never functioned properly and he died during an attempted second transplant. One girl with cystic fibrosis died 10 days after transplant with acute rejection and septicaemia; the second girl with cystic fibrosis died 20 months after heart-lung transplantation with obliterative bronchiolitis. A 13 year old girl with idiopathic pulmonary hypertension, stable over the previous eight years, was entering puberty and considered to be at high risk of death at sometime in the next few years. Though having severe cyanosis and considerable exercise limitation, she and her mother considered her life to be happy and fulfilled. She died within one week of transplant probably of acute rejection. This leaves six children who are alive in relatively good health, between two months and three and a half years after heart-lung transplantation. However, none has been spared the inevitable acute rejection episodes nor periods of sepsis.

### Discussion

Heart-lung transplantation is now being presented as the ultimate treatment for terminal respiratory failure and its existence has given new hope to a large number of patients and their families facing the prospect of premature death.<sup>3</sup> The success of this procedure in adults has inevitably led to its extension to the paediatric age range and the preliminary results are at least as good as in adults.<sup>1</sup> The experience of seeing a child in terminal respiratory failure miraculously given new life after a heart-lung transplantation can only encourage an intensely optimistic and positive approach to the procedure, but a balanced perspective of the pros and cons has been sadly lacking from publications.

The Papworth experience published in 1989 indicated that only five of 33 (15%) who were referred for heart-lung transplantation actually benefited from the procedure over an 18 month period.<sup>1</sup> Five were considered unsuitable, eight were on a provisional waiting list of whom four had died, and four were still waiting. Of the 15 accepted on to the transplant programme two had died waiting and eight were still waiting.<sup>1</sup> The figures I have presented over a three year period show 10 of 27 (37%) have ultimately received a transplant. I have deliberately excluded consideration of any patients who have been assessed over the last six months in order to give a complete presentation of the ultimate outcome. Thus the figures are comparable.

The three patients who were referred without adequate discussion about heart-lung transplantation between patient, parents, and referring physician were clearly handled extremely badly. The unnecessary transporting to an alien hospital under such circumstances was unforgivable and totally avoidable. Hopefully this problem will not recur. This leaves 10 of 24 (42%) who have been transplanted after assessment.

It is to be hoped that more appropriate referrals will be made in the future to reduce the numbers who are clearly unsuitable for heart-lung transplantation. The recrimination that is inevitable between the patients, parents, referring doctor, and the assessing doctor is very unpleasant for all concerned and causes immense upset for staff, parents, and patients alike. Firm handling at an early stage, indicating that certain medical circumstances preclude transplant, would prevent much of this difficulty arising. However, ultimately a third party may be required to provide an authoritative opinion. It has been particularly difficult to handle the patients who, for various reasons, have very poor compliance with treatment. This must be an absolute contraindication to transplant because rigid adherence to the immunosuppressive regimen after transplant is imperative. Missed doses of cyclosporin would be a death sentence. Equally adverse psychosocial circumstances, which are difficult to assess, will remain a contraindication but independent assessment will be required.

Some patients may be placed on a 'holding list' either because they are still reasonably healthy or because other adjustments to medical treatment are required before the patients are suitable for transplant. It is to be hoped that most of these patients will be found more effective medical treatment that will avoid the necessity for heart-lung transplantation. Only patients who have received maximal treatment and have failed with such approaches should ultimately end up on a transplant programme.

A total of 71% of those children accepted on to the programme have ultimately received a transplant. One suspects that in the future this figure will be very much lower as many more children who might be deemed suitable for heart-lung transplantation will actually be transferred to the transplant centres. Six of 10 are still alive after transplant. All have had acute rejection episodes and infections that have necessitated intensive medical supervision.

Even these figures do not give a clear representation of the anguish and suffering that is borne by the children and their families. Geographical and social dislocation during assessment and the subsequent wait for transplant and indeed the period of intensive medical care after transplant causes enormous problems. Indeed one of the successfully transplanted boys was faced with his parents' divorce after the procedure. His mother stayed in hospital with him for the nearly six months of inpatient treatment. Unfortunately, the family home was too far away for regular paternal visits. His parents' relationship broke down during the prolonged enforced separation.

A more exquisite form of torture could not be devised than to give a child with rapidly failing health a bleep that will sound once a week as a check and will go off once at any time in the future to indicate that suitable organs may have been found. As death approaches the desire to avoid palliative treatment can lead to totally unnecessary suffering. The issue of whether to use artificial ventilation when irreversible respiratory failure supervenes raises enormous medical and ethical problems. Intensive care units could very easily become blocked by children in respiratory failure being ventilated while awaiting transplantation. The results of heart-lung transplantation on patients who are being ventilated appears to be poor and therefore perhaps this is not a major issue.<sup>4</sup> It is most important that children in terminal respiratory failure are given appropriate treatment so that they die peacefully, with dignity, and certainly without pain. The patient and parents' grim determination to struggle on to the bitter and painful end is understandable but must be resisted.

The boy who died within three days of transplant had initially been assessed over 18 months before the procedure. At that stage he was very underweight and a poor complier with treatment. However, the use of gastrostomy tube feeding at night and an intensive programme of psychosocial support resulted in him gaining a considerable amount of weight with an improvement in his therapeutic compliance. Eighteen months of effort in making him suitable for heart-lung transplant culminated in disaster and his parents were clearly left wondering whether the 18 months had produced any tangible benefits. The girl who died 20 months after transplant had a one year period when she was remarkably well and able to sample a relatively normal life for the first time. Before transplant she had been totally resigned to her fate and able to face death in a remarkably mature and appropriate way. In the last six months of her life she became a frightened, desperate girl; she was assailed with morbid guilt about the donor of her heart and lungs and also excessively preoccupied with the child who had received her heart in a so called 'domino' transplant.

The spectre of heart-lung transplantation has fundamentally altered attitudes and medical practice in respiratory clinics. Sadly some families have seriously suggested that hastening deterioration by missing out treatment would

lead to earlier transplant and therefore avoid suffering. We have good evidence that steroids are very important in a number of chronic lung diseases including cystic fibrosis but are now more hesitant about their use because of transplantation.<sup>5</sup> Furthermore, pleurectomy is well established as the best treatment for recurrent pneumothoraces in cystic fibrosis but would contraindicate transplant.<sup>6</sup>

At a time of medical rationing with very limited resources in the health service, many paediatricians may question the wisdom of heart-lung transplantation. At present only a third of referrals will benefit from transplant, of whom two thirds may be expected to be alive at least for one year after the procedure. Many will be refused transplant for good medical reasons, and others will die waiting. I believe that heart-lung transplantation must be one final option for some patients in terminal respiratory failure. However, clear guidelines on suitability should be available to all so that unnecessary referral is avoided. Only the most psychologically robust families who fulfil appropriate criteria for severity of respiratory failure and without any of the known medical contraindications to transplant should be referred. Patients and parents should be fully aware of all the facts and figures related to the procedure. Emphasis should, however, remain on prevention, early diagnosis, and effective medical treatment for the management of the vast majority of problems that might ultimately lead to respiratory failure and the need for transplantation. No family should be left in any doubt that heart-lung transplantation is the last resort and will always remain so.

I would like to thank Ms Linda Romain for typing this paper and Ms Joanna Marchant for the diagram.

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### Commentary

Heart-lung transplantation is still a new therapeutic option for end stage lung disease. As with any new treatment it was only right that experience in adult patients should be established before extending it to a paediatric population.<sup>1,2</sup> An initial report demonstrated that the procedure was practical and at least in the short term gave similar results to those found in adults.<sup>3</sup>

Three papers in this current issue address three important areas of heart-lung transplantation: namely identification of suitable patients,<sup>4</sup> medium term outcome,<sup>5</sup> and the stresses involved for staff, patients, and their families.<sup>6</sup> The latter presents some of the problems encountered in the first three years of a heart-lung transplantation programme in a single

centre. Issues are raised which underline the importance of careful assessment before acceptance onto a transplantation programme and the important point is also made that organ supply is never likely to match demand. However, some improvements in donor supply may come from increased public awareness and the active support of paediatricians and anaesthetists responsible for intensive care. Supply is also limited by the relatively short time (four hours) that organs remain viable once removed from the donor, although there is some hope that this may be extended in the future with improved preservation techniques.<sup>7</sup>

In addition to highlighting important concerns about heart-lung transplantation, the experience presented does seem to have been a rather negative one with many children and their families experiencing 'increased and unnecessary suffering'. Many of the problems identified could in retrospect have been avoided. They indicate a need for greater awareness of potential problems and a high level of honesty, both within transplant teams and within those clinical teams referring patients. Hopefully this is exactly what this and the other two contributions in this issue will go some way towards achieving. Despite the problems of extrapolating from the experience of a single centre to 'all the facts' many of the underlying points made should not be discounted because of the small number of patients involved and the relative short time period. We all bear a great responsibility to introduce the transplantation option or suggest referral for assessment only when there is a realistic hope of it bringing benefit. The whole aim of transplantation should be to improve the quality of life not just to extend it. It would be more honest at this relatively early stage to view it as a palliation rather than a 'cure'. Heart-lung transplantation can provide a good quality of life for an indefinite period in exchange for continuing severe symptoms and the certainty of death.

The immediate outcomes of referral are: (i) acceptance onto an immediate or active waiting list, (ii) placing on a 'holding' or provisional list (no contraindications but not yet severe enough to transplant), and (iii) non-acceptance because either the patient is too sick (preterminal) or has major physical or psychological contraindications.<sup>3</sup> What has not been brought out is that patients accepted onto a provisional list may experience an increase in quality of life. This is because the decision communicates two important messages to the child and family: (i) the disease is not at a stage in which death is imminent or likely to occur in the next one to two years and (ii) transplantation offers an 'insurance policy' which may be drawn on at a later date.

Certainly no family should be assessed unless heart-lung transplantation had been fully discussed at the referral centre and the problem of ignorance on the part of the family or child should not arise. Inquiries should also be made as to the family dynamics, local family support, and major medical contraindications such as advanced liver disease and previous pleurectomy in order to forestall inappropriate refer-