

Kumaradasa Rajasuriya Oration 1998  
**ORGAN FAILURE ... FROM MASTRY TO EXCELLENCE**

Professor Rezvi Sheriff

I thank Professor Mahasara Gunaratne and the Late Prof K Rajasuriya Memorial Oration Committee for inviting me to deliver this 1998 Late Prof Kumaradasa Rajasuriya Memorial Oration. I consider this invitation a great honour, and am even more delighted for been given an opportunity to lecture in the memory of one of the greatest clinical teachers in medicine this country can boast of.

I have chosen the subject of “Organ Failure ... from Misery to Excellence”. Having worked with Prof Rajasuriya both as a keen medical student and postgraduate student and later been selected by him as a junior lecturer in medicine to work directly under him, I can unreservedly claim that he would have fully supported me to talk on this subject; for the misery of sick people touched his heart instantly, and what he would strive to achieve in all roles he played was excellence.

Prof Kumaradasa Rajasuriya, born on the 1st of December 1915 died of a heart attack which came on during the MD examination in 1975. The MD exam was always a stressful period for the late professor. He would worry more about the security of the paper as much as his preoccupation of maintaining a high standard of the examination.

He had a brilliant career and was an outstanding teacher and an excellent and astute clinician whose clinical judgements were sought after. He had a short stint as a medical administrator at the personal request of the Head of State at that time, Prime Minister Mrs. Sirimavo Bandaranaike. He came back to clinical Medicine as he did not seem to enjoy the powerful job as the Director General of Health Services. He held many positions including that of Editor of the Ceylon Medical Journal, and President of the Ceylon College of Physicians. He was an ardent Buddhist and member of the Board of Management of the YMBA and President of the Buddhist Brotherhood in the Faculty. He was also a member of the Red Cross Society Council and the Royal Asiatic Society.

Prof. Rajasuriya had 22 publications in reputed international publications, His research interest in medicine was wide, and he had publications on infectious diseases, liver diseases, haematological diseases, pancreatic disease and heart disease.

The late Professor Rajasuriya was a formidable personality and fulfilled his role as a leading academic, astute physician, researcher and administrator, and took on an active role in religion, community and national life. He enjoyed cricket and playing bridge with a close group of professional friends.

We need all our organs to function in harmony to give us good health. Each organ has a multitude of functions, and global loss of function of anyone organ usually has serious repercussions on health. When serious failure of an organ or several organs occurs acutely, one usually ends up in an intensive care unit, and life is taken over by machines and chemicals for survival. In the more chronic advancing organ failure, patients remain amongst their relatives, are miserable, having a poor quality of life in spite of all that modern medicine has to offer. Carefully tailored drug therapy in the case of heart failure or blood or blood component transfusion in bone marrow failure offers temporary relief. It is only with kidney failure that kidney machine treatment or Haemodialysis offers a reasonable option not only to survive but also enjoy at least a modified working life.

The treatment of organ failure is organ transplantation. All other therapies conservative or machine assisted do not off the fuller life as man would want. These are only considered as “holding” procedures. Kidney transplant introduced into clinical practice in early 1960's has today grown, and rich experiences gained worldwide has encouraged much research and enthusiasm. Heart transplants, liver transplants, lung transplants, heart-lung transplants, pancreatic transplants, kidney and pancreas transplants have all gone past the experimental phase and are now approved therapy worldwide for funding and insurance cover. Small bowel transplants are very much in the early stages of development.

After an initial period of pretransplant assessment, counselling and optimizing, while at the same time selecting a donor and doing donor work up, one proceeds to live related donor transplants. This can be done in kidney (one of two kidneys can be donated) or liver transplant (part of the liver can be donated), or in bone marrow transplant (as some parts of the bone marrow can be aspirated). For obvious reasons we cannot donate our hearts whilst we are living except perhaps in amorous surroundings with a matching heart!

The concept of brain death and brain stem death is now accepted worldwide, and cadaveric donation is widely practiced. Live donation which was popular to start off with has been replaced by donation of cadaveric organs whenever possible. Most countries are having organ shortage problems as the need for organs has increased in view of the good results of the procedures and greater acceptance by the profession and the people. Now live related transplants are again being done more and more to ease the organ shortage, particularly in kidney transplants.

The organ shortage is increasing as multiple organ transplants are also being done more often in recent times. Unrelated or paid donor transplants are also being considered ethical even in the west. Commercialism and donor organs for sale was rampant in India, South America and the Far East. Ethical standards and Codes of Conduct against unrelated transplants have been circulated by the international transplant societies. It is now commonplace to have poster presentations or even plenaries on the results of paid donor transplants, some even claiming better results.

In Sri Lanka we have done only live related donor transplants. I am personally not in favour of paid donor transplants. The Human Tissues Act is in place to enable us to start cadaveric transplants. Brain Death criteria have been defined, and Brain Death Certification Forms are used in our ITU appropriately. A Donor Card put out by the Sri Lanka Association of Nephrology and Transplantation (SLANT) has increased public awareness. We have not started cadaveric transplantation due to shortage of funds and lack of better facilities.

After transplantation, various regimens of immunosuppressive treatment and anti-rejection treatments are being used. A large dependence on the National Blood Transfusion Services is necessary particularly if bone marrow, liver and heart transplantation are started. Prednisolone, azathioprine, and ciclosporin are the main drugs used and are freely available in Sri Lanka. Ciclosporin costs nearly Rs 15000 per bottle for one months supply. ALG, OKT3, FK506, Myco-phenalate are some of the second line drugs used, and are not currently in use in Sri Lanka as they are more costly. Monitoring and long term follow up are usually done by transplant physicians and this has become a growing commitment in my life.

All transplants have complications. It is not easy to predict who will do well. However every program suffers from having to take on higher risk patients especially when the other option is death. The more popular the program the greater is the pressure to take on older persons, very young persons, those with complicating illnesses like diabetes, ischaemic heart disease etc, which will reduce the long term survival figures.

Also, developing countries have a large load of infectious diseases compared to the west. Transplanting and immune suppressing patients in such an environment considerably increases post transplant infection and attended morbidity and mortality.

### **Heart failure**

Let us first discuss the problem of resistant and chronic heart failure. Ischaemic heart disease, systemic hypertension, valvular heart disease, chronic lung disease and cardiomyopathies are the main causes of chronic heart failure

- \* Eliminate the cause if possible
- \* Avoid excess salt, alcohol, salt/fluid retaining drugs
- \* Drugs - ACE-I, Diuretics, Digoxin
- \* Devices – intraaortic balloon pump
- \* Coronary artery bypass graft
- \* Heart transplantation

In the United States during the period 1988 to 1994, 12627 heart transplants were performed. The figures for graft and patient survival are shown in table 1.

**Table 1**

Graft survival;		
1 year	:	81.7%
3 year	:	73.7%
Patient Survival		
1 year	:	82.5%
3 year	:	74.8%

### **Respiratory failure**

There are many causes of serious lung diseases leading to respiratory failure; Chronic obstructive lung diseases, chronic asthma, ankylosing spondylitis, Kyphoscoliosis, pulmonary fibrosis, ARDS, acute lung trauma, pulmonary oedema, pneumothorax etc. The principles of management of these conditions are as follows;

- Maintenance of air way
- Treat specific precipitating event
- Physiotherapy
- Nebulised bronchodilators / Antibiotics
- Controlled oxygen therapy
- Devices - IPPV
- Lung transplantation

While patients with acute reversible lung failure can be treated with intermittent positive pressure ventilation, those with chronic respiratory failure who suffer from the chronic effects of brain hypoxia can only be served best by lung transplantation. There are many forms of lung transplantation - single lung, double lung, heart-lung etc. The United States figures for lung transplantation are shown in table 2.

**Table 2**

Lung Transplants		
1 year	:	71%
3 year	:	54%
Heart Lung Transplants		
1 year	:	70%
3 year	:	50%

### **Liver Failure**

Liver disease leading to liver failure is commonly found in Sri Lanka because of the easy access to alcoholic beverages to our people. When one reaches a stage of irreversible liver failure, life can be miserable. I am reminded of the humorous epithet; 'Is life worth living? .... it depends on the liver'.

### **Bone marrow transplantation**

Bone marrow transplantation (BMT) is considered next. Although it is not strictly a solid organ, it does behave functionally in a similar manner. As HLA histocompatible donors are needed, the usual source is a brother or sister. International computer registries of Unrelated Volunteer Bone Marrow Transplant donors are used. In Autologous BMT techniques, the patients own bone marrow or peripheral blood stem cells are used; these are harvested and kept frozen for later use.

Bone marrow transplants differ from solid organ transplants in a few ways;

1. Only live donation is possible
2. No complex surgery is required for donor or recipient
3. One replaces both haemopoietic tissue and immune systems. Thus the serious complications of Graft vs Host disease can occur.
4. Since reconstituted haemopoietic and immune systems are both of donor origin, immunosuppressive therapy can be withdrawn in 6 to 12 months
5. Donor tissue can be collected conveniently and transplantation done at preplanned times
6. Ablative chemoradiotherapy is used prior to donor marrow infusion in certain diseases
7. Dependence on blood transfusion service is heavy

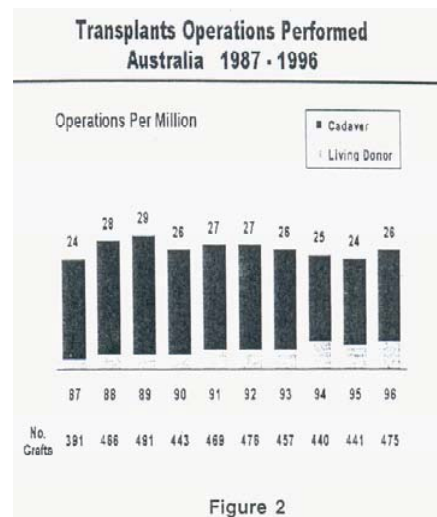
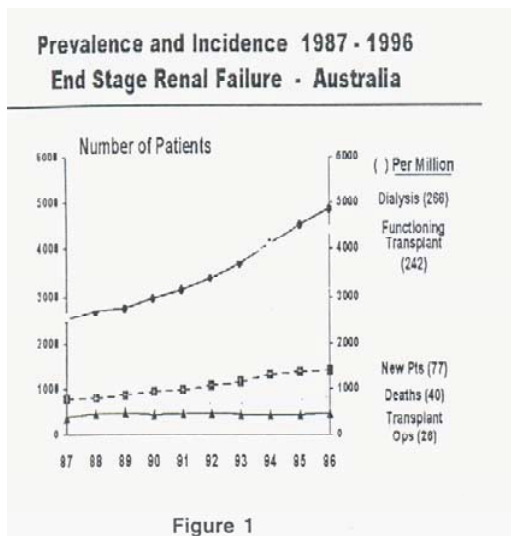
Initially results were depressing. Many technical problems of BMT have now been solved. New developments like monoclonal antibodies, recombinant haemopoietic growth factors are useful. The cost remains prohibitive at around 30000 pounds sterling per procedure in the UK. An estimate in Sri Lanka would be around Rs 2 million.

### Renal Failure

Renal failure one type of organ failure for which transplantation facilities are available in Sri Lanka. Our involvement in pioneering renal transplantation in this country has made it possible to study the impact of renal transplantation on the quality of life. Glomerulonephritis, hypertensive renal disease, obstructive uropathy, diabetes nephropathy, SLE renal disease, polycystic kidney disease and interstitial nephritis are among the common causes of renal failure. The principles of conservative management of end stage renal failure are shown below;

- |                        |                          |
|------------------------|--------------------------|
| * Dietary modification | * Fluid restriction      |
| * Nutritional Support  | * Blood pressure control |
| * Control of Diabetes  | * Vitamine D analogs     |
| * Erythropoietin       |                          |

These measures are usually temporary, and only renal transplantation will give a lasting cure. The figures for renal failure and renal transplants in Australia are shown in figures 1 & 2



The number of renal transplants done in Sri Lanka is 250. They were all live related donor transplants. The types of donors are shown in Figure 3. The mean age of donors was 42.8 years; 129 were males and 121 were females.

### Live Donor Kidney Transplants - Sri Lanka Donors Relationship

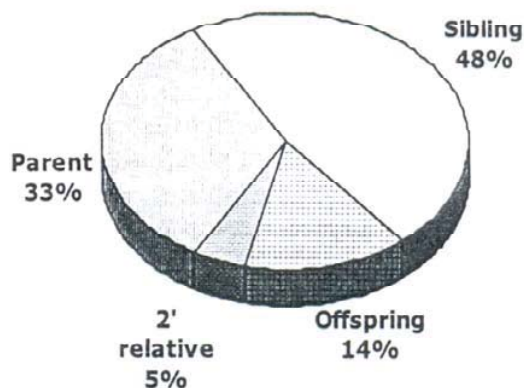


Figure 3

Transplantation is not without complications; the complications could be surgical, rejection, infection, vascular and malignancy etc. The decision to transplant should only be made if the anticipated prognosis is worse than the post transplant quality of life. Comorbid conditions like active sepsis, malignancy, psychosocial instability are a contraindication to transplantation. The success of a transplant also depends on several factors.

- Donor factors
- Tissue compatibility
- Warm ischaemia time
- Immunosuppression
- Recipient factors
- Cold ischaemia time
- Post surgical factors

Renal transplantation involves teamwork. The team usually comprises the Nephrologist and medical team, the dialysis team, the Transplant Surgeon and surgical team, the Anaesthetists, the Radiologists, Pathologists, Microbiologists, the nursing team and support staff.

Details of the Sri Lanka transplants are given in Table 3

**Table 3**

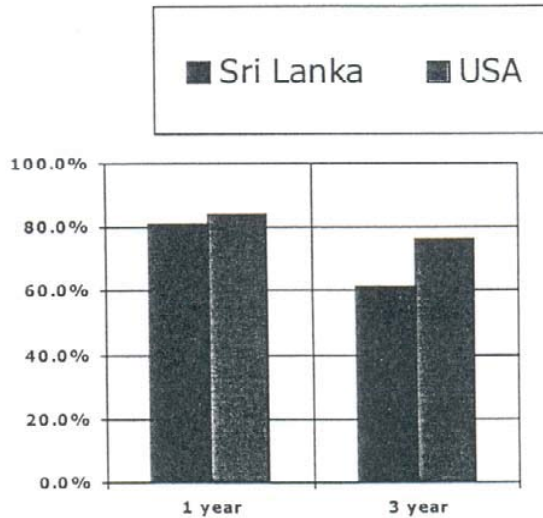
Males: 186      Females: 64  
 Mean age: 33.8 years  
 Ethnicity;  
     Sinhala - 195  
     Muslim - 37  
     Tamil- 18

Patient survival figures are shown in table 4. Graft survival usually equals patient survival in Sri Lanka, because if the graft fails, the patient cannot usually undergo a second transplant, for economic reasons.

**Table 4**

Patient Survival	
1 year	: 81.0%
3 year	: 61.2%
5 year	: 53.0%

Survival figures for Sri Lanka and USA are compared in Figure 4.



**Figure 4**

**Quality of life**

Measurement of the quality of life difficult, as it involves many aspects.

Most of the data on quality of life in this country comes from Government Hospital data and the Registrar Generals office. These institutions largely collect data related to numbers attending services or deaths / births. What perhaps matters more than the numbers who die is the numbers who suffer from the ill effects of a malady. The standard measurements for assessing medical or surgical procedures are clinical judgements, laboratory and other investigations and survival rates. However the measurement of perceived health is a very useful additional measure. A measure of Quality of Life would therefore require an assessment of the impact of ill health on aspects of everyday life of the individual.

From the 1940s the Karnofsky scale for cancer, American Rheumatology Association Scales, etc began to appear, as mortality/morbidity measures were inadequate in chronic diseases. More recently QOL measures are linked to effectiveness and economic costs of health services and extended to audits of clinical practice.

There are several instruments to measure QOL. Although QOL could be considered as a holistic judgement, this nebulous concept is broken into components or dimensions and this in turn into a number of questions or items. The administration and analysis of these questionnaires are susceptible to errors, and every effort must be made to avoid bias, selection etc.

We have an ongoing study in the Faculty of Medicine Kidney Transplant Programme to look at the QOL achieved as we move from chronic renal failure life through dialysis life to post transplant life. Two of the best known multidimensional instruments for general use in patient populations are known as;

1. Sickness Impact Profile
2. Nottingham Health Profile (NHP)
  - a. Pain (P)
  - b. physical Ability (PA)

- c. Energy Level (EL)
- d. Emotional reaction (ER)
- e. Sleep (S)
- f. Social Isolation (SI) Seven general questions  
Other disease specific questions

These issues were incorporated into a questionnaire specially formulated for our patients, with a few additional questions which were centrespecific. I am grateful to Prof Lalani Rajapakse and Dr. Varuna Gunatilake for their active role in these studies. We also obtained some data from the Obstetrics Department of the Faculty of Medicine to support the claim that we had several successful normal deliveries from marriages when one partner was a transplanted patient. Sexual desire, ability to perform sexually, fertility, menstrual periods, etc all improve with dialysis and transplantation in most patients.

The NHP employs weighted items. The questions concerning sleep are listed in this table, to quote as an example;

Question	Weightage
I take tablets to help me sleep	22.4
I wake up in the early hours of the morning	12.6
I lie awake for most of the night	27.3
It makes me along time to get to sleep	16.1
I sleep badly at night	21.7

The results from our studies showed that transplantation improved the quality of life much more than long term haemodialysis. The results are shown in figures 5 & 6.

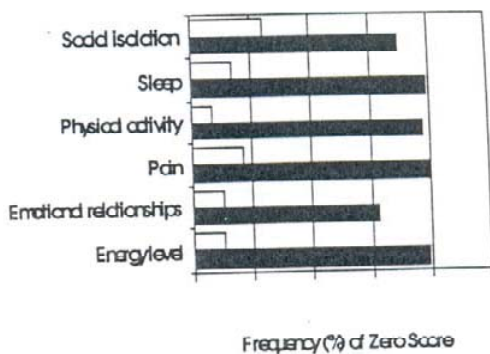


Figure 5

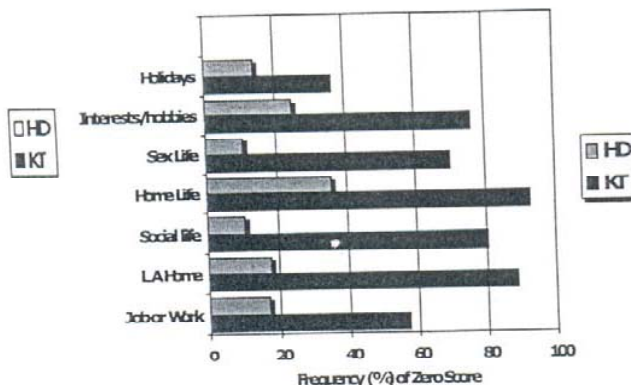


Figure 6

These QOL measurements are also correlated with other data, eg biochemical, radiological measurements. In the case of renal transplantation the general criteria associated with improvement of renal function include;

- \* Increase in Haemoglobin
- \* Fall in Blood urea
- \* Fall in Serum Creatinine
- \* Increase in body weight

The effects on these parameters after haemodialysis and after kidney transplantation are shown in figures 7, 8, 9 and 10.

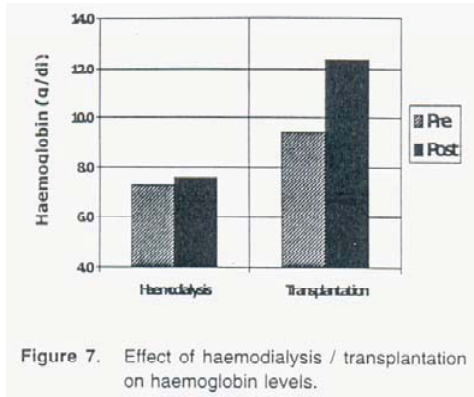


Figure 7. Effect of haemodialysis / transplantation on haemoglobin levels.

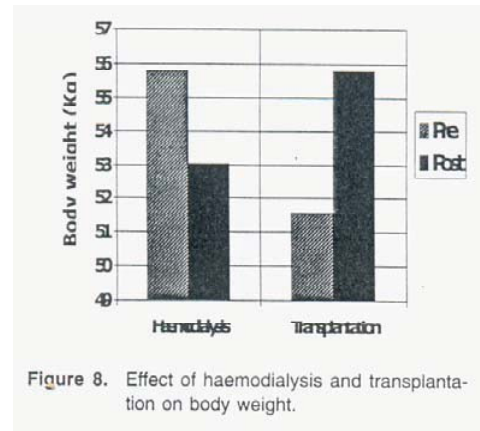


Figure 8. Effect of haemodialysis and transplantation on body weight.

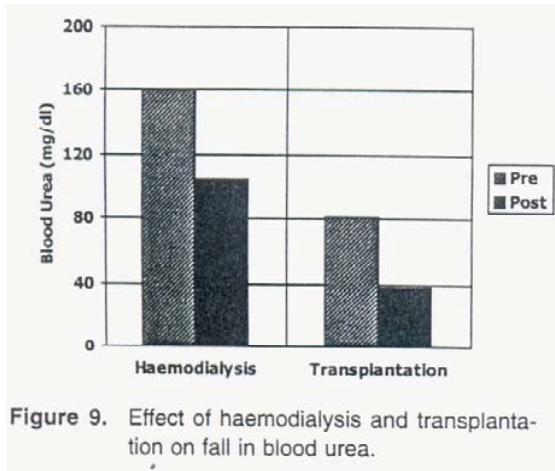


Figure 9. Effect of haemodialysis and transplantation on fall in blood urea.

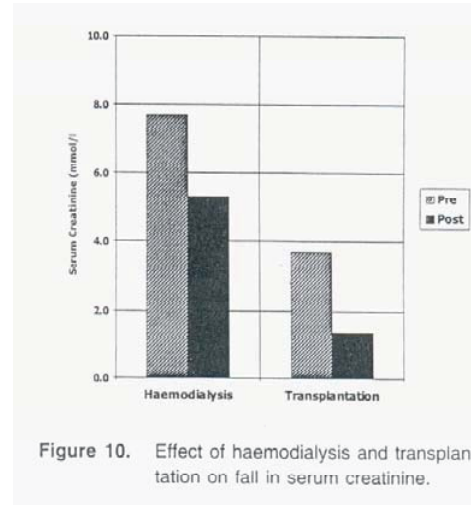
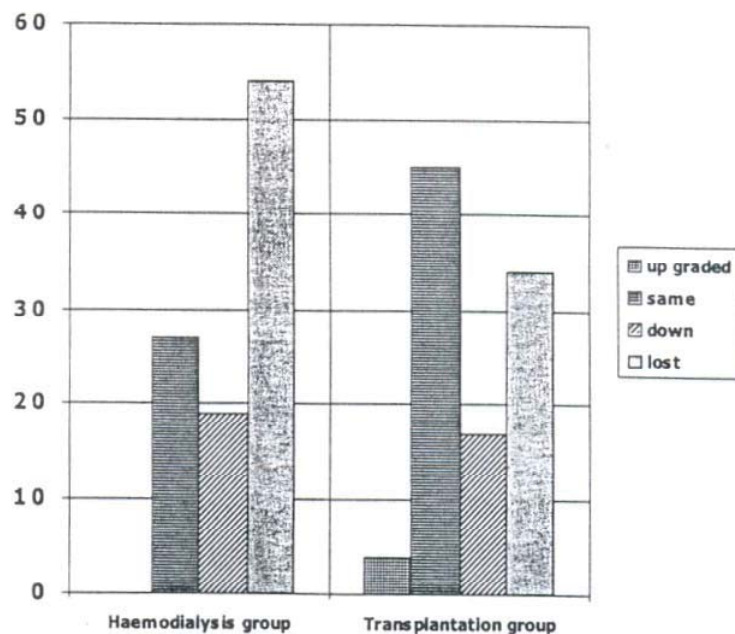


Figure 10. Effect of haemodialysis and transplantation on fall in serum creatinine.

Two other issues which adversely affect the mental health of patients include Occupation , Sex and reproductive life

The effects of either haemodialysis or transplantation on the patients occupation was assessed. The results are shown in Figure 11. Transplantation seemed to have a beneficial effect on patients occupation.

Figure 11  
Effect of haemodialysis  
or transplantation on occupation





Transplantation resulted in an improvement in patients sexual lives (Figure 12). A greater proportion of patients were able to perform normal sexual acts in the transplanted group.

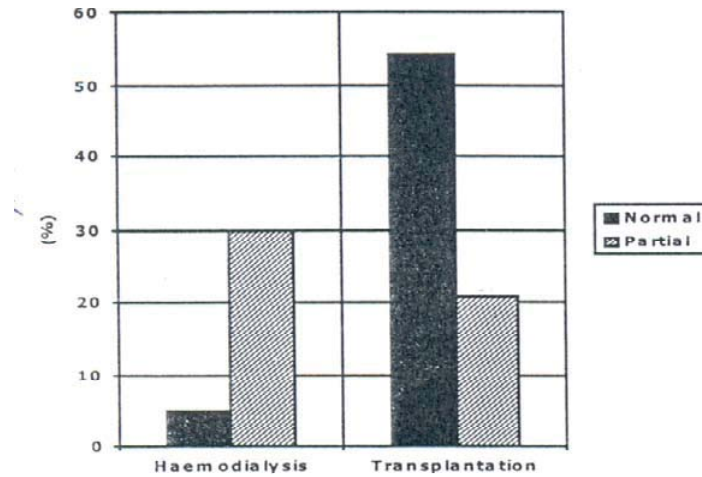


Figure 12. Sexual activity achieved after haemodialysis and transplantation.

### Pregnancy post transplant

Regarding pregnancy after transplantation, the international figures are as follows; 2000 pregnancies have occurred; 1 :50 women in child bearing age get pregnant following kidney transplant.; 40% of conceptions end in abortion in the first trimester. In our own series, 7 women conceived. Two of these were planned pregnancies, and five were unplanned. The two planned pregnancies had a successful outcome, while only two of the five unplanned pregnancies were successful. The importance of planning pregnancy after transplantation is obvious.

The final question which remains to be answered is the cost. All this at what cost? The effectiveness of the therapy is without doubt. The benefit to the user is unquestionable with the present results. None of the organ failure treatment strategies I mentioned are considered experimental any more. Presently a Kidney transplant will cost about 3 to 4 hundred thousand rupees when undertaken in the private sector.

In this country we have only one transplant program, and that to only for the kidney. We need more centres and more interest. It is not a University based specialty. I and the others in our team have performed our role in showing the medical community and the country the possibility of doing and sustaining such a program. We are ready to take on formal training programs in Transplantation. If Professor Rajasuriya were to come back, and I had the opportunity of presenting the ward round cases to him, I am sure he would be thrilled at the high standards in nephrology and transplantation in the University Medical Unit of the National Hospital.

I have come to a point where we cannot take on any more development in this field without facilities. If the Universities are to take on these challenges of medical development, every medical faculty must also have its own even modest specialized independent self funding health facility in addition to the Ministry service wards.

What is the future?

Cadaveric Kidney Transplantation  
Other organ transplantation

Organ Exchange programmes

You have seen what miserable lives these patients with organ failure have, and some of the treatment strategies available short of transplantation. I have briefly shown you the results of other organ failure management, and expanded on renal failure management as we have local experience.

Our results certainly fall short of USA or UK by 10-15% at 5-10 years survival, but if one looks at the cost benefit ratio, it will be a different story. Kidney transplants cost Rs 400 000 in Sri Lanka. In the UK it would cost about 10 times this amount. Our patients have to die if one transplant fails, as the family usually gives up after having gone through the ordeal of finding a donor, funding etc. We have had only 3 re-transplants so far out of 250' transplants.

In spite of our constraints, the patients who are doing well stimulated me to enter some of them to compete in the World Transplant Games. This event is considered internationally as a exhibition of maximum achievement following transplantation. The events athletics, swimming, cycling, contact sports etc, are held to international standards, and the 1997 event was special in that it was held in the year 2000 Olympics facility in Sydney, Australia.

Sri Lanka took 5 kidney transplant patient athletes to these games at short notice as we had difficulty in collecting funds. We are grateful to the Drug Industry, Sports Ministry, and others for their support. We needed a budget of over 1 million rupees.

One of our patients was placed 5th in the world for Cricket Ball Throw and this was our best placement. We could not win a medal. Our placements were better than India, Pakistan and Bangladesh - that too with much less facilities, exposure or training. In all this we cannot forget the thousands of people and relatives who make it all possible. It is their desire to donate, and their unselfish attitude which makes all this happen. Let me leave you with some sentiments of Robert Test.

Give my sight to the man who has never seen a sunrise.....

Give my heart to a person whose own heart has caused nothing but endless days of pain.

Give my blood to the teenager who was pulled from the wreckage of his car.

Give my kidneys to one who depends on a machine to exist.

Take my bones, every fibre and nerve in my body and find a way to make a crippled child walk ....

Burn what is left of me and scatter the ashes to the winds to help the flowers grow.

If you must bury something, let it be my faults, my weaknesses and all prejudice against my fellow man

Give my sins to the devil. Give my soul to God.

If, by chance, you wish to remember me, do it with a kind deed or word to someone who needs you.

If you do all I ask, I shall live forever.

#### Acknowledgements

To all members of the Faculty of Medicine Kidney Transplant Programme - the wider group inclusive of the Faculty Depts of Clinical Medicine, Surgery, Pathology, Microbiology, National Hospital wards 41, 48, Dialysis Unit, MICU. Pathology and Radiology Services and the Private Sector Dialysis unit at Western Infirmary (former Lanka Medicare). We are grateful to Ms. Amitha K. Peiris for her unstinted cooperation in counselling and coordination and Mrs. Gunawardene, Ms. Sadhana and Ms. Fernando for secretarial assistance.