



Kidney transplantation for Australian renal nurses

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Submitted: 4 April 2018, Accepted: 3 August 2018

Abstract

Kidney transplantation is a treatment option for people with end-stage renal disease. This educational supplement is written from an Australian perspective and gives an overview of transplantation, including the criteria for assessment of transplant recipients; care of the transplant recipient in the immediate post-operative period and the long term, including assessment of graft function and the role of immunosuppressive medication; and the common causes of graft dysfunction. It also gives a brief description of the different types of donors.

Objectives

- Define different types of kidney donors.
- List the criteria for transplant eligibility and the process of activation on the deceased donor waiting list.
- Discuss the allocation of deceased donor organs.
- Review the care of the renal transplant recipient in the immediate post-operative period.
- Describe the immunosuppressive medication commonly prescribed for renal transplant recipients.
- List the causes and management of graft dysfunction.
- Describe the long-term care of the renal transplant recipient.

Learning outcomes

- Have an understanding of transplant surgery, including a brief history of transplantation.
- Apply knowledge of the transplantation process to the nursing care of kidney transplant recipients.
- Have an understanding of the causes of graft dysfunction and their diagnosis and treatment.
- Provide emotional support and education for kidney transplant recipients.

Keywords

Transplant, graft dysfunction, nursing care, kidney donors, transplant suitability criteria.

Introduction

Kidney transplantation is a treatment option for people with end-stage renal disease (ESRD) (Danovitch, 2017). It is not a cure for renal disease, but it has been shown to allow better

health and an improved quality of life compared to life on dialysis (Czyżewski *et al.*, 2014). Kidney transplantation involves removing a kidney from a donor (either living or deceased) and surgically implanting it into the recipient, while suppressing

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the immune response with medication to prevent rejection of the donated organ (Mahendran & Barlow, 2014). The first successful kidney transplant took place on 23 December 1954 between identical twins in Boston, US (Starzl, 1990). The previous year, scientists in London had described acquired immunologic tolerance in rats, which was the beginning of the science, resulting in modern-day immunosuppressive medication (Danovitch, 2017). The development of both a surgical technique to successfully transplant an organ, along with medication to overcome the host's immune response, meant that transplantation became a viable treatment option for people with end-stage organ disease (Shrestha *et al.*, 2015).

Kidney donors

Donor kidneys may be from either living or deceased donors.

Living donors

Living donors may be either biologically or emotionally related to the recipient (Lentine *et al.*, 2017). Occasionally a person will come forward to offer one of their kidneys for transplantation without a specific donor in mind. These donors are called 'altruistic' or 'non-directed' donors.

Living donors go through an extensive work-up process designed to evaluate their physical and psychological suitability to donate a kidney. It is illegal in Australia for a living donor to be paid for their kidney, although there is some government funding available to recompense them for the time they need to take off work for the work-up tests and the surgery (Australian Government Department of Health, 2018).

Living donor transplantation is planned well ahead of time and gives people the opportunity to prepare for the surgery. People can receive a pre-emptive transplant from a living donor before they start dialysis. Because of the planned nature of living donor transplantation, it is also possible to perform transplants between individuals from different blood groups or where there are high levels of antibodies that require desensitisation treatment beforehand. For living donor/recipient pairs who are otherwise healthy but incompatible with each other, the Australian Paired Kidney Exchange programme exists to find suitable matches and 'swap' organs between pairs (Australian Government Organ and Tissue Authority, 2018).

Deceased donors

Deceased donors are people who are brain dead but maintained on life support within the ICU. Deceased donor kidneys are allocated to people on the transplant waiting list. The average length of time that people wait for a kidney from a deceased donor is between three and five years (ANZDATA Registry, 2017a). The type of deceased donor is dependent on the individual's co-morbidities and the cause and manner of their death.

Standard criteria donor (SCD)

A brain-dead person under 60 years of age with no history of hypertension or stroke is referred to as a standard criteria donor (SCD). The donor is taken to the operating theatre while still on life support, which maintains the blood supply to the organs for the maximum amount of time. The result of the reduced ischaemic time is that these kidneys usually last longer and function better than organs from other types of deceased donors.

Donation after circulatory death (DCD) donor

In donation after circulatory death the donor is removed from life support machinery and death is declared based on lack of a heartbeat. This increases the ischaemic time when the organs do not have a blood supply (Morrissey & Monaco, 2014). The protocol for the use of DCD donors in Australia was written in July 2010 (Australian Government Organ and Tissue Authority, 2010) and organs from DCD donors now constitute approximately 25% of transplanted kidneys in Australia (ANZOD Registry, 2017). Analysis of registry data has shown that in the short term, DCD organs have a higher incidence of delayed graft function than organs from an SCD donor, but in the medium to long term their overall outcomes are similar (Summers *et al.*, 2015).

Expanded criteria donor (ECD)

The definition of the expanded criteria donor (ECD) was formalised by the Organ Procurement and Transplantation Network (OPTN) in 2002 in response to the worldwide shortage of donor organs (Metzger *et al.*, 2003). An ECD is a DCD or SCD donor over the age of 60 years of age; or aged 50–59 years with a history of hypertension, death because of stroke or impaired kidney function at the time of death (Querard *et al.*, 2016).

Paediatric donors

Kidneys from donors under six years of age are given priority to go to recipients who are children, but may be used in adults if there are no suitable paediatric recipients waiting. When transplanted into an adult, the kidney grows to adult size in a few months. Where the donor is under two years old, both kidneys are transplanted 'en bloc'. This means they are attached to the aorta and vena cava (Hirukawa *et al.*, 2017).

High-risk donors

High-risk donors refer to individuals in the following categories who have a high risk of transmitting viral diseases:

- Men who have had sex with another man during the previous five years.
- Individuals who report non-medical injection of drugs during the previous five years.

- Men and women who have engaged in sex in exchange for money or drugs during the previous five years.
- Individuals who have had sex in the previous 12 months with anyone in the categories above or with a person known to have or suspected of having HIV-infection.
- Prison inmates due to a high risk of contact with people from the groups above.

Although there is a risk of disease transmission from these organs, it may be smaller than the risk of death whilst waiting on the transplant list. People are counselled concerning the use of these organs prior to any offer being made and they are only used if they are consenting (Trotter *et al.*, 2018).

Dual allocation

Sometimes where the kidney function of the deceased donor is less than optimal, both kidneys are used for one recipient. This is called dual allocation. The surgery takes approximately two hours longer than the transplantation of a single kidney, and carries a higher risk of surgical complications. Not all recipients are suitable for a dual kidney transplant, sometimes due to their small stature and the inability to fit two kidneys into the abdomen; or because they are obese and access to the blood vessels is difficult (Cravedi *et al.*, 2017).

Criteria for transplant eligibility

Criteria for entry to the renal transplant waiting list is specified by the Transplantation Society of Australia and New Zealand (TSANZ) (TSANZ, 2017). Inclusion criteria for deceased donor kidney transplantation in Australia includes:

- End-stage kidney disease requiring dialysis.
- A high likelihood of perioperative survival.
- At least an 80% likelihood of the transplant working for at least five years following transplantation. Factors that may influence this include risk of recurrent disease, and non-adherence with immunosuppressive medication.

Criteria for excluding people from the kidney transplant waiting list include:

- An estimated likelihood of surviving at least five years following transplant of less than 80%: co-morbidities such as cardiac disease, vascular disease, diabetes mellitus and malignancies influence post-transplant survival.
- Severe cardiovascular disease, for example, diastolic dysfunction, severe uncorrected coronary artery disease.
- Diabetes mellitus, whilst not an absolute contraindication, may lead to complications that affect an individual's anticipated five-year survival rate.

- Uncontrolled infection.
- Active malignancy.
- Non-adherence with treatment, which may indicate a person's difficulty in managing medications and maintaining follow-up appointments post-transplant.
- Whilst advanced age is not an absolute contraindication to kidney transplantation, less than 5% of people on the transplant waiting list in Australia are over the age of 65.

Diagnostic work-up

To evaluate whether a person is eligible for activation on the kidney transplant waiting list a person must undergo a full diagnostic work-up. The work-up is made up of a number of elements to ascertain whether the person is medically, surgically and psychologically fit for a transplant. Details of the work-up are tailored to the specific needs of the individual, but generally the essentials are as follows.

Medically, the emphasis is on establishing whether the person will be able to tolerate the immunosuppressive medication, and what the likely consequences will be. Past or family history of malignancy, and history of previous exposure to bacterial and viral infections are very important (Campbell *et al.*, 2013). Some units may also review diabetes control and bone health. Current TSANZ Guidelines demand that all potential kidney transplant recipients are reviewed by a nephrologist from the transplanting unit annually (TSANZ, 2017).

Surgically, the transplant surgeon will be concerned with previous history of any major surgeries or co-morbidities involving the blood vessels required for transplantation. Obesity can impact the accessibility of the abdominal vessels and surgeons may deem people surgically unsuitable for transplant based on their BMI and girth (Srinivas & Meier-Kriesche, 2013).

Cardiac health and the cardiac response to stress are very important and in people with previous cardiac disease it may be necessary for them to get clearance from their cardiologist before being deemed fit for transplant (Applegate *et al.*, 2017). People who may present a high anaesthetic risk will require an anaesthetic review.

Smoking status affects a person's medical and surgical suitability and also suggests a person's commitment to caring for their health. In some units, smoking is an absolute contraindication to suitability for transplantation. Other units allow smokers to be listed for transplant, although studies have shown that continued smoking is associated with adverse outcomes (Weinrauch *et al.*, 2018).

A person's psychological preparedness for renal transplant is evaluated in a variety of ways. Some units require potential

transplant recipients to meet with a psychiatrist, while others mandate that they must attend transplant education. A person's engagement with the work-up process and with their current treatment can be an indicator of how they are likely to behave when they receive a kidney transplant. Transplant suitability is re-examined every year for individuals who remain on the list (TSANZ, 2017).

A list of tests used in transplant recipient work-up is found in Table 1.

Table 1: Tests used in kidney transplant recipient work-up

Exposure to bacterial/viral infections
HIV
HBsAg, HBsAb, HBeAb
HCV Ab
CMV IgG Ab
EBV IgG Ab
HSV type 1&2 Ab
HTLV 1&2 Ab
Quantiferon gold (for exposure to TB)
Varicella-Zoster, strongyloides, toxoplasmosis
Dental check-up
Malignancy
Colonoscopy or faecal occult blood
PAP smear (women)
Mammogram (women)
PSA (men)
Renal ultrasound
Chest x-ray
Cardiac evaluation
Fasting serum lipid profile
ECG
Echo
Stress test
Coronary angiogram (if indicated)
Surgical evaluation
Carotid Doppler
Abdominal Doppler
Height, weight, BMI, waist circumference
Smoking status

Organ allocation

The waiting list for organs from a deceased donor is coordinated by the National Organ Matching System (NOMS), run jointly by the Organ and Tissue Authority (OTA) and the Australian Red Cross Blood Service (Australian Red Cross Blood Service, 2018). In Australia there are approximately 1100 people on the waiting list for a kidney transplant at any given time (ANZDATA Registry, 2017b). The number of deceased donors in Australia has been increasing steadily each year and in 2016 491 deceased donors resulted in 821 kidney transplant recipients (Australia and New Zealand Organ Donor Registry, 2017). Allocation of organs is calculated by a computer algorithm developed to create a system which is fair, whilst also ensuring the optimum use of the limited number of deceased donor organs available. Allocation is based on blood

group, tissue typing, HLA antibody levels and the length of time the person has been waiting (TSANZ, 2017). As a person's antibody levels fluctuate depending on sensitising events such as blood transfusions, pregnancies and infections, individuals on the transplant waiting list must send blood every month so that if the computer comes up with a match, the Red Cross staff can perform the crossmatch testing using an up-to-date blood sample.

When a donor organ is matched to a recipient on the waiting list, the transplanting unit has one hour to contact the potential recipient. If that person cannot be contacted, or if they are unfit to accept the offer, the kidney is offered to the next potential recipient matched with that organ until a suitable recipient is found.

Transplant surgery

Transplant surgery is performed by a vascular surgeon. The donated kidney is placed in either the left or right iliac fossa and the native kidneys are not removed unless they are chronically infected or exceptionally large. If nephrectomy of a native kidney were needed this would usually be undertaken prior to the transplant surgery, allowing the individual time to recover. Kidney transplant surgery takes around 3–4 hours. The donated kidney comes with its own blood vessels and ureter. The blood vessels are anastomosed to the recipient's large blood vessels, often the external or common iliac vessels. The donated ureter is attached to the recipient's own bladder and a stent is inserted to prevent a stricture from forming. The stent is removed at six weeks post-transplant (Barone *et al.*, 2004). The illustrations in Figure 1 show how the transplanted kidney is grafted into the recipient's body.

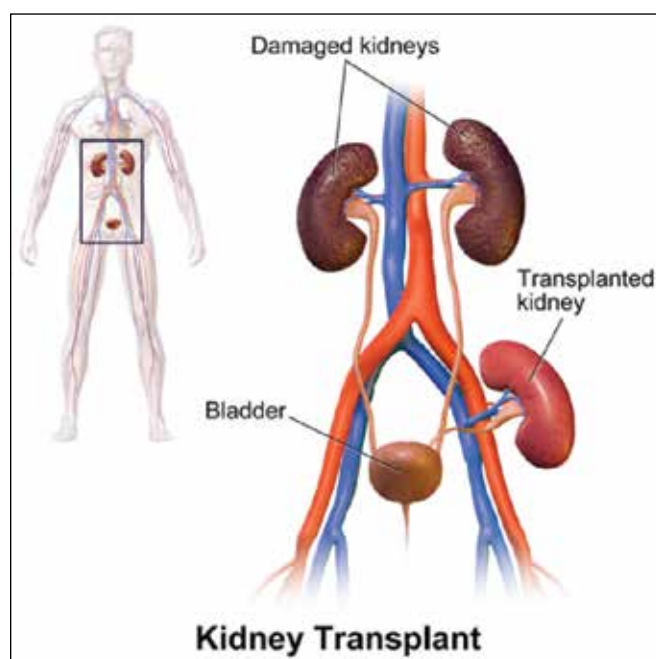


Figure 1: Kidney transplant surgery (Blaus, 2015)

Immediate post-operative care

After transplant surgery, people remain in hospital for approximately 5–7 days. Nursing care involves the monitoring of surgical wounds, care of drains (usually there will be one or two drains in situ), management of pain and prevention of infection and venous thromboembolism. As well as these general post-operative concerns, kidney transplantation presents the specific challenges of monitoring the function of the graft and administration of immunosuppressive medication (McPake & Burnapp, 2009; Murphy, 2007).

Assessment of graft function

- Urine output — a strict fluid balance record is essential. A urinary catheter remains in situ for the first 5–7 days and urine output is closely monitored. Daily weight is recorded.
- Serum biochemistry — urea and creatinine are markers for kidney function and the eGFR (estimated glomerular filtration rate) is often reported.
- Imaging — renal ultrasound and renal Doppler are used to identify any obstruction to the renal blood supply and urine flow.

Immunosuppression

At the time of transplant, intravenous monoclonal (Basiliximab) or polyclonal (Thymoglobulin) antibodies are given, which strongly suppresses the immune system. Oral immunosuppressive medications are commenced, which includes a combination of drugs that act upon the immune response in different ways. The various types of drugs commonly used and some of their side effects are listed below:

- Corticosteroids: prednisolone, prednisone, methyl prednisolone
Side effects: New onset diabetes after transplant (NODAT), which may or may not resolve when the steroid dose is reduced, worsening blood sugar control in people with pre-existing diabetes mellitus, weight gain, altered mood, osteoporosis, acne (MIMS Online, 2018c).
- Calcineurin inhibitors (CNI): Cyclosporin (Neoral), Tacrolimus (Prograf). These drugs are titrated depending on the circulating levels, which may be ineffective if too low or nephrotoxic if too high. Targets are set individually depending on the immunological risk.
Side effects: Nephrotoxicity, hypertension, tremor, hair thinning (MIMS Online, 2018d).
- Mycophenolic acid: Mycophenolate Mofetil (CellCept), Mycophenolate Sodium (Myfortic)
Side effects: Gastrointestinal upset, neutropenia, skin cancers, congenital defects and spontaneous abortion, so should be discontinued in transplant recipients planning pregnancy (MIMS Online, 2018a).

- mTOR Inhibitors: Sirolimus (Rapamune), Everolimus (Certican). Doses of these drugs are titrated depending on the circulating levels.
Side effects: GI upset, impaired wound healing, fatigue (MIMS Online, 2018e).
- Antimetabolites: Azathioprine (Imuran)
Side effects: bone marrow suppression, hair loss, skin reactions, neoplasms — this drug is cytotoxic, (MIMS Online, 2018b).

Typically, a transplant recipient will take a combination of three types of drugs: often a corticosteroid, a calcineurin inhibitor and mycophenolic acid. Immunosuppressive medication must be taken for the lifetime of the transplanted organ in order to prevent possible graft loss or damage from rejection (Holt, 2017).

Transplant recipients are also prescribed medication to counteract the effects of the immunosuppressive medication. Infections that are relatively minor in the general population may be severe or life-threatening in the immunosuppressed transplant recipient. To give some protection, transplant recipients may be given a prophylactic antibiotic (often Bactrim) to prevent *Pneumocystis jiroveci* pneumonia (Lee *et al.*, 2017) and an antiviral (often Valcyte, which is cytotoxic) to prevent Cytomegalovirus (CMV) infection (Gardiner *et al.*, 2017). They may also be prescribed anti-fungal mouthwash and antacids.

Long-term care of the renal transplant recipient

The main areas of focus in the long-term care of the renal transplant recipient include: graft function, prevention of infection, malignancy, co-morbidity and patient empowerment (Chadban *et al.*, 2012)

Graft function

There are four main causes of graft dysfunction: dehydration, drug toxicity, rejection and obstruction.

Dehydration

The transplanted kidney is particularly sensitive to dehydration. If a person has been on dialysis and living on a fluid restriction, it can be difficult for them to adjust to drinking enough fluids to maintain the functioning of the new kidney. Any time post-transplant the kidney may be affected by dehydration caused by infection, diarrhoea and vomiting, heat and exercise, and the recipient may need to be admitted for intravenous fluid replacement to aid the kidney recovery (McBryde & Kaiser, 2017).

Drug toxicity

If the circulating blood levels of calcineurin inhibitor become too high it can result in constricting the blood flow to the

kidney. Blood samples to check the CNI level must be taken either directly prior to the dose being taken (known as C0 or a trough level) or two hours after the drug is taken, known as C2. Calcineurin inhibitor drugs are usually taken twice-daily and should be spaced 12 hours apart so the circulating level is as consistent as possible (Holt, 2017).

Rejection

Rejection is the body's attempt to remove any foreign substance that it does not recognise as its own, such as a transplanted organ, by activation of the immune system.

- Hyperacute rejection is a very rare event that occurs in the first few hours/days following transplantation and results in widespread vascular thrombosis. It cannot be treated and the kidney has to be removed immediately.
- Acute rejection may be either cell-mediated or antibody-mediated, depending on the part of the immune system that has been activated. The microscopic appearance of the kidney looks different depending on the type of rejection; therefore a renal biopsy is required to confirm diagnosis. Treatment of acute rejection usually involves increased doses of corticosteroids, possibly supplemented with intravenous antibody therapy (Thymoglobulin or IVIG).
- Chronic rejection is a slow, insidious process that causes cumulative damage to the kidney over a long period of time. As with acute rejection, it has certain microscopic features that typically appear, so a renal biopsy is often helpful in diagnosis. Chronic rejection may be associated with non-adherence with immunosuppressive medication, although this is not always the case (Haas *et al.*, 2018)

Obstruction

Any mechanical obstruction to the renal blood supply or the urine flow may affect kidney functioning. This includes kinks and narrowing of the arteries, veins or ureters associated with the transplanted organ, and would be identified with renal ultrasound, Doppler and pyelogram. Renal artery stenosis is a cause of obstructive graft failure, which is also associated with high blood pressure (Chen *et al.*, 2014).

Infection

Due to the immunosuppressive medication, renal transplant recipients are at higher risk of contracting infections than other individuals. They must take particular care with the preparation and serving of food to prevent contracting food poisoning, and they must pay careful attention to hand hygiene, prior to preparing or eating food, after using the toilet and following any contact with other people. They should avoid people with active infections, particularly in the first few months following transplant. When admitted as an inpatient, renal transplant recipients should ideally be nursed in a single room with

private bathroom facilities. If no single rooms are available, they should not be placed in rooms with people who have infective symptoms (Prakash *et al.*, 2012).

Malignancy

Renal transplant recipients have a higher rate of malignancy than others, with approximately 7% of transplant recipients developing cancer after transplant (Wong *et al.*, 2013). It is important that transplant recipients maintain routine cancer screening. This includes screening for bowel cancer and regular skin checks, screening for prostate cancer in men, and screening for breast and cervical cancer in women (ANZDATA Registry, 2017c).

Co-morbidity

Co-morbid disease is treated aggressively after transplant to prevent damage to the new organ. Diabetes typically becomes more unstable following transplant due to the high doses of steroids that are used to prevent rejection. Sometimes people who were not previously diabetic develop a type of diabetes called 'New onset diabetes after transplant' (NODAT). When the steroid dose is reduced over the first few months, blood sugar control may settle and NODAT can sometimes disappear, although it does continue in a significant number of transplant recipients (Bzoma *et al.*, 2018).

Cardiovascular disease remains a significant cause of death post-transplant and so cardiovascular risk factors such as hypertension, dyslipidaemia, obesity and smoking are closely controlled (Mathur *et al.*, 2017).

Renal bone disease in transplant recipients may be related to renal failure, but is also affected by the long-term use of corticosteroids. Regular bone mineral density screening should be performed as well as monitoring calcium, phosphate and parathyroid hormone levels (Ketteler *et al.*, 2017).

Patient empowerment

To ensure the best outcomes, post-transplant renal transplant recipients are required to assume responsibility for their own health and strictly follow instructions provided by their medical team. This includes managing their medications, attending clinic appointments, maintaining a healthy lifestyle with diet and exercise, and committing to long-term follow-up. The development of therapeutic relationships with the health care team including doctors, nurses, clinic staff, pharmacists and dietitians may assist a renal transplant recipient with compliance (De Pasquale *et al.*, 2014). Because renal transplant recipients are encouraged to care for themselves, they should be kept informed of any changes to their treatment, particularly when admitted to hospital as an inpatient.

Renal transplant recipients are characterised as a generally well-educated group of people who generally view their kidney transplant as a precious gift (Turner *et al.*, 2018). At times when the kidney does not appear to be working they may experience feelings of anger, sadness, regret, guilt and fear — of the kidney failing and returning to dialysis. Health care staff who support renal transplant recipients need to understand the significance of the graft and be available to provide emotional support where possible (De Pasquale *et al.*, 2014).

Kidney transplantation and Indigenous Australians

Although comprising only 3% of the population, Aboriginal and Torres Strait Islander peoples make up 11% of people with ESRF in Australia (ANZDATA Registry, 2018); however, they are less likely to receive a kidney transplant as their renal replacement therapy (RRT) treatment. They are also less likely to receive a kidney from a living donor and experience poorer patient and graft survival compared to their non-Indigenous counterparts (ANZDATA Registry, 2017d).

There are many possible reasons given for these differences. The causes of renal failure are very different between the two groups, with 70% of ESRD in Indigenous Australians being due to diabetic nephropathy, compared to 33% in the non-Indigenous group (ANZDATA Registry, 2017d). As the acceptance criteria for transplant excludes individuals with poorly controlled diabetes, and also cardiovascular and peripheral vascular disease, this may partly explain why more Indigenous Australians are excluded from transplantation. It may also explain why fewer people are able to donate kidneys to their relatives, as diabetes, or the likelihood of developing diabetes in the future, is an absolute contraindication for living kidney donation (Tong *et al.*, 2011). The work-up for recipients and donors includes a lot of medical tests and appointments with a variety of specialists, and after a transplant there is intensive follow-up requiring frequent reviews. Another reason that Aboriginal and Torres Strait Islander peoples are under-represented in the kidney transplant population may be the lack of resources available in their locality, including pathology and imaging facilities as well as access to nephrologists and transplant coordinators (Burns, 2013). This is an area where further research is required.

Implications for nursing practice

- Renal transplant recipients remain at risk of graft failure and rejection. Nurses should be vigilant to monitor for signs of graft dysfunction, including decreased urine output, weight gain, positive fluid balance, oedema, and raised serum creatinine levels.

- Immunosuppressive medication must be taken correctly for the lifespan of the graft. Twice-daily doses should be given as close to 12 hours apart as possible to maintain constant serum concentrations and blood sampling for drug levels should be correctly timed, either directly before the dose is due (C0 — in the trough) or two hours after the dose (C2) depending on unit policy.
- Renal transplant recipients are at risk of developing serious infections due to their immunocompromised state and therefore should be nursed in a single room with private bathroom facilities, whenever possible.
- Renal transplant recipients have an increased risk of malignancy and should be encouraged to regularly undergo screening, such as colonoscopy, mammogram, PAP smear and dermatology reviews.
- Clear communication of progress and treatment is important when caring for people with kidney transplants as they are encouraged to be independent in their care. They may have many different emotional reactions when hospitalised and require education and support.

Conclusion

Kidney transplantation is a treatment option for people with ESRD. In Australia, close to 1000 people receive kidney transplants each year from either living or deceased donors. It is important that renal nurses understand the basic principles of transplantation and what is required of them when caring for a person who is a kidney transplant recipient.

Questions and activities

1. Explain the difference between standard criteria (SCD) donors and donation after circulatory death (DCD) donors. What difference does this make to the donated organs?
2. What are the criteria in Australia for a person to be activated in the waiting list for a deceased donor kidney?
3. Why it is important to accurately record fluid balance in a renal transplant recipient admitted with graft dysfunction?
4. Look up your unit's policy regarding the testing for serum drug levels. Should the blood sample be collected directly before the dose or at two hours after the dose is given (C0/C2)?
5. Talk to a renal transplant recipient and ask them about the difference their kidney transplant has made to their life.

Acknowledgements

We would like to acknowledge the nursing staff of St George Hospital renal ward and haemodialysis unit who inspired this education supplement and who contributed to reviewing it.

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KEY DATES

21 November	Call for abstracts opens
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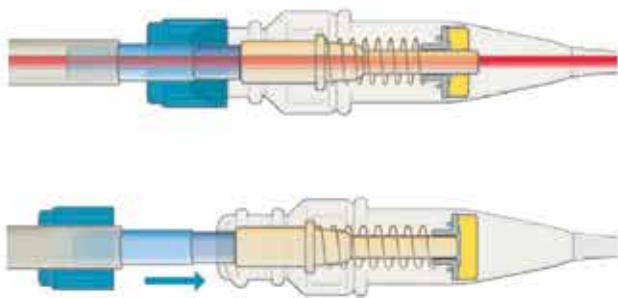


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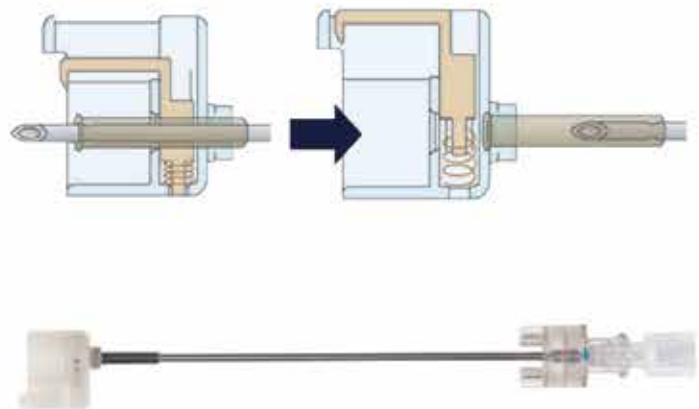


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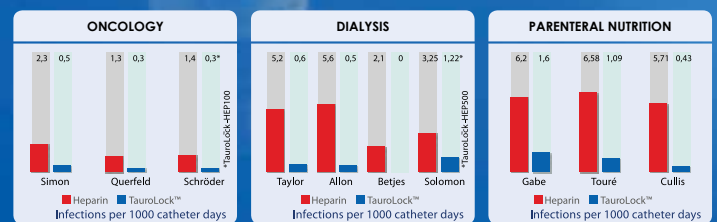
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