

KIDNEY TRANSPLANTATION - CHW

PROCEDURE[®]

DOCUMENT SUMMARY/KEY POINTS

- Kidney Transplantation is performed to replace renal function in children with end stage renal disease (ESRD).
- The majority of children will receive a living donor (LD) transplant usually from a parent. Others receive a deceased donor transplant.
- Patient work up prior to transplantation includes tissue typing, cross match, viral work-up.
- Donor work up includes tissue typing, viral workup, renal imaging and review by an adult nephrologist and the transplant surgeon.
- The majority of children will receive standard immunosuppression with an IL-2 receptor antagonist (basiliximab), steroids, mycophenolate mofetil (MMF), and tacrolimus. This may be varied because of diabetic risk, primary non-function, or risk of recurrent disease.
- The immediate post-operative period requires close monitoring of fluid, electrolyte and renal status usually in PICU with central venous pressure (CVP) monitoring as well as close surgical monitoring of the graft.
- Children require close monitoring of renal function, phosphorus and magnesium levels, tacrolimus levels, full blood count, medications and blood pressure with awareness of rejection, infections, and mechanical problems initially in the ward and then as an outpatient.
- This document provides information to staff in the renal, anaesthetic, surgical, PICU and Clancy teams on the management of a child receiving a kidney transplant.

This document reflects what is currently regarded as safe practice. However, as in any clinical situation, there may be factors which cannot be covered by a single set of guidelines. This document does not replace the need for the application of clinical judgement to each individual presentation.

Approved by:	SCHN Policy, Procedure and Guideline Committee	
Date Effective:	1 st January 2019	Review Period: 3 years
Team Leader:	Staff Specialist	Area/Dept: Nephrology

CHANGE SUMMARY

- Amendments have been made to the work-up for renal transplant recipients
- There is an additional appendix with donor work-up blood and urine testing to be done prior to referral to an adult nephrologist
- There is additional information about plasma exchange around the time of transplant
- The guideline for tacrolimus dosing has been amended
- There are guidelines for follow up investigations post-transplant
- There is additional information regarding surveillance for donor specific antibodies
- There is additional information about vaccinations pre and post-transplant
- Pre-transplant pregnancy testing has been added for girls of child-bearing age
- There is additional information about once daily immunosuppressive regimes

READ ACKNOWLEDGEMENT

- New renal registrars/fellows and the surgical transplant registrars/fellows should read the document at the beginning of their term(s).
- PICU/COU registrars/fellows caring for new renal transplant recipients should read the document
- The on-call subspeciality registrar should be aware of the document
- The nursing staff on Clancy ward, the Renal Treatment Centre and in PICU should be aware of the document
- The emergency staff should be aware of the document

This document reflects what is currently regarded as safe practice. However, as in any clinical situation, there may be factors which cannot be covered by a single set of guidelines. This document does not replace the need for the application of clinical judgement to each individual presentation.

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1 Kidney Transplantation

1.1 Background

End-stage renal failure (ESRF) in children is associated with a variety of primary and secondary disorders. The majority of renal transplants are done for children with end stage renal failure secondary to congenital structural disorders of the urinary tract and kidneys including congenital anomalies of the kidney and urinary tract (CAKUT) and posterior urethral valves. Other children develop end stage renal failure secondary to focal and segmental glomerulosclerosis (FSGS), systemic lupus erythematosus (SLE) and other causes of glomerulonephritis. A variety of other diseases make up the remainder of ESRF in children including Haemolytic Uremic Syndrome (HUS), malignancy most commonly bilateral Wilms tumour, genetic diseases such as nephronophthisis, Denys Drash, cystinosis and Alport's syndrome.

The majority of children receive kidneys from living donors, most of whom are related to the child. Most kidney transplants are blood group ABO compatible however there is now the ability to transplant across the ABO barrier (see separate protocol). If a parent or relative has been approved as a donor but is not acceptable as a donor to their child/relative (either because of blood group incompatibility or a positive cross-match/ donor specific antibodies) then they may be entered into the Australian Paired Kidney Exchange Programme (AKX). This programme uses a computer algorithm to match up potential donor-recipient pairs from a pool of entrants, to facilitate more living donations. (There is a separate protocol for AKX). When no suitable donor is available or there is a contraindication to living donor transplant, children are placed on the deceased donor waiting list. Changes were implemented in 2018 and now children aged less than 18 years receive priority on the deceased donor waiting list once they commence dialysis. In rare circumstances a child may undergo desensitisation treatment if they have significant antibodies.

Some children will circumvent the need for dialysis by receiving a living related transplant pre-emptively, however many children will undergo either peritoneal or haemodialysis before they receive a renal transplant.

2 Work up for recipients & donors for kidney transplantation

2.1 Renal Team

All children undergo transplant work up well before renal transplant. The renal Nurse Practitioner will see the family approximately 4 months prior to a planned living donor transplant. She will organise the following investigations and document the results on the work-up form, available in a folder in the Renal Treatment Centre (RTC):

- Blood group of recipient and potential donor (if any)
- Tissue typing: This will be scheduled by the Renal Treatment Centre staff with the Red Cross Tissue Typing Laboratory. For living donor renal transplants, blood from both donor and recipient is sent for an initial tissue typing (stage 1) and then a final cross match is performed about 3 weeks before the transplant. For potential deceased donor

transplant recipients, blood is sent on two separate occasions for tissue typing. As soon as the recipient is considered ready for transplant an activation form is sent to Red Cross, and the recipient is then active on the deceased donor transplant list. Serum (in a 10 ml gel tube), is sent monthly for antibody screening. The Tissue Typing Laboratory staff may request additional testing if antibodies are present, or the recipient has a sensitising event such as blood transfusion or immunisation.

- Chest X-ray and ECG (if not done in the previous 6 months)
- Viral Serology for CMV, EBV, HHV6, varicella, measles, HIV, hepatitis B antigen, hepatitis B antibody and hepatitis C antibody
- If the recipient is negative for IgG measles or varicella and is not immunosuppressed, he/she should be vaccinated if the transplant is more than 3 months later. If the patient has no hepatitis B titres, vaccination should be given if transplant is more than 3 months later. Please note that children on dialysis require a **double dose** of hepatitis B vaccine booster. Delay sending blood for tissue typing/cross match for 4 weeks following vaccination.
- In children aged less than 5 years, those with nephrotic syndrome or in those with increased thrombotic risk, check for Factor V Leiden levels, antithrombin III, Protein C and Protein S levels.
- Any recipient with congenital renal anomalies, spina bifida or caudal regression needs Doppler ultrasound of the lower aorta, inferior vena cava and iliac vessels. These children may need MRAV if the Doppler is unsatisfactory.
- Any recipient with a history of multiple central lines should have Doppler ultrasound of neck vessels to assess for patency.
- Measure a 24 hour urine volume in children with persisting urine output prior to a living transplant. This helps the renal physicians to interpret the urine output post-transplant.
- Research bloods for Prof S Alexander (page 6563). A parent information form and consent form is available electronically in the Renal Treatment Centre folder on the renal G drive.
- Swab throat, both nostrils and any stoma or dialysis catheter site for MRSA
- Tuberculosis gamma interferon assay
- Documentation of current vaccination status
- Documentation of the donor's CMV and EBV status for living donor transplantation. (This will be checked by the renal treatment centre nurses with the final cross match)
- There is now a pre-transplant work-up sheet in the renal Powerchart note and this should be completed. All patients will also be discussed in one of the quarterly transplant planning meetings.

The renal Nurse Practitioner will arrange the following in conjunction with the renal registrar or consultant:

- Consultation with the:
 - department of psychological medicine (often done in conjunction with consultation with the social worker)
 - dental department
 - urologist if required
 - Renal Transplant recipient surgeon
- Admission to Clancy ward if required the night before the transplant or admission to the Renal Treatment Centre on the day of transplantation.

The urologist and/or transplant surgeon will review the recipient either in the RTC or in their surgical clinic and they will arrange the admission forms and consent forms at this time.
- Potential living donors will have their blood pressure, height, weight, BMI calculation and screening bloods (see Appendix 1) done at The Children's Hospital at Westmead prior to referral to the Transplant Co-ordinator for donor work-up at Westmead Hospital. Appointments will include one with a renal physician and one with the donor surgeon. Referral is usually made at least 6 months prior to the transplant to allow adequate time for the work-up.

2.2 Surgical team

The surgical registrar is responsible for the following;

- Submitting the admission form for the PICU bed and booking the surgical pre-admission clinic for the recipient.
- The living donor information sheet that arrives with the kidney, with details about the cold ischaemic time etc., should be emailed to the nephrologist on call, the renal secretary and to the renal Nurse Practitioner. The original copy should be sent to medical records to be scanned into Powerchart.
- NB. Deceased donor details must NOT be filed in the recipient's records.
- The surgeon or surgical registrar should complete the intra-operative page in the renal Powerchart note.

3 Pre-transplant assessment

3.1 Living Donor Transplant

Living donor transplants are usually done on one Thursday each month according to the surgical schedules of both the donor and recipient surgeons. Children who are to undergo a living donor transplant will be reviewed in the RTC on the Tuesday morning prior to their transplant to complete their investigations and consultations.

3.2 Deceased donor Transplant

Organising the pre-transplant assessment for a child before a deceased donor transplant is urgent and all investigations must be marked as urgent. The patient and family are contacted immediately a kidney transplant is offered to the child. They are asked to attend the emergency department immediately. Transfer to Renal Treatment Centre or Clancy for pre-op preparation should then be negotiated with the Bed Manager and Nephrologist on call. The child should have nothing to eat or drink from the time that the family are asked to come to the hospital. If a child is on home peritoneal dialysis parents should be advised to drain the child's peritoneum prior to disconnect from the machine. If possible ask the parent to leave 20-50ml of fluid in situ to be tested for peritonitis on arrival at hospital.

3.3 Assessments and Investigations

- Cross match 2 units of packed CMV negative, irradiated red blood cells. Please make sure that "For renal transplant operation" is documented on the request form.
- Blood tests for electrolytes, creatinine, calcium, phosphorus, magnesium, albumin, liver function tests, glucose, PTH, FBC and coagulation studies
- Viral serology (unless taken in the previous month) for CMV, EBV, Herpes Simplex, Varicella Zoster, Hep B, Hep C, HIV, HHV6
- Pregnancy test in girls of child-bearing age
- Swab exit sites in children with peritoneal dialysis catheters, central venous haemodialysis access catheters and gastrostomy tubes or buttons and send for culture.
- CXR and ECG.
- Prescription of immunosuppressive medications required pre-transplant and in the post-operative period (see section on immunosuppressive medications below).
- Swab throat and both nostrils for MRSA culture if not done in the previous month
- History and physical examination
- Consultation with the anaesthetist
- Notify PICU of date and time for transplant (the surgical team will put in the admission form for PICU/Close observation unit).
- Pre transplant tour of COU/PICU with renal nurse specialist.
- Consultation with the renal transplant surgeon to complete the consent form (if not already done).
- Check with the child's consultant or the consultant on-call whether peritoneal dialysis catheters and/or gastrostomy buttons are to be removed during the procedure. Cuffed venous haemodialysis access lines are usually left in situ and a double or triple lumen central venous catheter placed on the opposite side.
- On the day of transplant notify the on-call ultrasonographer that a Doppler U/S will be required.
- On the day of transplant print off a copy of the protocol that will accompany the patient to theatre and to the PICU/Close observation unit.

- All patients will have a pre-implantation kidney biopsy done on the donor kidney in theatre.

3.4 Dialysis regimen for living donor transplant recipients

- Children on haemodialysis and scheduled for living donor transplant will receive haemodialysis on the day before transplant. Target ultrafiltration should be approximately 200-1000mls above dry weight depending on the size and urine output of the child.
- Children on peritoneal dialysis and scheduled for living donor transplant should undergo dialysis during the night before transplant. The parents will be given a “pre-transplant” dialysis program at the pre-admission clinic. This program will be set to end with an empty peritoneum.
- The dialysis schedule for peritoneal dialysis should be reviewed to ensure that the child completes peritoneal dialysis 0.2-1kg, depending on the size of the child, above the dry weight as it is important that children are well hydrated going into the transplant.
- Children on peritoneal dialysis should have their peritoneal dialysis fluid drained before going into the operating suite. This can be done at home prior to admission.

3.5 Dialysis regimen for deceased donor transplant recipients

- If a child is receiving haemodialysis and was not dialysed on the day before the transplant, he or she will need haemodialysis before going to the operating suite.
- The child should complete haemodialysis 0.2-1kg above dry weight, depending on the size of the child.
- Haemodialysis should be undertaken using no or minimal heparin
- If a child is having home peritoneal dialysis, they should be left empty when disconnected from the machine. Check with the parents whether this happened. If not, nursing staff should drain the fluid and collect a specimen for culture.

3.6 Plasma exchange peri-transplant

- Some children will require plasma exchange immediately pre or post-transplant, especially if they require antibody removal.
- Albumin is generally used for fluid replacement in plasma exchange but immediately prior to transplantation fresh frozen plasma is used to reduce the risk of bleeding at the time of transplantation.
- Children receiving fresh frozen plasma replacement may develop hypersensitivity reaction to the plasma. Therefore pre-medication with IV hydrocortisone and oral antihistamine may be ordered.

3.7 Fluid regimen for transplant recipients

Children should have full oral feeds/fluids up until the time that they have to be nil by mouth. Children with an increased urine output will require intravenous fluid replacement.

4 Immunosuppression and other Medications

TWO PHYSICIANS OR ONE PHYSICIAN AND THE RENAL NURSE PRACTITIONER **MUST** CHECK THE IMMUNOSUPPRESSIVE REGIMEN PRESCRIBED. IT WILL ALSO BE CHECKED BY THE RENAL PHARMACIST.

Once the medications have been prescribed and approved, the medication sheet should be taken to PICU or COU to ensure that the drugs are available in the ward on the day of transplant.

The day of transplant is regarded as day 0

***Tacrolimus*^{1,2} (Prograf):**

- 0.15mg/kg (maximum dose 7.5mg) orally at 8 am on day of living donor transplant or on admission for deceased donor transplant. Then give tacrolimus 0.15mg/kg (maximum dose 7.5mg) twice daily starting on the evening of transplant.

Please note that tacrolimus is removed by plasma exchange and dialysis so it must be given after plasma exchange/dialysis.

Pre-dose tacrolimus levels should be measured daily from the day after transplant. (This can be discussed with individual consultants as some are happy for alternate day levels). Aim for tacrolimus levels of 8-10ng/mL for the first month, then reducing to 6-10ng/mL for the next 3 months and 5-8ng/mL to 12 months or longer. In exceptional circumstances there may be some variation to these target levels.

PLEASE NOTE that children given antithymocyte globulin (ATG) (see ATG protocol in Appendix 23) for induction do not commence tacrolimus until Day 5 post transplant.

Common side effects of tacrolimus include tremor, hypomagnesemia, hypertension and increased risk of diabetes (especially in conjunction with high dose steroids).

***Mycophenolate* (Cellcept):**

- 10mg/kg (maximum dose 750mg) orally at 8 am on day of living donor transplant or on admission for deceased donor transplant. Then give mycophenolate mofetil (MMF) 10mg/kg twice daily (max dose 500mg) starting on the evening of transplant. MMF may cause leucopaenia. It also commonly causes short-term diarrhoea. This is sometimes alleviated by dividing the total daily dose into three separate doses instead of two and often after a period of a few weeks the child will then tolerate a twice daily dose.

Please note that MMF is removed by plasma exchange so it must be given after plasma exchange. There is no data about high flux dialysers so it should be given after dialysis to avoid potential removal by dialysis.

***Basiliximab*³ (Simulect):**

- Basiliximab is an IL-2 blocker.
- Give 12mg/m² (maximum dose 20 mg) mixed in 50 mL of 0.9% sodium chloride by IV infusion over 20 minutes 2 hours before transplant. (See basiliximab protocol in Appendix 2). Order the second dose of 12mg/m² basiliximab, which is given on day 4 post-transplant.
- Hypersensitivity reactions to basiliximab have been described so resuscitation medications and equipment should be immediately available.

Please note that basiliximab must be given after dialysis or plasma exchange.

Methylprednisolone:

- Give methylprednisolone IV in 50mL of 0.9% sodium chloride over 30min immediately before transplant and at 0800 on days 1 and 2 after transplant.
 - For children whose weight is below 20 kg, give 250 mg
 - For children whose weight is 20 kg or above, give 500 mg

Please note that methylprednisolone is removed by plasma exchange so it must be given after plasma exchange or dialysis.

Prednisone:

- From day 3 give prednisone 1mg/kg/day (maximum dose 20 mg) in the morning as a single dose orally. Prednisone is usually weaned from about 3 months. All children will be left on a small daily dose of prednisone (usually 5mg) by 6-12 months as determined by the primary consultant.

Other medications

- **Valganciclovir⁴** is given to all children unless the patient is a CMV negative recipient receiving a CMV negative kidney. Valganciclovir is given as a single morning dose with food and is continued for 6 months post-transplant. The dose of valganciclovir must be reduced in children with reduced renal function. Valganciclovir is available as 450mg tablets or as a 50mg/mL suspension. To prescribe the first dose of valganciclovir, assume that the creatinine clearance will be 50mL/min/1.73m².
 - The **daily oral dose required** is calculated from the formula:
 - 7 x body surface area x creatinine clearance in mg/day (max 900mg/day)
 - The **creatinine clearance** can be calculated from the formula below:

$$\frac{40 \times \text{height in cm}}{\text{Serum creatinine in } \mu\text{mol/L}}$$

Round off the dose to half or a whole tablet or to the nearest mL.

The predominant adverse reactions to valganciclovir are leucopenia, neutropenia, anaemia, thrombocytopenia, diarrhoea, nausea and vomiting.

- **Cefazolin** 50 mg/kg to be given as a single dose on induction of anaesthesia. Rarely an alternative or additional antibiotic will also be recommended depending on recent infectious history.
- **Sulfamethoxazole/trimethoprim (Cotrimoxazole)** (2 mg/kg/d of trimethoprim - maximum 80 mg) orally daily at 18.00. On discharge from hospital cotrimoxazole is given 3 times per week. This is continued for at least 12 months post transplantation as prophylaxis against *Pneumocystis jirovecii*.
- **Heparin** (sodium heparin) is given subcutaneously at a twice daily dose of 75units/kg/dose for 3 days following transplant starting on the evening of transplant. Heparin may be given by Insuflon subcutaneous catheter if necessary.
- **Nystatin** - orally at a dose of 100,000 IU (1mL) four times daily for 1-3 months post-transplantation.
- **Antacids**. There is emerging evidence that proton pump inhibitors (PPIs), such as omeprazole, reduce the absorption of mycophenolate mofetil. The use of ranitidine is preferable to PPIs, but may also reduce MMF absorption and ideally should be given at least 60mins after the MMF.

Proton pump inhibitors should be discontinued post-transplant.

5 Post-operative Management

The transplant kidney frequently acts as an open drain and has no capacity to retain fluid, so that post-operatively the patient can become either fluid overloaded or rapidly dehydrated. The urine output is no guide to the adequacy of perfusion of the kidney. Therefore the aim is to maintain good central pressure to promote good perfusion.

5.1 Fluid replacement regimen

The aim is to achieve a forced diuresis by maintaining the central venous pressure (CVP) between 8-12 mm Hg above the mid-axillary point. For unclear reasons it may not be possible to maintain CVPs at this level post-transplant so if the child is well hydrated and the urine output is satisfactory (>20mL/hr) in patients not in established acute tubular necrosis, it is not necessary to keep trying to achieve a CVP of 8mm Hg or more.

The initial regime for a kidney recipient is as follows:

- **Living donor kidneys**. Fluid replacement should be 15 mL/hr (0.45% sodium chloride + 5% dextrose) + previous hour's urine output. This is to be administered instead of maintenance fluids. Urine replacement fluid should alternate between 0.9% Sodium chloride and 0.45% sodium chloride. It is important to monitor the blood sugar level and sodium level. It may be necessary to use bags of fluid with dextrose for the urine replacement if the blood glucose level is low (<3.5mmol/L).
- **Deceased donor kidneys** often have some acute tubular necrosis and will therefore not produce much urine in the first 1-7 days. These children should therefore have 15mL/hr of 0.45% sodium chloride + 5% dextrose plus mL for mL urine replacement

with 0.9% sodium chloride +5% dextrose alternating with 0.45% sodium chloride + 5% dextrose, if required. If children are anuric then a fixed volume of fluid will be determined by the nephrologist.

- The required CVP and fluid replacement volumes will be determined by the nephrologist on call in conjunction with the Intensivist on call for each child.

If the patient's urine output drops suddenly, check that the catheter is functional and is not kinked. If there is no increase in urine output, immediately notify the Intensivist (if the child is still in PICU/COU **or the Renal physician on call** (if the child is in Clancy Ward).

- While the child is an inpatient there should be close observation of fluid balance and the child should be **weighed daily**.

5.2 Blood transfusion

- It is usually not necessary to transfuse children post-transplant and transfusion should be avoided if at all possible to avoid the risk of sensitisation. **Please contact the renal physician on call before giving a blood transfusion.**
- Blood is now leucocyte depleted so a white cell filter is no longer necessary.
- If the child is CMV negative, the child should receive CMV negative blood if this is available.
- In keeping with the network transfusion policy, blood for transplant recipients should be irradiated.

5.3 Acute Imaging post op Renal ultrasound/doppler studies/chest x-ray

- A chest x-ray must be obtained and viewed immediately on the patient's return from the operating theatres.
- A renal ultrasound with doppler studies must be performed immediately on the patient's return to the Intensive Care Unit, regardless of the time of day. In exceptional cases, the surgeon may permit the renal ultrasound to be performed the following morning.

5.4 Biochemistry and haematology

- Bloods for UEC and FBC should be obtained urgently on return from the operating theatres and then every 4-6 hours overnight.
- Bloods for UEC, calcium, phosphorus, glucose, albumin, LFTs, tacrolimus and FBC should be measured at 8-9 a.m. daily. Measure the first tacrolimus levels on the morning after the first evening dose. Tacrolimus levels are trough levels and obtained immediately before the morning dose. It is not necessary to wait for the result before giving the dose.
- Results of UEC and FBC should be obtained as soon as possible each day and reported to the consultant on call.

Urine:

- A urinalysis should be checked every 6 hours in PICU/COU and then daily on the ward. Urinary sodium, creatinine and protein: creatinine ratio should be checked daily in PICU/COU. In patients with underlying focal segmental glomerulosclerosis, if there is proteinuria, notify the renal consultant **immediately**.

5.5 Urinary catheters

Patients will return from theatres with a urinary catheter in place. If re-catheterisation is required this should be performed by the surgical registrar using a silastic catheter. Re-catheterisation may only be performed by the PICU registrar if requested to do so by the surgical team:

- Size 10 F for 10 - 20 kg.
- Size 12 F for > 20 kg.

Please ensure that the catheter is taped to the abdomen and not the child's leg as this prevents the catheter being pulled as the child abducts his/her leg.

5.6 Central venous catheters

- All children will usually have a double or triple lumen central venous catheter inserted in theatres even if they already have a cuffed central venous haemodialysis catheter in place.
- **Cuffed or uncuffed haemodialysis lines should only be used by the dialysis nursing staff for dialysis.** In exceptional circumstances the dialysis nurses may access the haemodialysis catheter for blood collection.
- In general arterial lines are not necessary and their use should be avoided to protect vessels for future haemodialysis access.
- Femoral lines should **not** be inserted because of the risk of thrombosis and infection.

5.7 Analgesia

Patient controlled analgesia or epidural infusion are preferred for administration of analgesia immediately post-op. When necessary, a morphine infusion can be given. The pain team will be involved whilst the patient is an in-patient and will supervise weaning of analgesia.

5.8 Isolation

- Patients should be nursed in isolation.
- All staff and visitors should wash their hands.
- Gowns need not be worn.
- People with respiratory or gastro infections should not visit the child.
- There should be no more than 3 visitors (including parents) in the room at any time.
- In general face masks are not necessary.

6 Problems post renal transplant

Hypertension

Hypertension is common following renal transplant. The levels of systolic and diastolic blood pressure requiring treatment will be determined by the Renal Physician on call in conjunction with the Intensivist on call.

- **IF NECESSARY, the following alternatives may be considered:**
 - Reduction in intravenous fluid volumes administered and/or intravenous frusemide 1mg/kg/dose.
 - Intravenous antihypertensive agent:
 - Clonidine 3-6 microgram/kg/dose. Mix in 10mL of 0.9% sodium chloride and infuse over 5-10 minutes.
 - Oral antihypertensive agent:
 - Nifedipine 10 mg (tablet) for children < 20 kg
 - Nifedipine 20 mg (tablet) for children ≥20 kg
 - Clonidine 6 microgram/kg/dose
 - Patients with persistent hypertension should be checked for evidence of angiotensin-1 receptor (AT1R) antibodies (discuss with the nurse practitioner).

Hyperkalaemia (i.e. $K > 5.5$ mmol/L)

- Refer to **CHW Administration of Potassium Practice Guideline:**
<http://webapps.schn.health.nsw.gov.au/epolicy/policy/469>
- Stop all exogenous sources of potassium

Hypophosphatemia

Most children will drop their serum phosphate in the first week and will require increased dietary intake plus supplementation with phosphate Sandoz

Hypomagnesemia

Tacrolimus will decrease the magnesium level. When the level is <0.5mmol/L children should be supplemented with Magmin (in older children) or Magnesium chloride (in younger children).

Fever

Fever may be due to a number of different problems but acute rejection should always be considered as a possible cause of fever.

- **Acute rejection:** Hyperacute rejection is very rare but occurs immediately post - transplant. Acute cellular or vascular rejection may occur anytime following transplant

but usually does not occur until the end of the first week or the second week post-transplant and is less likely to occur after the first 3 months post-transplant. It should be suspected if the patient has a fever, with a tender graft and rising creatinine. However not all of these have to be present and fever may be the first sign.

- **Acute bacterial infection:** This can occur at any time post-transplant. Appropriate cultures should be obtained. Knowledge of recent infections, such as exit site infections, may influence the choice of antibiotics.
- **Acute viral infection** (particularly CMV, EBV, BK and HHV6): These usually occur 3 - 6 weeks following a transplant, though CMV will often occur later because of the use of valganciclovir prophylaxis. Information on pre-transplant serology is usually available on donor and recipient. See the section on [viral surveillance](#).

Rising creatinine

- This may be due to:
 - Acute transplant rejection
 - Obstruction
 - Dehydration
 - Vascular problems
 - Infection
 - Tacrolimus toxicity
 - BK virus nephropathy

The creatinine result should be obtained urgently each day and the Renal Physician on call informed of the result. Note – there is no normal range for transplanted patients. Each individual patient will establish their own baseline creatinine over a period of about a week or two and variations of more than 10% of this baseline should be investigated. If the creatinine has risen in the acute period a renal ultrasound with doppler studies should be obtained urgently following discussion with the Renal Physician on call. The urinalysis should be checked and if indicated a urine sent for MC&S. Viral studies may be warranted. An urgent renal transplant biopsy is often required to determine the cause of a rising creatinine.

6.1 Treatment of acute cellular rejection

Acute cellular rejection is treated in the first instance with high dose intravenous methylprednisolone.

- Children weighing 25 kg or more should be given either 500 mg methylprednisolone IV for 3 consecutive days or 1 gram of methylprednidolone on Day 1, 500 mg on Day 2 and 250 mg on Day 3. Methylprednisolone is given as an infusion.
- Children weighing below 25 kg should be given either 250 mg methylprednisolone IV for 3 consecutive days or 500 mg of methylprednisolone on Day 1, 250 mg on Day 2 and 125 mg on Day 3.
- All patients will then revert to their previous dose of oral prednisolone unless determined otherwise by the Renal Physician on call if the patient is an inpatient or by the child's primary renal physician if the child is an outpatient.

- All children on high dose steroids are to have a daily urinalysis. If glucose is present then a blood glucose level is required at least daily.

6.2 Treatment of steroid resistant acute rejection

- ATG may be used in steroid resistant rejection (see [Appendix 3](#)).

6.3 Treatment of Antibody Mediated Rejection⁵

Donor specific antibody (DSA) testing is done by the Australian Red Cross. Patients should be routinely checked for *de novo* DSAs at 3 and 12 months post-transplant and annually thereafter. If *de novo* DSAs are identified, consider checking for binding of C1q as antibodies binding C1q are associated with a worse prognosis. Most patients with DSAs will be biopsied to look for evidence of antibody mediated rejection (AbMR). If the biopsy is benign then DSAs should be repeated 3 monthly. If there is histological evidence of AbMR the DSA levels should be checked monthly. DSA testing is arranged through the senior nurses in the Renal Treatment Centre. The patient will need to pick the blood bottles in the RTC and take them to pathology. They then return the filled bottles to the RTC. The blood tube and accompanying Red Cross request form should be double checked prior to hand delivery of the sample to the hospital blood bank staff, who will arrange for transport to the Red Cross.

There is currently no universally accepted protocol for the treatment of (AbMR) and there is a scarcity of randomised controlled trials. Interventions including plasma exchange, IVIG, rituximab, eculizumab and bortezomib have been used with variable success. In patients with donor specific antibodies and AbMR the management will be decided by the primary physician for the patient, but a suggested protocol is:

- 1.5 volume plasmapheresis on alternate days for 2 weeks

followed by

- 1g/kg of IVIG daily for 2 days.
- Patients are then maintained on 3 monthly infusions of 2g/kg IVIG (usually given over 2 days).

7 Discharge Guidelines

7.1 Ureteric stents

- All children will have double-J ureteric stents placed at the transplant procedure. At discharge patients will have appointments to return to Middleton ward 2 weeks after their transplant for stent removal, unless the stent has been removed prior to then.
- Haemodialysis or peritoneal dialysis catheters will also be removed at this time if no longer required and not already removed at the time of transplant.
Occasionally gastrostomy tubes can also be removed at this time but often they are needed for a little longer duration.

7.2 Follow up

- Patients are reviewed daily for the first month, then 3 times a week for 2 weeks, twice a week for 2 weeks, then weekly to 4-6 months, fortnightly until about 9 months and then monthly. Long-term stable patients should be seen at least every 3 months.
- A letter on discharge should go to the child's paediatrician and GP.

7.3 Immunosuppression Targets

The tacrolimus target level will be determined by the primary consultant for the patient but in general terms, tacrolimus levels are targeted between 8-10ng/mL for the first month, reducing to 6-10ng/mL for the next 3 months and then 5-8ng/mL. After a year most children will have a target of 5-6ng/mL.

7.4 Viral Surveillance

CMV

- Patients who are CMV IgG positive or those who are CMV IgG negative receiving a CMV positive kidney will remain on valganciclovir for 6 months.
- Patients should have CMV polymerase chain reaction (PCR) (0.3 mL EDTA blood) immediately before stopping valganciclovir and then at 1 month, 3 months, 6 months and then annually after ceasing prophylaxis. If positive a CMV quantitative PCR will be done and the log values monitored, with a 0.5 log change being significant.
- New CMV positivity on PCR should be discussed with the primary consultant.
- Patients who are CMV IgG negative should have annual serology checked until they become positive. Once a patient is IgG positive there is no need to repeat serology.

EBV

- Patients should have EBV PCR (0.3 mL EDTA blood) done monthly for 3 months post-transplant and then 3 monthly until 1 year post-transplant. It should be checked 6 monthly thereafter. Quantitative PCR will be performed if the qualitative EBV PCR is positive. Log values should be monitored, with a 0.5 log change being significant.

- Patients who develop de novo EBV in the first 6 months post-transplant should have repeat PCR done every 2-4 weeks until the levels stabilise or decrease.
- Patients who are EBV IgG negative should continue to have annual serology until they become positive.
- There is no proven treatment for EBV infection and the immunosuppression should be reviewed with the primary consultant, with a view to reducing overall immunosuppression to minimise the risk of post-transplant lymphoproliferative disease (PTLD).

BK Virus

- BK PCR (0.3 mL EDTA blood) should be checked every 3 months as part of the routine follow up until 24 months. After 2 years BK PCR should only be checked if clinically indicated.
- If there is a rise in creatinine BK virus should be considered.
- If the qualitative testing is positive, quantitative PCR will be sent to RPA.
- If a positive result is obtained the immunosuppression should be reviewed and repeat levels checked at 2-4 weekly intervals.
- A renal biopsy will be necessary to rule out BK nephropathy.
- Immunosuppression reduction will be sufficient to treat most cases though other treatments are available⁸.
- Urine BK PCR is non-specific and not helpful.

Hepatitis B and C

- Serology should be checked annually.

Other viruses such as varicella, herpes etc should be tested as clinically indicated.

8 Special Circumstances

Cyclosporin as an alternative to Tacrolimus can be considered if post-transplant diabetes is considered a risk. Also it may be an alternative immunosuppressive agent to tacrolimus in patients with FSGS, who are at a high risk of disease recurrence in their transplant.

- Cyclosporin 5mg/kg (max dose 250mg) orally at 0800 on the day of living donor transplant or on admission for deceased donor transplant. Then give cyclosporin 5mg/kg (max dose 250mg) twice daily starting on the evening of transplant.
- Blood levels should be taken two hours after the morning dose. Therefore the child should have the dose at 0700 and have bloods taken at 0900.
- The 2 hour peak cyclosporine level (C2) should be maintained between 800-1200ng/mL in children at risk of FSGS recurrence.
- Trough cyclosporine levels correlate less accurately than C2 with area under the curve and should be avoided if possible.

- When cyclosporin is used as an alternative to tacrolimus, mycophenolate mofetil (Cellcept) is given at a dose of 20mg/kg/dose twice daily because of an interaction between cyclosporin and mycophenolate.

Azathioprine is sometimes used as an alternative to mycophenolate mofetil.

- Children should have TPMT (thiopurine methyltransferase) levels checked prior to starting azathioprine.
- The dose is 2mg/kg daily

Once a day immunosuppression: Particularly for teenagers or non-compliant patients a once daily immunosuppressive regime may be preferable. This will consist of prednisone, azathioprine and long-acting tacrolimus (1:1 daily dose conversion from twice a day tacrolimus). Trough tacrolimus levels are monitored as previously described.

Plasma-Exchange: This is considered in patients with FSGS and atypical HUS where there is a high risk of disease recurrence. It may also be required when there are known donor specific antibodies.

ATG in place of Tacrolimus: This can be used as an alternative to Tacrolimus if there is primary graft dysfunction. Its use should be limited to 14 days (See Appendix 2).

Immunisation Post Renal Transplant:

- Children on immunosuppression cannot receive live vaccines (MMR and varicella). They can have killed attenuated or DNA vaccines but it is recommended that they wait at least 6 months after the transplant.
- Seronegative transplanted children who are in close contact with a child with varicella (>20 mins in a confined space such as a classroom or a household contact), should receive varicella zoster immunoglobulin (VZIG) as soon as possible, if within 10 days of exposure. If there are difficulties getting VZIG consider the use of chemoprophylaxis with acyclovir/valacyclovir⁷.
- The annual influenza vaccination is recommended for transplant recipients who received their graft at least 6 months prior.
- Children requiring a hepatitis B booster should receive a double dose and then have titres repeated after 4 weeks. If the titres are still low (<10 mIU per mL) follow the recommendations given in the Australian Immunisations Handbook for high risk patients. <https://immunisationhandbook.health.gov.au/recommendations/people-at-risk-of-hepatitis-b-are-recommended-to-have-serological-testing-4-8-weeks>
- Vaccinations can be given at the walk-in vaccination centre on level 1 of CHW.

Growth Hormone Post Renal Transplant:

- Some children will be on GH prior to transplant but this is stopped at the time of transplant. Children grow poorly for the first 6-12 months after a transplant because of the steroids but then most will show catch up growth. Some children will require re-evaluation for GH after transplantation but this is only done after 12 months.

9 References

1. Webster AC, Woodroffe RC, Taylor RS, Chapman JR, Craig JC. Tacrolimus versus ciclosporin as primary immunosuppression for kidney transplant recipients: meta-analysis and meta-regression of randomised trial data. *BMJ*. 2005 Oct 8;331(7520):810.
2. Filler G, Webb NJ, Milford DV, Watson AR, Gellermann J, Tyden G, Grenda R, Vondrak K, Hughes D, Offner G, Griebel M, Brekke IB, McGraw M, Balzar E, Friman S, Trompeter R. Four-year data after pediatric renal transplantation: a randomized trial of tacrolimus vs. cyclosporin microemulsion. *Pediatr Transplant*. 2005 Aug; 9(4):498-503.
3. Angela C Webster, Lorenn P Ruster, Richard McGee, Sandra L Matheson, Gail Y Higgins, Narelle S Willis, Jeremy R Chapman and Jonathan C Craig Interleukin 2 receptor antagonists for renal transplant recipients. *Cochrane Library* 2010.
4. Elisabeth M Hodson, Maleeka Ladhani, Angela C Webster, Giovanni FM Strippoli and Jonathan C Craig. Antiviral medications to prevent cytomegalovirus disease in solid organ transplant recipients. *Cochrane Library* 2013.
5. Djamali A, Kaufman DB, Ellis TM et al. Diagnosis and Management of Antibody-Mediated Rejection: Current Status and Novel Approaches. *American Journal of Transplantation* 2014; 14; 255-271
6. Kasiske BL, Zeier MG, Chapman JR et al. KDIGO clinical practice guideline for the care of kidney transplant recipients: a summary. *Kidney International* 2010;77 299-311.
7. S. A. Pergama, b, c, *, A. P. Limayea and the AST Infectious Diseases Community of Practice. Varicella Zoster Virus in Solid Organ Transplantation. *American Journal of Transplantation* 2013; 13, 138-146
8. Deirdre Sawinski and Simin Goral. BK virus infection: an update on diagnosis and treatment. *Nephrology, Dialysis and Transplantation* 2015; 30; 209-17.

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Appendix 1: Investigations for a potential living donor

Prior to sending a potential living donor to Westmead Hospital the following investigations should be done:

Fasting bloods for

FBC, EUC, CMP, LFT, GLU, TFT, Cholesterol and triglycerides

HBA1C, Quantiferon gold

EBV IgG, CMV IgG, Hepatitis B sAg, Hepatitis B cAb, Hepatitis C serology and HIV serology

Midstream Urine for:

Urinalysis

MC&S

Protein to creatinine ratio

Albumin to creatinine ratio

Please ask for a copy of the results to be sent to the nephrologist at Westmead Hospital and a copy to be sent to the Transplant Co-ordinator at Westmead Hospital.

Appendix 2: Basiliximab administration to renal transplant recipients

Basiliximab (Simulect) is a monoclonal antibody used in the prophylaxis of acute organ rejection following renal transplantation. Basiliximab is a murine/human chimeric monoclonal antibody that is directed against the interleukin-2 receptor alpha chain (CD25) in response to antigenic challenge. It specifically binds to the CD25 antigen on activated T-lymphocytes expressing the high affinity interleukin-2 receptor and thereby prevents binding of interleukin-2, the signal for T-cell proliferation.

It is available in packs of one glass vial containing 20mg freeze-dried powder and a vial of 5mL water for injection.

Dosage

NB: The day of transplant is considered to be Day 0.

- The recommended regimen is two doses of 12mg/m² to a maximum of 20mg per dose.
- The first dose is given two hours prior to transplantation (Day 0).
- The second dose is given on Day 4 after transplantation.
- It is administered as an intravenous infusion over 20 minutes diluted in 50mL of 0.9% sodium chloride.

Precautions

Ensure that resuscitation equipment is available when basiliximab is administered.

Medications for hypersensitivity reactions should be available (e.g. adrenaline).

Hypersensitivity reactions including anaphylaxis have been observed in clinical studies within 24 hours of the administration of basiliximab but these are rare (<1/1000 patients).

The second dose of basiliximab should be withheld if there is a hypersensitivity reaction with the first dose.

Adverse reactions

- Body pain
- Fever
- Headache
- Insomnia
- Constipation
- Vomiting
- No metabolic interaction is expected as basiliximab is an immunoglobulin. It does not cause cytokine release syndrome hence steroid prophylaxis is unnecessary.

Preparation of Basiliximab

Equipment required:

- 10mL vial containing 20mg freeze-dried basiliximab powder
- 5mL water for injection
- 19g needle
- 5mL syringe

To prepare injection solution, add 5mL water for injection to the vial containing the powder. Shake the vial gently and avoid foaming to dissolve the powder. Reconstituted solution should be used immediately but if needed can be stored at 2-8°C for 24 hours. Discard unused residue within 24 hours after reconstitution. Basiliximab should always be given through a separate infusion line as no data are available on the compatibility with other intravenous substances.

Appendix 3: ATG Administration

Introduction

Antithymocyte Globulin (ATG) is a polyclonal antibody product obtained from the serum of rabbits that have been immunised with human T-lymphoblasts. It is used for the treatment for renal transplant rejection where high dose prednisolone therapy has been ineffective. It is also used for prophylactic immunosuppressive therapy, in particular where recipients have a high panel reactive antibody level pre-transplant, are receiving second or subsequent transplant or who have persistent poor function post-transplant. In children the best long term results for graft survival have been obtained where ATG is used as part of a sequential quadruple immunosuppression protocol.

Currently there are two types of rabbit ATG available- ATG Fresenius, a German product available via SAS from Dutec Laboratories and Thymoglobuline, a French product registered in Australia. The potencies and doses of each product are different and the Transplant physician is responsible for the decision as to which ATG product is used. A small quantity of each rabbit ATG product is kept in Pharmacy but please inform the Pharmacy if ATG treatment is being considered to ensure adequate supply is available. Caution: There is an equine (horse) ATG product Atgam registered in Australia which is not usually used in solid organ transplantation.

Please Note: Information provided in the remainder of this appendix refers to the ATG-Fresenius product available from Pharmacy after a TGA SAS Cat A approval form has been provided.

Dosage

The dose used is 3.0 mg/kg/day for prophylaxis and 3.5 - 5 mg/kg/day for treatment of rejection. The dose for an individual patient will be determined by the nephrologist on call. The usual duration of therapy for prophylaxis will be 7 days but it may need to be given for up to 14 days where there is prolonged acute tubular necrosis and/or where the patient has evidence of sensitisation following failure of a previous transplant. It is given intravenously.

Precautions

- **Skin Prick Test**
 - Since ATG is a heterologous protein a skin test is used to identify possible hypersensitivity. An intradermal injection of 0.1mL of undiluted normal rabbit immunoglobulin is given into the medial side of the forearm. A reaction at the injection site within 15 minutes indicates that the person is intolerant to rabbit protein.
- **When ATG used at induction of immunosuppression:**
 - commence immediately post-transplant;
 - in combination with methylprednisolone and azathioprine;
 - Add Cyclosporin or tacrolimus approximately two days before the course of ATG is completed

When ATG is used to treat rejection, the doses of other immunosuppressive agents, particularly cyclosporin, need to be adjusted with the commencement and towards the completion of ATG therapy. Please check with the Nephrologist on call.

- **Premedication before the first dose**
 - Hydrocortisone 2 mg/kg IV (maximum dose 100 mg)
 - Paracetamol 20 mg/kg oral (maximum dose 1000 mg)
 - Promethazine 0.5 mg/kg/dose IV (maximum dose 25 mg)

Administration

Ensure that resuscitation equipment is available

- A physician must administer the first and second doses and be immediately available throughout the first and second infusions.
 - ATG-Fresenius is prepared in Pharmacy and is supplied in 0.9% sodium chloride .
 - Advance notice is required for preparation in the aseptic suite.
 - ATG is incompatible with glucose containing solutions.
 - It is administered over at least 4 hours in the ward.
 - When used for rejection the patient must remain in hospital overnight following the first dose.
 - If the first dose is well tolerated, subsequent doses may be given in the Mary Honan Renal Treatment Centre during day stay visits.

Blood samples

- **Before the first dose**
 - Titres for CMV, EBV, Herpes simplex and Toxoplasmosis unless obtained within the previous month.
- **Daily**
 - EUC, LFTs, FBC with differential white count
- **Twice weekly**
 - T cell subsets

Prophylaxis against CMV disease

All children receiving ATG will receive ganciclovir IV or valganciclovir orally during ATG administration whether ATG is used for induction or for treatment of rejection. If the child is CMV negative and has received a kidney transplant from a CMV negative donor, CMV prophylaxis is continued for the duration of ATG therapy only. All other children receive CMV prophylaxis for 3 months post-transplant.

Dosage reduction of IV ganciclovir and valganciclovir are required in renal failure as shown below:

- **IV Ganciclovir**
 - Calculated Creatinine Clearance >70 mL/min/1.73m² 5mg/kg/day
 - Calculated Creatinine Clearance 50-69 mL/min/1.73m² 2.5mg/kg/day
 - Calculated Creatinine Clearance 25-49 mL/min/1.73m² 1.25mg/kg/day
 - Calculated Creatinine Clearance 10-24 mL/min/1.73m² 0.625mg/kg/day
 - Calculated Creatinine Clearance <10 mL/min/1.73m² 0.625mg/kg three times/week.

- Valganciclovir
 - The oral dose of valganciclovir is calculated using the formula below:
7 X body surface area X creatinine clearance in mg/day (Maximum 900 mg daily).
Valganciclovir is given as a single morning dose. The predominant adverse reactions are leucopenia, anaemia, thrombocytopenia, diarrhoea, nausea and vomiting.

The creatinine clearance can be calculated from the formula below:

$$\frac{40 \times \text{height in cm}}{\text{Serum creatinine in micromoles/L}}$$

Side effects of ATG

Hypotension, chest tightness, urticaria and fever may occur and anaphylaxis is possible so adrenaline, antihistamines and corticosteroids must be available. These symptoms are usually only seen with the first doses of ATG.

Nursing protocol

1. Ensure that the skin test has been performed.
2. Ensure that resuscitation equipment and medications are available
3. Subsequent doses following the 1st and 2nd doses may be given by nursing staff.
4. During the first dose record pulse, temperature and blood pressure every 1/2 hour.
5. Then record these every hour for a further 4 hours.
6. For 2nd and subsequent doses record pulse, temperature and blood pressure every hour for 4 hours.
7. Paracetamol 20 mg/kg/dose (maximum dose 1000 mg) may be given every 4 hours for symptomatic treatment of fever for up to 4 doses.