Standard Operating Procedure on the Management of Paediatric Renal Transplantation

Renal Unit
Royal Hospital for Sick Children
Yorkhill Division
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1. SOP Development

1.1 SOP Group
The following SOP has been developed by the Paediatric Renal Transplant Group led by Dr Heather Maxwell, Consultant Paediatric Nephrologist, Mr Vlad Shumeyko, Consultant Transplant Surgeon, Mr Martyn Flett, Consultant Paediatric Urologist, Mrs Angela Lamb, Senior Paediatric Renal Pharmacist, Sr Karen Symington Ward Manager, Sr Kathleen Thomson in Theatres, Dr Alison Balfour Consultant Microbiologist, Dr Ann-Margaret Little Consultant Clinical Scientist Histopathology and Immunology, and Dr Chris Kidson, Consultant in Paediatric Intensive Care. Please contact Dr H Maxwell if there are issues with this SOP.

1.2 SOP Development
The SOP has been developed after assessing current practice in the light of published evidence and guidelines. Much of the guidance is based on shared expert opinion and experience. This SOP should be used in conjunction with the following GGC NOPS

NOP001 Donor and Organ Characterisation, Assessment and Allocation in Deceased and Living Donation and Transplantation

NOP002 Verification of Donor Identity, Consent/Authorisation and Organ and Donor Characterisation in Deceased and Living Donation and Transplantation

NOP003 Packaging, Labelling and Transport of Organs in Deceased and Living Donation Transplantation

NOP004 Management of Procurement Material and Equipment in Deceased and Living Donation and Transplantation

NOP005 Activities to Be Performed Under the Guidance of A Registered Medical Practitioner in Deceased and Living Donation and Transplantation

NOP006 Transfer And Storage Of Donor and Organ Characterisation Information and Storage of Traceability Data

SOP3888/1 Reporting an Organ Donation or Transplantation Incident to NHSBT

1.3 Objectives
This SOP is for use by the medical and nursing staff caring for paediatric renal transplant recipients, many of whom will not have looked after transplant patients before. The SOP helps outline the management of these patients and advises of situations when it is necessary to seek assistance. The appropriate management of transplant patients in the first hours and days after the operation is crucial to a positive outcome, hence the detailed sections on early post operative care. If in doubt seek advice from either the consultant paediatric nephrologist on call or from the surgeons involved in the procedure.
2. Introduction

Children will either receive a transplant from a relative (Living Donor - LD) or from a deceased donor (DD). An LD transplant will have been planned in advance; a DD transplant will take place when a suitable organ becomes available and often takes place out of hours. The duties of relevant personnel are outlined in NOP005.

2.1 Deceased Donor Kidney

The consultant paediatric nephrologist on call accepts a suitable kidney after phone calls from NHSB&T. The initial calls take place before the kidney has been harvested.

- The consultant paediatric nephrologist will phone Ward 6A to let them know a kidney has been accepted and will advise on the expected arrival time of the kidney and when the child should start fasting.
- The nephrologist will then contact the on call paediatric urologist (rota available).
- The urologist will then contact the on call transplant surgeon from the Western Infirmary Glasgow (rota available).
- The urologist will contact the duty anaesthetist to alert them to the fact that there is a deceased donor transplant planned and give the estimated time of operation. This information may be needed at the daily ‘bed huddle’.
- Ward 6A nursing staff will let the family know that a kidney may be available for their child.
- During this phone call, the ward 6A nursing staff will check if the patient has had any infections over the last 2 months and if they have had any recent blood transfusions.
- After the phone call, the ward 6A nursing staff will let the nephrologist know how the patient has been over the last two months.
- If the patient is on the virtual cross-match (vXM) list (no preformed antibodies and regular screening for 1 year or more), the nephrologist will then contact the Consultant Clinical Scientist on call (rota and numbers available on vXM Sheet) for confirmation that a vXM is acceptable. The laboratory crossmatch will be performed during working hours the next day. Contact should be made with the Histocompatibility and Immunogenetics (H&I) Laboratory during working hours to arrange transport of specimens (0141 301 7749).
- If the patient is not on the vXM list and therefore requires a prospective crossmatch, Ward 6A staff will contact the H&I laboratory during working hours, or if it is out of hours the tissue-typist on call via switchboard (0141-211-3000). This needs to be in sufficient time for a cross-match to take place as soon as the kidney arrives in the ward.
- Ward 6A nursing staff will inform PICU that a transplant is planned.
- Once the arrival time of the kidney is confirmed by NHSB&T, the nephrologist will inform Ward 6A. If necessary, the nephrologist will speak to the most senior of the medical receiving team on call.
- During working hours, the ward clerkess will obtain the casenotes; out of working hours, the ward 6A nursing staff will obtain the casenotes.

The patient should be fasted for 6 hours before the operation.
- The family should make their way straight to Ward 6A.
• If the patient is on peritoneal dialysis they should be left with no last fill. The parents should bring a sample of PD fluid with them. If during the night, the treatment should be interrupted and a manual drain performed.

• If the patient is on haemodialysis they may require an extra haemodialysis session before the transplant goes ahead.

The case notes for all children on call are held within the renal unit. A copy of this SOP should be printed out for use by the attending medical staff. Further information relating to the child (The Transplant Plan) is held in Clinical Portal. Print out this information. For most patients information can also be obtained from the renal unit database (SERPR). Admit as below.

2.2 Living Related Transplants
Living related transplants are planned in advance and the final cross-match will have already been carried out. Admit the child as below. Information will be available in the transplant plan and may include starting the immunosuppression a day or two before the transplant.
3. Admission

3.1 Admit the child directly to ward 6A
The patient should be clerked in by the most senior of the junior medical staff on call. Much of the past medical history will be documented in the transplant plan. Note any past medical history of hypertension, asthma or seizures. Attention should be paid to recent infections including peritonitis in PD patients and HD line infections, and any contact with infectious diseases. If the child is unwell or there are concerns, please discuss with the consultant paediatric nephrologist on call immediately.

3.2 Investigations

<table>
<thead>
<tr>
<th>Type</th>
<th>Investigation</th>
<th>Instructions</th>
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<tbody>
<tr>
<td>Haematology</td>
<td>FBC and coagulation</td>
<td></td>
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<tr>
<td>Blood Bank</td>
<td>Cross-match leuco-depleted packed red cells</td>
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</tr>
<tr>
<td></td>
<td>• &lt;20 kg: 2 units</td>
<td></td>
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<tr>
<td></td>
<td>• 20-40 kg: 3 units</td>
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</tr>
<tr>
<td></td>
<td>• &gt;40Kg: 4 units</td>
<td></td>
</tr>
<tr>
<td>Biochemistry</td>
<td>U+E, LFTs, Bone, Mg, Glucose, CRP</td>
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<tr>
<td>Virology</td>
<td>Serology (10mls clotted blood): CMV, EBV, VZV, Hep B, Hep C, And HTLV1</td>
<td>Send to South Sector Microbiology</td>
</tr>
<tr>
<td></td>
<td>PCR (3-5mls EDTA) EBV, CMV, adenovirus, BK</td>
<td>send to South Sector Microbiology</td>
</tr>
<tr>
<td>Bacteriology</td>
<td>PD fluid</td>
<td>In sterile universal</td>
</tr>
<tr>
<td></td>
<td>Urine</td>
<td>In boric acid container for culture</td>
</tr>
<tr>
<td>Tissue Typing</td>
<td>5-10ml clotted blood</td>
<td>Send to the H&amp;I Laboratory at Gartnavel General Hospital.</td>
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</table>

• Other investigations as clinically indicated e.g. CXR, ECG

3.3 Arrival of Deceased Donor Kidney
The donor kidney should be kept in ward 6A. Nursing staff should inform both the transplant surgeon and the paediatric surgeon when it has arrived (rotas available). If a prospective cross-match is required, the donor lymph node or spleen should be sent to H&I Laboratory at Gartnavel* along with a clotted sample of the patient’s blood. This should be sent by taxi not courier. Ensure the H&I lab / on-call tissue-typist is aware of the estimated time of arrival of specimens. Check where sample is to be sent. If a VXN is taking place, and samples arrive after 3pm (Mon-Fri), then they should be kept in the ward fridge ready for collection the next working day.

* Histocompatibility & Immunogenetics Service, Level 1, Laboratory Medicine Building, Gartnavel General Hospital, 21 Shelley Rd, Glasgow, G12 0ZD
The donor kidney will be taken out of ice, assessed by the operating surgeons to make sure that the kidney is suitable for grafting. This will take place before any immunosuppression has been given and before the patient is taken to theatre.

3.4 Medical Management

- Document anonymised deceased donor details in casenotes (Age, gender, blood group, tissue type, date and cause of death, weight, virology and creatinine)

- Fast for 6 hours pre-operatively (a cross match takes approximately 6 hours)

- Document the following: Weight, height, surface area and native urine output (mls/day) in the casenotes (Information available on Transplant Plan in Clinical Portal)

- Prescribe IV fluids once the child is fasting to cover measured urinary losses and insensible losses of 400ml/m². Use 0.45% saline/5% dextrose unless otherwise indicated. **Children should be well hydrated at the time of operation.** (Many CKD patients are polyuric and the use of large volumes of 0.9% saline has been associated with hypernatraemia).

- **Document BP.** Withhold long-acting anti-hypertensives. If BP elevated, discuss with consultant nephrologist.

- **Radiology.** Order an ultrasound of the transplant kidney (to be performed during or just after surgery) and make radiology aware that a transplant is about to take place.

- Calculate medication doses that will be necessary pre and post op. Discuss with renal pharmacist.

  i. **Prescribe immunosuppression.** The intended immunosuppressive regimen will be documented in the transplant plan. Doses are given below and details of all medicines used post transplant are available at the end of this protocol. Basiliximab is generally the only immunosuppressant given pre-operatively; methylprednisolone is given during surgery and the rest start after theatre. For LD transplants some immunosuppressants may be started pre-op. This will be documented in the transplant plan.

  ii. **Prescribe antibiotic cover.** Give Cefotaxime 50mg/kg at induction, to a maximum dose of 1.5g bd. This is for surgical prophylaxis and should be for a minimum of 24 hours or longer if indicated. This can be changed to a prophylactic oral dose to prevent UTIs whilst catheters remain in situ. If Co-trimoxazole has been started as PCP prophylaxis this will double as urinary prophylaxis.
iii. **Prescribe gastroprotection** as below to start pre-op.

iv. **Check CMV status** of recipient and donor. If the recipient is negative and donor is positive the patient will require valganciclovir. This is started post op once the patient is taking oral medication.

v. **Aspirin is started on the day of transplant and is given prior to going to theatre.** Any child deemed at increased risk of thrombosis will have a plan for low molecular weight heparin (LMWH) thromboprophylaxis outlined in their transplant plan.

At the discretion of the operating surgeon, thromboprophylaxis may be administered intra-operatively or LMWH may be recommended post operatively (See appendix V).

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dosage</th>
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</table>
| **Prednisolone**       | **Day 0:** Methyl prednisolone 600mg/m² max 1 gm given in theatre prior to the release of the vascular clamps  
**Day 1:** 60 mg/m²/day po (0800) maximum dose 80mg  
**Day 2:** 40 mg/m²/day po  
**Day 3:** 30 mg/m²/day po  
**Day 4:** 20 mg/m²/day po then stop. |
| **Tacrolimus**         | 0.15 mg/kg po bd (1000 & 2200) maximum dose of 5mg bd  
Specify Prograf® or Modigraf®, powder  
**Plasma level needed pre-dose at 09:00** |
| **Mycophenolate Mofetil** | 600 mg/m² po bd (0800 and 2000) max dose 1 gm bd |
| **Basiliximab**        | < 35 kg 10mg each dose  
≥ 35 kg 20 mg each dose  
Give first dose on day 0 when it is known that the transplant is going ahead. Basiliximab to be made up in the ward and administered prior to transfer to theatre.  
A second dose is given on Day 4 |
| **Cefotaxime**         | 50 mg/kg iv bd (1000 and 2200) to maximum of 1.5gm bd - adjust dose for GFR |
| **Omeprazole**         | **iv:** 1-12 years: start at 500mcg/kg (max 20mg) once daily increasing to 2 mg/kg/day (max 40mg) if necessary |
>12 yrs: max 40mg daily po:
10-20 kg 10mg once daily
>20kg 20mg once daily

### Valganciclovir
520 mg/m² po daily when tolerating oral fluids, if required – adjust dose for GFR (max. dose = 900mg daily)

### Aspirin
<25kg 37.5 mg po in the morning
>25kg 75 mg po in the morning
Continue for 3 months

- **Review blood results**
- **Haemodialysis:** children on haemodialysis will require dialysis pre-transplant unless they have had a satisfactory dialysis session within the previous 24 hours. Minimal anticoagulation should be used, and the line should be capped with hepsal only (please document). Fluid removal should be minimal unless fluid overloaded. Discuss with consultant on call.

- **Peritoneal Dialysis:** children should receive their usual overnight dialysis. Depending on the time of transplantation and biochemistry results, further cycles may be required. When going to theatre, the abdomen should be empty (no last fill), and the catheter capped prior to transfer to theatre. Fluid removal should be minimal unless fluid overloaded. Aim to leave child at or above their dry weight i.e. limit the UF or allow time to catch up with IV fluids if fluid removal greater than expected. Discuss with consultant on call.

#### 3.5 Surgical Considerations
- Consent will be obtained by the operating surgeons. Frequently consent will be taken by both Transplant and Paediatric Surgeons.
- Consideration should be given to the need for dialysis access (HD or PD) post operatively. Pre-emptive patients may need access inserted; for those with access in situ a decision needs to be made whether to keep the access or remove it (e.g. infected exit site or catheter). If dialysis is likely to be needed post op, replacement access may be necessary.

#### 3.6 Deceased Donor Cross-Match results
The patient can go to theatre if the cross-match result is negative. As soon as this result is known, the Basiliximab can be given, and once the infusion is complete, the patient should go promptly to theatre.

#### 3.7 Living Donor Transplantation
The donor nephrectomy takes place in the Western Infirmary theatres. As soon as the retrieving surgeon is happy that the kidney is suitable for use, they will phone ward 6A to say the transplant is going ahead. Nursing staff on Ward 6A will then phone theatre to inform them that the operation is proceeding. The Basiliximab will be given promptly to the patient who will then go to theatre as soon as the infusion is complete.
4. Receipt of Donor Organ at Recipient Centre

The arrival of the donor organ needs to be recorded in the Transplant Log which is held in the ward and in theatre. See also NOP002 and NOP003

5. Intra-operative management

See also NOP004. The operating surgeon is responsible for the correct identification of the donor organ used.

Children need to be kept 'well-filled' throughout the procedure and recovery period. Children should be well hydrated prior to going to theatre, and long-acting anti-hypertensives will have been withheld. Many children are polyuric and their native 24 hour urinary output will be clearly documented. On the day of transplant, these 24 hour urinary losses will be given as intravenous therapy with a crystalloid solution, the concentration of which will depend upon the urine sodium concentration. This is their 'maintenance' fluid, individualised to their needs, which will be running when the child reaches theatre and should be continued. This is usually given as 0.45% saline and 5% dextrose but will depend on the individual child. Serum sodium levels should be checked frequently.

The transplanted kidney needs to be well perfused. This is achieved by maintaining an adequate intra-vascular volume; as a guide, a central venous pressure in the range of 10-12 cm water and the absence of a core-peripheral temperature gradient. This is particularly important for small children receiving adult sized kidneys. When the clamps are released and the kidney is re-perfused, the child’s circulating volume will need to increase to be able to perfuse a large kidney at an appropriate pressure. A bolus of fluid (usually 5% albumin) should be given prior to the release of the clamps.

I. A double or triple lumen central venous catheter should be inserted for CVP monitoring, access and sampling, unless a haemodialysis catheter is already in situ. Consider a tunnelled line in children with sampling difficulties or other concerns. CVP should be maintained in the region of 10-12 cms H₂O.

II. Insert NG tube

III. IV fluids should be run to replace native urine output (as above)

IV. Pain relief will have been discussed with the child and family beforehand. Whilst thromboprophylaxis is no longer routine, epidurals should be avoided in those patients who will receive post operative low molecular weight heparin.

V. Replace intraoperative fluid losses with 5% albumin and packed red cells if warranted.
VI. Blood pressure should be maintained at levels appropriate for donor age. Information regarding donor age will be available in patient’s casenotes. (See also appendix I)

VII. Maintain a core-peripheral temperature gradient of no greater than 2°C

VIII. Infuse Dopamine 5microgram/kg/min or at a greater rate if BP is low.

IX. Give a bolus of 5% albumin prior to the release of the clamps. At least 10ml/kg 5% albumin should be given, but more may be required for large donor kidneys.

X. Consider mannitol 0.5g/kg infused over 5-10 minutes prior to removal of the clamps. Furosemide is an alternative. These are to be used at the surgeons’ discretion and should be discussed at the time of commencing surgery to confirm the appropriate dose and timing required.

XI. Give Methylprednisolone 600mg/m² (max 1gm) IV prior to the release of the vascular clamps.

XII. Continue IV fluids replacing both native and transplant urinary losses hourly until reaching ITU.

XIII. If TAP block to be placed, this can be done prior to skin closure.

XIV. Doppler USS of graft in theatre prior to transfer to PICU. USS may be performed by surgeon or may need to be arranged with radiology during the operation.

XV. Ensure dialysis access available if operative course suggests that dialysis is likely to be required. (see also section on Admission point 5). Consider removal of potentially infected dialysis access.

After the procedure I.V. fluids should continue and be run at a rate to replace both native and transplant urinary losses. This should continue until children reach ITU. Please document clearly all fluids received during the operation.

Human Tissue Authority Form B needs to be completed and faxed to NSHBT.
6. ITU management after return from theatre (Day 0)

The transplanted kidney needs to be well-perfused. Fluid management in the first 12 hours post-operatively is critical and needs careful attention. **Please discuss any concerns with the nephrologist on call.**

6.1 MEDICATION

I. The immunosuppression regimen will be documented in the drug chart from Ward 6A. Below is a summary of the usual medication used.

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Prednisolone</strong></td>
<td><strong>Day 0:</strong> No further steroid needed&lt;br&gt;&lt;br&gt;<strong>Day 1:</strong> 60 mg/m²/day po (0800) maximum dose 80mg&lt;br&gt;&lt;br&gt;<strong>Day 2:</strong> 40 mg/m²/day po&lt;br&gt;&lt;br&gt;<strong>Day 3:</strong> 30 mg/m²/day po&lt;br&gt;&lt;br&gt;<strong>Day 4:</strong> 20 mg/m²/day po then stop.</td>
</tr>
<tr>
<td><strong>Tacrolimus</strong></td>
<td>0.15 mg/kg po bd (0800 and 2000) max dose 5 mg bd&lt;br&gt;Specify Prograf® or Modigraf® (Powder)&lt;br&gt;<strong>Plasma level needed pre-dose at 09:00</strong></td>
</tr>
<tr>
<td><strong>Mycophenolate Mofetil</strong></td>
<td>600 mg/m² po bd (0800 and 2000) max dose 1 gm bd</td>
</tr>
<tr>
<td><strong>Cefotaxime</strong></td>
<td>50 mg/kg iv bd (1000 and 2200) to maximum of 1.5gm bd – adjust dose for GFR</td>
</tr>
<tr>
<td><strong>Omeprazole</strong></td>
<td>Prescribe omeprazole until eating well or feeds are re-started&lt;br&gt;iv:&lt;br&gt;1-12 years: start at 500mg/kg (max 20mg) once daily&lt;br&gt;increasing to 2 mg/kg/day (max 40mg) if necessary&lt;br&gt;&gt;12 yrs: max 40mg daily&lt;br&gt;po:&lt;br&gt;10-20 kg 10mg once daily&lt;br&gt;&gt;20kg 20mg once daily</td>
</tr>
<tr>
<td><strong>Aspirin</strong></td>
<td>&lt;25kg 37.5 mg po in the morning&lt;br&gt;≥25kg 75 mg po in the morning&lt;br&gt;Continue for 3 months</td>
</tr>
<tr>
<td><strong>Valganciclovir.</strong></td>
<td>Depends on CMV status. If the recipient is CMV negative and the donor CMV positive, then oral valganciclovir is given for the first 6 months. This should be started when the patient is tolerating oral fluids (usually day 1 or 2 post transplant)&lt;br&gt;520 mg/m² po daily when tolerating oral fluids, if required – adjust dose for GFR (max dose = 900mg daily)</td>
</tr>
</tbody>
</table>
II. Monitor CVP, urine output, BP and core-peripheral temperature gap

Aim to keep CVP at 8-10 cm H2O
Aim to keep systolic BP > 50th centile for donor age. For donors aged 17 and over this is 120/70. For younger donors age-specific centile charts are available (see appendix I).
Aim to keep core-peripheral temperature gradient ≤ 2°C
Measure the urine output hourly

III. Fluid and Electrolytes

i. Replace urine output ml for ml on an hourly basis with 0.9% saline and 5% dextrose initially. (This is the combined transplant and native urine output from the bladder). If serum sodium rises change to 0.45% saline and 5% dextrose

ii. Send a urinary sodium level and dip urine for glucose

iii. If combined urine output is greater than 150 ml/hr consider changing to 0.45% / 5% dextrose but be guided by urinary sodium losses

iv. Measure serum sodium frequently

v. If combined urine output is greater than 200ml/hr, consider reducing the dextrose concentration. Solutions of 0.45% saline/2.5% dextrose are available.

vi. K+ should not be added to replacement fluids until the serum K+ is normal and there is a good urine output

vii. Insensible losses will generally be covered by infusions of inotropes, morphine etc.

viii. Document drain losses - only replace, with 0.9% saline or blood, if losses are greater than 4-5 ml/kg/day (Discuss with nephrologist or surgeon on call.)

ix. Blood transfusion can result in sensitisation, therefore transfuse only if actively bleeding or Hb < 80 g/l or if there are concerns regarding adequacy of tissue oxygen delivery.

If clinically underfilled (CVP or BP low, large core-peripheral temp gap)

- Give 5% Albumin or 0.9% Saline at 5-10 ml/kg to keep CVP in the required range 8-10 cmH2O. Measure serum albumin 6-8 hourly

If urine output falls to less than 1.5ml/kg/hr

- Check for a full bladder and flush urinary catheter (and stent if present).
- Check for hypovolaemia and give 5% albumin or 0.9% saline 5-10ml/kg as appropriate
- If well-filled then consider IV furosemide (initially 0.25 - 0.5 mg/kg). Start with a low dose as the response can be dramatic particularly with LD transplants.

Polyuria

Large urinary losses of sodium, calcium, magnesium and phosphate can occur with a high urine output. Monitor serum electrolytes closely. Check for glycosuria.

IV. Delayed Graft Function

If there is no urine output, mechanical or surgical causes should be discussed and ruled out. If there is no obstruction and no urine output despite adequate hydration and furosemide, then there is likely to be delayed graft
V. Investigations
a. On admission measure FBC, coagulation, U&E, LFTs, Bone, glucose, magnesium, CRP and urinalysis. Thereafter measure U&E, LFTs, glucose and FBC 4-6 hourly.

b. Monitor serum Na on blood gas machine 3-4 hourly.

c. Renal USS and Doppler shortly after admission to ITU if not already performed in theatre and repeated if clinical situation changes.

d. Check Tacrolimus level at 0800 each day. For Tacrolimus level send 1 x 0.5 ml K EDTA Tubes which must be filled accurately.

e. Consider daily renal USS and doppler if concerns about renal blood flow.

f. Send daily urine (boric acid container) for culture

VI. CMV status
If the recipient is CMV negative and the donor CMV positive, then oral valganciclovir is given for the first 6 months. This should be started when the patient is tolerating oral fluids (usually day 1 or 2 post transplant).

VII. Analgesia / Sedation
This will have been started in theatre. If further analgesia is required, consider:

<table>
<thead>
<tr>
<th>Morphine:</th>
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<tbody>
<tr>
<td><strong>Dose</strong></td>
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<tr>
<td></td>
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<tr>
<td><strong>iv infusion</strong></td>
</tr>
</tbody>
</table>

Consult with pain service

Further information about medication is available in the medication appendix of the protocol.
7. Transfer to ward 6A

Time of transfer to ward 6a will depend on the patient’s clinical condition but ideally should take place during working hours. The patient should be nursed in a cubicle. Patients should have a daily weight, accurate 24 hour fluid balance and 4 hourly blood pressure. Monitor peripheral temperature and aim to keep this at or above 35°C.

7.1 INVESTIGATIONS

On admission measure FBC, coagulation, U&E, LFTs, bone, glucose, magnesium, CRP, urinalysis and urine culture. Thereafter measure U&E and LFTs 12 hourly or more often if clinically indicated. Check that a Renal USS and Doppler has been carried out within the previous 24 hours.

7.2 FLUID AND ELECTROLYTES

Measure urinary sodium losses to guide fluid prescription.

Replace transplant and native urine output ml for ml with either 0.9% saline/5% dextrose or 0.45% saline and 5% dextrose on an hourly basis. Insensible losses will generally be covered by infusions of morphine, antibiotics etc. and do not require a separate infusion. Document drain losses – only replace, with 0.9% saline or blood, if losses are greater than 4-5 ml/kg/day.

If clinically underfilled (BP low, large core-peripheral temp gap)
Give 4.5% Albumin or 0.9% Saline at 5-10 ml/kg to maintain intravascular volume. Measure serum albumin and keep within the normal range.

If urine output falls to less than 1.5ml/kg/hr, check for a full bladder and flush urinary catheter and stent. Check for hypovolaemia and give 5% albumin or 0.9% saline 5-10ml/kg as appropriate. If well-filled then consider iv furosemide (initially 0.25 - 0.5 mg/kg). Start with a low dose as the response can be dramatic particularly with LD transplants. Discuss with the consultant nephrologist who is on call.

If the urine output is large, urinary losses of sodium, calcium, magnesium and phosphate can occur. Monitor serum electrolytes closely and dip urine for glucose.

If there is delayed graft function with no transplant urine output, mechanical or surgical causes should discussed and ruled out. If there is no obstruction and no urine output despite adequate hydration and furosemide, then there is likely to be delayed graft function. Fluid replacement should cover insensible losses, any other losses and any urine output that is present.
7.3. MEDICATION

Immunosuppression
The immunosuppression regimen will be documented in the original drug chart from Ward 6A. Doses are available in the table below and in the section on medication at the end of the protocol.

Prescribe aspirin as below

Analgesia / Sedation
Most children will have a PCA in situ. If additional pain relief is required, consult with the pain service. For those not on a PCA, morphine can be given as below. Avoid non-steroidal analgesics.

Morphine:

| IV Bolus: | Up to 12 years: 100mcg/kg every 4 hrs |
| IV Bolus | 12-18 years: 5 mg every 4 hrs |
| IV Infusion: | 20-30 microgram/kg/hr up to 18 yrs |

Consult with pain service

Gastroprotection
Prescribe omeprazole until eating well or feeds re-started, or whilst high dose steroids are being used.

Antibiotics
Prescribe iv cefotaxime or oral co-trimoxazole as detailed in the table below. Cefotaxime is usually given for the first 48 hours, then oral co-trimoxazole is given thereafter. Co-trimoxazole is given for Pneumocystis prophylaxis and can double as urinary prophylaxis for patients at risk for UTI. This is given for 3 months. If urinary prophylaxis is required thereafter, change to an appropriate antibiotic.

CMV Status
If the recipient is CMV negative and the donor CMV positive, then oral valganciclovir is given for the first 6 months. This should be started when the patient is tolerating oral fluids (usually day 1 or 2 post transplant). The dose is given in the medication table below. Further information is available in the medication section of the protocol.

Aspirin
Aspirin should be given as thromboprophylaxis for the first 3 months post transplant. For patients deemed to be at increased risk of clotting low molecular heparin may be used.
Prescribe the following medication

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Prednisolone</strong></td>
<td><strong>Day 0:</strong> No further steroid needed</td>
</tr>
<tr>
<td></td>
<td><strong>Day 1:</strong> 60 mg/m²/day po (0800) maximum dose 80mg</td>
</tr>
<tr>
<td></td>
<td><strong>Day 2:</strong> 40 mg/m²/day po</td>
</tr>
<tr>
<td></td>
<td><strong>Day 3:</strong> 30 mg/m²/day po</td>
</tr>
<tr>
<td></td>
<td><strong>Day 4:</strong> 20 mg/m²/day po then stop.</td>
</tr>
<tr>
<td><strong>Tacrolimus</strong></td>
<td>0.15 mg/kg po bd (0800 &amp; 2000) max dose 5 mg bd</td>
</tr>
<tr>
<td></td>
<td>Specify Prograf® or Modigraf® (Powder)</td>
</tr>
<tr>
<td></td>
<td><strong>Plasma level needed pre-dose at 09:00</strong></td>
</tr>
<tr>
<td><strong>Mycophenolate Mofetil</strong></td>
<td>600 mg/m² po bd (0800 and 2000) max dose 1 gm bd</td>
</tr>
<tr>
<td><strong>Basiliximab</strong></td>
<td>&lt; 35 kg 10mg each dose</td>
</tr>
<tr>
<td></td>
<td>&gt; 35 kg 20 mg each dose</td>
</tr>
<tr>
<td></td>
<td>The second dose is given on Day 4.</td>
</tr>
<tr>
<td><strong>Aspirin</strong></td>
<td>&lt; 25kg 37.5 mg po in the morning</td>
</tr>
<tr>
<td></td>
<td>&gt; 25kg 75 mg po in the morning</td>
</tr>
<tr>
<td></td>
<td>Continue for 3 months</td>
</tr>
<tr>
<td><strong>Cefotaxime</strong></td>
<td>50 mg/kg iv bd (1000 and 2200) to maximum of 1.5gm bd – adjust dose for GFR</td>
</tr>
<tr>
<td><strong>Co-trimoxazole</strong></td>
<td>12 mg/kg nocte (max. 480 mg) to be given for a minimum of 3 months – adjust dose for GFR</td>
</tr>
<tr>
<td><strong>Omeprazole</strong></td>
<td>Prescribe omeprazole until eating well or feeds are re-started</td>
</tr>
<tr>
<td></td>
<td><strong>iv:</strong> 1-12 years: start at 500mcg/kg (max 20mg) once daily increasing to 2 mg/kg/day (max 40mg) if necessary &gt;12 yrs: max 40mg daily</td>
</tr>
<tr>
<td></td>
<td><strong>po:</strong> 10-20 kg 10mg once daily &gt;20kg 20mg once daily</td>
</tr>
<tr>
<td><strong>Valganciclovir (if necessary)</strong></td>
<td>520 mg/m² po daily when tolerating oral fluids, if required – adjust dose for GFR Give for 6 months post transplantation (max. dose = 900mg daily)</td>
</tr>
</tbody>
</table>
8. Daily management on ward 6A

8.1. Daily Investigations
Check U+E, LFTs, Bone, Glu, CRP, Mag and FBC each day. **Blood tests should be sent by 0800 so that results are available by midday at the latest.**

In addition
Check **Tacrolimus level** at 0800 each day. For Tacrolimus levels send 1 x 0.5 ml K EDTA tubes which must be filled accurately. Samples need to reach the lab by 1000. Assays are performed routinely Mon to Fri. If a level is required on a Saturday, discuss in advance with Dr Galloway or on call biochemist. Samples need to be in the RHSC biochemistry lab by 0900 on a Saturday.

Send daily urine for culture (boric acid container)

Consider daily **renal USS** if concerns about renal blood flow.

**If the creatinine is elevated**, it should be repeated (results to be back before 5pm) and the following considered:

1. Tacrolimus toxicity
2. Urinary tract infection
3. Obstruction to urine outflow
4. Dehydration
5. Rejection

Serum levels of phosphate, magnesium and potassium can fall post transplant and should be supplemented when below the normal range (See Appendix IV).

8.2. Other tests

**Weekly (Monday)**
- EBV / CMV / Adenovirus / Polyoma virus PCR (3-5 ml blood in EDTA tube to virology at South Sector Microbiology laboratory:)
- Urine protein/creatinine ratio

**Post Transplant HLA antibody Monitoring**
HLA antibody levels should be measured if there is suspected rejection, when performing a renal biopsy or if there is declining renal function. They should be checked 3 monthly until one year then yearly thereafter.

8.3 SURGICAL ISSUES

The following apply to routine (extraperitoneal) procedures. Always check operative notes and discuss with surgeons involved in all cases. The surgical team will review the morning after surgery. As both local Paediatric surgeons and the Transplant surgeons are involved, decisions may require a discussion. Unless by prior agreement any deterioration or concern should be passed on to both operating surgeons to ensure a coordinated plan can be made.
In principal:

**NG Tube / PEG**
- If minimal and improving drainage over the first 24hrs with a soft flat abdomen and normal bowel sounds, then spigot NG tube.
- Sips to drink initially building up as tolerated
- If there is any abdominal distension or vomiting, then stop fluids, place NG on free drainage and discuss with surgeons
- Aim for fluids, light diet and all medication taken orally by 24-48 hours or earlier if tolerated
- Remove NG tube when tolerating fluids and drugs

**Wound Drain**
- If drainage minimal then consider removal at 48-72 hours
- If drainage volumes change dramatically then discuss with surgeon

**Urethral catheter**
- Should remain in situ until days 6-7 (remove after wound drain and external stent if present)

**Ureteric Stent**
- Mostly these will be internal JJ stents which will be removed surgically after approximately 4 weeks. Theatre date to be arranged with the urologist prior to discharge. Often patients will be booked onto beginning of next LD list if possible. Patients may also need lines removed at that time.
- Occasionally external transplant ureteric stents are used which are usually of small calibre (4-6Fr) and therefore prone to blockage
- Flush 6 hourly with 5ml of 0.9% Sodium Chloride for first 24hours or longer if not draining well
- Aim to remove on day 5

**HD or PD catheters, Internal JJ Stents**
- Where PD or HD catheters remain in situ or an internal (JJ type) stent has been used patients should be booked for removal at about 4-6 weeks. This should be on the elective list of the operating paediatric surgeon or utilising the first hour of the LD Wednesday list. A booking should be made early to ensure patients are not delayed through waiting list pressures.

**8.4. RADIOLOGY**
- Renal USS as clinically indicated
- Consider USS pre and post catheter removal
- Consider Mag3 scan if there is persisting delayed graft function and concern about graft perfusion.
9 **Complications of transplantation**

### 9.1 Elevated Creatinine

**Can be due to:**
- Rejection
- Obstruction
- Vascular compromise (intrinsic or external compression)
- Infection (UTI or other)
- Dehydration
- Nephrotoxicity e.g. from Tacrolimus

**Therefore:**
- repeat bloods after 8-12 hours
- USS to exclude obstruction, assess vascularity and compression
- Tacrolimus (Ciclosporin) level
- Urine culture
- Virology (PCR) as above
- Consider fluid balance
- Measure donor specific anti-HLA antibodies
- Ensure operating consultant surgeons (or at least teams) aware (both Paediatric and Transplant)

### 9.2 The febrile transplant patient

**Check:**
- WCC and CRP
- urine culture (boric acid container) and urine virology (plain universal)– CMV, Adenovirus
- CVL culture(s)
- peripheral blood culture
- PD fluid culture if PD catheter in situ
- 3-5ml blood in EDTA tube for CMV/EBV/Adenovirus/Polyoma virus PCR
- Urine (plain universal) for polyoma virus PCR if suspected from clinical picture
- USS for abdominal collections
- Consider rejection as a cause of fever

### 9.3 Abdominal/graft pain in a transplant patient

**Consider**
- Rejection
- UTI
- Obstruction
- Haematoma / collection
- Thrombosis
- Ulcer
- Pancreatitis
- Graft rupture

### 9.4 Rejection

Rejection is a diagnosis of exclusion and when suspected should be confirmed by renal biopsy (See Guideline for Renal Biopsy). If confirmed rejection should be treated with intravenous methylprednisolone (600mg/m², max 1gm) for 3 days followed by a prednisolone taper. Consideration should be given to augmenting baseline immunosuppression. **Measure donor specific HLA**
antibody. If immunosuppression is increased consider CMV and PCP prophylaxis if these have already been discontinued.

9.5 Hypertension
High BP is common post transplant and often improves with time post transplant. Calcium channel blockers are often the first line agents to be used. Please refer to the hypertension protocol and discuss with nephrologist on call.
10. Discharge planning

10.1 Before the child is ready for discharge make sure the following have been arranged / carried out

I. Discharge summary to GP and other medical personnel involved in the child’s care. DISCHARGE SUMMARY MUST BE RECEIVED BY GP / LOCAL PAEDIATRICIAN WITHIN 2-5 DAYS. Refer to Discharge Summary Guideline for the information that needs to be included. Also copy IDL on Trakcare into renal database (SERPR) on day of discharge.

II. Supply of medications including where appropriate

III. 0.5 and 1.0 mg of Tacrolimus (Prograf®) capsules

IV. 0.2 and 1.0 mg Tacrolimus (Modigraf®) sachets

V. Renal Medication Information Book with up to date medication, and update ALL medications on renal database (SERPR).

VI. Ensure booking confirmed for removal of PD or HD catheters and internal JJ stent.

VII. Consider dietary advice, sun protection advice (leaflet available), advice re vaccination etc...

VIII. Co-trimoxazole should be used for the first 3 months post transplant.

IX. Prednisolone reducing schedule if appropriate (Avoid enteric coated prednisolone)

X. Aspirin should be continued for the first 3 months

XI. Valganciclovir should be continued for the first 6 months

10.2 Review after Discharge

The following is a rough guide.

- Weeks 1 and 2: Daily
- Weeks 3 and 4: Alternate days (but depends upon clinical status)
- Weeks 5 and 6: Three times per week
- Weeks 7 and 8: Twice weekly
- 3rd-4th months: Weekly
- 5th month: Every two weeks
- 6th-8th months: Every three weeks
- 9th month onwards: Monthly

If rejection episodes occur then visits will need to be more frequent.

At each visit: Weight, BP, bloods, urinalysis +/- urine culture as required.

Virology PCR screening as outlined below

Virology: If EBV, CMV, varicella IgG negative – repeat serology 6 mthly during first year (clotted blood)

Virology: If Hep BSag and Hep C screen negative – repeat serology yearly unless indicated more frequently

If creatinine elevated, measure viral PCRs and anti-HLA antibodies

10.3 Viral Screening

EBV, CMV, Adenovirus, Polyoma PCR – 3-5 ml EDTA blood sample

0 - 6 months post transplant: - monitor weekly or at each visit if seen less often

6-12 months: monitor monthly
Thereafter only at annual transplant assessment unless there is clinical concern

Clinical concern of **polyoma virus** – send urine in a plain universal

For further discussion on this guideline, please contact a consultant within the Renal Unit.
### 11. RHSC Renal Transplant Review

#### Tests Required

<table>
<thead>
<tr>
<th>Frequency</th>
<th>Tests Required</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Routine Review</strong></td>
<td>UE / LFT / Bone / Mag / Glu / CRP / Tacrolimus / FBC (EBV, CMV, BK and Adenovirus PCRs if &lt;1 yr post tx)</td>
</tr>
<tr>
<td><strong>Three monthly</strong></td>
<td>UE / LFT / Bone / Mag / Glu / CRP / Tacrolimus / urate / FBC / PTH, Ur Pro/Cr, Ferritin (EBV, CMV, BK and Adenovirus PCRs and PRA if &lt;1 yr post tx)</td>
</tr>
<tr>
<td><strong>Six monthly</strong></td>
<td>UE / LFT / Bone / Mag / Glu / CRP / Tacrolimus / urate / FBC / PTH, Ur Pro/Cr, Ferritin, TG and Cholesterol CMV IgG if seronegative EBV IgG if seronegative Varicella IgG if seronegative (EBV, CMV, BK and Adenovirus PCRs and PRA if &lt;1 yr post tx)</td>
</tr>
<tr>
<td><strong>Annual review</strong></td>
<td>Bloods &lt;br&gt; UE / LFT / Bone / Mag / Glu / CRP / Tacrolimus / urate / FBC PTH, Ur Pro/Cr, Ferritin &lt;br&gt; Fasting TG and Cholesterol CMV IgG if seronegative EBV IgG if seronegative Varicella IgG if seronegative Hep B and C IgG if seronegative EBV, CMV, BK and Adenovirus PCRs Anti-HLA Antibodies MPA level HBA1c 25 OH Vit D level</td>
</tr>
</tbody>
</table>

**Investigations**
- Renal USS
- Review rejection episodes
- Review medication -RE, anaemia, renal bone disease
- ABPM +/- ECHO
- Assess growth, nutrition & bone health
- Review education
- Review sun awareness
- Review sexual health
- Dental review
- Calculated GFR

*This is only a guide. If results are abnormal then they may need to be checked more frequently.*
12. Appendices

APPENDIX I BP Centiles

BP Centiles

APPENDIX II – MEDICATION INCLUDING ELECTROLYTE SUPPLEMENTS

Methylprednisolone/Prednisolone

<table>
<thead>
<tr>
<th>Start</th>
<th>Pre-transplant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dose</td>
<td>600 mg/m² iv (max dose 1 gm) at the time of anastomosis then give in reducing doses for a total of 5 days</td>
</tr>
<tr>
<td>Side Effects</td>
<td>Hypertension, hyperactivity, psychosis, acne, increase in appetite, weight gain, growth retardation, osteomalacia</td>
</tr>
</tbody>
</table>

Start with IV therapy and convert to oral Prednisolone as soon as tolerated. Most patients receive only 5 days of steroid.

Day 0 as above in theatre
Day 1 60 mg/m²/day (maximum dose 80mg)
Day 2 40 mg/m²/day
Day 3 30 mg/m²/day
Day 4 20 mg/m²/day then stop.

For patients receiving continuing steroid treatment, see appendix VIII.

Rapamycin (Sirolimus)

Switching to Sirolimus in renal transplant recipients from calcineurin inhibitor (CNI):

**Abrupt Switch**

- Stop CNI the night before.
- Next morning give loading dose 3mg/m² twice a day for three days.
- Thereafter give 3mg/m² daily adjusting dose according to trough levels. (Sirolimus has been shown to have shorter half-life in younger children who may require twice daily dosing).
- Approximate time to steady state 5-7 days. After dose changes allow at least 5 days before checking trough levels.

**Gradual Switch**

- Give fixed daily dose of Sirolimus 3mg/m² once a day. *(Sirolimus has been shown to have shorter half-life in younger children who may require twice daily dosing).
- Adjust dose according to trough levels. Discontinue CNI by 25% each week after reaching target level of Sirolimus.
### Alternative Gradual Switch

- Reduce CNI dose by 50% on day 1 or 2
- Introduce Sirolimus loading dose 3mg/m² twice a day for three days.
- Thereafter give 3mg/m² daily adjusting dose according to trough levels. (Sirolimus has been shown to have shorter half-life in younger children who may require twice daily dosing).
- Reduce CNI gradually over 1 to 4 weeks after reaching target level of Sirolimus.

Sirolimus 24 hour trough levels: 5-15ng/ml

*Alternative is to give a one-day loading dose of 3mg/m² twice a day.

NB: Ciclosporin increases plasma concentration of Sirolimus therefore careful adjustment of dosage is required when reducing/stopping the dose of Ciclosporin.

<table>
<thead>
<tr>
<th>Tacrolimus (Prograf ®)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Start</strong></td>
</tr>
<tr>
<td><strong>Dose</strong></td>
</tr>
<tr>
<td><strong>Plasma level needed pre-dose at 09:00</strong></td>
</tr>
<tr>
<td><strong>Side Effects</strong></td>
</tr>
</tbody>
</table>

IV treatment (0.06mg/kg/day as continuous infusion) can be associated with hypertension, therefore where possible start with oral therapy. Can be given NG by opening the capsules and dissolving the contents in at least 10 ml water. Flush with at least 10 ml water and clamp NG tube for 45 - 60 minutes.

- Aim for 12 hour trough levels of:
  - Day 0 - 21
    - 8 - 12 ng/ml
  - Week 3 to 6 mths
    - 5 - 10 ng/ml
  - 6 mths to 1 year
    - 4 - 8 ng/ml
  - After 1 year
    - 3 - 6 ng/ml

  - Trough level measured at 12 hours. One 0.5 ml EDTA is sufficient.
  - Interaction can occur with erythromycin, fluconazole and other imidazoles, warfarin. Do not administer with grapefruit or cranberry juice.
  - Prescribe as brand (Prograf® / Modigraf®) as other preparations are available
  - Modigraf® sachets can be used for those who have difficulty swallowing capsules.

<table>
<thead>
<tr>
<th>Mycophenolate Mofetil (MMF) (Cellcept ®)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Start</strong></td>
</tr>
<tr>
<td><strong>Dose</strong></td>
</tr>
<tr>
<td><strong>Side Effects</strong></td>
</tr>
</tbody>
</table>
Dose reductions will be needed if there are low platelets, low WCC or low haemoglobin. Available as 250mg capsule and 500mg tablet. Use liquid preparation rather than splitting capsules for doses in between. Side effects can be lessened by splitting the same daily dose tds or qid. If side effects are problematic, drug levels can be measured as an MPA trough.

If used in combination with ciclosporin continue on 600mg/m² bd after 2 weeks. Ciclosporin interacts with MMF and reduces the AUC. Where used with Tacrolimus, MMF can be continued at a dose of 600 mg/m² bd whilst aiming for slightly lower of Tacrolimus.

**Basiliximab (Simulect ®)**

<table>
<thead>
<tr>
<th>Start</th>
<th>Day 0</th>
<th>Day 4 post transplant (A total of 2 doses given)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dose</td>
<td>IV</td>
<td></td>
</tr>
<tr>
<td>35kg - 20mg each dose</td>
<td>&lt; 35kg - 10 mg each dose</td>
<td></td>
</tr>
</tbody>
</table>

**Side Effects**

Hypersensitivity reaction to infusion (rare)

Basiliximab is an IL-2 receptor blocking antibody, which can be used at induction. It is generally well tolerated. Only 2 doses are needed and this results in IL-2 receptor blockade for up to 4-6 weeks. The infusion: reconstitute with 5ml of water provided and then further dilute to a volume of 50 ml with 5% Glucose or 0.9% Sodium Chloride. Give over 20-30 minutes.

First dose is given on day 0 in ward 6A when it is known that the transplant is going ahead.

**Omeprazole**

<table>
<thead>
<tr>
<th>Start</th>
<th>Day 1</th>
</tr>
</thead>
<tbody>
<tr>
<td>iv:</td>
<td>1-12 years: start at 500mcg/kg (max 20mg) once daily increasing to 2 mg/kg/day (max 40mg) if necessary &gt;12 yrs: max 40mg daily</td>
</tr>
</tbody>
</table>

**Dose**

po: 10-20 kg 10mg once daily >20kg 20mg once daily

**Thromboprophylaxis**

**Dalteparin**

s/c: 40units/kg bd sub-cut (0600 and 1800) – measure heparin assay for anti-Xa level at 1000 next day

**Aspirin**

po: <25kg 37.5 mg po in the morning >25kg 75 mg po in the morning Continue for 3 months
### Phosphate

**Supplement if serum phosphate is below 0.7 mmol/l**

| **infusion:** | **0.4 mmol/kg** | adjust as necessary (See BNFc)  
Add 15 mmols Na Phosphate to 50 ml N saline (0.3 mmol/ml)  
and run at 0.5-3 ml/hr |
|----------------|-----------------|
| **po:**        | < 5yrs 2 -3 Phosphate sandoz tablets per day  
> 5yrs 4 - 6 Phosphate Sandoz tablets per day |

**Phosphate Sandoz tablet contains:**

- Phosphate 16.1 mmol
- Na 20.4 mmol
- K 3.1 mmol

### Magnesium

**Supplement if serum Magnesium is below 0.45 mmol/l or patient symptomatic**

| **iv:** | 1-12yrs: 0.2 mmol/kg Mg**+** bd  see BNFc  
12-18 yrs 4mmol Mg**+** bd  see BNFc  
Magnesium Sulphate 1g equivalent to ~4mmol Mg**+** |
|---------|-------------------------------------------------------------------|
| **po:** | 0.2 mmol/kg initially once daily increasing to 3 times daily if required  
One tablet of Magnesium Citrate contains 6 mmol magnesium  
Magnesiocard sachets contain 5 mmol magnesium per sachet |

### Calcium

**Supplement if calcium is below 2.00 mmol/l or patient symptomatic**

| **iv:** | Calcium gluconate 10% 0.5 ml (0.113 mmol)/kg with ECG monitoring as a slow injection through a central line if possible  
(max 4.5 mmols) |
|---------|-----------------------------------------------------------------|
| **infusion:** | 1 mmol/kg/day added to maintenance through central line  
(max 8.8mmols in 24 hrs) |
| **po:** | < 5 yrs 0.25 mmol/kg qid  
5-11 yrs 0.2 mmol/kg qid  
12-18 yrs 10 mmols qid |

**Calcium Sandoz liquid**  
(Calcium 0.54 mmol/ml)  

**Sandocal 1000 tablets**  
(Calcium 25 mmol / tab)
### PROPHYLAXIS

Patients who are CMV seronegative at the time of transplantation, should receive oral valganciclovir after transplantation if the donor is CMV seropositive. Valganciclovir should be started when the patient is tolerating oral fluids and continued for a duration of six months.

<table>
<thead>
<tr>
<th>Valganciclovir</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Note:</strong> The dose needs to be adjusted for renal function. After oral administration valganciclovir is rapidly metabolised to ganciclovir which is renally excreted.</td>
</tr>
</tbody>
</table>
| **Dose:** | All ages for GFR > 80 ml/min/1.73m²: 520 mg/m² po daily to a maximum of 900mg daily.  
All ages for GFR < 80 ml/min/1.73m²: The dose (mg) = 7 × BSA × CrCl (ml/min). Maximum dose is 900mg daily. |
| **Side effects:** | leucopenia, thrombocytopenia, anaemia, rash, abnormal LFTs |

Monitor CMV infection as required by CMV PCR: send 3-5 ml EDTA blood and urine (plain universal) for CMV PCR.

### TREATMENT OF CMV DISEASE

CMV disease is diagnosed by evidence of CMV in the blood by PCR and systemic symptoms: fever, abnormal LFTs, anaemia etc. Treatment is with oral valganciclovir

<table>
<thead>
<tr>
<th>Valganciclovir</th>
</tr>
</thead>
</table>
| **Dose:** | All ages for GFR > 80 ml/min/1.73m²: 520 mg/m² po twice daily for a minimum of 14 days (maximum dose 900mg twice daily).  
All ages for GFR < 80 ml/min/1.73m²: The dose (mg) = 7 × BSA × CrCl (ml/min) twice daily for at least 14 days (maximum dose is 900mg daily). |
| **Side effects:** | leucopenia, thrombocytopenia, anaemia, rash, abnormal LFTs |

The length of treatment will depend on the severity of the illness. Longer treatment may be required for gastrointestinal disease.
Immunosuppressed patients are at risk of pneumocystis jirovecii pneumonia (organism previously known as pneumocystis carinii, now known as pneumocystis jirovecii, but disease still referred to as PCP). This is particularly true for patients receiving augmented immunosuppression. Patients who develop CMV disease are susceptible to PCP. If clinically indicated send a bronchial alveolar lavage (BAL) to Virology for CMV PCR and to confirm the diagnosis of PCP by direct immunofluorescence and PCR.

**Prophylaxis**

**Co-trimoxazole** 12 mg/kg nocte (max. 480 mg) to be given for a minimum of 3 months. Can ‘double’ as urinary prophylaxis.

**Treatment**

<table>
<thead>
<tr>
<th>Co-trimoxazole</th>
<th>60mg/kg bd orally or intravenously for 10-14 days. When given intravenously give diluted via a central line. See BNFc for administration information.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Reduce the dose in renal failure:</strong></td>
<td>15-30 ml/min/1.73m²: Use half normal dose bd &lt; 15 ml/min/1.73m²: Avoid unless receiving haemodialysis, when 50% of the dose can be given.</td>
</tr>
<tr>
<td><strong>Side effects:</strong></td>
<td>Rash, agranulocytosis</td>
</tr>
</tbody>
</table>
APPENDIX V THROMBOPROPHYLAXIS

If the patient is deemed to be at increased risk of clotting then low molecular heparin may be used instead of aspirin. This is given as Dalteparin (Fragmin®) 40 units/kg bd by subcutaneous injection, starting within 2-4 hours post surgery. This is usually given at 1800 and 0600 and a heparin assay measuring the anti-Xa level is measured 4 hours after the second (usually morning) dose. If these times are missed, aim to give the first dose within 2-4 hours of surgery, the next at 10 to 14 hours and gradually work around to dosing at 0600 and 1800. Remember levels are only measured within working hours, but samples can be spun down and frozen.

Check an Anti-Xa level at 1000 each day (Purple Sodium Citrate tube). Withhold next dose until this result is available.

Aim for Anti-Xa levels of between 0.2 - 0.4 iu/dl. Patients with a pro-coagulant tendency may require a different therapeutic range.

Once patients are ambulant (approx day 5) or as directed by the medical team, dalteparin can be discontinued and aspirin commenced.

<table>
<thead>
<tr>
<th>Thromboprophylaxis</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dalteparin</strong></td>
<td>s/c:</td>
</tr>
<tr>
<td><strong>po:</strong></td>
<td></td>
</tr>
<tr>
<td><strong>s/c:</strong></td>
<td>40units/kg bd sub-cut (0600 and 1800) – measure heparin assay for anti-Xa level at 1000 next day</td>
</tr>
<tr>
<td><strong>po:</strong></td>
<td></td>
</tr>
<tr>
<td><strong>&lt;25kg:</strong></td>
<td>37.5 mg po in the morning</td>
</tr>
<tr>
<td><strong>≥25kg:</strong></td>
<td>75 mg po in the morning</td>
</tr>
<tr>
<td><strong>Continue for 3 months</strong></td>
<td></td>
</tr>
</tbody>
</table>
Appendix VI: Anti Thymocyte Globulin (ATG)

WIG Protocol for Use of ATG (Rabbit Anti T-lymphocyte Globulin/Thymoglobuline)

Updated by Heather Black, Renal Pharmacist 6.2.12
Reviewed by Neal Padmanabhan

Uses
Steroid resistant rejection in renal transplant patients. Use of ATG should only be on the instruction of the Consultant looking after the patient.

Supply

Dosage
The aim is to suppress absolute CD3 count to $<0.05 \times 10^9/L$ (50,000 cells/ml) for 14 days. On day 0 a test dose is administered, followed on day 1 by the first full dose of 1.5mg/kg. CD3 counts are monitored daily and further doses of 1.5mg/Kg are administered if the CD3 count is $\geq 0.05 \times 10^9/L$. Usually 3 doses will be required over a 10-14 day period. Length of treatment will be decided based on clinical status and laboratory results (approx 10-14 days) and may be suspended if total WCC falls to $<2 \times 10^9/L$, platelet count $<50 \times 10^9/L$, or if unacceptable side effects intervene. To avoid over-immunosuppression, tacrolimus dose is reduced to quarter dose and MMF is stopped during treatment. Cumulative doses between 10.5-21mg/kg may be required. Use ideal weight not actual weight and round the dose to nearest 25mg.

Presentation and Administration
- Thymoglobuline is presented in vials of 25mg freeze dried purified immunoglobulin + 5ml vial of diluent. The vials should be stored in the fridge.
- Although not essential, many units give a test dose due to infusion related symptoms including anaphylaxis.
- **Test dose:** no test dose is generally required
- **Full dose:**
  Premedicate with hydrocortisone 100mg IV and chlorphenamine 10mg IV. Reconstitute vials as above.
  Administer in NaCl 0.9%, allowing 50mls for every 25mg vial (total volume 250-500mls).
  Administer via a central line over at least 6 hours (preferably 8-12 hours if infusion related reactions are an issue). Observe the patient checking BP, pulse and temperature frequently during the infusion.

<table>
<thead>
<tr>
<th>Time after dose</th>
<th>Frequency of observations</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-2hrs</td>
<td>15mins</td>
</tr>
<tr>
<td>2-4hrs</td>
<td>30mins</td>
</tr>
<tr>
<td>4+ hrs</td>
<td>hourly</td>
</tr>
</tbody>
</table>

Stability
Once reconstituted, the infusion is only stable for a maximum of 24 hours but should be used as soon as possible.
**Contraindications**
- Allergy to rabbit protein
- Acute viral illness
- Full anaphylactic reaction to test dose

**Side Effects**
Severe acute infusion associated reactions associated cytokine release and rarely anaphylaxis can occur. Symptoms include headache, fever, arthralgia, rigors and hypotension. Pulmonary oedema may occur in severe cases. Reducing infusion rate and pre med with paracetamol, hydrocortisone and chlorpheniramine can reduce incidence and severity of these reactions. Caution if platelet count falls <50 or WBC<2- consider interrupting treatment.

**Interactions**
There is a risk of over-immunosuppression- review tacrolimus/ ciclosporin dose and stop mycophenolate.
Continue co-trimoxazole and valganciclovir prophylaxis for 3 months after treatment with ATG.

**Dosing schedule**

<table>
<thead>
<tr>
<th>Drug</th>
<th>1</th>
<th>2-7</th>
<th>7-14</th>
<th>14+</th>
</tr>
</thead>
<tbody>
<tr>
<td>ATG</td>
<td>Full</td>
<td>*CD3 Count</td>
<td>*CD3 Count</td>
<td></td>
</tr>
<tr>
<td>Tacrolimus</td>
<td>0.025mg/kg/day as 2 doses</td>
<td>0.025mg/kg/day as 2 doses</td>
<td>0.025mg/kg/day as 2 doses</td>
<td>0.05mg/Kg bd</td>
</tr>
<tr>
<td>MMF</td>
<td>stop</td>
<td>stop</td>
<td>stop</td>
<td>Full</td>
</tr>
<tr>
<td>Prednisolone</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
</tr>
</tbody>
</table>

*CD3 Count
Daily CD3 count. Further full dose if CD3 Count ≥0.05 x10^9/L (50,000 cells/ml). No dose if total WCC <2 x10^9/L or platelet count<50 x10^9/L.

**Tacrolimus/MMF**
Reduce Tacrolimus to 0.025mg/Kg as 2 doses until day 14, then increase to 0.05mg/Kg bd (Target level 8-12)
Stop MMF during treatment then reintroduce at full dose from day 14.

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1 http://www.dh.gov.uk/health/2012/03/sabto/