**Assessment for transplantation**

Abbreviated medical protocols from EdREN, the website of the Renal Unit of the Royal Infirmary of Edinburgh

**Assessment clinics**

In the East of Scotland, work-up for renal transplantation is carried out at local centres.

**Lothian, Borders and Fife patients** are seen at the transplant assessment clinic in Edinburgh.

A referral letter with a transplant recipient check-list and summary (appendix I+II) should be sent to the Transplant Unit (addressed to one of the Consultant Transplant Surgeons). All the referred patients will be sent an appointment for an outpatient visit.

At time of initial assessment some or all of the following personnel will provide clinical input:

- Transplant surgeon
- Renal physician
- Anaesthetist
- Transplant Co-ordinator

If indicated further assessment by social work department chiropody, dentistry, dietetics, dermatology, liaison psychiatry, and other relevant specialities may be sought.

Patients will have the opportunity for detailed discussion regarding kidney transplantation and will be counselled with respect to relative risks and benefits of cadaveric and living donor kidney transplantation.

An information booklet is also given to the patient to support the verbal information given at the assessment clinic.

**Before Listing**

Following initial outpatient assessment, those patients who are considered potentially suitable candidates and who remain willing to be considered for a transplant will undergo further investigation as required.

The transplant coordinator will arrange for copies of all the required investigations prior to listing.

When investigations are complete, the transplant team will review the results. Further
investigations and/or treatments may be required at this time.

The decision about listing the candidate for kidney transplantation will be made by the transplant surgeons after discussion with the multi-disciplinary team and the patient.

A detailed letter regarding the patient assessment will be sent to the referring centre with a copy to the general practitioner.

**Listing**

If the patient is to be listed, the patient will be directly informed, verbally and in writing, by the transplant co-ordinator.

Transport requirements in the event of being called in for transplantation will be determined and arranged by the transplant co-ordinator.

**UK Transplant** will be informed by the transplant co-ordinator as per unit procedure.

**Detailed protocols and other info**

These documents are all pdf files.

- [Transplant recipient check-list and summary](#) (Appendix 1)
- [Guidelines to be used with check-list](#) (Appendix 2)
- [Triggers to psychiatric referral in renal transplant assessment](#) (Appendix 3)
- [Protocol for tissue typing and antibody screening](#) (Appendix 4)

**Patient information**

- [Edren patient information on renal transplantation](#)

Transplant protocols developed on the Edinburgh Transplant Unit. This page first published January 2007 and last modified Tuesday, January 23, 2007.

**NOTE** that the accuracy of any statements in this information CANNOT be guaranteed. It is published in the belief that it is correct, and we endeavour to keep it so - but we do make mistakes. Furthermore, over some subjects there are differing opinions, or differing degrees of certainty. We have usually not attempted to discuss these here because the aim has been to provide an immediate and brief guide. In all areas, prior medical knowledge is assumed. The EdRenHANDBOOK is not suitable for use by those without such a background. Contact us by email or at the address given at the foot of the contents page with any comments or corrections.
Anti-thymocyte Immunoglobulins (ATG)

Indication

Rejection resistant to steroids is now uncommon but ATG may be used in some circumstances, e.g., persistent biopsy-proven rejection despite two courses of methylprednisolone.

Contra-indications

- known allergy to rabbit proteins
- acute viral illness
- full anaphylactic response to the test dose.

Dosage and administration

The aim of therapy is to suppress the absolute CD3 cell count (T cell count) to below 0.05x10^9/L (<50/microlitre) for 14 days. ATG is given daily until the CD3 cell count has reached this level, then repeated if it rises above this level. Response varies, but most patients need 2-3 full doses over the 14 day treatment period. A test dose is given and followed 24h later by the first full dose.

Test dose

Symptoms during or after an ATG infusion are common. This is due to a systemic inflammatory response which occurs when T cells are activated by binding ATG. Symptoms of this 'cytokine release syndrome' inculde headache, fever, arthralgia, rigors and hypotension. Pulmonary oedema may occur in severe cases. True anaphylaxis is rare but it may occur.

All patients should have a test dose first, to identify those who will develop severe reactions.
including anaphylaxis.

Signs of anaphylaxis are tingling in the extremities and around the mouth, swelling of the lips and larynx, bronchospasm, tenesmus, hypotension. It should be treated in the usual way with hydrocortisone 100mg IV, chlorpheniramine 10mg IV; 0.5ml adrenaline 1:1000 IM may be necessary.

- Give 5 mg ATG in 100ml NaCl 0.9% infused through a peripheral vein over 1 hour. Have hydrocortisone, chlorpheniramine and adrenaline available close by.
- Premedicate with paracetamol 1g orally, chlorpheniramine 10mg IV.
- Reconstitute the contents of one vial (25mg) with accompanying diluent (5 ml water for injections), giving a solution of 5 mg ATG per ml.
- Take 1 ml of solution and add to 100 ml NaCl 0.9%.
- Observe patient closely, monitoring BP, pulse and temperature according to the following schedule:

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

**First Full Dose**

Given the day after the Test Dose.

- Give ATG 2mg/kg in 0.9% NaCl given over 6-8h via a central venous catheter. Round the dose to the nearest 25mg.
- Reconstitute required number of vials with 5ml diluent per vial.
- Add contents of reconstituted vials to 0.9% NaCl, allowing 50ml per vial (250ml bag usually appropriate).
- Premedicate as for test dose, but if the patient experienced systemic symptoms with the test dose, consider hydrocortisone 100mg IV in addition to any oral prednisolone they are taking as part of their baseline immunosuppression.
- Observations as for test dose

**Further Doses**

- Further doses given according to absolute CD3 cell (=T cell) count. A second full dose should be given when CD3 count >0.05x10^9/L (<50/microlitre). Typically ATG will need to be given every 3-4 days, sometimes at much longer intervals.
- To obtain the absolute CD3 count,
• Give further doses as for 'First Full Dose'

**Monitoring**

• Daily absolute CD3 count whilst treated. In Edinburgh send a second FBC tube to the WGH haematology lab (tel 31914) urgently first thing every morning, using a separate request form. Same-day result will be provided.
• Daily FBC and U+E during treatment and over next 2 weeks.
• Interrupt treatment if platelet count <50x10⁹/L.
• Consider interrupting treatment if leukocytes <2x10⁹/L.

**Monitoring**

See also Test Dose section. Symptoms of some sort are common (approx 25%) during administration and may be unpleasant for the patient. They include rigors (4%), fever (15%), arthralgia (10%), erythema (10%) and pruritic skin eruptions (10%). Symptoms are most commonly seen after the first injection and decrease during the course of treatment.

Other side effects include thrombocytopenia (5%), neutropenia (5%) which may prevent continuation of the treatment course, and serum sickness. Severe cytokine release syndrome and true anaphylaxis are rare (<1%) but can be fatal.

**Interactions**

There is a risk of over-immunosuppression, hence the following schedule should be followed:

<table>
<thead>
<tr>
<th>DRUG</th>
<th>0</th>
<th>1</th>
<th>2-7</th>
<th>8-14</th>
<th>15-30</th>
<th>31+</th>
</tr>
</thead>
<tbody>
<tr>
<td>ATG</td>
<td>Test</td>
<td>Full</td>
<td>*</td>
<td>*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tacrolimus/Ciclosporin</td>
<td>Y</td>
<td>N</td>
<td>N</td>
<td>Half dose</td>
<td>Full dose</td>
<td>Full dose</td>
</tr>
<tr>
<td>Prednisolone</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>Azathioprine/MMF</td>
<td>Y</td>
<td>N</td>
<td>N</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
</tr>
</tbody>
</table>

* Depending on T cell count

Tacrolimus reinstated after 1 week at dose of 0.05mg/kg divided into two doses [or half previous established dose]. Ciclosporin at dose 3mg/kg divided into two doses [or half
previous doses].

Continue PCP and CMV/HSV prophylaxis for 3 months after treatment with ATG.

Ordering

Mon - Fri 08:30 - 17:00 - Contact unit pharmacist. Out of hours contact the resident pharmacist, bleep 2268. A small stock is held in pharmacy.

Storage

Both the dry powder and reconstituted solution should be stored in fridge (+4C), usually on ward 117; protect from light.
Azathioprine

Abbreviated medical protocols from EdREN, the website of the Renal Unit of the Royal Infirmary of Edinburgh

This page describes the Edinburgh regime for the use of the immunosuppressant Azathioprine.

Current indication

Third agent in standard triple therapy.

Dose

- Initial 1-2 mg/kg once daily.
- Maintenance 1 mg/kg once daily.
- Monitoring No monitoring of drug levels is required.

Preparation

Azathioprine is available as 25 mg and 50 mg tablets. There are both generic and brand (Imuran) forms on the market.

Administration

Virtually exclusively oral, although an IV preparation is available.

Contra-indications
• Pregnancy

• Bone marrow dysfunction, i.e. Patients who are known to be leucopaenic or thrombocytopaenic.

• Reduce dose if hepatic dysfunction is present.

Drug Interactions

Allopurinol must not be co-prescribed as an inhibition of xanthine oxidase results in potentially fatal accumulation of azathioprine and its metabolites. An alternative uricosuric- benz bromarone is available on a named patient basis. Contact transplant unit pharmacist for further details.

Side Effects

• Bone marrow suppression - usually reversible following cessation.

• Cholestatis and disturbed liver function - again usually reversible.

• Pancreatitis

• Dose may require to be altered depending on WCC, i.e., reduce if WCC<4.0, stop if WCC <3.0 and re-introduce at a lower doses when WCC>3.0.
Valganciclovir is prescribed for prevention of CMV disease in high risk transplant patients identified as follows:

- Renal transplant - CMV –ve recipient of CMV +ve donor
- Liver transplant - CMV –ve recipient of CMV +ve donor
- Simultaneous kidney-pancreas transplant (SKP) - All transplant recipients except CMV –ve recipients of CMV –ve donors

Prescription is initiated in hospital within 10 days of transplantation. Therapy will be continued in primary care for up to a total of 90 days treatment for which a shared-care protocol will be provided.

Valganciclovir is available as 450mg tablets (pink) and the brand name is Valcyte®. The tablets should be taken with food and not broken or crushed.

The initial valganciclovir dose is dependent on renal function as shown in the table below:

<table>
<thead>
<tr>
<th>Creatinine clearance (ml/min)</th>
<th>Prophylactic dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;60</td>
<td>900mg od</td>
</tr>
<tr>
<td>40 to 59</td>
<td>450mg od</td>
</tr>
<tr>
<td>25 to 39</td>
<td>450mg every 2 days</td>
</tr>
<tr>
<td>10 to 24</td>
<td>450mg twice weekly</td>
</tr>
</tbody>
</table>

FBC and LFTs must be monitored daily during therapy.

**Testing for CMV infection**

Surveillance is not routine since introduction of valganciclovir. Investigate any episode of illness which might be CMV related, at any stage following a transplant operation.

Check CMV serology together with samples of EDTA blood for buffy coat culture and serum sample for PCR. These should be requested following discussion with the Virologist.

An EDTA (9 ml or 3 x 2.5 mls sample for CMV should be sent to Virology whenever is clinically relevant. ON request form include details of illness (e.g. pyrexia or hepatitis etc.) Request CMV PCR and CMV culture. Please try to ensure samples reach Virus Lab by
midday, and within 2h. The rapid culture may provide an answer sooner than PCR in some cases.

It will often be appropriate to send respiratory or other samples to virology - bronchoalveolar lavage or induced sputum for investigation as usual or colon biopsies.

Transplant protocols developed on the Edinburgh Transplant Unit. This page first published March 2002 by Amit Adlakha, updated December 2006 and last modified Sunday, January 14, 2007.

NOTE that the accuracy of any statements in this information CANNOT be guaranteed. It is published in the belief that it is correct, and we endeavour to keep it so - but we do make mistakes. Furthermore, over some subjects there are differing opinions, or differing degrees of certainty. We have usually not attempted to discuss these here because the aim has been to provide an immediate and brief guide. In all areas, prior medical knowledge is assumed. The EdRenHANDBOOK is not suitable for use by those without such a background. Contact us by email or at the address given at the foot of the contents page with any comments or corrections.
Complementary medicines

Abbreviated medical protocols from EdREN, the website of the Renal Unit of the Royal Infirmary of Edinburgh

There is currently insufficient information on the pharmacokinetics of complementary medicines to enable a judgement on whether they are likely to interact with conventional medicines and whether dosage reduction is necessary in renal impairment. Due to a lack of regulation, adverse effects such as nephrotoxicity may be attributable to impurities rather than the active principle.

Below is an extremely limited list of information on complementary medicines - for specific queries the Welsh Drug Information Centre specialist file and Micromedex may be consulted via pharmacy. There is also a very useful databases at: http://www.nlm.nih.gov/medlineplus/druginformation.html

<table>
<thead>
<tr>
<th>Complementary medicine</th>
<th>Issue</th>
</tr>
</thead>
<tbody>
<tr>
<td>St John's Wort</td>
<td>Decreased CyA levels reported due to CYP450 3A4 induction. May therefore decrease tacrolimus levels also.</td>
</tr>
<tr>
<td>Garlic</td>
<td>Increases INR therefore avoid peri-operatively</td>
</tr>
<tr>
<td>Papaya</td>
<td></td>
</tr>
<tr>
<td>Danshen</td>
<td></td>
</tr>
<tr>
<td>Dong quai</td>
<td></td>
</tr>
<tr>
<td>Ginger</td>
<td></td>
</tr>
<tr>
<td>Xaiochai hutang</td>
<td>Increases Prednisolone levels</td>
</tr>
<tr>
<td>Chinese herb</td>
<td>Cause renal damage</td>
</tr>
<tr>
<td>(Aristolochia)</td>
<td></td>
</tr>
<tr>
<td>Juniper</td>
<td></td>
</tr>
<tr>
<td>Pennyroyal</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ginko</td>
</tr>
<tr>
<td>---</td>
<td>----------------------------</td>
</tr>
<tr>
<td></td>
<td>Echinaeea</td>
</tr>
</tbody>
</table>

Transplant protocols developed on the Edinburgh Transplant Unit. This page first published March 2002 by Amit Adlakha, reviewed December 2006 and last modified Sunday, January 14, 2007.

NOTE that the accuracy of any statements in this information CANNOT be guaranteed. It is published in the belief that it is correct, and we endeavour to keep it so - but we do make mistakes. Furthermore, over some subjects there are differing opinions, or differing degrees of certainty. We have usually not attempted to discuss these here because the aim has been to provide an immediate and brief guide. In all areas, prior medical knowledge is assumed. The EdRenHANDBOOK is not suitable for use by those without such a background. Contact us by email or at the address given at the foot of the contents page with any comments or corrections.
Ciclosporin

Abbreviated medical protocols from EdREN, the website of the Renal Unit of the Royal Infirmary of Edinburgh

This page describes the Edinburgh regime for the use of the immunosuppressant Cyclosporine (cyclosporin, ciclosporin).

Current Indication

No longer a first line agent but some transplant patients will still have Neoral (previous formulation Sandimmun but nearly all patients are on Neoral) as the lead agent in their immunosuppression regime.

Dosage

Starting dose is 8 mg/kg/day in 2 divided doses.

Preparation

Ciclosporin is available 10 mg (yellow / white), 25 mg (blue / grey), 50 mg (yellow / white) and 100 mg (blue / grey) capsules and as a 100 mg/ml oral solution. The brand name is Neoral.

Administration

- Oral route in most instances.
- It is administered usually at 10 am and 10 pm.
- Oral solution should be diluted immediately before taking. May be diluted in orange juice or squash, apple juice or water (not grapefruit juice - see interactions). Needs to be stirred well. Measuring device should not come into contact within the dilutent.
- One third of the oral dose can be given as a slow intravenous infusion in normal saline or dextrose 5% over 2-6 hours if absolutely necessary.
Contra-indications/Cautions

- Live vaccines are not to be given to immunocompromised patients.
- Neoral should be used with caution during pregnancy.
- Ciclosporin passes into breast milk so mothers should not breast feed their infants.

Side effects

- The most frequent side effects seen with ciclosporin include:
  - abnormal kidney function
  - hypertrichosis
  - tremor
  - hypertension
  - hepatic dysfunction
  - gingival hypertrophy
  - gastointestinal disturbances
  - burning sensations of hands and feet

- Less common side effects are:
  - headaches
  - weight increase
  - mild anaemia
  - hyperkalemia
  - hyperuricaemia
  - hypomagnasaemia
  - hypercholesterolaemia
  - rashes (possible allergic origin)
  - oedema
  - pancreatitis
  - neuropathy
  - reversible dysmenorrhoea
  - muscle weakness cramps or myopathy
Interactions

- **Potential interactions due to effects on hepatic microsomal enzymes.**

Inhibitors of cytochrome P450 which may *decrease* metabolism of Ciclosporin and thus *increase* Ciclosporin blood levels include:

<table>
<thead>
<tr>
<th>clarithromycin</th>
<th>erythromycin</th>
<th>nicardipine</th>
</tr>
</thead>
<tbody>
<tr>
<td>danazol</td>
<td>fluconazole</td>
<td>oral contraception</td>
</tr>
<tr>
<td>diltiazem</td>
<td>ketoconazole</td>
<td>verapamil</td>
</tr>
</tbody>
</table>

Inducers of cytochrome P450 which may *increase* metabolism of Ciclosporin and thus *decrease* blood levels include:

<table>
<thead>
<tr>
<th>Barbiturates</th>
<th>phenytoin</th>
</tr>
</thead>
<tbody>
<tr>
<td>carbamazepine</td>
<td>rifampicin</td>
</tr>
</tbody>
</table>

- **Interactions due to cumulative toxicity / synergistic effects**

  - Take care when using Ciclosporin in combination with compounds known to have nephrotoxic effects, e.g.: aminoglycosides, ciprofloxacin, trimethoprim, amphotericin B, melphalan and NSAIDs.

  - Concurrent administration of Ciclosporin with HMG-CoA reductase inhibitors may enhance risk of rhabdomyolysis.

  - Concomitant administration of nifedipine and Ciclosporin increases the rate of gingival hyperplasia when compared to that for Ciclosporin alone, particularly in the presence of poor oral hygiene.

  - Since Ciclosporin may cause hyperkalemia, potassium sparing diuretics, potassium supplements and high potassium intake should be avoided.

- **Other interactions**

  - Vaccines may be less effective and the use of live attenuated vaccines should be avoided.

  - Owing to its possible interference with the gastrointestinal cytochrome P450 enzyme system, grapefruit or grapefruit juice should not be taken 1 hour prior to Ciclosporin dosing and grapefruit juice should not be used as a diluent for the oral solution.

  - This is not a comprehensive list of all potential interactions with Ciclosporin. For further information please ask senior members of staff or consult the transplant unit pharmacist.
Levels

Whole blood trough levels are measured by the laboratory on Mondays, Wednesdays and Fridays. The assay changed on January 10th 2005 as shown.

The table shows results pre and post 10th January 2005

_Ciclosporin Assay (nmol/L)_

<table>
<thead>
<tr>
<th>OLD</th>
<th>NEW</th>
</tr>
</thead>
<tbody>
<tr>
<td>50</td>
<td>32</td>
</tr>
<tr>
<td>100</td>
<td>69</td>
</tr>
<tr>
<td>150</td>
<td>107</td>
</tr>
<tr>
<td>200</td>
<td>144</td>
</tr>
<tr>
<td>250</td>
<td>182</td>
</tr>
<tr>
<td>300</td>
<td>219</td>
</tr>
<tr>
<td>350</td>
<td>257</td>
</tr>
<tr>
<td>400</td>
<td>294</td>
</tr>
<tr>
<td>450</td>
<td>332</td>
</tr>
<tr>
<td>500</td>
<td>369</td>
</tr>
<tr>
<td>550</td>
<td>407</td>
</tr>
<tr>
<td>600</td>
<td>444</td>
</tr>
<tr>
<td>650</td>
<td>482</td>
</tr>
<tr>
<td>700</td>
<td>519</td>
</tr>
<tr>
<td>750</td>
<td>557</td>
</tr>
</tbody>
</table>
Target Range

For first 6 months 100 - 125 mmol/L (new assay)

After 6 months 50 - 100 mmol/L

Transplant protocols developed on the Edinburgh Transplant Unit. This page first published March 2002 by Amit Adlakha, reviewed November 2006 and last modified Sunday, January 14, 2007.

NOTE that the accuracy of any statements in this information CANNOT be guaranteed. It is published in the belief that it is correct, and we endeavour to keep it so - but we do make mistakes. Furthermore, over some subjects there are differing opinions, or differing degrees of certainty. We have usually not attempted to discuss these here because the aim has been to provide an immediate and brief guide. In all areas, prior medical knowledge is assumed. The EdRenHANDBOOK is not suitable for use by those without such a background. Contact us by email or at the address given at the foot of the contents page with any comments or corrections.
Immunosuppression

Abbreviated medical protocols from EdREN, the website of the Renal Unit of the Royal Infirmary of Edinburgh

- Methyl Prednisolone 500 mg IV just prior to releasing clamps and again at 24 hours.
- **Standard** immunosuppression will be Tacrolimus (FK506) led triple therapy.
  - **Tacrolimus** 0.1 mg/kg/day given as two doses at 1000 and 2200
  - **Prednisolone** 20 mg once daily at 0800
  - **Azathioprine** 1-2 mg/kg (usually 75-100 mg) once daily at 0800

- **Patients who have an increased risk** of rejection will receive Tacrolimus led triple therapy, but with MMF substituted for Azathioprine.
  - **Tacrolimus** as per standard regime
  - **Prednisolone** as per standard regime
  - **Mycophenolate Mofetil** 2 grams/day given as two doses at 0800 and 2000 (note: not at the same time as Tacrolimus)

**High risk Patients Include:**

- Previously sensitised patients - those with panel reactive antibody titres of > 50%.
- FACS +ve crossmatch
- B cell +ve crossmatch
- More than one transplant in the past
- Past episodes of graft loss due to acute rejection
- HLA mismatch - non favourable
Basiliximab

May also be given to patients with expected delayed graft function to allow reduced Tacrolimus dose (0.05mg/kg/day given as two doses), and sometimes to patients believed to be at increased risk of rejection.

Links

Treatment of acute rejection


NOTE that the accuracy of any statements in this information CANNOT be guaranteed. It is published in the belief that it is correct, and we endeavour to keep it so - but we do make mistakes. Furthermore, over some subjects there are differing opinions, or differing degrees of certainty. We have usually not attempted to discuss these here because the aim has been to provide an immediate and brief guide. In all areas, prior medical knowledge is assumed. The EdRenHANDBOOK is not suitable for use by those without such a background. Contact us by email or at the address given at the foot of the contents page with any comments or corrections.
Live kidney donor management

Abbreviated medical protocols from EdREN, the website of the Renal Unit of the Royal Infirmary of Edinburgh

Live kidney donors should be managed as follows.

- Live kidney donors will be seen at the Transplant Assessment Clinic two weeks prior to the scheduled transplant date.
- Blood samples will be taken at this visit for:
  - repeat virology
  - lymphocytotoxic crossmatch
  - advance group and save

- Admission is arranged 24 hours pre-op to the Transplant Unit. In exceptional circumstances if there are no beds available on Ward 206 then a bed will be found for the donor according to the nurse-charge of ward 206 in liaison with the hospital bed-manager.
- On admission the donor should have received a full physical examination; blood pressure; temperature; urinalysis and urine specimen sent to bacteriology.
- **No** pre-op X-Ray/ECG/ blood tests are necessary unless requested by Consultant.
- Written consent for a nephrectomy should be obtained by the Consultant Transplant surgeon.
- All donors should receive DVT prophylaxis with TED stockings, intra-operative pneumatic compression and heparin. Post-operative: heparin sub-cut 5000u BD.
  - Pre-op heparin should not be administered unless the Consultant Anaesthetist specifically requests.
  - Post-op fluid management: 4 - 6 hourly dextrose/saline.

Any problems should be reported directly to the Consultant Surgeon.
NOTE that the accuracy of any statements in this information CANNOT be guaranteed. It is published in the belief that it is correct, and we endeavour to keep it so - but we do make mistakes. Furthermore, over some subjects there are differing opinions, or differing degrees of certainty. We have usually not attempted to discuss these here because the aim has been to provide an immediate and brief guide. In all areas, prior medical knowledge is assumed. The EdRenHANDBOOK is not suitable for use by those without such a background. Contact us by email or at the address given at the foot of the contents page with any comments or corrections.
PRETRANSPLANT - kidney offers

Abbreviated medical protocols from EdREN, the website of the Renal Unit of the Royal Infirmary of Edinburgh

Local retrieval

Once a kidney becomes available, the following procedure should be observed.

1. Tissue type to be established as soon as possible, usually from peripheral blood lymphocytes.
2. Tissue type will phone the results of donor tissue-type and results of highly sensitised patients to donor transplant co-ordinator. Tissue typist will also fax tissue type results to UK Transplant (UKT)
3. UKT will inform the donor transplant co-ordinator of the allocation of the kidneys as per National and Scotland & Northern and Ireland allocation schemes so that the kidneys can be packed and addressed to the appropriate centre.

UKT Offer of a Kidney

1. The on-call donor/renal recipient transplant co-ordinator will receive the offer of a kidney from UKT.
2. Transplant co-ordinator contacts transplant surgeon and asks for a decision as to whether the kidney should be accepted.
3. If the decision has been made to go ahead, then the transplant co-ordinator contacts the patient's own local Consultant Nephrologist and the RIE on call Consultant Nephrologist, to ensure that the patient is fit and should be called.
4. Transplant co-ordinator performs the following tasks:
   - Contact of the patient.
   - Arrangement of transport for the patient and his/her notes to the renal transplant unit; NB. APD patients to bring own machine.
   - Alert renal transplant unit and give details of patient and
dialysis needs.

- Alert the renal registrar with the patient details.
- Alert the tissue typist with the patient details.

5 It is the responsibility of the surgeon and the transplant co-ordinator to
arrange theatre and inform the anaesthetist to book the first available
operating space.

6 It is the responsibility of the renal registrar to ensure the chosen patient is
adequately dialysed and medically fit prior to operation.

7 The on-call renal / transplant SHO also liaises with BTS regarding
    grouping and saving.

Patients from other centres (Fife, Dundee, Aberdeen &
Inverness)

1 Transplant co-ordinator will discuss the patient with surgeon and patient's
local nephrologist. If the kidney is to be accepted, the transplant
co-ordinator will also inform the RIE consultant nephrologist on call.

2 The nephrologist or the transplant co-ordinator to contact the patient and
arrange transport of the patient to the RIE.

3 The nephrologist arranges the patients notes and x-rays to be sent to the
    transplant unit ASAP.

4 If the patient requires dialysis this to be organised in Edinburgh. The
    MRSA and virology status of the patient must be known.

5 As per 4-7 above.

When the kidney arrives at the Unit

- The kidney will arrive at the Transplant Unit HDU Ward 117.
- Check that the kidney is surrounded by sufficient ice, if not, top up. (This
  is the responsibility of Ward 117 Nursing staff).
- Send spleen and lymph nodes to BTS for lymphocytotoxic crossmatch.
  Please ensure that a SNBTS histocompatibility platelet immunohaematology
  form is completed and sent with the lymph node and spleen to tissue-typing.
Note: Two kidneys may arrive in UNit if the kidneys are from a local donor. These kidneys will be allocated according to UKT and may need to be sent to another centre. For kidney allocation rules please see UK Transplant web site.

In this case the box containing the kidney to be sent should not be disturbed, it will be picked up by the courier service as arranged by UKT. UKT will inform the transplant unit where the kidney is going to. Transplant unit to clearly write name and address of where the kidney is going. Check with UKT whether it is right or left kidney if in any doubt contact donor transplant co-ordinator.
Mycophenolate Mofetil (MMF)

This page describes the Edinburgh regimen for the use of the immunosuppressant Mycophenolate Mofetil.

Current indication

As a substitute for azathioprine in alternative triple therapy regimen for patients at high risk of rejection and following resistant rejection in patients treated with standard triple therapy.

Dose

- (500 mg to) 1g twice daily, depending on concomitant immunosuppression and renal function.
- MMF is best absorbed on an empty stomach, either one hour before or two hours after a meal, but gastrointestinal side-effects may be alleviated by taking MMF with food and further splitting the daily dose.
- Monitoring of MMF blood levels is not needed.

Mode of action

- MMF is rapidly hydrolysed following absorption to mycophenolic acid (MPA), the active metabolite.
- MPA is a potent inhibitor of inosine monophosphate dehydrogenase (IMPDH) and therefore inhibits the denovo pathway of guanosine nucleotide synthesis.
B and T lymphocytes are critically dependent on the de novo pathway and so MPA inhibits B and T lymphocyte proliferation and also B-cell antibody formation.

**Preparation**

MMF is available as 250 mg capsules (blue-brown) and 500 mg tablets (lavender). The brand name is **CELLCEPT**.

**Contra-indications**

Pregnancy

**Side-effects**

- neutropenia
- gastro-intestinal bloating
- cramps
- diarrhoea
- vomiting

**Drug Interactions**

- Tacrolimus increases the AUC of MPA, the active metabolite of MMF. By 3 months past transplant the increase is such that the dose of MMF may need to be reduced with time post-transplant to maintain stable systemic exposure to MPA.
- Cholestyramine and antacids - may bind MMF and significantly reduce its absorption.
- Drugs which undergo tubular secretion e.g., Aciclovir, theoretically may impair secretion of MMF and have raised blood levels themselves during concurrent administration.
Drugs which interfere with enterohepatic recirculation potentially may reduce the efficacy of MMF.
Pneumocystis Prophylaxis

Standard prophylaxis is cotrimoxazole 480mg once daily for the first three months. If extra treatment for acute rejection has been required, prophylaxis should extend to 3 months after that treatment.

Desensitisation should be considered if patients are unable to tolerate low dose Co-trimoxazole for PCP prophylaxis.

**Desensitisation protocol**

**First Line**

*Paediatric Co-trimoxazole suspension (240mg/5ml) diluted 1:20. (2.4mg/ml Co-trimoxazole).*

<table>
<thead>
<tr>
<th>Day</th>
<th>Volume</th>
<th>Dose of Sulphamethoxazole</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1ml</td>
<td>2mg</td>
</tr>
<tr>
<td>2</td>
<td>2ml</td>
<td>4mg</td>
</tr>
<tr>
<td>3</td>
<td>4ml</td>
<td>8mg</td>
</tr>
<tr>
<td>4</td>
<td>8ml</td>
<td>16mg</td>
</tr>
<tr>
<td>5</td>
<td>12ml</td>
<td>24mg</td>
</tr>
</tbody>
</table>

*Paediatric Co-trimoxazole suspension (240mg/5ml)*

<table>
<thead>
<tr>
<th>Day</th>
<th>Volume</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>1.25ml</td>
<td>50mg</td>
</tr>
<tr>
<td>7</td>
<td>2.5ml</td>
<td>110mg</td>
</tr>
<tr>
<td>8</td>
<td>5ml</td>
<td>240mg</td>
</tr>
<tr>
<td>9</td>
<td>10ml</td>
<td>480mg</td>
</tr>
<tr>
<td>10</td>
<td>10ml/1 tablet</td>
<td>480mg</td>
</tr>
</tbody>
</table>

**Second Line**

Dapsone 100mg od

Consider dose reduction to 50mg od in severe renal dysfunction (reatinine clearnace <10ml/min).
Third Line

Nebulised pentamidine 300mg every 4 weeks - details from pharmacy.


NOTE that the accuracy of any statements in this information CANNOT be guaranteed. It is published in the belief that it is correct, and we endeavour to keep it so - but we do make mistakes. Furthermore, over some subjects there are differing opinions, or differing degrees of certainty. We have usually not attempted to discuss these here because the aim has been to provide an immediate and brief guide. In all areas, prior medical knowledge is assumed. The EdRenHANDBOOK is not suitable for use by those without such a background. Contact us by email or at the address given at the foot of the contents page with any comments or corrections.

Go to top of page

Go back to EdRenHANDBOOK contents page

Go to EdREN home page
# Post-op management of a renal transplant

Abbreviated medical protocols from [EdREN](http://renux.dmed.ed.ac.uk/EdREN/Handbookbits/TPHdbkbit...), the website of the Renal Unit of the Royal Infirmary of Edinburgh

## On return to the Unit

### Day one and early days

<table>
<thead>
<tr>
<th>Allograft biopsy</th>
<th>Three months</th>
</tr>
</thead>
</table>

### Early problems

<table>
<thead>
<tr>
<th>Early anuria</th>
<th>Outpatient review</th>
<th>Long-term follow-up</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Delayed graft function</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Graft dysfunction</th>
</tr>
</thead>
</table>

The page describes the immediate and later post-operative management of renal transplant patients in Edinburgh.

## On return to the Unit

1. Check FBC and Us&Es immediately post-op. Serum K+ must be known and result discussed with Registrar, if possible hyperkalaemia should be managed with Insulin/dextrose and nebulised Salbutamol rather than haemodialysis. Subsequent repeat Us & Es 12 hourly (more frequently if indicated or as decided by Registrar).

2. Arrange chest X-ray for position of central line.

3. Initial IV fluid replacement is Normal Saline at 40 mls/hr + last hour's output. This should be adjusted according to clinical assessment and CVP. Usual target CVP is 5-10 cm water. Boluses of Normal Saline (or colloid) may be needed to raise a low CVP. Failure of the patient to respond to IV Fluid with a rise in CVP or BP should raise possibility of bleeding. These measures should always be instigated by a senior member of staff. If there is a possibility of bleeding a transplant surgeon must be contacted.
4. Continuing IV fluid replacement should be maintained with alternating 5% Dextrose and Normal Saline initially - more dextrose if high volumes of urine.

5. Analgesia is by PCA morphine/Fentanyl. Inadequate pain relief may herald serious pathology and should be discussed with a senior surgical colleague/Anaesthetist. NSAIDs are absolutely avoided. Live donors will receive an epidural infusion (see Appendix VI).

Immunosuppression

See Immunosuppression section

Infection prophylaxis

All patients on triple therapy receive COTRIMOXAZOLE 480mg daily for the first three months to prevent Pneumocystis carinii pneumonia. For more info see Pneumocystis page. If the patient is sensitive to Septrin then the Sulphonamide de-sensitisation protocol should be instigated. (See Pneumocystis).

For the management of CMV negative recipients who receive a kidney from a CMV positive donor refer to the CMV protocol.

Blood Tests

- U's & E's daily marked "PRIORITY"; result returned by fax
- FBC daily
- LFTs, glucose, urate, Ca and PO4 - daily
- Tacrolimus or Ciclosporin level - M/W/F
- MSU each Monday and at other times if clinically indicated
- Chart all results on flow sheets and plot creatinine on log graph daily

Tubes and Drains
Redivac drain removed at 24 - 48 hours at surgeon's discretion.

Urinary catheter removed at day 5 unless

- the patient is anuric (may be removed earlier)
- the patient is polyuric (may be removed later)

**Post-op Anuria**

Check catheter function. Gentle catheter irrigation should only be performed after surgical consultation and preferably by the surgeon. Seek advice urgently if urine output has started but subsequently ceased.

**Graft Dysfunction**

Any drop in urine output, rise in creatinine or change in log creatinine slope should be discussed immediately with a senior colleague. Management will depend on the clinical situation but acute rejection must always be suspected. The physical signs are often absent and urgent investigation is required.

- Review fluid tolerance and clinical signs (fluid balances, graft tenderness, wound)
- Check Tacrolimus / Ciclosporin result, and also show lymphoreoel etc.
- Graft ultrasound scan - will exclude obstruction.
- Graft Doppler - assesses flow in renal artery and vein (may also comment on intra-renal vascular resistance).
- Graft biopsy - for definite diagnosis of rejection.

**Renal Allograft Biopsy**

A routine graft biopsy is preformed around day 5 if there is a delayed graft function and subsequently at weekly intervals until function is established. This is to diagnoses acute rejection co-existing with ATN.

Any deterioration in graft function may require a graft biopsy which will be requested by a senior member of staff. Refer to full biopsy protocol.

**Treatment of Rejection**
See **approach to altered graft function** and **full protocol for treatment of rejection**

### Delayed graft function

Due to prolonged ischaemic times/ATN etc., not all kidneys function immediately and some take a few days or even weeks before functioning. During this time the aim is to ensure that we are not missing concomitant rejection or other catastrophe.

**DAY 1**
- Duplex scan
- Routine immunosuppression.
- Alternatively Basiliximab may be given Day 0 and Tacrolimus dosage halted.

**DAY 5**
- If no evidence of improvement then biopsy to exclude rejection.

**Around DAY 12**
- Repeat Duplex/biopsy.

### Discharge and follow-up

Uncomplicated patients usually discharged day 10-14.

See below for patients from other hospitals. Patients are usually seen three times monthly at first, in the OPD1 Transplant Clinic on Monday, Wednesday and Friday mornings. An appointment and transport if required must be arranged prior to discharge. If there is no clinic or if patient needs to be seen more frequently then they will be seen in Ward 206 following discussion with the nurse in-charge.

Appointments in ward 206 - If patient needs to attend for bloods on day when there is no transplant clinic in OPD1 the patient will attend ward 206. Appointments should be recorded in the Diary including what tests are required, any special arrangements and the date of the next appointment. Patients should always attend before 9.15 am so that their drug assays may be run the same day. Blood forms should be completed in advance so that the phlebotomist can take their blood during the ward round.

Tacrolimus / Ciclosporin / MMF shared care protocol must be included with the immediate discharge letter. Formal discharge summary is dictated as soon as possible.
Outpatient review

At each out-patient review the following are checked:

- Blood pressure, (pulse, temperature; if necessary)
- Weight
- Blood taken for U & Es, LFT, CAP, FBC and Tacrolimus/Ciclosporin
- MSU
- Urine dipstick
- Medication - any alteration to immunosuppression required should be documented on the patients medication sheet which was issued to the patient on discharge, and up-dated on the patient's computerised record by the clinician making the alteration.
- PTH checked 1 month, 3 months and 6 months.

Results of out-patient bloods must be checked as soon as possible and patients may be recalled for repeat checks or 'phoned' to alter their dose of Tacrolimus/Cyclosporin. Any alteration to dose should be documented in the patients case notes and on the drug screen of Proton.

Patients from other units (Aberdeen, Dundee & Inverness)

Transferred when stable as an in-patient to the Renal Unit at the referring Hospital (as out patients only if recovery quick or transfer delayed).

Prior to discharge the centre must be contacted before and on day of discharge. A copy of the patient transfer details sheet (medical and nursing) (See Appendix 5) with a computer printout of the biochemistry, haematology, Tacrolimus results and discharge letter should accompany patient on transfer and/or faxed to receiving unit.

Patients from Fife

Transferred from Out-patient department when stable. A letter must be sent to the patient’s local consultant prior to transfer.

Return to top

Three months

- Ureteral Stent and CAPD catheter should be removed at this time unless specific reasons for leaving or removing earlier.

- Check PTH, Lipids.
- Prednisolone dosage should be 10mg in patients not treated for rejection (see *steroid reduction*)

**Six months**

- Check PTH, Lipids.
- Prednisolone dosage should be 5-7.5mg in patients not treated for rejection - consider withdrawal at 12 months (see *steroid reduction and withdrawal*)

**Long-term follow-up**

There are many factors to be considered. More detailed guidance is available in the outpatient protocols booklet, available separately. Major considerations besides graft function include:

- Immunosuppression: consider long-term level
- Urine infections
- Hypertension
- Hyperlipidaemia
- Glucose intolerance
- Arterial disease risk profile - weight, smoking, diet (lipids, hypertension)
- Gout and uric acid (note *dangerous interaction between allopurinol and azathioprine*)
- Bones - osteoporosis, renal osteodystrophy, hyperparathyroidism
- SKIN - sun avoidance, surveillance
- Contraception
- Pregnancy advice
- Cervical smears - annually

**Late (>3 months) presentation with altered function**

Acute rejection and drug toxicity remain important causes at all stages of a transplant. Review all the features mentioned above under post-op management – graft dysfunction. Consider too:

- Recurrent primary disease
- Infection – polyoma virus, CMV or other
- Graft artery stenosis
Biopsies should be examined with all these possibilities in mind – so include samples for electron microscopy and immunofluorescence.

**Supplementary documents**

These are pdf files:

- [Transfer details form - Appendix 5](#)
- [Epidural analgesia policy - Appendix 6](#)

Transplant protocols developed on the Edinburgh Transplant Unit. This page first published September 2002, updated December 2006 and last modified Tuesday, January 23, 2007.

NOTE that the accuracy of any statements in this information CANNOT be guaranteed. It is published in the belief that it is correct, and we endeavour to keep it so - but we do make mistakes. Furthermore, over some subjects there are differing opinions, or differing degrees of certainty. We have usually not attempted to discuss these here because the aim has been to provide an immediate and brief guide. In all areas, prior medical knowledge is assumed. The EdRenHANDBOOK is not suitable for use by those without such a background. Contact us by email or at the address given at the foot of the contents page with any comments or corrections.

Go to top of page

Go back to EdRenHANDBOOK contents page

Go to EdREN home page
Preparing the recipient for a renal transplant operation

Abbreviated medical protocols from EdREN, the website of the Renal Unit of the Royal Infirmary of Edinburgh

History and examination

Investigations

Communication

Consent

Other Considerations

1. Full History and Examination

Particular points of note:

- **History**
  - cause of renal failure
  - dialysis - type, when commenced
  - time of last dialysis - normal target or dry weight
  - access and any related problems
  - Volume of urine output and history of past/present, urinary tract problems
  - infections - any recent
  - CAPD peritonitis/exit site/access related
  - other operations
  - ischaemic heart disease
  - peripheral vascular disease

**Recipient** blood group, tissue typing and virology (CMV, EBV, HIV, Hep B & C) **must** be recorded in the notes.

**Donor** details should also be included in recipient clerking - age, cause of death, blood group, tissue typing, virology and ischaemic time. The transplant co-ordinator will provide this information. **Avoid noting any further details that could compromise donor confidentiality if read by the patient.**
**Examination** - a full physical examination of the patient should be performed and should include observation of

- fluid status
- peripheral pulses
- abdominal scars/hernias

2. Investigations

**Blood Tests**

(Phone laboratory to alert staff that sample is arriving)

60-70 mls blood required and should be taken as soon as patient is admitted.

- *FBC
- *U&E’s + creatinine
- Baseline calcium/LFT’s (results available post-op)
- *Clotting screen/INR (if on Warfarin)
- *Tissue Typing (white clotted bottle for lymphocytotoxic Antibody, plus 5 ml EDTA sample) See Apendix IV
- Virology - CMV, HIV, Hep B + C (only if >1/12 since last test)
- *Glucose
- BM test on ward

*Asterisked results must be requested as urgent.

If patient requires dialysis pre-op, repeat biochem 30 mins after dialysis.

**Chest X-ray**

**MSSU** - for gram stain and subsequent culture

**PD fluid** - for WCC and gram stain / culture if appropriate
3. Communication

- **Patient** (See also consent section below)

  Ensure potential recipients are aware that they will not definitely be getting the kidney until the result of the cross-match is known.

  Inform patient re: ureteric stent insertion with cystoscopic removal required at 3 months, (usually as a day case). CAPD catheter also removed at the same time as ureteric stent. Do not give donor info to the recipient beyond what is necessary to explain any particular risks/techniques of the transplant.

  Patients who are not suitable for transplant need discharge sheet with appropriate reasons.

- **Staff**

  Inform theatre and anaesthetist of any special problems.

4. Consent

Consent for HIV test - verbal consent should be obtained by the physician who clerks in the recipient

Consent for the transplant operation should be obtained by the transplant surgeon (mention central line, surgical drain, urinary catheter and ureteric stent).
5. Other Considerations

Diabetes

Subcutaneous insulin should be omitted.

Insulin / Dextrose infusion must be established pre-operatively: standard sliding scale -

- **BM < 6 mmol/l**
  - add 6 units Actrapid in 500mls Glucose 10%
- **BM 6 - 9 mmol/l**
  - add 10 units Actrapid in 500mls Glucose 10%
- **BM >9 mmol/l**
  - add 14 units Actrapid in 500mls Glucose 10%

Run Infusion @ 100 ml/hr and check glucose (BM stick) hourly

Anti-viral and CMV prophylaxis

Further info in dedicated section

Rhesus Sensitisation

Rh-ve young female recipients with Rh +ve donor require anti D immunoglobulin at induction (can be given up to 72 hours later if overlooked initially).


NOTE that the accuracy of any statements in this information CANNOT be guaranteed. It is published in the belief that it is correct, and we endeavour to keep it so - but we do make mistakes. Furthermore, over some subjects there are differing opinions, or differing degrees of certainty. We have usually not attempted to discuss these here because the aim has been to provide an immediate and brief guide. In all areas, prior medical knowledge is assumed. The EdRenHANDBOOK is not suitable for use by those without such a background. Contact us by email or at the address given at the foot of the contents page with any comments or corrections.

Go to top of page
Prednisolone

Abbreviated medical protocols from EdREN, the website of the Renal Unit of the Royal Infirmary of Edinburgh

This page describes the Edinburgh regimen for the use of the immunosuppressant Prednisolone.

**Reduction; Withdrawal; Prevention of osteoporosis**

### Prescription and reduction

Prednisolone is normally reduced according to the following schedule:

- 20 mg daily x 1 month started on day 2
- 15 mg daily x 1 month
- 10 mg daily x 1 month
- 5 mg daily thereafter

This schedule may be altered if rejection occurs.

All patients to receive Ranitidine (150 mgs od) along with Prednisolone.

After 3 months continue minimum of 5 mg or 7.5 mg if >75 kg in weight.

Keep on maintenance dose until the end of the first year and then review.

At one year, cessation of prednisolone should be considered - see steroid withdrawal protocol. Caution should be exercised in patients with an "increased risk" of rejection. Cautions relating to Steroid withdrawal include:

- FACs + ve
- >2 transplants
- Panel reactive antibodies >50% / highly sensitised patients
- Rejection episodes >1 or more acute rejection episodes Banff grade > II
- Late acute rejection i.e., occurring after 6 months
Steroid withdrawal

Steroid withdrawal should be discussed with the patient and they should be informed of the risk of rejection. The steroids should be withdrawn according to the following schedule.

- Decrease by 1mg per month til 0mg
- Monthly measurements till at least 3 months after cessation

Steroid-induced osteoporosis

All patients should receive additional elemental calcium, this may be as one or two tablets per day depending on dietary intake.

- If GFR > 50 mls/min AdCalD3 (or similar) should be used.
- If GFR < 50 mls/min Alfacalcidol and Calcichew should be used.

Bisphosphonates

IV Pamidronate may be used in the initial post transplant period in patients with known osteopenia or osteoporosis, a history of one or more previous transplants, 2 or more episodes of rejection (treated with high dose steroid therapy) or a history of previous disease management with steroids.

All patients should be given advice on:

- Diet
- Weight
- Exercise
- Smoking cessation

NOTE that the accuracy of any statements in this information CANNOT be guaranteed. It is published in the belief that it is correct, and we endeavour to keep it so - but we do make mistakes. Furthermore, over some subjects there are differing opinions, or differing degrees of certainty. We have usually not attempted to discuss these here because the aim has been to provide an immediate and brief guide. In all areas, prior medical knowledge is assumed. The EdRenHANDBOOK is not suitable for use by those without such a background. Contact us by email or at the address given at the foot of the contents page with any comments or corrections.
Sirolimus

(Rapamune - should not be prescribed as rapamycin)

Abbreviated medical protocols from EdREN, the website of the Renal Unit of the Royal Infirmary of Edinburgh

This page describes the Edinburgh regimen for the use of the immunosuppressant sirolimus.

**Indication**

As an adjunct or substitute to a calcineurin phosphatase inhibitor for immunosuppression in patients in whom ciclosporin/tacrolimus have been implicated in allograft pathology.

**Contra- indications**

Hypersensitivity to Sirolimus and its derivatives

Pregnancy and breast feeding

**Presentation, Dosage and Administration**

* 1mg and 2mg tablets. Doses should be given on an empty stomach.

<table>
<thead>
<tr>
<th>Day</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>8mg daily</td>
</tr>
<tr>
<td>2</td>
<td>6mg daily</td>
</tr>
<tr>
<td>3+</td>
<td>2mg daily adjusted according to levels</td>
</tr>
</tbody>
</table>
Monitoring

Target range 5-15ng/ml depending on whether it is an adjunct to or substitute for a CNI.

Side Effects

- Raised triglycerides and cholesterol
- Thrombocytopenia
- Mouth Ulceration
- Anaemia
- Neutropenia
- Proteinuria
- Hypokalaemia
- Arthralgia
- Epistaxis
- Delayed wound healing
- Lymphocele
- Rash
- Oedema
- Infections
- PTLD
- Diarrhoea
- Pulmonary syndrome

Drug Interactions
Compounds which modulate CYP3A4 activity may effect Sirolimus levels. Drugs and substances which may increase sirolimus levels include:

- Diltiazem
- Azole antifungals
- Macrolide antibiotics
- Prokinetic agents
- Grapefruit
- Bromocriptine
- Cimetidine
- Danazol
- Protease inhibitors

Drugs which may decrease Sirolimus levels:

- Anticonvulsants
- Rifampicin

Caution should be exercised with concomitant administration of nephrotoxic drugs.


NOTE that the accuracy of any statements in this information CANNOT be guaranteed. It is published in the belief that it is correct, and we endeavour to keep it so - but we do make mistakes. Furthermore, over some subjects there are differing opinions, or differing degrees of certainty. We have usually not attempted to discuss these here because the aim has been to provide an immediate and brief guide. In all areas, prior medical knowledge is assumed. The EdRenHANDBOOK is not suitable for use by those without such a background. Contact us by email or at the address given at the foot of the contents page with any comments or corrections.

Go to top of page

Go back to EdRenHANDBOOK contents page

Go to EdREN home page
Renal Allograft Biopsy

Abbreviated medical protocols from EdREN, the website of the Renal Unit of the Royal Infirmary of Edinburgh

Renal allograft biopsies are usually performed under USS guidance in x-ray department by the radiologist. Urgent biopsy requests should be discussed with a Consultant Radiologist.

All patients must have:

Consent - must be obtained by the doctor requesting the biopsy, and patients informed of risks:

- significant bleeding (requiring blood transfusion / further surgical intervention) is approximately 1-2%.
- the risk of graft loss is <1 in 250 biopsies.

Clotting screen - For biopsy to proceed results required:

- Platelets > or = to 60 x 109L
- PT - prolongation of < 3 seconds.
- if patient on Warfarin an INR of < or = 1.5. APTT normal.

Group and save

Heparin discontinued

Aspirin / Warfarin discontinued

Fluids only for a while before the procedure.

Results, Consent Form and Pathology Form must be attached to front of case notes for the attention of radiologist. If samples are required for EM and immunofluorescence then this must be clearly indicated on the request card. These are required if de novo / recurrence of a primary glomerulonephritis is suspected – consider in any biopsy more than 3 months post-transplant.

Pathology Department contacted and told of the biopsy and arrangements made to collect the specimens. INCLUDE request for electron microscopy and immunofluorescence in all samples over 3 months post transplant.

Pathology request forms must be filled in by the doctor requesting the biopsy. Unless otherwise stated it will be assumed that samples for light microscopy and frozen section are required. If sample for immunofluorescentce or electron microscopy is required this must be stated on the form.
Out of hours, the on call Pathologist can be contacted via RIE switchboard

Post biopsy observations – every 15 mins for first 30 mins, every 30 mins for 2 hours, 4 hourly.
Renal transplantation: anaesthetic protocol

Abbreviated medical protocols from EdREN, the website of the Renal Unit of the Royal Infirmary of Edinburgh

2007: this page replaced by Appendix 8 Anaesthetic protocol (pdf file)

Transplant protocols developed on the Edinburgh Transplant Unit. This page first published March 2002 by Amit Adlakha, updated November 2006 and last modified Tuesday, January 23, 2007.

NOTE that the accuracy of any statements in this information CANNOT be guaranteed. It is published in the belief that it is correct, and we endeavour to keep it so - but we do make mistakes. Furthermore, over some subjects there are differing opinions, or differing degrees of certainty. We have usually not attempted to discuss these here because the aim has been to provide an immediate and brief guide. In all areas, prior medical knowledge is assumed. The EdRenHANDBOOK is not suitable for use by those without such a background. Contact us by email or at the address given at the foot of the contents page with any comments or corrections.

Go to top of page

Go back to EdRenHANDBOOK contents page

Go to EdREN home page
Altered Graft Function

Abbreviated medical protocols from EdREN, the website of the Renal Unit of the Royal Infirmary of Edinburgh

An increase in creatinine may be caused by a number of processes, but common causes are:

- Rejection
- Infection, e.g. urine, CMV
- Tacrolimus / Ciclosporin toxicity
- Altered fluid balance

Less common causes are:

- Vascular catastrophe
- Mechanical problem - urinary obstruction (less likely if ureteric stent present), lymphocele

A patient whose creatinine has increased requires careful assessment, as the classic signs of rejection (pyrexia, tender graft) are rarely present with current immunosuppressive agents.

- Review patient's fluid status and fluid balance charts;
- Check FBC
- Note particular decrease in urine volumes, tender graft;
- Check for pyrexia;
- Culture urine, PD fluid;
- Consider CMV PCR and rapid culture.
- Get Tacro / CyA level
- Consider USS to exclude mechanical/vascular problem, with Duplex to confirm patency of major vessels

Transplant protocols developed on the Edinburgh Transplant Unit. This page first published in December 2006, last modified Sunday, January 14, 2007.

NOTE that the accuracy of any statements in this information CANNOT be guaranteed. It is published in the
belief that it is correct, and we endeavour to keep it so - but we do make mistakes. Furthermore, over some subjects there are differing opinions, or differing degrees of certainty. We have usually not attempted to discuss these here because the aim has been to provide an immediate and brief guide. In all areas, prior medical knowledge is assumed. The EdRenHANDBOOK is not suitable for use by those without such a background. Contact us by email or at the address given at the foot of the contents page with any comments or corrections.
Self-administration of medicines programme within the transplant unit, RIE

Abbreviated medical protocols from EdREN, the website of the Renal Unit of the Royal Infirmary of Edinburgh

2007: This page has been replaced by the pdf file Self-administration of Medicines (Appendix 9)

Transplant protocols developed on the Edinburgh Transplant Unit. This page first published March 2002 by Amit Adlakha. Last updated in December 2006 and last modified Tuesday, January 23, 2007.

NOTE that the accuracy of any statements in this information CANNOT be guaranteed. It is published in the belief that it is correct, and we endeavour to keep it so - but we do make mistakes. Furthermore, over some subjects there are differing opinions, or differing degrees of certainty. We have usually not attempted to discuss these here because the aim has been to provide an immediate and brief guide. In all areas, prior medical knowledge is assumed. The EdRenHANDBOOK is not suitable for use by those without such a background. Contact us by email or at the address given at the foot of the contents page with any comments or corrections.

Go to top of page

Go back to EdRenHANDBOOK contents page

Go to EdREN home page
Tacrolimus
(FK506/PROGRAF)

Abbreviated medical protocols from EdREN, the website of the Renal Unit of the Royal Infirmary of Edinburgh

This page describes the Edinburgh regime for the use of the immunosuppressant Tacrolimus.

Current indication
As the lead agent in standard triple therapy for all patients.

Dosage
0.1 mg/kg/day in 2 divided doses (normally between 2 mg and 5 mg bd).

Preparation
Tacrolimus is available as 0.5 mg (cream), 1 mg (white) and 5 mg (greyish red) capsules. The brand is Prograf.

Administration
- Oral route in most instances (well absorbed even in those with NG tubes).
- It is administered usually at 10 am and 10 pm.
- The capsules are taken on an empty stomach either 1 hour before or 2 - 3 hours after meals.
- Contents of the capsule can be suspended in water for NG administration.
- One fifth of the oral dose can be given as a continuous IV infusion in saline via non PVC bags/tubing if absolutely necessary.

Levels
Whole blood trough levels to be checked on Mondays, Wednesdays and Fridays. The target level for the first six months is 10 ng/ml (range 8-12 ng/ml) and 5-10 ng/ml after six months. In adult kidney transplant patients steady state may be reached 2-3 days after starting therapy or changing dose.

**Contra-indications**

Live vaccines are not to be given to immunosuppressed patients (see vaccinations).

Tacrolimus is contra-indicated in pregnancy. Since it is not known to what extent tacrolimus may influence the efficacy of oral contraceptives it is generally recommended that other forms of contraception be used.

**Side Effects**

- The most frequent side effects seen with tacrolimus include:
  - abnormal kidney function (similar to Ciclosporin)
  - tremor
  - headache
  - paraesthesiae

- Less common side effects are:
  - diarrhoea
  - hypertension
  - hyperglycaemia
  - hyperkalemia
  - hypomagnesaemia
  - visual and neurological disturbances (affected patients should not drive or operate machinery)
  - hypertrophic cardiomyopathy (in paediatric patients with trough levels >25 mg/ml).

**Interactions**

- *Potential interactions due to effects on hepatic microsomal enzymes.*

Tacrolimus is extensively metabolised via the hepatic microsomal cytochrome P450 3A4 isoenzyme. Concomitant use of substances known to inhibit or induce cytochrome P450 3A4 (CYP3A4) may affect the metabolism of tacrolimus. Therefore:

- Inhibitors of CYP3A4 may decrease metabolism of tacrolimus and thus increase tacrolimus blood levels, e.g.
Inducers of CYP3A4 may increase metabolism of tacrolimus and thus decrease blood levels, e.g.

- rifampicin
- phenobarbital
- phenytoin

(Drugs in red will require a dose adjustment of tacrolimus in nearly all patients. Other listed drugs may require dose adjustment only in individual cases).

Tacrolimus itself has a powerful inhibitory effect on CYP3A4. Thus concomitant use of tacrolimus with drugs metabolised by CYP3A4 dependant pathways may affect the metabolism of such drugs. For this reason Ciclosporin A should not be co-prescribed with tacrolimus. Patients switched from Ciclosporin to tacrolimus should receive the first tacrolimus dose at least 24 hours after the last Ciclosporin dose.

**Interactions due to cumulative toxicity/synergistic effects**

Concurrent use of tacrolimus with drugs known to have nephrotoxic or neurotoxic effects may increase the degree of toxicity. Enhanced nephrotoxicity has been observed with co-administration of:

- Cyclosporin A
- Amphotericin B
- Ibuprofen
- Sirolimus (Rapamune)

**Hyperkalaemia**

As Tacrolimus may cause hyperkalemia, high potassium intake or potassium sparing diuretics should be avoided.
**Interactions due to plasma protein binding of tacrolimus**

- Tacrolimus is extensively bound (>98%) to plasma proteins so competition with other highly protein bound drugs may result in displacement of either drug. This displacement may not be reflected in the blood levels of Tacrolimus or other drugs. Therefore, dosage adjustment may not be needed unless clinical signs and symptoms suggest otherwise.

**Other interactions**

- Vaccinations may be less effective and the use of live attenuated vaccines should be avoided.
- Administration of Tacrolimus with a meal of moderate fat content reduces the oral bioavailability of the drug.
- Complementary medicines may cause a variety of interactions (see more info).

This is not a comprehensive list of potential interactions with tacrolimus. For further information please ask a member of staff or consult the transplant unit pharmacist.
Treatment of Rejection

Abbreviated medical protocols from EdREN, the website of the Renal Unit of the Royal Infirmary of Edinburgh

**First Episode of Rejection**
Methylprednisolone 250mg IV for 3 days

- **Good Response**
  - Ensure adequate Tacrolimus levels

- **No Response**
  - Re-Biopsy
  - Consider MMF

- **Partial Response**
  - Steroid tail?
  - Switch to MMF?
  - Re-biopsy?

**Second Episode of Rejection**
OR Incomplete response to treatment of first Episode

- Methyl Prednisolone 500mg IV for 3 days
- Re-biopsy

If there is response add in MMF

If there is no response consider MMF or ATG/OKT3

**NB** Patients should receive PCP prophylaxis and CMV prophylaxis for 3 months from the time of the last dose of methyl prednisolone.
discuss these here because the aim has been to provide an immediate and brief guide. In all areas, prior medical knowledge is assumed. The EdRenHANDBOOK is not suitable for use by those without such a background. Contact us by email or at the address given at the foot of the contents page with any comments or corrections.
Vaccinations

Abbreviated medical protocols from EdREN, the website of the Renal Unit of the Royal Infirmary of Edinburgh

Pre-transplant, Post-transplant, Malaria/ yellow fever

Pre- Transplant

If previously unimmunised, adults should receive Polio, Tetanus and Diphtheria vaccines.

Administration of Pneumococcal, Menningococcal and Haemophilus Influenza type B vaccinations are desirable. Live Varicella vaccine may also be considered it is available on a named patient basis from pharmacy. Vaccinations should be documented in admission clerk in.

Post- transplant

Live vaccines should not be given to immunosuppressed patients. Influenza vaccine is inactivated and therefore safe.

The following are live vaccines:

- Oral Polio vaccine (OPV, Sabin)
- Oral Typhoid vaccine (Vivotif)
- Measles, Mumps, Rubella - MMR vaccine (MMR II, Priorix )
- Rubella vaccine (Erverax)
- BCG vaccine
- Varicella vaccine - not in UK
- Yellow fever (Arilvax)

Polio/Typhoid
There are inactive alternatives for the oral polio and typhoid vaccines. Household contacts of immunosuppressed patients should also receive the inactive polio vaccine as they will excrete live polio for up to 6 weeks post-vaccination if they receive the live polio vaccine.

Inactivated vaccine is available on a named patient basis via the pharmacy.

**MMR**

There is no risk of infection from vaccinees. Immunosuppressed patients who have come into contact with measles should receive HNIG (Human Normal Immunoglobulin) as soon as possible after exposure. HNIG may be given to pregnant women with proven Rubella infection where termination is unacceptable.

**Varicella**

Varicella Zoster Immunoglobulin (VZIG) is indicated in patients who have had significant exposure to Chickenpox or Herpes Zoster and who have no antibodies to the VZ Virus. If required VZIG should be administered within 7 days of the initial contact.

**Yellow Fever**

For patients intending to travel to countries where a Yellow Fever certificate is required they should obtain a letter of exemption from a medical practitioner. Yellow Fever occurs in tropical Africa and South America. Up-to-date information is available from a pharmacy or WHO publications.

**Malaria Prophylaxis**

Up to date information on Malaria prophylaxis for a given destination is available from pharmacy.

The following table gives an indication of interactions:

<table>
<thead>
<tr>
<th></th>
<th>Tacrolimus</th>
<th>Ciclosporin</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Choloroquine</strong></td>
<td>? increased tacrolimus (cP450 3A4)</td>
<td>increased CyA (CP450 3A4)</td>
</tr>
<tr>
<td>Medicine</td>
<td>Interaction Description</td>
<td>No interactions likely</td>
</tr>
<tr>
<td>------------</td>
<td>-----------------------------------------------</td>
<td>------------------------</td>
</tr>
<tr>
<td>Proguanil</td>
<td></td>
<td>No interactions likely</td>
</tr>
<tr>
<td>Mefloquine</td>
<td>? increased tacrolimus (displacement from plasma protein)</td>
<td>No interactions likely</td>
</tr>
<tr>
<td>Doxycycline</td>
<td>? increased tacrolimus (CP450 3A4)</td>
<td>increased CyA (CP450 3A4)</td>
</tr>
</tbody>
</table>

Transplant protocols developed on the Edinburgh Transplant Unit. This page first published March 2002 by Amit Adlakha, updated December 2006 and last modified Sunday, January 14, 2007.

NOTE that the accuracy of any statements in this information CANNOT be guaranteed. It is published in the belief that it is correct, and we endeavour to keep it so - but we do make mistakes. Furthermore, over some subjects there are differing opinions, or differing degrees of certainty. We have usually not attempted to discuss these here because the aim has been to provide an immediate and brief guide. In all areas, prior medical knowledge is assumed. The EdRenHANDBOOK is not suitable for use by those without such a background. Contact us by email or at the address given at the foot of the contents page with any comments or corrections.
Transplant Recipient Check List and Summary
(Please read in conjunction with referral letter)

<table>
<thead>
<tr>
<th>Patient ID Sticker</th>
<th>Date:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Renal Consultant:

Referring Doctor:

Referring Centre:

Primary Renal Disease:
Current Dialysis Modality:
Date of 1st RRT:
Estimated ESRF date:
Weight: BMI: Allergies:

Previous Transplant History:

Date of Transplant:

Reason for Failure:

Date of Failure:

<table>
<thead>
<tr>
<th>Other Conditions</th>
<th>Y/N</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ischaemic Heart disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Respiratory Disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peripheral Vascular Disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>GI disease / Activity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urological History</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TB</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smoker</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Investigation Checklist

<table>
<thead>
<tr>
<th>Test</th>
<th>Done (✓)</th>
<th>Normal/Abnormal</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>FBC</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LFTs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Virology</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hep B</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hep C</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HIV</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CMV</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VZV</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EBV</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blood Group</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tissue Typing</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anti-HLA Ab</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CXR (within 6 months)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EGC</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Renal USS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MSU</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urinalysis</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Recommended Pre-transplant clinical review

<table>
<thead>
<tr>
<th>Referrals</th>
<th>Y/N</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiology Opinion Requested</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urological Investigation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vascular investigation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Psychiatric opinion</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Up to date cervical smear</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Good dentition</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Referral Letter: Y / N
Date of Referral: 
Appointment Transplant Assessment Clinic: Y / N
Renal transplantation
All patients with ESRF should be considered for transplantation unless there are absolute contraindications.

Entry to the transplant list

Best Practice: Every local transplant service should agree criteria for the acceptance of patients onto the Transplant waiting list.

- Age, gender, social background or ethnicity should not influence entry onto the Transplant waiting list.

- Patients on the Transplant waiting list should undergo regular, structured review to ensure that they remain fit for transplantation.

Suitability for renal transplantation

Best Practice:

- A transplant surgeon and a nephrologist should formally assess all patients who wish to be considered for renal transplantation.

- At least 40% of dialysis patients in most units will be suitable for transplantation.

- All patients should be given specific and written information with regard to transplant procedures and outcomes, including discussion and consent in advance regarding the use of organs from marginal donors.

- Cardiovascular disease, diabetes, previous malignant disease and other comorbidity should be assessed and recorded. Assessment should be repeated at least annually while on the waiting list.

- Patients should be placed on or permanently removed from the transplant list only after discussion and with the agreement of transplant surgeons, nephrologists and the patients themselves. The decision should be recorded in the patients’ notes.
Guidelines to be used with the Renal Transplant Assessment Check List

**Patient ID**  As computerised label
*Rationale:* Correct identification of all results for given patient

**Nephrologist**
*Rationale:* Direct liaison to appropriate consultant from Transplant assessment team

<table>
<thead>
<tr>
<th>Wt</th>
<th>kg</th>
<th>Ht</th>
<th>cm</th>
<th>BMI</th>
<th>kg/m^2</th>
</tr>
</thead>
</table>

*If BMI >30, refer for dietary advice and weight loss programme*

*Rationale:* Obesity increases the risk of technical failure
Baseline for monitoring weight changes post transplantation

BMI of greater than or equal to 40 is an ABSOLUTE contra-indication to transplant
BMI of 35-40 is a relative contra-indication to transplant. Other factors such as diabetes, cardiovascular risk, waist/hip ratio and peripheral vascular disease should be taken into account, and patients will be considered on a case to case basis.

**Allergies**
*Rationale:* 

**Original Disease**
*Rationale:* Risk of recurrence and early graft failure must be discussed with patient

<table>
<thead>
<tr>
<th>Smoker</th>
<th>Malignancy</th>
<th>IHD</th>
<th>VU reflux</th>
</tr>
</thead>
<tbody>
<tr>
<td>DM</td>
<td>Peptic Ulcer</td>
<td>PVD</td>
<td>Neurogenic bladder</td>
</tr>
<tr>
<td>HBV</td>
<td>HCV</td>
<td>TB</td>
<td>Kidney Stones</td>
</tr>
</tbody>
</table>

See comorbidity

**Hypertension**  Y/N  BP /  Anti HT Rx
*Rationale:* Uncontrolled Hypertension associated with significant cardiovascular disease/anaesthetic risk
Baseline data - hypertensive effects of immunosuppressives

**Date of first Dialysis / Type / Access / Previous Transplant ± Nephrectomy**

**Dialysis History**
*Year  RRT mode*

*Rationale:* Longer time on RRT = poorer outcome
Collected as registry data
Ischaemic Heart Disease

UK Transplant 2003 Waiting list criteria

**Absolute contraindication**
IHD the prognosis of which cannot be improved by revascularisation and/or cardiac failure with a predicted risk of death greater than 50% at 5 years.

**Suggested Algorithm (J Sim, Dundee)**

```
  Symptomatic
   ↓
  Asymptomatic
   ↓
  Abnormal
   ↓
  Normal
   ↓
  ECG
   ↓
  Normal
   ↓
  LIST
   ↓
  Exercise Tolerance Test or Thallium
   ↓
  Abnormal
   ↓
  Angiography
   ↓
  Treat
   ↓
  LIST
```

Above is for IHD.

Patients with Hx of severe hypertension or possible cardiac failure/valve lesions need ECHO.

* Will need liaison with local cardiology services

**Chronic Lung Disease**

**CXR** all

**Rationale:** information on lung injury/heart size; silent tumours in smokers.

**Pulmonary function tests** - if significant symptoms if significantly abnormal, respiratory opinion.

**Rationale:** Anaesthetic risk increased in chronic lung disease; increased risk of opportunistic infections in post-Tx period.
**Urological Abnormalities**

**Renal USS and bladder pre-post micturition** (within last year)
Discuss significant abnormalities with Tx Sx before referral

*Rationale:* Abnormal bladder drainage increases the risk of serious UTIs and poorer long term outcome
Polycystic kidneys, if large, may need to be removed to create space
Chronically infected kidneys/ stones may need to be removed to reduce infective risk post Tx
Risk of renal cell Ca in acquired cystic disease in pts on long-term RRT

**Peripheral Vascular Disease**

**Peripheral pulses absent/Bruits present** - ABPI/Duplex scanning (remember carotid)
Above positive or symptomatic - refer to vascular surgeon for assessment/intervention before Tx referral

*Rationale:* Technical problems if PVD present increasing risk of Tx/limb loss

**Drug Abuse (including alcohol) / Non-compliance / Psychiatric disorders**
Psychiatric assessment of all patients whose pre Tx state may influence compliance in post transplant period. Consider if
History of attempted suicide
Prior medical non-compliance
Psychosis
Inadequate neurocognitive function
Alcohol or Drug abuse
**Drug dependency** - Requirement (?) of 6 months abstinence before listing

*Rationale:* Poor drug compliance in post Tx period = kidney loss

**Viral Hepatitis / HIV / Other chronic infections**

**Hep B/C pos:** Assessment by hepatologist.
*Rationale:* may require liver Bx/ interferon pre Tx, ? combined liver/kidney Tx
Hep B sAg pos are at inc risk of death post Tx compared to sAg neg and inc risk of progressive liver disease and should be informed

**HIV pos:** will be considered on a case by case basis

**Chronic bacterial infection:** (including TB) must be clear of infection off antibiotics before referral. In some cases eg. chronic suppurative bronchiectasis, this may not be possible.

If there is a suggestion of previous exposure from CXR and incomplete or no treatment for TB, prophylaxis with anti-TB chemotherapy should be considered

**Other**

**Dental Clearance**
*Rationale:* Source of infection post Tx

**Cancer Screening**
*Last cervical smear in* all women
*Last mammogram* women >40
*Pelv/Vag US* if above pos or symptoms
*Rationale:* Candidates >50 yrs should be screened for pre-existing cancer
  - Initial Hx and examination should be done with this in mind
  - Many early bowel Ca asymptomatic
  - Done in yearly assessment post Tx

**Previous thrombotic history/family history**
  - Thrombophilia screen
*Rationale:* Graft loss due to vascular thrombosis higher
  - Increased risk of post-op DVT/PE
TRIGGERS TO PSYCHIATRIC REFERRAL IN RENAL TRANSPLANT ASSESSMENT

(cadaveric kidney, combined kidney & pancreas, live donor kidney transplant)

Pre-transplant assessments cover a potentially wide range of factors, including at times psychological and psychiatric problems. The following are suggested as factors which may require patients to be referred on for psychiatric assessment, either in the Department of Psychological Medicine at the Royal Infirmary (where Dr Potts will see most cases), or to local psychiatric services for those living at a distance from Edinburgh. The aims of these assessments are:

1. to identify patients who may need additional support before or after transplantation and to engage them with appropriate local support services.
2. to identify patients for whom transplantation may be inappropriate on psychosocial grounds.

FACTORS TO CONSIDER:

1. Active current substance misuse (where current means within the last six months)
   a) Alcohol – either
      - (i) high levels of consumption without harm;
      - (ii) harmful use
      - (iii) dependence
   b) Illicit drug misuse
   c) Dependence on prescribed medication (particularly for example opiates and/pr benzodiazepines)

2. Evidence of problematic non-compliance with current or previous medical treatments (including for example, insulin and other treatments for diabetes, anti-hypertensives, antibiotics and so on, and non-attendance at appointments in hospital clinics and primary care).

3. Evidence of mental illness which is either:
   a) current
   b) recurrent
   c) previous but severe

4. Most commonly any such mental illness will be depression, which can vary widely in severity but the following count as severe, even if currently stable and require further psychiatric referral:
   i) bipolar affective disorder
   ii) schizophrenia or other psychotic illness
   iii) learning disability or other cognitive impairments
5. Previous deliberate self-harm(either overdose or self-mutilation). Any episode within the last 5 years or a life total of more than 5 episodes should act as factors to trigger psychiatric referral.

6. Live Donors

Evidence of:
   a) Any of the above factors affecting potential donors, as well as recipients or
   b) Significantly dysfunctional family relationships particularly between the recipient and prospective donors.

If there is doubt about whether a psychiatric referral is appropriate or not, Dr Potts would be happy to discuss this.

Contacts:

Dr SG Potts
Consultant Liaison Psychiatrist
Renal Transplant Unit
Royal Infirmary of Edinburgh

0131 242 1398
fax: 0131 242 1393
email: psychmed.rie@luht.scot.nhs.uk
APPENDIX IV

Protocol for Tissue Typing and Antibody Screening
Royal Infirmary of Edinburgh
Scottish National Blood Transfusion Service / Renal Transplant Unit
March 2009

H&I work-up for Renal Transplant Recipients

HLA typing and HLA antibody screening for all East of Scotland patients/donors is carried out at the SNBTS H&I laboratory at the Royal Infirmary of Edinburgh.

Assessment for Renal Transplant Waiting List

Samples required:

1. HLA typing
   10ml Lithium Heparin
   10ml EDTA
2. HLA antibody screening
   10ml clotted sample
3. ABO blood group (sent to blood bank)
   4.5ml EDTA
4. Confirmatory HLA typing
   5ml EDTA

It is essential that a 10ml clotted antibody screening sample is received by the labs every 3 months so that a patient’s HLA antibody status can be updated and so that a crossmatch may be carried out prior to bringing in a patient for transplantation from a NHBD. The recipients Renal Consultant should arrange this sample.

Living Donor Transplants

Recipient samples required:

1. HLA typing
   10ml Lithium Heparin
   10ml EDTA
2. HLA antibody screening
   10ml clotted sample
3. ABO blood group (sent to blood bank)
   4.5ml EDTA
4. Confirmatory HLA typing
   5ml EDTA

Donor samples required:

1. HLA typing
   10ml Lithium Heparin
   10ml EDTA
2. ABO blood group (sent to blood bank)
   4.5ml EDTA
3. Confirmatory HLA typing
   5ml EDTA

Deceased Donor HLA Type and Crossmatch

Local (East of Scotland) Heart Beating Donors
HLA typing information is sent to UKT and a copy to the donor transplant co-ordinator. Information on which patient(s) to crossmatch will be relayed to the laboratory via the transplant coordinator.

If the donor is a potential pancreas donor then the H&I lab should be alerted at this time so that the crossmatch can commence.

Donor samples required:

1. HLA typing and KP XM 10ml Lithium Heparin
2. ABO blood group (sent to blood bank) 4.5 ml EDTA

Local (East of Scotland) Non Heart Beating Donors
HLA typing information is sent to UK Transplant and a copy to the donor transplant co-ordinator. On receipt of the local match run from UKT a decision will be made on which patient(s) to crossmatch.

Donor samples required:

1. HLA Typing and XM 20ml Lithium Heparin
2. ABO blood group (sent to blood bank) 4.5 ml EDTA

Patient samples required:

1. Crossmatch (allo and auto) 10ml clotted

Referred donors (imported)
Tissue samples (lymph nodes and spleen) should be sent to the H&I lab as soon as available to enable the crossmatch to be undertaken. The crossmatch test takes approximately 4 hours.

Donor samples required:

1. HLA Typing and XM Lymph nodes and spleen

Patient samples required:
1. Crossmatch (allo and auto)  
  10ml clotted  
  10ml EDTA
Dear Dr

Re: (Patient sticker)

This patient came to Royal Infirmary of Edinburgh in anticipation of a kidney or kidney/pancreas transplant. This was not performed for the following reason(s):

The patient has been told the following:

Signed

Fax copy of this form to the specific consultant:-
Aberdeen 01224 550713 (Dr Fluck/Dr Miller/Dr Waulbaum)
Aberdeen 01224 551134 (Dr Khan/Dr Brunton)
Inverness 01463 704586 (Dr Peel/Dr Lambie/Dr Joss/Dr Macdonald)
Fife 01383 627096 (Dr Wood/Dr Alfonso/Dr Buck/Dr Doyle)
Patient Transfer Details (Nursing)
This form must accompany all patients being transferred back to referring hospital following kidney or kidney/pancreas transplantation. A photocopy of this form should be filed in the transplant notes.

From: Transplant Unit, Royal Infirmary of Edinburgh
TO: ...............................................................

For completion by Transplant Nursing Staff

1. Ward informed by telephone of transfer □
2. Transport arranged □
3. Next of kin informed □
4. Valuables returned □
5. Own drugs returned □
6. Local notes/X-rays returned □
7. Drug chart photocopied and attached □
8. Urine out-put previous 24 hours: ...............mls
9. Most recent vital signs: Temp: BP: Pulse:
10. Further comments (i.e wound/diet/mobility / issues):

Signed............................................Block Capitals........................................

Position.........................................Date:........................................

Please do not hesitate to contact the transplant unit ward 206 if there is further information required:  Tel: 0131 242 2068   Fax:0131 242 2065
Patient Transfer Details (Medical)

This form must accompany all patients being transferred back to referring hospital following kidney or kidney/pancreas transplantation. A photocopy of this form should be filed in the transplant notes.

From: Transplant Unit, Royal Infirmary of Edinburgh

TO: .................................................................

For completion by Transplant Medical Staff (Renal Registrar)

1. Medical staff informed by telephone of transfer □
2. Type of transplant
   □ Cadaveric kidney
   □ Simultaneous kidney/pancreas
   □ Pancreas after kidney
   □ Pancreas alone
   □ Living donor kidney (relationship............................)

3. Pre transplant lymphocytotoxic crossmatch
   T cell........B cell............FACS T.........FACS B

4. HLA Mismatch ............... 

5. Immunosupression on discharge: .................................................................
   a. Most recent level............Date...../..../....
      Current dose .................

6. Dialysis required post transplant? Yes / NO (please circle)
   Indication: hyperkalaemia only Yes/No
   If yes date of last dialysis treatment............./...../.....

7. Episode of rejection? Yes / NO  Biopsy proven? Yes/NO (please circle)
   State Banff grade.................................................................
   If yes state treatment for rejection and dates.................................

8. Computer printout of Biochemistry, Haematology, Tacrolimus level results

Signed..............................................Block Capitals.................................

Position..............................................Date:.......................................... 

Please do not hesitate to contact the transplant unit ward 206 if there is further information required: Tel: 0131 242 2068      Fax:0131 242 2065

Discharge letter to follow:

Introduction

This policy complements but does not replace p24-32 of the LUHT “Guidelines for the Management of post-operative pain”. This is available in paper form and on the Intranet. Users are referred to this document for guidance on general principles of Epidural Analgesia, risks and Side Effects, patient Mobilisation and Epidural Catheter Removal.

This policy adds only comments specifically in relation to transplant patients which have been agreed by all the Transplant Anaesthetists.

Anaesthetist who places epidural will inform the pain team: Page 5247 (pain nurse) or 2140 (SHO)

1. Epidural Infusions of Local Anaesthetic and Opioids

There is one standard recipe for use in the Transplant Unit.

- Fentanyl 2µg/ml

These infusions run as prescribed by the anaesthetist on the epidural chart.

2. Co-prescribed Analgesia or Sedative Drugs

Analgesia

- Paracetamol 1g qds PO/PR given regularly while epidural running.
  - DO NOT give NSAID’s eg Diclofenac, Ibuprofen.
  - DO NOT give other opioids or sedative drugs with epidural opioids.

This includes Tramadol and Nefopam.

3. Duration of Epidural Analgesia

This will usually be for 72 hours. This should not hinder sitting out of bed or mobilising around the bed. The aim is to then go on to oral analgesia.

Mobilisation

One of the advantages of good quality epidural analgesia is that it allows mobilisation. This should be actively encouraged.

4. Failure of Epidural Analgesia

This is usually a partial failure and may be solved by catheter manipulation or top-ups by anaesthetic /pain staff. If however, this still fails, the standard position will be to change to:

- 0.1% Bupivacaine PLAIN (if the epidural still has any function) plus IV PCA
- Fentanyl or Morphine (depending on circumstances).

Patients in renal failure or post renal transplant use Fentanyl (NOT Morphine)
5. Step-down Analgesia After Epidural

DO NOT REMOVE EPIDURAL CATHETER UNTIL ORAL ANALGESIA IS ESTABLISHED AS EFFECTIVE

1. Continue Regular Paracetamol 1g QDS PO plus
2. Dihydrocodeine 30mg PO 4 hrly as required for pain to a maximum of 120mg in 24 hours – give a dose as the epidural infusion is turned off.
3. Tramadol 50mg 6hrly as required for pain in addition if significant pain despite the above, given to a maximum of 200mg in 24 hours.
4. If pain is still a problem, may need further time with epidural and needs discussion with anaesthetic/pain staff.

Top-Ups

Initial top-ups should be given as specified by the anaesthetist who places the epidural on the epidural form.

Contacts for Top-Ups or Problems with Epidurals/Pain

1. Transplant Anaesthetist – the anaesthetist who sited the epidural will have left contact details and times on the Epidural Chart.

2. Acute Pain Team – they will visit routinely to review patients with epidurals between 9 and 10am and again at about 5pm.

3. At other times:  
   Day: Pain Nurses Page 5247  
   And Top-Ups  
   Nights: General Duties Anaesthetic ST1/2 Page 2140

4. Emergencies:  
   Anaesthetic ST1/2 Page 2140  
   ICU Middle Grade Page 2306

Replacement Bags when they run out

The need for replacement bags is predictable and should not occur at unsociable times eg between 10pm and 9am. If a bag is going to run out overnight – inform page 2140 or 2306 before 10pm.

Dr Rory Mayes  
Consultant Anaesthetist
Appendix VII

Example Drug Kardex
Introduction
Valganciclovir is licensed for the prevention of cytomegalovirus (CMV) in CMV-negative patients who have received a solid organ transplant from a CMV-positive donor.

Shared Care
As outlined in the NHS circular 1962 (Gen 11) a consultant may seek the GP’s involvement in prescribing for a patient where there is a shared care agreement. This leaflet provides information on valganciclovir prophylaxis following solid organ transplantation and guidelines for the shared commitment between the consultant and GP concerned.

Absolute Contraindications
Valganciclovir is contra-indicated in patients hypersensitive to valganciclovir, ganciclovir, valaciclovir and aciclovir. It is also contraindicated in pregnancy and lactation.

Preparations Available
Valganciclovir is available as 450mg tablets (pink). The brand name is Valcyte®.

Recommended Dosage and Administration
Valganciclovir is rapidly and extensively metabolised to ganciclovir after oral dosing.

The initial valganciclovir dose is dependent on renal function as shown in the following table. Serum creatinine or creatinine clearance should be monitored every two weeks.

<table>
<thead>
<tr>
<th>Creatinine clearance (ml/min)</th>
<th>Prophylactic Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 60</td>
<td>900mg od</td>
</tr>
<tr>
<td>40 to 59</td>
<td>450mg od</td>
</tr>
<tr>
<td>25 to 39</td>
<td>450mg every 2 days</td>
</tr>
<tr>
<td>10 to 24</td>
<td>450mg twice weekly</td>
</tr>
</tbody>
</table>

Valganciclovir is not recommended for patients on haemodialysis (CrCl < 10ml/min).

To calculate an estimated creatinine clearance:
For males \( \frac{(140 \text{- age (years)}) \times \text{weight (kg)}}{(0.81) \times \text{serum creatinine (umol/L)}} \)
For females \( 0.85 \times \text{male value} \)

Valganciclovir tablets should be taken with food. The tablets should not be broken or crushed. Treatment should continue for 90 days.

Cost
The cost per patient varies depending on the dose used. Based on the average creatinine clearance post transplant the estimated cost per patient ranges from £1370-£3590 (ex VAT) for 90 days.

Shared Care Responsibilities

Option 1: Initiation of prescribing by Consultant

Aspects of Care for which the Consultant is responsible
- Initiate prescription and provide initial supply of medicine
- Monitor weight, urea and electrolytes, whole blood count and liver function tests at clinic visits - results to be communicated to GP
- Dose adjustment in response to changes in creatinine clearance with changes being communicated to GP

Aspects of Care for which the General Practitioner is responsible
- Once the dose is predictable monitoring of urea and electrolytes and whole blood counts between clinic visits
- Sending results to and contacting consultant if concerned about the results
- Prescribe and adjust the dose of valganciclovir in response to changes in creatinine clearance as recommended by hospital medical staff
Precautions
Valganciclovir is a potential carcinogen, mutagen and teratogen. It may cause temporary or permanent inhibition of spermatogenesis and suppression of female fertility. Barrier contraception is recommended in male patients during therapy and for 90 days following treatment. Women of childbearing potential should use effective contraception during treatment.

Severe leucopenia, thrombocytopenia, anaemia, neutropenia, pancytopenia and aplastic anaemia may occur. Treatment should not be initiated if the absolute neutrophil count is less than 0.5 x 10^9/L or the platelet count is less than 25 x 10^9/L or haemoglobin level is less than 8g/dl.

Drug Interactions
In-vivo drug interaction studies with valganciclovir have not been performed. Since valganciclovir is extensively and rapidly metabolised to ganciclovir; drug interactions associated with ganciclovir will be expected for valganciclovir.

Additive toxicity is possible when valganciclovir is co-administered with other medicines that inhibit replication of rapidly dividing cells such as trimethoprim/sulpha combinations, dapsone, pentamidine, flucytosine, vincristine, vinblastine, Adriamycin, amphotericin B and other nucleoside analogues. Combination therapy with valganciclovir and such agents should be used only if the potential benefits outweigh the risks.

Toxicity may also be enhanced when valganciclovir is co-administered with other medicines that may reduce renal clearance of valganciclovir such as probenecid or nucleoside analogues (which inhibit renal tubular secretion) or nephrotoxic agents.

Concomitant use of valganciclovir with zidovudine and didanosine may increase zidovudine blood levels (17%) and increase didanosine blood levels (approx 80%).

Avoid the concomitant use of imipenem-claustin and valganciclovir due to the risk of seizures.

Side-effects
The most frequent side effects associated with valganciclovir include neutropenia, anaemia, diarrhoea and dyspnœa. Common side effects include infections, blood dyscrasias, anorexia, depression, anxiety, confusion, headache, insomnia, dizziness, pain, myalgia, gastrointestinal upsets and abnormal LFTs.

Referral Criteria
The patient will be referred to the GP after the initial hospital period (approx 14 – 21 days post transplant). The patient will receive at least a 7-day supply of medicines from the hospital pharmacy.

Adverse Reaction Reporting
Any adverse drug reactions noted should be reported to the Transplant Unit at RIE.

Contact Points
Contacts at the Royal Infirmary of Edinburgh Transplant Unit:

Consultants and registrars for the unit are available 24 hours a day – contact the Transplant Ward on 0131 242 2068.

The transplant unit pharmacist can be contacted Mon – Fri 8.30am – 5.00pm on 0131 536 1000 bleep 8006/2294 (renal / renal pancreas) or 5132 (liver).

The secretaries for the Transplant Unit can be contacted 9am - 5pm Mon - Fri on 0131 242 1717.

Version 1.0: January 2004 Revision Date: January 2006

This information was prepared by the physicians and pharmacists of the Transplant Unit at the Royal Infirmary of Edinburgh, through liaison with the General Practice Prescribing Committee and the Drug and Therapeutics Committee, NHS Lothian - University Hospitals Division.