

ROYAL INFIRMARY OF EDINBURGH

**SIMULTANEOUS ISLET/ KIDNEY
TRANSPLANTATION
PROTOCOL**

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**Mr Andrew Sutherland
Mr John Casey
Dr Shareen Forbes
Dr Paul Phelan
Dr Lorna Henderson
Kirsty Duncan
Christine Jansen**

Pre-operative recipient work-up

1. Admit under Transplant team (Ward 206 Transplant, RIE)
2. Diagnosis: Type 1 diabetes for combined Kidney and Islet cell transplantation
3. Obtain hospital notes from transplant office, notes stored in the transplant filing cabinets
4. Record:
 - Height, weight, waist circumference on admission
 - HR, BP lying and standing, Temp and oxygen saturations 4 hourly
 - Blood glucose monitoring hourly
5. Send blood to lab for:
 - Full blood count and differential*
 - Platelets*
 - INR*
 - PT , APTT, APTT Ratio*
 - HbA1c
 - Electrolytes, urea, creatinine*
 - Liver function tests*
 - Serum pregnancy test in fertile females*
 - Serum CMV IgG, EBV, HBcAb, HBsAg, Hep C, HIV
 - HLA type and Lymphocytotoxic Cross-match (10ml EDTA and 10ml clotted sample) negative cross-match result must be available pre-transplant unless vXM and retrospective cross-match specifically agreed by the H&I team. (discuss with on call transplant coordinator)
 - ABO Group and X match 2 units
 - Blood culture x 2 – C&S and fungi, if pt in hospital in previous week
6. Urinalysis and MSU
7. If on peritoneal dialysis send PD fluid for MC+S.
8. MRSA screen
9. Send sputum for C&S and fungi
10. Request CXR and ECG
11. Patients must be fasted for at least 4 hours prior to the anticipated time of transplant. At this time convert to intravenous insulin with intravenous fluids (as per protocol – appendix 1). Place 18 Fg IV cannula in large arm vein.
12. Please prescribe all fluids on patient's drug chart. Discuss fluids and infusion rate with Renal Physician:
 - a. A critical appraisal of the patient's fluid status must be performed and pre-operative fluids prescribed accordingly.
 - b. If dialysis is planned prior to theatre, patients should not have fluid removed unless they are grossly fluid overloaded.

* = urgent Result required prior to procedure

13. Pre-operative dialysis

- a. **Patients on peritoneal dialysis:** Continue peritoneal dialysis until immediately pre-op (abdomen should be emptied 30 - 45 minutes pre-operatively).
- b. **Patients on haemodialysis:** Patient may require haemodialysis either because dialysis is due irrespective of transplant or based on the results of admission U&Es. In practice, unscheduled haemodialysis is unlikely to be required except for hyperkalaemia. (If ECD or DCD and delayed graft function likely, consider dialysis if time permits). Patients will often not require their full dialysis time, and theatre should not be delayed because of dialysis unless absolutely necessary.
- c. **Management of high potassium:** Once serum potassium is obtained discuss with the SpR/Cons on call. If potassium >5.5 then patient should have dialysis.
- d. **Dialysis should be prescribed without heparin using saline flushes instead.**

14. Medications

- a. Patient's "routine" medication (STOP metformin if patient using it on admission and for 48 hours post procedure)
- b. Anti-hypertensives are withheld except for beta-blockers and centrally acting agents. This decision should be discussed with SpR and/or anaesthetist.
- c. **ACE inhibitors and angiotensin II antagonists are omitted.**
- d. Omit NSAIDS, Diuretics.
- e. Review aspirin. If any doubt as to whether or not to continue, discuss with surgeon.
- f. Warfarin: patients on the waiting list on warfarin should have a plan for reversal and timing of reintroduction of anticoagulation, discussed with haematology prior to listing.
- g. Antibiotic prophylaxis - given at induction of anaesthesia Piperacillin/tazobactam 4.5g IV, unless patient is allergic to penicillin. If patient is allergic to penicillin give Vancomycin 1 Gram IV in Normal Saline over 2 hours and Ciprofloxacin 400 mgs infused over 60 mins.
- h. Anti-viral prophylaxis- as per renal protocol
- i. Pneumocystis jirovecii prophylaxis – as per renal protocol
- j. DVT prophylaxis: Heparin 5000U/SC at anaesthetic induction and 5000U/SC/bd thereafter until mobile post operatively (adhering to hospital protocol)
- k. Gastric protection: Ranitidine 150mg bd unless already on PPI in which case use or switch to lansoprazole 30mg.
- l. Bone prophylaxis: Calcichew 2 tablets nocte, Alphacalcidol 0.25mcg mane)

15. Immunosuppression (standard steroid sparing regime)

- a. Paracetamol 1g PO, 30 mins before Alemtuzumab (Campath-1H)
- b. Chlorpheniramine 10mg IV, 30 mins before Alemtuzumab (Campath-1H)
- c. Methylprednisolone 500mg IV, 30 mins before Alemtuzumab (Campath-1H)
- d. Alemtuzumab (MabCampath)* 30mg SC (stored in Transplant fridge, 30mg/1ml vial in solution – draw up 1ml into syringe in interventional radiology suite) and give SC into thighs, arms or buttocks over 1-2 minutes, (Pharmacist Bleep 2294 / 8006)
Alemtuzumab to be given in anaesthetic room once kidney has been reviewed by surgeon and deemed suitable for transplant.
- e. Post-op Mycophenolate Mofetil 500mg BD (10.00 and 22.00) – unless other specific regimen appropriate. To discuss with Transplant Team
- f. Prograf (Tacrolimus) 0.05mg/kg bd at 10.00 and 22.00 (check trough level (target 8-10ug/L) *if in target, usual dose of Prograf (Tacrolimus) BD (10.00 and 22.00) - unless other specific regimen appropriate. To discuss with Transplant Team.
- g. **Campath-1H 30mg 24 hours after first dose (only if recipient <60 years old).**
 - i. Paracetamol 1g PO, 30 mins before Alemtuzumab (Campath-1H)
 - ii. Chlorpheniramine 10mg IV, 30 mins before Alemtuzumab (Campath-1H)

iii. Methylprednisolone 500mg IV, 30 mins before Alemtuzumab (Campath-1H)

*** For highly sensitized patients, an individualized protocol will be decided by the MDT in discussion with the renal physicians.**

16. Intravenous insulin regime to be prescribed by Renal Registrar. (See Healthcare A – Z section of the NHS Lothian Intranet: Healthcare → Healthcare a-z → D → Diabetes → Metabolic unit handbook → Diabetes protocols)

17. Consent:

Obtaining consent is the responsibility of the operating surgeon. The transplanting surgeon must check donor blood group is compatible with two copies of the recipient blood group prior to the start of the transplant. The surgeon must sign the blood group check form to document that the blood groups of the donor and recipient have been checked.

Early post-operative management (after renal transplant)

Surgical registrar contacts renal team on #6394 once patient in recovery to communicate intraoperative course / concerns and facilitate nephrology review. Post op review by surgical team (either in recovery or HDU) to consider fluid status, wound and drain output. Admit to ward 215 post-operatively. The renal transplant coordinator on-call will update team if islet cells are suitable to transplant and when this will take place (usually 24-48 hours post- renal transplant).

Post-operative Investigations

1. Arrange chest X-ray for position of central in recovery
2. Check FBC and U&Es immediately post-op
 - a. Serum K⁺ must be known and result discussed with Registrar.
 - b. Hyperkalaemia should be managed with Insulin/Dextrose and nebulised Salbutamol rather than haemodialysis when possible.
 - c. Subsequent repeat U&Es 12 hourly (more frequently if indicated or as decided by Registrar).
3. Doppler US in recovery only if requested by Surgeon.

Fluid Management

1. Initial IV fluid replacement is Normal Saline at 60 mls/hr + last hour's urine output. This should be guided by clinical status and the CVP with a target of 8-10.
2. Fluid regimen should take into consideration: amount of fluid given in theatre, total blood loss, native urine output, cardiac status of patient, age of patient (caution if >65), if DGF expected.
3. If expected immediate graft function and urine output <40mls/hr:
 - a. Ensure catheter not blocked. Member of surgical team should flush out catheter at this early stage.
 - b. Discuss with surgeons and consider renal transplant doppler.
 - c. Gelofusine bolus 200mls to achieve CVP of 8-10.
 - d. Consider IV NaCl at continuous rate of 100 mls/hr initially.
 - e. Response must be carefully assessed (hourly initially) before continuing infusion at this rate and especially if remains oligoanuric. NB Any concerns should be discussed with transplant surgeon and renal team.
4. If Delayed graft function expected
 - a. CVP <6: GELOFUSINE 250MLS BOLUS + TOTAL OUTPUT +60mls/hr
 - b. CVP 6-10: TOTAL OUTPUT +60mls/hr
 - c. Careful monitoring of fluid status is required as higher risk of precipitating pulmonary oedema **Failure of the patient to respond to IV Fluid with a rise in CVP or BP should raise possibility of bleeding. If there is a possibility of bleeding a transplant surgeon must be contacted.**
 - d. **Maintenance IV fluids:** Continuing IV fluid replacement should be maintained with alternating 5% Dextrose and Normal Saline.
5. Insulin Sliding Scale to be continued as prescribed pre-operatively

Post-operative analgesia

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.

Post-operative Management prior to Islet Transplant

1. Infection prophylaxis: CMV prophylaxis (as per renal transplant protocol).
2. Blood Tests
 - a. U&Es daily
 - b. FBC daily
 - c. LFTs, glucose, CRP daily
 - d. Repeat Coagulation screen
Tacrolimus level - M/W/F
3. MSU each Monday and at other times if clinically indicated.
4. Urinary catheter removed at day 5 unless directed by transplant surgeon. If a patient develops urinary retention after removal of catheter in the post-operative period it should be replaced as soon as possible. This does not need to be a surgeon if it will cause undue delay.
5. A routine graft biopsy is performed around day 5 if there is delayed graft function and subsequently at weekly intervals until function is established. This is to diagnose acute rejection co-existing with ATN.
6. Any deterioration in graft function may require a graft biopsy, which will be requested by a senior member of staff.
7. Treatment of Acute rejection as per renal transplant protocol.

Preparation for Islet cell Transplant (day 2 post renal transplant)

1. Please inform Diabetes Registrar (on call up to 8pm), Dr Shareen Forbes, Islet Transplant Diabetologist, Debbie Anderson, Diabetes Dietitian on ext 21460 and Diabetes Specialist Nurse on ext. 21470 or bleep 5955 of patient.(Transplant co-ordinator will inform Dr Forbes).
2. Diabetes registrar to review patient and insulin sliding scale.
3. Obtain blood glucose monitoring sensor from Diabetes Specialist Nurse / Dietitian who will attach to patient.
4. Check clotting and FBC the day before islet cell transplant.
5. Order islet transplant on TRAK
6. Repeat antibody sample for tissue typing lab day of islet transplant

ISLET Transplant (approximately 48 hours following renal transplant)

Clear fluids may be taken orally up to two hours pre-procedure. Nil by mouth for at least 2 hours pre procedure. Ensure an 18G IV cannula in large arm vein is in place. The following should be prescribed:

1. Omeprazole 40mg PO, 4 hours before transplant
2. Piperacillin/Tazobactam 4.5 gm IV 8hrly for 24 hours (only 2 doses if patient is anuric or has DGF). Start 1-2 hours pre-transplant. If allergic to penicillin give Vancomycin 1g IV in 250ml sodium chloride 0.9% over 2 hours (one dose only, adjust dose if renal impairment) and Ciprofloxacin 400mg IV over one hour (12hrly for 24 hours (2 doses)).
3. Chlorpheniramine 10mg IV, 30 mins before expected islet cell transplant
4. Hydrocortisone 100mg IV, 30 mins before expected islet cell transplant
5. Tacrolimus and Mycophenolate maintenance to continue as prescribed after renal transplant.

Radiology

- Radiologist to prepare, prescribe and administer sedation.
- Surgeon to prepare and add heparin to islet bags prior to infusion (usually 35 units per kg body weight, (intraportal), into bag containing islets (not the rinse solutions)
- Surgeon check donor blood group arriving with islet cells compatible with recipient blood group

Post-islet cell transplant:

1. Observations: Temperature, heart rate, blood pressure, oxygen saturations, respirations every 15 minutes x 1 hours; then every 30 minutes x 2 hours; then every 1 hour x4 hours.

Call transplant team: (> greater than, < less than)

- Temp > 38° C.
- HR > 100 or < 60.
- Systolic BP > 160 or < 100 mmHg.
- Diastolic BP > 100 or < 60 mmHg.

2. Activity: Bed rest for 4 hours lying on right side, then activity as tolerated.

3. Bloods: Full clotting screen. FBC including, WBC and differential.

4. Doppler US: Ensure Doppler USS of liver has been arranged for within 24 hours post-procedure

5. Diet: Nil By Mouth for 4 hours post-transplant, then clear fluids. If patient tolerating clear fluids they can choose from Islet Transplant Carbohydrate Restricted Menu which should have already been arranged by, Diabetes Dietitian (ext 21460)., If there are any catering queries contact the catering supervisor (ext 24242) and liaise with Diabetes Dietitian (ext 21460).

Note: While Nil By Mouth patient must continue on intravenous insulin treatment with intravenous fluids as indicated overleaf.

Fluid Management:

Patient to be reviewed by renal registrar post procedure to manage fluid requirements

Insulin Management: Please contact on-call Diabetes registrar (Bleep #6800) (Mon – Friday 0900 - 2000; Sat/Sun 0900 - 1700) or Diabetes team with any concerns.

- Target glucose 4 – 7 mmol/l
- Intention: avoid stimulation of beta cells
- Note: the islet solution contains free insulin from disrupted islets
- CHECK Capillary glucose on patient's return to ward, then hourly for the first 48 hours. If patient fitted with continuous glucose monitor, capillary glucose readings MUST still be taken for verification of blood glucose concentrations.
- After 48 hours, check capillary glucose pre meals, two hours post meals and at bed time.

Insulin Infusion Instructions for First 4 Hours or until eating

(GOAL: Glucose between 4 – 7 mmol/L).

- 50 units Human Actrapid made up to 50 mls 0.9% sodium chloride (= 1 unit/ml) – see adult intravenous insulin prescribing chart page 3.
- Continue 0.45% sodium chloride / 5% glucose 500ml infusion as previously until drinking
- Continue 5% glucose 500ml infusion with 20 mmol of KCl at 50ml/hr or 100 ml/hr (Discuss with diabetologist, appropriate glucose concentration and rate) for first 8 hours, or until eating, whichever is sooner
- Check blood glucose hourly but every 15 minutes if glucose <4mmol/L* until glucose >4mmol/L

*If glucose <4mmol/L, switch insulin off, administer 100ml 10% dextrose stat – repeat every 15 mins until blood glucose >4mmol/L. If patient is NOT Nil By Mouth give 5 dextrose tablets or 100ml lucozade.

Note: Intravenous insulin has a half-life of 2.5 minutes, so if stopped for any length of time, **hyperglycemia will occur.**

Note: If the blood glucose \geq 14mmol/l, the glucose infusion should be deferred until the intravenous insulin has lowered the blood glucose to <14 mmol/l.

Note: The insulin and glucose infusions are given through the same IV cannula, with a non-returning valve.

Subcutaneous Insulin Instructions ONCE EATING (GOAL: Glucose between 4 – 7 mmol/L):

Continue hourly blood glucose monitoring and intravenous insulin scale until reviewed by Diabetes Team.

Once eating, discontinue intravenous glucose

Re-commence basal insulin, or if patient on a pump this may be restarted.

Administer subcutaneous insulin based on pre-meal capillary glucose readings and carbohydrate load (approx. 30-35G carbohydrate or snack of 15G or 0G carbohydrate).

Note: patients will have a particular ratio of amount of insulin required per 10G carbohydrate (please discuss with Debbie Anderson, Dietitian or Janet Barclay, Diabetes Specialist Nurse).

Note: The amount of insulin required for a carbohydrate restricted meal is individualised to the patient, reflecting amount needed to cover amount of carbohydrate as well as the amount needed to correct the glucose reading to a target value of 6 mmol/L

If patient was on metformin do not start until at least 48 hours post-procedure. Ensure eGFR > 40 mmol/l, serum creatinine < 150 µmol/l.

7. OTHER MEDICATIONS: (To prescribe on drug Kardex)

1. 2 further doses of Piperacillin/Tazobactam 4.5 g IV (8 hours apart); If allergic to penicillin give x1 further dose of Ciprofloxacin 400mg IV over one hour (12 hours apart from first dose)
total of 7 days. Consider continuing unfractionated heparin post-discharge if CrCl < 30ml/min

11. Glucagon 1 mg IM PRN if blood glucose < 2.8 mmol/l and patient cannot be treated orally

8. LABORATORY / DIAGNOSTIC STUDIES:

4 hours post transplant:

FBC including WBC and differential. Coagulation screen.

Routine Studies (Routine Requisition):

1. DAILY: FBC including WBC with differential, coagulation screen, glucose (fasting), c-peptide (only if off insulin), insulin (if off insulin).
2. ALTERNATE DAYS: trough Tacrolimus level (Monday, Wednesday, Friday)
On discharge, patient may need to attend the ward for bloods prior to the Monday clinic, depending upon day of discharge.

Radiology:

Doppler Ultrasound of liver EARLY AM post-islet cell transplant and on Day 7 at the Monday clinic.

9. BLOOD PRODUCTS

If blood products are required then the patient should be given **IRRADIATED BLOOD** only post Alemtuzumab administration. This procedure should be followed for subsequent islet cell transplants.

10. DISCHARGE

On discharge the patient will be provided with a sheet containing:

1. Subcutaneous insulin regimen
2. Medication booklet including immunosuppression schedule. See over-leaf for table of drugs.
Note TOTAL duration of drug treatment is shown.
3. Follow up appointments for the Monday transplant clinic and other studies (to liaise with Kirsty Duncan / Christine Jansen/ Mel Philips)
4. Renal transplant follow-up Wednesday and Friday, as per local renal transplant follow-up protocol.
4. Contact numbers
5. General Health Care Advice in relation to transplant and immunosuppression.

TABLE OF DRUGS AND TOTAL DURATION OF TREATMENT

DRUG	DOSE	ROUTE	FREQUENCY
INSULIN	As indicated	SC	
MYCOPHENOLATE MOFETIL*	500mg or alternative dose	PO	BD (1000; 2200)
PROGRAF (TACROLIMUS)*	0.05mg / kg Or usual dose if on drug	PO	BD (1000; 2200)
CO-TRIMOXAZOLE	480mg	PO	OD (8am) for 6 months
VALGANCICLOVIR	900mg (adjust dose if impaired renal function)	PO	OD (8am) for 6 months
HEPARIN	5000 UNITS	SC	BD (while in-patient - withhold prior to islet transplant)

*In some patients alternative immunosuppression may be appropriate

** If patient has Cr Cl<30ml/min, unfractionated heparin 5000 units SC to be prescribed

IN SOME PATIENTS, THE FOLLOWING DRUGS MAY BE APPROPRIATE

DRUG	DOSE	ROUTE	FREQUENCY
ISONIAZID TB PROPHYLAXIS	300 mg	PO	OD 3 months
PYRIDOXINE PROPHYLAXIS OF ISONIAZID INDUCED NEUROPATHY	10 mg	PO	OD 3 months

