

Management of Islet Transplantation.		<i>Addressograph or Name Address</i>	
Pre-transplant		<i>Dob</i>	
Date:	Ward:	<i>Unit no.</i>	<i>CHI</i>

NHS Lothian- University Hospitals Division

Consultant Surgeon: Transplant Nurse:

Consultant Diabetologist: Diabetes Specialist Nurse: Dietitian:

Consultant Radiologist:

Recipient	Donor
CMV Status	CMV Status
EBV Status	EBV Status

1. Admit under Transplant team (Ward 206 Transplant, RIE)
2. Diagnosis: Type 1 diabetes for islet transplantation
3. Transplant consent form to be completed
4. Obtain hospital notes from transplant office, notes stored in the transplant filing cabinets
5. Record:
 - Height, weight, waist circumference on admission
 - HR, BP lying and standing, Temp and oxygen saturations 4 hourly
 - Blood glucose monitoring hourly
6. 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 admission.
7. **Note** patient will be contacted the night before admission. The regimen will be individualised to the patient and must be discussed with the Diabetes team.
 - If on multiple dose insulin (MDI) regimen and procedure is planned for the **morning**: usual dose of long acting insulin (eg. Lantus or Levemir) at night, and omit breakfast and omit morning short acting insulin. If on long acting insulin in the morning this may be taken.
 - If on MDI regimen and procedure is planned for the **afternoon (including late afternoon)**: Usual short acting insulin with breakfast before 07.30h and omit lunch and omit usual short acting lunchtime insulin. If on long acting insulin in the morning this may be taken.
 - If on Continuous Subcutaneous Insulin Infusion (CSII) and procedure planned for **morning**: omit breakfast **but** continue on pump at usual basal rate until two hours pre-procedure
 - If on CSII and procedure planned for **afternoon**: have bolus of insulin with breakfast before 7.30 am then continue on normal/usual basal rate until two hours pre-procedure. If procedure planned for late afternoon then theoretically light lunch may be taken.
8. When patient admitted, obtain blood glucose monitoring probe (Guardian) from Diabetes Specialist Nurse / Dietitian who will attach to patient.

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9. Clear fluids may be taken orally up to two hours pre-procedure. Nil by mouth for at least 2 hours pre procedure. At this time convert to intravenous insulin with intravenous fluids. Place 18 Fg IV cannula in large arm vein.

10. Send blood to lab for:

* = urgent Result required prior to procedure

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.
ABO Group and X match 2 units
Blood culture x 2 – C&S and fungi, if pt in hospital in previous week

11. Send urine for:

MSU for C&S and fungi
Urinalysis (Inform Diabetes Team if > ++ ketouria)

12. MRSA screen

13. Send sputum for C&S and fungi

14. Urgent CXR if not done in last 3 months and ECG

15. STOP metformin if patient using it on admission and for 48 hours post procedure

16. Telephone 24242 to inform catering supervisor of need to issue Islet Transplant Carbohydrate Restricted Menu. Contact and liaise with Debbie Anderson, Diabetes Dietitian on ext 21460 and inform ward Dietitian of patient admission

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

Note patient's usual total dose of insulin over 24 hours:

Adjust insulin regimen to achieve blood glucose 4 – 7 mmol/L

50 units Human Actrapid made up to 50 mls 0.9% sodium chloride (= 1 unit/ml)

Check blood glucose at least 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 BM>4mmol/L

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

Intravenous Fluids
<p>Please prescribe all fluids on patient's drug chart. The fluids below are a guide only. Discuss fluids and infusion rate with Diabetologist</p> <p>Commence 5% glucose 500ml infusion with 20 mmol of KCl at 50ml/hr (or 100 ml/hr) usually alternating with 5% glucose 500ml infusion at 50ml/hr</p> <p>In parallel administer "mixed bag" of 0.45% saline/ 5% glucose 500ml at 50ml/hr</p> <p>Individualise infusion rate for islets after kidney to keep patient hydrated while nil by mouth</p> <p>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. In this case it may be appropriate to use 0.9% sodium chloride</p> <p>Note: The insulin and glucose infusions are given through the same IV cannula, with a non-returning valve</p>

NHS Lothian Adult Intravenous Insulin Prescribing Chart

Ward:Date:

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Insulin infusions are continuous and made up of: 50 units soluble insulin (Actrapid) in 50ml of 0.9% Sodium Chloride so that 1ml = 1 unit. Commence 5% glucose 500ml infusion with 20 mmol of KCl at 50ml/hr (or 100 ml/hr). Alternate with 5% glucose 500ml infusion at 50ml/hr.

Assess which scale to use based on the patient's **total daily insulin dose**. If patient is persistently hypoglycaemic or hyperglycaemic **while the infusion is running**, consider moving down or up respectively to an alternative scale. A fourth scale may be prescribed if necessary.

Notes	Capillary Blood Glucose	Scale 1	Scale 2	Scale 3	Scale 4
		For Insulin Sensitive Patients Total Insulin Dose <25 Units per day	Standard Rate Total Insulin Dose 25-35 Units per day	For Insulin Resistant Patients Total Insulin Dose >35 Units per day	
TREAT HYPOGLYCAEMIA SEE BELOW	Mmol/L	Units/hr	Units/hr	Units/hr	Units/hr
	< 4.0	0 ←	0 ←	0	
	4.1 - 8.0	0.2	0.5	1	
	8.1 - 12.0	0.5	1	2	
MEDICAL REVIEW IF GLUCOSE PERSISTENTLY ABOVE 14mmol/L	12.1 - 16.0	1	2	4	
	16.1 - 20.0	1.5 →	3 →	5	
	20.1 - 24.0	3	4	6	
	> 24.1	4	6	8	
Doctor Signature and Print					

Check capillary blood glucose hourly while on IV insulin

MONITORING CHART	Time (24hour clock)	Blood Glucose (mmol/l)	Scale	Insulin rate (units/hr)	Signature	Time (24hour clock)	Blood Glucose (mmol/l)	Scale	Insulin rate (units/hr)	Signature	

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For ISLET ALONE

For patient having first transplant (please prescribe on patient Kardex):

1. Omeprazole 40mg PO, 4 hours before transplant
2. Piperacillin/Tazobactam 4.5 gm IV 8hrly for 24 hours (3 doses). 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. Paracetamol 1g PO, 30 mins before Alemtuzumab (MabCampath)
4. Chlorpheniramine 10mg IV, 30 mins before Alemtuzumab (MabCampath)
5. Hydrocortisone 100mg IV, 30 mins before Alemtuzumab (MabCampath)
6. Alemtuzumab (MabCampath)* 30mg SC (stored in transplant fridge, 30mg/1ml vial in solution – draw up 1ml into syringe) and give SC into thighs, arms or buttocks over 1-2 minutes, (Pharmacist Bleep 2294 / 8006).

Alemtuzumab to be given on ward prior to going down to radiology for islet cell transplant. Transplant Co-ordinator will advise once final cell count has been confirmed.

All patients to go down with 5% glucose infusion. Additional 20% glucose must be taken down to radiology for treatment of hypoglycaemia.

*** For second and third transplants, Alemtuzumab only to be prescribed on Transplant Surgeon's instructions. See post transplant orders for subsequent Prograf (Tacrolimus) and Mycophenolate Mofetil (MMF) doses. Aim for Tacrolimus trough level 8-10 µg/L.**

For ISLET AFTER KIDNEY

For patient with previous transplant, still on full immunosuppression including Prograf (Tacrolimus) aim for Tacrolimus trough level 8-10 µg/L. If in target range give as per usual dose BD*. Patients should continue their normal dose of oral prednisolone

1. Omeprazole 40mg PO, 4 hours before transplant
2. Piperacillin/Tazobactam 4.5 gm IV 8hrly for 24 hours (3 doses). 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. Paracetamol 1g PO, 30 mins before Alemtuzumab (MabCampath)
4. Chlorpheniramine 10mg IV, 30 mins before Alemtuzumab (MabCampath)
5. Hydrocortisone 100mg IV, 30 mins before Alemtuzumab (MabCampath)
6. 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 on ward prior to going down to radiology for islet cell transplant. Transplant Co-ordinator will advise once final cell count has been confirmed.**
7. Mycophenolate Mofetil 500mg BD (10.00 and 22.00) – unless other specific regimen appropriate. To discuss with Transplant Team.
8. Prograf (Tacrolimus) (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.
All patients to go down with 5% glucose infusion.

* For second and third transplants, Alemtuzumab only to be prescribed on Transplant Surgeon's instructions.

If blood products are required IRRADIATED blood only to be given post transplant.

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FOR ISLET AFTER KIDNEY:

A different regimen may be required from standard CAMPATH/ Prograf / MMF. Discuss with transplant team.

18. Analgesia (To be prescribed on patient's Kardex)

Paracetamol 1g QDS

Additional analgesic requirements to be prescribed by Transplant Team

Ondansetron 4 mgs QDS/Cyclizine 50 mgs TDS depending on patient's analgesic requirements.

19. 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)

Islet infusion summary form

(to be completed in radiology and inserted into the patient records)

Date: ___/___/___ Time of islet infusion _____

Radiologist: _____

Surgeon/physician: _____

Islet lab sign off: _____

Time of X clamp (24 hr clock): _____

Total ischaemic time (X clamp) _____ hrs

Donor details:

Blood group: _____

Transplant Protocol:

Transplant #: 1st 2nd 3rd

Recipient weight: _____ kg Blood group _____

Packed volume (Bag with purified islets) _____ mls

*Heparin added to bag prior to infusion _____ units (1000 units/ml)

Total volume _____ mls

Residual volume (not infused) _____ mls

TOTAL islet packed cell volume infused _____ mls

Must be less than 10 mls

Wash medium (total volume infused) _____ mls

*State heparin dose: usually 35units per kg only in bag containing islets (not the rinse solutions):

Portal access: _____ Routine / complicated: _____

Portal Pressures: Pre Infusion- _____ During Infusion- _____ Post Infusion- _____

Catheter tip (main pv): Y / N Catheter size used (4 Fr): _____

Other comments: _____

Signed: _____ Date: _____

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On return from radiology

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. STAT BLOODS: Full clotting screen. FBC including, WBC and differential.

4. DOPPLER USS: 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.

6. INTRAVENOUS THERAPY:

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.

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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.

NHS Lothian Adult Intravenous Insulin Prescribing Chart
POST TRANSPLANT
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 Assess which scale to use based on the patients **total daily insulin dose**. If the patient is persistently hypoglycaemic **while the infusion is running**, consider using scale 1. If the patient is consistently hyperglycaemic during infusion, consider moving to scale 3. A fourth scale may be prescribed if necessary.

Notes	Capillary Blood Glucose	Scale 1	Scale 2	Scale 3	Scale 4
		For Insulin Sensitive Patients Total Insulin Dose <25 Units per day	Standard Rate Total Insulin Dose 25-35 Units per day	For Insulin Resistant Patients Total Insulin Dose >35 Units per day	
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	4.1 - 8.0	0.2	0.5	1	
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	16.1 - 20.0	1.5 →	3 →	5	
	20.1 - 24.0	3	4	6	
	> 24.1	4	6	8	
Doctor Signature and Print					

Check capillary blood glucose hourly while on IV insulin

MONITORING CHART	Time (24hour clock)	Blood Glucose (mmol/l)	Scale	Insulin rate (units/hr)	Signature	Time (24hour clock)	Blood Glucose (mmol/l)	Scale	Insulin rate (units/hr)	Signature	

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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, CSII 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)
2. Omeprazole 40mg PO OD to continue post discharge
3. Mycophenolate Mofetil (MMF) 500mg PO BD at 1000 and 2200 hours (*or alternative dose / immunosuppression if appropriate*)
4. Tacrolimus (Prograf) 0.05mg/kg PO BD at 1000 and 2200 hours; or usual dose if already on drug (*or alternative Dose / immunosuppression if appropriate*)
5. Co-Trimoxazole 480mg PO OD for 6 months for PCP prophylaxis. If patient allergic to Co-Trimoxazole Dapsone 100mg PO OD is second line treatment.
6. Unfractionated Heparin sodium (minihep) 5000 units sc BD. Withhold if APTR > 1.5. One day before discharge convert to Dalteparin 2,500 units sc once daily. Continue heparin sc for total of 7 days. Consider continuing unfractionated heparin post-discharge if CrCl < 30ml/min

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7. Valganciclovir 900 mg PO OD for 6 months for CMV prophylaxis.

For all transplant recipients except CMV –‘ve recipients of CMV –‘ve donors. Dose as per creatinine clearance (see table below)

Creatinine clearance (ml/min)	Prophylactic dose
>60	900mg OD
40 to 59	450mg OD
25 to 39	450mg every 2 days
10 to 24	450mg twice weekly

8. Paracetamol 1g PO QDS

9. Additional analgesic requirements to be prescribed by Transplant Team

10. Ondansetron 4mg/Cyclizine 50mg TDS

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

12. TB prophylaxis only for those with a history of TB, or born in the Asian/African continent: isoniazid PO 300mg OD and pyridoxine PO 10mg OD (prophylaxis of isoniazid induced neuropathy)

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:

EARLY AM post-procedure and on Day 7 +/- at the Monday am Doppler ultrasound clinic

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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. 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		SC	
OMEPRAZOLE	40mg	PO	OD (1000)
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
DALTEPARIN**	2,500 UNITS	SC	OD 7 days total on sc heparin

*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