ROYAL INFIRMARY OF EDINBURGH

SIMULTANEOUS PANCREAS TRANSPLANTATION IN-PATIENT PROTOCOL

Revised August 2024

Pancreas Transplant Team

INPATIENT MANAGEMENT

1 Offer of Organs

Organ allocation will be carried out according to the NPAS.

https://nhsbtdbe.blob.core.windows.net/umbraco-assets-corp/27964/pol185.pdf

Following the offer of a pancreas and kidney for transplantation, the recipient renal/pancreas transplant co-ordinator will contact the on-call consultant transplant surgeon to discuss the donor and recipient details. Prior to accepting the organs further discussion with the recipient's consultant renal physician may be required before the decision is made to accept the organs.

NHS BT duty office is then informed of the decision to accept or decline the pancreas and /or kidney.

The recipient transplant coordinator will inform all members of the transplanting team including:

- Critical Care / Ward 206 Transplant
- Anaesthetist
- Theatre staff
- Renal registrar / renal transplant SHO
- Renal Consultant
- Tissue typing

The patient will be contacted by the transplant co-ordinator and asked to come to the transplant unit. The patient will be asked to fast if required with regard to transplant timings. The transplant co-ordinator will arrange transport of the patient from home to Transplant Unit if required.

All prospective recipients should be admitted after the offer has been accepted, allowing time for assessment, dialysis and cross-match if required.

2 Pre-operative recipient work-up on admission

At the time of admission the MDT decision to list will be documented on trak and vital data. Documentation of all assessment investigations will be in the patient's transplant case notes.

Investigations:

- *FBC
- *U&E
- *Baseline calcium/phosphorus/LFT's (results available post-op)
- *Clotting screen/INR (if on Warfarin)
- *Blood Group and save
- Tissue Typing (10mls clotted, plus 5ml EDTA sample.)
- Virology – CMV IgG, EBV VCA IgG, HIV Ag/Ab COMBO, Hep B SAg, Hep B CoreAb, Hep CAb

- *Glucose
- Blood glucose test on ward

***Blood results must be obtained urgently** as patient may require dialysis prior to operation depending on this result.

In practice:
- If K+ >5.5: dialysis.
- If 5-5.5: dialysis if there is time/risk factors for delayed graft function.

Repeat U&Es are required 30 minutes following dialysis.

- **Chest X-ray**
- **ECG**
- **MSSU –** for gram stain and subsequent culture
- **PD fluid –** for WCC and gram stain / culture if appropriate
- **Covid PCR**
- **Serum/Urine HCG pregnancy test for women of child bearing age**

History and Examination:

- Duration of DM
- Complications of DM
- Recent glycaemic control
- Daily insulin requirement
- 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 + history of past/present, urinary tract problems
- Infections -any recent urinary, CAPD peritonitis/exit site/access related
- Other operations
- Ischaemic heart disease
- Peripheral vascular disease
- Previous renal transplants, timing and cause of failure
- Current medications

- **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 coordinator will provide this information.

NOTE: Donor confidentiality must be maintained at all times

A full physical examination of the patient must be performed and should include:
- assessment of fluid status
  supine and erect blood pressure recordings
  JVP
  Peripheries

any oedema
weight vs 'dry weight' if on dialysis

- peripheral pulses
- abdominal scars/hernias
- presence of failed transplant / previous transplant nephrectomy

Fasting:

Solids food should not be given to the patient from 6 hours prior to the anticipated theatre time unless otherwise stated by surgeons or anaesthetists. The patient may consume sips of clear fluid up to 2 hours prior to going to theatre.

Consent:

Obtaining consent is the responsibility of the operating surgeon. The patient will have signed the pancreas transplant consent proforma (Appendix 1) in the assessment clinic and have been given a copy. **At the time of transplant, 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.

Medications:

Routine medications should all be charted and be taken except as stated:

- Anti-hypertensives are withheld except for beta-blockers and centrally acting agents. This decision should be discussed with SpR and/or anaesthetist.
- ACE inhibitors and angiotensin II antagonists are omitted.
- Omit NSAIDS, Diuretics.
- Review aspirin. If any doubt as to whether or not to continue, discuss with surgeon.
- 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.

Glycaemic control: Once patients are fasting, they should be commenced on a variable rate insulin infusion. As below.

You will require the following charts:
Adult Insulin Prescription & Administration Record
Blood Glucose Monitoring Chart

http://intranet.lothian.scot.nhs.uk/Directory/anaestheticsandtheatres/AnaestheticsTheatresDocs/Documents/Preoperative Assessment and Perioperative Care/Diabetes and perioperative management.docx

Antibiotic and antifungal prophylaxis:

Given at induction of anaesthesia: Piperacillin/tazobactam 4.5g IV, unless patient is allergic to penicillin. Anidulafungin 200mg IV

Piperacillin/tazobactam 4.5g Continue once daily for 3 days and then stop.

Anidulafungin 100mg IV od for 3 days or until the results of the duodenal swab known. If positive continue for 7 days in total.

If patient is allergic to penicillin give Vancomycin 1g IV in Normal Saline over 2 hours and Ciprofloxacin 400 mgs infused over 60 mins. In the event of mild penicillin sensitivity, ceftazidime 1g daily in 250mls 0.9% NaCl over one hour with metronidazole 500mg iv/ 400mg orally daily for 3 days may be given. If severe penicillin allergy is present, vancomycin 500mg/d with ciprofloxacin 400mg iv/ 500mg orally once daily with metronidazole 500mg iv/ 400mg orally daily. This should be continued for 3 days.

Immunosuppression: The standard protocol for SPK patients is a steroid sparing T-cell depleting (alemtuzumab/Campath) protocol. For patients identified as at higher risk from a T-cell depleting protocol (e.g. increased risk of infection) they will receive a non-depleting Basiliximab based protocol. The decision for which protocol a patient will receive should be discuss and documented at the listing MDT.

Standard/Campath Protocol (T-cell depleting/steroid sparing)

Pre-op (at admission)	MMF	750mg
	Tacrolimus	0.05mg/kg
Peri-op	Alemtuzumab	30mg s/c in theatre
	Methylprednisolone	500mg in theatre.
Post-op	MMF	750mg bd at 08:00 and 20:00 hrs
	Tacrolimus (Adoport)	0.05mg/kg bd at 10:00 and 22:00

<u>No further steroids are given after the induction dose.</u>

Basiliximab Protocol (Non-T-cell depleting)

Pre-op (at admission)	MMF	1g
	Tacrolimus	0.05mg/kg
Peri-op	Basiliximab	20mg
	Methylprednisolone	500mg in theatre.
		500mg at 24hrs post-op
Post-op	Prednisolone	20mg daily from day 2
		(Reducing to 5mg at 3 months)
	MMF	1g bd at 08:00 and 20:00 hrs
	Tacrolimus (Adoport)	0.05mg/kg bd at 10:00 and 22:00
Day 4	Basiliximab	20mg

Target Tacrolimus levels for both protocols:

Tacrolimus	Target trough level 8-11 in first 3 months
	Target trough level 6 – 9 after 3 months

Note: No immunosuppression should be administered until it is confirmed that operation is to proceed

Anti-viral prophylaxis: All transplant recipients except CMV IgG negative recipients of CMV IgG negative donors (D-/R-) receive CMV prophylaxis with valganciclovir for 6 months. If T-Cell depleting induction [ATG/Alemtuzumab (Campath)] is used, CMV D-/R- cases will also receive 6 months valganciclovir.

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

Creatinine clearance (ml/min)	Prophylactic dose of valganciclovir
>40	450mg od
25 to 39	450mg every 2 days
10 to 24	450mg twice weekly

Note that our maximum dose of valganciclovir is 450mg od (even if creatinine clearance >60 ml/min).
Valganciclovir is available as 450mg tablets. The tablets should be taken with food and not broken or crushed.
FBC and LFTs must be monitored during therapy.

For CMV IgG neg/neg transplant recipients not on prophylaxis a CMV PCR should be checked weekly until 8 weeks post transplant, then at 10, 12, 26 weeks post transplant.

Pneumocystis prophylaxis: **Pneumocystis prophylaxis – edren.org**

DVT prophylaxis: Heparin 5000U/SC at anaesthetic induction and 5000U/SC/bd thereafter until mobile post operatively (adhering to hospital protocol).

Gastric protection: Ranitidine 150mg bd unless already on PPI in which case use or switch to lansoprazole 30mg. (In the context of supply issues with ranitidine use lansoprazole 30mg)

Prophylaxis against corticosteroid induced bone loss: For 1 year and then review if needed
Calcichew 2 tablets nocte.
Alfacalcidol 250 nanograms once daily.

The above initial management should be changed before discharge to *Calcichew D3 Forte* 2 tablets per day, if eGFR>30mls/min/1.73m^2. This provides cholecalciferol (25-vitamin D) instead of activated vitamin D.
If already on high dose alfacalcidol consider whether this dose needs to be continued.
If serum calcium is high, omit Calcichew. Vitamin D can be prescribed as Fultium D3 800 iu daily.

Note - Patients with tertiary hyperparathyroidism may require altered bone prophylaxis and should be considered in an individual basis.

Rh -ve female recipients: Rhesus negative female recipients – edren.org

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3 Cross-match result

Virtual Cross match: If patient eligible for a virtual crossmatch, tissue typing will inform the transplant coordinator who will ensure there is a copy of the virtual crossmatch in the patients notes, or out of hours emailed to the transplanting surgeon. If a full crossmatch is required, this will take about 4 hours and the result will be communicated to the coordinator who will document this in the notes.

If the Crossmatch is positive: The duty team will decide whether the transplant can go ahead and if so what immunosuppression will be used. The patient will be advised accordingly.
Should the transplant not go ahead an immediate discharge letter should be generated and sent to the referring centre.

If the crossmatch is negative: The patient will be advised, and surgeon, anaesthetist, and theatre will be informed by the transplant co-ordinator.

4 Post-operative recipient care

Immediate post-operative period:

First 24 hours – (ICU ward 118 protocol)

On arrival from theatre/ theatre recovery the patient will be admitted in the routine fashion.

The major early management issues are:

1. **Potential for bleeding.**
2. **Fluid balance** – these patients in generally require larger volumes of fluid than kidney transplantation alone. Frequent assessment of volume status required.
3. **Blood Glucose control** – pancreatic function will dramatically reduce previous insulin requirements.
    a) Patients often have transient hypoglycaemia in the first 24 hours following pancreas transplant and require IV glucose.
    b) Hourly blood glucose measurement is essential
    c) A BG > 12 for 2 hours may indicate graft dysfunction and the on-call surgeon should be immediately notified.
4. **Electrolyte disturbance.**

DO NOT USE STANDARD WARD 118 MAINTENCE FLUID OR INSULIN REGIMES FOR THIS PATIENT GROUP.

Investigations

Admission:

- FBC, U&E, LFT's, Coagulation screen, Lab glucose, Amylase, ABG, Drain Amylase
- CXR – central line position: NG position – left in-situ for 24 hours- remove following discussion with transplant surgeon.
- 1 hourly glucose via ABG

8hours post transplant

- Repeat FBC, U&E, Formal Glucose Serum and Drain AMYLASE
- Repeat coagulation screen if clinically indicated.

PRESCRIBE

All routine medications except ACE inhibitors, AT2 receptor inhibitors NSAIDS, s/c insulin, oral phosphate binders, erythropoietin

DVT prophylaxis heparin 5000 units sc bd

GI prophylaxis Pantoprazole 40mg IV od

IV Fluid Initially crystalloid at urine output + 80mls/hr
250mls bolus if clinical signs of hypovolaemia
NEEDS REGULAR CLINICAL REVIEW

Blood Glucose Hyperglycaemia: Insulin if BM > 12 for 2 hours **call on-call surgeon to review patient** and start sliding scale (50 units Actrapid in 50mls N Saline):

BG 8.1 – 10	1 unit per hour
BG 10.1 – 12	2 units per hour
BG > 12	3 units per hour

Hypoglycaemia: Check blood glucose hourly.
Keep blood glucose > 4mmol/L with IV dextrose 10% or 20% at 50mls/hour and adjust rate to maintain > 4mmol/L
Every 6 hours stop dextrose infusion to assess for ongoing. hypoglycaemia
Restart dextrose infusion if BG < 4mmol/L

Analgesia Epidural and/or Fentanyl PCA as charted
Regular Paracetamol 1g qds
Avoid NSAIDS

Immunosuppression If the Basiliximab (Non T-cell depleting) protocol be used:
Methylprednisolone 500mg - 24 hours after clamps released.
Prednisolone 20mg mane thereafter.

For both the Campath (T-cell) and Basiliximab (Non T-cell) depleting protocols:
Ongoing immunosuppression in consultation with the transplant team.

Antimicrobials Co-trimoxazole 480mg daily
In addition, until duodenal swab culture known
Anidulafungin 100mg IV od
Tazocin 4.5g od

Day 2 post transplant

Discussion with the duty team if further imaging is required.

- Blood Glucose should continue 2 hourly.

Blood glucose control**:** If BG>12 – **call surgeon to review patient as may be a sign pancreas graft compromise.** Start sliding scale.

- **IV fluid replacement:**

  Crystalloid at urine output + 60 mls/hour.
  Aim for CVP 5-11 cm H2O. If CVP low, then give colloid (4.5% HAS 200 ml aliquots) or crystalloid**. However it should be noted that SPK patients are likely to require more IV fluid than patients who have undergone kidney transplant alone.**

- Analgesia –. Some patients will have an epidural. If epidural is providing adequate analgesia it should run for 36-48 hours. If no epidural, or epidural is discontinued use PCA. Avoid NSAIDS. If pain increase consider cause e.g. bleed, graft thrombosis, contact on-call transplant surgeon. Discuss pain management with pain team as necessary.
- NG tube for 24 hours usually.
- Urinary catheter should normally be removed on day 5. If catheter obstruction suspected, gentle catheter irrigation should be performed after surgical consultation and preferably by the surgeon.

- Nutrition: Patients will remain fasted until the surgeons allow oral intake. Patients ar classed as low or high nutritional risk during their assessment. High nutritional risk patients will be reviewed by the dietician (Appendix 2)

  NOTE: If the patient's condition changes and there is any cause for concern – do not hesitate to contact on-call transplant surgeon – at any time of day

5 Potential problems (Days 0-5) –

Note: Contact on-call surgeon if concerned at any time

- bleeding
- urinary leak
- renal vein thrombosis
- renal arterial occlusion
- pancreatic vascular thrombosis
- allograft pancreatitis

- **Post-op anuria** - Exclude catheter occlusion and hypovolaemia and treat as delayed graft function (see below)

- **Hypotension/low CVP unresponsive to IV fluids**

    - Suspect bleeding.
    - Exclude narcosis, cardiac event or ECF volume depletion.
    - Arrange urgent abdominal USS.
    - ECG
    - Check FBC and X-Match
    - Inform on call transplant surgical registrar/consultant.
    - Review need for epidural

- **Pain**

    - Suspect bleeding, graft infarction secondary to arterial or venous occlusion, urinary catheter occlusion, allograft pancreatitis
    - Urgent amylase
    - Inform surgeons.
    - Arrange urgent abdominal USS and Doppler of vessels (if required)

- **Delayed graft function**

    - Renal +/- pancreatic ultrasound – Doppler on first post-op day. Additional imaging for pancreas may be required.
    - Renal biopsy may also be required on day 5-7 to exclude rejection and at weekly intervals thereafter until function is established.

- **Renal allograft dysfunction**

    - A rise in Creatinine, a change in slope of plotted log Creatinine or a decrease in urine output may result for a number of reasons. ECF depletion, Tacrolimus toxicity or infection should be excluded. Acute rejection should always be suspected.
    - An USS, Doppler +/- renal biopsy should be arranged.

- **Pancreatic allograft dysfunction**

    - Isolated pancreatic rejection in the absence of renal allograft acute rejection is relatively uncommon. Problems with vascular supply should be first considered.
    - An abdominal USS and Doppler of pancreas should be arranged. If the pancreas is not visualised well, consider CT-angiogram or MRA in discussion with consultant surgeon.
    - Request serum and drain amylase.
    - Pancreas biopsy should be considered as there can be a discrepancy between the renal and pancreas biopsy.

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6 Routine management of post-operative transplant patients

Routine Investigations:

- **Blood Glucose** should be measured at least 4xday after the first 24 hours for the first week

- **Daily:**
  - U&E, Creatinine (plotted on log graph)
  - LFT
  - Lab Glucose (fasting)
  - Calcium, Albumin and Phosphate
  - FBC – if WBC above normal level check CRP daily
  - Clotting Screen
  - **Serum amylase**
  - **Drain fluid amylase.**

- **Monday / Wednesday /Friday**
  - Tacrolimus level *(trough)

*For the first month the desired trough Tacrolimus level will be 8-11. In cases of delayed primary renal allograft function this may be reduced.

- **Weekly (Mon)**
- MSU or CSU if indicated.
- PCR for CMV (9mls EDTA) for patients not on Valganciclovir prophylaxis.

Management of hyperglycaemia

Some patients may require some additional insulin if there is combined effects of pancreatic allograft dysfunction and steroids and Tacrolimus. Management should be discussed with the diabetes physicians. **If hyperglycaemia develops suddenly, please discuss with surgeon as it may indicate a problem with the pancreas graft.**

Management of hypertension

If BP control is not adequate on the patient's routine medication (excluding ACEi or AT2A for the first three months) then additional therapy should be introduced. Dihydropyridine Calcium channel blockers would be a suitable first line choice.

Prevention / Management of infection

Prompt diagnosis and treatment with appropriate anti-microbial therapy is required. Cultures of blood and urine in event of a pyrexia are mandatory. Chest physiotherapy in the post-operative period is required. Remember interaction of Erythromycin, Clarithromycin with Tacrolimus. (These drugs should be avoided if possible). Check with edren

Medications

The patients will start on the self-medication protocol when appropriate.

Wound Care

Wound clips should be removed following discussion with consultant transplant surgeon and no earlier than 2 weeks after transplantation.

Drains

Drain fluid should be measured every 24 hours and sample of fluid sent for drain amylase.

Pancreas drains to be removed / shortened as per instruction from consultant transplant surgeon.

Discharge / Follow-up (details in Out-patient protocol)

All patients should have a Mixed Meal Tolerance Test before discharge. (Appendix 3)

When patients are considered fit for discharge:

The referring unit will be informed by immediate discharge letter and telephone call. If patients are transferred to the local hospital prior to discharge home the centre must be contacted before and on day of discharge.

A copy of the patient transfer details sheet (Appendix 4) with a computer printout of the biochemistry, haematology, Tacrolimus results and discharge letter should accompany patient on transfer and/or emailed to receiving unit. The GP should be copied into this correspondence.

The discharge letter can be generated on vital data and must include details of:

- Mismatch
- Operation (including confirmation of appendicectomy or otherwise)
- Immediate graft function or otherwise
- Details of rejection episodes and required treatment.
- Any complications and discharge requirements
- Creatinine and blood glucose/insulin requirements
- Drug prescription
- Follow-up plan including timing for stent removal (3-4 weeks post-operatively)

A copy should be filed in the patient's transplant case notes.

Follow up plan for SPK patients post transplant at RIE

For **all** SPK patients to be offered follow up at 3 and 12 months and yearly thereafter at RIE.

If patients have followed up at their own centre, there will be provision for dial – in updates.

For Inverness/Dundee/Aberdeen – through the existing kidney MDT monthly meetings

For Glasgow/NI – through bimonthly MDT meetings

Referring Centre	Follow up Clinics	3-month Review	Annual Review
Lothian	RIE	RIE	RIE
Fife	Fife	RIE	RIE
Tayside	Dundee	RIE/Dundee	RIE
Greater Glasgow	Glasgow	RIE	RIE
Northern Ireland	NI	RIE	RIE
Grampian	Aberdeen	RIE	RIE
Borders	Borders	RIE	RIE
Lanarkshire	Glasgow> 3months	RIE	RIE
Dumfries and Galloway	Glasgow	RIE	RIE
Highland	Inverness	RIE/Inverness	RIE
Ayrshire and Arran	Glasgow	RIE	RIE
Shetland	Aberdeen	RIE/Aberdeen	RIE
Orkney	Aberdeen	RIE/Aberdeen	RIE
Western Isles	Inverness	RIE/Aberdeen	RIE
Forth valley	Glasgow	RIE	RIE

Please note any patient with pancreas complications resulting from SPK transplant will have follow- up at RIE.

All patients offered 3 month Follow up at RIE: Three-month clinics to be surgically led, annual review transplant co-ordinator with medical/surgical support if required.

For Referring centres that are doing follow-up:

Follow-up will **be at least weekly until 6 weeks post-transplant**. This will be either at RIE or referring unit but could also be a combination of both.

All patients should be offered a **3-month Surgical Follow up** appointment at RIE.

From 12 **weeks to 6 months** outpatient visit intervals will be gradually increased to monthly visits.

Beyond 12 months follow-up will be normally at the local referring centre. Patients should be seen every 3-4 months.

NOTE: To ensure satisfactory shared care, prompt communication between units will be necessary.

Monitoring

Ideally patients should monitor their blood glucose frequently for the first 3 months and record them in a diary. Recommend blood glucose check – pre-breakfast and pre-evening meal. Patients should also monitor weight daily and adjust fluid intake accordingly.
At each out-patient review the following should be done.

- BP
- Weight
- Urinalysis
- Bloods taken for U&E, Glucose, Amylase, HBA1c (3, 6 and 12 months thereafter), LFT, CAP, Tacrolimus trough level* FBC
- MSSU
- Urine Albumin/Creatinine ratio
- Lipids every 6 months
- PTH every 6 months if evidence of renal allograft dysfunction or previous hyperparathyroidism.
- Post transplant donor specific antibody levels checked at the time of any significant change in function of either graft.

Patients should be advised to have annual check for diabetic complications at their diabetic unit, annual retinal examination, annual podiatry.

Patients will be asked to omit their morning Tacrolimus dose until after bloods have been taken

Targets

- **Blood Pressure** 130/80
- **Blood Glucose** <6 mmol/l
- **Lipids** LDL cholesterol >3.0 dietary advice and statin.
  or total cholesterol > 5.0 dietary advice and statin.

Immunosuppression

Tacrolimus trough level	0 –3 month	8-11
	3+ months	6-9

Prednisolone dose on Basiliximab (non T-Cell) depleting protocol.

0 – 4 weeks	20mg/day
4 – 8 weeks	15mg/day
8 –12 weeks	10mg/day
>12 weeks	5mg/day

Mycophenolate (MMF) 1g bd (Campath protocol)

750mg (Basiliximab protocol)

Dose may need to be adjusted according to absolute neutrophil count (ANC) especially for patients in the T-cell depleting Campath protocol. A guide for dose adjustment is as follows:

ANC > 1.5-2 reduce dose to 500mg bd

ANC > 1-1.5 reduce dose to 250mg bd

ANC < 1 stop MMF

- **Prophylaxis against infection**

Co-trimoxazole discontinued at 3 months.
CMV prophylaxis discontinued at 6 months

BK Screening

BK Virus – edren.org

CMV Screening: When considered clinically relevant/annually. The threshold for CMV PCR should be lower after the 6 months given the increased risk of CMV disease following completion of the prophylaxis period.

Three month follow-up clinics

Three month follow up to be medically led in RIE
Location: OPD1/Near Me

Structure:

- Medications review
- BP / weight
- Wound check
- Neuropathy assessment
- Stent removal check
- Fluid balance
- Compliance review
- Pancreas function – patient blood glucose check before am food and before pm food 2-3 times/week
- Review of recent blood tests, amylase, HbA1c, C-Peptide
- MMT test (Appendix 3)/stimulated C-peptide to be requested from local centre.

Definition of graft function

Functioning: HbA1c 42 mmol/mol (<6%) on NO anti-diabetic medication

Partial function: HbA1c 42mmol/mol (>6%) OR requiring medication to maintain HbA1c

< 42mmol/mol (<6%). C-peptide >50 pmol/l [or C-peptide > pre-transplant C-peptide]

Graft failure: C-peptide < 50 pmol/l OR C-peptide lower than pre-tx C-peptide

C-peptide tests should be accompanied by a glucose value and should ideally be stimulated. The gold standard would be a MMTT (Appendix 3). A functioning pancreas graft would usually be expected to have a stimulated c-peptide in the 1000pmol/l - 3000pmol/l range.

Management of altered pancreas graft function.

Normal function equates to normal fasting blood glucose (less than 5.5mmol/L) and HbA1c less than 42mmol/mol (<6%). Routine outpatient monitoring of HbA1c should raise concern if level is greater than 42mmol/mol or increasing trend towards 42mmol/mol over 6- 12 month period. Partial function can be considered with elevated fasting glucose (5.5-7.0mmol/L) or upward trend in HbA1c.

If present, the following should be considered and the Edinburgh Transplant Team contacted:

1. CT angiogram pancreas
2. Auto-antibody screen (Anti-GAD, Anti-islet cell antibody)
3. Donor Specific Antibody screen
4. Review weight change since transplant, medication, tacrolimus levels
5. Perform MMTT and consider CGMS probe monitoring

In discussion with the Edinburgh Transplant Team, pancreas biopsy may also be indicated but should only be performed at the Edinburgh Transplant Centre.

Post Transplant Virology Screening

Patients undergoing solid organ or islet transplantation will undergo testing for the HBV, HCV, HIV and HEV when they have reached a time-point of **3 months post transplantation** (Appendix 5)

Testing will be arranged by the clinical team undertaking follow up at that time and sent to the local clinical laboratory.

Appendix 1 – SPK Consent Proforma

At time of attendance at transplant assessment clinic: **Initial**

- I have read and understood the patient information booklet explaining SPK transplant, including pre-assessment, operation, and post-operative care. ----
- I understand there are alternatives to SPK transplantation including kidney transplant alone +/- islet transplant or standard insulin therapy ----
- I understand the different types of kidney/pancreas which may be offered to me including kidneys from neurological criteria death (DBD) and circulatory death (DCD) donors ----
- I understand current pancreas and kidney transplant success rates and the risk of death following an SPK transplant ----
- I understand at the time of the operation the appendix is routinely removed ----
- I understand that, following my SPK transplant, I need to be followed up for the long term and I understand the consequences of not following medical advice ----
- I understand the risks that smoking can have on my recovery and the transplant. function and may result in me being removed from the list. ----
- I understand that if my weight increases and my BMI is over 30 I may be removed from the waiting list ----
- I understand the effects of the COVID 19 pandemic on donation and transplantation. and the risks of catching COVID 19 whilst on immunosupression. ----

The following risks have been discussed and I understand:

- There can be a delay in the start of the kidney working (approx 20 in 100 people) ----
- There may be a need for a biopsy of the transplant kidney before or after transplantation ----
- I may need treatment for kidney/pancreas transplant rejection (approx 10 – 20 in 100 people) ----
- Some donors have diseases that we may not know about (such as cancer or infections) and these can be passed to me in the transplanted kidney/pancreas (< 1 in 1000 people) ----
- There may be side effects from the essential treatment with anti-rejection medicines, including diarrhoea, sleep disturbance, tremor, skin changes, weight gain and long term damage to the kidney ----
- Other complications of anti-rejection medicines can include:
    - Diabetes – new onset ----
    - Infection– bacterial, viral, fungal ----
    - Reactivation of previous infections I have been exposed to e.g. shingles, polyoma virus ----
    - Increased risk of developing cancers such as skin cancer and lymphoma ----

Perioperative Risks

My kidney or pancreas may never work (approx 2 in 100 people), ----

After my surgery approximately 1 in 5 people require further surgery due to :

- Pancreatitis (5-10 in 100 people) ----
- Collections of fluid around the kidney/pancreas needing drainage or surgery (approx 8 in 100 people) ----

- Infection (10-20 in 100 people) ----
- Duodenal leak (approx 5-10 in 100 people) ----
- Bleeding (approx 15 in 100 people) ----
- Clotting of the vessels to/from the kidney/pancreas (approx 3-5 in 100 people) ----
- Urine leak or narrowing of the ureter (approx 2 in 100 people) ----
- Blockages of the intestine (2-5 in 100 people) ----
- Graft pancreatectomy (removal of the pancreas transplant) (10 in 100 people) ----

- Damage to other organs including bowels and blood vessels leading to lower limbs (1 in 65 people) ----
- Blood clots in the legs (DVTs) or lungs (PE) (approx 1 in 100 people) ----
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- Illness related to the cardiovascular system such as a heart attack (1-5 in 100 people), stroke (< 1 in 100 people) or pneumonia ----
- Dying after the operation (approx. 1 in 100 people) ----

With respect to the SPK offers I may receive:

- I am happy to consider any kidney and pancreas that are thought to be suitable for me by the transplant team Yes/No
- I would be willing to consider a kidney from a donor whose lifestyle may increase the risk of transmitting blood borne viruses to me.
  Blood borne viruses include hepatitis C, hepatitis B and HIV. This is in the knowledge that the viruses, if transmitted, are treatable and the treatment is unlikely to affect the life of the kidney/pancreas transplant Yes/No
- I would like to be notified if a kidney offer is declined for me because of a lack of resources Yes/No

I confirm that I have understood and consent to the procedure. I will have the opportunity to ask questions and re-affirm my consent at time of review and prior to the operation itself.

Patient	***Clinician***
Signed……	Signed……
Date: / /	***Date:*** / /

Appendix 2: Nutritional Protocol

Simultaneous Pancreas and Kidney Transplantation (SPK) Nutritional Support Protocol

When patient admitted for potential SPK:
Inform Transplant Dietitian on x. 21255.

All patients from Day 1 post-op (or when surgically indicated):
•Offer Fresubin 2kcal oral nutritional supplement (ONS) 200ml 2 x day *(or Ensure Plus Juce 220ml 2 x day if dislikes milk style ONS).*

From Day 3 post-op (or when surgically indicated):
•Commence light diet and offer ward snacks between meals.
•Start food record charts.
•If managing negligible amounts orally, to consider supplementary enteral feeding (or parenteral feeding if has non-functional gut).

If unable to meet 50% of estimated nutrition requirements by **Day 5 post-op**, to consider supplementary enteral feeding (or parenteral feeding if has non-functional gut).

On discharge:
Transplant Dietitian to provide 'Healthy Living' booklet including food safety advice. Update local dietitians.

Transplant Dietitian to identify level of nutrition risk for SPK during work-up process with SPK MDT:

LOW nutrition risk	HIGH nutrition risk
• BMI 19-30 (note BMI > 30 contraindicated for SPK surgery) • Meeting nutritional requirements • No significant or unexplained weight gain/loss • Nil/mild gastroparesis	• BMI < 19 • Not meeting nutritional requirements • Disordered eating behaviours • Significant or unintentional weight loss/gain • Significant gastroparesis e.g. nausea, vomiting, bloating, early satiety, abdominal pain. **= For optimisation of nutritional status pre-operatively via liaison with local dietitians**

Renal Dietitians, Edinburgh Royal Infirmary
April 2022 (Review April 2023)

Appendix 3: Mixed Meal tolerance Test

MMTT Quick Guide

Patients undergoing a MMTT must **fast from midnight** and *if still* on insulin omit their morning dose of short acting insulin. Long-acting insulin to be taken as usual. Patients still on insulin pump should keep their basal rate continued and not take any bolus.Ideally the test should be done first thing in the morning. Patients may drink plenty of plain water to stay hydrated.

1. **Explain the purpose of the test.** *C-peptide is produced at the same time as endogenous insulin, giving a very good indication of islet cell/ pancreas function. The higher the C-peptide result the better the function. In order to stimulate the cells to produce insulin, and thus C-peptide, we must give you a 'mixed meal' containing protein, fat and carb. This is the 'Fortisip Compact' or 'Ensure Compact'.*

2. **Take ZERO baseline blood samples** including glucose, c-peptide and insulin and any routine blood tests required.

3. **Check the patient's blood glucose using their own monitor.** If their fasting blood glucose is over 16mmol/L consider rescheduling the test.

4. **Administer 150 ml supplement drink** (bottles are 125ml so will need 2 x bottles + measuring cup)

5. **Record the time at which the drink was completely consumed,** you may calculate the 90-minute sample time point and complete the table below.

6. **Take 90-minute sample as close as possible to the calculated time.**

7. **Recheck blood glucose using patients own meter.**

8. **Send samples to lab as soon as possible, if there will be a delay keep cold but not frozen.**

Equipment

- C-peptide/ Insulin – Clotted (serum) tube x 2 (RIE – brown tube)
- Glucose tube x 2 (RIE – yellow tube)
- Venepuncture set + tourniquet
- Sharps box
- Measuring cup

Product Used: **Ensure Compact (125ml bottles)**
Volume used: **150ml**

Time Supplement Finished	

	0 minutes	**90 minutes**
Planned Sample Time		
Actual Time *(if different)*		
Blood Glucose (mmol/L)		

Appendix 4: Transfer document

Royal Infirmary of Edinburgh

Renal Transplant Unit

SPK Patient Transfer Information

Patient name: **CHI:**	
Consultant Surgeon **Consultant Nephrologist**	
Date of Transplant	
Date of Transfer / Discharge	
Type of transplant	
Extended Criteria Donor?	[ECD = Donor over age 60 or over age 50 ***plus*** history of HTN **or** death due to ICH **or** baseline Cr > 133umol/l]
Donor Details Sex Age Cause of death Other relevant detail / PMHx (if LD include isotope GFR + split function)	
Cold Ischaemic Time	
HLA MM Pre-formed DSA Monitoring required If Y, is table attached?	
CMV status	
EBV status	

Induction therapy	IL2RA / Methylprednisolone
Maintenance therapy CNI Levels and dose adjustments. CNI target trough	**Tacrolimus** trough level 0 –3 month 8-11 > 3 months 6-9 [Target levels per protocol: https://edren.org/ren/handbook/transplant-handbook/immunosuppression-protocol/tacrolimus-levels/ "Acceptable ranges of trough (12 hour) tacrolimus levels may be wide, and general principles dictate that levels should be higher early on, and in those with high immunological risk. However, many factors such as drug adverse effects, dose of MMF, tolerated, infectious risk, and prior clinical events also influence the target range.
Surgical complications	
If Y, details	
Operation notes attached?	
If Y, details	
DGF (Delayed Graft Function) ?	
If Y, duration of dialysis	
Implantation biopsy?	
Graft biopsy? Number	
Findings	
Acute rejection?	
If Y, details	
Treatment	
Serious infection?	
If Y, details	
Treatment and duration	

Attached reports.

Copied and pasted below (Attach as screen shots of relevant VitalData screens)

Operation notes -

Pathology reports –

Radiology reports –

CNI dosing chart –

Biochemistry -

Haematology -

Microbiology -

H&I post op DSA screen -

BK screening form –

Stent removal required ? Yes – at ~ 3 weeks post-operatively as per protocol

Operation Note:

Pathology reports: Nil

Radiology reports:

Biochemistry (include U+Es ++, LFT/Bone)

Haematology (include Coag, FBC):

Microbiology (Include CMV/HIV, Microbiology (including detail of any relevant +ve results):

Appendix 5: Protocol for Blood-Borne Virus Testing Following Solid Organ and Islet Cell Transplantation

Authors

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Dr Ingolfur Johannessen Clinical Director Laboratory Medicine NHS Lothian

Review Date

1st August 2018

Aim of Testing

To confirm that a blood-borne virus (BBV) has not been transmitted during solid organ or islet transplantation.

To confirm that hepatitis E virus has not been transmitted during solid organ or islet transplantation

Rationale

Hepatitis B Virus, Hepatitis C Virus and Human Immunodeficiency Virus

Transmission may occur as a consequence of solid organ transplantation. Pathogens that can be transmitted include blood borne viruses (BBV) such as hepatitis B virus (HBV), hepatitis C virus (HCV) and human immunodeficiency virus (HIV).

Given the potential for pathogen transmission during transplantation, an assessment of potential organ donors is undertaken. This assessment includes obtaining a history from close relatives and health professionals followed by a panel of routine microbiological/virological tests.

The donor history may document a previously known BBV or identify BBV-risk factors that are associated with increased risk of BBV infection. Such risk factors include injecting drug use (persons who inject drugs PWID), commercial sex workers (CSW) and men who have sex with men (MSM).

Although BBV risk factors may be identified in the donor history, an accurate history cannot be guaranteed in the setting of both deceased and live organ donation given the sensitive nature of some of these risk factors. Blood donation surveys consistently reveal poor self-reporting of risk factors. Consequently, the apparent "absence" of a risk factor in the donor history for BBV infection does not guarantee its true absence.

Microbiological/virological testing in organ donation is for the most part based on the humoral immune response of the individual with the detection of an antibody response to a specific pathogen. Consequently, there is a window period between the acquisition of infection and the development of pathogen-specific antibodies, during which time the individual poses an infectious risk to the recipient if organ donation were to occur. In this

window period a negative microbiological/virological antibody test can be falsely reassuring, unless correct interpretation of the test is undertaken in the setting of the patient history. For some agents, antigen tests are also available that help further assess infectious risk and have entered out-of-hours diagnostic test service.

The risk of transmitting an infection in the setting of negative microbiological/virological antibody tests may be quantified and is termed the residual risk. The residual risk for transmitting an infection is not solely dependent on the characteristics of the specific test used to test for the pathogen (sensitivity and specificity) but is also dependent on the incidence of the pathogen infection within a defined population and the length of the window period (positive and negative predictive value).

The incidence of infection within a population will vary according to the presence or absence of risk factors for the acquisition of the pathogen (e.g. IDU, CSW, MSM).

The residual risk may be reduced by antigen tests and/or nucleic acid (molecular) tests (NAT; generally, not available out-of-hours, yet), which have reduced window periods when compared to antibody-only tests.

Residual risk estimates have been calculated for solid organ donors in the United States of America and although they may act as a rough guide for use in the UK, the figures will not be equal because of the differing incidence and prevalence of BBV in the two populations. Similarly, residual risk estimates dersived for UK blood donors cannot be used in the context of solid organ transplantation partly because of a different population of individuals donating and the routine use of molecular tests for blood donations. Work is underway at a UK level to provide estimates of residual risk in the UK solid organ donor population.

Increased-risk donor criteria	HIV		HCV	
	Serology alone	Serology plus NAT	Serology alone	Serology plus NAT
Men who have sex with men	8.3	3.4	36.0	3.8
Nonmedical intravenous, intramuscular or subcutaneous drug use	12.9	5.3	350.0	37.8
Individuals with haemophilia	0.05	0.02	0.46	0.05
Persons who have had sex in exchange for money or drugs	2.9	1.2	107.8	11.5
Partners with any of the above risk factors	2.7	1.1	126.2	13.5
Individuals who have been exposed to blood or blood products from a person with HIV or HCV	1.3	0.5	22.0	2.3
Incarcerated individuals	1.5	0.6	68.6	7.3

Abbreviations: HCV, hepatitis C virus; NAT, nucleic acid test.

Figure 1: Residual risk estimates for HCV and HIV infection from solid organ transplantation in the USA. Risk of transmission of disease per 10,000 donors in the setting of a negative microbiological test.[12]

[1] Kucirka, L. M. *et al.* Risk of window period hepatitis-C infection in high infectious risk donors: systematic review and meta-analysis. *Am. J. Transplant.* 11, 1188–1200 (2011).
[2] Kucirka, L. M. *et al.* Risk of window period HIV infection in high infectious risk donors: systematic review and meta-analysis. *Am. J. Transplant* 11, 1176–1187 (2011).

Donors with higher risk of infection may be used following careful consideration and discussion with the proposed transplant recipient of the risk of transmission following transplant and the risk of foregoing the solid organ transplant and remaining on the transplant waiting list. The Advisory Committee on the Safety of Blood, Tissue and Organs (SaBTO) stated in guidance issued in 2011[3] that "*We accept that there may be clinical need for transplantation of such urgency that it may be appropriate to consider the use of organs and tissues for life-preserving purposes from donors who would not otherwise be considered eligible to donate, due to a known or perceived infection risk….. Fully informed consent to such a procedure is required from the recipient of such transplantation and all measures for risk reduction, including onward transmission, must be taken*" and that "*intensive immediate post-transplant monitoring and long-term follow-up of the infection status of recipients should be set in place and the long-term outcome of the recipient recorded centrally by the transplant community*".

Furthermore SaBTO guidelines state "*As a matter of principle for effective surveillance, there is value in the clinician looking after a surviving recipient considering the routine screening of recipients at one year follow-up from transplantation for microbial infection potentially transmitted from the donor to the recipient*".

The major BBVs now have effective antiviral management strategies that may either cure (HCV) or control (HBV, HIV) infection. Early identification of infection allows for timely introduction of effective management for the individual but will also allow for measures that reduce the risk of pathogen transmission from the infected transplant recipient to others.
w
Hepatitis E Virus

Hepatitis E virus (HEV) infection is increasing in incidence in the UK, and indeed is now the most frequently acquired hepatitis virus infection. HEV infection with genotype 3, the predominant genotype found in the UK, is frequently a mild self-limiting infection but chronic infection may occur in the setting of immunosuppressed patients. Although HEV is usually transmitted through dietary intake, it can also be transmitted through transfusion of blood products or solid organ transplantation. Consequently, the Advisory Committee on the Safety of Blood, Tissues and Organs (SaBTO), consulting with NHS Blood and Transplant (NHSBT) and other stakeholders, are in the process of making recommendations regarding both donor and recipient HEV testing. Consideration had been previously given to HEV RNA testing at 3-months post transplant to identify cases of donor transmitted infection, with advice to consider further recipient testing on an annual basis in order to identify chronic HEV infections acquired later through the dietary route. It had been hoped that definitive recommendations would be provided at the April 2016 SaBTO meeting however work is on-going with plans to discuss at the September 2016 meeting.

The present document deals solely with the transmission of infection from the donor and so testing requirements will be restricted to the 3-month post-transplant review.

Procedure

[3] https://www.gov.uk/government/publications/guidance-on-the-microbiological-safety-of-human-organs-tissues-and-cells-used-in-transplantation

Patients undergoing solid organ or islet transplantation will undergo testing for the HBV, HCV, HIV and HEV when they have reached a time-point of 3 months post transplantation. Testing of living donor and deceased donor transplant recipients will be undertaken.

Consent for testing will be according to local policy regarding BBV testing.

Testing will be arranged by the clinical team undertaking the follow up at that time and sent to the local clinical laboratory.

The following tests will be undertaken:

Pathogen	Test
Hepatitis B virus (HBV)	HBcAb and HBsAg
Human Immunodeficiency virus (HIV)	HIV Ag/Ab combo
Hepatitis C virus (HCV)	HCV PCR and HCV Ab
Hepatitis E virus (HEV)	HEV RNA PCR[4]

Samples sent for recipient virological testing will be stored for a period of 2 years in keeping with current NHS Lothian practice for virological testing. The policy of sample storage allows for testing of pre-transplant samples should concern arise over potential donor transmitted infection. It should be noted that samples sent for virological testing of organ donors are stored for an indefinite period.

A test result suggesting transmission of a BBV will require the clinician looking after the patient to

- Initiate further investigation of the recipient to confirm acquisition of a BBV. This will require specialist advice from a consultant virologist with experience of transplantation.
- Initiate appropriate management of the BBV in the transplant recipient. Specialist advice should be sought.
- Notify the Transplant Unit Clinical Director
- Notify NHSBT of possible BBV transmission by telephone call[5] and through the online reporting system[6]
- If blood products have been used either during or after transplantation then the blood transfusion services must be notified with submission to Serious Adverse Blood Reactions and Events (SABRE)[7]

In the event of a transmission of a BBV, the Clinical Director of Transplant Surgery will

- Ensure that a DATIX submission has been made
- Inform the Associate Medical Director
- Inform the Transplant Unit Clinical Service Manager
- Inform the Medical Director (Procurement, Commissioning and Facilities) NHS National Services Scotland

[4] It is noted that final SaBTO recommendations are awaited.
[5] 01179757580
[6] https://safe.nhsbt.nhs.uk/IncidentSubmission/Pages/IncidentSubmissionForm.aspx
[7] https://aic.mhra.gov.uk/mda/sabresystem.nsf/Login?Open