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Dear Colleague,

Thank you for resuming the clinical care of our shared patient who has received a kidney transplant in Auckland. By now you will have received a discharge letter and telephone call from our service detailing the progress of your patient up until the time of transfer to your care.

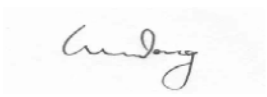
The following is a shared protocol explaining the requirements of care for your patient after this transfer. We will remain in close communication with you and the patient during the first 12 months and thereafter. We ask your local laboratory to send us copies of all laboratory tests undertaken on your patient. We will follow up any relevant results as soon as they come to hand and appreciate being informed promptly of any concerning result or clinical concern that you may have. The renal nurse specialist coordinates clinical care for renal transplant children and should be your first point of contact. Any changes to treatment will be communicated to you and the parents of the patient.

The patient will be scheduled for a 2-3 day review in Starship Hospital at 3 and 12 months post transplantation. The details of the review are in the Outpatient visits section of the protocol. During the first 12 months after transplantation, all diagnostic procedures (except simple blood tests) related to the care of a renal transplant patient (e.g. biopsy) will be undertaken in Auckland unless there is prior agreement.

I hope the shared cared protocol will help with your care of this renal transplant patient. We are happy to discuss any issues with you.

Kind regards

Yours sincerely



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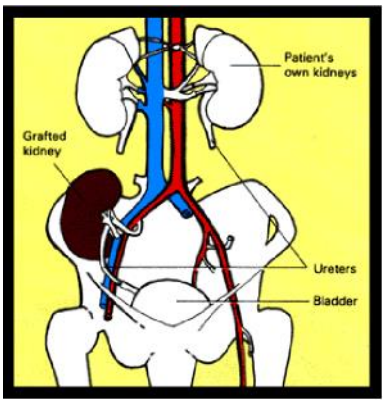
Department of Paediatric Nephrology

Shared Care Guidelines

Paediatric Renal Transplant Recipient



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Outpatient Visits

For the first 28 days the patient will have been monitored intensively with frequent bloods and review by a Paediatric Nephrologist/ renal nurse specialist at Starship. This is a guide only for a well functioning graft in a stable post transplant patient. NB In order to preserve veins and forearm vasculature for potential haemodialysis access in the future, it is recommended that blood draws be done as microcollections

Time after transplant	Visit Interval[a]	Surveillance for
Month 1	**3 days per week**	Acute rejection, post op complications, adverse drug reactions, hypertension
Month 2	**2 days per week**	Acute rejection, infections, adverse drug reactions, hypertension, unexplained lymphadenopathy
Months 3&4	**1 day per week**	Acute rejection, infections, adherence, adverse drug reactions, hypertension, unexplained lymphadenopathy
Months 5&6	**Every other week**	Acute rejection, adverse drug reactions, infections, adherence, hypertension, unexplained lymphadenopathy, growth
Months 6-12	**Monthly**	Acute rejection, adverse drug reactions, infections,adherence, hypertension, unexplained lymphadenopathy, growth, vaccinations
>12 months	**1-3 monthly visit[b]** **1 monthly labs**	Acute rejection, adverse drug reactions, infections, adherence, hypertension, unexplained lymphadenopathy, growth, skin, vaccinations

a. **Visit requires blood test plus medical review**
b. **Timing of visits dependant upon clinical course and interval concerns**

Clinic visits should be recorded on the proforma and faxed to 09 307 8938. If a dictated letter is sent please ensure it includes all information that would be included on the proforma.

All paediatric renal transplant recipients should be seen by a Paediatric Nephrologist whenever they have outreach clinics at the patient's local hospital.

Post transplant, children will be reviewed at Starship Children's Hospital over 2-3 days at 3 and 12 months for a surveillance biopsy and at 36 and 60 months for general review including consideration of GFR measurement, blood pressure monitoring, growth assessment, vaccination review and possible biopsy.

Post Renal Transplant Routine Blood and Urine Tests

Please ensure blood test forms state copy to be sent to renal team at Starship on fax number (09) 3078938.

Additional tests or change in frequency of these tests may be required for more complex patients or those with chronic kidney disease, these patients may have an individualized plan.

Investigation	Frequency
Full Electrolytes Sodium Calcium Potassium Phosphate Urea Magnesium Creatinine Albumin Glucose	As per visit schedule - see above.
Full Blood Count	As per visit schedule - see above.
Tacrolimus Level (trough)	As per visit schedule - see above.
EBV PCR	Monthly for first year. Monitoring thereafter dependent on antibody status.
CMV PCR	Monthly for first year after taking valganciclovir prophlyaxis (monitoring not required whilst on). Monitoring may resume post increased immune suppression. For CMV R-/D- transplants (no valgan) q 3/12 for first year.
BKV PCR	Monthly for first 6 months, 3 monthly from month 7 to 24, then annually until 5 years post- transplant. Monitoring may resume post increased immune suppression.
25-OH Vitamin D **ALP**	Annual Annual (suggest these are done at time of transplant anniversary)
PTH	Annual if eGFR>60, biannual 30-60, q 3 monthly <30.
HBsAb **VZV and Measles IgG**	6 and 12 months post transplant then annually (unless documented non-responder). Annually unless IgG neg.
Urine microscopy & culture, protein:creatinine ratio	Monthly – first morning urine specimen should be obtained for confirmation if proteinuria detected.

Graft Dysfunction

Significant rejection can present with only small rises in creatinine. Other causes of graft dysfunction can include, dehydration, infection (including UTI, EBV/CMV/BKV), obstruction and nephrotoxicity secondary to high levels of calcineurin inhibitors (tacrolimus, cyclosporine).

All elevations in creatinine (>10-20% above baseline) should be reviewed/investigated re underlying cause and discussed urgently with Starship. If thought to be hydration related this should be addressed with a follow-up creatinine measurement within 48 hours. Any rising or persistently elevated creatinine levels should be re-discussed with Starship. Patients may be required to return to Starship urgently for transplant biopsy.

Persistent Proteinuria and Haematuria

Urine microscopy and a protein:creatinine ratio should be evaluated monthly. Persistent proteinuria and haematuria, even in the setting of otherwise stable graft function, can signify significant pathologies including rejection, recurrence of original renal disease, de novo renal disease in allograft, BK virus nephropathy, nephrolithiasis, malignancy etc. These findings should be discussed with Starship and specific investigations, which might include a renal biopsy will be recommended.

Surveillance for Viral Infections

CMV and EBV infections are associated with significant morbidity, and the possible development of post transplant lymphoproliferative disease (PTLD). BKV infections may cause an inflammatory nephropathy with subsequent renal scarring and permanent loss of allograft function. These infections may require treatment or changes in immunosuppression. Early detection may prevent the development of more serious disease.

CMV Infection

Routine CMV Quantitative PCR monitoring

- CMV PCR at monthly intervals for the first year post transplant unless whilst taking valganciclovir prophylaxis.
- IF transplant was CMV D-/R- with no valganciclovir prescribed, q 3 monthly CMV PCR for first year.
- Monthly CMV PCR for three months following IV steroids/ATG.
- Required routine frequency after one year should be documented at their 12 month review at Starship.

Additional

- CMV PCR should be checked during episodes of allograft dysfunction.
- CMV should be checked in all patients who develop unexplained fever, diarrhoea, persistent cough, unexplained lymphadenopathy, abnormal liver function tests, or persistent haematological abnormality.
- CMV should be checked in children presenting with EBV, HSV or Varicella.
- In a patient with previous CMV PCR positive results, if beyond the first year post transplant, continued monitoring can be discontinued following three consecutive months of negative test results. This should be discussed with Starship Nephrology.

CMV Serology

- If the recipient is CMV IgG negative then serology should be checked annually as silent seroconversion is possible.
- If a CMV IgG negative recipient develops a positive CMV PCR then CMV IgM and IgG should be checked.

EBV Infection

Routine CMV Quantitative PCR monitoring

- Monthly EBV PCR for first year.
- Monthly EBV PCR for three months following IV steroids/ATG.
- After first year those who are seronegative should continue to have routine PCRs every 3 months. Those who are seropositive do not require routine testing. Both groups require additional testing as documented below.
- Required level of EBV testing should be documented at 12 month review at Starship.
- If the PCR is found to be positive this should be checked monthly or more frequently at the discretion of the Paediatric Nephrology team.

Additional

- EBV PCR should be checked during episodes of allograft dysfunction.
- EBV should be checked in all patients who develop unexplained fever, diarrhoea, persistent cough, unexplained lymphadenopathy, abnormal liver function tests or persistent haematological abnormality.
- EBV should be checked in children presenting with CMV, HSV or Varicella.
- In a patient with previous EBV PCR positive results, if beyond the first year post transplant, continued monitoring can be discontinued following three consecutive months of negative test results. This should be discussed with Starship Nephrology.

EBV Serology

- If the recipient is EBV negative then serology should be checked annually as silent seroconversion is possible.
- If an EBV negative recipient develops a positive EBV PCR then EBV IgM and IgG should be checked.
- A change in viral status should be discussed with a Paediatric Nephrologist.

BKV Infection

Routine BKV Quantitative PCR monitoring

- Monthly BKV PCR for first six months then 3 monthly until 24 months post-transplant, then annually until 5 years post-transplant.

- If the PCR is found to be positive this should be discussed urgently with the Paediatric Nephrology team, as renal biopsy and medication adjustment will likely be required. Subsequent monitoring will be at the discretion of the Paediatric Nephrology team depending on viral load and clinical status (including biopsy findings and graft function) however a general approach would be to repeat viral load q2 weekly until $<10^3$ then q monthly until negative x 3.

- Following any episode of BKV infection we recommend resumption of screening 3 monthly for the 12 month period following resumption of full immune suppression (nb. it is likely they will remain on lower immunosuppressive doses than prior to the diagnosis of BK infection).

Additional

- BKV PCR should be checked during episodes of allograft dysfunction or gross haematuria.
- Monthly BKV PCR for three months following IV steroids/ATG.

Medications

Routine Post Transplant Medications

Nystatin	Stop after 6 weeks
Ranitidine	Stop after 6 weeks
Cotrimoxazole	Stop after 6 months (protocol can change based on local risk)
Valgancyclovir (CMV prophylaxis)	Stop at 12 weeks

Maintenance Immunosuppressive Regime

Any changes in immunosuppression drugs must be discussed with a Paediatric Nephrologist first.

Prednisone

This will be weaned as per the individualised protocol and will depend on graft function and growth.

Tacrolimus

In general target levels are:

> 30 days post RTX	6.0-8.0ug/l
90-180 days post RTX	5.0 – 7.0ug/l

Note: Levels of around 4.0ug/l after 6 months are acceptable if there has been no history of acute rejection. However we may aim for different levels under certain circumstances eg EBV viraemia. Any changes or concerns should be discussed with the renal team.

Long Term Surveillance

Histological Surveillance of Renal Transplant by Graft Biopsy

Rationale

- To detect CNI toxicity
- To detect chronic allograft nephropathy
- To detect sub-clinical rejection

Timing

- Time Intervals for surveillance biopsy: 3 months and 12 months and discretionary biopsies thereafter depending on GFR.
- The biopsy at 3 months will be undertaken before switching to alternate day steroids. Conversion to alternate day steroids will only take place if there is no history of acute rejection and the biopsy is satisfactory.

Surveillance of Glomerular Filtration Rate (GFR)

- ^{51}Chromium EDTA GFR will be considered at 12, 36, 60 months post transplant when at Starship for review.
- To be arranged by Starship renal team with Nuclear Medicine Department of Auckland City Hospital.

Cardiovascular Surveillance

- Target blood pressure after the first three months post transplant is 50th-90th percentile for gender/height/age. Any patient with persistent hypertension should be discussed with Starship nephrology.
- 24 hour ambulatory blood pressure profiles recommended annually (where facility is available) to assess blood pressure control - we will do this at their routine Starship reviews when possible.
- In those patients who are on anti hypertensive medications, best practice recommendation is biannual ambulatory blood pressure profile.
- Annual serum lipid profiles measuring fasting cholesterol, triglycerides, and glucose.

Bone Health Surveillance

- Evaluation of serum calcium, phosphate, alkaline phosphatase, PTH, in all post transplant patients twice in the first year and at annual intervals thereafter, more frequently if CKD stage 3 or higher.

- Vitamin D level annually and more frequently based on advancing CKD.

Ultrasound Surveillance of Native Kidneys and Allograft:

Ultrasound surveillance of native kidneys and the allograft should be performed routinely at 1, 5 and 10 years post transplant.

Skin Surveillance:

Patients should be given regular reminders about sunblock.
If there is concern about changing moles or other new skin lesions they should be discussed with a dermatologist.

Vaccinations and Post-Exposure Prophylaxis Recommendations:

You should receive a copy of your patients Starship CKD Vaccination Record documenting their pre-transplant vaccinations and highlighting those that are still required.

It is recommended to avoid vaccinations, except influenza vaccination (see below), in the first 6 months following kidney transplantation. **All live vaccinations and BCG are contraindicated whilst immunosuppressed post renal transplantation.**

Hepatitis B

- Check HBsAb titres 6 & 12 months post transplant and then annually (unless patient is known to be HBsAb <10 and a documented vaccine non-responder).
- Give Hep B booster vaccination if antibody titer falls below 20mIU/mL.
- Recheck HBsAb 1 month post vaccination to determine response.
- A single "booster" dose may be provided annually as long as patient continues to mount a response.
- To maximise response can administer vaccine intradermally.
- Booster dose recommendation:
    - HBvaxPro; <16yrs = 10ug, 16+ yrs 20ug
    - Engerix B (if above unavailable); <16 yrs =10ug, 16+ yrs 40ug

- If patient was a documented non-responder pre transplant recommend a repeat standard 3 dose series with repeat serology 1 month after completion. If continued non-response not for further vaccination. A non-responder who is exposed to blood or body fluids should be given 2 doses of HBIg, 1 month apart.

Varicella and Measles

We check VZV IgG and Measles IgG prior to discharge post-transplant and then it should be done annually (unless known IgG negative).

Ig is **not** indicated in immunosuppressed contacts with detectable antibody as the amount of

antibody provided by VZIG will not significantly increase varicella antibody titres in those who are already positive. Be aware that if the patient has recently had increased immunosuppression, their current status may have changed.

- **Post transplant patients should receive immunoglobulin (IG) prophylaxis* if Varicella or Measles exposed AND:**

    - **<u>known seronegative</u>**
    - **OR if status is unknown and urgent result cannot be obtained**
    - **OR if patient has recently had increased immunosuppression (pulse steroids/ ATG/ increased baseline IS) without subsequent VZV/measles IgG result.**

    *For **varicella** exposure IG prophylaxis is given as VZIG (i.m.) or IVIG as soon as possible, but up to 10 days following exposure may be beneficial. If IG given greater than 96hours post exposure Acyclovir can also be offered for post exposure prophylaxis: oral acyclovir 20mg/ kg four times daily for 7 days from day 7 post exposure, plus strict instruction to present to medical care if lesions develop. In severely immune suppressed patients both modalities may be offered.

    For **measles** exposure IG prophylaxis is given as normal IG (i.m.) or IVIG, as soon as possible within 6 days of exposure.

- **<u>Additionally</u>** ensure household contacts are immunised/ have immunity:
    - Varicella vaccine is now funded for all household contacts of immunosuppressed patients and should be given to household contacts with no prior history of chicken pox or vaccination
    - MMR vaccine is on the National Immunisation schedule and is free for any susceptible individual: all household contacts should have received 2 doses of measles containing vaccine (unless born prior to 1969).

<u>Influenza</u>

- All kidney transplant recipients who are at least 1-month post-transplant, should receive the influenza vaccination prior to the onset of the annual influenza season, regardless of status of immunosuppression.
- Household contacts also recommended and funded to receive the annual flu vaccine.
- Even while transplant recipients are receiving high levels of immunosuppression, the benefits of timely vaccination outweigh the risks of delaying vaccination.

<u>HPV (Gardasil)</u>

- Recommended and funded (from age 9) for all male and female transplant patients.

Renal Transplant Follow Up Clinic Proforma

Renal Transplant Follow Up Clinic Proforma	Date seen: ___/ ___/ ___
Name Sticker	Date of transplant: ___/ ___/ ___ Time Since Transplant:
Background History	**1.** ESKD secondary to **2.** Transplanted **3.**
Current Issues	
Medications	**1.** **2.** **3.**
Examination **Height %** **Weight %** **BSA m2**	BP: Nodes: ENT:
Investigations	
Creatinine Urea Hb Plt WCC N L Tac Urine PCR Urine microscopy CMV PCR EBV PCR	
Date of next clinic visit	
Please ensure results are copied to fax 093078938 WHEN COMPLETED PLEASE FAX TO 093078938 If completed electronically email to: renalnurse@adhb.govt.nz	Please do bloods/urine as per protocol