



General Information For Primary Care Physicians Regarding Renal Transplant Patient Management

Immunosuppression

General

Following transplantation, patients are maintained on life long immunosuppression. Standard immunosuppressive therapy usually consists of alternate day or daily prednisone in addition to cyclosporine (Neoral) or tacrolimus (Prograf) and mycophenolate (MMF). Prednisone dosages range considerably but most patients take 10 to 15 mg every other day, and should never be stopped abruptly. Some patients may be on azathioprine (Imuran) and usually take between 50 -150 mg/day (1-2 mg/kg/day) provided the WBC is > 4000. Additionally, some patients are on investigational drugs and any questions regarding these should be referred to us directly.

Cyclosporine (Neoral) or Tacrolimus (Prograf, FK506)

These drugs are similar in their actions and side effects. Both are taken twice daily (every 12 hours). Patients are followed by drug levels which are obtained at clinic visits and adjustments are common within the first year. Once patients have established the times they will take their drug, they should rarely deviate from this regimen. If they forget a dose, they should take it if they remember within 6 hours. If it is greater than 6 hours, they should skip the dose and return to their regular schedule. Patients should never double dose. If they vomit within an hour of taking a dose, they should repeat the dose when they are able. If they are unable to keep anything down or if they have prolonged diarrhea (1 - 2 days) they should contact their nephrologist.

Trough drug levels are measured at clinic visits. Toxicity is associated with elevated blood levels. Dosage adjustments are made by the transplant physician. Due to metabolism via the cytochrome p450 system, these medications are involved in a significant number of drug interactions. All transplant recipients are instructed to check with their physician or pharmacist prior to taking any new prescription or over the counter medications. Three effects can occur:

1. increased drug level (increased risk of side effects)
2. decreased drug level (risk of rejection)
3. additive nephrotoxicity.

The table below lists common drug interactions. This list is by no means complete, but will give you an idea of what types of drugs interact.

Drug Class	Increased Serum Drug Levels	Decreased Serum Drug Levels	Additive Nephrotoxicity	No Effect
Antibiotics/ Antibacterials	erythromycin clarithromycin	trimethoprim rifampin isoniazid sulfadimine	aminoglycosides cotrimoxazole trimethoprim	penicillin norfloxacin cephalosporins
Anti-fungals	ketoconazole fluconazole			
Calcium Channel Blockers	diltiazem verapamil nicardipine			nifedipine
Anti-convulsants		carbamazepine phenytoin pheobarbital		
Others	cimetidine metoclopramide oral contraceptives			ranitidine

Hypertension

Hypertension is a common problem in renal transplant patients and it often predates their transplant. It is aggravated by the immunosuppressant agents post transplantation. We usually begin treatment with adjustment of their immunosuppression and mild diuretics if edema is present. Long acting calcium channel antagonists or Beta blockers are added if they are not contraindicated. We tend to avoid ACE inhibitors as they can all decrease renal function abruptly. However, if ACE inhibitors are required, we follow patients' renal function (creatinine and potassium) closely for several weeks before returning to usual monitoring.

Non-Steroidal Anti-Inflammatory Agents

All of the NSAIDs have the potential to decrease transplanted renal function and we generally avoid them, particularly indomethacin. There is no evidence that the newer COX2 inhibitor class of drugs is protective of renal transplants. However, under some conditions NSAIDs are unavoidable and if prescribed renal function (creatinine and potassium) must be monitored weekly for several weeks before returning to usual monitoring.

Gout

Gout is common in transplant patients on cyclosporine. We rule out other causes of acute joint pain, and then begin with colchicine 0.6 mgm one to two times a day. It can be stopped when symptoms subside or if severe diarrhea develops. We try to avoid NSAIDs as mentioned above, but if necessary we will use them other than **indomethacin**. Allopurinol can be given to patients with recurrent problems with gout after the acute episode subsides. However if the patient is on **azathioprine (Imuran)**, we

recommend that the patient be reviewed in our clinic to begin allopurinol as fatal bone marrow suppression can occur as a result of altered azathioprine metabolism, and dosage adjustments must be made. The drug MMF does not have this high risk but we ask to review these patients as well before starting allopurinol.

Hyperlipidemia

If a patient is identified with a cholesterol > 5.5 mmol/l, a dietary consultation is obtained. Careful attention to diet is then tried for three months. If the fasting cholesterol remains > 5.2 mmol/l, then the patient is started on Pravastatin (Pravachol) at a dose of 10 mgm at hs. The patient is monitored for signs of rhabdomyolysis, liver injury and renal impairment. CPK, AST, Creatinine, and Potassium should be checked every two weeks for two months. If at the end of two months the cholesterol has still not fallen below 5.1 mmol/l, the dose is increased to 20 mgm at hs. The same bloodwork is monitored at the same intervals. The dose can be increased again to 40 mgm. If severe myalgias or an elevation in enzymes occurs to three times the normal, the therapy is stopped.

Pneumocystis Carnii Prophylaxis

Transplant patients are placed on one tablet of Septra DS every Monday, Wednesday, and Friday for the first year following their transplant as prophylaxis against pneumocystis carinii. This coincides with the the period of the highest level of immunosuppression.

Dental Prophylaxis

Prophylactic antibiotic coverage is recommended for bacteria-inducing procedures such as probing, cleaning, extractions, and oral surgery if the patient has foreign material such as a gortex graft or heart valve or a prominent heart murmur. The benefit of prophylaxis in transplant patients otherwise has not been established. Dosage adjustments for current short term prophylaxis is not required for either penicillin or erythromycin. Penicillin based treatment will not affect cyclosporine levels. Erythromycin should not cause sustained increases in cyclosporin if given only for 1 - 2 days.

Immunizations

Patients should be advised that the effectiveness of vaccines is considerably reduced while on immunosuppressive therapy and they may not receive protection from immunization. However, the Ministry of Health will cover the cost of some vaccinations even if low rates of response occur. The table below outlines which ones **adult** patients may or may not have. Patients should not be immunized with vaccines prepared from live sources (attenuated vaccines). If you have a question, please call the general nephrology information line.

Recipients may be given:	Recipients may not be given:
Diphtheria	Mumps
Pertussis	Measles
Tetanus toxoid	Smallpox
Polio (Salk form)	Rubella
Influenza	Polio (Sabin form--oral)
Hemophilus B Influenza	B.C.G.
Hepatitis B	
Pneumococcus	

Pregnancy

Patients with functioning transplants may become pregnant. If they do not wish to become pregnant, some form of contraception should be used. Issues of graft function should be discussed with the transplant team.

Malignancy

Skin cancers, particularly squamous cell carcinoma, and lymphomas are more common in patients receiving immunosuppression and monitoring physicians need to be watchful for any signs and symptoms. Patients are advised to avoid sun exposure and suspicious or persistent skin lesions should be investigated.

Lab Results and Consult Notes

Transplant patients are followed by four nephrologists (Dr. Norman Muirhead, Dr. Andrew House, Dr. David Hollomby and Dr. Anthony Jevnikar) at the University Campus of the London Health Sciences Centre and do not have a specific attachment to any one nephrologist. As many patients are seen each week without major problems, unless unusual issues arise or the patient is admitted we do not provide dictated notes to referring physicians. However, we can provide notes and copies of any investigations if requested, along with lab results for the patient to bring to their next visit with their primary care physician. We encourage our patients to maintain a close relationship with their primary care physician to co-ordinate their care between specialists and to provide ongoing followup of problems not directly related to their renal function or immunosuppression. We are also happy to discuss any additional concerns or questions which can be directed to the nephrologist on call (519) 685-8500.

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