CCHCS Care Guide: Post Renal Transplant

SUMMARY | **DECISION SUPPORT** | **PATIENT EDUCATION/SELF MANAGEMENT**

GOALS

- ✓ Effectively monitor patients post-renal transplant to avoid re-hospitalization and surgery complications.
- ✓ Appropriately utilize immunosuppressant and other common post-renal transplant medications with the Transplant Team.
- ✓ Understand graft dysfunction and monitor for acute and chronic rejection to allow for prompt treatment.
- ✓ Improve care and manage post-renal transplant complications.

ALERTS

- Notify the Loma Linda University Transplant Team (LLUTT) of signs and symptoms of medication issues and graft dysfunction or rejection: extreme diarrhea, inability to retain meds due to nausea/vomiting, medication refusals, fevers, pain at the graft site, fever, flu-like symptoms, malaise, creatinine (CREAT) fails to drop or rises, decreased urine output (UO), and proteinuria.
- Notify the LLUTT if UO drops below 1 L/day or unanticipated acute drop from usual.

EVALUATION

- **History**: Review operative report and discharge summary (note graft kidney quality). General state of being, malaise, pain, swelling noted, bowel status, weight gain, how long on dialysis (longer = decreased graft and patient survival), comorbid conditions, substance use disorder (SUD), mental health (MH), what type of kidney? (i.e., donor or deceased, high kidney donor profile index [KDPI] or high risk [high KDPI is a lower quality kidney and have worse graft outcomes]), any problems peri-operatively?
- **Physical Exam**: Temp and other vitals, consider UO a vital sign, 24 hour UO should be > 1 L/day, Foley, Jackson-Pratt (JP) or other drain volumes, color and trends. Heart, lungs, abdomen, extremities, extremity edema, incision site, drain attachment site, organ site/retroperitoneal edema, redness or heat. Many will have a ureteral stent, some will have peritoneal or hemodialysis (HD) catheter. Note: working arteriovenous fistula (AVF)/arteriovenous graft (AVG) should have functionality sustained after transplant.
- **Labs**: CREAT, spot urinary protein to CREAT ratio (Spot UPCR), and immunosuppressant troughs.
- Ensure patient/care team members are all familiar with plan, labs, and visit intervals, etc.

TREATMENT

- **Patient Education**: See patient education pages for detailed information on: infection risks and prevention, understanding medications, understanding immunosuppression, diet (especially hyperkalemia and glucose intolerance), rejection, daily life after transplant, empowering patients, and self care. Patients will have had a detailed medication session with LLUTT before discharge.
- Encourage the patient's use of the "purple book" from LLUTT for recording fluid intake and output for at least 2-3 weeks (wks).
- The patient must understand doses of medications and their Medical Action Plan from LLUTT and understand they may be altered frequently to ensure effective treatment of comorbid conditions such as diabetes or hypertension (HTN).

IMMUNOSUPPRESANT INDUCTION (high dose immediately after surgery), generally to be tapered to a maintenance dose by 1 month post-op. Doses usually decrease over time. Most will use a combo of the top three listed below.

Immunosuppressant	Indication
Calcineurin Inhibitors (CNI)	• 92% use **tacrolimus** (Prograf® or FK506®), the rest use **cyclosporine–**(Neoral®, Gengraf®, Sandimmune®) • Action: Suppress T cells and T cell-dependent B cell activation (inhibits interleukin-2)
Glucocorticoids	• Nearly all use **prednisone** • Action: Profound suppression of lymphocyte proliferation, inhibits antigen presentation and cytokines.
Anti-Metabolite Agents	• Most use **mycophenolate mofetil** (MMF or CellCept®), enteric-coated mycophenolate sodium (EC-MPS®) or azathioprine (Imuran®) • Action: Inhibit proliferation of B and T cells
Mammalian Target of Rapamycin (mTOR) Inhibitor	• Sirolimus/rapamycin (Rapamune®) and everolimus (Zortress®, Afinitor®) • Second tier alternative if unable to take tacrolimus or cyclosporine • Action: Suppress T cells and T cell-dependent B cell activation (inhibits interleukin-2)
Category-Belatacept (Nulojix®)	• Second tier alternative if unable to take tacrolimus or cyclosporine • Action: Humanized antibody that inhibits T cell co-stimulation
Anti-Lymphocyte-Depleting Agents	• Anti-thymocyte globulin (ATG) rabbit (r-ATG®), and horse (h-ATG®) (Thymoglobulin®), ATGAM®, basiliximab (Simulect®), alemtuzumab (Campath-1H®), and rituximab • *Proposed* Action: Anti-monoclonal antibodies that inhibit pathway to development of Human Leukocyte Antigen (HLA)–and ABO blood type–incompatibility antibodies via inhibitory effect on hematopoietic stem and progenitor lymphocyte cells, reduces certain specific B cells types

MONITORING

Monitor:

- Labs (See pages 9-11)
- Vaccines (See page 12)
- MH status: Nonadherence, depression, and other psychological issues (See page 13)
- Delayed graft dysfunction, rejection and other complications (See pages 14-20)
- Infection (See pages 21-23)

TABLE OF CONTENTS

Information contained in the care guide is not a substitute for a health care professional's clinical judgment. Evaluation and treatment should be tailored to the patient's unique clinical circumstances. Furthermore, using this information will not guarantee a specific outcome for each patient. In addition, the recommendations in this care guide are solely to provide global guidance for providers. Patient care after transplant is highly individualized and the Loma Linda University Transplant Team (LLUTT) gives CDCR providers very specific instructions for patient care after transplant. LLUTT instructions will always supersede the care guide recommendation. Refer to "Disclaimer Regarding Care Guides" for further clarification. https://cchcs.ca.gov/clinical-resources/

POST-RENAL TRANSPLANT ALGORITHM PAGE 1

(LLUTT management supersedes**)

PATIENT UNDERGOES RENAL TRANSPLANTATION (RT)

Overall Survival Benefit, Improved Quality of Life, and Lower Cost than lifelong HD

Post-Op Day 1-6: *See details page 5*

Patient remains in the hospital typically for 4-6 days and will be discharged to an institution with a personalized Medication Action Plan from LLUTT and will have had detailed medication training

Monitoring:

LLUTT manages

- Fluids ins and outs. Goal: 2 L/day in and > 20 mL/kg/day out
- Blood pressure (BP)
- Weight

Medications:

LLUTT manages

- 90% discharge on tacrolimus (high dose), prednisone (high dose), and mycophenolate
- Order tacrolimus for an empty stomach: no food 2 hrs before and 1 hr after

Special Needs/Orders:

- Correctional Treatment Center (CTC)/ Outpatient Housing Unit (OHU) dedicated bed needed, non-cocci facility
- Single cell
- Hot water (when available)
- Mask when out of cell
- Patient hygiene is important
- Separate yard than general population
- Maintain at an institution with close proximity to Loma Linda University Medical Center (LLUMC) for 1-2 years (See general guidance page 4)

Complications:

- Possible delayed graft function or dysfunction may be related to intraoperative insults or intrinsic graft issues
- Graft vascular thrombosis
- Watch for infections, especially urinary tract infection (UTI) (Foley), wound infections, and drain infections

Post-Op Day 7-30: *See details page 5*

Primary Care Physician (PCP)/Care Team and LLUTT keep close follow-up

Monitor:

LLUTT manages

- Fluid ins and outs
- BP
- Weight
- CREAT and for proteinuria-Spot UPCR; proteinuria has worse graft outcomes
- 2x/wk labs (See lab pages 9-11)
- LLUTT clinic visits (See details of visits on next page)

Medications:

LLUTT manages

- LLUTT will attempt to lower immunosuppressant dosages to maintenance doses
- Goal to avoid over immunosuppression and drug toxicity to new kidney-narrow therapeutic window-requires very close monitoring with 12-hour post-med trough levels for tacrolimus

Special Needs/ Orders:

- Same as above
- Keep kidney perfused-patients need to drink a minimum of 2 L/day

Complications:

- Same as day 1-6 above
- Focus is: Infection, calcineurin inhibitor (CNI) (tacrolimus or cyclosporin) medication toxicity to new organ, graft dysfunction and early rejection, prednisone side effects including hyperglycemia
- Watch for leaks
  - Urinomas, hematomas, etc.
- Early rejection
- Anemia due to post-op bone marrow not recovered

Post-Op Day 31-90: *See details page 6*

Primary Care Physician PCP/Care Team and LLUTT keep close follow-up

Monitor:

LLUTT manages

- Urine output
- BP
- CREAT and for proteinuria-Spot UPCR
- Labs 1-2x/mo for 1 mo, then monthly for 12 mos (See lab pages 9-11)
- LLUTT clinic visits (See details of visits on next page)

Medications:

LLUTT manages

- Stabilize medication doses
- Do not treat HCV in first 3 mos after transplant

Special Needs/Orders:

- Inpatient CTC or OHU bed through third month
- After first 4 wks, the patient does not have to wear a mask and can be in yards with general population
- Patients should avoid other patients with signs/ symptoms of infection

Complications:

- Same as day 7-30 above
- Opportunistic Infections* highest risk 1-3 mos post transplant
- HTN
- New-onset diabetes after transplant (NODAT)-common, typically develops in first few mos
- Elevated lipids (common)
- Anemia (post op recovery usually by 2-3 months if no complications)
- Allograft dysfunction due to donor kidney disease or CNI nephrotoxicity

***Common Opportunistic Infections:**
Cytomegalovirus (CMV), BK virus, Epstein- Barr (EBV), Nocardia, Listeria, Aspergillus, Pneumocystis, Hepatitis B (HBV), Human Herpes Virus (HHV6/8), Hep C (HCV), Herpes Simplex (HSV), Vesicular Stomatitis (VSV), Tuberculosis (TB), Varicella Zoster (VZV), & ParvoB-19

POST-RENAL TRANSPLANT ALGORITHM PAGE 2

(LLUTT management supersedes**)

Post-Op Months 4-12: ***See details page 6***

Routine PCP, Care Team, and LLUTT follow-up. If indicated, treat for HCV at ≥ 3 mos post transplant after approval from LLUTT (See page 22)

Monitor:

LLUTT manages results

- Labs (See lab pages 9-11)
- Coping, adapting, and adherence
- Monthly clinic visits^
- Continue scheduled LLUTT visits. If LLUTT approves-may initiate telemedicine visits when available

Medications:

LLUTT manages

- Maintenance dosing
- Ok to give influenza vaccine when > 3 mos post op. Do not use live vaccine

Special Needs/Orders:

- Manual lab requisitions for pre-telemedicine appts
- At 12 mos, if approved by LLUTT for facility transfer, careful discharge planning to receiving institutional care team

Complications:

- Same as month 1-3 on prior page
- Drug-Drug Interactions (DDI) with new medications
- Allograft dysfunction progressing to chronic rejection most need biopsy (1/2500 biopsies cause graft failure)
- Donor-related disease
- Recurrent original disease (especially focal segmental glomerulosclerosis [FSGS])
- Arteriosclerotic Cardiovascular Disease (ASCVD) and cardiomyopathy
- Weight gain
- Malignancy-3x lifetime higher risk. Keep high index of suspicion (See pages 27-29)
- Persistent hyperparathyroid hormone (PTH) 50%,
- Calcium/phosphate (Phos) and consequent bone disorders, Dual-energy X-ray absorptiometry (DEXA) screening if will affect management
- Electrolyte and metabolic disorders
- Hematologic disorders
- Hyperuricemia and gout
- Resumption of secondary comorbidities due to chronic kidney disease (CKD)
- Upper respiratory infection (URI) and UTI
  - As immunosuppressant doses decrease, less opportunistic infections but community acquired risk increases, especially after 6 mos post-op
- New HBV/HCV infections

Lifelong Post Transplant: ***See details page 6***

Monitor:

- Watch for ulcers, cataracts, diabetes mellitus (DM), bone disease, poor wound healing and other side effects of prednisone
  - HgA1c q 3 mos for first 12 mos, then annually thereafter
  - Measure bone mineral density (BMD) within first 3 mos of post-transplant period if it will change management (See page 26)
  - Annual ophthalmology eval is recommended for glaucoma and cataract screening
- Renal function will never be normal, estimated glomerular filtration rate (eGFR) universally< 60 and CREAT > 1.1
- Tacrolimus, cyclosporine levels will be obtained 1 wk prior to clinic^ or tele-visit with transplant nephrologist
- Monthly to quarterly labs (See lab pages 9-11)
- Quarterly, biannual, or annual clinic visits. If LLUTT approves-may initiate telemedicine visits when available

Medications:

- NO LIVE VACCINES, NSAIDS or DECONGESTANTS (pseudoephedrine)
- 70% of patients remain on lifelong prednisone
- 100% remain on lifelong tacrolimus, cyclosporine, or other non-glucocorticoid immunosuppressant

Special Needs:

- When approved by LLUTT for facility transfer, careful discharge planning to receiving institutional care team
- Forever non-cocci facility

Complications:

- Same as month 1-12 on previous page and above
- All grafts ultimately fail. Depending on graft ~5-10 years expected
- After graft failure, patient can be evaluated for replacement on United Network for Organ Sharing (UNOS) list

^LLU In Person Clinic Visits:

- Patient follow-ups with LLUTT at 1, 2, & 4 wks post-transplant
- Arrange transportation from institution to LLUMC Clinic
- Ensure patients bring all medications, Medical Action Plan, water, and breakfast to every visit
- Patients should wear a mask to the lab and clinic *for the first 4 wks*
- Same day fasting and 12-hr trough labs prior to every clinic visit
- Patients can drink water anytime
- Check into the lab fasting and wearing a mask at 6:30 a.m.
- Take AM tacrolimus immediately AFTER blood is drawn
- Check into the clinic at 7:00 a.m.
- One hr after taking tacrolimus, all other morning medications should be taken with breakfast
- Labs need to be drawn 11-12 hrs from the last time tacrolimus was given (Example: Patient takes tacrolimus at 8:00 p.m., labs need to be drawn no later than 8:00 a.m. the next day)

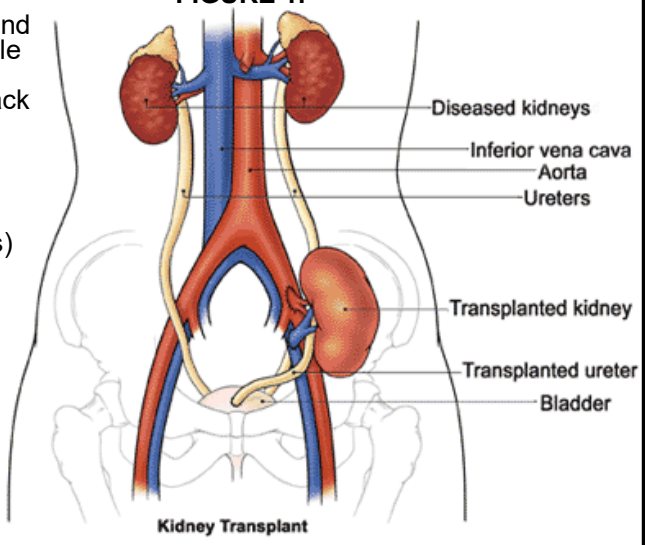
SUMMARY | DECISION SUPPORT | PATIENT EDUCATION/SELF MANAGEMENT

POST-TRANSPLANT GENERAL GUIDANCE**

What providers can expect after RT surgery:

- The renal allograft is placed **extraperitoneally in the right or left iliac fossa** (See Figure 1). Vascular anastomosis are usually between the donor renal vessels and the external iliac vessels of the recipient. Urinary reconstruction is almost always via uretero-neocystostomy (donor ureter to recipient bladder), although at times, other types of reconstruction may be chosen.
- The patient will be discharged often day 4 post-surgery with a personalized Medication Action Plan from LLUTT. This is a list of all their medications and when to take each
- A Foley catheter is usually put in place post-op and possibly left in up to 7 days (LLUTT removes or approves removal).
- Possible JP rubber drain for blood/serous fluid is left in near surgical site to remove fluid (LLUTT removes)
- Possible ureteral stent removed by LLUTT 5-6 wks post-transplant under sedation
- Possible delayed graft function requiring continued temporary dialysis (or graft failure with resumption of dialysis)
- If rare case of pre-op peritoneal dialysis (PD) used, PD catheter–removed in operating room (OR) 4-6 wks post-transplant
- AVF and AVG are not removed and usual care to maintain graft patency should be emphasized
- Patient on CNI* tacrolimus (90% or more of patients) or cyclosporine (CSA), prednisone, and an antimetabolic agent (most often mycophenolate). Order tacrolimus for an empty stomach. No eating 2 hrs before and 1 hr after the medication dose (See page 31)
  - *Calcineurin is a calcium and calmodulin dependent phosphatase that activates the T cells of the immune system
- The patient will have had extensive education on the medications, and most patients are able to transition to keep on person (KOP) when stable
- The patient will have a "purple book" for tracking fluid ins and outs
- All the other medications should be taken with food, including a snack with nighttime medications

FIGURE 1.



Kidney Transplant

LLUTT post-transplant general patient guidance:

- No lifting over 10 lbs for the first 4 wks
- No sexual activity in the first 4 wks or while the incision is healing
- No core exercises for 3 months (mos) (e.g., sit ups, crunches, or planks)
- No running, or vigorous exercise for 3 mos; walking is best
- No contact sports for 6 mos
- Showers are fine
- Wear a mask when outside of the clinic for the first 4 wks
- Practice good hygiene and wash hands with hot water (when available)
- ALWAYS wear a mask to the clinic and laboratory for the first 4 wks
- Avoid crowds when possible, especially for the first 4 wks
- Always avoid sick people or people with signs and symptoms of illness
- Stay out of the sun, wear lip sunscreen, limit the skin that is exposed and protect your head, face and skin with cloth barriers and clothing
- Vascular access is usually left in; continue access preservation. No blood draws, BP cuffs, constriction, etc.
- Wait to return to work is typically 4-12 wks post-transplant
- If the patient has in-person visitation privileges, avoid secretions of children who have received live vaccines
- Promptly report wounds, injuries, UTI symptoms, or respiratory ailments to the health care team

LLUMC CLINIC VISITS

- Patients will have follow-up visits at LLUMC at 2x/wk first mo, q wk second mo, q 1-2 wks third mo, then monthly to 1 yr
- Ensure the patient brings all medications, Med Action Plan, water and breakfast to every visit
- Patients should wear a mask to the lab and clinic *for the first 4 wks*
- Same day fasting and 12-hr trough labs prior to every clinic visit
- Patients can drink water anytime

LLUMC Appointment Locations:

Lab: Faculty Medical Office
11370 Anderson St.
Loma Linda, CA 92354

Clinic: Transplant Institute
197 East Caroline St. Ste 1400
San Bernardino, CA 92408

Note: When LLUTT clears the patient for telemedicine visits (and telemed available) labs will be drawn by CDCR phlebotomists and the blood picked up by Quest as per usual routine. If STAT level needed, call local Quest lab to notify. The tacrolimus levels are only run Tues-Sat, so Saturday nights, Sundays, and holidays, STAT labs will not be available (confirm with local lab). If need STAT and Quest unable to run, transfer the patient to LLUMC. ***Results must be sent to LLUTT immediately****. LLUTT will direct providers if dose changes are needed.*

Clinic Day Schedule:

- Work with the institution Offsite Specialty Team/custody
- Use telemedicine when available and approved by LLUTT
- The patient should be advised to gather: medications, Med Action Plan, water, and breakfast to go check into the lab fasting and wearing a mask at 6:30 a.m.
- Take AM tacrolimus immediately AFTER blood is drawn–lab turnaround is generally 1-2 days and up to 72 hrs with a holiday
- Check into the clinic at 7:00 a.m.
- One hour after taking tacrolimus, all other morning medications should be taken with breakfast
  - Labs need to be drawn 11-12 hrs from the last time tacrolimus was given
  - Example: If the patient takes tacrolimus at 8:00 p.m., labs need to be drawn no later than 8:00 a.m. the next day

MONITORING POTENTIAL COMPLICATIONS POST-TRANSPLANT

(LLUTT management supersedes**)

Immediate Post-Op Issues (Day 1-6)

- Medically stabilize the patient–vital signs (UO/weight), drains, Foley & stent removal, graft functioning?
- Most will discharge to an institution (non-cocci) 4-6 days post-surgery
- Will need: single cells, mask precautions when out, separate activity yard, hot water when available, advance to solid diet as soon as tolerated
- Incision is generally in the lower abdomen and graft in the peritoneal (not retroperitoneal) cavity
- Immunosuppressant induction therapy characterized by high dose steroids and high dose tacrolimus or CSA
- > 90% of patients will be on tacrolimus, mycophenolate, and steroids. Job of mycophenolate is to lower CNI doses
- Primary graft failure (transplanted kidney never starts working)
  - May be related to intra-operative "hits" to graft/kidney quality (long ischemic cold times, long graft re-warm times (ice is used while performing the anastomosis), poor intravascular volume repletion)
- Monitor:
  - Daily: fluid ins and outs, weight–patients to drink a ***minimum* of 2 L/day (or customized target).** Assess fluid status–especially if history of congestive heart failure (CHF). Consistent UO indicates graft perfusion. **UO > 20 mL/kg/day**
  - Educate patients NOT to empty Foley bags and only to use the bedside urinal and not the toilet after Foley removal
  - Daily BP
  - Infections: Wound infections, drain entry infections, graft infections, UTI (Foley)
  - Surgical complications (thromboses, nicked bladder, ureter, or vessel, etc.), abnormal bleeding or swelling, ↑ pain
  - Medications
    - ⇒ Tacrolimus level at LLUTT target?
      - ◊ Tacrolimus order: "take on an empty stomach. No food 2 hrs before and 1 hr after pill"
      - ◊ Tacrolimus monitored by 12-hr trough, CSA 12-hr trough or 2-hrs post dose
    - ⇒ Drug toxicity and Side effects
      - ◊ Tacrolimus (or CSA) (CNIs–narrow therapeutic window: Too low of dose = rejection, too high of dose = over-immunosuppression and drug nephrotoxicity. (Increasing ↑ CREAT and/or new/↑ protein)
    - ⇒ Patients will be on or started on antiviral, antifungal and antibacterial prophylaxis as clinically indicated
    - ⇒ Consider consultation for any patients on warfarin and especially if on direct oral anticoagulants (DOACs). Reassess risk benefit ratio
  - Delayed graft function (See page 14)
    - ⇒ Sx: Oliguria (relative or < 400 mL/day), anuria, CREAT fails to decline, or proteinuria > 1 gm/day. See conversion of Spot UPCR to 24 hr protein: Urinary Protein Excretion Estimation Calculator*
    - ⇒ Requiring dialysis in the first week (wk) post-operatively
    - ⇒ **Rule out thrombosis/**reversible causes, but may be related to intra-operative "hits" to graft/kidney quality (long ischemic cold times, long re-warm times [anastomosis], poor intravascular volume repletion)
  - Hyperacute rejection-oliguria (relative or < 400 mL/day), anuria, graft tenderness. Surgical urgency (See pages 16-19)
  - Labs 2-3x/wk–per LLUTT, watch international normalized ratio (INR) closely if on warfarin anticoagulation
  - Physical appointments to LLU 2-3x/wk–per LLUTT

Early Post-Op Issues (Day 7-30)

- Keep kidney perfused: continue minimum 2 L/day of fluids (unless CHF or other co-morbid condition precludes)
- LLUTT will begin to lower immunosuppressant doses to maintenance (lower prednisone and tacrolimus)
- Monitor:
  - Fluid ins and outs, BP, weight–continue to drink a *minimum* of 2 L/day/(or customized target) fluid status-especially if history of CHF; consistent UO indicates graft perfusion
    - ⇒ CREAT trend and proteinuria (Spot UPCR–order "Protein, Total, Random Urine with CREAT" test code 1715).
    - ⇒ See conversion of spot UPCR to 24 hr protein: Urinary Protein Excretion Estimation Calculator*
  - Infections: wound site, drain entry, graft, UTI, URI
  - Surgical complications: especially leaks–urinomas, hematomas, abnormal bleeding or swellings, and pain
  - Medications
    - ⇒ Tacrolimus (or CSA) level at LLUTT target? (12-hr trough, no food 2 hrs before and 1 hr after pill)
    - ⇒ Nephrotoxicity from tacrolimus/CSA, high stakes if over (toxicity) or under (graft loss) dose (increasing CREAT and/or protein appearance or increase)
    - ⇒ Close monitoring of levels with frequent post 12-hr trough levels of meds
    - ⇒ Prednisone side effects (weight gain, cushingoid faces, bone weakening/loss, dyspepsia and ulcers, insomnia, HTN, hyperglycemia, striae, edema, and poor wound healing)
  - Early acute rejection-high risk this timeframe: Asymptomatic or flu-like symptoms, ↓UO, graft pain (See page 16)
  - Graft dysfunction: CREAT ↑ >25% from baseline, > 1 g/day proteinuria, Failure of CREAT to ↓ (See page 15)
  - Anemia: Common, post-op marrow recovery may take 2-3 mos to resolve (See page 26)
  - Labs 2-3x/wk for first 4 wks, monitor INR closely if on warfarin anticoagulation
  - Physical LLU appointments to LLU 2-3x/wk– per LLUTT

* https://www.mdcalc.com/urinary-protein-excretion-estimation#pearls-pitfalls

MONITORING POTENTIAL COMPLICATIONS POST-TRANSPLANT

Late Post-Op Issues (Day 31-90)

- Maintenance, optimization of medication doses to lowest necessary, and return to normalcy
- Keep kidney perfused: continue goal of 2 L/day minimum of fluids or per LLU (customize as indicated/CHF risk)
- Monitor:
  - Fluid ins and outs, BP, weight, consistent UO indicates graft perfusion and body water regulatory ability
  - CREAT trend and proteinuria (Spot UPCR–order "Protein, Total, Random Urine with Creatinine"–test code 1715)
    - ⇒ CREAT post-transplant will never be normal–nearly always > 1.1 and eGFR < 60
      - ◊ Monitor for decline and if so, rate of decline
    - ⇒ Development of proteinuria has worse prognosis
  - Infections
    - ⇒ Highest risk of infections between 1-3 mos
    - ⇒ Opportunistic infections begin
      - ◊ CMV, BK (polyoma virus) Virus, Epstein-Barr Virus (EBV), Nocardia, Listeria, Aspergillus, Pneumocystis, HBV, HCV, HSV-HHV, VSV, TB, and VZV (See page 21)
  - Medications
    - ⇒ Tacrolimus level at LLUTT target?
      - ◊ Nephrotoxicity from tacrolimus/CSA (increasing CREAT and/or protein appearance or increase)
      - ◊ Close monitoring of levels with frequent post 12-hr trough levels of meds
      - ◊ No dose changes unless rejection or side effects
    - ⇒ Prednisone side effects (weight gain, cushingoid faces, bone weakening/loss, dyspepsia and ulcers, insomnia, HTN, hyperglycemia, striae, edema, and poor wound healing)
    - ⇒ DDIs–clear new medications with LLUTT, check DDIs new and ↑ doses
  - Acute rejection–highest risk 1-3 mos. Asymptomatic or flu-like syndrome, UO changes, graft pain (See page 16)
  - Graft dysfunction–CREAT ↑ >25% from baseline, > 1 g/day proteinuria, failure of CREAT to ↓ (See pages 15-16)
  - Donor kidney disease–risk factor for allograft dysfunction (See pages 15-16)
  - Anemia–common, post-op marrow recovery time usually ends by 2-3 mos if no complications (See page 26)
  - Weight gain–give lifestyle recommendations: exercise, healthy diet, consider dietary consult (See page 24)
  - HTN–very common. Goal < 130/80 if Ualbumin > 30 mL/24 hrs. Use amlodipine/nifedipine first (See page 23)
  - Hyperglycemia and post-transplant diabetes mellitus (new-onset diabetes after transplant [NODAT])–usually first few mos post-transplant (See page 24)
  - Elevated lipids–atorvastatin or simvastatin recommended (See pages 23-24)
  - Myocardial infarctions–rate 50x higher than general population. Assess CV Risk % (See page 24)
  - Post-transplant lymphoproliferative disorder (PTLD)–related to EBV and immunosuppression. Highest risk 1-3 mos after RT. Associated with high mortality (50%) (See page 28)
  - **Do not treat HCV yet. Wait until 3 mos after RT** (See page 22)
  - **Do not give influenza vaccine until after 3-6 mos, but may give after 1 mo if needed** (See page 12)
  - Adherence–be vigilant. Associated with high risk of acute rejection and allograft loss (See page 13)
  - Labs: as needed and 1x/wk for 4 wks second mo, every other wk the third mo–per LLUTT (See page 9)
  - Switch from physical appointment to telemedicine LLUTT appointments when available and per LLUTT

Chronic Issues (Day 91 Onward)

- Maintenance phase and vigilance for complications
- 70% of patients will remain on steroids lifelong
- Monitor:
  - Consistent UO
  - CREAT trend and proteinuria (Spot UPCR–order "Protein, Total, Random Urine with Creatinine"–test code 1715)
    - ⇒ CREAT never normal–nearly always > 1.1 and eGFR < 60
      - ◊ Monitor for decline and if so, rate of decline
      - ◊ Development of proteinuria has worse prognosis
  - Infections
    - ⇒ Typically after 6 mos community acquired infections more likely
    - ⇒ Opportunistic infection risk remains: CMV, BK, EBV, Nocardia, Listeria, Aspergillus, Pneumocystis, HBV, HCV, HSV-HHV, VSV and Mycobacterium TB– Keep high index of suspicion, atypical molds
    - ⇒ Exotic community acquired infections such as coronavirus severe acute respiratory syndrome (SARS)/West Nile
  - Medications
    - ⇒ Tacrolimus level at LLUTT target
    - ⇒ Nephrotoxicity from tacrolimus/CSA
    - ⇒ Close monitoring of levels with frequent post 12-hr trough levels of meds

MONITORING POTENTIAL COMPLICATIONS POST-TRANSPLANT (CONTINUED)

Chronic Issues (Day 91 Onward–Continued)

- Monitor (continued)
  - Medications (continued)
    - ⇒ Side effects of medications
      - ◊ Longer term side effects of prednisone–including: weight gain, cushingoid faces, bone weakening/loss, dyspepsia and ulcers, insomnia, HTN, hyperglycemia, striae, edema, and poor wound healing
      - ◊ DDIs–clear new meds with LLUTT, check DDIs new medications and dose increases–CCHCS DDI Checker*
  - Allograft dysfunction into chronic rejection, most need biopsy. 1/2500 biopsies result in graft loss (See page 15)
    - ⇒ > 12 mos post RT, much lower risk of rejection
  - Donor kidney disease–prior and de novo
  - Anemia–post-op marrow usually ends by 3 mos if no complications. ↑ Risk if CREAT > 2 mg/dL (See page 26)
  - HTN poor control common, goal < 130/80 if albuminuria. 30 mg/24 hrs and tolerated, use amlodipine and nifedipine first. Avoid angiotensin-converting enzyme (ACE)/angiotensin receptor blocker (ARB) x 6 mos post RT (See page 23)
  - Hyperglycemia and post-transplant diabetes mellitus (NODAT)–less common this phase. Goal A1c 7% (See page 24)
  - Elevated lipids–use atorvastatin/simvastatin first. Moderate dose in eGFR ≥ 60 mL/min/1.73m^2 (See pages 23-24)
  - Atherosclerotic Cardiovascular Disease (ASCVD) (See page 24-25)
    - ⇒ Myocardial infarctions–rate 50x higher than general population. Assess CV Risk % regularly
    - ⇒ ASCVD and risk management: HTN, DM, Lipids, weight. Very high risk. Start acetylsalicylic acid (ASA), statins, ACE/ARB NOTE: ACE/ARB give only after > 6 mos post, and beta blockers, as indicated
    - ⇒ Counsel against smoking. Multiple studies show smoking increases mortality rates, graft loss, infections, and cardiovascular disease. Also decreases non-CV related 5 year survival.[2] 60% increased risk in the composite endpoint of return to dialysis or death[45]
  - Cardiomyopathy
    - ⇒ With or without clinical CHF is common among RT recipients. CHF is second only to infection as a cause of hospitalization after a kidney transplant. (Risk factors: Age, DM, anemia, HTN, obesity, suboptimal graft function, and graft loss)
    - ⇒ ACE/ARB
    - ⇒ NOTE: ACE/ARB give only after > 6 mos post,
  - PTLD–related to Epstein-Barr Virus (EBV) and immunosuppression. Bimodal risk again at > 2 years post RT. Mortality up to 90% (See page 28)
  - HCV treatment > 3 mos post. If HCV to be treated with Mavyret, note that the **only statin compatible with Mavyret is rosuvastatin**. Associated with increased morbidity (See page 22)
  - Vaccines–no live vaccines. Give influenza vaccines ≥ 3-6 mos after transplant surgery (See page 12)
  - Adherence (See page 13)
    - ⇒ Monitor for coping and adapting difficulties, adjustment disorder and other mood disorders
  - Weight gain–provide recommendations on healthy diet and exercise. Consider dietary consult (See page 24)
  - Malignancy–high risk–high index of suspicion, monthly self-skin check, annual experienced diagnostic provider or dermatologist skin check. Check lymph nodes when examining for acute complaints (See page 27)
  - Persistent hyper parathyroid hormone (PTH), calcium (Ca)/Phos disorders–31% will have after first yr. Leads to fractures (See page 26)
  - Electrolyte and metabolic acidosis–keep HCO3 28-30 mmol/L. Low potassium ion (K+) and magnesium ion (Mg++) especially (See page 25)
  - Bone disease due to the two above–DEXA if will change management
  - Bisphosphonates may not be helpful to lower fracture risk after the first year post RT (See page 26)
  - HEME: Anemia, leukopenia/neutropenia (meds–call LLUTT & viral infections), erythrocytosis (See page 26)
  - Hyperuricemia and gout–especially with cyclosporine, ↑risk if poor renal function & loop diuretic (See page 25)
  - 100% lifelong CNI, 70% will have lifelong prednisone (monitor side effects)
  - Lifelong NO LIVE VACCINES, NO NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS), NO DECONGESTANTS (pseudoephedrine vasoconstriction)
  - Labs monthly x12 mos, then monthly to quarterly per LLUTT
  - May have monthly labs for life, some may be q 3 or q 6 mos, some annual (See page 9)
- LLUTT (telemedicine when available) appointments per LLUTT
- When ready for leaving CA Institute for Men (CIM)/no cocci locations/keeping LLUTT communication/discharge planning and communication
- Survival (deceased graft–living donor) 5 yr: 85-92%. 10 yr: 64-79%

* http://www.clinicalpharmacology-ip.com/Forms/login.aspx?ReturnUrl=%2fForms%2fReports%2fintereport.aspx

SUMMARY | DECISION SUPPORT | PATIENT EDUCATION/SELF MANAGEMENT

UNITED NETWORK FOR ORGAN SHARING (UNOS) LISTING PARAMETERS THAT AFFECT GRAFT SURVIVAL

Dialysis Start Date	The longer the patient is on dialysis, the worse the graft outcomes.
Blood Type	ABO incompatible grafts have more complications. Mitigating pre-treatment regimens improving.
Kidney Donor Risk Index (KDRI)	Risk for kidney graft failure which is based on: donor's age, height, weight, ethnicity, cause of death, whether donated after circulatory death (DCD) or not, medical history, HTN, HCV status, DM/CREAT/ protein levels. It is the relative risk compared with the average (50th percentile) donor as a reference donor. Used to calculate the KDPI below.
Kidney Donor Profile Index (KDPI)	Lower KDPI is better (higher post-transplant longevity). Low score (< 20) = younger and healthier kidney, typically lasts 11 yrs; score 20-85 = standard kidney, typically last 9 yrs, high score = > 85, older sicker donor, typically last 5½ yrs. KDPI based on risk for kidney graft failure which is based on the Kidney Donor KDRI above. The patient agrees to what risk they'll accept. (The worse the kidney is, the faster the chance of transplant)
Estimated Post-Transplant Survival Score (EPTS)	Assigned to all patients on UNOS list Scale 0-100% Estimated Post-Transplant Survival (EPTS) Score Calculator*. Lower is better (higher post-transplant longevity). Takes into account: Age, DM, prior solid organ transplants, and time on consistent, ongoing dialysis. Scores < 20% are matched first with offers for kidneys from donors with KDPI scores of 20% or less. This means that the kidney is in the "top 20%" and thus likely to function longer than 80% of other available kidneys. After EPTS < 20% offered, those with KDPI < 20% are offered. (KDPI > 20% kidneys are not matched for priority)
Calculated Panel Reactive Antibodies (CPRA) Level	Scale 0-99%, percent of specific **HLA antibody** reactions within given panel. Lower is better (higher post-transplant longevity). CPRA of > 20% is considered sensitized (~30% of transplant patients) and > 98% = "highly sensitized". Theoretically, the PRA is the % chance of acute rejection. For example: PRA of 80% = rejection likely 80% of the time. Pre-treatment to desensitize patients improving outcomes.
Public Health Service (PHS) Kidney Consent	Kidney with history of past or current IV drug use, history of incarceration, or risky sexual behavior and a higher chance of human immunodeficiency virus (HIV), HCV, and other blood diseases. Patients have a choice of + nucleic acid testing (active infection) or only history of risk or disease, but nucleic acid negative. Nov 2019 American Association for the Study of Liver Disease guidelines state that HCV positive donors may be considered for recipients without chronic infection. AASLD HCV Guidance‡
HCV Status	HCV viral load (VL)+ and cirrhosis have worse graft outcomes.
Prior Transplant	Creates sensitization and higher CPRA. (Above)

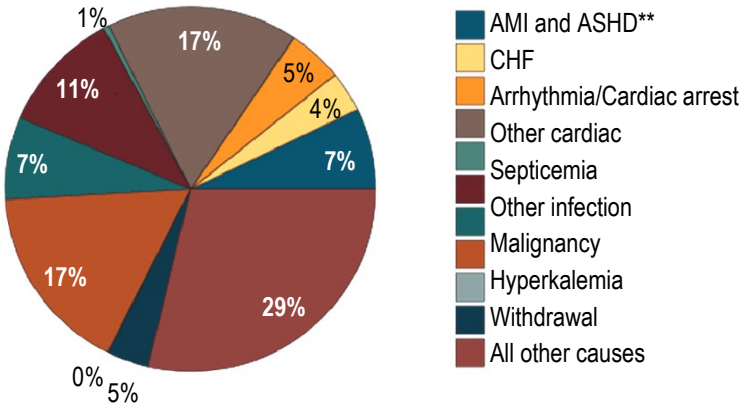
Table 1: Renal Transplant Graft Survival Data

Years from Transplant	Type of graft	
	Deceased Donor	Living Donor
1 Year	97%	99%
5 Year	85%	92%
10 Year	64%	79%

United States Renal Data Systems (USRDS) 2015†

Causes of Death in Renal Transplant recipients:
Highest:

- All other causes 29%
- Arrhythmia/Cardiac Event 17%
- Malignancy 17%
- Septicemia 13%
- Cerebro-vascular accident (CVA) 5%



* https://www.thecalculator.co/health/Estimated-Post-Transplant-Survival-(EPTS)-Score-Calculator-1081.html
† https://www.usrds.org/
‡ https://www.hcvguidelines.org/unique-populations/post-liver-transplant
**AMI: Acute myocardial infarction; ASHD: Atherosclerotic heart disease

MONITORING

(LLUTT management supersedes**)

Monitor for infection, graft dysfunction, rejection, medication side effects, medication adjustments as CREAT down or graft dysfunction, electrolyte, PTH/CA abnormalities often persist, hematologic abnormalities. First few mos–diabetes development, later–bone abnormalities, cancer and CVD. (See pages 14-30)

- **Infection**: Fever, malaise, chills, productive cough, incision site pain, swelling, or redness, drain attachment site pain, swelling, redness, or drainage, cloudy urine and/or dysuria–especially females, new or increased drainage volume in drains. (Note: Typical post-op pain usually resolves in 1 wk)
  - Common infections: UTI, influenza, BKV (polyoma virus), CMV and EBV virus
- **Graft Dysfunction**: Flu like symptoms–malaise, chills, fever, body aches, joint pain, nausea, cough, shortness of breath (SOB); decreased UO, failure of CREAT to decline or increases, proteinuria, pain/tenderness at grafted organ site, fluid retention and edema
- **Medication Side Effects**: See pages 30 & 33-41 for details
- **Lab monitoring**: As requested by LLUTT. First 1-2 mos labs are done at LLUMC lab, prior to clinic appointments, INR if prescribed warfarin anticoagulation
  (Note: Nearly all RT patients will never have normal eGFR, generally always > 1.1 and eGFR <60)
  - Every visit (2x/wk x first 4 wks, then weekly x 4 wks, then q 1-2 wks x 4 wks. Then monthly x 12 mos unless cleared to go quarterly. After 1 year quarterly to annually per LLUTT nephrologist) complete blood count (CBC), basic metabolic panel (BMP), FK506/tacrolimus level, Magnesium (Mg), phos, urinalysis (UA), urine protein/CREAT (UP/C)
  - Also, monthly: polymerase chain reaction (PCR) for CMV, EBV and BK Virus
  - If received increased risk donor kidney (KDPI > 85%)–q 1, 2, 6, and 12 mos: PCR for HIV, HCV, HBV, and HCV antibodies (Ab)
- **Bone monitoring**: **DEXA–**test within first 3-12 mos post-RT if will alter therapy (See page 10)

Labs

- Initial monitoring lab work will be conveyed by LLUTT to institutional care team for ordering during the first year post-op
- Coming Soon: Telemedicine visits and lab courier for patients with stable vital signs, stable UO, and are without drains
- Suggested frequency of laboratory tests following kidney transplantation: LLUTT^, *UptoDate, ** Kidney Disease-Improving Global Outcomes (KDIGO), ***American College of Cardiology/American Heart Association (ACC/AHA)

^*Every visit = at least 2xwk first mo, weekly second mo, biweekly 3rd and 4th mo, monthly until liberalized by LLUTT*– generally every 2 mos until the end of year 2, and every 3-4 mos, thereafter

TABLE 2: LAB MONITORING DETAILS

TEST	FREQUENCY
Basic chemistry panel (includes eGFR and Ca), Mg, and Phos	• Every visit^
Complete blood count (CBC) and differential	• Every visit^ then at least q 3-6 mos or after any chance in meds with hematologic complications
Tacrolimus (Test code 70007) **Sirolimus/everolimus** *(Test code 36712/18883)* **Cyclosporine** *(Test code 15220 trough, 10719 2 hr peak, 10720 panel with trough 1 hr and 2 hr post)*	• Every visit^ • Note: Tacrolimus Trough reference range for LLUMC lab: 4.0-24.9 ng/mL • Concentrations measured q 1-2 days while hospitalized. After discharge, levels should be measured 1-2x/weekly for the first mo, then weekly until 3 mos. post-transplantation, then q 2 wks until 6 mos post-transplant, and then monthly. Some stable, low-risk patients may have concentrations monitored q 2-3 mos
UA with sediment examination	• Every visit^
Spot urine protein-to-CREAT ratio (Protein, Total, Random Urine with CREAT- UP/C [Test code: 1715] or 24 hr Urinary protein)**	• Every visit^ • Note: Patients at risk for recurrent idiopathic focal segmental glomerulosclerosis (FSGS): q 2 wks for the first 2 mos after transplantation
Fasting blood glucose and/or **Hemoglobin A1c (HbA1c)** after first 4-6 wks	• Weekly for the first 4 wks, then q 3 mos for first year post-transplant, annually thereafter** • Screen HbA1c after substantial increases in dose of CNI, mTOR, or steroids**
Alkaline Phosphatase	• First wk after transplant, then annually or more frequently in presence of elevated PTH**
HIV, HCV, HBV PCR testing and **HCV Ab** (in patients with KDPI > 85%)	• 1, 2, 6 and 12 mos

MONITORING

Labs (Continued)

TEST	FREQUENCY
HCV VL until treated	• Monthly with alanine aminotransferase (ALT) for first 6 mos, then q 3-6 mos thereafter** • 1, 2, 6, and 12 mos if received increased risk donor kidney **(KDPI >85%)** • 3 mos after transplant if prior systemic vascular resistance (SVR) before transplant and if liver dysfunction**, q 6 mos or at discretion of HCV treating provider, untreated HCV+ RT recipients follow the American Association for the Study of Liver Disease (AASLD) guidelines[†] for follow up**
HBV DNA VL	• q 3 mos with alanine aminotransferase (ALT), if on antivirals for HBV • q 1, 2, 6, and 12 mos in patients with KDPI > 85%
HBsAb titer	• Booster to keep titers of HbSAB to ≥ 100mIU/mL**
Serum Albumin	• At least 2-3x in the first post-transplant year and then annually**
CMV blood PCR testing (in patients not receiving CMV prophylaxis therapy) *(Test code 10600 Cytomegalovirus DNA, Quantitative, Real-Time PCR)*	• Weekly for the first 3 mos, then monthly*
EBV PCR testing *(Test code 10186 Epstein-Barr Virus DNA, Quantitative, Real-Time PCR)*	• Monthly • Screen at least once the first wk after transplant, then at least monthly for the first 3-6 mos post-RT, then q 3 mos until the end of the first yr**
BK Virus blood PCR testing *(Test code 11274 BK Virus deoxyribonucleic acid (DNA), Quantitative, Real-Time PCR, Plasma)*	• Monthly for the first 6 mos, and then at 9, 12, 18, and 24 mos */ ** • And at unexplained rise in CREAT or after treatment for acute rejection**
PTH	• After immediate post-op period, measure based on presence, magnitude, and progression rate of abnormalities and chronic kidney disease (CKD). General Guide for PTH: CKD I-IIIb once, CKD IV q 6-12 mos, CKD V q 3-6 mos
25-Hydroxy Vitamin D	• Immediately post-transplant, then by baseline and interventions. **Increase frequency if on bone mineral density (BMD) treatment****
Uric Acid	• At least once during the first 2-3 mos after RT. Then additional screening if reduced renal function, on cyclosporine or diuretics
Fasting Lipid Profile	• Before treatment and if level would change management**
INR (if on warfarin)	• Frequency per PCP/anticoagulation clinic recommendations

Diagnostics

TABLE 3: DIAGNOSTIC STUDY DETAILS

TEST	FREQUENCY
Liver Ultrasound	• HBV infected (HCV neg)–with cirrhosis–annually with alpha fetoprotein (AFP)** (check AASLD website for updates) • HCV infected q 6 mo with AFP (check AASLD website for updates) • All cirrhosis of any cause q 12 mos with AFP**
DEXA	• Fracture risk is 4x higher in CKD than the general population and 34% higher in post RT than if on HD • Test within first 3-12 mos post-RT if will alter therapy • When eGFR post-RT is >30 mL/min/1,73m^2 and bone density is found to be low on DEXA, **BONE BIOPSY** should be considered before treatment with bisphosphonates, for unexplained fractures, or persistent bone pain • There is insufficient data to guide treatment after the first year • There is growing evidence that bone density predicts fracture risk in CKD but much less clear for post-RT recipients

[†] https://www.hcvguidelines.org/

MONITORING

Labs (Continued)

Table 4: Laboratory Screening Intervals Summary Sheet *Intervals depicted reflect following order LLU> KDIGO> UpToDate> other

	Month Post Transplant												After First Year
	1	2	3	4	5	6	7	8	9	10	11	12	
Basic chemistry panel (includes eGFR, Ca, Mg, and Phos)	2x/ Week	Weekly	Every other week		Monthly until liberalized								
CBC with differential													
Tacrolimus Sirolimus/everolimus													
UA with micro													
Spot UCPR													
Fasting blood glucose or Hemoglobin A1c (HbA1c)	Weekly			X			X			X			Annually
	Also screen HbA1c after substantial increases in dose of CNI, mTOR, or steroids												
Alkaline Phosphatase	Frequency dependent on presence and degree of elevated PTH												Annually
HIV, HCV Ab (HCV naïve) if received KDPI > 85% kidney	X	X				X						X	
HCV Positive VL until treated Follow the American Association for the Study of Liver Disease (AASLD) guidelines[†] for follow up	Monthly with ALT						Every 3-6 months						
HCV VL if received KDPI > 85% kidney	X	X				X						X	
HCV VL with prior SVR before transplant			X						X	q 6 months thereafter			
HBV positive DNA VL with ALT if HBV+ and on antivirals			X			X			X			X	
HBV if received KDPI > 85% kidney	X	X				X						X	
HBsAb titer													Annually
Serum Albumin	2-3x												Annually
CMV blood PCR testing (in patients not receiving CMV prophylaxis therapy)	Weekly				Monthly								
EBV PCR testing	At least once during the first week	Monthly							X			X	
BK virus PCR testing	Monthly									X			18 & 24 months
	Every 24 months after first year and at unexplained rise in CREAT or after treatment for acute rejection												
PTH	Measure after immediate post-op period based on presence, magnitude, and progression rate of abnormalities and CKD. General Guide: CKD I-IIIb once, CKD IV q 6-12 mos, CKD V q 3-6 mos												
25-hydroxy vitamin D	Once and then by baseline and interventions. Increase frequency if on BMD treatment												
Uric Acid	Once in the first 2-3 mos after transplant												
	Additional screening if reduced renal function, on cyclosporine or diuretics												
Fasting lipid profile	Before treatment and if level would change management												
INR (if on warfarin)	Frequency per PCP/anticoagulation clinic recommendations												

[†] https://www.hcvguidelines.org/

VACCINES CDC on RT Vaccines[†]

(LLUTT management supersedes**)

Kidney transplant recipients are at an increased risk of developing infections, including vaccine-preventable diseases. Some of these vaccines may not be beneficial, whereas others could even be harmful to transplant recipients.

- In general, it is best to wait until the first 3-6 mos after kidney transplantation, the period of intense immunosuppression, before attempting vaccination. However, inactivated influenza vaccination can be administered as early as 1 mo after kidney transplant to time it before onset of the flu season. KDIGO recommends only influenza in the first 6 mos after RT. Give influenza to all at least 1 mo post-RT if season-appropriate, regardless of level of immunosuppression.
- Vaccinations are most likely to be effective when immunosuppression is lowest, when transplant recipients are receiving the lowest possible doses of immunosuppressive medication (during maintenance generally after the first month). NOTE: Live vaccines are contraindicated in post-RT patients and life threatening infections can occur.
- Although immunity may be less regularly achieved and may be of shorter duration in transplant recipients, compared with the general population, vaccination is usually effective.

Table 5: Safe Vaccines for Post Renal Transplant Patients

Diphtheria-pertussis-tetanus (TDAP)	**Meningococcus:** Administer if recipient is high risk* * High Risk for Meningococcus: • *They have complement component deficiency (e.g., C5-C9, properdin, factor H, factor D, or are taking Soliris®)* • *They have functional or anatomic asplenia* • *They are living with HIV* • *They are a microbiologist who is routinely exposed to Neisseria meningitides (the causal pathogen)* • *They are traveling or residing in countries in which the disease is common* • *They are part of a population identified to be at increased risk because of a serogroup A, C, W or Y meningococcal disease outbreak* • *They are a first-year college student living in a residence hall* • *They are a military recruit*
Tetanus (inactivated toxoid– Td)	
Haemophilus influenza B (not recommended for HIV patients): One dose should be given if previously unvaccinated	
Hepatitis A (for travel, occupational or other specific risk, and endemic regions)	
Hepatitis B test immunity annually and booster if titer <10 mIU/mL	
Human Papillomavirus (HPV) avoid except catch-up vaccination to men and women ≤ 26 y/o who have not previously been vaccinated	
Inactivated polio (injectable)	
Influenza types A and B (inactivated): Annually	
(Salmonella Typhi) Typhoid Vi (killed polysaccharide) for exposure travel, occupational or other specific risk, and endemic regions–consult ID/public health	**Pneumococcus:** PCV13 is recommended once for all adults who have not previously received PCV13 and have an immunocompromising condition, which includes iatrogenic immunosuppression. If PPSV23 has been given previously, PCV13 should be given at least 8 weeks after. PPSV23 re-vaccination every 5 years until 65 is recommended. A final dose of PPSV23 is recommended for adults > 65 y/o and should be given at least 8 weeks after PCV13 is given and 5 years after prior PPSV23 (See diagram below). Adults > 65 y/o with iatrogenic immunosuppression only need to receive PCV13 once, and so will only require it after age 65 if they did not previously get a dose < 65. (CDC: When to vaccinate[‡])
(Salmonella Typhi) Typhoid (killed subunit) for exposure travel, occupational or other specific risk, and endemic regions–consult ID/public health	
Rabies ok to treat as per the general population, but additional doses may be needed	
Tick-borne meningoencephalitis inactivated for travel, occupational or other specific risk, and endemic regions–consult ID or public health	
Japanese B encephalitis inactivated for travel, occupational or other specific risk, and endemic regions–consult ID or Public Health	

Figure 2: Pneumococcal Vaccination Recommendations for Transplant Recipients

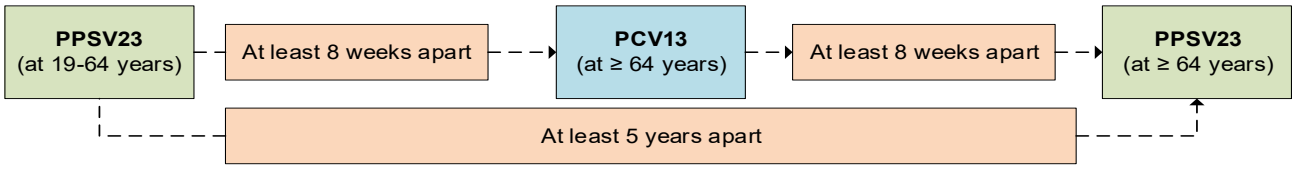


Table 6: Vaccines to Avoid After Kidney Transplant

Contraindicated		Avoid
• Influenza (live attenuated) • Varicella (live) • Zoster (live attenuated) • Yellow Fever (live attenuated) • MMR (live) • MMRV (live)	• Oral polio (live) • Typhoid Live Oral • Cholera Live Oral • BCG (bacille Calmette-Guerin) • Rotavirus	• Adjuvanted influenza vaccines • HPV–unless catch up and prior unvaccinated ≤ 26 y/o

[†] https://www.cdc.gov/vaccines/hcp/acip-recs/general-recs/immunocompetence.html
[‡] https://www.cdc.gov/vaccines/vpd/pneumo/hcp/who-when-to-vaccinate.html

MONITORING (CONTINUED)

NONADHERENCE

Nonadherence is common in the first mos after kidney transplantation and increases by duration of follow-up. Nonadherence is associated with a high risk of acute rejection and allograft loss. Measures can be taken to reduce nonadherence and improve clinical outcomes. Measurement of adherence to medications can be by direct observation that medication was consumed and indirect measures that medication has been consumed (nursing medication administration record [MAR] or self-reporting).

Nonadherence is multidimensional and can include any of the following:
- Nonadherence with immunosuppressive medication use
- Nonadherence to diet, exercise, abstinence from alcohol, drug-use, and tobacco
- Nonadherence to self-monitoring of vital signs (e.g., BP, body weight, and clinical appointments)

Risk Factors for Medication Nonadherence include:
- Nonadherence behavior prior to transplantation
- Psychiatric illness
- Personality disorders
- Poor social support
- Substance abuse and other high-risk behavior
- Time since transplantation (higher earlier)
- Lack of adequate follow-up with transplant specialists
- Inadequate pre-transplant education
- Multiple adverse effects from medications
- Complex medication regimens

Education and Medical Interventions:
- Ensure patients know their medications by name, dosage, and reason for prescription; reinforce every clinic visit
- Inform patients about the common adverse effects of drugs
- Provide written instructions for each change in medication dose or frequency
- Reduce the number and frequency of medications (i.e., 1x per day versus multiple times) if possible
- Ensure patients understand that they need to continue taking immunosuppressive medications even if the transplanted organ is functioning well
- Teach patients that chronic rejection is insidious in onset, hard to diagnose in early stages, often not reversible once established, and that all grafts ultimately fail one day
- Attempt to treat medication adverse effects by means other than dose reduction
- Inquire about problems during every clinic visit and address specific patient concerns
- Monitor compliance with laboratory work, clinic visits, and prescription refills

Behavioral and Psychosocial Approaches:
- Provide positive support to encourage adherent behaviors during preparation for transplant
- Encourage the patient to demonstrate a track record of medication adherence and knowledge
- Encourage all care team members to develop rapport with the patient
- Identify and involve a back up support system (e.g., family or friends, HD Unit social worker, MH professional)
- Treat depression, anxiety or other psychological issues (Consider consult to MH)
- Elicit a personal promise of adherence (consider a written contract with certain patients)
- Employ Motivational Interviewing techniques*
- Use a non-judgmental approach to the discussion of adherence
- Tailor interventions for nonadherence to its root cause
- Integrate taking medication into the daily routine
- Provide ongoing education, discussion, and easily accessible counseling

PATIENT EDUCATION

- See Patient Education handouts at the end of this care guide (pages PE1-PE10) for guidance on:
  - Infection risks and prevention of infection/rejection,
  - Understanding medications,
  - Understanding immunosuppression,
  - Diet (especially hyperkalemia and glucose intolerance), sodium restriction if fluid retention a problem, CHF, or HTN
  - Daily life after transplant,
  - Empowering patients, and
  - Self care
- Patients will have had a detailed medication session at LLUMC before discharge and have a Medical Action Plan
- For additional patient education materials, the National Kidney Foundation has a comprehensive A to Z post-RT Health Guide† to kidney disease and related conditions and topics

* https://motivationalinterviewing.org/
† https://www.kidney.org/atoz

MANAGING POTENTIAL COMPLICATIONS POST-TRANSPLANT**

COMPLICATIONS TABLE OF CONTENTS

Allograft Dysfunction Related Complications

General

- Definition: failure of graft to function as expected with decrease in eGFR
- Most common complication of RT
- Classified as immediate, early (< 1 wk post-transplant) or late (> 3 mos post-transplant)
- Involve LLU immediately
- **Recognition vital as often the dysfunction is reversible if timely intervention**
- Presents with low UO, failure of CREAT to decrease after transplant, and/or proteinuria > 1gm/day
  - Must use both UO and CREAT parameters to monitor
    Note: **UO > 20 mL/kg/day** in the immediate post-operative period is generally a good indicator of kidney function, except in the minority of cases where large urine volumes were still produced by the patient's native kidneys before transplant
- Vascular etiologies (thrombosis) in the first wk are transplant emergencies
- See other causes on Figure 3, page 17
- For causes that may resolve with decreasing immunosuppressant doses, the risk for rejection is in proportion to needed immunosuppressant dose decrease
- For irreversible causes and rejection refractory to treatment, the risk for early graft failure is high
- Often asymptomatic
- Can lead to graft loss
- Monitor anticoagulation closely if prescribed post-transplant
- What to do: (See pages 17-19)

Delayed Graft Function (DGF)

Be vigilant! Undetected and untreated rejection can lead to graft failure and loss

If immediate allograft dysfunction requires dialysis during the first wk after transplantation, it is called DGF.

- Usually oliguria or anuria (< 50 mL/hr), and/or failure of CREAT to decline, and/or proteinuria > 1 gm/day. DGF > 8 days has worse prognosis than < 8 days post-operatively
- The CREAT level reached by the second wk may predict long term graft function; a baseline level greater than 2 mg/dL warrants further investigation
- Elevations in CREAT greater than 25% from baseline almost always indicate a clinically significant and potentially graft-endangering event, and it is advisable to repeat within 48 hrs
- Monitor CREAT levels: should be measured at least twice weekly in the first mo, weekly in the second mo, biweekly in the third and fourth mos, then monthly until LLUTT liberalizes. (Generally every 2 mos until the end of year 2, and every 3 to 4 mos thereafter)
- Risk markedly increased if high KDPI (measures quality of the organ, lower is better)
- KDPI > 85% (risk of rejection is more likely than 85% of donor kidneys) vs standard (< 85%) thought due to inherent donor disease–arteriosclerosis and acute tubular necrosis (ATN)
- More common in deceased donors vs living
- DGF increases risk of rejection

Etiology: Most common cause is post-ischemic ATN or reperfusion injury–but diagnosis of exclusion. Incidence reported to occur in 20-25% of patients. Symptoms treated by: hydration, limiting salt, protein, potassium in diet or by dialysis

IMPORTANT: A number of studies have found that developing post-transplant ATN does not have long-term consequences provided that rejection does not occur, lending support to the theory that it is the immunological consequences of ATN that are responsible for its prognostic significance.

Other DGF causes: Hyperacute antibody medical rejection (ABMR), volume depletion–especially intraoperative third spacing, surgical complications (vascular thrombosis and fluid leaks–urinomas, hematomas, lymphocele, multiple renal arteries ligated during surgery), arterial or venous thrombosis, renal artery stenosis, thrombotic microangiopathy, recurrence of primary glomerular disease (especially FSGS), catheter or ureteral obstruction, neurogenic bladder, benign prostatic hyperplasia (BPH), atheroemboli (cholesterol crystal)–rare and calcium oxalate deposit (primary–is why uncontrolled hyperPTH is not eligible for transplant; or secondary–seen in post-bariatric, Crohn's disease, or Cystic Fibrosis) and possible but unproven: CNI nephrotoxicity
*Note: Screen for thrombotic microangiopathy with: platelet count, peripheral smear for blood cell morphology, plasma haptoglobin, and serum Lactic Acid Dehydrogenase (LDH).

MANAGING POTENTIAL COMPLICATIONS POST-TRANSPLANT (CONTINUED)

Allograft Dysfunction Related Complications (Continued)

Delayed Graft Function (DGF) (Continued)

Risks for DGF:
- Cold ischemia time exceeding 24 hrs with CSA induction treatment, especially at doses > 10 mg/kg/day
- Prior sensitization in re-transplanted patients
- Peritoneal dialysis immediately pre-RT
- Quality of the donor (older, history of HTN worse)
- Donor brain death
- Intravascular volume depletion or hypotension
- Preservation of the allograft in Euro-Collins solution
- Severe PVD in donor (or recipient–but at CDCR/LLUMC patients with severe PVD are ineligible)
- Administration of mTOR inhibitors (protein kinase inhibitor)
  - mTOR is a crucial molecule in the pathogenesis of renal inflammation, including regulating the expression of inflammatory factors. Used as adjunct or alternative to CNI which has greater nephrotoxicity (see next page)
- Possibly laparoscopic donor nephropathy
- Possibly use of dopamine or pump perfusion in donor

Protective against DGF: Intraoperative thymoglobulin administration and possibly the renotrophic factor hepatocyte growth factor/scatter factor (HGF/SF) whose activity is expected to preserve tissue viability

What to Do:
For Allograft Dysfunction in first wk: Contact LLUTT
1. H&P, check fluid balance, blood loss, hypotension (including intraoperatively)
2. Ensure the Foley catheter is not obstructed
3. Give 500 cc bolus of isotonic saline fluid challenge with 1-2 doses of IV furosemide (100 mg to deceased donor and 20 mg to living donor recipients) to increase UO
4. If hypervolemic–give Lasix® without fluid
5. Test for donor specific antibodies (DSAs) (Test codes: 95731 [HLA Class I], 97111 [HLA Class II])
6. Doppler Renal US with radionuclide scan–rule out obstruction, vascular thrombosis, and a urinary leak
   - If negative US and negative DSAs, most likely cause is post-ischemic ATN
   - If negative US and positive DSAs–send for immediate biopsy to evaluate for acute active ABMR
     - ABMR = DSAs = ABO isoagglutinins (test code: 29837), anti-endothelial Abs (test code: 16690), and HLA Ab. Causes intra-renal coagulopathy and frequently leads to allograft loss in first 24 hrs. Usually diagnosed intraoperatively–pink kidney becomes mottled and cyanotic. Little or no UO
7. Monitor UO and CREAT for 1 wk, if no improvement, biopsy to discern acute rejection from differential diagnosis (DDX) of early recurrent disease (FSGS), oxalate deposition, thrombotic microangiopathy
   - If hyperoxaluria, consider interventions: pyridoxine, high calcium/low oxalate diet, increased fluids, potassium or sodium citrate (alkalinize urine), orthophosphate, magnesium oxide, and dialysis

Acute Allograft Dysfunction

Allograft Dysfunction > 1 wk post-transplant–Contact LLU
- Increase in CREAT > 25% from baseline, > 1 g/day proteinuria, failure of CREAT to decrease after first wk from RT
- Usual causes: Acute rejection (one of most common) due to acute T cell mediated cellular rejection, or acute ABMR. Also: pyelonephritis, hypovolemia, nephrotoxic medications, calcineurin caused inhibitor nephrotoxicity, thrombotic microangiopathy, recurrent primary disease (especially FSGS), transplant renal artery stenosis, urinary obstruction, viral infections (especially BK virus), de novo glomerular disease not related to original disease

What to do: (See algorithm page 17-19)
- Assess for fever, abdominal pain, graft tenderness, drainage at site of surgical wound–antibiotics if indicated
- Check for proteinuria– > 1 gm/day may be sign of recurrent or de novo FSGS–send for biopsy, regardless of CREAT (native kidney proteinuria resolves over 4-6 wks post-transplant as function ceases)
- Assess volume status–replete volume if indicated
- Assess adherence to medications and if changes to med regimen
- Measure tacrolimus or CSA concentration and if elevated reduce q 2-3 days
- Draw for DSAs
- Measure PCR for BK polyomavirus and CMV VL
- Labs for thrombotic microangiopathy (HUS and multifactorial)–platelets, LDH, haptoglobin, and RBC morphology
- Assess function of the contralateral kidney of the deceased donor to compare
- If no cause found or fails to improve after treatment, obtain Doppler US to evaluate for perinephric fluid collections (urinary leak–urinoma), perinephric hematoma, urinary obstruction, transplant RAS–treat as appropriate (nephro-ureteral stent, drain fluid and evaluate, angioplasty of RAS)
- If negative US or still no improvement–send for biopsy

Allograft Dysfunction–Late (> 3 mos) post-transplant (chronic): (See page 17-19 under graft loss)
- Irreversible damage to the allograft occurs over a period of wks to mos. Chronic allograft nephropathy or injury (defined as allograft dysfunction > 3 mos duration **in absence of acute rejection**, drug toxicity/CI toxicity, or other diseases, DDX: de novo graft disease, BK, late or recurrent rejection, RAS, and occasionally ureteric obstruction
- Gradual deterioration of graft function. Precursor to the majority of graft failures

MANAGING POTENTIAL COMPLICATIONS POST-TRANSPLANT (CONTINUED)

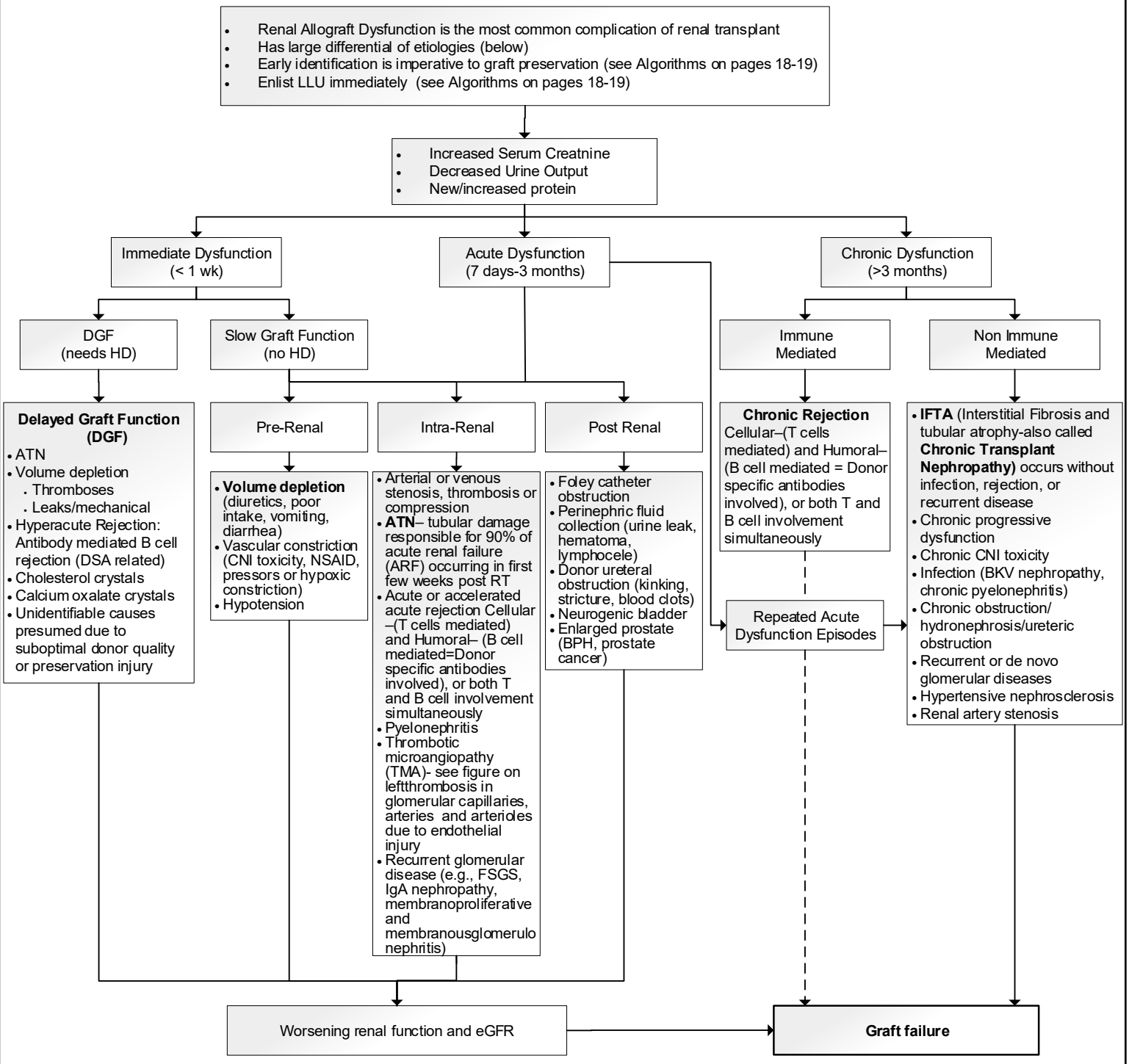
Allograft Dysfunction Related Complications (Continued)

Acute Allograft Dysfunction (Continued)	• Risk Factors: Development of chronic allograft nephropathy (aka interstitial fibrosis/tubular atrophy IFTA) which in turn is related to donor factors, ischemia-re-perfusion injury, repeated episodes of acute dysfunction, subclinical rejection, CNI nephrotoxicity and hypertensive disease. Biopsy shows interstitial fibrosis, tubular atrophy and glomerulosclerosis • Poorly understood
Rejection (See pages 17-19 for details)	**Hyperacute Rejection/Hyperacute Antibody Mediated Rejection (ABMR)/Accelerated Acute Rejection**: Immediate antibody attack mounted by recipient's DSAs which are encoded by the organ donor's cellular HLA complex (anti-HLA DSAs). **15-30% of RT recipients**. Usually occurs within minutes to days post-RT and leads to graft loss. Increased risk if positive crossmatch with high level of antibodies towards donor's kidney or many tissue types (generally from prior transplant, pregnancy, or blood transfusions) • **Signs/Symptoms:** Oliguria or anuria, graft tenderness, little or no uptake on renal scan, intravascular coagulation. Needs prompt surgical exploration and most need removal **Acute Cellular (T cell delayed type hypersensitivity–majority) rejection and/or ABMR–(worse prognosis)**: The prevalence of clinically silent acute rejection is 4-27% at 3 mos. Generally occurs 1-3 mos. In the early post-transplantation period, acute rejection is the most important potentially reversible threat to graft function. Can happen at any time post-transplant or as beginning of chronic rejection. Can be related to CMV or BK virus. Poor prognosis. Rarely can occur in latter part of first wk of transplantation where it will look like DGF. Have low threshold to perform allograft biopsy if any suspicion. Biopsy is the gold standard for diagnosis. Noninvasive biomarkers under study • **Signs/Symptoms**: Majority are **asymptomatic.** Rise in CREAT and/or development of proteinuria can mimic signs/symptoms of the flu, fever, changes in UO, pain over incision site, swelling of retroperitoneal/graft site and extremities **Chronic Rejection**: **The prevalence of clinically silent acute rejection at 2 years is 9-12%.** B and T Cells. • May happen mos or years after the transplant; is resistant to treatment with current medications • Progresses from dysfunction to graft failure over time. Biopsy is usually needed to ascertain cause and thus treatment

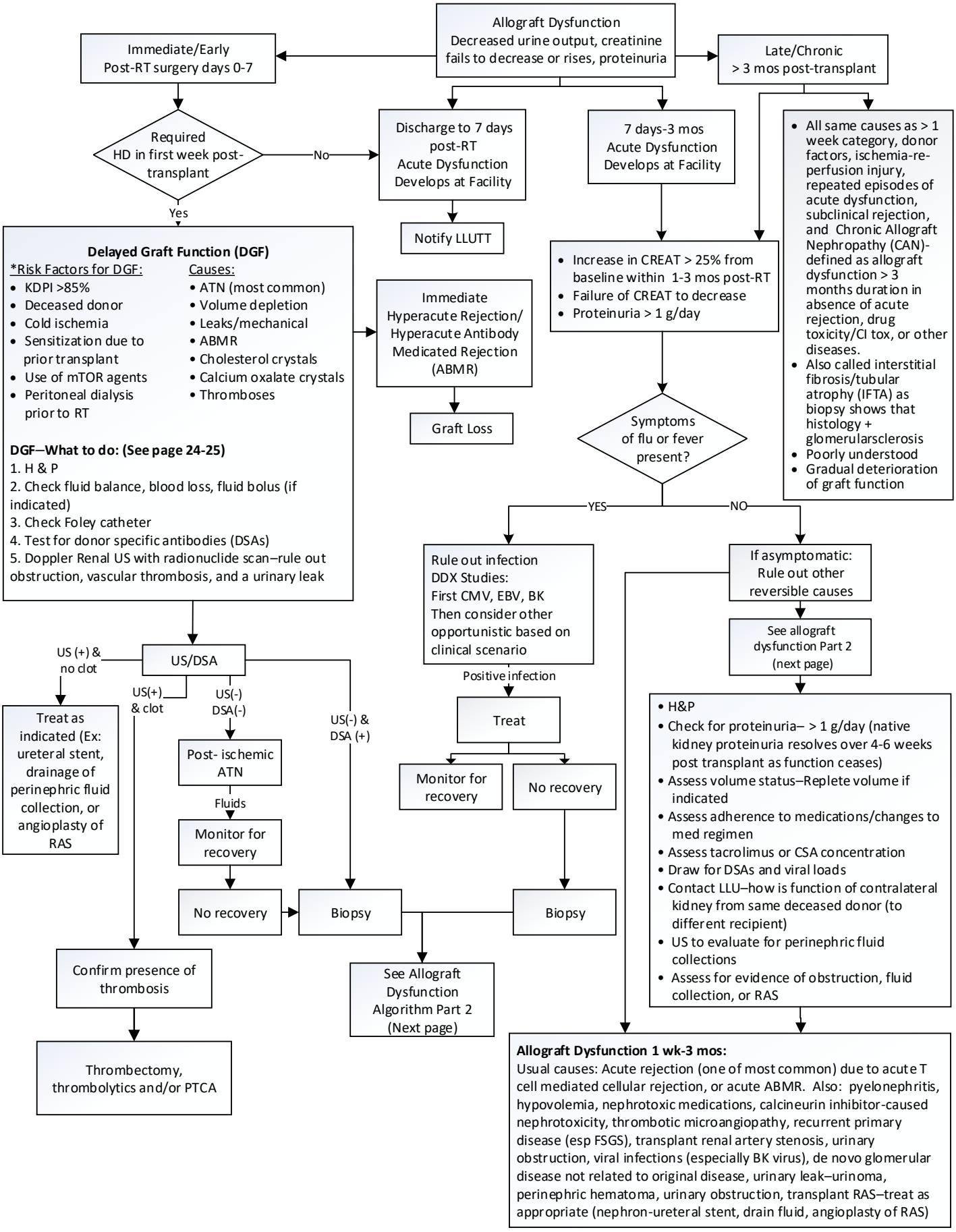
Graft Loss	• Overall 1-year unadjusted survival of a renal allograft is 89% for deceased donor and 95% for living donor. Adjusted 1-year survival is 97% and 99% respectively
	• Longer on dialysis pre-RT = less graft survival
	• Most common cause of graft failure after the first year is chronic allograft nephropathy (CAN). CAN is an incompletely understood clinicopathological entity variously called IFTA, chronic rejection, transplant nephropathy, chronic renal allograft dysfunction, transplant glomerulopathy (TG), chronic allograft injury, or chronic renal allograft nephropathy. Also, there is a relationship to chronic T cell-mediated rejection and chronic antibody-mediated rejection
	• There are no universally accepted clinical syndrome diagnostic criteria for this disorder. In general, it is a poorly understood process that is defined as renal allograft dysfunction (occurring at least three mos post-transplant) in the absence of active acute rejection, drug toxicity (principally CNIs), or other diseases. There are histologic diagnostic features on biopsy (called **Banff criteria** or Banff grading system: Grade I, II, III = mild, moderate, and severe respectively, revised in 2017)
	• Clinical syndrome: slowly rising CREAT, increasing proteinuria and worsening HTN. However, these **symptoms probably manifest much later than the pathologic process in the kidney**
	• 20% of kidney transplants in U.S. go to patients who have previously failed one or more allografts
	• Risk Factors for graft loss:
	  ◦ Prior sensitization with > 50% panel reactivity
	  ◦ Number and severity of rejection episodes
	  ◦ 2nd or 3rd transplant
	  ◦ Donor age < 5 or > 60 y/o
	  ◦ Greater degrees of HLA mismatching (and it's associated high Panel Reactive Antibody activity)
	  ◦ Allograft dysfunction at post-transplant hospital discharge (CREAT > 2 mg/dL)
	  ◦ Presence of DGF requiring HD first wk after RT
	  ◦ BK virus (polyoma virus allograft nephropathy or PVAN)
	  ◦ Injury promotors: HTN, glomerular hyperfiltration, de novo parenchymal disease, hyperlipidemia
	• The most common causes of later graft loss are chronic allograft dysfunction, CAN/IFTA, death with functioning graft, and recurrent glomerulonephritis
	• The overall incidence of recurrent glomerulonephritis in RT recipients is approximately 10% and it is a feared outcome. For those who develop recurrence, just under half will lose their grafts within 5 years of the recurrence. RT recipients who have recurrent glomerular disease have a 50%-100% increased risk of allograft loss over those who do not, depending on the study. The predominant disease entities are: IgA nephropathy (20%), FSGS (13-50%), membranoproliferative nephropathy (11-19%), and membranous glomerulonephritis (10-18%). Membranoproliferative nephropathy has the worst graft survival, with only 30% of grafts surviving 5 yrs. Graft survival for FSGS, IgA and membranous were 57-59% at 5 yrs
	• Note: In order to be considered for immediate re-listing after early graft loss, the graft must have been deemed never to have worked. A nonfunctioning graft is formally defined as: Kidney graft removal, documentation that the patient is on dialysis, or an eGFR ≤ 20 mL/min within the first 90 days after transplant

POST-RENAL TRANSPLANT ALLOGRAFT DYSFUNCTION GENERAL ALGORITHM (LLUTT management supersedes**)

Figure 3: Causes of Renal Allograft Dysfunction

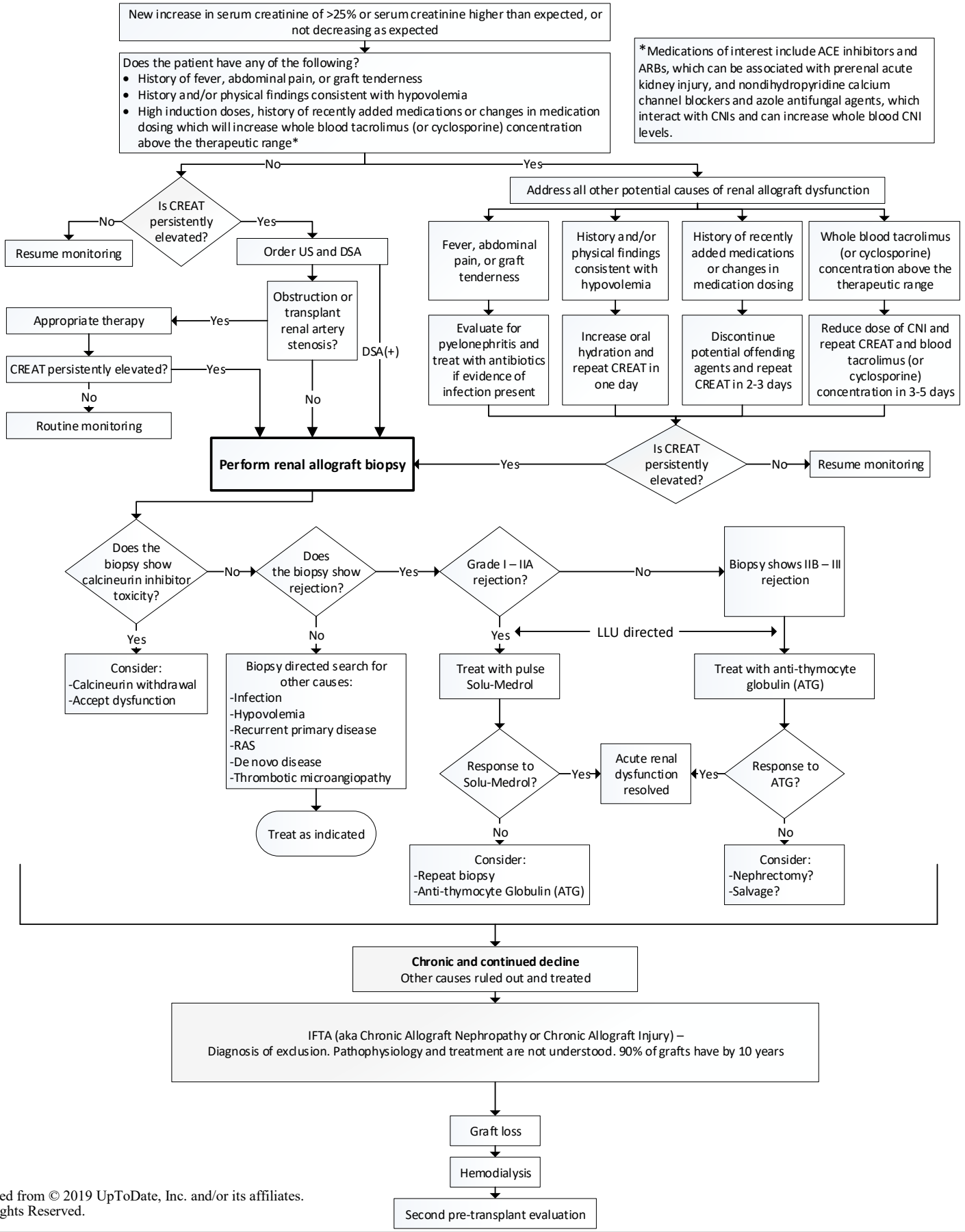


POST-RENAL TRANSPLANT ALLOGRAFT DYSFUNCTION DETAILED ALGORITHM PART 1



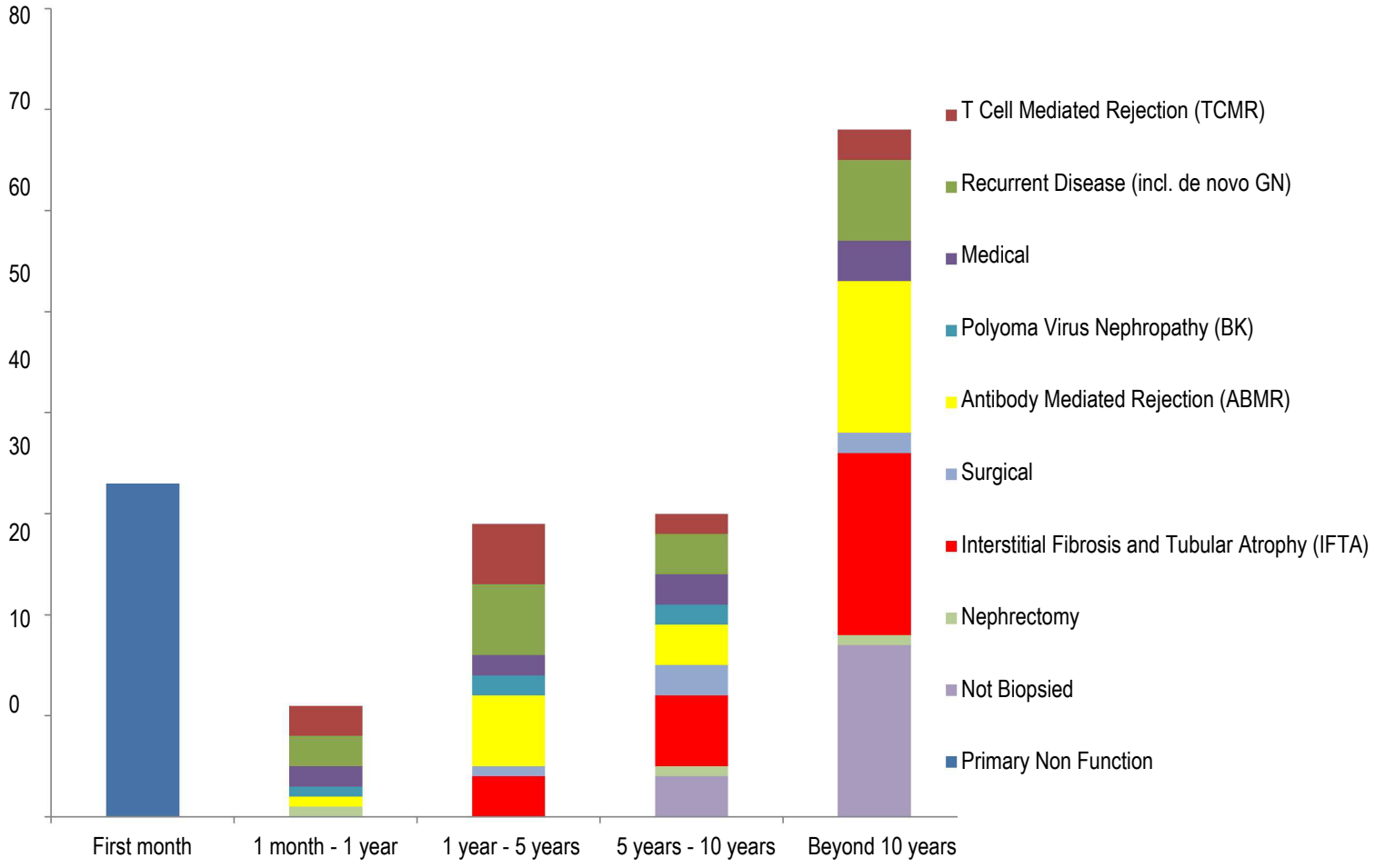
POST-RENAL TRANSPLANT ALLOGRAFT DYSFUNCTION DETAILED ALGORITHM PART 2

Figure 4: Early and Late Allograft Dysfunction (> first wk post RT) same differential



Causes of Graft Failure by Time from Transplantation

FIGURE 5.



^Chand, Sourabh, PLOS, The spectrum of renal allograft failure, journal pone.0162278, Sept 2016

MANAGING POTENTIAL COMPLICATIONS POST-TRANSPLANT (CONTINUED)

Infectious Complications

General	• Infection can lead to rejection which is life and graft threatening and is extremely costly to treat (intravenous immunoglobulin [IVIG], rituximab, apheresis [antibody removal process], thymoglobulin and steroids) • CMV is a common infection seen after transplant. Highest risk of CMV in first 4 mos after transplant surgery when on highest doses of immunosuppressant medications. The patient may have flu-like symptoms, fatigue, and/or joint pain • Other common post-transplant infections include: UTI, influenza, varicella, herpes, EBV, BK virus, and adenovirus • With CMV, EBV, Parvo B19, Human Herpesvirus 6 (HHV6) and influenza–white blood count (WBC) may also be very low • Opportunistic infections* have highest risk between 1-3 mos *Including: Nocardia, Listeria, Aspergillus, Pneumocystis Jiroveci Pneumonia (previously thought carinii), HBV, HCV, HSV, HHV 6/8, Parvo B-19, mycobacterium TB, toxoplasmosis, cryptococcus neoformans, C-difficile, and JC polyoma virus Note: Liver function tests (LFTs) are poor markers of viral hepatitis activity–use serology/DNA (nucleic acid testing [NAT]) • Severe "exotic" community acquired infections, e.g., SARS and West Nile Virus
Treatment	• Adjustment of immunosuppressant medications, antibiotics, IVIG, intravenous (IV) fluids, possible hospitalization
Prevention	• Ensure the patient knows their role in preventing infection by washing their hands with soap and water often, brushing their teeth 2x/day, avoiding people who are sick or have infections, avoid sharing drinking cups or utensils, keep cuts or scratches clean and covered, wear a facemask for all medical visits for the first 4 wks after transplant surgery, separate yard

CMV[31]	• Associated with substantial morbidity, mortality, and decreased allograft survival rates
	• **Signs/symptoms:**
	  ▪ Acute viral syndrome: fever, chills, splenomegaly, arthralgia, thrombocytopenia and leukopenia
	  ▪ Acute **tissue-invasive CMV disease** have symptoms and signs of end-organ disease (e.g., enteritis, colitis, pancreatitis, hepatitis, nephritis, pneumonitis, meningitis, encephalitis, cystitis, myocarditis, and retinitis), gastrointestinal (GI) most common
	  ▪ Later transplant vascular sclerosis and chronic graft dysfunction. Also associated with accelerated atherosclerosis and fungal/bacterial superinfections
	• **Screening:** Patients identified as likely to develop symptomatic CMV with treatment will be given prophylaxis
	• Periodic post-transplant screening is recommended as follows: antibody titer assays, conventional viral cultures, qualitative PCR assays to detect CMV DNA, quantitative PCR assays and other methods to quantify CMV DNA, rapid culture methods, e.g., shell vial cultures, and methods to detect CMV antigenemia
	• Prophylaxis recommendations are as follows: Recipient (R)(+)/Donor (D)(+) with antilymphocyte immunosuppression, R(+)/D(+) without antilymphocyte immunosuppression, R(+)/D(-) with antilymphocyte immunosuppression, R(+)/D(-) without antilymphocyte immunosuppression, R(-)/D(+) with antilymphocyte immunosuppression, R(-)/D(+) without antilymphocyte immunosuppression
	• Prophylaxis is for at least 3 mos after RT and for 6 wks after treatment with T-cell depleting antibody (ATG)
	• **Treatment:**
	  ▪ If active disease, KDIGO recommends weekly NAT
	  ▪ Treat serious disease with IV anti-viral, mild can be treated with oral or IV anti-viral. Treat until NAT or Antigen testing is no longer detectable
	  ▪ If life-threatening disease, KDIGO recommends reduce immunosuppression

BK Virus[17, 30]	• Named after discovered in an RT recipient whose initials were B.K. • Common childhood virus remains latent in the urinary tract and can reactivate with immunosuppression (virtually only seen in transplant patients) and often is transmitted by the donor • Associated with polyomavirus associated nephropathy (aka BKV-induced nephropathy–BVIN) in 1-10% with a mean of 5%, which in turn is significant cause of renal allograft failure (50% with BVIN) • Can cause ureteral stenosis and other organ system involvement, but much less common • Associated with graft damage and graft loss • Increased risk in: older, male, Caucasian, DM, deceased donor, greater HLA mismatches, longer cold ischemia, ureteral stent use, high donor titer, sooner after RT, delayed graft function, acute rejection • Symptoms: Often asymptomatic rise in CREAT, hematuria, dysuria, difficulty urinating, urinary frequency, URI symptoms, myalgia, seizures. UA: pyuria, hematuria, cellular casts (viruria precedes viremia) • KDIGO recommends reducing immunosuppression when NAT is persistently > 10K copies/mL. There is general consensus that reduction of immunosuppression is appropriate for management of significant BKV replication • Test monthly for 6 mos, then q 3 mos for 1 yr, on unexplained rise in CREAT, and after acute rejection treatment

MANAGING POTENTIAL COMPLICATIONS POST-TRANSPLANT (CONTINUED)

Infectious Complications (Continued)

EBV[4, 38]	• May be marker for over-immunosuppression • Viremia first 12 mos post-RT associated with graft loss (first 6 mos worse risk than later) • Associated with other opportunistic infections (e.g., HSV, Pneumocystis Jiroveci Pneumonia [PJP], TB, Nocardia, Legionella, Aspergillus) • Associated with PTLD including B, T, Hodgkin, and Burkitt Lymphoma • PTLD occurs late, generally beyond the first yr, 50% of cases are associated with EBV. Poor prognosis • EBV "mono" viral syndrome: fever, sweats, anorexia and weight loss, sinus congestion, swollen lymph nodes (can jeopardize airway), pharyngitis, abdominal pain, hepatosplenomegaly and potentially fatal splenic rupture. EBV can affect virtually any organ system and is associated with diverse disease manifestations (ex: hematologic, neurologic, pneumonia, myocarditis, pancreatitis, mesenteric adenitis, myositis, glomerulonephritis, and genital ulceration) • Associated with nasopharyngeal and head and neck carcinomas and oral hairy leukoplakia • Prevalence of viremia increases with time from transplant, less viremia if EBV-1 (EBV VCA+) antigen positive before transplant and use of MMF post-RT • Highest risk from seronegative recipient and seropositive donor • After first post-RT year, viremia level does NOT correlate with the active viral syndrome or PTLD and the significance of asymptomatic increases in DNA levels beyond the first year post-RT are unclear • KDIGO recommends: screen at least once the first wk after transplant, then at least monthly for the first 3-6 mos post-RT, q 3-6 mos, then q 3 mos until the end of the first year • KDIGO recommends EBV seronegative patients with an increasing EBV VL and patients with PTLD reduce immunosuppression
HCV[21]	• HCV+ should be followed by a hepatologist after transplant and if the patient is cirrhotic–screening for hepatocellular carcinoma (HCC) and varices, should follow AASLD guidelines for HCV* (q 6 mos ultrasound [US]) and EGD or HCV Care Guide[†] on Lifeline • HCV VLs often increase due to immunosuppression • RT recipients with unexplained hepatic dysfunction, always check HCV and HBV • During HCV treatment, if prior HBV infection (Core Ab+ with or without hepatitis surface antibody [HbSAB]), monitor for reactivation with serial HBV DNA and LFT • HCV is risk factor for development of proteinuria post-transplant. All HCV+ patients need proteinuria (UPCR) and microhematuria (UA with micro) screening starting 2 wks after transplant (or when stable) and q 3-6 mos • UPCR > 1 or 24-hr urine protein > 1 gram x 2 occasions or microhematuria– need biopsy • In recipients of HCV-infected kidney test for proteinuria at least q 6 mos • HCV+ RT recipients have worse allograft survival vs. non-infected • Previously treated HCV with SVR are unlikely to recur. If prior treatment and SVR, check ribonucleic acid (RNA) 3 mos after transplant or if liver dysfunction occurs • Do not initiate treatment for HCV before 3 mos post-transplant and without approval from LLUTT Hepatologist. Review AASLD[^] and email HCV Central Treatment Team[§] as needed. For DDIs consult AASLD[‡] and Liverpool[‖]. Dose adjustments for CKD are not required for RT recipients if eGFR > 30 mL/min/1.71m^2 • Limited data, but HCV cure rates seem to be equivalent in RT recipients • Do not use interferon in transplant recipients • Direct-acting antivirals are metabolized by cytochrome P450 and there is substrate competition. Monitor CNI levels during and after HCV treatment • HCV+ patients are at risk for: HCV-related kidney disease, HCV-related liver disease: chronic hepatitis and fibrosing cholestatic hepatitis with rapidly progressive liver failure, NODAT, PTLD and higher mortality from PTLD • HCV associated with recurrent glomerular disease, de novo Membranoproliferative Glomerulonephritis (MPGN), membranous nephropathy (MN), renal thrombotic microangiopathy. If de novo MPGN or transplant glomerulopathy develops, is more likely to progress to allograft failure and end-stage renal disease (ESRD) • Use ACE/ARB for HCV+ RT recipients with proteinuria, after 6 mos post-RT, and as tolerated

*https://www.hcvguidelines.org
† http://lifeline/HealthCareOperations/MedicalServices/Care%20Guides%20and%20Tools/Hepatitis-C-Care-Guide.pdf
^ https://www.hcvguidelines.org/unique-populations/kidney-transplant
§ CPHCSHCVQuestions@cdcr.ca.gov
‡ https://www.hcvguidelines.org/unique-populations/post-liver-transplant (Direct-acting antivirals interaction with CNIs, last page)
‖ https://www.hep-druginteractions.org./

MANAGING POTENTIAL COMPLICATIONS POST-TRANSPLANT (CONTINUED)

Infectious Complications (Continued)

HBV[23]	• AVOID INTERFERON • Prophylax all HBV Ag+ with tenofovir, entecavir or lamivudine • During antivirals treatment, measure HBV DNA with ALT q 3 mos to monitor efficacy and detect drug resistance • HBV with cirrhosis (HCV negative) q 6 mos liver US for HCC (w/ alpha feto-protein, AASLD with or w/o AFP) • Give HBV booster vaccine when HBsAB titer < 10 mIU/mL to raise titer ≥ 100 mIU/mL
HIV[23]	• Consult with HIV Specialist
Herpes Simplex and Varicella Virus (HSV/VZV)[23]	• Treat superficial HSV and VZV infections with antivirals until all lesions have resolved • Use suppression if frequent recurrences • Treat systemic infections with IV antivirals and reduce immunosuppression • VZV treat with IV or oral antivirals and temporary immunosuppression reduction • Exposed VZV susceptible patients: prophylaxis with IVIG within 96 hrs of exposure or if not available or past 96 hrs, a 7-day course of oral acyclovir starting 7-10 days after exposure
Influenza Virus	• Potentially fatal and significant morbidity. Vaccine does not cause rejection or other major adverse effects in RT recipients and should be given annually. Use prophylactic treatment (amantadine, rimantadine, zanamivir, or oseltamivir) if not yet vaccinated or on high doses of immunosuppressants (questionable immune response). If symptomatic, use antiviral therapy during first 48 hrs of symptoms
Tuberculosis	• RT recipients should be considered at increased risk for TB • Patients who have never received adequate treatment and who are purified protein derivative (PPD) positive, have a history of TB, have a chest X-ray suggesting latent TB, have a recent exposure history, or received a kidney from a PPD+ donor should undergo 6-9 mos of therapy with isoniazid (and pyridoxine) • TB prophylaxis and treatment regimens the same as general population[23] • If needed, consider using rifabutin instead of rifampin to minimize CNI and mTOR interactions[23]
Pneumocystis Jiroveci Pneumonia (PJP)[23]	• Daily medical prophylaxis for 3-6 mos post-RT and for at least 6 wks after acute rejection • Diagnose by bronchial alveolar lavage and/or lung biopsy • Treat active pneumonia with high-dose IV trimethoprim-sulfamethoxazole, steroids, and lower immunosuppression. Treat with steroids if room air PaO_2 < 70mm Hg or alveolar gradient of > 35 mmHg
Candida[23]	• Oral and esophageal prophylaxis with lozenges, nystatin, or fluconazole for 1-3 mos post-RT and for 1 mo after treatment with anti-lymphocyte antibody

Cardiovascular Related Complications

Hypertension (HTN)	• **50-80% of RT recipients will have HTN prior to transplant or develop HTN post-transplant** • Risk factors: Allograft dysfunction, deceased donor, especially if history of HTN, increased body weight, volume overload, presence of native kidneys, renal artery stenosis (occurs in 20% of post-RT patients) and is correctable, resistant HTN refer to nephrology for possible angiogram (See HTN Care Guide*) • Associated with worse graft outcomes • Exacerbated by CNI vasoconstriction, especially cyclosporine • May be exacerbated by steroids–salt retention, weight gain and mineralocorticoid effect • Poor control is common • Can lead to left ventricular hypertrophy (LVH) which is independent risk factor for heart failure and death in RT recipients • Goal: **< 130/80** Kidney Disease Outcomes Quality Initiative (KDOQI) and KDIGO 2012. European best practices goal = 125/75 if proteinuric • If develop post-RT HTN, improved outcomes proven with control < 140/90 vs not • DIHYDROPYRIDINE CALCIUM CHANNEL BLOCKERS (amlodipine and nifedipine) ARE TREATMENT OF CHOICE AFTER RT (evidence based benefit) • USE DIURETICS IF EDEMA OR HYPERKALEMIA AFTER INVESTIGATION OF ETIOLOGY • **AVOID ACEI/ARB UNTIL ≥ 6 MOS**, STABLE ALLOGRAFT FUNCTION, NO HYPERKALEMIA • After 6 mos, consider ACE/ARB if urine protein is ≥ 1 g/day[23]
Hyperlipidemia	• Common, even with near-normal allograft function. **80-90% of RT recipients by 1 year** post-transplant, 60% of post RT recipients with total cholesterol > 240 mg/dL (high risk) • Associated with reduced allograft survival and chronic allograft vasculopathy • Increases low-density lipoprotein (LDL), total cholesterol, and thyroglobulins (TGs)

*http://lifeline/HealthCareOperations/MedicalServices/Care%20Guides%20and%20Tools/Hypertension-CG.pdf

MANAGING POTENTIAL COMPLICATIONS POST-TRANSPLANT (CONTINUED)

Cardiovascular Related Complications (Continued)

Hyperlipidemia (Continued)	• Especially associated with glucocorticoid, sirolimus, cyclosporine, and rapamycin use • Exacerbated by hypothyroidism, DM, obesity, chronic liver disease, nephrotic syndrome, lack of exercise, and alcohol use • Measure fasting lipid panel before treatment, then 4-12 wks after and repeat q 3-12 mos for adherence checks • Shared decision making if < 29 y/o and no history of ASCVD or DM and CV risk < 10% • **2013 KDIGO recommends treating all RT patients with statin, regardless of age,** but studies with benefit were for >30 y/o. No target dose recommendations given. For general CKD and eGFR < 60 mL/min/1.73 m^2 then moderate dosing only. If eGFR > 60 mL/min/1.73m^2 , any regimen for general population • ACC/AHA 2018 recommendations, "clear benefit in RT, recommend statins", but no dosing guideline and discusses 2013 KDIGO (as above) • If on cyclosporine, UptoDate recommends start with atorvastatin 10 mg or simvastatin mg and remain on low dose • If **not** on cyclosporine, UptoDate recommends start with atorvastatin 10 mg or simvastatin 20 mg and increase to target doses of 20 and 40 mg respectively • Screen q 3 mos or every LLUMC visit once visits are > q 3mos, then at least annually (Note: Maintenance of allograft function may increase high-density lipoprotein [HDL])
High Blood Sugars and New-Onset Diabetes After Transplant (NODAT)	• Approximately **30% post-RT, but only 5% at 1 yr.** Common first few mos post RT, but continued risk persists for life • Multifactorial: including pre-existing risk factors, caused by medications (prednisone, tacrolimus > cyclosporine), new kidney metabolizes insulin more efficiently than failing native kidneys and the transplanted kidney is gluconeogenic, CMV infection, HLA mismatching, possibly hypomagnesemia • Increased risk in HCV infected RT recipients on tacrolimus • Adverse effect on patient and allograft survival • Increased risk of infections, sepsis, UTI, pneumonia and CMV • Screen with fasting blood sugar weekly first 4 wks, then HgA1c q 3 mos for first year post-transplant, annually thereafter[23] • Screen after substantial increases in dose of CNI, mTOR, or steroids[23] • If pre-RT HgA1c is > 6%, monitor A1c quarterly after the first 4 wks • Treat if A1c > 7% • Can use metformin if eGFR > 45% • Insulin often needed, may decrease need after glucocorticoid doses decrease • Use ASA 65-100 mg/day for primary prevention if CVD risk prevention outweighs GI risks[23]
Weight Gain	• Common. **40% are obese 1 year post RT** associated with CVD/CVD risk factors • Due to prednisone, improved appetite off dialysis, and physical inactivity (evaluate for fluid overload) • Using selective serotonin reuptake inhibitors (SSRI), St. John's Wort or weight loss medications (orlistat) are NOT recommended due to DDIs • Studies on risks and benefits of bariatric surgery are lacking • Measure body mass index (BMI) often. If BMI < 35 kg/m^2 but central obesity, measure waist circumference[23] • Lifestyle: Maintain BMI ≤ 25 kg/m^2, engage in physical activity recommendations for their age as for general population or DM/HTN if appropriate (generally at least 150 minutes of moderate physical activity or 75 minutes of vigorous physical activity [or combination] each wk) (See HTN Care Guide* and Type 2 Diabetes Care Guide† for more information about lifestyle changes)
ASCVD	• **23% of RT recipients develop ischemic heart disease, 15% cerebral vascular disease, and 15% peripheral vascular disease (PVD) by 15 years after RT. Annual rate of fatal and non-fatal CVD events is 50 times higher than general population** • Highest ASCVD risk group (lower risk of fatal and nonfatal cardiovascular events vs. waitlisted on HD, but significantly higher than in the general population) • Considered a coronary heart disease equivalent • Markedly increased rate of acute myocardial infarction (MI) in first 3 mos post-surgery • Framingham calculation underestimates risk in RT recipients • **Major cause of death and graft loss (greatest rates early after transplant)** • 50-60% of post-transplant deaths are directly attributable to CVD • **#1 cause of death for transplant recipients with DM** • Independently associated with post-transplant CV disease: Age, DM, male sex, smoking cigarettes, HTN, cholesterol, reduced kidney function following transplant, length of dialysis prior to transplant, rejection, hyperhomocysteinemia, elevated lipoprotein, elevated C-reactive protein (CRP) and interleukin-6 (IL-6) levels, proteinuria, low levels of physical activity, elevated pre-transplant troponin I (each 0.01 mcg/L increase = 17% increase in major cardiac events < 3 mos post-transplant), and reduced homoargine levels

* http://lifeline/HealthCareOperations/MedicalServices/Care%20Guides%20and%20Tools/Hypertension-CG.pdf

† http://lifeline/HealthCareOperations/MedicalServices/Care%20Guides%20and%20Tools/Type-2-Diabetes-Care-Guide.pdf

MANAGING POTENTIAL COMPLICATIONS POST-TRANSPLANT (CONTINUED)

Cardiovascular Related Complications (Continued)

ASCVD (Continued)	• Independently associated with MI: Age, kidneys from older donors or deceased donors, delayed allograft function, pre-transplant comorbidities (DM, angina, PVD, and prior MI), post-transplant DM, allograft failure, total cholesterol, and prior acute rejection • Independently associated with cardiac death: Age, DM, electrocardiograms (EKG) stress tests (ST-T) changes, elevated CREAT • Insufficient evidence that screening asymptomatic patients with EKG, ST-T, or carotid duplex reduces mortality or morbidity after transplant • 65-325 mg aspirin is indicated if known ischemic HD or at high risk of ischemic HD, and tolerated • Offer education and cessation counseling to all patients who use tobacco[23]

Kidney Function Related Complications

Proteinuria	• **10-25% of RT recipients** exhibit proteinuria of > 1 g/24 hr for ≥ 6 mos • Associated with decreased graft survival rates • Causes of persistent proteinuria include chronic allograft nephropathy, transplant glomerulopathy, glomerulonephritis (de novo or recurrent), diabetic nephropathy, and calcineurin nephrotoxicity • Recommended monitoring: . First 2 wks after transplantation or as soon as the patient is in stable condition. Thereafter, screen at least every 3-6 mos for the first 1 year and then every 6-12 mos . If at risk for recurrent idiopathic focal segmental glomerulosclerosis (FSGS): screen at least every 2 wks for the first 2 mos after transplantation. If proteinuria is caused by FSGS, screen for proteinuria at least daily for 1 wk, q wk for 4 wks, q 3 mos for the first year and every year thereafter[23] . Active HCV viremic patients, check at least q 3-6 mos for proteinuria . Use UPCR, 24-hr urine rarely needed unless clinical nuances dictate . General urine dipstick reading of 1+ or greater should prompt UPCR or 24-hr timed collection test (Note: Insufficient evidence for or against screening for urine albumin excretion)
Electrolyte and Acid Base Abnormalities	• Common: Hypomagnesemia, hyperkalemia, hypercalcemia, hypophosphatemia, and metabolic acidosis • Hypomagnesemia generally related to CNIs. If severe, weakness and risk for arrhythmias. Occurs in 25% if on cyclosporine. Monitor EKG • Hypokalemia–from impaired allograft function, CNIs and multiple medication interactions. Discontinue offending agent, correct metabolic acidosis, and possibly cautious use of loop diuretic. Monitor EKG • Metabolic acidosis–frequent, but usually mild. Thought due to impaired allograft function, CNIs (type 4 renal tubular acidosis, non-gap hyperchloremic), impaired renal acid handling. Treatment is similar to non-RT CKD–use sodium bicarbonate, sodium citrate, calcium citrate/acetate/carbonate[26] • Calcium, phosphorus–see BMD next page • Screen at every LLUMC visit. At least monthly for the first 6 mos, then q 1-6 mos depending on levels • Consider dietary consult
Malnutrition (Hypo-Albuminuria)	• **10% of RT recipients** exhibit low serum albumin levels at 1 year and **20% at 10 years** after transplant • Associated with ↑ risk of infection, delayed wound healing, muscle weakness, and general debility • Measure serum albumin at least 2-3 times in the first post-RT year and then annually • Measure pre-albumin if clinical findings suggest malnutrition
Hypophosphatemia	• **More than 50% of RT recipients** may exhibit mild hypophosphatemia • May cause muscle weakness and possibly osteomalacia • Measure at every LLUMC visit, at least monthly for the first 6 mos, q 2 mos until the end of the first yr, then annually • Check PTH and calcium • Treat under guidance of LLUTT/nephrologist: oral phosphorus, vitamin D, and calcium supplements • See HyperPTH, and BMD on next page
Hyperuricemia	• Common, especially with **cyclosporine (up to 80%**) • New-onset **gout** occurs in **up to 13% of transplant recipients,** and can be of great severity • Risks increase with impaired renal function and use of loop or thiazide diuretics • Uncommonly causes nephrolithiasis and rarely renal failure itself • Screen at least once during the first 2-3 mos after RT. Then additional screening if reduced renal function, on cyclosporine or diuretics. If signs or symptoms: **Rule out joint infection** • KDIGO recommends treatment with eGFR-adjusted colchicine for acute gout, tophi, or stones • UptoDate recommends pulse oral and intra-articular glucocorticoids as part of treatment choices • Avoid allopurinol in those using azathioprine[23] • Avoid NSAIDs and COX2 inhibitors whenever possible[23]

MANAGING POTENTIAL COMPLICATIONS POST-TRANSPLANT (CONTINUED)

Endocrine Related Complications

Persistent hyper parathyroid (PTH)

- **Discuss with nephrologist, differing recommendations amongst transplant nephrologists**
- **Up to 50% of RT recipients**
- **40-90% with hypophosphatemia in early period after RT**, often resolves over time
- **31% hypercalcemia first year after RT**
- Associated with increased mortality and lower graft survival (hypercalcemic vasoconstriction and renal artery stenosis [RAS])
- Present with elevated Ca and low Phos, but some only have elevated PTH
- Cause of BMD and increased risk of fractures
- UptoDate defines as 2-3x the upper limit of normal
- Treatment: Cinacalcet, parathyroidectomy. Dependent on level of hypercalcemia, vitamin D status and degree of hypophosphatemia
- Total serum calcium levels measured at least monthly for first 6 mos, then every 2 mos until the end of 1st yr, then annually
  - Use corrected calcium*, if low serum albumin or order ionized calcium
    *__Corrected calcium__ (mg/dL) = measured total **Ca** (mg/dL) + 0.8 (4.0 - serum **albumin** [g/dL]), where 4.0 represents the average **albumin** level

BMD

- **Discuss with nephrologist–Approach to vitamin D and bisphosphonates is controversial**
- **Up to 60% post-RT**
- Occurs rapidly after RT, especially due to glucocorticoids, CNIs, elevated PTH, metabolic acidosis, DM
- Also general population risks: renal failure, low testosterone, Caucasian race, thin/small body habitus, smoking, lack of exercise, poor nutrition, use of proton pump inhibitors (PPIs) and steroids, family history, age > 50yrs, female, body mass index (BMI) < 20 kg/m^2
- Diagnosis:[27] Test bone mineral density if risk factors for osteoporosis and **fracture risk will alter therapy**. If overt BMD or low bone mineral density in first 12 mos post-RT and eGFR is > 30 mL/min/1.73m^2, consider treat with vitamin D, calcitriol/alfa-calcidol, and/or anti-resorptive agent. Treatment depends on abnormalities in Ca, Phos, PTH, Alkaline Phos, and vitamin D. Consider bone biopsy. Insufficient data to guide treatment after 12 mos
- If no DEXA scan in year prior to RT, obtain DEXA within first 3 mos after RT. Screen q 2 years if initial is normal. If indicated, treat for 12 mos and may discontinue if prednisone dose < 5 mg q day. Check DEXA in 1 year to assess compliance. If compliant and still low, consider treatment 1 more year
- DEXA within 6 mos of the start of prednisone treatment and every 2-3 years if testing will change management
- Overt BMD or low bone density, treat as for CKD 4-5 (no dialysis): Lower PTH toward normal, but no optimal PTH is known. Avoid hypercalcemia. Consider use of phosphate-lowering treatment for persistent or progressive elevated serum phosphorus. If receiving phosphate-lowering treatment, restrict dose of Ca-based binders. Recommend use calcitriol and vitamin D analogs only for severe and progressive hyperPTH. Consider parathyroidectomy if fail to respond to medical therapy[27]
- KDIGO suggests not to routinely measure bone turn-over markers[27]
- Lateral abdominal X-ray/echo with vascular Ca may lean treatment decision toward bisphosphonates. Recent research suggests choice of bisphosphonate matters[27]
- Use lateral spine films or vertebral fracture assessment (VFA) with DEXA to look for vertebral fractures
- Lifestyle recommendations: weight bearing exercise, no smoking, fall prevention, early mobilization

Hematologic Related Complications

Anemia

- **30-40% of RT recipients (8-10% severe):** 10-40% even if normal graft function
- Associated with increased mortality and morbidity rates
- Universal before transplant. After RT, persists due to blood loss, inflammation, bone morrow suppression from surgery, abrupt cessation of erythropoietin (EPO) stimulating agents and immunosuppressant medications
- Typically resolves 6-12 mos post-RT
- Increased risk of late post-RT anemia if decreased allograft function, especially CREAT > 2 mg/dL, antiviral agents, infection prophylaxis agents, (especially ganciclovir and trimethoprim-sulfamethoxazole) infections (viral, TB and staphylococcus), and use of ACE/ARB
- Tacrolimus, sirolimus, cyclosporine can cause hemolytic anemia and associated with hemolytic uremic syndrome (HUS)
- Passenger Leukocyte Syndrome—ABO compatible but not identical—Coombs + hemolytic anemia
- Screen routinely, CBC should be part of regular labs: at least weekly first 3 mos, q 2-4 wks for a year and then q 3 mos thereafter
- Measurement of EPO concentrations is NOT helpful in RT patients
- Enlist help of nephrologist for treatment

MANAGING POTENTIAL COMPLICATIONS POST-TRANSPLANT (CONTINUED)

Hematologic Related Complications (Continued)

Leukopenia/ Neutropenia	• **20-60% of RT recipients will have at least one episode** of leukopenia or neutropenia, typically in the first year post-RT • Generally due to medications and viral infections • Work with transplant team regarding medication changes • Some will need granulocyte stimulating factor (G-CSF) • Test for EBV, CMV, Parvo19, HHV6, and influenza
Erythrocytosis	• **Consult hematology and nephrology** • Definition: Hemoglobin > 17 g/dL; Hematocrit > 51% • **8-22% of RT recipients patients** • Usually develops 8-24 mos after RT • Persists for 6 mos or more, spontaneous remission in 25% within 2 yrs • Symptoms: Malaise, headache, plethora, lethargy and dizziness,10-30% thromboembolic events (veins and arteries), 1-2% mortality due to complications • Risk factors: Male sex, smoking, DM, retained native kidney and possibly: polycystic kidneys, glomerulonephritis, and renal artery stenosis • BE WARY of MALIGNANCY-associated erythrocytosis, especially renal cell, breast and HCC. Also chronic obstructive pulmonary disorder (COPD), cerebellar hemangiomas, uterine myomata, and pheochromocytomas can cause • Work up: US with Doppler waveform of renal arteries of native and transplanted kidneys, 3 morning urine cytology, mammogram, if history of viral hepatitis: liver US and alpha fetoprotein, if smoking history > 20 yrs: chest X-ray, pulmonary function tests (PFT) • Measurement of EPO concentrations is NOT helpful in RT patients • Treatment: > 18.5 g/dl hemoglobin phlebotomy. Milder cases–ACEI or ARB at 2.5-5 mg/day. Relapse is common if stop treatment. ACEI/ARBs suppress renin substrate which in turn stimulates EPO and erythropoiesis. Rarely: theophylline and azathioprine, mycophenolate are used in refractory cases • Check CBC at every LLUMC clinic visit and at least every other wk for mos 3 and 4, at least monthly for mos 4-12, then at least q 3-6 mos
Mental Health	• Depression and anxiety are more common than in the general population • May be associated with nonadherence, sleep disorders, and other adverse effects that could affect the graft success • Include direct questioning about depression and anxiety in the routine follow up for RT patients
Sexual Dysfunction	• Sexual dysfunction is common in both male and female RT recipients • May be particularly distressing if paroling. Consider discussion and counsel as appropriate

Malignancy Related Complications

Cancer	• Principal risk factor is overall level of immunosuppression • Complete history assessments and physical exams are recommended at least every 3 mos during first yr, then annually (See Cancer Screening page 29) • Pre-transplant cancers may recur (0 to > 25% recur depending on the cancer type) • Typically must reduce and sometimes must stop immunosuppression • Overall 3x more likely than general population to develop any cancer. Same screenings as general population except for skin cancer and gynecologic cancers (see below). Retain high index of suspicion. Digital rectal exam (DRE) and prostate-specific antigen (PSA) annually
The following have a ≥ 5x increased risk in RT recipients over general population	
Skin, Lip Cancers and Squamous Cell Carcinoma (SCC) of the Eye	• **40-60% by 20 years post-RT**: Monthly self exam, q 6-12 mos[23] by dermatology or experienced diagnostic provider. SCC can **occur repeatedly and can be aggressive and cause severe tissue destruction and metastases. Approximately 5% of RT recipients with skin cancer die as a consequence of their malignancy**
Ano-Genital and **Vaginal Carcinoma**	• Related to HPV • Multiple and extensive cancers are common, 11% of RT recipients die as a result of these neoplasms. • Exams yearly: anogenital/pelvic and cytologic for women • Cervical–highly mortal if advanced (5 year survival 14%) Note: No convincing data for or against HPV screening in RT recipients ≥ 70 years of age

MANAGING POTENTIAL COMPLICATIONS POST-TRANSPLANT (CONTINUED)

Malignancy Related Complications (Continued)

The following have a ≥ 5x increased risk in RT recipients over general population (Continued)

Kaposi's Sarcoma (KS)	• Related to HHV8, especially high in Arab, Jewish, or Mediterranean patients. Mortality rate > 50% if visceral involvement, 100% if disseminated and so immunosuppression must be reduced with possible graft loss • At least annually examine the skin, conjunctival and oropharyngeal mucosa and if patient is HHV8+. More frequent exams should be done if patient is of above ethnic heritage
Non-Hodgkin Lymphoma	• Related to EBV
Hepatobiliary	• HCC risk is 30-100x general population. 40% of all malignancies of RT recipients in some countries • Very poor survival unless early diagnosis • Alpha fetoprotein q 6-12 mos and US q 6 mos if liver disease, chronic hepatitis, or otherwise at risk
Post-Transplant Lymphoproliferative Disorder	• A spectrum from lymphocyte excess to lymphoma (16% of all post-RT tumors) associated with EBV and immunosuppressive medications • Highest risk first few mos after transplant when immunosuppression is highest and may also occur several years after transplant • Mortality rates are as high as 50% (early after RT): 90% (several years post-RT) • The signs and symptoms are variable depending on location of involvement. Symptoms include: fever, pharyngitis, adenopathy, fatigue, night sweats, weight loss, enlarged lymph node/mass and atypical lymphocytosis • More than half of PTLD presents with extranodal masses of the gastrointestinal tract, lungs, skin, liver, central nervous system, and the allograft itself (causes dysfunction and demise) • Screening is a full exam every 3 mos for the first post-transplant year. Afterwards, there is no formal recommended screening for PTLD • Patients should be educated to alert the health care team for any new/enlarging masses

The following cancers have a statistically significant ($p < 0.001$) increased risk in RT recipients

Lung	• Computed tomography (CT) screening same as general population
Renal Carcinoma	• Aggressive, often asymptomatic early on, 40% mortality rate, and **uroepithelial cancer (transitional cell)**. • US or UA screening NOT recommended
Colon and Rectum	• Not increased first few years post-RT, but increased by 2-4x that of general population after 10 years. Screening recommended for ≥ 50 y/o is annual fecal occult blood testing and flex sig q 5 years or colonoscopy q 10 years

Pancreas, Hodgkin Lymphoma, and Melanoma

The following cancers have significantly increased risk, but to lesser extent in RT recipients:

Stomach, oral cavity, larynx, pharynx, vulva, penis, thyroid, esophagus, salivary glands, soft tissue sarcomas, small intestine, testis, biliary tract primary, acute myeloid leukemia, plasma cell neoplasms, and chronic myeloid leukemia

Cancers that are not at higher risk in RT recipients than the general population: Breast and prostate

Breast	• Incidence of breast CA not increased overall in RT recipients and the **risk of developing breast CA during the first year after transplant is actually reduced 49% of that for general population.** If it develops, the outcomes are poor and in prior breast cancer patients who relapse after transplant, the risk of death is very high • Little evidence for or against mammography screening in the population ≥ 70 years of age
Prostate	• The incidence of prostate CA is underdiagnosed • Treatment response to localized CA is same as general population. If extensive, rapidly progress. Men ≥ 50 y/o (40 for African American)–screen with DRE and PSA annually

MANAGING POTENTIAL COMPLICATIONS POST-TRANSPLANT (CONTINUED)

Malignancy Related Complications (Continued)

Table 7: Suggested Guidelines for Cancer Screening in Patients Undergoing Solid Organ Transplantation^

Cancer Type	Suggested Guidelines
Breast (Women)	• 40-44 yrs: give opportunity, but the benefit of screening is less certain and should be left to the decision of the clinician and patient • 45-69 yrs: annual screening mammography with or without clinical breast examination • ≥ 70 yrs: annual screening is appropriate as long as estimated life expectancy is ≥ 8 yrs
Skin	• Monthly self-examination; clinician examination at least annually, with early referral for suspected lesions
Cervical	• All women ≥ 18 y/o and sexually active girls < 18 y/o should undergo an annual pelvic examination and Pap smear
Anogenital	• Yearly physical examination of the anogenital area, including pelvic examination and cytologic studies for women • At menopause, women should be informed about the risks and symptoms of endometrial cancer and strongly encouraged to report any unexpected bleeding or spotting • Insufficient evidence to recommend for or against screening anoscopy and biopsies of anal epithelium
Kaposi's Sarcoma (KS)/Other Sarcomas	• Examination of skin, conjunctivae, and other oropharyngeal mucosa annually • Patients at higher risk (ethnicity, geographic area of residence or serologic positivity for human Herpes Virus [HHV]) may benefit from more frequent screening
Prostate	• Unlike the general population, annual screening with digital rectal examination and PSA recommended for men ≥ age 50 if their estimated life expectancy is at least 10 years (for RT patients) • If positive family history or African-American race, may start annual screening earlier (e.g., age 40 years)
Colorectal	• Starting at age 50: annual fecal occult blood test (FOBT)/Fecal immunochemical testing (FIT) and either sigmoidoscopy every 5 years or colonoscopy every 10 years*
Post-Transplant Lymphoproliferative Disorder (PTLD)	• Complete history and physical (H&P) examination every 3 mos, particularly in the first post-transplant yr; patients at increased risk of PTLD may benefit from more frequent screening • EBV serologies are NOT for PTLD screening. Insufficient data to recommend for or against EBV VL or tissue gene expression. Screening ↑EBV VL as a marker for PTLD is not recommended by KDIGO or the 2017 European Clinical Practice Guidelines. Patients should be educated to alert the health care team for any new/changing lumps

Lung	• 2019 American Cancer Society (ACS) and US Preventative Services Task Force (USPSTF) for general population:
	  ◦ Annual low-dose CT in adults 55-80 years of age who have a 30 pack/year smoking history and currently smoke or quit within the past 15 years
	  ◦ Have undergone a process of informed or shared decision-making that included information about the potential benefits, limitations, and harms of screening with low-dose CT
	  ◦ ACS further recommends criteria of "access to a high-volume, high-quality lung cancer screening and treatment center"

Hepatocellular Carcinoma (HCC)	• Patients with chronic hepatitis B or C and cirrhosis, serum AFP (see pages 10-11 & 22-23) and liver US every 6 mos
Renal Cell	• Screening via cytologic or radiographic means is not recommended, except possibly for patients with a history of analgesic abuse. Some suggest regular US on the native kidneys

*At some institutions, screening is started at age 40 years or 5 years after transplant, whichever comes first

^*Modified from Kasiske BL, Vazquez MA, Harmon WE, et al. Recommendations for the outpatient surveillance of renal transplant recipients. American Society of Transplantation. J Am Soc Nephrol 2000; 11 Suppl 15:S1, Wong, Cancer Screening in Renal Transplant Recipients: What is the Evidence, Clin J Am Soc Nephrol 2008 Mar, 3(Suppl 2): S87-S100, 2014 Clinica Summary of the USPSTF Recommendation on Screening for Lung Cancer and the 2019*

MANAGING POTENTIAL COMPLICATIONS POST-TRANSPLANT (CONTINUED)

Medication Related Complications

General

- Medication side effects are very common and can be difficult to manage. Seek LLUTT guidance for any suspected need for medication changes
- Discuss medication problems and side effects with patients. Foster trust and team approach with the patient
- Check DDIs on all new medications–consult LLUTT if new medicines have immunosuppressant interactions

Medication Side Effects

- See pharmacy pages 33-41
- See below for CNI toxicity
- Side effects of common immunosuppressants:
  - **Tacrolimus**–Elevated BP, hand tremors, hair thinning, elevated blood sugar (BS), nausea/vomiting, seizures, elevated potassium (K+), nephrotoxicity
  - **Cyclosporin**–Hirsutism, elevated BP, diarrhea, nausea/vomiting, gingival hyperplasia, tremor, nephro/hepato toxicity
  - **Prednisone**–Elevated BP, weight gain, edema, cushingoid faces, striae, bruising, insomnia, elevated BS, osteopenia, ulcers, mood changes, poor wound healing
  - **Mycophenolate**–Diarrhea, decreased WBC/neutropenia (may need G-CSF), anemia, nausea/vomiting
  - **Sirolimus**–Rash, bone marrow suppression, edema, proteinuria, hepatotoxicity
  - **Azathioprine**–Bone marrow suppression, diarrhea, joint pain, myalgia, loss of balance/coordination, weakness, hepatotoxicity

Calcineurin Inhibitor (CNI)-Mediated Nephrotoxicity

- Cyclosporine and tacrolimus selectively inhibit calcineurin (calcium and calmodulin dependent phosphatase that activates T cells), thereby impairing the transcription of interleukin (IL)-2 and several other cytokines in T lymphocytes. CNIs have been mainstays of immunosuppression in solid organ transplantation for over three decades
- CNIs produce a dose-related, reversible, renal vasoconstriction that particularly affects the afferent arteriole
- **Inadequate therapeutic levels may lead to acute rejection, whereas very high levels are more likely to be associated with nephrotoxicity. Other adverse effects may occur independently of blood level**
- Evidence of CNI toxicity should be sought during periodic history assessments and physical examinations
- Manifests clinically as a blood-level-dependent elevation in CREAT concentration that may be difficult to distinguish from other causes of graft dysfunction
- High blood levels of CNIs do not preclude a diagnosis of rejection
- In the acute phase, tubular function is intact
- CNI nephrotoxicity may develop at low drug levels, especially in malnourished patients with diminished protein binding where the free drug concentration is increased; some degree of toxicity may be intrinsic to their use. In practice, particularly when CREAT elevation is modest, it is reasonable to initially presume that a patient with a very high CNI level probably has nephrotoxicity and that a patient with deteriorating graft function and a very low drug level is likely undergoing rejection
- CNI toxicity usually resolves within 24-48 hrs of dose reduction. Progressive elevation of the plasma CREAT level, even in the face of persistently high drug levels, warrants consideration of rejection
- Few studies address the optimal interval for monitoring, but levels should be measured more frequently early after transplantation, after CNI dose changes, during periods of growth in pediatric patients, and when there are changes in medications or other factors that may influence CNI levels

Adverse effect	Tac	CSA	Steroids	MMF	mTORi	AZA
New-onset diabetes mellitus	XX	X	X		X	
Dyslipidemias		X	X		XX	
Hypertension	X	XX	XX			
Osteopenia	X	X	XX			
Anemia and leucopenia				X	X	X
Delayed wound healing					X	
Diarrhea, nausea/vomiting	X			XX		
Proteinuria					XX	
Decreased GFR	X	X				

X- indicates a mild to moderate adverse effect on the complication

XX- indicates a moderate to severe adverse effect on the complication.

MEDICATIONS

(LLUTT management supersedes**)

Calcineurin Inhibitors (CNI) Pharmacology

- The cornerstone of post-transplant immunosuppression is the use and close monitoring of CNIs
- Cyclosporine and tacrolimus selectively inhibit calcineurin, thereby impairing the transcription of interleukin (IL)-2 and several other cytokines in T lymphocytes. CNIs have been mainstays of immunosuppression in solid organ transplantation for over three decades
- In addition to standard immediate-release tacrolimus, there are two extended-release formulations of tacrolimus (capsules [Astagraf] and tablets [Envarsus]) designed for 1x/daily administration
- Therapeutic monitoring of cyclosporine and tacrolimus is complicated by the narrow margin between adequate immunosuppression and toxicity. Whole blood should be used as a sample for both drugs
- Tacrolimus and cyclosporine reach steady-state concentrations after 4-6 doses
- Blood concentrations should be checked 2-3 days after starting cyclosporine or tacrolimus and after any dose change. Typically, after transplant, concentrations are measured every 1-2 days while hospitalized. After discharge, levels should be measured 1-2x/weekly for the first mo, then weekly until 3 mos post-transplantation, then q 2 wks until 6 mos post-transplant, and then monthly. Some stable, low-risk patients may have concentrations monitored every 2-3 mos. However, if drugs that affect cyclosporine or tacrolimus metabolism are added or withdrawn, more frequent measurement of trough concentrations will be required (see 'Food and Drug interactions' below)

Factors Influencing Pharmacokinetics of CNIs:

- **Absorption:** Interacting medications like cholestyramine, motility agents, diarrhea or constipation, presence or absence of food, brand vs generic formulations
- **Distribution:** Hematocrit
- **Metabolism:** DDIs (see pages 33-34), grapefruit juice, genetic polymorphism in Cytochrome P450 3A5 (CYP3A5), hepatic impairment
- **Other:** Timing of concentration, type of laboratory immunoassay, schedule, frequency and adherence

Dosing– CNI Target Levels

Tacrolimus: Starting dose ~ 0.08 mg/kg BID

- In patients treated with tacrolimus, whole-blood 12-hr trough concentrations are used for immediate-release preparations and 24-hour troughs are used for extended-release preparations
- **Tacrolimus target levels for 12-hr trough are not well established**. Different formulations are not interchangeable.
  - Research shows that a level ≥ 8 ng/mL in first month is important to prevent rejection
  - LLU reference range is 4-24.9 ng/mL and sometimes the trough will be a 10-hr trough (and adjusted accordingly)
  - Each patient has unique goal depending on the clinical scenario, but generally levels are maintained between 8-10 ng/mL first mo, then generally 5-8 ng/mL thereafter, range: 3 ng/mL (low risk)–10 ng/mL (high risk patients)
  - After three mos, doses are generally not decreased unless there are compelling side effects
- **Dose Adjustments**: In clinical practice, dose adjustments are made in small increments with subsequent drug concentration monitoring. It is important to determine whether the concentration was obtained correctly before making any dose adjustments. Always consider adherence
  - For tacrolimus, dose adjustments are typically 0.5-1 mg per dose
  - If supra-therapeutic (> 30 ng/mL for tacrolimus), the dose may be held until the concentration returns to the therapeutic range. Tacrolimus reaches steady-state concentrations after 4-6 doses, and therefore, **dose adjustments can be assessed via drug concentration monitoring 2-3 days after an adjustment**. Safety and efficacy must be monitored after adjustments
- **Common side effects of tacrolimus:**
  - Headache, tremor, insomnia, paresthesias, diarrhea, nausea, constipation, elevated LFTs, anorexia, vomiting, HTN, pruritus, rash, alopecia, hyperglycemia, lymphoproliferative diseases, anemia, leukocytosis, thrombocytopenia, CMV infection, abdominal pain, fever, asthenia, back pain, ascites, nephrotoxicity

Envarsus XR (extended release tacrolimus): Starting dose is 0.14mg.kg

- Titrate for 12-hr trough of 6-11 ng/mL the first mo and 4-11 ng/mL after the first month

Cyclosporine: Starting dose ~ 0.04-0.05 mg/kg BID

- In most patients treated with cyclosporine, whole-blood 12-hr trough concentrations are monitored. Formulations are not interchangeable
- **CSA target levels for 12-hr trough:**
  - 200-300 ng/mL in mos 1-3 after transplantation
  - 50-150 ng/mL for subsequent mos
- **Dose Adjustments:** In clinical practice, dose adjustments are made in small increments with subsequent drug concentration monitoring. It is important to determine whether the concentration was obtained correctly before making any dose adjustments. Always consider adherence
  - If a drug concentration is supratherapeutic (> 400 ng/mL for cyclosporine), then the dose may be held until the concentration returns to the therapeutic range
  - If a cyclosporine concentration is high, then the dose of cyclosporine may be decreased by 25-50 mg per dose
  - If the concentration is low, then the dose may be increased by 25-50 mg per dose
  - Cyclosporine reach steady-state concentrations after 4-6 doses, and therefore, **dose adjustments can be assessed via drug concentration monitoring 2-3 days after an adjustment**
  - Safety and efficacy must be monitored after adjustments
- **Common side effects of cyclosporine:**
  - Tremor, headache, dizziness, hirsutism, elevated BP, diarrhea, nausea and vomiting, dyspepsia, flushing, gingival hyperplasia, tremor/shakiness, drowsiness, pruritus, muscle spasms, ear pounding, thrombocytopenia, brady or

MEDICATIONS

Below is a list of medications that most recipients are placed on after they receive a kidney transplant. This list may or may not include all medications a patient may be prescribed, and the medications each patient is prescribed will vary depending on individual needs.

Medication	Action	Length of Time
Cyclosporine or tacrolimus (Prograf®)	Immunosuppressant/antirejection	Lifetime
Mycophenolate (Cellcept®) or sirolimus (Rapamune®)	Immunosuppressant/antirejection	Lifetime
Thymoglobulin	Treats allograft rejection	Acute use
Orthoclone IV	T cell suppressant (MCAB to CD3 receptor)	Acute use
Methylprednisolone (Solu-Medrol®)	Acute Immunosuppressant/antirejection or allergic reaction	Acute use
Rituximab	Treats acute allograft rejection	Acute use
Lymphocyte Immune Globulin (ATGAM IV®)	Treats allograft rejection	Acute use
IV Immunoglobulin (IVIg®)	Treats antibody mediated allograft rejection	Acute use
Bactrim DS/Sulfa, Cipro, Dapsone	UTI and PJP prophylaxis	2 mos* Cipro: 2 doses for ureteral stent removal Dapsone: 1 yr
Diflucan (Fluconazole®) or Mycelex®	Antifungal prophylaxis	3 mos
Valcyte® or acyclovir (Zovirax®)	CMV and other antiviral prophylaxis	6 mos
Hep B Immunoglobulin (H-BIG) if pre-transplant HBV and lamivudine (Epivir®), Entecavir (Baraclude®), or tenofovir (Viread®)	Hep B re-infection prophylaxis	All HBV Antigen + patients should receive lamivudine at time of transplant and continuing for at least 18-24 mos
Ranitidine or Proton Pump Inhibitor	GI prophylaxis	Approx. 1 yr
Magnesium oxide	Replaces magnesium	As needed
MiraLAX®, Colace® and other stool softeners and stimulants	Constipation	As needed
K Phos Neutral	Replaces phosphorus	As needed
Antihypertensive medications (First line: amlodipine and nifedipine)	Lowers BP	As needed
Insulin	Lowers blood sugar	As needed
Opioids	Pain control	As needed, first wk post-op
Patiromer (Veltassa®) or polystyrene sulfonate (Kayexalate®)	Hyperkalemia	PRN
Multivitamin	General nutrition	Lifetime

*Fluconazole: Prophylaxis lifelong if history of cocci; 1 year post-transplant if they live in a cocci endemic location. When therapy is complete, the Prograf® level will drop significantly so the dose will need to be modified concurrently.

MEDICATIONS

Drug Interactions of Immunosuppressants Used in Solid-Organ Transplant

Important note: Drug therapy **choices and doses** should be managed by transplant specialists with expertise in therapeutic drug monitoring, and doses should be adjusted based upon measurement of immunosuppressant concentrations.

- Cyclosporine, tacrolimus, and sirolimus are highly dependent upon CYP3A metabolism for clearance and are also substrates of P-glycoprotein (Pgp) drug efflux pump. Some interactions can lead to subtherapeutic or dangerously toxic levels of immunosuppressant concentrations.
- When appropriate non-interacting alternatives are readily available, discuss with the transplant team regarding modifying treatment to avoid combined use with potent metabolic inhibitors/inducers or agents known to have additive toxicities with immunosuppressants.
- If there are any concerns about the safety of a given medication or supplement, they should be discussed with the patient's transplant center prior to initiation.

This is **not** a complete list and many other significant drug interactions can occur. Below are resources to check DDIs:

- CCHCS Pharmacy DDI checker*
- UptoDate Lexicomp DDI checker†

Common Types of Drug Interactions	Examples of Interacting Drug	Approach to Management in the Absence of Appropriate Non-interacting Alternatives
Co-administration of drugs that inhibit CYP3A metabolism and/or P-gp efflux can **increase immunosuppressant serum concentrations**, leading to significant toxicities	• Amiodarone • Antiretroviral-boosting agents (e.g., ritonavir, cobicistat) • Azole antifungals (e.g., fluconazole, posaconazole, voriconazole) • HIV protease inhibitors (e.g., atazanavir, nelfinavir, saquinavir) • Macrolide antibiotics • Non-dihydropyridine calcium channel blockers (diltiazem, verapamil, nifedipine) • Ombitasvir-paritaprevir-ritonavir with or without dasabuvir (an HCV/direct-acting antiviral regimen) • Grapefruit juice • Antidepressants: fluoxetine and fluvoxamine, sertraline, venlafaxine, mirtazapine, and paroxetine	• Closely monitor immunosuppressant concentrations and signs of toxicity (e.g., tremors and headaches) • Substantial, including preemptive, dose reduction of immunosuppressant drug may be needed (e.g., on average, only 25% of the standard dose of cyclosporine is required if administered concomitantly with HIV protease inhibitors) • Some combinations are considered contraindicated according to product labeling; refer to appropriate topic reviews for detail
Co-administration of drugs that induce CYP3A metabolism and/or P-gp efflux pumping can **decrease immunosuppressant serum concentrations**, increasing the risk of organ rejection	• Anti-seizure drugs, enzyme inducing (e.g., carbamazepine, fosphenytoin, oxcarbazepine, phenobarbital, phenytoin, primidone) • Enzalutamide • Nafcillin • Rifampin and Rifamycins (e.g., rifabutin, rifapentine) • St. John's Wort	• Closely monitor immunosuppressant serum concentrations and signs of organ rejection • Significant immunosuppressant dose increases may be needed • Avoid concomitant treatment with everolimus if possible • Enzyme induction can require up to 2 wks to achieve maximum effect and persists for up to 2 wks after discontinuation of the interacting medication. Clinically significant effects can occur within hours to days of starting a CYP inducer

Adapted from: Chandraker, M.D., et. Al. Overview of care of the adult kidney transplant recipient. UpToDate. March 2019.

* http://www.clinicalpharmacology-ip.com/Forms/login.aspx?ReturnUrl=%2fForms%2fReports%2fintereport.aspx
† https://www.uptodate.com/drug-interactions/#di-druglist

MEDICATIONS

Drug Interactions of Immunosuppressants Used in Solid-Organ Transplant (Continued)

Common Types of Drug Interactions	Examples of Interacting Drug	Approach to Management in the Absence of Appropriate Noninteracting Alternatives
Co-administration of nephrotoxic drugs with cyclosporine or tacrolimus can cause **additive or synergistic kidney injury**	• Aminoglycosides • Amphotericin B • NSAIDs • Colchicine	• Concomitant administration of cyclosporine and/or tacrolimus with other potentially nephrotoxic drugs should be avoided • Suggested dose adjustments for use with colchicine are available in the Lexicomp monograph* included within UpToDate
Co-administration of drugs that increase serum potassium with cyclosporine or tacrolimus may cause **severe hyperkalemia**	• ACEI/ARBs • Amilioride • Spironolactone • Triamterene • Trimethoprim, trimethoprim-sulfamethoxazole (cotrimoxazole)	• Closely monitor serum potassium levels
Co-administration of cyclosporine with sirolimus can **increase sirolimus concentrations**	• Cyclosporine	• Separate administration of sirolimus from cyclosporine by four hours; give sirolimus at a consistent time with respect to cyclosporine • Closely monitor immunosuppressant serum concentrations
Co-administration of common drugs with cyclosporine **or tacrolimus** that can **increase statin/drug levels and risk of myotoxicity or other toxicities**	• Atorvastatin • Lovastatin • Pitavastatin • Rosuvastatin • Simvastatin • Colchicine • Ezetimibe	• Pravastatin and fluvastatin are preferred due to decreased interactions • Tacrolimus may be preferred over cyclosporine in patients receiving statin therapy • Cyclosporine and simvastatin should not be used together • Some combinations are considered contraindicated or statin daily dose limits are recommended in the product labeling
Co-administration of nifedipine and phenytoin with Cyclosporine (CSA)	• Additive incidence of gingival hyperplasia (from 8% CSA alone to 51% in combination)	• Monitor and consider a different antihypertensive or antiepileptic • Avoid long term use if possible • Good dental/oral hygiene with regular dental visits
Digoxin	• INCREASED DIGOXIN LEVELS • Decreased volume of distribution of digoxin by 50-70% • Increased digoxin half-life by 30-40% • Digoxin toxicity (vomiting, cardiac arrhythmias, etc.)	• Initiate low dose and follow up with serum digoxin levels • Closely monitor for symptoms of digoxin toxicity

Table 8: DAA Interactions With Calcineurin Inhibitors†

	Cyclosporine (CSA)	Tacrolimus (TAC)
Sofosbuvir (SOF)	4.5-fold ↑ in SOF AUC, but GS-331007 metabolite unchanged; no a priori dose adjustment	No interaction observed; no a priori dose adjustment
Ledipasvir	No data; no a priori dose adjustment	No data; no a priori dose adjustment
Velpatasvir	No interaction observed; no a priori dose adjustment	No data; no a priori dose adjustment
Sofosbuvir/ velpatasvir/ voxilaprevir (SOF/ VEL/VOX)	9.4-fold ↑ in VOX AUC; combination is not recommended	No data; no a priori dose adjustment
AUC=area under the curve		

* https://www.uptodate.com/drug-interactions/#di-druglist

† https://www.hcvguidelines.org/unique-populations/post-liver-transplant

MEDICATIONS

MEDICATION CLASS/ MEDICATION	DOSING	ADVERSE EFFECTS/ INTERACTIONS*	COMMENTS*
IMMUNOSUPPRESSANTS			

Tacrolimus (Prograf®)
 	
Capsule:
0.5 mg,
1 mg,
5 mg
 	
First-Line CNI
 	
$$$$$
 	
Note: Other formulations of tacrolimus, including Envarus XR® (extended-release), are rarely used by LLU. If a patient comes in from the community or the hospital on the extended release product it should be continued (although NOT formulary) until consultation with transplant nephrologist to determine if transition to formulary product is acceptable.
	• Dosing based on Observed Whole Blood Trough Concentrations
	• Prescribe based on LLUTT recommendations
	• Initial Oral Dosage: 0.1-0.2 mg/kg/day
	• Standard Dose: Adjust dose to keep 12-hr trough levels (C_0) of 10 (5-15) ng/mL
	• Low Dose: Adjust to keep C_0 of 5 (3-7) ng/mL
	• Hepatic/Renal Impaired Dosing: Dose at the lowest value of the dosing range. Close monitoring of whole blood concentrations are recommended
	
	NOTE: Take on an empty stomach: 1 hour before and 2 hours after a meal This is usually for the extended release products. To minimize variations in bioavailability for the immediate release products, administer consistently with or without food.
		• Adverse Effects: tremor, headache, diarrhea, N/V, dyspepsia, insomnia, hair loss, weight gain, mood changes, nephrotoxicity, dizziness, thrombocytopenia, bruising bleeding, hepatitis, hepatotoxicity, abnormal liver function tests, muscle weakness, leg pain (can be severe), CHF, hypertension, peripheral edema, pruritus, persistent erythema of skin, constipation, anemia, increased CREAT, paresthesia, cough, hypercholesterolemia, hyperlipidemia, hypertriglyceridemia, infection, malignancy
		
		Due to the large number of interactions* which can affect tacrolimus level or level of the interacting medication, it is imperative to **CHECK DDI CHECKER ANY TIME STARTING OR STOPPING MEDICATIONS** CCHCS DDI Checker.
		
		Follow levels after any medication change and ensure LLUTT is informed of the changes.
		
		• Drug Interactions*: colchicine voriconazole, sirolimus, esomeprazole, omeprazole, lofexidine, hydroxychloroquine, fentanyl, posaconazole, ketoconazole, donepezil, metronidazole, NSAIDS, phenobarbital, verapamil, ranitidine, diltiazem, darunavir, fosaprepitant, imatinib, aprepitant, moxifloxacin, ombitasvir, fluoxetine, nicardipine, efavirenz, nafcillin, dexamethasone, prednisone, oxcarbazepine, modafinil, rifapentin, armodafinil, etravirine, bosentan, clarithromycin, itraconazole, quetiapine, metoclopramide, levofloxacin, cyclosporine, nefazodone, indinavir, lopinavir, cobicistat, idelalisib, cobicistat, hydroxyzine, clozapine, amiodarone, erythromycin, ciprofloxacin, nilotinib, crizotinib, atazanavir, aripiprazole, escitalopram, amlodipine, quinidine, disopyramine, procainamide, chloroquine, quinine, methadone, promethazine, haloperidol, imipramine, prochloperazine, amitriptyline, doxepin, chlorpromazine, tamoxifen, cyclobenzaprine, trazodone, famotidine, ofloxacin, sotalol, mefloquine, paroxetine, azithromycin, clomipramine, venlafaxine, risperidone, citalopram, olanzapine, tetrabenazine, ondansetron, live vaccines
			• **BLACK BOX WARNING**
			  • Only physicians experienced in immunosuppressive therapy and management of organ transplant patients should prescribe tacrolimus
			  • Immunosuppression may lead to increased susceptibility to infection and possible development of lymphoma and other malignancies
			
			Different Formulations: Tacrolimus immediate release (Prograf®), **is NOT interchangeable with the extended release versions (Envarus XR®) and Astagraf XL®**). Use only the formulations prescribed by LLUTT.
			
			• Contraindications: hypersensitivity to castor oil derivatives (IV form), liver transplant use XR Cap form, uncorrected electrolyte abnormalities, congenital long QT syndrome, hypersensitivity to tacrolimus or any component of the product, concurrent use with **fluconazole, ziprasidone, saquinavir, ritonavir, mifepristone, thioridazine, pimozide, dronedarone, nelfinavir, live vaccines**
			
			• Caution in the following: QT prolongation or family history of, history of torsades de pointes, ventricular arrhythmias, bradycardia, recent MI, CHF, African-American, Hispanic, renal impairment, hepatic impairment, concomitant use of oral and topical product
			
			• Length of time to take: Lifetime
			
			• As shown in Adverse Effects/Interactions column, there are multiple DDIs. Must run DDI checker when starting or stopping any medication. Follow levels with any change, LLUTT should be informed of changes.

Bold = Formulary *See prescribing information for complete description of contraindications/precautions, adverse effects and drug interactions.

The cost scale $-$$$$$ represents the relative cost of acquisition of medication only. Frequency and complexity of medication administration (institution workload, effect on adherence) should be considered when determining overall cost-effectiveness of treatment.

MEDICATIONS

MEDICATION CLASS/ MEDICATION	DOSING	ADVERSE EFFECTS/ INTERACTIONS*	COMMENTS*
IMMUNOSUPPRESSANTS			

Cyclosporine (Sandimmune®)
 	
Capsule:
25 mg,
100 mg
 	
$$$$$
 	
Note: Other formulations of cyclosporine are rarely used by LLU. If a patient comes in from the community or the hospital on cyclosporine, it is available, but is not formulary. Do not change formulations without first consulting a nephrologist
	• Dosing based on Observed Whole Blood Trough Concentrations.
	
	Prescribe based on LLUTT recommendations
	
	• Standard Dose: 10-14 mg/kg/day Adjust to keep 12-hr trough level (C_0) of 200 (150-300) ng/mL
	
	• Suspected Poor CSA Absorption Dose: (rare), a higher dose and a 2 hr post-trough (C_2) is used. Dose adjusted to keep C_2 level 800-1800 ng/mL early and 400-1200 ng/mL later after transplantation
	
	• Note: In most cases, C_0 should be used to adjust drug levels NOT C_2
	
	• Low Dose: C_0 of 75 (50-100)
	
	• Hepatic Dosing: Specific guidelines are not available, however, patients with hepatic impairment may require a dose reduction. Cyclosporine concentrations should be monitored closely
	
	• Renal Dosing: Specific guidelines for dosage adjustments are not available, it appears that no dosage adjustments are needed
		• Adverse Effects: Headache, diarrhea, N/V, tremor, hirsutism/hair growth, HTN, gum tissue overgrowth, conjunctivitis, infection, nephrotoxicity, hepatotoxicity, seizure, edema
		
		Due to the large number of interactions* which can affect cyclosporine level or level of the interacting medication, it is imperative to **CHECK DDI CHECKER ANY TIME STARTING OR STOPPING MEDICATIONS**
		CCHCS DDI Checker.
		
		Follow levels after any medication change and ensure LLUTT is informed of the changes.
		
		• Drug Interactions*: Ritonavir, fentanyl, lovastatin, itraconazole, glecaprevir/pibrentasvir, NSAIDS, voriconazole, etoposide, diltiazem, rosuvastatin, morphine, nafcillin, rifabutin, pravastatin, metoclopramide, fluconazole, atorvastatin, aliskiren, felodipine, posaconazole, rifampin, mycophenolic acid, amlodipine, bupropion, domperidone, tacrolimus, vaccines, dabigatran
			• **BLACK BOX WARNING**
			  • Only physicians experienced in immunosuppressive therapy and management of organ transplant patients should prescribe cyclosporine
			  • Immunosuppression may lead to increased susceptibility to infection and possible development of lymphoma
			  • The physician responsible for maintenance therapy should have complete information requisite for the follow-up of the patient
			
			• Different Formulations: Cyclosporine and Cyclosporine Modified are NOT interchangeable. Use only the formulation prescribed by LLUTT
			
			• Contraindications: Hypersensitivity to cyclosporine or any ingredient in the formulation of the product. Concurrent use with the following: **simvastatin, colchicine, bosentan, grazoprevir, dronedarone, eliglustat, live vaccines**
			
			• Length of time to take: Lifetime
			
			• As shown in Adverse Effects/Interactions column, there are multiple DDIs. Must run DDI checker when starting or stopping any medication. Follow levels with any change, LLUTT should be informed of changes.

Cyclosporine Modified (Neoral®)
 	
Capsule:
25 mg,
50 mg,
100 mg
 	
$$$$$
 	
Note: Other formulations of cyclosporine are rarely used by LLU. If a patient comes in from the community or the hospital on cyclosporine, it is available, but is not formulary. Do not change formulations without first consulting a nephrologist
	• Dosing based on Observed Whole Blood Trough Concentrations.
	
	Prescribe based on LLUTT recommendations
	
	• Standard Dose: 10-14 mg/kg/day Adjust to keep 12-hr trough level (C_0) of 200 (150-300) ng/mL
	
	• Suspected Poor CSA Absorption Dose: (rare), a higher dose and a 2 hr post-trough (C_2) is used. Dose adjusted to keep C_2 level of 800-1800 ng/mL early and 400-1200 ng/mL later after transplantation
	
	• Low Dose: Adjust to keep C_0 of 75 (50-100)
	
	• Hepatic Dosing: Specific guidelines are not available, however, patients with hepatic impairment may require a dose reduction. Cyclosporine concentrations should be monitored closely
	
	• Renal Dosing: Specific guidelines for dosage adjustments are not available, it appears that no dosage adjustments are needed
		• Adverse Effects: Headache, diarrhea, N/V, tremor, hirsutism/hair growth, HTN, gum tissue overgrowth, optic disc edema, infection, nephrotoxicity, hepatotoxicity, seizure, edema, increase in serum triglycerides, paresthesia
		
		Due to the large number of interactions* which can affect cyclosporine level or level of the interacting medication, it is imperative to **CHECK DDI CHECKER ANY TIME STARTING OR STOPPING MEDICATIONS**
		CCHCS DDI Checker.
		
		• Drug Interactions: Ritonavir, fentanyl, lovastatin, itraconazole, glecaprevir/pibrentasvir, NSAIDS, voriconazole, etoposide, diltiazem, rosuvastatin, morphine, nafcillin, rifabutin, pravastatin, metoclopramide, fluconazole, atorvastatin, aliskiren, felodipine, posaconazole, rifampin, mycophenolic acid, amlodipine, bupropion, domperidone, tacrolimus, vaccines, dabigatran
			• **BLACK BOX WARNING**
			  • Only physicians experienced in immunosuppressive therapy and management of organ transplant patients should prescribe cyclosporine modified
			  • Immunosuppression may lead to increased susceptibility to infection and possible development of lymphoma
			  • The physician responsible for maintenance therapy should have complete information requisite for the follow-up of the patient
			
			• Different Formulations: Cyclosporine Modified and Cyclosporine are NOT interchangeable. Use only the formulation recommended by LLUTT.
			
			• Contraindications: Hypersensitivity to cyclosporine or any ingredient in the formulation of the product. Concurrent use with the following: simvastatin, colchicine, bosentan, grazoprevir, dronedarone, eliglustat, live vaccines
			
			• Length of time to take: Lifetime
			
			• As shown in Adverse Effects/Interactions column, there are multiple DDIs. Must run DDI checker when starting or stopping any medication. Follow levels with any change, LLUTT should be informed of changes.

Bold = Formulary

*See prescribing information for complete description of contraindications/precautions, adverse effects and drug interactions.

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MEDICATIONS

MEDICATION CLASS/ MEDICATION	DOSING	ADVERSE EFFECTS/ INTERACTIONS*	COMMENTS*
IMMUNOSUPPRESSANTS			

Mycophenolate mofetil (MMF) (CellCept®)
 	
Capsule:
250 mg
 	
Tablet:
500 mg
 	
First-Line anti-proliferative agent
 	
$$-$$$$
	• Usual Dose: 1 g orally twice daily on an empty stomach
	• Max Dose: 3 g/day
	• Note: Doses of 3 g/day did not show any advantage over 2 g/day
	• Hepatic Dosing: No dosage adjustment is recommended for renal transplant patients with severe hepatic parenchymal disease
	• Renal Dosing: GFR < 25 mL/min outside immediate post-transplant period: 1 g orally twice daily
	• MMF blood levels are not ordinarily used for routine management
		• Adverse Effects: Constipation, N/V, diarrhea, dyspepsia, headache, flatulence, insomnia, tremor, arrhythmia, fatigue, thrombocytopenia, edema, balance and coordination problems, decreased cognition, seizures, dizziness, rash, hypertension, abdominal pain, musculoskeletal pain, hypotension, tachycardia, depression, chills, confusion, drowsiness, hypertonia, malaise, ecchymosis, cellulitis, fever, acidosis
		• Drug Interactions: ciprofloxacin, amoxicillin/clavulanic acid, proton pump inhibitors, telmisartan, antacids with magnesium or aluminum hydroxide, rifampin, bile acid sequestrants, isavuconazonium, tofacitinib, cyclosporine, ethinyl estradiol, calcium-free phosphate binders, fenofibrate, vaccines (live and inactivated), acyclovir, valacyclovir, anticoagulants
			• **BLACK BOX WARNING**
			  • Only physicians experienced in immunosuppressive therapy and management of organ transplant patients should prescribe mycophenolate mofetil. Immunosuppression may lead to increased susceptibility to infection and possible development of lymphoma
			  • The physician responsible for maintenance therapy should have complete information requisite for the follow-up of the patient
			  • Female users of childbearing potential must use contraception due to association with increased pregnancy loss and congenital malformations
			• Contraindications: hypersensitivity to polysorbate 80 (IV form), pregnancy, breastfeeding, Lesch-Nyhan syndrome, concurrent use with live vaccines
			• Caution in the following: HBV or HCV infection, GI disorder, severe renal disease, bone marrow depression, PKU (phenylalanine-containing forms)
			• Length of time to take: Lifetime

Sirolimus (Rapamune®)
 	
(An mTOR [mammalian target of rapamycin], not CNI. A second line immunosuppressant, used if complications on CNIs)
 	
Tablet:
0.5 mg,
1 mg,
2 mg
 	
Solution:
1 mg/mL
 	
$$$$$
	• Usual Maintenance Dose:
	Low to moderate immunologic risk: 2 mg orally once daily. Titrate to obtain a whole blood trough concentration of 3-11 ng/mL (chromatographic method) for the first year after transplantation; a target concentration of 12-20 ng/mL (chromatographic method*) is recommended after year 1. Used in combination with cyclosporine and tacrolimus
	High Immunologic Risk: 5 mg orally once daily. Titrate to obtain a whole blood trough concentration of 10-15 ng/mL (chromatographic assay) for the first year after transplantation. 12-hr trough level should be drawn between days 5 and 7 after initiation of therapy.
	When a maintenance dose is adjusted, wait 7-14 days before additional adjustments are made based on concentration monitoring.
	Therapy > 12 mos should be individualized and adjusted according to the clinical status of the patient and will depend on doses of other immunosuppressants used simultaneously.
	• Max Dose: 40 mg/day
	• Hepatic Dosing:
	Loading dose: no dose adjustment needed
	Maintenance dose:
	Mild or moderate impairment: reduce dose by approximately one-third.
	Severe hepatic impairment: reduce dose by approximately one-half.
	Close monitoring of whole blood concentrations are recommended
	• Renal Dosing: No dosage adjustments are necessary in patients with renal impairment
	• Food changes levels, take medication either consistently with or without food
	* chromatographic and immunoassay methodologies are NOT interchangeable
		• Adverse Effects: Diarrhea, joint pain, acne, elevated hepatic enzymes, hepatotoxicity, muscle cramps, nausea, fatigue, bone pain, edema, headache (can be severe), impaired wound healing, elevated cholesterol, rash– common, hyperlipidemia, hypertriglyceridemia, chest pain, abdominal pain, constipation, stomatitis, anemia, thrombocytopenia, dizziness, increased CREAT, urinary tract infections, proteinuria, fever, pain, upper respiratory infection, epistaxis, gingivitis, infection
		• Drug Interactions: posaconazole, voriconazole, mifepristone, ritonavir, ACE inhibitors, fluconazole, rifampin, tacrolimus, amiodarone, ketoconazole, itraconazole, live vaccines, verapamil, phenobarbital, clarithromycin, dronedarone, metoclopramide, cobicistat, pazopanib, saquinavir, etravirine, efavirenz, phenytoin, erythromycin, diltiazem, rifabutin, rifapentine, cisapride, cimetidine,indinavir,
			• **BLACK BOX WARNING**
			  • Only physicians experienced in immunosuppressive therapy and management of renal transplant patients should prescribe sirolimus
			  • Immunosuppression may lead to increased susceptibility to infection and possible development of lymphoma and other malignancies
			• Contraindications: lung or liver transplant use. Concurrent use with posaconazole, voriconazole, mifepristone, and ritonavir, live vaccines
			• Caution in the following: concurrent nephrotoxic agent use, delayed graft fxn, BMI >30, hepatic impairment, renal impairment, hyperlipidemia
			• Length of time to take: Lifetime

Bold = Formulary *See prescribing information for complete description of contraindications/precautions, adverse effects and drug interactions.

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MEDICATIONS

MEDICATION CLASS/ MEDICATION	DOSING	ADVERSE EFFECTS/ INTERACTIONS*	COMMENTS
IMMUNOSUPPRESSANTS			
Prednisone (Deltasone®) Tablet: 1 mg, 2.5 mg, **5 mg,** **10 mg,** **20 mg**, 50 mg **$** Prednisone is used as a third immunosuppressant agent in most patients and is continued lifelong in approximately 70%	• Usual Dose: 5-30 mg orally once daily. Titrate to response. • Long-Term Maintenance Dose: 5 mg orally once daily • Max Dose: No absolute maximum dose– consult Transplant Team • Hepatic Dosing: Specific guidelines are not available; prednisone is converted to prednisolone, the active moiety, by the liver. The use of oral prednisolone instead of oral prednisone may be preferred in patients with significant hepatic dysfunction • Renal Dosing: Specific guidelines are not available	• Adverse Effects: acne, poor wound healing, gastritis, hair growth, moon facies, abdominal obesity, edema, cataracts, hyperglycemia, hypertension, increased appetite, weight gain, osteoporosis, disturbance in mood • Drug Interactions: fluoroquinolones, fentanyl, dronedarone, nifedipine, lopinavir, elvitegravir, ritonavir, bupropion, tramadol, tacrolimus, methadone, oxycodone, hydrocodone, hormonal contraceptives, telaprevir, velpatasvir, buprenorphine, meperidine, codeine, darunavir, daclatasvir, NSAIDS, salicylates, rifapentine, montelukast, rifampin, fluconazole, ketoconazole, clarithromycin, phenytoin, lurasidone, selegiline, indinavir, cyclosporine, propranolol	• Contraindications: systemic fungal infection, cerebral malaria, avoid abrupt withdrawal (high dose or long-term use), hypersensitivity to prednisone or any component of the product, administration of live or live attenuated vaccines with immunosuppressive corticosteroid doses, concurrent use with desmopressin • Caution in the following: immunosuppressed, active infection, TB infection (active or latent), infection risk, measles or varicella exposure, hypertension, pheochromocytoma risk, CHF, recent MI, DM, peptic ulcer disease, ulcerative colitis, diverticulitis, recent intestinal anastomosis, GI perforation risk, seizure disorder, psychiatric disorder, thyroid disorder, osteoporosis or risk for, myasthenia gravis, optic neuritis, ocular HSV, renal impairment, cirrhosis • Length of time to take: lifetime • Some evidence exists that steroids may be safely stopped in most patients after 3-12 mos on combination therapy with a CNI and mycophenolate. Data suggest that the risk of steroid withdrawal depends on the use of concomitant immunosuppressives, immunological risk, ethnicity, and time after transplantation. However, current guidelines recommend continuing corticosteroids if used beyond the first wk after transplantation The risk of fractures is high. Measure BMD within first 3 mos of post transplant period if patient on steroids post RT and it will change management. Bone mineral density in post RT patients has not been shown to predict fracture risk as it does in the general population and does not predict the type of kidney transplant bone disease. Bone biopsy is recommended. (See page 26) Annual ophthalmology evaluation is recommended for glaucoma and cataract screening.
Anti-Thymocyte Immune Globulin (Rabbit) (Thymoglobulin®) 25 mg powder for injection $$$$$ Used in the treatment of high grade acute rejection and lower grade rejection refractory to high dose steroids and other treatments.	• Premedication needed: Give acetaminophen, corticosteroids, and/or antihistamine one hour before infusion • Usual dose: Acute rejection treatment in combination with other immunosuppressive agents: 1.5 mg/kg/day for 7-14 days • Rejection prophylaxis in combination with other immunosuppressive agents: 1.5 mg/kg/day IV once daily for 4-7 days with the first dose given prior to reperfusion of the donor kidney; infuse over a minimum of 6 hours for first infusion, over at least 4 hrs on subsequent days of therapy • Hepatic/Renal Dosing: Specific guidelines for dosage adjustments are not available, it appears that no dosage adjustments are needed	• Adverse Effects: chills, leukopenia, headache, abdominal pain, HTN, nausea, hyperkalemia, constipation, diarrhea, anemia, myalgia, anxiety, urinary tract infectious disease, dyspnea, fever, hypertension, peripheral edema, tachycardia, thrombocytopenia, anaphylaxis, cytokine release syndrome, acute renal failure, infectious disease, sepsis, serum sickness due to drug, infusion site pain, swelling and erythema • Drug Interactions: vaccines (live and inactivated), belatacept, tofacitinib, anticoagulants, NSAIDs, baricitinib, cladribine, denosumab, trastuzumab, pimecrolimus, tacrolimus (topical), salicylates	• **BLACK BOX WARNING** • Anti-Thymocyte Immune Globulin (rabbit) should only be used by physicians experienced in immunosuppressive therapy in transplantation • Contraindications: hypersensitivity to rabbit protein, active infection, hypersensitivity to any component of the product; concurrent use with live vaccines • Caution: ensure appropriate dose is used—protein composition and concentration varies based on source of anti-thymocyte globulin—products are not interchangeable, immunization with attenuated live vaccines not recommended with recent or current use, serious immune-mediated reactions have been reported especially with rapid infusion and can lead to serious cardiorespiratory events or death, increased incidence of lymphoma, lymphoproliferative disorders, or other malignancies may occur, life-threatening infections, reactivation of infection and sepsis have been reported; monitoring recommended

Bold = Formulary *See prescribing information for complete description of contraindications/precautions, adverse effects and drug interactions.

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MEDICATIONS

MEDICATION CLASS/ MEDICATION	DOSING	ADVERSE EFFECTS/ INTERACTIONS*	COMMENTS*
RAPID METABOLIZER IMMUNOSUPPRESSANT			
Envarsus XR (tacrolimus extended release) Dosage forms: ER TAB: 0.75 mg, 1 mg, 4 mg Info: tacrolimus ER products not interchangeable w/ other ER or IR products; do not substitute on a mg to mg basis	• Usual Dose: 0.14 mg/kg PO q am, adjust dose based on serum levels • Max Dose: Titrate to 12 hour trough of 6-11 ng/mL during month 1 and to 4-11 ng/mL after 1 month. Doses of 0.17mg/kg produced higher than recommended tacrolimus levels • Hepatic Dosing: moderate impairment: caution advised, monitor closely; Child-Pugh Score >10: decr. dose, amount not defined • Renal Dosing: renal impairment: give lowest recommended dose, may consider further dose decrease • Give on empty stomach; do not cut/crush/chew tab • **[pts converting from IR formulations]** Dose: individualize dose PO qam; Start: approx. 80% of total daily IR tacrolimus dose; Info: adjust dose based on serum levels; give on empty stomach; do not cut/crush/chew tab	• Adverse Effects: Serious Reactions-immunosuppression, malignancy, lymphoma, post-transplant lymphoproliferative disorder, infection, severe, CMV infection, PML, BK virus-assoc. nephropathy, Stevens-Johnson syndrome, toxic epidermal necrolysis, anaphylaxis, nephrotoxicity, neurotoxicity, posterior reversible encephalopathy syndrome, seizures, calcineurin inhibitor-induced pain syndrome, myocardial hypertrophy, pericardial effusion, QT prolongation, torsades de pointes, hyperkalemia, severe, HTN, severe, diabetes mellitus, myelosuppression, DIC, thrombocytopenic purpura, hemolytic anemia, pure red cell aplasia Common– tremor, diarrhea, headache, HTN, Cr incr., infection, nausea, vomiting, insomnia, pain, hypophosphatemia, constipation, asthenia, edema-peripheral, hypomagnesemia, fever, anemia, diabetes mellitus, paresthesia, LFTs elevated, hyperlipidemia, hyperkalemia, anorexia, dyspepsia, arthralgia, dyspnea, pruritus/rash, hypokalemia, dizziness, cough, leukopenia, photosensitivity, bronchitis • Drug Interactions: adenovirus vaccine-live, BCG live intravesical, cholera vaccine- live, cidofovir, influenza nasal vaccine- live, lefamulin, measles/mumps/ rubella vaccine- live, mifepristone, pimozide, ritonavir, rotavirus vaccine- live effects), saquinavir, smallpox vaccine (live vaccinia virus), talimogene laherparepvec, thioridazine, typhoid vaccine- live, varicella vaccine- live, yellow fever vaccine- live, ziprasidone, zoster vaccine, live	• Contraindications: hypersensitivity to tacrolimus or any component of the formulation, hypersensitivity to castor oil derivatives (IV form), liver transplant use (ER cap form), electrolyte abnormalities-uncorrected, congenital long QT syndrome • Caution if: QT prolongation, QT prolongation family history, torsades de pointes history, ventricular arrhythmias, bradycardia, recent MI, CHF, black patients, Hispanic patients, negative EBV serostatus, renal impairment, hepatic impairment Due to the large number of interactions* which can affect tacrolimus level or level of the interacting medication, it is imperative to **CHECK DDI CHECKER ANY TIME STARTING OR STOPPING MEDICATIONS** CCHCS DDI Checker. Follow levels after any medication change and ensure LLUTT is informed of the changes.
ACUTE REJECTION			

Lymphocyte immune globulin Anti-Thymocyte Immune Globulin (ATG) (Equine) (ATGAM®)
 	
50 mg/mL
 	
$$$$$
 	
Used in the treatment of high grade acute rejection and lower grade rejection refractory to high dose steroids and other treatments
	• Usual Dose: 10-15 mg/kg/day IV for 14 days in conjunction with concomitant immunosuppression, may continue with 7 additional doses on an every-other-day schedule if needed (up to a total of 21 doses)
	• Max Dose: 30 mg/kg/day IV
	• Hepatic/Renal Dosing: specific guidelines for dosage adjustments are not available. Appears no dosage adjustments are needed
		• Adverse Effects: chest pain, rash, pruritus, shivering, headache, diarrhea, N/V, thrombocytopenia, backache, abnormal renal function tests, fever, leukopenia, dyspnea, sepsis, arthralgia, joint stiffness, myalgia, hypertension, hypotension, agitation, dizziness, lethargy, diaphoresis, abdominal pain, hyperkalemia, hypokalemia, infection, hyperlipidemia
		• Drug Interactions: vaccines (live and inactivated), belatacept, tofacitinib, anticoagulants, NSAIDs, salicylates, baricitinib, cladribine, denosumab, trastuzumab, pimecrolimus, tacrolimus (topical)
			• **BLACK BOX WARNING:**
			  ◦ Anti-thymocyte globulins can cause anaphylaxis. Although Anti-Thymocyte Immune Globulin (equine) is processed to reduce the level of antibodies that will react to non-T cells, physicians should be prepared for the potential risk of anaphylaxis and monitor patients for signs and symptoms during infusion
			  ◦ Only physicians experienced in immunosuppressive therapy in the treatment of renal transplant patients should use lymphocyte immune globulin, anti-thymocyte globulin equine
			• Contraindications: systemic reaction (e.g., anaphylactic reaction) during prior administration of any equine gamma globulin preparations, or any component of the formulation; concurrent use with live vaccines
			• Caution with severe and unremitting leukopenia or thrombocytopenia—discontinue therapy
			• Skin testing potential recipients is strongly recommended before starting treatment to identify those at greatest risk of systemic anaphylaxis
			• During repeat courses, observe patients for signs of allergic reactions
			• Used with concomitant immunosuppressants
			• Indication: Treat allograft acute rejection

Bold = Formulary *See prescribing information for complete description of contraindications/precautions, adverse effects and drug interactions.

The cost scale $-$$$$$ represents the relative cost of acquisition of medication only. Frequency and complexity of medication administration (institution workload, effect on adherence) should be considered when determining overall cost-effectiveness of treatment.

SUMMARY | DECISION SUPPORT | PATIENT EDUCATION/SELF MANAGEMENT

MEDICATIONS

MEDICATION CLASS/ MEDICATION	DOSING	ADVERSE EFFECTS/ INTERACTIONS*	COMMENTS
ACUTE REJECTION			

Rituximab
 	
10 mg/mL
 	
$$$$$
	• Usual Dose: 375mg/m² IV infusion generally 50 mg/hr initially, then 100 mg/hr-but may depend on type of lymphoproliferative disorder (For IV infusion ONLY. Do not administer as an IV push or bolus). Timing of administration, dosing schedule and duration of treatment are still being determined. Defer to LLUTT or hematology oncology specialist.
	• Monitor patients closely during each infusion
	• Hepatic/Renal Dosing: specific guidelines for dosage adjustments are not available. Appears no dosage adjustments are needed
	• Studies to define the optimal treatment of acute humoral rejection are needed
		• Adverse Effects: peripheral edema, pruritus, diarrhea, nausea, anemia, lymphocytopenia, neutropenia, spasms, asthenia, headache, urinary tract infections, nasopharyngitis, respiratory tract infection, fever, shivering, Stevens-Johnson syndrome
		• Drug Interactions: live vaccines, cisplatin, etanercept, infliximab, abatacept, adalimumab, azathioprine, beclomethasone, betamethasone, cyclophosphamide, dexamethasone, methotrexate, hydroxychloroquine, prednisolone, triamcinolone, prednisone
			• **BLACK BOX WARNING:**
			  • Fatal infusion related reactions with 24 hours of infusion; ~80% of fatal reactions occurred with first infusion. Monitor patients and discontinue rituximab infusion for severe reactions
			  • Severe mucocutaneous reactions, some with fatal outcomes
			  • Hepatitis B virus reactivation, in some cases resulting in fulminant hepatitis, hepatic failure and death
			  • Progressive multifocal leukoencephalopathy (PML) resulting in death
			• Should only be administered by a health care professional with appropriate medical support to manage severe infusion-related reactions that can be fatal
			• Contraindications: hypersensitivity to murine proteins or any component of the formulation, severe active infection; concurrent use with live vaccines
			• Caution in the following: chronic or latent infection, HBV carrier, elderly, cardiovascular disease or history of, angina or history of, pulmonary disease, high tumor burden
			• Prior to initiating therapy, screen all patients for hepatitis B virus infection by measuring HBsAg and anti-HBc and obtain CBC including platelets

IMMUNE SYSTEM DISORDERS			

Intravenous immune globulin (IVIG) (Bivigam™ , Carimune® NF, Flebogamma® DIF, Gamastan®, Gammagard®, Gammagard® S/D, Gammaked™, Gammaplex®, Gamunex® C, Octagam®, Privigen®)
 	
Depending on product:
50 mg/mL,
100 mg/mL,
150-180 mg/mL,
5 gm, 10 gm,
6 gm, 12 gm
 	
Do not mix immune globulin products of different formulations or from different manufacturers
 	
$$$$$
	• Usual Dose: varies depending on indication
	• Max Dose: dependent on indication and patient response
	• Hepatic Dosing: specific guidelines for dosage adjustments are not available. Appears no dosage adjustments are needed
	• Renal Dosing: administer IV at the minimum dose and infusion rate possible in patients at risk of renal dysfunction. Recommended infusion rates may vary by product. Avoid sucrose-containing IVIG products if possible. Discontinue if renal function deteriorates during treatment
		• Adverse Effects: heart murmur, hypertension, hypotension, increased heart rate, increased systolic arterial pressure, peripheral edema, injection site reaction, pruritus, rash, swelling at injection site, urticaria, increased body temperature, nausea, diarrhea, upper abdominal pain, aphthous ulcers of the mouth, arthralgia, muscle weakness, myalgia, pain in limb, spasm, asthenia, dizziness, headache, lethargy, migraine, otalgia, asthma, cough, nasal congestion, pain in throat, pharyngitis, pharyngolaryngitis, sinusitis, wheezing, dehydration, fatigue, fever, pain, rigor, shivering, chest pain, backache, anaphylaxis
		• Drug Interactions: live vaccines, NSAIDS, salicylates, acyclovir, amikacin, aminoglycosides, amphotericin B, bacitracin, cyclosporine, gentamicin, tacrolimus. Tobramycin, valacyclovir, vancomycin, zoledronic acid
			• **BLACK BOX WARNING**
			  • Thrombosis may occur with or without known risk factors, including advanced age, prolonged immobilization, hypercoagulable conditions, history of venous or arterial thrombosis, estrogen use, indwelling central vascular catheters, hyperviscosity, and cardiovascular risk factors. For patients at risk of thrombosis, administer immune globulin at the minimum dose and infusion rate practicable. Ensure adequate hydration in patients before administration; monitor for signs and symptoms of thrombosis and assess blood viscosity in patients at risk for hyperviscosity
			  • Renal dysfunction, acute renal failure, osmotic nephrosis, and death may occur in predisposed patients who receive immune globulin IV (IVIG) products. Patients predisposed to renal dysfunction include those with any degree of preexisting renal insufficiency, diabetes mellitus, age greater than 65, volume depletion, sepsis, paraproteinemia, or patients receiving known nephrotoxic drugs. Higher rates of renal failure were associated with IVIG products that contain sucrose
			• Contraindications: anaphylaxis or severe systemic reaction to human immunoglobulins or to any component of the product, corn hypersensitivity, hereditary fructose intolerance, hyperprolinemia, IgA deficiency, maltose hypersensitivity
			• Caution in the following: cardiac disease, coronary artery disease, dehydration, elderly, breastfeeding, pregnancy, hypertension, hyper/hypovolemia, renal disease, history of migraines

Bold = Formulary *See prescribing information for complete description of contraindications/precautions, adverse effects and drug interactions.

The cost scale $-$$$$$ represents the relative cost of acquisition of medication only. Frequency and complexity of medication administration (institution workload, effect on adherence) should be considered when determining overall cost-effectiveness of treatment.

MEDICATIONS

MEDICATION CLASS/ MEDICATION	DOSING	ADVERSE EFFECTS/ INTERACTIONS*	COMMENTS
PERSISTENT HYPERPARATHYROIDISM			
Cinacalcet (Sensipar®) Tablet: **30 mg**, 60 mg, 90 mg $$$$$ Note: Off-Label use for hypercalcemia in renal transplant recipients with persistent hyperparathyroidism	• Initial Dose: 30 mg orally daily • Titration: titrate as necessary, 30 mg every 4 wks, based on intact parathyroid levels and corrected total serum calcium (60, 90, 120, and 180 mg/day) • Max Dose: 180 mg/day • Hepatic Dosing: Child-Pugh class B or C: serum calcium, serum phosphorus and parathyroid hormone concentrations should be closely monitored. Dose reduction may be necessary, however, specific dose adjustments not defined • Renal Dosing: no dosage adjustment necessary. See dose adjustments for hypocalcemia under comments • Give with food or shortly after a meal • Tablets should be swallowed whole; do not cut, chew, or crush • May be used alone or in combination with vitamin D and/or phosphate binders • See dose adjustments for hypocalcemia under comments to the right	• Adverse Effects: hypotension, hyper/ hypocalcemia, abdominal pain, constipation, diarrhea, loss of appetite, n/v, anemia, arthralgia, backache, myalgia, spasm, fracture of bone, dizziness, headache, cough, paresthesia, depression, URI, dyspnea, dehydration, fatigue, seizures, weakness • Drug Interactions: eliglustat, tramadol, codeine, fluoxetine, tamoxifen, donepezil, brexpiprazole, desipramine, ketoconazole, amitriptyline, amoxapine, imipramine, clomipramine, carvedilol, clarithromycin, nefazodone, nortriptyline, flecainide, erythromycin, propranolol, ritonavir, doxepin, tamsulosin, thioridazine	• Contraindications: hypocalcemia, concurrent use with eliglustat, hypersensitivity to cinacalcet or any component in the formulation • Caution in the following: hepatic impairment (Child-Pugh classes B and C), seizure disorder, long QT syndrome, history of QT interval prolongation, family history of long QT syndrome or sudden cardiac death, conditions that predispose to QT interval prolongation, pregnancy, breast-feeding, esophagitis, heart failure, peptic ulcer disease, severe vomiting Package Insert: https://www.pi.amgen.com/~/media/amgen/repositorysites/pi-amgen-com/sensipar/sensipar_pi_hcp_english.pdf • **Conversion from etelcalcetide ^:** Discontinue etelcalcetide for at least 4 weeks prior to initiating cinacalcet • **Dosage adjustment for hypocalcemia^:** • If iPTH <150 pg/mL: Reduce dose or discontinue cinacalcet and/or vitamin D • If serum calcium >7.5 mg/dL but <8.4 mg/dL **or** if hypocalcemia symptoms occur: Use calcium-containing phosphate binders and/or vitamin D to raise calcium levels • If serum calcium <7.5 mg/dL **or** if hypocalcemia symptoms persist and the dose of vitamin D cannot be increased: Withhold cinacalcet until serum calcium ≥8 mg/dL and/or symptoms of hypocalcemia resolve. Reinitiate cinacalcet at the next lowest dose ^ https://www.uptodate.com/contents/cinacalcet-drug-information?search=persistent%20hyperparathyroidism%20after%20renal%20transplant&topicRef=7299&source=see_link
HYPERKALEMIA			
Patiromer (Veltassa®) 8.4 gm, 16.8 gm, 25.2 gm powder for suspension $$-$$$	• Usual Dose: initial: 8.4 g orally once daily Dose titration: Adjust in increments of 8.4 g at 1-week or longer intervals to goal serum potassium levels • Max Dose: 25.2 g/day • Hepatic/Renal Dosing: specific guidelines for dosage adjustments are not available. Appears no dosage adjustments are needed	• Adverse Effects: hypomagnesemia, constipation, hypokalemia, diarrhea, nausea, abdominal discomfort, flatulence • Drug Interactions: metformin, levothyroxine, ciprofloxacin	• Contraindications: GI obstruction, severe constipation, fecal impaction, GI motility disorder, hypersensitivity to patiromer or any component of the formulation • Caution: hypomagnesemia may occur; monitoring recommended and magnesium supplementation may be required. GI motility may become worse and result in decreased efficacy
Sodium polystyrene sulfonate (SPS®, Kionex®) **15 gm/60 mL Suspension** **$-$$**	• Usual Dose: oral suspension: 15 g orally 1-4 times per day Rectal Suspension: 30-50 g rectally every 6 hrs • Max Dose: information not available. Individualize dosage based on serum potassium concentrations and other clinical parameters • Hepatic/Renal Dosing: specific guidelines for dosage adjustments are not available. Appears no dosage adjustments are needed	• Adverse Effects: constipation, nausea, vomiting, hypervolemia, hypocalcemia, hypokalemia, fecal impaction, GI hemorrhage, GI necrosis, GI obstruction, GI perforation, ischemic colitis • Drug Interactions: sorbitol, Aluminum, calcium or magnesium containing products, meloxicam, liothyronine, levothyroxine, lithium	• Contraindications: hypokalemia, GI obstruction, reduced GI motility, constipation, fecal impaction risk, hypersensitivity to polystyrene sulfonate or any component of the formulation • Caution in the following: GI disease or history of surgery, marked edema, severe CHF, severe hypertension, hypernatremia, sodium restriction, severe hyperkalemia, hypovolemia, renal impairment, aspiration risk, impaired gag reflex • Concomitant administration of sorbitol and sodium polystyrene sulfonate is not recommended due to risk for colonic necrosis. However, the manufacturer of sodium polystyrene sulfonate recommends that the resin is sometimes administered as an enema mixed with an aqueous vehicle such as sorbitol. Such usage requires subsequent administration of a non-sodium containing cleansing enema

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SUMMARY | DECISION SUPPORT | PATIENT EDUCATION/SELF MANAGEMENT

POST KIDNEY TRANSPLANT

Most patients feel better after a kidney transplant but you are more likely to face big health challenges as well.

MEDICATIONS AFTER TRANSPLANT

After a kidney transplant, you will need to take medications to help prevent your immune system from attacking (or rejecting) the donor kidney.

- These are called immunosuppressant (anti-rejection) medications.
- Usually they must be taken for the rest of your life.

There are other medications you will need to take to help the anti-rejection drugs do their job or control their side effects. You may also need to take other medications for different health conditions.

Your transplant hospital will give you detailed information on your specific medications. You will get a purple book from them to help you understand your medications and track when you take them.

WHAT ARE THE POTENTIAL SIDE EFFECTS OF THE MEDICATIONS?

After a transplant, you may experience medication side-effects such as:

- Hair growth or loss
- Acne
- Mood swings
- Round face
- Weight gain
- Diarrhea
- High blood pressure
- High cholesterol
- High blood sugars
- Infection
- Bone thinning
- Diabetes (See below)

If you notice any side effects, let your health care team know. They can adjust your medications to lower side effects without increasing your risk for kidney rejection.

New-Onset Diabetes After Transplant (NODAT) - Even if you did not have diabetes before, you may develop diabetes after transplant. This can occur as a side effect of the medications that you need to prevent rejection of your new kidney. Sometimes it gets better when it's time for your prednisone dose to be lowered.

WHAT SHOULD I DO AFTER A TRANSPLANT?

After a kidney transplant it is important that you:

- **Keep all doctor appointments and do all blood tests/lab tests**.
  - ⇒ You will have very frequent blood tests–sometimes twice a week–you must do every test.
  - ⇒ You will have frequent follow-up visits at the transplant hospital and will have to do lab test before each visit.
  - ⇒ This is very important to make sure you are not having any complications from surgery and your body is accepting the donor kidney.
- **Take all your prescribed medications exactly as the transplant doctor directed.**
- **Wear your mask everywhere you go for at least 4 weeks after surgery to avoid getting other people's germs.**
- **Tell your health care provider if you have any signs or symptoms of infection** such as:
  - ⇒ Fever, chills, body aches, swelling/itching/pain or drainage at transplant site, or pain when going to the bathroom

Control your blood pressure, blood sugar, and blood cholesterol by eating as well as you can, avoiding junk food, and exercise regularly! Usually only walking for the first 6 months.

POST KIDNEY TRANSPLANT (CONTINUED)

WHAT ARE IMMUNOSUPPRESSANTS AND REJECTION?

When you get a kidney transplant, your body knows that the new kidney is foreign (that is, not originally part of your body). Your body will attack the new kidney and try to reject it by damaging or destroying it. The immunosuppressant drugs keep your body from attacking the new kidney and damaging or destroying it. **Rejection can happen at any time, early or long after your transplant surgery.**

Immunosuppressants are medicines that lower the body's ability to reject a transplanted kidney. These are also called anti-rejection drugs.

The goal is to adjust these medications to prevent rejection and to minimize any side effects of the drugs.

Almost everyone who has a transplant must take these drugs every day as directed for the rest of their life to prevent rejection and losing the kidney.

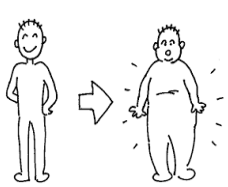
WHAT SHOULD I DO IF I MISS A DOSE?

Take it as soon as you remember and tell your health care team immediately. If it is time for the next dose, do not take a double dose.

ARE THERE ANY SIGNS OR SYMPTOMS I SHOULD WATCH FOR?

Yes. Even though you are taking your medicines every day, you may still develop rejection of the kidney transplant. You also can get bad infections. You need to know your body very well. If you have any of the following, you should notify your health care team right away:

- A fever above 100 degrees
- Flu-like feelings, chills, body aches, flu-like symptoms
- A cough or cold that will not go away, extreme fatigue, and/or nausea vomiting or diarrhea
- Tenderness of your new kidney
- Drainage from your surgical scar
- Decrease in how much urine you pass, bloody urine, or burning when you pass urine
- Weight gain (more than 3 pounds in two days) especially if making less urine or swelling



ARE THERE ANY SIDE EFFECTS FROM THESE DRUGS?

The most common side effects of these drugs is an increased chance of infections. This is more of a problem in the early time after transplant, or following treatment of a rejection because the dosage of these medicines is higher at these times.

Specific side effects for specific drugs include:

- **Tacrolimus**: tremors, hair loss, headaches and increased risk of developing diabetes
- **Cyclosporine**: hair growth (does not grow hair if you are already bald), gum enlargement, and tremors
- **Sirolimus**: rash, bone marrow problems (anemia, low white count and low platelets), swelling of ankles, frothy urine (because of protein leakage from urine)
- **Prednisone**: weight gain, water retention, diabetes, acne, bone thinning

If you are having stomach pains as a side effect of these medications, talk to your health care team about taking your medicine at a different time to help with this problem.

Wash your hands and avoid sick people!

Remind your doctor to check drug interactions whenever starting a new medicine!

Don't let anyone give you a vaccine that is live and don't use the nasal flu vaccine. Always get the recommended vaccines. Tell anyone who wants to give you a vaccine that you have a transplant and can only take "killed vaccines."

POST KIDNEY TRANSPLANT (CONTINUED)

DO I NEED TO EAT A SPECIAL DIET?

A healthy lifestyle is important for everyone. It is even more important after a kidney transplant. Poor lifestyle habits can increase the risk of organ rejection.

- **Eat a healthy diet:** Your diet will play a big role after a kidney transplant. A healthy, balanced diet will help prevent high blood sugar, excess weight gain and promote overall health.
  - ⇒ The CDCR Heart Healthy Diet, along with making healthy canteen choices will help you eat healthy. Make good choices by limiting junk food (high fat, high salt, and high sugar foods like chips and cookies). Eat fiber-rich foods like vegetables and beans and lentils to keep you full.
  - ⇒ Eat high protein* foods like lean meat, eggs, and beans.
    - * Kidney recipients need a **higher protein diet** right after transplant to help build up the muscle tissue that has been broken down by the large doses of steroids. Protein needs will be the same as a healthy individual after several months of transplant.
  - ⇒ You should plan to follow a diet low in salt.
  - ⇒ Make sure to drink plenty of water.
  - ⇒ There is no **potassium** restriction for kidney transplant patients as long as their transplant is working well. However, some transplant medicines can increase blood level of potassium, while other medicines may decrease it. If so, you may need to modify your diet.
  - ⇒ As kidney function gets lower, extra **phosphorus** can start building up in the blood. High phosphorus levels can cause bones to get weaker. Your dietician or health care provider can tell you if you need to limit foods that are high in phosphorus.
  - ⇒ Foods that are good sources of **calcium** are often high in phosphorus. Your dietitian or health care provider will tell you if you need to limit calcium.
  - ⇒ If you get **gout,** your health care provider will help you learn what not to eat.
  - ⇒ **If you have diabetes**, your transplant team and primary care provider will help you manage your blood sugar. High blood sugar is usually maintained by: a carbohydrate-controlled diet, exercise (as allowed by your doctor), and diabetes medications. It's important to treat diabetes because it can hurt your new kidney and also cause damage to your heart, blood vessels, eyes, feet, and nerves.

WHAT ARE SOME OF THE FOODS I NEED TO AVOID?

You may need to avoid certain foods. Your health care team will help you understand which foods you should avoid when you are back in the community and why.

Do not eat foods that are spoiled, moldy, or past the "use by" date, as well as the foods listed below.

- Raw or undercooked meat, poultry, fish, seafood
- Unpasteurized dairy products
- Uncooked or undercooked eggs or products that have them
- Grapefruit or grapefruit juice
- Pomegranate or pomegranate juice
- Unwashed raw fruits and damaged fruits
- Unwashed raw vegetables and unwashed salads
- Unpasteurized juices or ciders
- Sprouts (like alfalfa or bean sprouts)

DO I NEED TO EXERCISE?

- Start with low-impact activity such as walking for 10-20 minutes and gradually increase your workout intensity to jogging or weight bearing activities.
  - ⇒ Regular exercise will help you control your cholesterol levels, blood pressure, weight, and blood sugar.
  - ⇒ Work with your health care team to establish an exercise plan.

Follow all directions received from your Loma Linda University Transplant Team.

POST KIDNEY TRANSPLANT CONTINUED

TIPS FROM KIDNEY TRANSPLANT RECIPIENTS FOR POST-TRANSPLANT SUCCESS!

1. ***Learn about your medications and take ALL as prescribed***. Your health care team may adjust your medication or dosing until they find the right regimen for you. Keep a list of your medications with you in case of an emergency. Consider using pillboxes to help ensure you do not miss doses.

2. ***Attend ALL follow up appointments***. Often, follow-up appointments are weekly, then monthly, then at least yearly.

3. ***Complete ALL the lab tests requested done on time.*** Blood tests are very important to monitor your new kidney, detect rejection, and monitor drug levels. They allow your doctor to react quickly to treat any abnormal results. At first, there are many lab tests required, but in time they will be much less frequent.

4. ***Be honest with your health care team about any side effects you experience or concerns you have.*** If you are not feeling well or are experiencing side effects, explain your symptoms to your health care team as accurately as possible. Your health care team may need to adjust your medications.

5. ***Let ALL of your health care providers know about your transplant.*** This is especially important for your primary care team and any other medical professionals you see regularly. If you switch to new health care professionals in the future or need testing for other medical problems, be sure to let them know you are a kidney transplant recipient.

6. ***Ask questions!*** If you are wondering or worried – ASK! It might help to write out your questions before your appointment so you don't forget to ask your providers.

7. ***Be informed.*** Make sure you understand why tests or procedures are being done or why medication is being prescribed.

8. ***Seek support.*** If you have any concerns, talk with your health care practitioner and ask for a referral to a specialist who can help (e.g., a Social Worker can help if you are feeling anxious or depressed).

9. ***Live a healthy lifestyle. Make healthy food choices and exercise regularly.*** Control your blood pressure, blood sugars, and blood cholesterol**!** Having kidney disease puts you at high risk for heart disease (heart attacks or weak heart).

DAILY LIFE AFTER TRANSPLANT

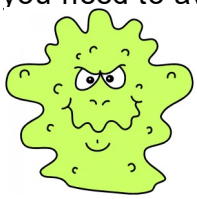
Do NOT smoke, drink any alcohol, or do any street drugs.

- Smoking damages the lungs and puts you at risk for lung infections. Smoking also hurts the circulation to the new kidney.
- Cancer is the leading cause of death after transplant surgery- smoking increases this risk.

Wear sunscreen at all times when outside to prevent sun burns and skin cancer.

- Skin cancer is more common in patients who have had a transplant.
- Limit exposure to the sun and protect yourself with proper clothing and sunscreen.

Prevent infections: Because of your suppressed immune system you need to avoid infections as much as possible.



- Wash your hands with soap and water many times per day.
- Brush your teeth 2 times per day and gently floss.
- Avoid people who are sick.
- Do not share cups or utensils.
- Keep cuts or scrapes clean/covered.
- Tell your health care team immediately if you are not feeling well or have a new rash or sore.

Vaccines: Your provider will be ordering vaccines for you like the flu shot every year, pneumonia vaccine every 1-5 years, HPV if you are young, Hepatitis B if your immunity drops, and tetanus every 10 years.

Vaccines to AVOID–transplant patients cannot get "live" vaccines. Do not accept any of these and ask if you have any questions:

- Influenza nasal (Flu Mist). The nasal mist is NOT Ok, ***the flu shot that is injected is an inactive vaccine and ok.***
- Chicken-pox (varicella)–NOT ok
- Shingles (Herpes Zoster)–NOT ok
- Measles, Mumps, Rubella (MMR)–NOT ok
- Yellow Fever–NOT ok

CANCER–After transplant you are at higher risk for many cancers due to the immunosuppressant medications. All patients will need regular skin and colon cancer testing. Men need a digital rectal exam and prostate blood test (Prostate Specific Antigen-PSA) and women need a pap smear, pelvic exam, and mammograms. Some patients will need lung or liver cancer testing if they have a history of smoking or liver disease. Your health care team will tell you what you need and when as it can be different for everyone (If they don't, ask!). It is very important to complete the tests your health care team recommends.

Complications after Transplant:

- Infections
- New kidney slow to work or stops working well
- Original disease may come back to the new kidney
- Gout (crystals build up and lodge in joints)
- High blood pressure–exercise and eat a healthy diet, work with your provider on medicines if needed
- High cholesterol–exercise and eat a healthy diet, work with your provider on medicines if needed
- Bleeding or low blood count that needs transfusion. If you have anemia, your doctor may prescribe an iron supplement or other medications
- Loss of the new kidney
- Urinary system problems that might need re-operation
- Weight gain–exercise and eat a healthy diet
- Cancers–get all the recommended tests and check your skin and lips every month
- New onset of diabetes–exercise and eat a healthy diet, work with your provider on medicines if needed
- Bone disease (weak bones)–your provider may order tests to check them. Work with your provider if medicines are needed.
- Heart attacks and strokes–exercise and eat a healthy diet, work with your provider on medicines if needed. You may need aspirin or blood thinners or other special medicines.

DESPUÉS DEL TRASPLANTE RENAL

La mayoría de los pacientes se siente bien después de un trasplante renal; pero, asimismo, pueden enfrentar grandes desafíos para la salud.

MEDICAMENTOS DESPUÉS DEL TRASPLANTE

Después del trasplante, deberá tomar medicamentos que eviten que su sistema inmunológico ataque (o rechace) el riñón donado.

- Estos medicamentos se denominan inmunosupresores o antirrechazo.
- Por lo general, deben tomarse por el resto de su vida.

Existen otros medicamentos que necesitará tomar para que los medicamentos antirrechazo surtan efecto o para controlar los efectos secundarios. Es posible que tenga que tomar otros medicamentos para diversas afecciones de salud.

El hospital donde se le realizó el trasplante le dará información detallada sobre esos medicamentos específicos. Le entregarán un libro violeta que lo ayudará a entender sus medicamentos y a llevar un registro de cuándo los toma.

¿CUÁLES SON LOS POSIBLES EFECTOS SECUNDARIOS?

Después de un trasplante, puede experimentar efectos secundarios de los medicamentos como:

- Crecimiento o pérdida de cabello
- Acné
- Cambios de ánimo
- Cara redonda
- Aumento de peso
- Diarrea
- Presión alta
- Colesterol alto
- Azúcar alta en sangre
- Infecciones
- Adelgazamiento de los huesos
- Diabetes (ver más adelante)

Si experimenta cualquier efecto secundario, infórmeselo a su elenco tratante médico. Ellos pueden pueden ajustar sus medicamentos para disminuir los efectos secundarios sin aumentar el riesgo de rechazo del riñón.

Diabetes de Novo Postrasplante (NODAT): aunque no haya sufrido anteriormente de diabetes, puede desarrollarla después del trasplante. Puede presentarse como un efecto secundario de los medicamentos que necesita para evitar el rechazo del nuevo riñón. En ocasiones, mejora cuando se baja la dosis de prednisona.

¿QUÉ DEBO HACER DESPUÉS DEL TRASPLANTE?

Después del trasplante, es importante que:

- **Vaya a todas las citas médicas y se haga todas las pruebas o exámenes de laboratorio.**
  - ⇒ Le harán pruebas sanguíneas con frecuencia, en ocasiones, dos veces a la semana. No debe omitir ninguna.
  - ⇒ Le harán consultas médicas frecuentes en el hospital que realizó el trasplante y pruebas de laboratorio antes de cada consulta.
  - ⇒ Es muy importante asegurarse de que no está presentando complicaciones resultantes de la cirugía y que su cuerpo está aceptando el riñón donado.
- **Tome todos los medicamentos prescritos exactamente según lo indica el médico que realizó el trasplante.**
- **Use su máscara en todo momento por al menos 4 semanas después de la cirugía para evitar el contagio de gérmenes.**
- **Le diga a su proveedor de atención médica si tiene indicios o síntomas de infección** como:
  - ⇒ Fiebre, escalofríos, dolores corporales, inflamación/picazón/dolor o supuración en el sitio del trasplante o dolor al ir al baño

¡Controle su presión arterial, azúcar en la sangre y el colesterol comiendo lo mejor que pueda, evitando la comida chatarra y ejercitándose con regularidad! Por lo general, los primeros 6 meses solo se ejercitará caminando.

DESPUÉS DEL TRASPLANTE RENAL (CONTINUACIÓN)

¿QUÉ SON LOS INMUNOSUPRESORES Y EL RECHAZO?

Cuando se le hace un trasplante de riñón, su cuerpo sabe que ese nuevo órgano es extraño (es decir, que no era parte de su cuerpo originalmente). Su cuerpo atacará al nuevo riñón y tratará de rechazarlo, dañándolo o destruyéndolo. Los medicamentos inmunosupresores evitan que su cuerpo ataque al nuevo riñón y que lo dañe o lo destruya. **El rechazo puede ocurrir en cualquier momento, inmediatamente o mucho después del trasplante.**

Los inmunosupresores son medicinas que disminuyen la capacidad del cuerpo de rechazar el órgano trasplantado. También se les llama medicamentos antirrechazo.

La meta es ajustar esos medicamentos para que eviten el rechazo y reducir cualquier efecto secundario de los medicamentos.

Casi todas las personas con un trasplante deben tomar estos medicamentos diariamente, según lo prescrito, por el resto de su vida para evitar el rechazo y la pérdida del riñón.

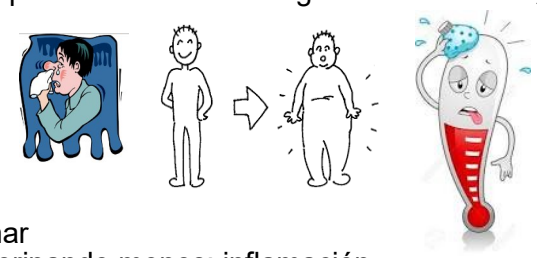
¿QUÉ DEBO HACER SI OLVIDO TOMAR UNA DOSIS?

Tómese el medicamento tan pronto lo recuerde y avise a su equipo médico de inmediato. Si ya es el momento de tomar otra dosis, no tome una dosis doble.

¿HAY INDICIOS O SÍNTOMAS A LOS QUE DEBERÍA PRESTAR ATENCIÓN?

Sí. Aunque tome sus medicamentos diariamente, aún puede desarrollar un rechazo del riñón trasplantado. También puede contraer infecciones graves. Debe conocer muy bien su cuerpo. Si presenta uno de los siguientes síntomas, debe avisarle a su elenco tratante médico inmediatamente:

- Fiebre sobre los 100 ºF
- Sensación de gripe, escalofríos, dolores corporales, síntomas de gripe
- Tos o resfriado que no se cura, fatiga excesiva o náuseas, vómitos o diarrea
- Sensibilidad en la zona del nuevo riñón
- Supuración de la cicatriz de la cirugía
- Disminución de la cantidad que orina, sangre en la orina o ardor al orinar
- Aumento de peso (más de 3 libras en dos días) especialmente si está orinando menos; inflamación



¿ESTOS MEDICAMENTOS OCASIONAN EFECTOS SECUNDARIOS?

El aumento del riesgo a contraer infecciones es el efecto secundario más común. Este es un problema sobre todo en los primeros momentos después del trasplante, o después del tratamiento de rechazo, ya que la dosis de los medicamentos es más alta en ese lapso de tiempo.

Los siguientes medicamentos incluyen los efectos secundarios especificados:

- **Tacrolimus:** temblores, pérdida del cabello, dolores de cabeza y riesgo aumentado de desarrollar diabetes
- **Ciclosporina:** crecimiento del cabello (no ocurre si ya es calvo), recrecimiento de las encías y temblores
- **Sirolimus:** sarpullido, problemas de la medula ósea (anemia, recuento bajo de glóbulos blancos y de plaquetas), inflamación de los tobillos, orina espumosa (a causa de la fuga de proteína por esta vía).
- **Prednisona:** aumento de peso, retención de líquidos, diabetes, acné, adelgazamiento de los huesos

Si tiene dolores estomacales como efecto secundario de los medicamentos, hable con su elenco tratante médico sobre tomarlos en momentos diferentes para paliar este problema.

¡Lávese las manos y no se acerque a personas enfermas!

¡Recuérdele a su médico de revisar las interacciones de medicamentos siempre que comience a tomar uno nuevo!

No permita que le apliquen una vacuna viva y no se aplique la vacuna nasal contra la influenza. Aplíquese siempre las vacunas recomendadas. Dígales a las personas que lo vayan a vacunar que es un paciente trasplantado y que solo puede recibir “vacunas muertas”.

DESPUÉS DEL TRASPLANTE RENAL (CONTINUACIÓN)

¿NECESITO UNA DIETA ESPECIAL?

Para todos es importante llevar un estilo de vida saludable y esto es aún más importante después de un trasplante de riñón. Los malos hábitos pueden aumentar el riesgo de rechazo de un órgano.

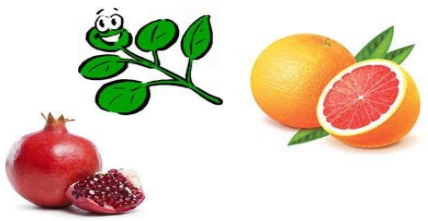
- **Siga una dieta saludable:** su dieta jugará un rol esencial después de un trasplante de riñón. Una dieta sana y equilibrada lo ayudará a evitar altos niveles de azúcar en la sangre, aumento excesivo de peso y favorecerá su salud en general.
  - ⇒ La Dieta para la Salud Cardíaca del Departamento de Correcciones y Rehabilitación de California (CDCR), así como las elecciones saludables en la cantina lo ayudarán a comer de manera saludable.
  - ⇒ Tome decisiones saludables limitando la comida chatarra (alimentos altos en grasa, en sal y azúcar, como las papas fritas y galletas). Coma alimentos ricos en fibra como vegetales, granos y lentejas para sentir saciedad.
  - ⇒ Coma alimentos altos en proteína* como carnes magras, huevos, nueces sin sal, atún y granos.
    - * Los receptores de un riñón necesitan una dieta más rica en proteínas justo después del trasplante para contribuir a la generación del tejido muscular que se ha perdido por las grandes dosis de esteroides. Las necesidades proteicas serán las mismas que las de una persona sana después de varios meses posteriores al trasplante.
  - ⇒ Debe planificar seguir una dieta baja en sal.
  - ⇒ Asegúrese de beber mucha agua.
  - ⇒ No hay restricciones de **potasio** para pacientes trasplantados siempre que el trasplante funcione bien. Sin embargo, algunas medicinas para el trasplante pueden elevar los niveles de potasio en la sangre, mientras que otras pueden disminuirlo. Si así ocurre, es posible que tenga que modificar su dieta.
  - ⇒ Puesto que la función del riñón se vuelve más lenta, posiblemente se produzca una acumulación de **fósforo** en la sangre. Los niveles altos de fósforo pueden debilitar los huesos. Su dietista o médico pueden indicarle si debe restringir los alimentos ricos en fósforo.
  - ⇒ Los alimentos que son buena fuente de **calcio** con frecuencia lo son también en fósforo. Su dietista o médico puede indicarle si debe restringir los alimentos ricos en calcio.
  - ⇒ Si le da **gota**, su médico le indicará lo que no debe comer.
  - ⇒ **Si padece diabetes,** su equipo del trasplante y médico de atención primaria lo ayudarán a controlar su nivel de azúcar en la sangre. Esto normalmente se logra con una dieta baja en carbohidratos, ejercicio (según lo indique el médico) y medicamentos para la diabetes. Es importante controlar la diabetes, ya que esta puede dañar su nuevo riñón, así como su corazón, vasos sanguíneos, ojos, pies y nervios.

¿QUÉ ALIMENTOS TENGO QUE EVITAR?

Es posible que deba evitar ciertos alimentos. Su elenco tratante médico lo ayudará a entender cuáles debe evitar cuando vuelva a su comunidad y por qué.

No coma alimentos dañados, mohosos o con fecha vencida, así como los alimentos mencionados a continuación:

- Carne, pollo, pescado o mariscos crudos o poco cocidos
- Productos lácteos no pasteurizados
- Huevos crudos o poco cocidos o productos que los contengan
- Toronja o su jugo
- Granada o su jugo
- Frutas crudas sin lavar y frutas estropeadas
- Vegetales crudos sin lavar y ensaladas de vegetales no lavados
- Jugos o sidras no pasteurizados
- Brotes (como alfalfa o germinados)



¿NECESITO HACER EJERCICIO?

- Empiece con actividades de bajo impacto, como caminatas de 10 a 20 minutos, y aumente gradualmente la intensidad de entrenamiento hasta hacer trote o actividades en las que deba levantar peso.
  - ⇒ El ejercicio regular lo ayudará a controlar sus niveles de colesterol, presión arterial, peso y azúcar en la sangre.
  - ⇒ Trabaje con su elenco trantante médico para establecer un plan de ejercicios.

Siga todas las indicaciones del Equipo de Trasplante de la Universidad de Loma Linda.

DESPUÉS DEL TRASPLANTE RENAL (CONTINUACIÓN)

¡CONSEJOS DE RECEPTORES DE TRASPLANTE PARA TENER ÉXITO EN EL SUYO!

1. ***Aprenda sobre sus medicamentos y tómelos TODOS según la prescripción.*** Su elenco tratante médico puede ajustar sus medicamentos o dosis hasta que encuentren el mejor régimen para usted. Lleve consigo una lista de medicamentos con usted en caso de emergencia. Considere el uso de pastilleros para asegurarse de tomar todas las dosis.

2. ***Asista a TODAS las consultas de seguimiento.*** Con frecuencia, las consultas de seguimiento son semanales, luego mensuales y luego al menos una vez al año.

3. ***Realícese a tiempo TODAS las pruebas de laboratorio solicitadas.*** Las pruebas sanguíneas son muy importantes para supervisar su nuevo riñón, detectar el rechazo y revisar los niveles de los medicamentos. Las pruebas permiten a su médico abordar rápidamente cualquier resultado anormal. Al principio, se necesitan muchas pruebas, pero con el tiempo serán mucho menos frecuentes.

4. ***Sea honesto con su elenco tratante médico sobre los efectos secundarios o las preocupaciones que tenga.*** Si no se siente bien o experimenta efectos secundarios, explique sus síntomas a su equipo médico tan exactamente como sea posible. Es posible que tengan que hacer modificaciones a sus medicamentos.

5. ***TODOS sus proveedores de atención médica deben saber que fue trasplantado.*** Esto es de gran importancia para su elenco tratante de atención médica primaria y otros médicos a los que vea regularmente. Si cambia de médicos en el futuro o necesita consultar otros problemas médicos, asegúrese de que sepan que usted es un paciente trasplantado de riñón.

6. ***¡Pregunte!*** Si quiere saber algo o algo lo preocupa ¡PREGUNTE! Escribir sus preguntas antes de su cita médica tal vez lo ayude para no olvidar preguntar lo que necesita.

7. ***Infórmese.*** Asegúrese de que entiende por qué se hacen ciertas pruebas o procedimientos o por qué se le prescribe un medicamento.

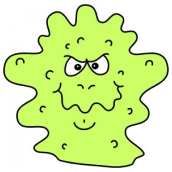
8. ***Busque apoyo.*** Si se siente preocupado, hable con su profesional de la salud y pida una referencia a un especialista que lo ayude (por ejemplo, un trabajador social puede ayudarlo si se siente ansioso o deprimido).

9. ***Lleve un estilo de vida saludable. Elija alimentos sanos y ejercítese regularmente.*** ¡Controle su presión arterial, el azúcar y el colesterol en la sangre! Las enfermedades renales lo hacen propenso a padecer enfermedades del corazón (como ataques cardíacos o debilidad cardíaca).

VIDA DIARIA DESPUÉS DEL TRASPLANTE

NO fume, ni beba alcohol ni consuma ninguna droga ilícita.
- Fumar daña los pulmones y puede causarle infecciones pulmonares. Asimismo, daña la circulación hacia el nuevo riñón.
- El cáncer es la primera causa de muerte después de la cirugia trasplante y fumar aumenta el riesgo de padecerlo.

Use protector solar cada vez que esté al aire libre para evitar quemaduras de sol y cáncer de piel.
- El cáncer de la piel es más común en pacientes trasplantados.
- Limite su exposición al sol y protéjase con la ropa apropiada y protector solar.



Para evitar infecciones: como resultado de su sistema inmunológico suprimido, debe evitar las infecciones tanto como sea posible.
- Lávese las manos con agua y jabón varias veces al día
- Cepíllese los dientes 2 veces al día y use hilo dental con cuidado
- Evite el contacto con personas enfermas
- No comparta vasos ni cubiertos
- Mantenga las heridas y rasguños limpios y cubiertos
- Si no se siente bien o tiene un nuevo sarpullido o úlcera, informe inmediatamente a su elenco tratante médico

Vacunas: su médico le prescribirá vacunas anuales como la de la gripe, la de la neumonía cada 1 a 5 años, la del VPH si es joven, la de hepatitis B si su inmunidad decae y el tétanos cada 10 años.

Vacunas que debe evitar: los pacientes trasplantados no pueden recibir vacunas "vivas". No acepte ninguna de las siguientes vacunas y pregunte si tiene dudas:
- Vacuna nasal contra la influenza (Flu Mist). NO debe recibir la vacuna nasal. **La vacuna que es inyectada sí es una vacuna inactiva y puede recibirla.**
- Vacuna de la varicela: NO la acepte
- Vacuna del herpes zóster: NO la acepte
- Vacuna del sarampión, rubéola y paperas (SRP): NO la acepte
- Vacuna de la fiebre amarilla: NO la acepte

CÁNCER: después del trasplante, tiene un riesgo mayor de sufrir cáncer debido a los medicamentos inmunosupresores. Todos los pacientes deben hacerse una prueba de cáncer de piel y de colon. Los hombres necesitan un examen rectal digital y el examen sanguíneo de la próstata (el antígeno prostático específico, PSA), y las mujeres la citología cervical, examen pélvico y mamografías. Algunos pacientes deberán realizarse pruebas de cáncer de pulmón o hígado si tienen antecedentes de tabaquismo o de enfermedades del hígado. Su equipo médico le dirá lo que necesita, ya que cada persona es diferente (si ellos no le dicen, ¡pregúnteles!) Es muy importante que se haga las pruebas que su elenco tratante médico le recomiende.

Complicaciones después del trasplante:

- Infecciones
- El nuevo riñón trabaja lentamente o deja de hacerlo
- La enfermedad original afecta al nuevo riñón.
- Gota (cristales que se acumulan y alojan en las articulaciones)
- Presión arterial alta: ejercítese y lleve una dieta sana, consulte con su médico sobre los medicamentos si es necesario
- Colesterol alto: ejercítese y lleve una dieta sana, consulte con su médico sobre los medicamentos si es necesario.
- Sangrado o recuento bajo sanguíneo que amerita transfusión. Si tiene anemia, el médico puede recetarle un suplemento de hierro u otros medicamentos
- Pérdida del nuevo riñón
- Problemas del sistema urinario que pueden necesitar una nueva operación.
- Aumento de peso: haga ejercicio y siga una dieta sana
- Cáncer: hágase todas las pruebas recomendadas y revise su piel y labios mensualmente
- Diabetes de aparición reciente: ejercítese y lleve una dieta sana, consulte con su médico sobre los medicamentos si es necesario
- Enfermedades de los huesos (huesos frágiles): es posible que su médico le pida hacerse pruebas para controlarlos. Consulte con su médico si necesita tomar medicinas
- Ataques cardiacos y accidentes cerebrovasculares: ejercítese y lleve una dieta sana, consulte con su médico sobre los medicamentos si es necesario. Puede necesitar aspirina o anticoagulantes u otros medicamentos especiales