- If a patient makes it past the first year without rejection, they are markedly less likely to ever experience rejection.
- Importance of immunomodulating medications:
  - Cardiac transplant recipients are typically not HLA matched.
  - As a result, missing even a dose or two can have a significant impact on rejection.
  - If a patient has missed medications for any reason, discuss the use of short-course, high-dose steroids with the transplant team.

Pediatric Transplant Patients

Ilene Claudius, Tim Ruttan, and Brittany DeFabio

- Approach to fever in a child with a history of transplant:
  - Fever can be an indicator of infection or rejection.
  - If septic, treat like you would anyone else.
  - If not septic, think about the timeline after the transplant:
    - <1 month: surgical, nosocomial, or donor-derived infection?
    - 1-6 months: the patient is still very immunocompromised and at risk for opportunistic infection (eg, PJP, histoplasmosis, coccidiomycosis) and will need more specialized testing as an inpatient.
    - >6 months: immunosuppression will be tapered and the patient will start to be at risk for infections like everyone else.
- Be aware that kids on immunosuppressant medications may not mount a leukocytosis or even manifest an elevated C-reactive protein, which could be falsely reassuring, so sending cultures and giving antibiotics would still be advised.
- Specific types of solid organ transplants and considerations:
  - Renal
    - Patients can have recurrence of their primary disease that caused them to get the transplant in the first place, so it is important to screen for renal failure.
    - Small changes in creatinine can be very significant in these kids, so take a careful look back at their historical values; even if it's a minor increase, talk to the transplant team.
    - Urinary tract infections are common (with equal incidence among males and females) and they will require treatment; if they have pyelonephritis, they get IV antibiotics and are admitted.

- Recommendation in terms of urgent treatment: IV fluids are fine to give but hold steroids until you talk to the transplant team.
- Be aware of nephrotoxicity concerns, particularly with medication interactions with all of their immunosuppressants. Lots of seemingly benign drugs can interact with those medications, so check with a pharmacist or the transplant team.

- Cardiac (these patients are a little scarier)
  - The clinical picture of rejection can include hemodynamic instability.
  - The transplanted heart is denervated so they will not have chest pain, even if they have ongoing ischemia.
  - Fluid boluses should be small; start with 10 mL/kg and reassess.
  - Can use epinephrine (preferred over norepinephrine).
  - Atropine won't work due to the denervation.
  - Induction agents that have myocardial depressant properties may have an amplified effect, so beware.
  - Adenosine was once contraindicated but recent studies say that it's ok to use at 25% of the dose for supraventricular tachycardia.
  - Will need a rapid formal echocardiogram. If not accessible, consider point-of-care ultrasound.
  - If you do not have access to the transplant team or there will be delays, consider giving high-dose steroids at a dose of 30 mg/kg methylprednisolone (up to 1 g maximum).
  - Compare their current ECG to the old ECG. Even subtle changes could be meaningful. These patients can develop a coronary vasculopathy as part of a chronic rejection pattern and it will manifest as global ischemia.
- Medications
  - These patients are usually on a triple therapy combination
    - Calcineurin inhibitor: Tacrolimus or cyclosporine
      - These are very nephrotoxic drugs, so watch for renal failure, and do not give nonsteroidal anti-inflammatory drugs. Patients can have a hypertensive emergency and are at risk for posterior reversible encephalopathy syndrome (PRES) and will need magnetic resonance imaging if altered.
    - Anti-metabolite: Mycophenolate or azathioprine
      - GI side effects, cytopenias
    - Steroids

- Stem cell/bone marrow transplant patients
  - Timeline considerations are similar.
  - Up until about 100 days, they still have T cells that are not fully functional, so patients are at risk for viral infections.
  - They can get hemorrhagic cystitis, which can progress to renal failure. Start fluids and obtain a renal ultrasound.
  - Otherwise, treat these patients the same as solid-organ transplant patients.
- Graft vs host disease
  - Acute graft vs host disease:
    - Maculopapular rash (painful or pruritic) that can involve palms and soles and can progress to erythroderma +/- bullous formation; looks like Stevens-Johnson syndrome
    - GI symptoms: nausea, vomiting, diarrhea and total bilirubin elevation can also occur
  - Chronic graft vs host disease
    - Chronic graft vs host disease looks like a chronic autoimmune process with sclerotic, lichenoid lesions, dry eyes, and conjunctival inflammation.
    - GI symptoms are common but patients can also get esophageal webs/strictures and mucositis/oral ulcers.
    - Bronchiolitis obliterans is hard to treat and can present with shortness of breath, cough, and wheezing.
- Post-transplant lymphoproliferative disease (PTLD)
  - PTLD is a broad term to describe the neoplastic changes seen after transplant.
  - Most cases are due to EBV infection.
  - Patients are most at risk in the first year after transplant.
  - In patients with fever/malaise-type symptoms, think about getting an EBV titer and speak with the team for outpatient follow-up.

References:

CorePendium: Children with Special Needs

CorePendium: Renal Transplant Related Emergencies