



# Interactive Case: Immunology in Solid Organ Transplantation

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## LEARNING OBJECTIVES

1. Evaluate the differences in vaccine considerations as they apply to candidates for and recipients of solid organ transplantation (SOT).
2. Develop a schedule for catch-up vaccinations for patients with a SOT.
3. Design an appropriate strategy for providing vaccinations to parents and siblings of a SOT recipient.
4. Devise a pharmacotherapeutic plan for SOT recipients based on the individual patient's endogenous and passively transferred antibody status.
5. Develop a plan for managing immunoglobulins and preventing adverse effects using different immunoglobulin preparations.

## ABBREVIATIONS IN THIS CHAPTER

AMR	Antibody-mediated rejection
CMV	Cytomegalovirus
DSA	Donor-specific antibody
DTaP	Diphtheria, tetanus, and acellular pertussis vaccine
Hib	<i>Haemophilus influenzae</i> type b
IDSA	Infectious Diseases Society of America
IIV	Inactivated influenza vaccine
IVIG	Intravenous immunoglobulin
LAIV	Live, attenuated influenza vaccine
MMR	Measles, mumps, and rubella
PCV	Pneumococcal conjugate vaccine (7-valent, 13-valent)
PPSV23	23-valent pneumococcal polysaccharide vaccine
PRA	Panel of reactive antibody
RSV	Respiratory syncytial virus
SCIG	Subcutaneous immunoglobulin
SOT	Solid organ transplantation
VarIZIG	Varicella zoster immunoglobulin

[\*Table of other common abbreviations.\*](#)

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## INTERACTIVE CASE

- [Click here to begin this PedSAP activity.](#)

## BASELINE KNOWLEDGE STATEMENTS

Readers of this chapter are presumed to be familiar with the following:

- Interpreting basic laboratory tests
- Assessing appropriateness of vaccines for healthy children
- Understanding the pathophysiology of vaccine-preventable diseases
- Recognizing the mechanism of action and common adverse reactions with solid organ transplant maintenance immunosuppressive agents

## ADDITIONAL READINGS

The following free resources have additional background information on this topic:

- CDC. [Vaccines & Immunization Topics.](#)
- Advisory Committee for Immunization Practices. [Vaccine Recommendations.](#)
- Infectious Diseases Society of America. [2013 Clinical Practice Guideline for Vaccination of the Immunocompromised Host.](#)
- American Society of Transplantation. [2013 Infectious Disease Guidelines, 3rd ed.](#)

[\*Table of common pediatric laboratory reference values.\*](#)

# Self-Assessment Questions

- The day after Christmas, a 9-month-old, former 35-week premature boy receives a heart transplant for a complex congenital heart defect with heart failure. Four weeks later, he is ready for discharge home. He was hospitalized for 3 months while awaiting a transplant and had several infections, including *Staphylococcus aureus* bacteremia and a parainfluenza respiratory viral infection, during that period. He is up-to-date with his 6-month immunizations. The patient will receive the inactivated influenza vaccine (IIV) before leaving, but his mother is concerned about respiratory syncytial virus (RSV) because the patient's 4-year-old sister attends day care. Which one of the following is best to recommend regarding palivizumab administration for this child?

  - Do not administer; standard precautions should be sufficient because he is not a less than 29-week premature infant and no longer has congenital heart disease.
  - Administer; he recently had a heart transplant, and it is RSV season.
  - Administer; he should have received palivizumab while hospitalized in November and December as well as continuing treatment as an outpatient.
  - Do not administer; he should receive the RSV vaccine.
- A 14-year-old girl is admitted for a kidney transplant from a deceased donor. The patient has end-stage renal disease caused by renal dysplasia and has received hemodialysis three times a week for the past 2 years with a baseline SCr of about 5.5 mg/dL. Her last panel of reactive antibody (PRA) measurement 1 month ago was class I 25% and class II 46%. She received induction therapy with methylprednisolone and antithymocyte globulin and cefazolin for surgical antibiotic prophylaxis. Immediately after the transplant and during the first 24 hours post-transplantation, her SCr measurements were 5.5 mg/dL, 4.3 mg/dL, and 3.5 mg/dL; however, the last two measurements were 4.6 mg/dL and 6.7 mg/dL. The surgeons inform you that they are concerned about atypical hemolytic uremic syndrome/thrombotic microangiopathy or hyperacute rejection. The patient receives intravenous immunoglobulin (IVIG) 1 g/kg and rituximab 375 mg/m<sup>2</sup>, and the team suggests blocking the membrane attack complex with eculizumab. The patient receives her dose before you arrive at the hospital in the morning. As soon as you arrive at the hospital, which one of the following actions is best to take for this patient?

  - Review her vaccination record for meningococcal vaccine against serotypes ACWY and B; initiate penicillin VK orally for prophylaxis of *N. meningitidis*.
  - Administer the measles, mumps, and rubella (MMR) and varicella vaccines regardless of immune status.
  - Initiate levofloxacin prophylaxis for all bacterial infections because she has received significant immunosuppression.
  - Review her vaccination record for meningococcal vaccine ACWY; initiate levofloxacin for prophylaxis of *N. meningitidis*.
- You are seeing a 12-month-old girl for a follow-up biopsy in November 1.5 months after an orthotopic heart transplant. Because influenza season began early, everyone in the waiting room is wearing a mask. The patient is at the office with her mother, 4-year-old sister, and 8-year-old brother. The patient was given a diagnosis of viral myocarditis at 7 months of age and, within 3 weeks of hospital admission, was listed as status 1a for a heart transplant. For her maintenance immunosuppression, she receives tacrolimus (goal 10–12), mycophenolate (600 mg/m<sup>2</sup> every 12 hours), and prednisolone (0.5 mg/kg/dose every 12 hours). Before transplantation, she received her 6-month vaccinations. Which one of the following plans is best to recommend for catch-up vaccinations for this patient?

  - She should receive all of her 12-month vaccinations including MMR, varicella vaccine, and influenza vaccine because she has school-aged siblings who may expose her to these infections.
  - She should only receive inactivated influenza vaccine (IIV) because it is flu season and she is greater than 1 month post-transplantation.
  - She should only receive her inactivated vaccines such as *Haemophilus influenzae* type B (Hib) and pneumococcal conjugate vaccine 13-valent (PCV13) because live vaccines are not indicated post-transplantation.
  - She should wait until 6 months post-transplantation and then receive her entire 12-month vaccinations including MMR and varicella vaccine.
- A 4-year-old girl, a new patient in your liver transplant follow-up clinic, received a deceased donor liver transplant 1.5 years ago for biliary atresia with a failed Kasai procedure. Her immunosuppressive regimen consists of tacrolimus 1.5 mg twice daily with a goal concentration of 6–8 ng/dL and mycophenolate mofetil 200 mg/m<sup>2</sup>/dose twice daily. About 3 months ago, she received a 3-day steroid burst for acute cellular rejection. Her family recently transferred her from a children's hospital in Atlanta, and her vaccine records are en route. The patient's mother states that she is hesitant for her daughter to receive too many vaccines at once. She also says

that her daughter once “got the flu from a shot” so never again received the influenza vaccine. However, because the girl’s healthy cousin was just hospitalized with influenza, the mother is now interested in the vaccine. Which one of the following counseling points is best to provide this patient’s mother?

- A. The girl should not receive any vaccines because she recently had an episode of rejection, which might cause her to have another episode.
  - B. The girl should receive LAIV (live, attenuated influenza vaccine) because it is the only influenza vaccine available in the clinic today.
  - C. The girl should receive IIV; her mother does not need to receive her vaccine because her daughter will have full immunity.
  - D. The girl should receive IIV and another vaccine in 1 month to complete her first series of influenza vaccine.
5. A 7-year-old girl presents 3 years after a deceased donor kidney transplant for end-stage renal disease related to nephrotic syndrome. She is at the clinic for her yearly visit and is in good health with no acute issues. Before transplantation, the patient took steroids since diagnosis at 2 years of age. She has done relatively well but has had some episodes of acute cellular rejection, requiring short 3-day courses of pulse intravenous methylprednisolone in the past 3 years with brief escalations in maintenance therapy. She has not received many of her vaccinations because she was taking steroids before the transplant. She has received enough maintenance immunosuppression that her physician has not wanted her to receive vaccinations. She has not received any vaccinations since her 1-year-old shots. By looking at her serologies before transplantation, you conclude that she is protected against MMR and hepatitis B but is not immune to varicella. One week ago, the patient was visited by an out-of-state cousin who now has chickenpox. According to the CDC’s recommendations for using varicella zoster immunoglobulin (VariZIG), which one of the following strategies is best to recommend for this patient?
- A. Admit her to the hospital for acyclovir intravenously 10 mg/kg/dose every 8 hours for a total of 7 days.
  - B. Administer acyclovir orally at home together with a varicella vaccine to try to confer immunity before infection.
  - C. Administer VariZIG because she does not have immunity, as evidenced by her serology, and it is less than 10 days from exposure.
  - D. Do not administer VariZIG because the exposure was more than 96 hours ago. She is many years out from transplantation and is therefore at less risk of developing infection from exposure.

6. A 5-year-old girl has a medical history of a deceased donor renal transplant about 2 years ago for end-stage renal disease caused by a small left solitary kidney at birth. The patient also has a history of vesicoureteral reflux and hypertension related to transplantation. One month ago, she received methylprednisolone 10 mg/kg/day intravenously for 3 days for mild acute cellular rejection. Two days ago, she presented to the inpatient acute care unit for a renal biopsy as a workup for recurrent rejection, given her recent increase in SCr. The final biopsy today reveals acute cellular rejection without acute antibody-mediated rejection (AMR) (negative C4d staining). The Luminex assay reveals no evidence of donor-specific antibodies. Her maintenance drugs include amlodipine 2.5 mg by mouth daily; sulfamethoxazole/trimethoprim 400 mg/80 mg by mouth daily; prednisolone 3 mg by mouth every Monday, Wednesday, Friday, and Saturday; mycophenolate mofetil 300 mg by mouth twice daily; and tacrolimus 2 mg by mouth twice daily. According to the KDIGO guidelines, which one of the following regimens would best treat this patient’s acute cellular rejection episode?
- A. Rituximab.
  - B. Intravenous rabbit antithymocyte globulin.
  - C. Subcutaneous immunoglobulin (SCIG).
  - D. Plasmapheresis plus intravenous immunoglobulin (IVIg).
7. A 12-year-old African-American girl presents in the kidney transplant clinic. She received a living unrelated donor kidney transplant 1 year ago because of end-stage renal disease secondary to focal segmental glomerulosclerosis. At transplantation, she received induction with intravenous basiliximab and has had no rejection episodes since transplantation. Her drugs include tacrolimus 3 mg by mouth twice daily, prednisone 5 mg by mouth daily, pantoprazole 40 mg by mouth daily, amlodipine 10 mg by mouth daily, atenolol 25 mg by mouth daily, and isradipine 2.5 mg by mouth every 6 hours as needed for blood pressure greater than 140/90 mm Hg. The patient has a new 2-month-old brother who is healthy. According to their mother, the patient’s brother is due for the following vaccines: inactivated poliovirus vaccine (IPV), PCV13, Hib, rotavirus, and diphtheria, tetanus, and acellular pertussis (DTaP). The mother asks you which of these vaccines can safely be administered. According to the 2013 IDSA clinical practice guideline for vaccination of the immunocompromised host, which one of the following vaccines is best to recommend for this patient’s brother?
- A. The IPV, PCV13, Hib, and DTaP vaccines but not the rotavirus vaccine.
  - B. The PCV13, Hib, rotavirus, and DTaP vaccines but not the IPV vaccine.

- C. The IPV, PCV13, Hib, and DTaP vaccines but not the rotavirus and IPV vaccines.
- D. The IPV, PCV13, Hib, DTaP, and rotavirus vaccines, but the patient should avoid handling her brother's diapers for 1 month after vaccinations.
8. Three months ago, a 16-year-old white girl received a bilateral lung transplant for end-stage lung disease secondary to cystic fibrosis. Her medical history also includes gastroesophageal reflux disease, pancreatic insufficiency, and chronic kidney disease caused by a significant history of aminoglycoside therapy. The patient's postoperative course was complicated by *Aspergillus flavus* and *Pseudomonas aeruginosa* pneumonia. Five days ago, she was readmitted to the hospital medical ICU for acute-on-chronic respiratory failure requiring endotracheal intubation and mechanical ventilation. She had alveolar infiltrates suggestive of rejection. A transbronchial lung biopsy yesterday revealed acute AMR (acute lung injury with neutrophil infiltration of the alveolar septae with capillaritis and C4d deposition in the alveolar capillaries). Furthermore, the Luminex assay revealed strong de novo donor-specific antibodies to HLA-B44 and DR53 (mean fluorescence intensity of 5649 and 7034, respectively). The patient's immunosuppressive regimen includes tacrolimus 1.5 mg by mouth twice daily, mycophenolate sodium 720 mg by mouth twice daily, and prednisone 15 mg by mouth once daily. The team decides to treat the acute AMR episode with five plasmapheresis sessions followed by immunoglobulin 100 mg/kg/dose after the first four sessions and 1 g/kg/dose after the final plasmapheresis session. Depending on her response, the patient may also receive rituximab. When considering the immunoglobulin preparation to select for therapy, which one of the following stabilizing agents used in immunoglobulin preparations is best to avoid in this patient?
- Maltose.
  - Sucrose.
  - Glucose.
  - Proline.
9. A 12-year-old Hispanic girl with chronic liver disease secondary to autoimmune hepatitis (AIH) is hospitalized for an AIH flare caused by medication nonadherence. The patient and her grandmother, her primary caregiver, are being seen for a pre-liver transplant pharmacotherapy consultation. The patient has no other significant medical or surgical history. She takes prednisone, azathioprine, and phytonadione. Her vaccine records, reviewed as part of her liver transplant evaluation, show the following:
- Three doses of hepatitis B vaccine, with a recent hepatitis B surface antibody of 100 mIU/mL
  - One dose of Tdap (tetanus, diphtheria, and acellular pertussis) vaccine at 11 years of age
  - One dose of PCV13 at 10 years of age
  - Three doses of Hib vaccine before 6 months of age
  - Four doses of inactive polio vaccine
  - One dose of meningococcal conjugate (MCV4) vaccine
  - Two doses of MMR vaccine
  - Two doses of varicella vaccine
  - One dose of influenza vaccine during the most recent influenza season
  - Three doses of human papillomavirus 4 vaccine
- According to the 2015–2016 CDC immunization schedule guidelines, which one of the following strategies is best to ensure that this patient is up-to-date on vaccinations for potential liver transplantation?
- Patient is up-to-date on vaccinations.
  - Give meningococcal serotype group B vaccine.
  - Give PPSV23 (23-valent pneumococcal polysaccharide vaccine).
  - Give cytomegalovirus (CMV) vaccine.
10. Yesterday morning, a 5-month-old Hispanic boy received a deceased donor split liver transplant for biliary atresia. He received induction with intravenous basiliximab and is receiving a maintenance immunosuppressive regimen of intravenous methylprednisolone and oral tacrolimus. The transplant donor was a 12-year-old girl. The donor was CMV IgG positive, and the recipient was CMV IgG positive at transplantation. According to the 2013 American Society of Transplantation ID guideline, which one of the following regimens would be the best strategy for CMV prophylaxis in this patient?
- Intravenous ganciclovir followed by conversion to oral valganciclovir when he is considered stable.
  - Intravenous ganciclovir for 7 days followed by conversion to oral ganciclovir.
  - Intravenous ganciclovir for 7 days followed by conversion to oral acyclovir with pre-emptive monitoring.
  - Intravenous cidofovir followed by conversion to oral brincidofovir when he is considered stable.