**Test Your Knowledge: Management of Kidney Transplant Recipients**

A recent Core Curriculum by [Voora and Adey](www.ajkdblog.org) published in *AJKD* reviews the mechanisms of immunosuppression, types of rejection, complications of recurrent disease, common infectious diseases, and the nonrenal complications commonly encountered in the kidney transplant recipient. Test your knowledge on your understanding of this topic with the quiz below.

1. Which of the following medications is an inducer of cytochrome P450 and when given with tacrolimus will result in low levels if the dose is not adjusted?
   - A. Erythromycin
   - B. Fluconazole
   - C. Ritonavir
   - D. Rifampin

2. Which of the following is true regarding cyclosporine?
   - A. The 2 formulations, Sandimmune and Neoral, are not equivalent in dose
   - B. Modified cyclosporine (Neoral) correlates better with 2-hour peak levels, whereas non-modified Sandimmune usually requires 12-hour troughs
   - C. When switching between formulations, the drugs can be used interchangeably due to similar bioavailability
   - D. The primary toxicity of cyclosporine are gastrointestinal symptoms

3. Which of the following immunosuppressive drugs can increase the incidence of posttransplantation lymphoproliferative disease (PTLD)?
   - A. MMF
   - B. CNIs
   - C. Belatacept
   - D. mTOR inhibitors
   - E. Corticosteroids
4. A 47-year-old white man with end-stage renal disease (ESRD) secondary to idiopathic focal segmental glomerulosclerosis (FSGS) who received a deceased donor kidney transplant 1 year ago presents for follow-up. Four weeks prior, he had presented to the emergency department with seizure, was discharged with Phenytoin, and told to continue his home immunosuppressive medications, which include prednisone, mycophenolate mofetil (MMF), and tacrolimus.

Today, he complains of a low-grade fever, poor appetite, and graft tenderness. In clinic, his pulse is 85, temperature is 99F, blood pressure is 141/98 mm Hg. His lab values from today are notable for serum creatinine increase from a baseline of 0.8 mg/dL to 1.8 mg/dL and urinalysis with 5 WBCs, 5 RBCs, as well as 100 mg/dL protein. Urine culture and tacrolimus level is pending.

Which of the following is the most likely diagnosis?

A. Medication toxicity  
B. Allograft pyelonephritis  
C. Rejection  
D. Volume depletion from poor appetite  
E. Recurrent FSGS

5. A 56-year-old woman with a medical history of advanced chronic kidney disease (CKD) from diabetes who received a living-related donor kidney transplant 2 years ago with no complications presents to a transplant center in Texas for follow-up. Her immunosuppression regimen consists of tacrolimus, MMF and prednisone. She denies any complaints and informs you that she plans to move to Bakersfield, California, within the next 6 months. You note that coccidiomycoses is endemic to this region. What should you do next?

A. Check a titer for coccidiomycosis; if positive, treat with fluconazole; if negative, do not treat  
B. Plan to start prophylactic fluconazole once patient moves  
C. Plan to start prophylactic fluconazole once patient moves and decrease dose of tacrolimus  
D. Do nothing
6. Which of the following cases is an ideal scenario to start discussing post-transplant conception?

A. A 36-year-old woman 9 months post-transplant with a serum creatinine 0.7 mg/dL, no history of rejection, urinalysis negative for protein, and BP of 111/77 mm Hg
B. A 36-year-old woman 3 years post-transplant with a serum creatinine 2 mg/dL, no history of rejection, urinalysis with 300 mg/dL protein, and BP of 123/78 mm Hg
C. A 36-year-old woman 2 years post-transplant with a serum creatinine 0.9 mg/dL, history of rejection 2 months ago, negative protein on urinalysis, and BP of 141/90 mm Hg
D. A 36-year-old woman 1.5 years post-transplant with a serum creatinine 0.8 mg/dL, no history of rejection, urinalysis negative for protein, and BP of 123/89 mm Hg

- Quiz prepared by Natasha N. Dave, AJKDBlog Contributor. Follow her @NatashaNDave.

To view Voora and Adey (FREE), please visit AJKD.org.

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1. D. Rifampin

When drug interactions with the cytochrome P450 are possible, consultation with a transplantation pharmacist or physician is important to prevent drug toxicity or underdosing, which can put the patient at risk for acute rejection. Notable drugs that interact are shown in Table 1:

<table>
<thead>
<tr>
<th>Common Drug Interactions</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Agent</strong></td>
</tr>
<tr>
<td><strong>Common Drugs That Increase CNI Level</strong></td>
</tr>
<tr>
<td>Erythromycin, clarithromycin</td>
</tr>
<tr>
<td>Azole antifungals</td>
</tr>
<tr>
<td>Diltiazem, verapamil</td>
</tr>
<tr>
<td>Protease inhibitors (e.g., ritonavir, darunavir, indinavir)</td>
</tr>
<tr>
<td><strong>Common Drugs That Decrease CNI Level</strong></td>
</tr>
<tr>
<td>Rifampin</td>
</tr>
<tr>
<td>Rifabutin</td>
</tr>
<tr>
<td>Carbamazepine</td>
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<tr>
<td>Phenobarbital</td>
</tr>
</tbody>
</table>

*View Table in HTML*

*Note: This is by no means an exhaustive list. It is advised to check for drug interactions when initiating new medications in transplant recipients.*

*Abbreviation: CNI, calcineurin inhibitor.*
2. **B. Modified cyclosporine (Neoral) correlates better with 2-hour peak levels, whereas non-modified Sandimmune usually requires 12-hour troughs**

Cyclosporine is available in 2 formulations: Sandimmune (non-modified) and Neoral (modified). Twelve-hour trough levels are measured for Sandimmune because the levels correlate with drug exposure and toxicity. Neoral drug exposure correlates better with 2-hour peak levels (C2 levels) due to more consistent drug absorption. Caution should be taken when switching between formulations due to variations in bioavailability. Gastrointestinal symptoms are the primary side effect of MMF. CNIs have multiple toxicities including vasoconstriction, thrombotic microangiopathy, chronic interstitial fibrosis, alopecia, gingival hyperplasia, and new onset diabetes.

3. **C. Belatacept**

Belatacept is an infusion that blocks the costimulatory signal between CD28 on T cells and antigen-presenting cells. It typically supplants the use of CNIs and is used in conjunction with MMF or mTOR inhibitors and steroids. There is an increased risk of PTLD with belatacept compared to cyclosporine, particularly in EBV negative patients. As a result, it is contraindicated in patients who are EBV negative or whose EBV status is unknown.

4. **C. Rejection**

Rejection is likely due to low tacrolimus levels after starting phenytoin, as it interacts with cytochrome p450 and may cause lower levels of the CNI.

5. **C. Plan to start prophylactic fluconazole once patient moves and decrease dose of tacrolimus**

Coccidiomycosis is endemic in southwestern United States, especially the San Joaquin Valley of California. Lifelong prophylactic fluconazole therapy is used by some transplant centers to prevent coccidiomycosis for patients residing in these endemic areas.
6. D. A 36-year-old woman 1.5 years post-transplant with a serum creatinine 0.8 mg/dL, no history of rejection, urinalysis negative for protein, and BP of 123/89 mm Hg

Women who wish to conceive are encouraged to discuss this with their physicians. The optimal scenario for conception is for the patient to:
1) Substitute azathioprine for mycophenolate 3 months before conception
2) Be at least 1 year posttransplantation
3) Have a stable eGFR with SCr < 1.5 mg/dL with no recent rejection episodes
4) Have no significant proteinuria
5) Have well-controlled blood pressure without using an ACE-I or ARB

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