American Society of Nephrology Quiz and Questionnaire 2013: RRT

Rajnish Mehrotra,* Mark A. Perazella,† and Michael J. Choi‡

Abstract
The Nephrology Quiz and Questionnaire (NQ&Q) remains an extremely popular session for attendees of the Annual Meeting of the American Society of Nephrology. As in past years, the conference hall of the 2013 meeting was overflowing with interested audience members. Topics covered by expert discussants included electrolyte and acid-base disorders, glomerular disease, ESRD/dialysis, and transplantation. Complex cases representing each of these categories, along with single best answer questions, were prepared by a panel of experts. Before the meeting, program directors of United States nephrology training programs answered questions through an Internet-based questionnaire. A new addition to the NQ&Q was participation in the questionnaire by nephrology fellows. To review the process, members of the audience test their knowledge and judgment on a series of case-oriented questions prepared and discussed by experts. Their answers are compared in real time using audience response devices with the answers of nephrology fellows and training program directors. The correct and incorrect answers are then briefly discussed after the audience responses and the results of the questionnaire are displayed. This article recapitulates the session and reproduces its educational value for CJASN readers. Enjoy the clinical cases and expert discussions.


Introduction: Mark A. Perazella and Michael J. Choi (Comoderators)
For most American Society of Nephrology (ASN) Kidney Week attendees, case-based clinical nephrology talks are the most exciting venues of the meeting. The Nephrology Quiz and Questionnaire (NQ&Q) is the essence of clinical nephrology and represents what drew many of us into the field of nephrology. The 2013 NQ&Q in Atlanta, with full-house attendance, was no exception. Each of the discussants prepared vignettes of puzzling cases, each illustrating some topical, challenging, or controversial aspect of the diagnosis or management of various areas of nephrology. These eight interesting cases were presented and eloquently discussed by our four expert ASN faculty. Subsequently, each discussant prepared a manuscript summarizing his or her discussion of the cases, which serves as the main text of this article.

In this NQ&Q, Dr. Rajnish Mehrotra challenges the reader with his two interesting dialysis cases and discusses the appropriate diagnostic and management approaches for these complicated cases. The audience responses are reviewed along with the training program director and nephrology fellow responses obtained before the meeting, giving an interesting perspective into the thoughts processes of nephrologists with varying levels of training and experience. Dr. Mehrotra thoughtfully synthesizes the essential clinical, laboratory, and renal pathology data and walks the reader through the diagnosis and management of two complicated cases that highlight challenging issues related to RRTs in patients with ESRD. Overall, this event was an educational experience for all who participated. We hope that this “distillate” from Atlanta will serve CJASN subscribers well and provide some fresh insights into the complexity and vibrancy of clinical nephrology for those who were unable to attend the meeting.

RRT Case 1: Rajnish Mehrotra (Discussant)
A 63-year-old woman with type 2 diabetes and ESRD, undergoing treatment with automated peritoneal dialysis (PD) for the last 4 months, presented to the dialysis facility 48 hours earlier with a 1-day history of abdominal pain and cloudy dialysate. She had no associated fever, nausea, vomiting, or any other symptoms. She had completed a 2-week course of treatment for coagulase-negative staphylococcal peritonitis only 3 weeks ago (Figure 1). The PD effluent had been sent for cell count, Gram stain, and culture, and empirical treatment was started with cefazolin and ceftazidime. She now presents with peritonitis only 3 weeks ago (Figure 1). The PD effluent had been sent for cell count, Gram stain, and culture, and empirical treatment was started with cefazolin and ceftazidime. She now presents with peritonitis only 3 weeks ago (Figure 1). The PD effluent had been sent for cell count, Gram stain, and culture, and empirical treatment was started with cefazolin and ceftazidime. She now presents with peritonitis only 3 weeks ago (Figure 1). The PD effluent had been sent for cell count, Gram stain, and culture, and empirical treatment was started with cefazolin and ceftazidime. She now presents with

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overnight and a 2-L last bag fill for the long day dwell. The last measured weekly \( \text{Kt/V}_{\text{urea}} \) was 2.30 (0.56 dialysate-to-plasma ratio of creatinine on peritoneal equilibration test). She lives with her daughter, who reports that her mother has become increasingly irritable, is not infrequently tearful, and needs her assistance in setting up the cycler at night. The patient has an additional medical history of diabetic retinopathy for which she has had multiple laser procedures, hypertension, and dyslipidemia. She has had two episodes of volume overload over the last 4 months from dietary and dialysis nonadherence. She has also been complaining of problems with falling asleep and awakens frequently throughout the night. She also has difficulty in adhering to a low-phosphorus diet and to her prescribed phosphate binders, resulting in persistent hyperphosphatemia. Her oral medications include glipizide, sevelamer carbonate, calcitriol, metoprolol, simvastatin, renal vitamins, amlodipine, furosemide, zolpidem, and aspirin, with a total pill burden of 29 tablets. The patient is also prescribed to take insulin glargine once daily and erythropoietin once a week.

Upon physical examination, her BP was 150/90 mmHg and she had pitting edema (2+) on both of her lower extremities. She had no abdominal tenderness and the rest of the physical examination was unremarkable.

**Question 1A**

Which of the following terms BEST characterizes the pattern of peritonitis in this patient?

A. Refractory  
B. Relapsing  
C. Recurrent  
D. Repeat

**Question 1B**

Which of the following represents the BEST option for reducing the long-term risk of peritonitis in this patient?

A. Simultaneous removal and replacement of the PD catheter  
B. Trial of sertraline monotherapy  
C. Transfer to in-center hemodialysis  
D. Change topical gentamicin to polysporin  
E. Use of icodextrin for the long day dwell

**Discussion of Case 1, Questions 1A and 1B**

This 63-year-old woman with ESRD has had two episodes of peritonitis with two different organisms, with the second episode occurring within 3 weeks of completion of antibiotic therapy for the first episode (Figure 1). This constitutes recurrent peritonitis (question 1A, choice C is correct; Figure 2). The causative organisms for the two episodes may reflect repeated episodes of touch contamination from poor technique in performing exchanges. It is also possible that the second episode of peritonitis (*S. viridans* organism) may be an endogenous infection from poor oral hygiene or gum disease. In addition to episodes of peritonitis, the patient has had difficulty adhering to other aspects of her treatment, including dietary sodium and phosphorus restriction and medications. She has also had difficulty with her sleep and her daughter has noticed her to be increasingly irritable with crying spells. These symptoms are highly suggestive of underlying depression and a trial of antidepressant drug therapy would be the most appropriate next step (question 1B, choice B is correct; Figure 3).

Over the last 3 decades, the risk for peritonitis in PD patients has decreased quite substantially (1). As a result, most PD patients never experience an episode of peritonitis. However, some patients develop several episodes of peritonitis over a relatively short period of time. Depending upon the interval between episodes and the causative organisms for the two consecutive episodes, patients can be grouped into having recurrent, relapsing, or repeat peritonitis (Table 1) (2). This patient has had two episodes of peritonitis within 4 weeks of completion of treatment of the first episode with two different microorganisms. Hence, she has a recurrent pattern of peritonitis (question 1A, choice C is correct, whereas choices A, B, and D are incorrect).

Recognizing these different patterns of peritonitis is important because each of them is associated with a different frequency of various microorganisms causing the infection; this, in turn, has implications for selection of empirical antibiotic regimen for the second episode. Moreover, the risk for removal of the PD catheter varies by the pattern of peritonitis. The largest series describing these different patterns of peritonitis included 356 episodes of relapsing peritonitis and 165 episodes of recurrent peritonitis compared with 2021 control episodes (3). The three most common organisms associated with relapsing peritonitis were coagulase-negative staphylococci (30%), non-**Pseudomonas** Gram-negative rods (23%), and *Staphylococcus aureus* (18%). By contrast, although non-**Pseudomonas** Gram-negative rods were the single most common group of organisms associated with recurrent peritonitis (25%), the second episode was significantly more likely be a fungal peritonitis compared with controls (13% versus 5%) (3). Patients who experienced either a relapsing or recurrent episode were significantly more likely to require removal of the PD catheter for the treatment of peritonitis compared with controls (30% and 37%, respectively, compared with 22%) (3).
The long-term management of patients with multiple episodes of peritonitis also depends upon an understanding of the pathophysiology of the different patterns of infection. Patients with relapsing peritonitis (infection with the same microorganism within 4 weeks of stopping antibiotics for the first episode) are thought to have microorganisms embedded in the biofilm (4). It is difficult for antibiotics to penetrate the biofilm, and a complete cure often requires removal of the infected PD catheter. If the primary infection responds to antimicrobial therapy, a simultaneous removal of the old PD catheter and replacement with a new PD catheter can be safely performed while the patient is taking antibiotics (question 1B, choice A is incorrect because this patient does not have a relapsing pattern of peritonitis) (2,5). This patient, by contrast, has had infections with two different microorganisms, each of which enters the peritoneal cavity to cause peritonitis because of a break in the sterility of the PD procedure (touch contamination). This implies a patient’s inability to perform PD exchanges aseptically and it may result from inadequate training or problems with manual dexterity or vision. Transfer to in-center hemodialysis would be premature at this time (question 1B, choice C is incorrect); instead, observing such individuals perform PD exchanges in a dialysis facility and retraining may help reduce the risk for peritonitis. Daily application of antibiotics at the exit site is ineffective in reducing the risk of peritonitis from touch contamination and changing the prophylactic agent is not expected to help this patient (question 1B, choice D is incorrect). Furthermore, there is no difference in the risk for peritonitis in patients using icodextrin or glucose-based dialysate (6) (question 1B, choice E is incorrect).

In the patient under discussion, recurrent episodes of peritonitis from touch contamination need to be judged in
light of her difficulty in adhering to dietary restrictions and medications for other aspects of the management of her ESRD, as evidenced by volume overload and hyperphosphatemia. Furthermore, she has increased irritability, crying spells, and sleep disturbances and this constellation of symptoms is highly concerning for the presence of comorbid depression. In a systematic review that included 198 cohorts with 46,505 patients, the summary prevalence of depression in patients undergoing maintenance dialysis using a structured clinical interview was estimated to be 23% (7). In addition to its association with poor patient-reported outcomes, the presence of comorbid depression is associated with nonadherence in patients undergoing maintenance dialysis (8). In PD patients, this is characterized by a significantly higher risk for peritonitis (9). In patients undergoing in-center hemodialysis, greater severity of depressive symptoms is associated with higher interdialytic weight gain, shortening dialysis treatment sessions, and skipping dialysis treatments altogether (10–14). In part because of nonadherence, at least 10 studies have demonstrated an association of depressive symptoms with higher risk for death.

Despite the evident importance of comorbid depression, it is diagnosed infrequently; even when comorbid depression is recognized, it is rarely treated in patients undergoing maintenance dialysis (15,16). This may be, in part, secondary to lack of high-level evidence for the efficacy of different approaches for treatment of depression in patients undergoing maintenance dialysis. Although single-center randomized controlled trials have demonstrated the efficacy of cognitive behavioral therapy for the treatment of depressive symptoms in patients undergoing in-center hemodialysis, there are no such studies in patients undergoing PD (17,18). To date, two single-center, uncontrolled studies have reported improvement in depressive symptoms with antidepressant drug therapy; similar uncontrolled studies have been published regarding the efficacy of medications for patients undergoing in-center hemodialysis (19,20). Until high-level evidence is available, given the high likelihood of comorbid depression and significant consequences on the health of the patient under discussion, a trial of treatment is warranted. Hence, in this patient with recurrent peritonitis and difficulty in coping with the treatment of ESRD, a trial of antidepressant therapy (sertraline) is warranted and is the most appropriate next step.

### Table 1. Definition of recurrent, relapsing, and repeat peritonitis

<table>
<thead>
<tr>
<th>Type of Peritonitis</th>
<th>Interval between the Two Episodes of Peritonitis</th>
<th>Causative Organism for the First and Second Infections</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recurrent</td>
<td>≤4 wk</td>
<td>Different</td>
</tr>
<tr>
<td>Relapse</td>
<td>≤4 wk</td>
<td>Same or the culture from one of the two episodes is sterile</td>
</tr>
<tr>
<td>Repeat</td>
<td>&gt;4 wk</td>
<td>Same</td>
</tr>
<tr>
<td>Refractory</td>
<td>Failure of effluent to clear after 5 d of antibiotic therapy</td>
<td></td>
</tr>
</tbody>
</table>


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**RRT Case 2: Rajnish Mehrotra (Discussant)**

The rehabilitation medicine service asks you to evaluate an 82-year-old woman who was transferred from another hospital. She has ESRD and has been undergoing maintenance hemodialysis for the last 4 years. She lives in a nursing home and was brought to the other hospital about a week ago after sustaining a fall. She was found to have a small intracerebral hematoma, of uncertain chronicity, had no focal neurologic deficit, and was transferred for physical therapy. Her last hemodialysis treatment was 2 days ago.

Her past medical history was significant for hypertension, early cognitive decline, coronary artery disease with a history of myocardial infarction, and congestive heart failure. She had a poorly functioning left upper arm fistula that had been ligated 4 weeks ago and a new right upper extremity arteriovenous graft was placed at the same time. Her current medications were aspirin, carvedilol, amlodipine, renal multivitamins, erythropoietin, paricalcitol, and calcium carbonate.

At the time of her evaluation, her BP was 135/65 mmHg and she was hemodynamically stable. She had a right internal jugular venous catheter in place; the exit site for the catheter was clean and dry. There was significant swelling of the right upper extremity even though there was a strong thrill and bruit over the arteriovenous graft. The left upper extremity arteriovenous fistula was pulsatile with aneurysmal dilation. Her neurologic examination was normal, with no focal deficits.

An ultrasound of the upper extremity and neck showed an extensive clot in the right subclavian and internal jugular veins encasing the tunneled central venous catheter.

**Question 2A**

Which vascular access site would you use for the next hemodialysis treatment?

A. Left upper arm arteriovenous fistula
B. Right internal jugular venous tunneled catheter
C. Left internal jugular venous temporary catheter
D. Right upper arm arteriovenous graft

**Question 2B**

What is the BEST next step in the management of this patient?

A. Therapeutic anticoagulation with a heparin bridge
B. Removal of the right central venous catheter after completion of hemodialysis treatment today
C. Thrombolysis with a tissue plasminogen activator  
D. No additional intervention at this time

Discussion of Case 2, Questions 2A and 2B

This 82-year-old nursing home resident with multiple comorbidities and ESRD undergoing maintenance hemodialysis has a new arteriovenous graft with edema over the right upper extremity that was out of proportion to what would be expected with an ipsilateral central venous catheter. Evaluation for the edema demonstrated right upper extremity central venous catheter-associated deep venous thrombosis. The presence of a thrombus around the catheter does not preclude its use for the next dialysis treatment and is preferable over using the arteriovenous graft, given the significant overlying edema at the time of evaluation (question 2A, choice B is correct; Figure 4). To prevent clot propagation and embolization, it is advisable for the patient to undergo therapeutic anticoagulation before removal of the right internal jugular catheter (question 2B, choice A is correct; Figure 5).

Hemodialysis patients with a central venous catheter have a high incidence of complications. In a recent series of 3213 central venous catheters, the incidence of complications was 6.98 per 1000 catheter-days (21). Whereas catheter-associated bloodstream infections were most frequent (5.1 per 1000 catheter-days), thrombotic complications were the second most common (0.80 per 1000 catheter-days) (21). Thrombotic complications with central venous catheters include a fibrin sheath, an intraluminal clot, mural thrombosis, catheter-associated venous thrombosis (or secondary deep venous thrombosis as in this patient), or catheter-associated right atrial thrombus (22,23).

Endothelial damage is likely to be the primary trigger for catheter-associated thrombosis and published case series suggest that the risk is higher with placement in the left internal jugular vein, malposition of the catheter tip, larger lumen size, and infections (22). Most patients with catheter-associated thrombosis are asymptomatic but up to one-third can have a variety of consequences that include catheter dysfunction resulting in inadequate or unsuccessful dialysis, infection, pulmonary thromboembolism, and failure of maturation of the ipsilateral arteriovenous fistula (22). Although venography is the gold standard for the diagnosis of upper extremity deep venous thrombosis, duplex ultrasonography is the method of choice (24). When combined with Doppler, duplex ultrasonography has 100% sensitivity and 93% specificity for the diagnosis of upper extremity deep venous thrombosis and catheter-associated thrombosis (24).

There is only one clinical trial that has tested the efficacy of prophylaxis for preventing thrombotic complications in patients with central venous catheters undergoing hemodialysis. In a recent study, 174 hemodialysis patients were randomly assigned to receive either low-dose warfarin with a target international normalized ratio of 1.4–1.9 or placebo (25). There was no significant difference in time to first mechanical catheter failure not caused by kinking or extrusion between the two arms (25). Similarly, there is no evidence for any benefit with thromboprophylaxis with unfractionated heparin, low molecular weight heparin, or warfarin in patients with cancer with long-term central venous catheters (26). Hence, prophylactic antithrombotic therapies cannot be recommended at this time with the expectation to reduce the risk for thrombotic complications with central venous catheters.

There are very limited data on the optimal management of patients with dialysis catheter-associated thrombosis; the recommendations are based upon experience with patients with central venous catheters placed for other indications such as for cancer chemotherapy. In patients with catheter-associated thrombosis, there is no contraindication to the continued use of the central venous catheter (27). Hence, in this patient, if the right upper extremity central venous catheter allows for good flow, it is the vascular access of choice for the next hemodialysis treatment. The left upper extremity arteriovenous fistula has been ligated and hence is no longer
available for use for hemodialysis treatments (question 2A, choice A is incorrect). Although the right upper extremity arteriovenous graft could be used for hemodialysis, the overlying edema will make it challenging (question 2A, choice D is incorrect). Placement of a temporary left central venous catheter in a patient with right-sided deep venous thrombosis is not advisable (question 2A, choice C is incorrect).

Patients with deep venous thrombosis are at potential risk for pulmonary embolism; whether the risk is amplified with immediate removal of the central venous catheter without intervening anticoagulation is not clear. It is generally recommended that patients with catheter-associated thrombosis at high risk of embolization receive therapeutic anticoagulation with unfractionated or low molecular weight heparin for 3–5 days before removal of the central venous catheter (question 2B, choice D is incorrect) (22,27). Small case series seem to suggest that thrombolytics are associated with a higher risk for bleeding in individuals with catheter-associated upper extremity deep venous thrombosis (27). This is an important consideration for this patient, who may have had a recent stroke (question 2B, choice C is incorrect). If there is no continued need for the central venous catheter, it should be removed only after 3–5 days of treatment with heparin (question 2B, choice B is incorrect because it recommends immediate removal of the catheter without heparin therapy). Even after removal of the central venous catheter, it is recommended that patients continue to receive therapeutic anticoagulation therapy with warfarin for at least 3 months. If, however, there is a continued need for central venous catheters, a longer duration of treatment with warfarin may be considered (3–12 months) (27).

This patient has a functioning arteriovenous graft and the swelling over the upper arm is expected to diminish with recanalization of the central veins and removal of the central venous catheter. Hence, the central venous catheter was removed after 1 week of systemic heparin administration. By that time, the swelling over the right arm had diminished sufficiently to permit long-term dialysis using the right upper arm arteriovenous graft.

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Disclosures
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References

Figure 5. Question 2B: Distribution of answers from fellows in training, training program directors (TPD), and audience members at the Kidney Week meeting. *The correct answer is A.


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