Nephrology Quiz and Questionnaire: Renal Replacement Therapy

Thomas A. Golper (Discussant), Richard J. Glassock (Co-Moderator),† and Anthony J. Bleyer (Co-Moderator)‡*

Summary

Presentation of the Nephrology Quiz and Questionnaire has become an annual "tradition" at the meetings of the American Society of Nephrology. It is a very popular session judged by consistently large attendance. Members of the audience test their knowledge and judgment on a series of case-oriented questions prepared and discussed by experts. They can also compare their answers in real time, using audience response devices, with those of program directors of nephrology training programs in the United States, acquired through an Internet-based questionnaire. Topics presented here include fluid and electrolyte disorders, transplantation, and ESRD and dialysis. Cases representing each of these categories along with single best answer questions were prepared by a panel of experts (Drs. Palmer, Hricik, and Golper, respectively). After the audience responses, the "correct" and "incorrect" answers then were briefly discussed and the results of the questionnaire were displayed. This article aims to recapitulate the session and reproduce its educational value for a larger audience—readers of the *Clinical Journal of the American Society of Nephrology*. Have fun.

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*Vanderbilt Medical School, Vanderbilt University, Nashville, Tennessee; †David Geffen School of Medicine, University of California, Los Angeles, California; and ‡Section on Nephrology, Wake Forest University School of Medicine, Winston-Salem, North Carolina

Correspondence: Dr. Anthony J. Bleyer, Section on Nephrology, Wake Forest University School of Medicine, Medical Center Boulevard, Winston-Salem, NC 27157. Email: ableyer@wakehealth.edu

Case 1

A 50-year-old male municipal manager on automated peritoneal dialysis (APD) for 2 years underwent semi-elective coronary artery bypass surgery. He was doing well before this event and had 500–1000 ml/d of urine output, which provided a weekly Kt/V of 0.3 to go along with his peritoneal dialysis (PD) Kt/V of 1.5 for a total weekly Kt/V of 1.8. He was a low-average transporter who spent 9 hours nightly on the cycler performing three exchanges of 2500 ml, a last bag fill of 2000 ml and a mid-day exchange also of 2000 ml. His body surface area was 1.9 m^2. Most of his solution utilization was 1.5% dextrose, and he was usually clinically euvolemic but required antihypertensive medications and diuretics.

After the bypass surgery, he was hypotensive with apparently compromised cardiac output. Residual kidney function (RKF) deteriorated. He did not thrive upon hospital discharge and rehabilitation, and he lost muscle mass. It was decided to increase the delivered dose of dialysis to see if that could help improve his overall failure to thrive. He preferred to continue APD.

Renal Replacement Therapy Question 1

Given the patient's circumstances and lifestyle choices, how could his dose of PD BEST be increased in a most cost-efficient manner (Figure 1)?

A. Increase the number of exchanges per day.
B. Increase the fill volume per cycler exchange.
C. Increase his ultrafiltration per day.
D. Increase dwell time on the cycler and thus his time on the cycler.
E. Increase his transport status.

Discussion of Case 1

The best choice is B: Increase the fill volume per cycler exchange. It would be ideal if the patient were to regain the lost RKF. In fact, this did occur over the next 3 months; however, because this could not be predicted, it was necessary to increase the delivered dose of PD. His ultrafiltration had always been good, as expected from his low-average transport status. Fortunately, this situation persisted after the bypass.

Using a cycler is a lifestyle decision for PD patients, allowing them to perform the majority of their therapy during sleep. Over time, as RKF is lost, there may be a need to alter the PD regimen. After his heart surgery, our patient was considered underdialyzed but he desired to remain on APD.

Sterile peritoneal dialysate is the limiting resource in PD, because the solution is provided in bags and increasing the amount of fluid used increases cost. Clearance is the product of the effluent volume times the ratio of the dialysate solute concentration over the plasma solute concentration (D/P). To increase the product, one must increase either or both components. In other words, to increase PD dose, one must increase effluent volume per week and/or have more solute per unit volume. Therefore, the limited resource must be increased because there is no feasible way to increase D/P (see below).

For the effluent to have a concentration of solute approaching that of plasma, the solute must move faster across the peritoneal membrane, or it must have longer time to dwell within the peritoneal cavity to reach equilibrium with the plasma concentration. Transmembrane solute transport status is characterized by the speed of this equilibration, ranging from low (or slow) to high (or rapid) with two average

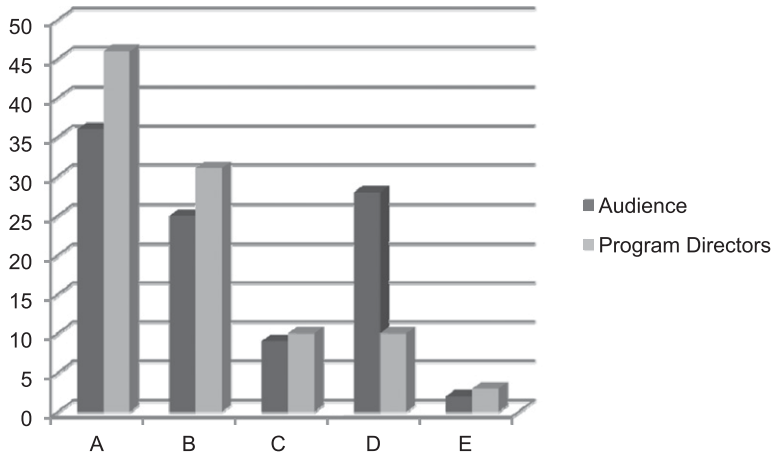

Figure 1. | **Question 1: Which is the best option for increasing the dialysis dose in this patient?** The correct answer is A.

positions between those extremes (1). There are chemicals such as vasodilators that have been used to temporarily increase this transport speed (2), but this strategy has not been clinically practical. Peritoneal inflammation is an example of vasodilation and is most often caused by microorganism contamination of the dialysate, causing peritonitis. In active peritonitis, and for several weeks of the recovery phase, peritoneal transport is accelerated. Severe infections as well as recurrent infections may lead to a permanent conversion to a higher transport state (3). There is concern that this contributes to loss of peritoneal membrane function over time, and is not a desirable method to increasing solute clearance. Furthermore, increasing the solute transport status may have other more immediate detrimental effects. Not only would uremic solutes move faster from plasma to dialysate, but so would proteins, leading to significant protein losses and potential malnutrition as seen in nephrotic syndrome. High transporters also transport glucose rapidly from dialysate to plasma, leading to excessive glucose absorption, which may exacerbate malnutrition by impairing appetite. In addition, the rapid absorption of the dialysate glucose dissipates the osmotic gradient driving force for ultrafiltration. Thus, high transporters lose more protein, absorb more glucose, and ultrafilter more poorly than do patients with lower transport status. Consequently, it is no surprise that observational studies suggest that outcomes are worse in higher transport states (4). Choice E is not correct.

The option to increase dialysate solute concentration by keeping the fluid in the peritoneal cavity longer is attractive. Our patient was already leaving fluid in as he left the cycler in the morning and already performed a manual exchange during the day. Option A, increasing the number of exchanges per day, has two undesirable aspects. First is the intrusion on his lifestyle to perform another 30-minute exchange during the day. Second, peritonitis rates are increased with more frequent exchanges (5–7). Although a second day exchange (option A) would increase the dialysis dose, it is a less attractive alternative in this setting.

To keep fresh fluid in longer to equilibrate better, the patient must spend more time on the cycler. Option D, increasing overall cycler time by increasing exchange duration, would increase dialysis dose but affects lifestyle. For this approach to significantly increase the dialysis dose, the cycler time would likely need to increase by 2 hours. This would be a good strategy if this alteration fit into the patient's lifestyle. However, many patients, including ours, do not want to be "tethered" (his word) to their cycler for an additional 2 hours. The patient was already spending 9 hours "tethered," and he did not want to increase this further. In fact, PD patients in the United States have recently increased their time on the cycler (8) up to levels seen in our patient. In summary, the option of leaving the fluid in longer by increasing the cycler time commitment is feasible if it fits into the patient's lifestyle; in our case, it was not preferred.

Another option, but intentionally not offered as an answer, is to increase the number of exchanges performed during the 9 hours of cycling. This strategy would almost certainly increase small solute clearance (9). As fresh dialysate enters the peritoneal cavity, the rate of solute transfer is at its fastest at the start, slowing down as equilibrium is approached. The constant inflow of fresh dialysate will maximize solute removal into the dialysate and is the basis behind an experimental therapy called continuous flow PD (10). Because this requires either two catheters or a special two-directional flow catheter (11), PD is not yet performed in this manner.

The current approach is rapid exchanges on the cycler with infusion of fresh dialysate at short intervals. This maximizes the concentration gradient from blood to dialysate and increases the rate of small solute (*e.g.*, urea and creatinine) removal (9). This may not be true for slower-moving solutes because surface area is not being utilized during inflow and drainage. For each cycle, a conservative estimate is that 25 minutes is used to fill and drain. Thus, for a cycle length of 60 minutes, 25 minutes are spent with a less than full peritoneal cavity in what is marginal or insignificant therapy and only 35 minutes are devoted to maximal surface area utilization where there is effective therapy. If the cycle length is 2 hours and 35 minutes are used to fill and drain, there are 85 minutes of fully effective therapy. Therefore, speeding up exchanges on a cycler may not always increase solute clearance due to the proportion of the cycle being inefficient during fill and drain

(12). This may not matter for urea but it will for larger solutes, especially in the low and low-average transporters. In addition, rapid cycling stimulates aquaporin channels due to the increased osmotic activity of the dialysate; this results in more solute-free water movement into the peritoneal cavity. This sodium-free water movement dilutes the sodium concentration in the dialysate, and is called "sodium sieving." If the aquaporin-derived water is not allowed to dwell in the peritoneal cavity long enough for sodium to diffuse from plasma into the dialysate through the (nonaquaporin) intercellular pores, then the drained effluent will remain sodium poor relative to the sodium concentration in the plasma. Essentially, more free water then leaves the body relative to interstitial water. When this occurs, the patient becomes hypernatremic, which stimulates thirst. Thus, rapid cycling results in the use of large volumes of dialysis, poorer large solute removal, and potentially inadequate sodium removal (13).

Option C is to increase solute removal by convection, which translates to increasing ultrafiltration per day. Convective transport removes larger molecules better than diffusion and would be attractive for our patient's uremia. However, to really improve his uremic symptoms, his convective transport would likely need to increase by at least a liter per day. Achieving this would require an increased use of hypertonic exchanges (2.5% and 4.25% dextrose solutions) and perhaps the replacement of one of his day exchanges with icodextrin. We discourage the use of hypertonic exchanges in our program because of the long-term adverse effects of glucose exposure on the peritoneal membrane (14,15). Hypertonic exchanges are reserved for higher transporters or emergencies. Icodextrin is an alternative, unattractive only because of its extra expense. Increasing the number of exchanges on the cycler would increase ultrafiltration and small solute clearance but would decrease diffusion time for larger solutes. This might be compensated by increased convective transport of these larger molecules. As discussed above, increasing exchanges on the cycler increases dialysate inflow volume and costs but was not offered as an answer.

In our opinion, increasing fill volume per cycler exchange (option B) is the best answer. The number of connections is not changed so contamination risk is not increased. Surface area is maximized, and lifestyle is not altered. When we increase fill volumes in an APD patient in our program, we start with increasing only the fills from the cycler and we increase in increments of 100 ml per exchange every 1 or 2 weeks so that the patient is essentially unaware of the sensation of the increased volumes. A blinded study has shown that patients infrequently complain of either mild or moderate discomfort with larger fill volumes in the sitting position (16) and patients are even more tolerant of such volumes when supine on the cycler. The benefit of incrementally increasing cycler fill volumes on peritoneal Kt/V is exemplified in Figure 2. Dialysate for cyclers comes in large volume bags and increasing fill volume in this way rarely leads to increased dialysate cost. Thus, from the aspect of ease of operation and cost benefit, option B to increase fill volumes is the best of the offered choices.

Case 2

A 55-year-old male farmer, weighing 120 kg, being treated by in-center hemodialysis requested transfer to home dialysis. He already placed his own needles into a well functioning fistula, and his wife participated actively in his care. He had always taken in very large quantities of fluids daily even before ESRD, and this behavior continued on in-center hemodialysis. He preferred to perform home hemodialysis 3–4 times per week, needing to remove 2–6 L at each session. He tolerated this well but eventually developed both rhythm disturbances and left ventricular dysfunction. His fluid gains persisted despite his increasing intolerance of the ultrafiltration demands. He was offered more frequent home hemodialysis. For ease of set-up and take-down, he switched from his Fresenius K machine to NxStage "short" daily home hemodialysis, with his medical condition mandating at least six dialysis sessions per week. Despite his low BP, his fistula performance remained outstanding and he routinely achieved a blood flow rate (Qb) of 450 ml/min.

His interdialytic fluid gains remained at 3 L/d, mandating 3000 ml of ultrafiltration at each dialysis session. Because his dry weight body size yielded a urea volume of distribution of 72 L (75 L when wet), each dialysis session required 30 L of dialysate. The 30 L of dialysate required 3 hours and 20 minutes of dialysis time (200 total minutes) to process.

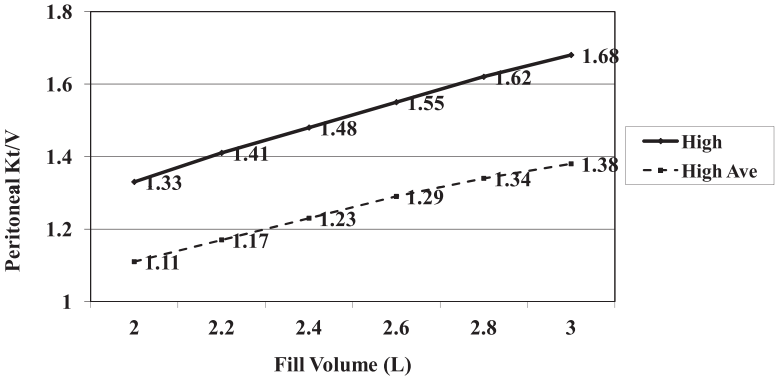

Figure 2. | Increments in fill volumes of 100–200 ml have minimal effect on sensation of fullness, intra-abdominal pressure, and clearance. However, if fill volumes are nudged up by these amounts every few weeks the clearance benefits add up and symptoms are avoided. Ave, average. (Courtesy of Dr. Salim Mujais.)

Renal Replacement Therapy Question 2

How much extra time per treatment session would be required to remove the 3 L of fluid by ultrafiltration under several different operating conditions (Qb and flow fraction) described below (Figure 3)?

A. Blood flow rate (Qb) 400 ml/min, flow fraction 25%, would require 25 minutes more.
B. Blood flow rate (Qb) 400 ml/min, flow fraction 25%, would require 20 minutes more.
C. Blood flow rate (Qb) 450 ml/min, flow fraction 33.33%, would require 25 minutes more.
D. Blood flow rate (Qb) 450 ml/min, flow fraction 33.33%, would require 20 minutes more.
E. None of the above.

Discussion of Case 2

Answer D is the most correct choice. In 2011, the Centers for Medicare and Medicaid services implemented a prospective payment system for dialysis services in the United States. One feature of this new policy was to provide a financial incentive for the use of home dialysis. Furthermore, the Frequent Hemodialysis Network Trial demonstrated a cardiovascular benefit to more frequent hemodialysis (17). This was followed by several reports from the Following Rehabilitation, Economics, and Everyday-Dialysis Outcome Measurements (FREEDOM) study, suggesting that restless leg syndrome, sleep disturbances, postdialysis recovery time, and depression were also improved with short daily hemodialysis (18,19). This constellation of events contributed to the growth of home hemodialysis.

The simplicity of the NxStage system has made it the most popular current version of home hemodialysis. Some of the benefits of this system are that it generally only requires 3 weeks for training, it does not require home plumbing modifications, and the equipment is small and portable.

Gotch popularized the concept of standard weekly Kt/V to help equate in terms of urea clearance intermittent versus continuous kidney replacement therapies and the frequency of the applied intermittent treatments (20). This is one of several mathematical models that allow the comparison of different kidney replacement therapies with the clearance of urea over a week's duration. Although they are not clinically validated, many clinicians have found them useful and they certainly are helpful in quantitative comparison of urea clearance by differing dialytic modalities. Figure 4 shows where the currently prescribed therapies relate relative to each other on a standardized weekly Kt/V scale.

In the NxStage system, dialysate fluid is provided. As with PD, the dialysate is a scarce commodity because it must be ultrapure. Also as in PD, to maximize clearance in the setting of scarce dialysate, the dialysate must be highly saturated with solute. To do this efficiently requires increased contact time between blood and dialysate. The practical application is to operate with a low ratio of dialysate flow rate (Qd) to blood flow rate (Qb). A large surface area for such contact also facilitates saturation of dialysate. These are features of the NxStage system. Conventional hemodialysis operates with high Qd (thus huge water requirements) and high Qb, whereas NxStage uses low Qd but high Qb. Conventional hemodialysis is not concerned with saving dialysate, so dialysate saturation is unimportant.

NxStage developed the term *flow fraction*, which is the ratio of effluent flow (spent dialysate + ultrafiltration) divided by Qb. Fully saturated dialysate would mean that clearance is equal to effluent flow rate. For a small solute which moves rapidly across dialyzer membranes, using urea as the example and in-house data from NxStage, a flow fraction of 25% would yield a saturation of about 95%, which then equates to a clearance that is approximately 95% of effluent flow rate. Increasing the flow fraction to 33% would drop the saturation to about 92%. Preferable (cost-effective) flow fractions are in this range. This generally requires accesses to deliver a Qb of ≥400 ml/min. If the Qb is not this high, then the flow fraction will be greater than preferred, and consequently dialysate will be less saturated and essentially wasted. This would increase treatment time and require more dialysate to deliver the same dialytic dose. For this reason, NxStage requires a well functioning access for frequent short-duration treatments.

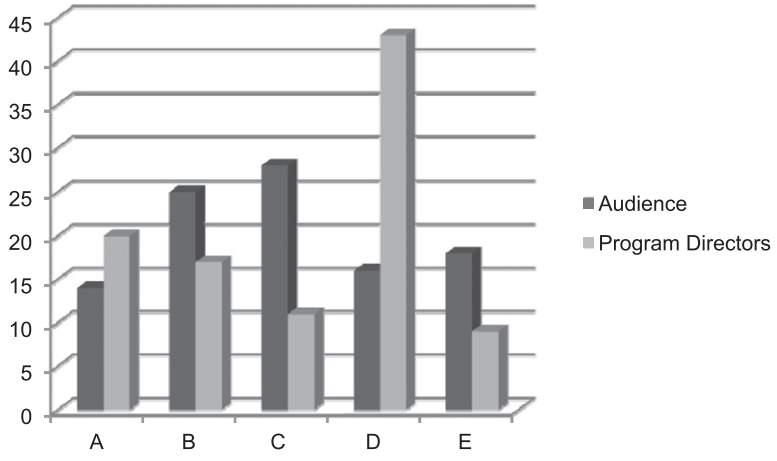

Figure 3. | **Question 2: How much extra time would be required at varying flow fractions?** The correct answer is D.

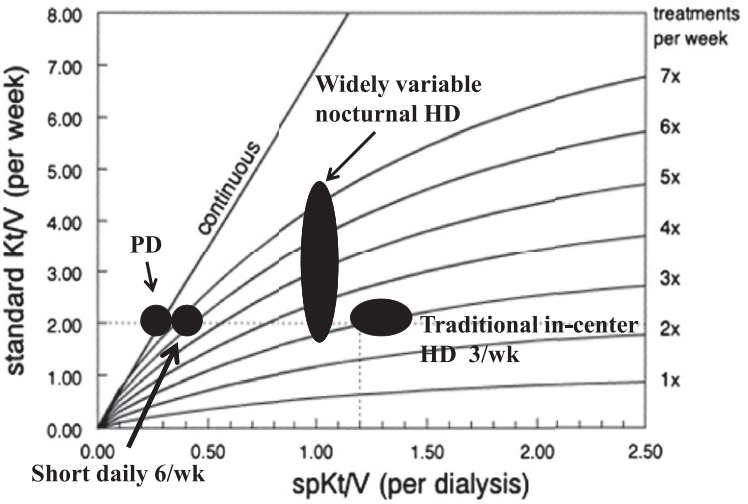

Figure 4. | **The weekly standardized Kt/V is a useful method to compare the dose equivalency of various dialysis modalities**. Shown here are different modalities, all delivering a standardized weekly dose approaching 2.0 but requiring continuous or frequent applications to do so. HD, hemodialysis. Modified with permission from reference 20.

Answers A and B stipulate a Qb of 400 ml/min and a flow fraction of 25%. Because the flow fraction is the ratio of effluent flow (spent dialysate + ultrafiltration) divided by Qb, this means that the effluent flow (Qd) will be 100 ml/min (100/400=0.25, or 25%). With a Qd of 100 ml/min, this means that it will require for 30 L of dialysate for 300 minutes (5 hours). For the 3000 ml that needs to be ultrafiltered, this will then require (at 100 ml/min) an additional 30 minutes of treatment. This means that Qd is 100 ml/min and 3000 extra ml must be removed at this rate; 3000 ml at 100 ml/min requires 30 additional minutes. Thus, answers A and B are incorrect.

Answers C and D stipulate a Qb of 450 ml/min with a flow fraction of 33.33%. This means that Qd is 150 ml/min and 3000 extra ml must be removed at this rate; 3000 ml at 150 ml/min requires 20 additional minutes. Thus, answer C is incorrect, whereas answer D is correct.

Another simple solution is that without any ultrafiltration and a Qd of 150 ml/min, our patient requires 3 hours and 20 minutes (200 minutes) to process 30 L of dialysate. He has an additional 3 L of ultrafiltrate to process. If 30 L requires 200 minutes, then an additional 3 L would require 20 additional minutes. The lesson to learn with this case is that ultrafiltration extends treatment time with NxStage therapy.

The prescription for this patient with a urea volume of distribution of 72 L was 30 L of dialysate with 92% saturation yielding a Kt/V of 0.38 per treatment. Without any convective urea removal, his six treatments per week with a Kt/V of 0.38 per dialysis would yield a standardized Kt/V approaching our 2.0 target (Figure 4). However, with 3 L of ultrafiltration 100% saturated with urea, there is an increase in treatment time but an increase in Kt/V of approximately 4% (3/75) to 0.395 per treatment.

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Disclosures

None.

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