The Nephrology Quiz and Questionnaire: 2005

Robert G. Narins (Moderator)*; Participants: Mitchell Halperin,† Gabriel Danovitch,‡ Ronald Falk,§ and Joanne Bargman†

*American Society of Nephrology, Washington, DC; †University of Toronto, Toronto, Canada; ‡University of California Los Angeles, Los Angeles, California; §University of North Carolina, Chapel Hill, North Carolina


The Nephrology Quiz and Questionnaire (NQQ) continues to be the most popular of the 2-hr Clinical Nephrology Conferences held at our annual Renal Week. Our faculty presented eight puzzling cases that prompted some lively discussions at the recent Philadelphia meeting.

As most of you know, each of the four faculty is charged with developing two cases, each of which involve some controversial aspect of diagnosis, management, or pathophysiology related to a renal or an electrolyte disorder. One or two questions follow each case. Before Renal Week, we e-mail these cases and multiple-choice questions to all our members and ask them to send us their answers. At the meeting, the collated answers to each question are presented by the faculty, and they discuss their “correct” answer to each question. The responses from the Nephrology Training Program Directors and those from all other nephrologists are assessed and presented separately. In years past, we have e-mailed the answers to the membership after the Renal Week meeting. CJASN will now be the new home for the discussions of NQQ cases. We hope that this “distillate from Philadelphia” will serve as a good review for those of you who were at the session and will provide fresh insights for those of you who missed the Clinical Nephrology Conferences.

Case 1: Mitchell L. Halperin (NQQ Presenter), Kamel S. Kamel, and Desmond Bohn

Two days ago, a 24-yr-old, healthy, 50-kg man developed profuse diarrhea (“rice water” consistency) after drinking contaminated water. On physical examination, he appeared very ill and cyanotic. His BP was 90/60 mmHg, his heart rate was 110 beats/min, and his jugular venous column height was below the sternal angle. The remainder of the examination was not relevant.

Laboratory studies on admission included serum electrolytes (in mM) Na 140, HCO3 24, K 4.6, Cl 95; pH 7.39, Pco2 (arterial) 39 mmHg, glucose 72 mg/dl (4.0 mM), creatinine 3.0 mg/dl (345 μM), total protein 132 g/L (13.2 g/dl), and hematocrit 60%.

On day 1, the volume of his diarrhea was approximately 5 L and contained (in mM) 140 Na, 15 K, 115 Cl, and 40 HCO3.

Question 1A
What type(s) of acid–base disorder(s) was (were) present on admission?

a. Metabolic acidosis
b. Respiratory acidosis
c. Metabolic and respiratory acidosis
d. Metabolic acidosis and metabolic alkalosis
e. None

Question 1B
Should NaHCO3 be added to the intravenous fluids?

a. Yes
b. No
c. Cannot tell without more information

Answers from Drs. Halperin, Kamel, and Bohn and the membership (Figures 1 and 2).

Question 1A: d. Metabolic acidosis and metabolic alkalosis
Question 1B: a. Yes

Discussion of Case 1

Ingestion of water heavily contaminated with the vibrio cholera bacillus causes the abrupt onset of massive diarrhea. Stool volume is often approximately 5 L/d and contains approximately 40 mM HCO3 (1). These massive and acute losses of alkali dwarf its potential replacement by ingestion (limited in these sick patients), generation by gastric HCl loss, or renal new HCO3 formation linked to the urinary excretion of NH4 (2). Predictably, these patients should develop a metabolic acidosis.

Notwithstanding, our patient (and many others like him [1]) has normal arterial pH, Pco2 and plasma HCO3 concentration (P HCO3).

Question 1A. From analysis of the laboratory data, either the patient does not have a metabolic acid-base disorder because the arterial pH (7.39) and P HCO3 (24 mM) are in the normal range, or he has both metabolic acidosis (NaHCO3 loss in diarrhea fluid) and metabolic alkalosis. Because the patient had a large increase in his plasma anion gap (21 mEq/L, excluding K\(^{-}\)), one might conclude incorrectly that he has an acid overproduction type of metabolic acidosis. Because he has a normal pH and P HCO3, he must also have metabolic alkalosis. Most of the respondents preferred this diagnosis.

Could the same diagnosis have been made without knowing the diarrhea volume and composition? The answer is yes providing that a quantitative estimate of his extracellular fluid
PHCO$_3$ is 24 mM in the face of such a large deficit of NaHCO$_3$. Therefore, this patient has metabolic acidosis as a result of large diarrheal losses of NaHCO$_3$. 

Because he still has 2 L of RBC, his current plasma volume is 1.33 L (3.33 − 2 L), a value that is reduced from normal by ~50%. With a normal P$_{HCO_3}$ and an ECF volume that is <50% of normal (3), his ECF content of HCO$_3^−$ is ~<50% of normal. Therefore, this patient has metabolic acidosis as a result of large diarrheal losses of NaHCO$_3$.

What is his P$_{HCO_3}$ in the normal range? One must examine the numerator (content of HCO$_3^−$) and the denominator (ECF volume) of the HCO$_3^−$ concentration term to determine why his P$_{HCO_3}$ is 24 mM in the face of such a large deficit of NaHCO$_3$. Regarding the numerator, although there were a few episodes of vomiting, the loss of HCl and the resultant gain of HCO$_3^−$ in the ECF (4) are trivial compared with the large loss in diarrhea fluid. Furthermore, he did not ingest NaHCO$_3$, and very little new HCO$_3^−$ would be generated by this anuric patient’s kidneys (2). Therefore, the major reason for his metabolic alkalosis is a denominator effect, a markedly contracted ECF volume causing a contraction type of metabolic alkalosis (eq. 1). As we will explain below, because the content of HCO$_3^−$ in the ECF was greater than expected from the measured loss of HCO$_3^−$ in diarrhea fluid and ECF contraction, an additional source of new HCO$_3^−$ must have been present.

What is the basis for the high value for his plasma anion gap? Before attributing this to the addition of acids and retention of their conjugate bases, other causes for the high plasma anion gap should be considered. The normal value largely is due to the net negative charge on plasma albumin. Because he has the same amount of albumin, which now is contained in less than half the plasma volume, he will have approximately twice the albumin concentration in plasma (1). This alone should more than double the contribution of the anionic charge on albumin to the plasma anion gap. In addition, the net negative valence on albumin is higher when the ECF volume is contracted (5). The minimal increase in lactate levels further supports the role of albumin as the cause of the elevated plasma anion gap.

Does this patient have respiratory acidosis? The usual definition of respiratory acidosis is an acid-base disorder with high plasma [H$^+$] and high arterial P$_{CO_2}$. This definition considers only a “ventilation” form of respiratory acidosis. When the arterial P$_{CO_2}$ is not low enough in an acidemic patient, the P$_{CO_2}$ in all cells of the body will be too high. Because our patient had a normal arterial pH and P$_{CO_2}$, he does not have this type of respiratory acidosis. The definition of respiratory acidosis also should include a “tissue” form in which the cell has a P$_{CO_2}$ that is too high to permit the majority of intracellular H$^+$ to be buffered by the HCO$_3^−$ buffer system (6). Accumulating cellular H$^+$ will bind to intracellular proteins, changing their charge and shape and possibly adversely affecting their function. A high cell P$_{CO_2}$ is reflected by a high P$_{CO_2}$ in venous blood draining that organ. When the majority of oxygen is extracted from each liter of blood that traverses an organ, either because of a higher overall CO$_2$ production rate or a much slower blood flow rate, the P$_{CO_2}$ in draining venous blood is increased. As a result, the P$_{CO_2}$ in these cells also must be high because CO$_2$ diffuses from cells. Because this patient had a marked degree of ECF volume contraction and hence slower blood flow rate to organs, his venous P$_{CO_2}$ was high and he does have a tissue form of respiratory acidosis.

What is the source of new HCO$_3^−$ added to the ECF compartment? An elevated P$_{CO_2}$ in cells leads to the formation of H$^+$ and HCO$_3^−$. The H$^+$ so produced binds to proteins with potentially adverse effects, whereas HCO$_3^−$ is released into the ECF compartment. The converse also is true (see discussion of question 2).

Question 1B. The following facts indicate that it is very important to treat this patient with NaHCO$_3$. First, if he is given enough isotonic saline to raise his ECF volume to normal, then his P$_{HCO_3}$ will halve to approximately 12 mM. Second, when enough saline is infused to improve the blood flow, the P$_{CO_2}$
will decline in veins and in cells. As a result, H+ ions will be released from intracellular proteins, further lowering the pHCO3 (7). Third, renal addition of new HCO3− will not increase promptly owing to the very low GFR (2). Parenthetically, his GFR is low because of vasoconstriction plus the presence of very viscous blood (low hydrostatic pressure in his glomerular capillaries) together with a very high colloid osmotic pressure exerted by the high plasma albumin concentration. Fourth, when blood flow to his small intestine increases, diarrheal fluid loss will increase markedly (1). The delivery of more Na+ and Cl− to his colon will lead to a large loss of NaHCO3. This probably reflects the larger capacity of the colonic Cl−/HCO3 anion exchanger as compared with the colonic Na+/H+ exchanger.

Overall, one can expect a very severe metabolic acidosis to develop unless the intravenous solution contains at least 30 mM NaHCO3. Parenthetically, just as in patients with diabetic ketoacidosis, these patients are K+ depleted, yet their plasma [K+] is not in the hypokalemic range, therefore, the intravenous solution also should contain KCl (8).

Although the data were not robust, when severely ill patients with cholera were given isotonic saline very aggressively, five of 40 patients developed pulmonary edema even though the positive balance of saline did not re-expand their ECF volume to its normal value (9). In contrast, pulmonary edema was not reported in patients who received HCO3−-containing intravenous fluid. Most surprising, briskly infusing isotonic NaHCO3 to saline-treated patients who developed pulmonary edema reversed the cardiopulmonary disorder. This might be due to the effect of acidemia to cause peripheral vasoconstriction and venoconstriction, which increases the central blood volume (10).

**Case 2: Mitchell L. Halperin (NQQ Presenter), Kamel S. Kamel, and Desmond Bohn**

A 14-yr-old, 50-kg girl had a craniopharyngioma resected. There was no previous evidence of central diabetes insipidus (CDI). Polyuria developed within 1 h of surgery (average urine flow rate in the first 5 h was 10 ml/min, and the urine osmolality was 120 mOsm/kg H2O). During the induction of anesthesia and during the first 5 h of surgery, she received 3 L of isotonic saline to maintain a normal BP. During this period, her plasma Na concentration (PNa) increased from 140 to 150 mM.

**Question 2A**
Which ONE of the following choices contributes the most to her hypernatremia?

- a. Negative balance for water
- b. Positive balance for Na
- c. Both negative balance for water and positive balance for Na

CDI was diagnosed, and she was treated with dDAVP. Two hours later, her urine flow rate was 0.5 ml/min and her urine osmolality was 800 mOsm/kg H2O. During the next 20 h in the intensive care unit, she received hypotonic saline (30 mM) at hourly rates that successfully replaced each previous hour’s urine output. She also received some boluses of saline for perceived ECF volume contraction. Her peripheral vein PNa decreased progressively to a nadir of 124 mM. In the 2 h before death, her urine output increased to 25 ml/min and her urine osmolality was 40 mOsm/kg H2O. She was given dDAVP, and again her urine output decreased and urine osmolality increased. Urine output was fully replaced with hypotonic saline. Her PNa was 122 mM. Nevertheless, her condition deteriorated suddenly, and she died with autopsy-proven brain stem herniation.

**Question 2B**
Which ONE of the following choices best explains why this patient developed brain stem herniation?

- a. She had unique brain cell pathology
- b. She had a greater number of brain cells for her size
- c. Her brain was exposed to a greater degree of hyponatremia
- d. She was given too much dDAVP

Answers from the membership (Figures 3 and 4).

**Question 2A:** a. Positive balance for Na

**Question 2B:** c. Her brain was exposed to a greater degree of hyponatremia
Discussion of Case 2
This case emphasizes two main points. First, it illustrates the reliability of calculating separate balances for water and for Na⁺—we call this a *tonicity balance*—for determining why the PNa increased (11). In contrast, the more commonly used approach calculates an electrolyte-free water balance. Although the latter will confirm that the PNa rose, it will not reveal why the PNa changed or what the goals for therapy should be to restore the tonicity and composition of both the ECF and the intracellular fluid (ICF) compartments (Table 1). Second, we emphasize that it is the PNa in arterial rather than in venous blood that best quantifies the risk for brain cell swelling.

**Clinical Diagnosis.** The patient had an extremely large diuresis (projected over 24 h, she would have lost half her total body water). Because her urine osmolality was 120 mOsm/kg H₂O, the basis for the polyuria was a water diuresis (her osmole excretion rate, however, was increased: 120 mOsm/L × 14.4 L = 1728 mOsmol/d). Because she had hypernatremia in this interval and her urine flow rate declined dramatically when dDAVP was given, her water diuresis undoubtedly was due to lack of vasopressin’s action as a result of CDI. Conceivably, destruction of vasopressin by a circulating vasopressinase could account for this picture (12). We emphasize that balances—-for determining why the PNa changed or what the goals for therapy should be to restore the tonicity and composition of both the ECF and the intracellular fluid (ICF) compartments (Table 1). Second, we emphasize that it is the PNa in arterial rather than in venous blood that best quantifies the risk for brain cell swelling.

**Balance for Water.** The input of water over 5 h was 3 L (as 3 L of isotonic saline). Because the overall urine flow rate was 10 ml/min for 300 min, water output also was 3 L. Therefore, she did not have an important negative balance for water (nonrenal water loss is trivial in this period). The hypernatremia likely is due to positive Na⁺ balance.

**Positive Balance for Na⁺.** The 3 L of isotonic saline delivered 450 mmol of Na⁺ (and Cl⁻). Urine osmolality is 120 mOsm/kg H₂O, so the maximum Na⁺ + K⁺ concentration in the urine is 60 mM (plus 60 mM anions, Cl⁻ and some HCO₃⁻). With the usual rate of urea excretion, urine Na⁺ + K⁺ concentrations would be even less; in fact, the measured value was 50 mM (13). The output of Na⁺ + K⁺ was 150 mmol (3 L × 50 mM) in this initial 5-h period. Therefore, there was a positive balance of 300 mmol of Na⁺ + K⁺.

**Goals for Therapy.** For removing the surplus of 300 mmol of Na⁺, the patient was given dDAVP to decrease the urine volume and, more important, to raise the urinary concentrations of Na⁺ + K⁺ (which rose to 175 mM) (13). For ridding the 300 mmol of Na⁺, the infusate was half-isotonic saline (approximately 75 mM, 100 mM less than the urine Na⁺ + K⁺ concentration), and the rate of infusion should be equal to the urine output until 3 L of urine is excreted. As soon as the PNa reaches 140 mM, the patient should have received intravenous fluids with the same Na⁺ concentration as in the urine and at a rate equal to that of urine flow to keep the PNa in this safe range. Note that dDAVP quickly caused the urine to become hypertonic. Unfortunately, this was not the therapy given to the patient—she continued to receive hypotonic saline at a rate equal to the urine output, so her PNa fell to dangerously low levels.

**Comment on Audience Responses.** In each category, fewer than one third of the respondents recognized the importance of surplus Na⁺. Had a tonicity balance been calculated, the positive balance of Na⁺ would have been obvious.

**Question 2B**
The vast majority of respondents concluded correctly that her brain was exposed to a greater degree of hyponatremia.

**Explain Why the PNa Fell.** For the PNa to decline by approximately 15% (140 to 124 mM) from only one cause, there had to be either a positive balance of 4.5 L of water (15% of 30 L) or a deficit of approximately 480 mmol of Na⁺ (a decrease of 16 mmol Na⁺/L of total body water × 30 L) (14). Because the infusion volume was equal to the previous hour’s urine output, it is very unlikely that the patient was given 4.5 L of “occult” water (e.g., as ice chips) during this interval. Therefore, we must

| Table 1. Comparison of EFW and tonicity balances when the PNa changes* |
|------------------|----------|---------|----------|----------|
|                  | Na + K (mmol) | Water (L) | EFW (L) | Therapy from Balances |
| Patient given 3 L of isotonic saline |                     |          |          |
| input            | 450       | 3        | 0        | +2 L      |
| output           | 150       | 3        | 2        | 0 Na      |
| balance          | +300      | 0        | −2       | −300 mmol Na |
| Same patient with no intravenous fluid administration, and urine output was unchanged |                     |          |          |
| input            | 0         | 0        | 0        | +2 L      |
| output           | 150       | 3        | 2        | 0 Na      |
| balance          | −150      | −3       | −2       | +150 mmol Na |

*Two situations are described in which the plasma Na concentration (PNa) rose from 140 to 150 mM in a patient with 30 L of total body water (TBW); only the volume of isotonic saline infused in the two settings differed. In both settings, there is a negative balance of 2 L of electrolyte-free water (EFW). Nevertheless, the goals for correcting the hypernatremia become clear only after calculating a tonicity balance.
turn our attention to a huge Na\(^{+}\) loss. It is possible that she had cerebral salt wasting, even though the diagnosis cannot be confirmed until the patient has a contracted ECF volume (15). In addition, “desalination” of several of the liters of isotonic saline that was administered in the perioperative period could play a role (16). While Na\(^{+}\) is being excreted, the medullary tonicity rises because dDAVP was administered (urine [Na\(^{+}\)] rose to 300 mM). This resulted in a gain of 1 L of pure water for every 2 L of saline that was infused. Hence, a combination of water gain and Na\(^{+}\) loss caused the fall in the P\(Na\).

**Explain Why Brain Herniation Occurred.** Brain cell swelling depends on the P\(Na\) near brain cells. If a hypotonic solution is infused rapidly, then the arterial P\(Na\) will decline more than the brachial venous P\(Na\) (Figure 5) (17). Because blood flow to the brain and skeletal muscle is approximately 1 L/min at rest and the size of the ICF compartment of the brain is approximately 5\% of that of skeletal muscle (1 versus 20 kg lean body wt), brain cells will swell much more rapidly (the same volume enters both organs, but each brain cell must swell by a larger amount). Because the brain is in the bony skull, intracranial pressure rises and herniation can result. Moreover, simply looking at the brachial venous P\(Na\) underestimates the very serious risk for the patient.

**The Specific Danger.** When the actions of dDAVP wore off, the urine output rose to 25 ml/min, equivalent to the excretion of 1.5 L/h water. Replacing this urine output with hypotonic saline in this setting is not dangerous as long as the same volume of water will be lost in the current hour. In contrast, if dDAVP is given, then there likely would be an abrupt and large fall in the urine output. With a large positive water balance, arterial P\(Na\) will decrease significantly. Therefore, *not* giving an infusion in this hour is the correct therapy, especially if the patient has hyponatremia. Moreover, giving such a large infusion of water (hypotonic saline) while the urine output is reduced is a fatal error (Figure 5).

**Case 3: Gabriel Danovitch**

A 35-yr-old Caucasian man with type 1 diabetes and chronic kidney disease (CKD) received a one-haplotype matched living-donor transplant from his sister in June 2004. No pretransplantation sensitization was noted. The early posttransplantation course was unremarkable, and the baseline serum creatinine level was 1.6 mg/dl. He received tacrolimus (maintaining trough levels of approximately 10 mg/dl), mycophenolate mofetil (MMF) 2000 mg/d, and prednisone 10 mg/d at 3 mo after transplantation and 5 mg/d by 6 mo after transplantation.

At 6 mo after transplantation, the MMF was held by the patient for 3 to 4 d because of an episode of diarrhea and then restarted at a dose of 1500 mg/d. At 12 mo after transplantation, his creatinine level increased asymptotically to 2.4 mg/dl. The patient adhered to his immunosuppressive regimen.

A presumptive diagnosis of acute rejection was made and an "empiric" steroid pulse was given (Solu-Medrol 5 mg/kg for 3 d). Allograft function was unchanged, and he was referred back to the transplant program for further work-up. A renal biopsy was planned, but the pretransplant ultrasound showed moderate hydronephrosis. An antegrade nephrostomy was placed, and a nephrograms subsequently showed distal ureteric obstruction. Urinalysis revealed 2\% protein with more than 100 RBC per high-power field (hpf) and 60 white blood cells (WBC)/hpf; urine was sent for culture and cytology. Serum creatinine remained 2.4 mg/dl. Renal biopsy showed a dense interstitial infiltrate on light microscopy.

**Question 3**
Which ONE of the following choices offers the best therapeutic option?

a. Repeat the steroid pulse. If the creatinine level remains unchanged, then re-biopsy and give Thymoglobulin if the infiltrate persists.

b. Give Thymoglobulin or OKT3
c. Give antibiotics for presumed urinary tract infection with pyelonephritis
d. Do nothing; await further analysis of the biopsy

Answer from Dr. Danovitch and the membership.

Question 3: d. Do nothing; await further analysis of the biopsy

Discussion of Case 3

Whenever possible, the results of key laboratory tests should be reviewed before assuming that acute rejection is present. In a patient with deteriorating renal function, persistence of a dense interstitial mononuclear infiltrate (Figure 7) despite relief of obstruction suggests acute rejection. Transient discontinuation of MMF also may increase the subsequent development of acute rejection (18). If indeed this were an acute rejection, then either option a or option b would have been reasonable answers. However, this compliant patient was taking high-dosage immunosuppression and the MMF had been discontinued only briefly. It is unusual for acute rejection to occur at this stage posttransplantation. Moreover, approximately 75% of acute rejection episodes respond to steroids. For these reasons, there should have been a high level of suspicion that the mononuclear infiltrate may not have represented typical acute rejection.

Causes other than acute rejection should have been considered to explain the interstitial infiltration. A polymorphonuclear infiltrate would, of course, suggest acute pyelonephritis. Drug-induced interstitial nephritis can be difficult to differentiate from acute rejection, but in this case, there were no obvious culprits. Posttransplantation lymphoproliferative disease can present as graft dysfunction. The finding of a high proportion of plasma cells would suggest this diagnosis, but the patient had not received immunosuppression with the lymphocytic depletonal agents (Thymoglobulin or OKT3), which are associated with posttransplantation lymphoproliferative disease (19).

Careful inspection of the lymphocytic infiltrate revealed viral inclusions that were suspicious of polyoma (BK) virus infection (Figure 8). The pathologists and clinicians elected to wait until this diagnosis could be confirmed with special histologic stains (Figure 9) and to determine whether the BK virus genome could be identified in blood and urine.

Polyoma virus–associated nephropathy is increasingly being recognized as a cause of kidney transplant failure that may affect up to 10% of patients (20). Most cases are caused by the BK virus and occur in intensely immunosuppressed patients, who usually are receiving the combination of tacrolimus, MMF, and steroids. Once diagnosed, the dose of immunosuppression should be reduced. The two principal antiviral agents that have...
been used to manage the infection are leflunomide and cidofovir, but randomized trials are not yet available. The success rate of intervention is increased by early diagnosis. Screening for this infection has been recommended (testing for BK virus replication in the urine) in the following settings: At 3-mo intervals during the first 2 yr after transplantation, in the setting of allograft dysfunction, and when allograft biopsy is performed. A positive screening test should be confirmed by quantitative assays in blood and urine. Definitive diagnosis requires allograft biopsy. In this case, treatment with antibiotics (option c), until the correct diagnosis was made, would have been harmless.

Case 4: Gabriel Danovitch
A 26-yr-old African-American woman received her first deceased-donor transplant at age 21. After initially functioning well, the transplant was lost in the third month because of repeated cell-mediated rejection. She developed high levels of preformed antibodies and had a positive cross-match to several potential deceased donors. Her ABO-compatible brother, a one-haplotype match, donated a kidney. Standard cytotoxic and FACS cross-matching were repeatedly negative.

Transplant surgery was uneventful, and the graft initially functioned well. After 4 d of anti-thymocyte polyclonal antibody, she received standard doses of cyclosporine, MMF, and steroids. By day 7, the serum creatinine was 1.2 mg/dl. On day 8, her urine output decreased and the serum creatinine increased to 2.4 mg/dl. An ultrasound with color Doppler showed good flow without obstruction. Urinalysis revealed 1+ protein with no cellular elements. Her biopsy displayed evidence of tubular injury with occasional perivascular polymorphs (Figures 11 and 12).

Question 4
Which ONE of the following choices offers the most likely diagnosis for her allograft dysfunction?

a. Delayed posttransplantation acute tubular necrosis (ATN)
b. Early pyelonephritis
c. Antibody-mediated rejection
d. Subclinical acute cell-mediated rejection.

Answer from Dr. Danovitch and the membership.
Answer to Question 4: c. Antibody-mediated rejection

Discussion of Case 4

Option a: incorrect. The histologic features are consistent with ATN (option a), but at day 8, this diagnosis is unlikely without some new precipitating insult. Peritubular capillary infiltrates are unusual in ATN.

Option b: incorrect. If pyelonephritis were present, then various clinical signs, pyuria, and an interstitial polymorphonuclear leukocyte infiltrate should have been present. Pyelonephritis also is unusual so soon after surgery.

Option c: correct. The patient is at risk for antibody-mediated rejection because her first transplant failed and she had a high level of preformed antibodies. The minimal findings seen on light microscopy can lead to a mistaken diagnosis of ATN. The introduction of the C4d stain (the “footprint” of antibody-mediated rejection) now avoids this error. Donor-specific antibodies (DSA) also are present. Therapy requires high-dose intravenous Ig (IVIg) either alone or with plasmapheresis (Figure 11).

Option d: incorrect. An interstitial infiltrate involving tubules (tubulitis) is present even in borderline cases of cell-mediated rejection. Subclinical rejection refers to these findings that are seen on so-called “protocol biopsies” that are performed at fixed intervals after transplantation in the absence of any clinically detectable deterioration in renal function.

Acute allograft failure at the end of a seemingly uneventful first posttransplantation week demands an immediate diagnostic response. A normal renal ultrasound and color Doppler rule out acute obstruction or a vascular catastrophe, making a histologic diagnosis an urgent requirement because the clinical differentiation from among rejection, nephrotoxicity, and other causes of
Graft dysfunction is notoriously unreliable. Initially, light microscopy suggested a diagnosis of ATN (Figure 11), but in the absence of a precipitating cause and in the presence of excellent graft function, especially at this early stage posttransplantation, that diagnosis is virtually excluded. As noted above, the diagnosis of pyelonephritis also is unusual at such an early posttransplantation stage, and the absence of clinical and histologic findings that are consistent with this disorder exclude it from consideration. Although acute cellular rejection typically occurs later in the posttransplantation course, early rejections may occur particularly in recipients of living-donor transplants; however, the absence of an interstitial lymphocytic infiltrate with tubulitis excludes this diagnosis (Figure 12).

This patient is at risk for both antibody-mediated (AMR) and humoral rejection because of her history and the presence of preformed antibodies. The use of sensitive cross-matching techniques has made antibody-mediated hyperacute rejection a rarity. The disorder typically led to rapid graft loss either immediately or within the first few posttransplantation days. However, even in the absence of a positive cross-match, early rejections may occur particularly in recipients of living-donor transplants; however, the absence of an interstitial lymphocytic infiltrate with tubulitis excludes this diagnosis (Figure 12).

The diagnosis of AMR has been greatly facilitated by the availability of the C4d immunostain, which is strongly associated with the presence of anti-human leukocyte antibody DSA (21). C4d is an advanced product of complement activation, and its diffuse deposition on peritubular capillaries (Figure 13) has been described as the “footprint” of humoral rejection (22). Type 1 AMR has an ATN-like histology and minimal inflammation, type II describes a capillary glomerulitis with margination and thrombosis that can mimic calcineurin inhibitor–related thrombotic thrombocytopenic purpura, and type III is characterized by arterial involvement.

The discrete histologic findings that are described in this case are typical of type 1 AMR. Tubular injury is nonspecific at this stage posttransplantation, and the peritubular capillary infiltrate has only an approximately 50% concordance with AMR. If the C4d stain had not been performed, then the diagnosis easily could have been missed and treatment delayed. The diagnosis was confirmed by the finding of DSA. Treatment typically consists of IVlg in high dose (2 g/kg) or low dose (0.4 g/kg), often combined with plasmapheresis (23). The administration of IVlg may be followed by the development of so-called “osmotic nephropathy,” a form of acute renal failure that is caused by the high osmotic pressure of the infusate. Although renal function typically improves rapidly, the renal dysfunction that is caused by the IVlg infusion produces a confusing clinical picture if it is not recognized.

**Case 5: Ronald Falk**

Mildly abnormal kidney function was recently discovered in a 27-yr-old African-American man. He had childhood asthma and was taking lithium for a bipolar disorder, nutritional supplements for body-building, and acetaminophen for associated muscle pain. He was athletic appearing with a BP of 130/72 mmHg. Other physical findings included widely scattered nevi; several cherry angiomas on his back; and small, pigmented, hardened nodules on his face. These skin findings had been present for “some time.” Laboratory studies on admission: Serum electrolytes (in mM) were 140 Na, 4.0 K, 105 Cl, 25 CO₂; blood urea nitrogen (BUN) was 25 mg/dl, creatinine was 1.6 mg/dl, calcium was 10.8 mg/dl, albumin was 3.4 g/dl, and hemoglobin was 14.1 g/dl. All other chemistries, including the usual serologic studies, were unremarkable. Urinalysis revealed 1+ protein and 1+ heme. The urine sediment showed 3 to 5 RBC/hpf, 4 WBC/hpf, and coarsely granular casts. The urine protein-creatinine ratio was 0.7. Ultrasound revealed two 11-cm kidneys with mild echogenicity.

Clinical course: The patient returned 1 mo after discontinuing acetaminophen and all nutritional supplements. His serum creatinine remained 1.6 mg/dl. A kidney biopsy revealed com-
pletely normal glomeruli and extensive tubulointerstitial nephritis (TIN) with occasional eosinophils and a loosely formed granuloma. There was one obsolescent glomerulus.

**Question 5A**
Which ONE of the following choices is the most likely diagnosis for this patient’s kidney disease?

a. TIN from lithium  
b. TIN from a dietary supplement  
c. Analgesic nephropathy  
d. Sarcoidosis  
e. Sjögren syndrome

**Question 5B**
Which ONE of the following choices would most likely confirm the correct diagnosis?

a. Response to a short course of glucocorticoids  
b. Response to discontinuation of lithium  
c. Response to prolonged discontinuation of the analgesics

d. Biopsy of a salivary gland  
e. Biopsy of a facial nodule

**Answers from Dr. Falk and the membership (Figures 14 and 15).**

**Question 5A:** d. Sarcoidosis  
**Question 5B:** e. Biopsy a facial nodule

**Discussion of Case 5**

This athletic young man developed renal insufficiency of uncertain duration and origin. Historical clues and preliminary clinical evaluation suggested an interstitial process, yet short-term elimination of potential causes by discontinuing acetaminophen and dietary supplements did not improve his renal function. A kidney biopsy revealed normal glomeruli but an extensive granulomatous TIN with occasional eosinophils.

Pharmaceutical agents and illicit drugs are the most common causes of acute TIN, but other causes include infections, idiopathic conditions, the syndrome of TIN and uveitis, and sarcoidosis. It is more likely that this patient has a chronic interstitial nephritis (CIN) with his history of stable renal dysfunction.

The causes of CIN include drugs; metabolic disturbances; and immune-mediated abnormalities, including Sjögren syndrome and sarcoidosis. Sjögren syndrome causes an autoimmune TIN associated with dry mouth and eyes, enlarged salivary glands, arthralgias (seen in up to 60%), and Raynaud’s phenomenon (30%). Less commonly seen are cutaneous, pulmonary, and renal manifestations of the disease. Granulomas would be an unusual histologic finding in Sjögren syndrome.

This black man most likely has sarcoidosis. His mildly elevated serum calcium concentration and the loose granuloma seen on biopsy add to the likelihood of this diagnosis. Hypercalciuria and/or hypercalcemia are found in 50% of patients with sarcoidosis, and nephrolithiasis is found in up to 14%. The disordered calcium metabolism is caused by calcitriol production by the granulomata. The vitamin D excess causes hyperabsorption of dietary calcium, subsequent suppression of parathyroid hormone secretion, and hypercalciuria. In this setting, renal calcium excretion prevents hypercalcemia. However, when renal dysfunction, from any cause, supervenes, hypercalcemia may occur. Hypercalcemia is, in fact, a more common cause of renal dysfunction than is granulomatous interstitial nephritis.

Confirmation of the diagnosis of sarcoidosis may prove difficult as shown by the responses from the membership (Figures 14 and 15). Both the training program directors and other ASN members largely voted for one of two options: “Treat with a course of glucocorticoids” or “Biopsy a facial nodule.” In fact, the facial nodule biopsy revealed a necrotizing granulomatous lesion (24). Not known to the audience, this patient had hilar adenopathy as well, so this constellation of findings makes sarcoidosis the most likely diagnosis (25,26).

In general, the prognosis of patients with sarcoidosis is most difficult to predict at the time of presentation. At least half of patients improve without any kind of therapy—some very slowly, and some very quickly. Approximately 20% of patients stabilize with glucocorticoid therapy, whereas, unfortunately, one fourth of
patients have progressive disease even with glucocorticoid or other immunomodulating drugs.

Most agree that glucocorticoids should be administered to patients with severe lung disease with or without upper airway obstruction, posterior uveitis and vision loss, central nervous system disease, cardiac disease, disfiguring skin disease, and progressive kidney disease. All of these target-organ dysfunctions may improve. In this case, prednisone therapy was used for 3 to 4 mo, and at the end of therapy, the patient's creatinine stabilized at 0.9 mg/dl, where it has remained for almost 3 yr (Figures 16 and 17).

Case 6: Ronald Falk

A 23-yr-old Caucasian woman with an unremarkable medical history presented with 3 d of malaise and diarrhea. She denied any history of urinary tract infection or recent illness. She lives with her husband and 3-yr-old child and works at home. There is no family history of kidney disease. Medications are daily multivitamins and ibuprofen once or twice a month for headaches. Physical examination revealed BP of 155/86 mmHg; there were no other relevant findings. Initial laboratory studies included serum creatinine 2.1 mg/dl; BUN 50 mg/dl; urinalysis 1+ proteinuria, bland sediment; 24-h urine 1.6 g of protein; and complete blood count (WBC 18 K/µl, hemoglobin 13 g/dl, platelets 120 K/µl). Renal ultrasound revealed bilaterally echoric kidneys of normal size and no structural abnormality.

Question 6A
Which ONE of the following choices provides for the most likely diagnosis of this patient's illness?
   a. HIV nephropathy
   b. Focal segmental glomerulosclerosis
   c. Nonsteroid anti-inflammatory drug–induced acute interstitial nephritis
   d. Acute renal failure of unknown cause

Two days later, she became increasingly more somnolent and oliguric (producing only 160 ml of urine/24 h), and her BUN and creatinine rose to 65 and 3.8 mg/dl, respectively. Repeat complete blood count revealed WBC 25 K/µl, hemoglobin 9.5 g/dl, and platelets 95 K/µl. Hemodialysis (HD) is initiated. A kidney biopsy is performed.

Question 6B
Which ONE of the following histologic findings is most likely to be found?
   a. Focal segmental glomerulosclerosis
   b. Acute tubular necrosis
   c. Thrombotic microangiopathy
   d. Class IIIa lupus nephritis

Question 6C
Which ONE of the following therapeutic options would be best?
   a. Ciprofloxacin
   b. Plasma exchange
   c. Oral prednisone
   d. Pulse Solu-Medrol
   e. Supportive care

Answers from Dr. Falk and the membership (Figures 18, 19, and 20).

Question 6A: d. Acute renal failure of unknown cause
Question 6B: c. Thrombotic microangiopathy
Question 6C: e. Supportive care
Discussion of Case 6

The salient clinical features in this case are 3 d of diarrhea, hypertension, renal insufficiency, and thrombocytopenia. Two days later, this patient became increasingly somnolent and oliguric with a rise in both her BUN and serum creatinine. This patient has confirmed infection with Shiga-toxin Escherichia coli (STEC). The primary habitat of this Gram-negative organism is the intestine of large animals, such as

Figure 18. Answers from the membership: Responses to question 6A.

Figure 19. Answers from the membership: Responses to question 6B.

Figure 20. Answers from the membership: Responses to question 6C.

Figure 21. Pathology of hemolytic uremic syndrome demonstrating in A and B narrowed glomerular capillary lumens, endothelial cell swelling, and damaged and widened subendothelial spaces (courtesy of Drs. David Thomas and Jennifer Slickers).
cows or goats. Intestinal excretion and subsequent re-colonization maintain the reservoir and promote continuing exposure to *E. coli* (27).

A secondary habitat is water, soil, or sediment. STEC travels on neutrophils and platelets, attaching to the Gb3 receptor on endothelial cells, where they cause endothelial cell injury. STEC and endothelial cell interactions produce an inflammatory storm of IL-1, IL-6, and TNF, further upregulating the Gb3 receptor expression. Endothelial injury and activation of the coagulation cascade results in the clinicopathologic presentation of the hemolytic uremic syndrome (HUS).

The pathology of HUS is well depicted in the accompanying photomicrograph (Figure 21). The typical clinical course begins with ingestion of the toxin followed by abdominal pain, fever, and vomiting and the production of bloody diarrhea. The latter typically improves spontaneously with resolution of the disease or a more virulent expression of the HUS (28,29).

Therapy of the HUS requires supportive care, controlling BP, and avoiding antimotility agents. The debate over the utility of antibiotics remains unresolved. Antithrombotics or anticoagulants do not work, and they increase the risk for stroke. Glucocorticoids may improve renal function, but they offer no appreciable long-term benefit. There is no evidence that plasma exchange or plasmapheresis in diarrhea-induced HUS exerts a positive effect. Whether removing the toxin with antibodies or small molecules proves to be an effective therapy remains to be explored.

Outbreaks of diarrhea-induced HUS that have occurred at state fairs have gained wide coverage in the media. During the 2004 North Carolina State Fair, 108 people were infected by an *E. coli*–induced outbreak, and 15 children developed life-threatening disease from exposure to animals at the petting zoo. The patient discussed above did remarkably well with good supportive care and has had a complete resolution of her clinical renal dysfunction.

**Case 7: Joanne Bargman**

A 30-yr-old Caucasian man with “unspecified nephritis” and no residual renal function had been on HD for 18 mo. His target weight was 70 kg, and average interdialytic weight gain was 5.2 kg. He failed to restrict dietary Na and water despite repeated warnings. Frequent episodes of cramping, nausea, weakness, and hypotension complicated his dialyses, especially toward the end of each session. His dialysis prescription was 4 h thrice weekly, blood pump speed was 400 ml/min, dialysis flow was 760 ml/min, and dialysate (Na) was 140 mM. His average pre- and postdialysis BP were 165/95 and 150/90 mmHg, respectively, but it often fell to 100/70 mmHg toward the session’s end. His predialysis serum (Na) was 138 mM. Medications included ramipril and amlodipine for his hypertension. The patient refused peritoneal dialysis (PD) or more frequent hemodialyses.

**Question 7**

Which ONE of the following therapeutic options would be best for managing the patient’s intradialytic hypotension?

**a. Increase his target weight**

**b. Ramp ultrafiltration: Remove fluid more rapidly at the start of dialysis and more slowly thereafter**

**c. Ramp ultrafiltration: As in b and ramp Na: 143, 139, and 135 mM for the first, middle, and final thirds of his dialysis sessions, respectively**

**d. Ramp Na: Set the dialysate Na at 150, 145, and 140 mM for the first, middle, and final thirds of the session, respectively**

**e. Withhold ramipril and amlodipine therapy on the day of dialysis**

**Answers from Dr. Bargman and the membership (Figure 22).**

**Question 7:** c. Ramp ultrafiltration: As in b and ramp Na: 143, 139, and 135 mM for the first, middle, and final thirds of his dialysis sessions, respectively.

**Discussion of Case 7**

Episodes of hypotension during conventional HD occur commonly and can be distressful and adversely affect the patient’s quality of life. Repeated falls in BP cause a more rapid decline in residual kidney function in both HD and PD patients (30), and intradialytic hypotension is associated with shortened survival (31). The many causes of hypotension during HD include the following.

**Plasma Volume Depletion.** To achieve euolemia after interdialytic gain of several kilograms of salt and water, the amount of fluid removal over 4 h of HD often approximates that of plasma volume (PV). If the PV were not re-filled during the course of ultrafiltration, then circulatory collapse would develop rapidly. The re-filling of the PV derives principally from the interstitial compartment (ISF) of the ECF. This transcompartmental movement of fluid is not problematic when the ISF is expanded and there is no impediment to its mobilization. However, if the ISF is not that “full” and/or there are constraints to its mobilization (e.g., transient oncotic or tonicity pressure differences between PV
and ISF, “3rd spacing” of a portion of the ISF) then there may be diminished re-filling of the PV, leading to a fall in BP. A remediable cause of PV depletion is ultrafiltering to a target weight lower than the true euvoicemal weight. When the appetite of a previously uremic patient improves and gains in lean body mass are achieved, the target weight for dialysis must be increased. Failing to make this adjustment will cause PV depletion.

Rapid dialytic removal of uremic solutes by HD may reduce the toxicity of the ECF more quickly than that of the ICF. This transient difference in toxicity between the compartments causes plasma water to move into the relatively hypertonic cells. This flux may cause headache and transient depletion of the PV.

Cardiac Dysfunction. Maintenance of BP depends on the balance of cardiac output and peripheral vascular resistance. Suboptimal cardiac function, therefore, can cause or contribute to intradialytic hypotension. Patients who reach dialysis after years of CKD and hypertension commonly have left ventricular hypertrophy associated with a stiff left ventricle and diastolic dysfunction. In the face of vigorous ultrafiltration, the thickened left ventricle may not effect sufficient output to prevent a fall in BP. Ischemic cardiac dysfunction may manifest as either systolic or diastolic failure or some combination of the two. Intracardiomyocytic fibrosis from hyperparathyroidism or some other uremic progenitor also may adversely affect cardiac function. Finally, pericardial disease that leads to fibrosis and cardiac constriction also can affect detrimentally optimal function of the heart.

Autonomic Vascular Tone. Autonomic neuropathy that is associated with diabetes or the uremic state, per se, can affect baroreceptor sensing and response to hypovolemic and hypotensive states. Sympathetic responses also may be affected by net heat gain during dialysis and by the use of antihypertensive agents that are sympathetic or vasodilatory. Finally, abnormal venous compliance can lead to pooling of the blood peripherally, compromising venous return to the heart and thereby diminish cardiac output (reviewed in [32]).

Least Correct Answers

a. Increasing the target weight would reduce net fluid removal, at least at the outset of HD. This reduction of ultrafiltration would minimize the incidence of intradialytic hypotension and its symptoms. However, the patient is likely to have the same interdialytic salt and water intake, so the same problem eventually would recur, albeit at a greater weight and total fluid volume. The resulting chronic hypervolemia likely would lead to deleterious changes in left ventricular geometry and an increase in sympathetic traffic, so although increasing the target weight may help to relieve dialysis-associated hypotension in the short term, it will not be effective in the long term.

b. Ramping ultrafiltration refers to the more rapid removal of fluid early in the session followed by less fluid removal later. The slower rate of fluid removal later in the dialysis allows more time for the ECF to re-fill the “shrink-removal later. The slower rate of fluid removal later in the session followed by less fluid removal, at least at the outset of HD. This reduction of ultrafiltration would minimize the incidence of intradialytic hypotension and its symptoms. However, the patient is likely to have the same interdialytic salt and water intake, so the same problem eventually would recur, albeit at a greater weight and total fluid volume. The resulting chronic hypervolemia likely would lead to deleterious changes in left ventricular geometry and an increase in sympathetic traffic, so although increasing the target weight may help to relieve dialysis-associated hypotension in the short term, it will not be effective in the long term.

Case 8: Joanne Bargman

A 42-yr-old Caucasian woman with CKD from “glomerulonephritis” started PD in 1992. She received a deceased-donor kidney transplant in 1996, but chronic allograft nephropathy caused her to restart PD in 2002. She did very well on PD and worked as a legal secretary. Her dialysis prescription was 2.5 L × 3 exchanges overnight, with a 2-L “last fill.” Her transplant kidney GFR was 6 ml/min, and urine volume was 1100 ml/d.
Medications were low-dose prednisone, MMF, and mupirocin at the catheter exit site.

At a routine clinic visit, her exit site was erythematous with some dried pus on the gauze dressing. The tunnel was not swollen, and no pus could be expressed from the catheter tunnel. A swab that was taken of the pus at the exit site grew *Pseudomonas aeruginosa*.

**Question 8A**
Which ONE of the following choices offers the best course of action?

a. Change mupirocin to gentamicin sulfate cream at the exit site  
b. Hospitalize for a course of intravenous gentamicin  
c. Remove catheter and re-implant a new one at the same visit  
d. Administer a trial of oral quinolones  
e. Remove the PD catheter, insert a tunneled internal jugular (IJ) catheter, and transfer to HD

Two days after the clinic visit, she returned with fever, mild abdominal pain, and cloudy PD fluid that had a WBC of $2000 \times 10^6$, and the culture grew *P. aeruginosa*. She received intraperitoneal tobramycin and ceftazidime, and the PD catheter was scheduled for removal. A tunneled IJ line was inserted for HD. Despite the delay in catheter removal, she felt much better by the second day of admission. The PD fluid cell count decreased to $300 \times 10^6$. By the third day, the PD cell count was $<100$, she became pain-free, and cultures from day 2 revealed no growth.

**Question 8B**
Which ONE of the following choices offers the most appropriate next step?

a. Cancel the catheter removal and continue PD  
b. Decide about catheter removal after observing for 2 to 3 d to determine whether the PD fluid remains clear  
c. Failed PD requires permanent HD  
d. Remove the catheter and plan to re-implant it in several weeks  
e. Her rapidly improved peritonitis allows for discontinuation of the intraperitoneal antibiotics and continuation of PD

Answers from Dr. Bargman and the membership (Figures 23 and 24).

**Discussion of Case 8A**

This stable PD patient developed a symptomatic *P. aeruginosa* exit-site infection despite using mupirocin. Although infection at the catheter exit site can be uncomfortable and unsightly, the principal concern is that the infecting bacterium will migrate along the catheter into the subcutaneous tunnel. Tunnel infections cause tenderness, swelling, and erythema along the catheter track. Even if asymptomatic, the bacteria can migrate into the peritoneal cavity, causing bacterial peritonitis. When the same organism is cultured at the exit site and in the peritoneal fluid, it is assumed that this migration has occurred. *Pseudomonas* peritonitis is particularly difficult to treat, because the organism can attach to bioprosthetic materials such as the catheter and secrete a protective biofilm. Spontaneous *Pseudomonas* peritonitis sometimes is eradicated with intraperitoneal antibiotics, but *Pseudomonas* peritonitis that arises from an exit-site infection rarely can be treated successfully without catheter removal (35).

**Least Correct Answers to Question 8A**

a. Change her exit-site mupirocin ointment to gentamicin sulfate cream. Prophylaxis with mupirocin ointment at
the catheter exit site reduces infections by approximately 50%, as shown by retrospective studies (36). However, mupirocin exerts its greatest efficacy against Gram-positive organisms, allowing the resistant ones, such as *Pseudomonas*, to become overrepresented in exit-site infections (37). A recent randomized, controlled trial compared prophylaxis with mupirocin and gentamicin. The topical aminoglycoside was as effective in preventing infection with *S. aureus* and was more effective in reducing exit-site infection with *Pseudomonas* (38). However, this was a study of prevention of exit-site infection, not treatment of established infection. Although the gentamicin sulfate would supply better antimicrobial coverage for the Gram-negative organism, it is unlikely to cure established *Pseudomonas* exit-site and tunnel infection without additional maneuvers.

b. Hospitalize for a course of intravenous gentamicin. Parenteral aminoglycosides may more effectively treat *Pseudomonas* infection, but it is costly, inconvenient for the patient, and still unlikely to eradicate the infection permanently. Furthermore, renal and vestibular aminoglycoside toxicity should be considered.

c. Arrange for catheter removal and re-implantation at the same session. This approach is acceptable but should be undertaken only after a trial of antibiotic therapy to eradicate the infection. Failed therapy may lead to eventual *Pseudomonas* peritonitis, which, when associated with exit-site and tunnel infection, almost always mandates catheter removal and an interim period on HD. Therefore, preemptive removal and replacement of the catheter (under anti-pseudomonal antibiotic coverage) may prevent an episode of peritonitis with this organism, but requires insertion of a temporary line for HD, and risks permanent technique failure.

e. Arrange for removal of the PD catheter, insertion of a tunneled IJ catheter, and transfer the patient to HD. *P. aeruginosa* infection is not sufficient reason to transfer the patient to HD. This is especially unappealing if transfer will entail placing another indwelling line with its attendant risk for infection.

**Most Correct Answer to Question 8A**

d. Administer a trial of oral quinolones. These agents are well absorbed, have good bioavailability, and are preferred to parenteral aminoglycosides. Quinolones will resolve the infection in some cases. When the exit-site infection is slow to resolve, a second agent with anti-pseudomonal activity probably should be added (39). If therapy with two agents does not work, then catheter removal and replacement should follow. Adding strength to the decision to remove the catheter, however, are reports of subsequent development of *Pseudomonas* peritonitis within a few months of clinical resolution of the *Pseudomonas* exit-site infection (40).

**Discussion of Case 8B**

The patient quickly developed PD peritonitis with *P. aeruginosa*, suggesting that the bacterium now has extended from the exit site into the peritoneum along the course of the catheter. The likelihood that this infection will be eradicated without removal of the catheter is very low (35). While arrangements were being made to remove the PD catheter, insert a tunneled line for interim HD, and then re-implant the peritoneal catheter 2 mo later, the patient was treated with intraperitoneal tobramycin and ceftazidime. After 3 d of therapy, the peritoneal WBC normalized and dialysate cultures became sterile. The question is what to do at this juncture.

**Least Correct Answers to Questions 8B**

a. Cancel the catheter removal and continue PD. This is a tempting option because removing the catheter, changing the patient to interim HD, and then re-implanting a new catheter several weeks later involves three different procedures, considerable expense, and a major upheaval to the patient’s life. However, the chances are very great that the peritonitis will recur soon after discontinuation of the antibiotics (35). Given that the whole catheter tract is infected with *P. aeruginosa*, a sticky, resistant organism, the best course of action is to remove the catheter.

b. Decide about catheter removal after observing for 2 to 3 d to determine whether the PD fluid remains clear. The peritonitis will not recur in 2 or 3 d while the patient is on potent anti-pseudomonal antibiotics. It likely will relapse, however, soon after discontinuation of the therapy. Therefore, nothing is apt to change after 2 or 3 d, and one should not be fooled into believing that the infection has been eradicated.

c. Failed PD requires that she be transferred to permanent HD. *Pseudomonas* peritonitis is a serious complication of PD but does not suggest that the therapy has failed, any more than an episode of bacteremia suggests that HD has failed as a renal replacement modality.

e. Her rapidly improved peritonitis allows for discontinuation of the intraperitoneal antibiotics and continuation of PD. Although there are no good studies to support this contention in PD, experience with infections for which there is co-infection of biomaterial suggests that prolonged antibiotic therapy is necessary. Sterile dialysate and normalization of the peritoneal leukocytosis is heartening, but it is very unlikely that the infection has been eradicated (this applies to any infecting bacterium, not just *Pseudomonas*). Therefore discontinuing antibiotics after just 2 or 3 d is unlikely to cure the infection.

**Most Correct Answer to Question 8B**

d. Remove catheter with plans to re-implant in several weeks. The chances of successful eradication of *Pseudomonas* infection in the face of exit-site, tunnel, and peritoneal infection are very small (35). Without antibiotics, the risk for re-infection is great; therefore, given the morbidity and even mortality associated with peritonitis, the risk-benefit ratio of this option is unfavorable.

Another option would be to remove and replace the dialysis catheter at the same setting (41). This combined procedure saves the patient placement of a temporary HD catheter, a period of in-center HD, and a second operation. Unfortunately, results with this one-step procedure are not as good for *Pseudomonas* as with other infections (42). Therefore, on balance, the most prudent approach would be to remove the catheter, continue antibiotic
coverage for at least 2 wk, and plan for catheter re-implantation after a minimum of 6 wk.

References
34. Song JH, Park GH, Lee SY, Lee SW, Lee SW, Kim M-J: Effect of sodium balance and the combination of ultrafiltration profile during sodium profiling hemodialysis on


