FLUID AND ELECTROLYTES: MITCHELL HALPERIN

CASE I:

Medical History: This is the fourth admission with similar findings for a 22-year old male who has mild cerebral palsy. He is normal between these episodes, taking the same medications for control of his depression. There was no history to suggest that he has diabetes mellitus.

Acute Episode: Each episode begins with extreme agitation and an inability to sleep. Intake of sweetened soft drinks increases markedly and is accompanied by crampy lower abdominal pain. The syndrome is not associated with the intake of alcohol or toxins and his P_{osm} gap has not been increased. On physical examination, there were no signs of ECF volume contraction. Acetone was detected on his breath and in plasma.

Laboratory Data (plasma): Before therapy:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH</td>
<td>7.20</td>
</tr>
<tr>
<td>HCO_{3}</td>
<td>mM</td>
</tr>
<tr>
<td>Anion gap</td>
<td>mM</td>
</tr>
<tr>
<td>Albumin</td>
<td>g/dl</td>
</tr>
<tr>
<td>Glucose</td>
<td>mg/dl (mM)</td>
</tr>
<tr>
<td>ß-hydroxybutyrate</td>
<td>mM</td>
</tr>
<tr>
<td>L-Lactate</td>
<td>mM</td>
</tr>
<tr>
<td>K</td>
<td>mM</td>
</tr>
<tr>
<td>Creatinine</td>
<td>mg/dl (µM)</td>
</tr>
<tr>
<td>Osmolality</td>
<td>mOsm/kg H_{2}O</td>
</tr>
</tbody>
</table>

Because diabetic ketoacidosis was considered, his plasma insulin level was measured and found to be in the normal range; his hemoglobin A_{1C} was not elevated (4.4 %).

Course: His treatment consisted of 1 L of isotonic saline and 1 L of D_{5}W and his acid-base values normalized within 24-h.
QUESTION 1:
Which ONE of the following choices is the most likely cause of his metabolic acidosis?

A. Diabetic ketoacidosis
B. Alcoholic ketoacidosis
C. Starvation ketoacidosis
D. D-Lactic acidosis
E. Sugar-induced acidosis

ANSWER TO QUESTION 1:

Background: The objective was to define the basis of the metabolic acidosis. Clearly, it was a form of metabolic acidosis with a large increase in the anion gap in plasma. Since the plasma $\text{HCO}_3^-$ concentration ($P_{\text{HCO}_3}$) returned to normal within 24-hours without receiving NaHCO$_3$, one can presume that the retained unmeasured anions were ones that could really be converted to HCO$_3^-$ by metabolism. Biochemical evidence indicated that at least part of the increase in the anion gap was due to ketoacidosis. By assay there was no L-lactic acidosis. The absence of GI stasis or antibiotic use made D-lactic acidosis unlikely and this was confirmed by direct assay. Nevertheless the combination of the very large intake of sugar, the GI complaints and the need for a source of precursors for ketoacidosis for the liver suggest an important role for the intestinal tract in the etiology of the ketoacidosis.

Discussion: Virtually all agreed that there was no solid basis for diabetic, alcoholic or hypoglycemic forms of ketoacidosis. Therefore, the possibility was raised that fermentation in the GI tract produced acetic acid and butyric acids which could serve as precursors for hepatic ketoacid synthesis. The source of the fuel for fermentation is likely to be the fructose in the sugar-containing soft drinks that he consumed. A very high adrenergic surge could convert the liver into a ketogenic mode because of inhibition of fatty acid synthesis at acetyl-CoA carboxylase. The reason for this adrenergic surge seemed to be the panic reaction and a caffeine overdose (1 L of most soda drinks have 100 mg of caffeine, and he drank many liters). Drug interactions could have contributed because his antidepressant down-regulates the cytochrome P$_{450}$ that metabolized caffeine. Finally his CNS lesion might have reduced his ability of oxidize $\beta$-hydroxybutyrate.

Final diagnosis: (E) Sugar (fructose) induced ketoacidosis plus other organic acids formed in the colon by fermentation. The development of the acidosis required the additional step of a high adrenergic surge (1).
CASE II:

Medical History: A 22-year old, 40-kg Asian female has myasthenia gravis. During the past 6 months she became listless, weak, developed a poor appetite leading to a weight loss of 3-kg. On physical examination in the Emergency Room her blood pressure was 60/40 mm Hg, pulse rate was 126/min, the jugular venous column height was below the sternal angle and there was no edema.

Laboratory Data (on admission and before therapy):

<table>
<thead>
<tr>
<th></th>
<th>Plasma</th>
<th>Urine (spot)</th>
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</thead>
<tbody>
<tr>
<td>Na (mM)</td>
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</tr>
<tr>
<td>K (mM)</td>
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<td>18</td>
</tr>
<tr>
<td>Cl (mM)</td>
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<tr>
<td>HCO₃ (mM)</td>
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<tr>
<td>BUN (Urea)</td>
<td>94 (34)</td>
<td>-</td>
</tr>
<tr>
<td>Creatinine</td>
<td>5.3 (460)</td>
<td>-</td>
</tr>
<tr>
<td>Osmolality</td>
<td>265</td>
<td>438</td>
</tr>
</tbody>
</table>

QUESTIONS 2 & 3:

2. With regard to the increment in her Pₙa concentration in first 24-hours, which ONE of the following choices would be safest?

A. 0 mM
B. 4 mM
C. 8 mM
D. 12 mM

Reference:

3. Which ONE of the following initial therapies would be most effective in preventing a CNS complication?

A. Hypertonic saline alone
B. Normal Saline alone
C. Half-isotonic saline alone
D. Rapid bolus of normal saline (150 mM) plus furosemide
E. Normal Saline plus DDAVP

ANSWERS TO QUESTIONS 2 & 3:

Diagnosis: This is a straightforward case of adrenal insufficiency with hyponatremia (113 mM), hyperkalemia (5.7 mM) and a very low excretion of potassium (K). Unfortunately an aggressive infusion of isotonic saline led to permanent brain damage [osmotic demyelination (ODS)]. Hence we need to re-think this ‘obvious’ mode of therapy.

Warning signs for impending ODS: First, hyponatremia accompanied by weight loss suggests that there is a catabolic state. Second, the very high BUN might cause a urea-induced osmotic diuresis when the GFR rises—this could explain why the sum of urinary Na and K concentrations ($U_{Na+K}$) decreased from near isotonic values to 1/2 isotonic values. This together with a rise in the urine flow rate may cause the plasma Na concentration ($P_{Na}$) to rise too rapidly when a large volume of isotonic saline is infused. Third, when cortisol is administered to patients with improved hemodynamic parameters, ADH levels will further decline and the distal delivery of filtrate will increase. These events may conspire to cause a rapid water diuresis and contribute to the development of ODS. Fourth, she had very reduced muscle mass (weight 40 kg). In this setting, the same negative water balance and/or positive Na balance will cause a much greater rise in her $P_{Na}$ because of her smaller total body water.

Answers: When first seen this patient’s $P_{Na}$ 12-hrs previously was unknown and it was clear that she had many risk factors for developing ODS. If I could go back in time and re-craft my therapy, I would set a maximum limit (not a target) for a rise in $P_{Na}$ of 4 mM in the first 12-24 hr. I would want to avoid a sudden water diuresis so I would administer dDAVP at the outset. I would give cortisol to improve her hemodynamic status as soon as possible to thereby diminish the need for rapid infusion of saline (1). As soon as the urine flow rate rose, one must monitor the $U_{Na+K}$. To avoid an unwanted rapid rise in the $P_{Na}$, the input and output concentrations of Na + K should be similar. Extra saline at a value close to the $P_{Na}$ should be given to re-expend the ECF volume (2).

Summary: My best guesses for the answers to the question are: Limit the $P_{Na}$ rise to < 4 mM in the 1st 24-hours. Give dDAVP plus less isotonic saline. Include cortisol in your initial therapy. Monitor the $U_{Na+K}$ if the urine output rises.

The correct answer for Question 2 is B, and the correct answer for Question 3 is E.
References:

TRANSPLANTATION: GABRIEL DANOVITCH

CASE III.

A 58 year old obese African-American female with hepatitis C and a history of gestational diabetes mellitus is scheduled to receive a deceased donor kidney from a 62 year old female who died of an intracerebral hemorrhage. Cold ischemia time is anticipated to be 28 hours. Prior to organ harvest the donor serum creatinine level rose from a baseline value of 1.2mg/dl to 1.9mg/dl though urine output remained high.

QUESTION 4:

Which ONE of the following immunosuppressive regimens would be best for this transplant candidate?

A. Tacrolimus; mycophenolate mofetil; standard taper to low dose corticosteroids
B. Tacrolimus; sirolimus; rapid total corticosteroid withdrawal
C. Cyclosporine; mycophenolate mofetil; standard taper to low dose corticosteroids
D. Mycophenolate mofetil; sirolimus; standard taper to low dose corticosteroids

ANSWERS TO QUESTION 4:

There is no ‘right’ answer to this question. While a legitimate case can be made for each of these protocols, the following factors should be part of the decision making process.

1. This patient is at high risk of developing posttransplant diabetes (PTDM) and insulin dependence because of her African-American ethnicity and the presence of hepatitis C and obesity. The magnitude of this risk would be further amplified by the use of tacrolimus-based protocols (as offered by options A and B). The risk of PTDM would be less with option C because the diabetogenicity of tacrolimus is two-to-three times that of cyclosporine. The risk would be least with option D because the protocol does not include a calcineurin inhibitor, although corticosteroids would still be required.
2. This patient is at high risk of developing posttransplant delayed graft function (DGF). This risk may be exaggerated by the use of sirolimus (options B and D).

3. The patient’s obesity puts her at risk of developing incisional dehiscence. Sirolimus may, indeed, impair wound healing.

4. Rapid corticosteroid withdrawal (option B) has become increasingly more popular. Clinical trials have shown that these agents can be withdrawn safely with a low incidence of acute rejection. Some studies, however, suggest that steroid withdrawal entails more risk in African Americans.

5. Calcineurin inhibitor avoidance (option D) is attractive because it minimizes the possibility of causing nephrotoxicity. The combination of mycophenolate mofetil and sirolimus has been used effectively but has not been rigorously studied with randomized trials. Currently this option is not a conventional protocol. The higher risk of rejection in African Americans makes them less attractive candidates for calcineurin inhibitor avoidance.

For the above reasons Dr. Danovitch chooses option C.

References:

CASE IV.

A 45 year old type 1 diabetic male has been dialysis dependent for two years. Diabetic complications include retinopathy with loss of vision in the right eye; coronary artery disease that has required a two vessel coronary artery by-pass and peripheral neuropathy with a right ankle Charcot joint. The patient can now walk one mile without chest pain and a recent nuclear cardiac stress test showed no reversible ischemia.

QUESTION 5:

Which ONE of the following treatment options would you now recommend for this patient?

A. Because the morbidity and mortality of transplantation for this patient would be excessive, he should remain on dialysis
B. List the patient for combined kidney and pancreas transplant (SPK)
C. List the patient for deceased donor transplantation with consideration of pancreatic transplantation if clinical stability is sustained for 3-to-6 months following renal transplantation
D. A living donor transplantation from the patient’s consenting one-haplotype matched brother should be recommended with consideration of pancreas transplantation after 3-to-6 months of stability

ANSWERS TO QUESTION 5:

A. Incorrect. The estimated mortality of diabetic patients on dialysis approximates 10% per year and is greater than their mortality would be following transplantation. Although this patient is at greater surgical risk because of his coronary artery disease, the negative stress test would suggest that it is safe to proceed with transplantation.

B. Not Incorrect, but not deemed as Acceptable as D. A successful SPK would indeed make this patient insulin independent. Some transplant programs regard significant coronary artery disease to be a contraindication to SPK because of the procedure’s greater surgical risk. Although the pathological changes of diabetic nephropathy frequently recur in kidneys transplanted alone, this finding is an unusual cause of graft loss. It is unlikely, at least in the short-term, that this patient’s non-renal complications will improve significantly post-SPK. If this patient did not have a living donor, and in countries where the deceased donor waiting list is long, SPK would be a more attractive option because of the shorter waiting time for an SPK as compared to a deceased kidney-alone.

C. Incorrect. The availability of a living donor would be far preferable and the anticipated long wait for a deceased donor organ make this option unacceptable.

D. Most Acceptable. Living donor transplantation (LRD) from a biologically related or non-related living donor provides the safest and most rapid way to improve this patient’s quality and length of life. Most transplant programs recommend LRD as the prime treatment modality for type 1 diabetics although some patients elect to take upon themselves the additional risk of SPK. The decision to recommend posttransplant pancreas transplantation (PAK) requires careful consideration. Some data suggests that when renal function is good, mortality is greater when a pancreas is transplanted alone. If successful, the patient’s quality of life may improve with the advent of insulin independence.

Dr. Danovitch recognizes that options B and D are not mutually exclusive, but for the reasons outlined, prefers option D.

References:
ESRD: JOANNE BARGMAN

CASE V.

A 45-year-old female accountant developed ESRD from lupus nephritis. She opted for treatment with home peritoneal dialysis and a catheter was successfully inserted by a blind surgical technique. There was satisfactory inflow and outflow of dialysis solution at the time of insertion.

At the PD unit 2 weeks later the inflow of dialysate was normal, but outflow was slow and intermittent. An abdominal flatplate showed that the tip of the dialysis catheter had migrated to the right upper quadrant. There was also evidence of stool-filled bowel. An intensive laxative regimen was prescribed, but the location of the catheter tip remained unchanged and the dialysis outflow remained slow. Under fluoroscopy the catheter was re-positioned into the pelvis.

She was trained and discharged on home cycler peritoneal dialysis. One month later, a peritoneal equilibration test (PET) showed that she was a high-average transporter, with a dialysate to plasma (D/P) creatinine of 0.68.

Her course was uneventful for 18 months, at which time she noted the abrupt onset of diminished effluent volume. She also experienced a 2.5 kg weight gain and new hypertension. In clinic she looked well and her BP was 180/95 mmHg (usually 145/90 mmHg). The abdomen was neither protuberant nor edematous. There was slight swelling of the ankles.

Repeat PET showed the D/P creatinine unchanged at 0.66. She was anuric. She was put on rapid-cycling peritoneal dialysis in the unit, which successfully ultrafiltered several liters of fluid.

This is a patient with lupus and recurrent pancreatitis who reaches dialysis dependence on the basis of lupus nephritis. She had a PD catheter inserted but the catheter tip migrated and so it was moved back under radiological guidance into the pelvis by the insertion of a rigid trocar. The catheter worked thereafter and she was shown to be a high-average transporter. After eighteen months she suddenly developed diminished effluent volume with consequent fluid retention. Repeat investigation showed the catheter to be in the correct position and a repeat PET test showed that the D/P creatinine is essentially unchanged, that is, she had not become a more rapid transporter. She was brought into the PD unit and given rapid cycling dialysis, which was able to remove fluid, despite the unchanged transport characteristics.
QUESTION 6:

Which ONE of the following options would be best for this patient?

A. Discontinue PD and begin permanent in-center hemodialysis
B. Continue PD but add polyglucose (icodextrin) to the long daytime dwell
C. Continue PD but switch to an intermittent rapid-cycling regimen
D. Order an abdominal CT scan with intraperitoneal instillation of dye

ANSWERS TO QUESTION 6:

Correct Answer: (D) “ordering an abdominal CT scan with the intraperitoneal installation of dye.” There are two important clues suggesting that the cause of the diminished effluent volume is mechanical in nature. The first is the suddenness of the change in drain volume, and the second is that there has been no change in the PET results. The observation that rapid cycling, in contrast to long dwells, is able to remove fluid may be explained by the presence of a slow leak of dialysis fluid into some other compartment. The rapid in-and-out cycles may well occur too quickly for the slow leak to become manifest. Long dwells would allow the time required for significant amounts of the dialysis fluid to escape into an abnormal loculation or compartment.

Less Appropriate Answers: PD should not be discontinued. If we did that with hemodialysis patients every time a resolvable problem arose, we’d be discontinuing dialysis all the time! However, there is a lower threshold to switch a patient from PD to hemodialysis when a problem is encountered. For this patient, home dialysis and, in particular, home peritoneal dialysis, was a successful modality. It allowed her to travel freely to her home country in the Caribbean where she had a job. Discontinuing peritoneal dialysis and switching to in-center hemodialysis should be a decision of last resort.

Icodextrin is a glucose polymer that ultrafilters by colloid oncotic pressure during a long dwell. It is indicated for patients who are rapid transporters and experience rapid absorption of glucose from the dialysate, dissipating the osmotic gradient and thereby, the ultrafiltration process. Icodextrin is also useful during peritonitis where even those subjects with more normal peritoneal transport can temporarily become rapid transporters secondary to the inflammation. Here again icodextrin is more successful at promoting ultrafiltration as compared to glucose-based dialysis fluid. Given that this patient had a complicating mechanical event, and that she had definitely not become a rapid transporter, there was no indication for icodextrin. Indeed, long dwells with icodextrin with increased ultrafiltration volumes and pressure could have theoretically increased the amount of fluid migrating out of the peritoneal compartment. Intermittent rapid cycling seemed to be effective in removing fluid from this patient. It would be possible to manage her ultrafiltration needs with this regimen, but she was anuric. An intermittent peritoneal dialysis regimen would not prove to be adequate dialysis, even if urea kinetics
could be increased to meet “guideline” values. A key benefit of peritoneal dialysis lies in its continuous nature, and this would be compromised by a long-term intermittent rapid cycling regimen.

The abdominal CT scan did show a sizeable retroperitoneal leak. It is unclear whether this was a late event related to the rigid trocar manipulation of the catheter eighteen months earlier or to damage related to previous episodes of pancreatitis or perhaps even to a lupus-related serositis.

She was devastated by the decision to put her on a two-month course of in-center hemodialysis while waiting and hoping that the retroperitoneal defect would seal spontaneously. Her devastation again highlights the inappropriateness of immediately resorting to option (A), discontinuing PD.

References:


CASE VI.

A 58 year-old woman with ESRD from autosomal-dominant polycystic kidney disease is receiving in-center hemodialysis. There were no suitable living donors available for transplantation. She required parathyroidectomy (1/3rd of one gland was left in the neck) for worsening autonomous hyperparathyroidism. Because of two episodes of graft thrombosis she was placed on 1mg coumadin daily. She declined workup for renal transplantation.

Two years later, she developed atrial fibrillation. Anti-arrhythmic therapy was started, and the Coumadin increased to maintain the INR at 2.0 – 2.5.

Six months after this she bruised her upper left thigh against the edge of a table resulting in an ecchymosis and eventual breakdown of the overlying skin. The thigh area became ulcerated. Soon thereafter a patch of skin ulceration developed on the opposite thigh without preceding trauma. The skin ulcers on both thighs continued to enlarge and became painful. Livedo reticularis developed on both lower limbs.
Current laboratory Data:

Corrected calcium  2.51 mmol/l (10.04 mg/dl)
Phosphorus   2.20 mmol/l (7.0 mg/dl)
PTH (intact)   154 pg/ml
Blood sugar   normal
Hemoglobin   102 g/l (10.2 g/dl)
ANCA (Elisa)  negative

A skin biopsy from the edge of one of the ulcerated lesions showed vascular calcification and associated ischemic necrosis. A diagnosis of calcemic uremic arteriolopathy (calciphylaxis) was made.

QUESTION 7:

Which ONE of the following courses of action would be LEAST appropriate in this setting?

A. Consider re-exploration of the neck for remnant parathyroid tissue  
B. Consider discontinuing calcitriol and eliminating oral calcium  
C. Consider discontinuing Coumadin or replacing it with another anticoagulant  
D. Consultation should be sought from plastic surgery for wound care

ANSWERS TO QUESTION 7:

Case Summary: This ESRD patient with polycystic kidney disease had a subtotal parathyroidectomy for autonomous hyperparathyroidism. She was receiving in-center hemodialysis, thrice-weekly. Coumadin therapy was originally given to maintain graft patency and the dose was increased once she developed atrial fibrillation. Trauma to her thigh caused ecchymosis, skin breakdown and progressive ulceration. In the absence of trauma, the contralateral thigh underwent the same process. A clinical and pathological diagnosis of calciphylaxis was made. Current laboratory studies revealed hyperphosphatemia, high-normal calcium concentration and a PTH level at the lower limit of normal. ANCA and other tests looking for an alternate cause of the skin necrosis were negative.

Least Appropriate Answer: A) “Re-exploration of the neck for remnant parathyroid tissue.” The patient has already had a partial parathyroidectomy and her PTH level is at the lower limit of normal making it very unlikely that the hormone underlies the calciphylaxis. Indeed, calciphylaxis appears to be an evolving disease, less associated now with hyperparathyroidism than it had been in previous decades. Increasing use of coumadin, as outlined below, has been implicated as a cause of calciphylaxis.

The More Appropriate Answers: Discontinuation or substitution of another anticoagulant for coumadin. Coumadin inhibits the cycling of vitamin K which itself is important in the regeneration of matrix GLA protein. The GLA protein appears to be important in the tonic prevention of vascular calcification. Indeed, GLA-knockout
animals develop striking and complete vascular calcification. This patient is receiving coumadin for stroke prophylaxis, a disease with a relatively low incidence per annum in patients with atrial fibrillation. The death rate for patients developing calciphylaxis is, by contrast, quite high. On balance it would seem best to discontinue the coumadin. If another anticoagulant is thought to be indicated, either for stroke prophylaxis or for graft patency, this could be used instead. (We have to be cognizant of the long-term effects of coumadin in our dialysis patients who already have accelerated levels of vascular calcification.)

There is little indication for calcitriol given the low-normal PTH level, and the vitamin’s potential for exacerbating the hyperphosphatemia and borderline hypercalcemia. Therefore, that agent should be discontinued along with the oral calcium, replacing the latter with another phosphorus binding agent. Given the severity and high mortality associated with calciphylaxis, if at all possible, this patient should have her dialysis prescription increased to long-daily dialysis.

Finally, consultations from a plastic surgeon for wound care would be important. Many patients with calciphylaxis die of sepsis emanating from the wounds. Careful attention to sterility of the wound and appropriate debridement would be indicated.

References:


GINGERULONEPHRITIS: RONALD FALK

CASE VII.

A 53 year-old Caucasian man presented with a history of nasal crusting, intermittent episodes of “red eyes and skin rash” a serum creatinine of 2.0 mg/dl and his urinalysis revealed glomerular hematuria. A 24-hour urine collection contained 800 mg of protein. Serologic studies included normal complement levels, negative anti-nuclear and anti-dsDNA antibody tests but a positive proteinase-3 ANCA. Kidney biopsy showed focal necrotizing glomerulonephritis with 10% crescents. Thirty percent of glomeruli were globally sclerotic and there was focal mild-to-moderate interstitial fibrosis and tubular atrophy.

The patient was treated with three intravenous doses of solumedrol (7 mg/kg/day x 3) and was started on cyclophosphamide. He suddenly developed significant hemoptysis, hypoxemia and a chest X-ray consistent with diffuse alveolar hemorrhage. He was then treated with plasmapheresis in addition to corticosteroid and cyclophosphamide, and prompt resolution of his pulmonary process ensued. Three months after the start of
therapy, the patient was in remission with no evidence of active vasculitis. At six months, he was still taking cyclophosphamide.

**QUESTION 8:**

Given his most current status and therapeutic regimen, which ONE of the follow choices would now be his best therapeutic option?

A. Discontinue all immunosuppressive therapy  
B. Continue oral cyclophosphamide for another six months  
C. Convert the patient to methotrexate as immunomodulating therapy  
D. Convert the patient to azathioprine or mycophenolate mofetil

**ANSWERS TO QUESTION 8:**

This patient had many of the manifestations of ANCA small vessel vasculitis at the time of his initial presentation. The different manifestations of vasculitis do not necessarily occur in a synchronous fashion. The findings on biopsy of glomerulosclerosis and interstitial fibrosis which accompanied those of necrosis and a minimal number of crescents, suggests that the patient may have had an indolent, waxing and waning disease process. Although clinically inapparent, these changes resulted in a substantial loss of GFR and elevation of his serum creatinine. The presence of skin disease typically alerts patients to the onset of their disease process and prompts a more rapid diagnosis. Pulmonary hemorrhage represents one of the most worrisome complications of small vessel vasculitis. In such cases the addition of plasmapheresis to immunotherapy with corticosteroids and cyclophosphamide affords an improved survival. Based on anecdotal reports, the use of recombinant Factor VIIA to stop the alveolar hemorrhage may also be of benefit. This patient entered a clinical remission quite quickly with cyclophosphamide given either intravenously or orally.

At issue is the question of this patient’s long-term care. Use of azathioprine has been documented to be as efficacious as oral cyclophosphamide in the EUVAS CYCAZAREM trial. CellCept may also prove to be of benefit, although this has not been subjected to a similar kind of study. Methotrexate should not be used in individuals who have kidney dysfunction. This patient with both proteinase-3 ANCA and respiratory tract disease has a high likelihood of developing another relapse, and some form of maintenance immunosuppression is in order.

**Thus, Dr. Falk chooses option D as the best response to this question.**
References


CASE VIII.

Four years ago this 23 year-old Caucasian man had a renal biopsy that revealed a diffuse proliferative glomerulonephritis with no crescents, but 30% of his glomeruli were obsolescent, and there was mild to moderate interstitial fibrosis. Immunofluorescence microscopy demonstrated IgA 3+, IgG 2+, IgM 2+, C1q negative, C3 2+ and electron microscopy detected electron dense deposits within the mesangium. A diagnosis of IgA nephropathy was made.

The patient has been treated with an angiotensin receptor blocker (ARB) and his blood pressure taken at home has ranged between 120-125/70 mm Hg. On three separate occasions during the past four years his serum creatinine has transiently increased from 0.9 mg/dl to 2.0 mg/dl, each occurring at the time of synpharyngitic flares of his disease. One year ago, he had another synpharyngitic flare with a flu-like illness (despite having had the influenza vaccine) that resulted in another episode of gross hematuria and his serum creatinine rose to 1.3 mg/dl. He now presents with yet another synpharyngitic episode of glomerulonephritis with no other constitutional symptoms. The gross hematuria has dissipated and his serum creatinine is 1.4 mg/dl. He still has persistent microscopic hematuria. His blood pressure remains under excellent control, although in addition to an ARB, he also takes a small dose of an angiotensin converting enzyme inhibitor. His protein excretion has increased from 1.2 g/day to 2 g/day over the past 4 years.
QUESTION 9:

Given his past history and current status, which ONE of the following choices offers the best course of therapy for this man?

A. Continued supportive care without change in his medical regimen.
B. Institution of pulse methylprednisolone therapy every other month and alternate-day oral prednisone.
C. Institution of cyclophosphamide for 6 months.
D. High dose oral steroids for the next 2 years.
E. Institution of mycophenolate mofetil at a dose of 1 gram twice daily.

ANSWERS TO QUESTION 9:

Considering this patient’s progressive loss of renal function over the last four years, it is unlikely that supportive care alone will be sufficient. Several studies suggest a possible beneficial role for corticosteroid therapy. In a prospective trial of 86 patients with proteinuria of 1 to 3.5 grams/day and a serum creatinine <1.5 mg/dl, the combination of methylprednisolone for 3 days at the beginning of months 1, 3 and 5 and 0.5 mg/kg of oral prednisolone given every-other day for 6 months, resulted in improved kidney function over the period of observation. Immunosuppressive therapy with methylprednisolone plus cyclophosphamide for three months followed by azathioprine for two years has been used in individuals who have more significant renal disease. Compared with the control group, renal survival in this population was higher among the treatment group at two years and was sustained for up to five years. The use of prolonged oral glucocorticoids has not been proven to be efficacious. The role for mycophenolate mofetil in the treatment of IgA nephropathy is the focus of several randomized trials including one that has negative results (personal communication).

Thus, Dr. Falk chooses option B as the best response to this question.

References: