

**Pathophysiology Renal Exam**  
**March 2, 1998**

**Questions 1-4: Slide Questions**

**1. SLIDE 1**

A 67 year-old male develops back pain and acute renal failure, with rise in serum creatinine from 1.2 mg/dl to 5.6 mg/dl over the course of four weeks. Lytic bone lesions are detected in the ribs and spine. Urinalysis reveals 1+ protein with 0-3 rbc per high power field, no wbc and no eosinophils. Urine cultures are negative and serologies (including ANA, Hepatitis B surface antigen, Hepatitis C antibody, and serum complements) are negative or normal. Renal biopsy shows the changes depicted in this slide. The most likely diagnosis is:

- a. Acute pyelonephritis
- b. Chronic pyelonephritis
- c. Myeloma cast nephropathy
- d. Acute tubular necrosis
- e. Allergic interstitial nephritis

**2. SLIDE 2**

The condition depicted here may be caused by all of the following EXCEPT:

- a. Renal artery stenosis
- b. Diabetic nephropathy
- c. Obstructive uropathy with acute pyelonephritis
- d. Analgesic nephropathy
- e. Sickle cell anemia

**3. SLIDE 3**

The gross appearance of the kidney shown here is MOST consistent with which of the following?

- a. Cholesterol embolization
- b. Multifocal renal infarction
- c. Acute pyelonephritis
- d. Acute post-infectious glomerulonephritis
- e. Acute tubular necrosis

**4. SLIDE 4**

The glomerulus depicted here is MOST consistent with which of the following?

- a. Acute post-streptococcal glomerulonephritis
- b. Membranous glomerulopathy
- c. Minimal change disease
- d. Membranoproliferative glomerulonephritis

e. Anti-GBM disease

**CASE HISTORY (questions 5 through 8)**

A 25 year-old white female hairdresser presents to her local medical doctor with 2 week history of malar rash, fever, fatigue and arthralgias of the small joint of the hands. Laboratory work-up discloses serum creatinine 3.2 mg/dl, urine protein 2.5 grams/day, serum albumin 3.8 g/dl, urinalysis with active urine sediment including 20-25 rbc per high power field, reduced serum complements C3 and C4, and high titer positive ANA (anti-nuclear antibody). A renal biopsy is performed.

5. Renal biopsy would be most likely to show which of the following by light microscopy?

- a. SLIDE 1
- b. SLIDE 2
- c. SLIDE 3
- d. SLIDE 4
- e. SLIDE 5

6. Immunofluorescence microscopy would be most likely to show which of the following staining patterns for IgG?

- a. SLIDE 1
- b. SLIDE 2
- c. SLIDE 3
- d. SLIDE 4
- e. SLIDE 5

7. By electron microscopy, the glomeruli would be most likely to show which of the following?

- a. SLIDE 1
- b. SLIDE 2
- c. SLIDE 3
- d. SLIDE 4
- e. SLIDE 5

8. Microscopic examination of the urinary sediment would be most likely to show which of the following?

- a. SLIDE 1
- b. SLIDE 2
- c. SLIDE 3
- d. SLIDE 4
- e. SLIDE 5

**E** 9. Hypocomplementemia is commonly detected in all of the following conditions EXCEPT:

- a. Lupus nephritis
- b. Acute post-streptococcal glomerulonephritis
- c. Membranoproliferative glomerulonephritis
- d. Acute-post infectious glomerulonephritis associated with bacterial endocarditis
- e. Crescentic glomerulonephritis associated with polyarteritis nodosa

**D** 10. Which of the following is NOT a feature of chronic pyelonephritis?

- a. Asymmetric broad flat cortical scars
- b. Dilated calyces
- c. Blunted papillae
- d. Acute tubular necrosis
- e. Thyroidization of the tubules

**D** 11. In Goodpasture's disease, the anti-GBM antibody has specificity for:

- a. The podocyte cell membrane
- b. The endothelial cell membrane
- c. The heparan sulfate proteoglycans
- d. The alpha 3 subunit of collagen IV
- e. Laminin

**D** ↓

**B** 12. Which of the following statements about acute post-streptococcal glomerulonephritis is FALSE?

- a. It usually presents with nephritic syndrome.
- b. Onset is usually 1 to 2 days following infection with Group A Beta-hemolytic streptococcus.
- c. It may follow pharyngeal or skin infection.
- d. Most cases resolve clinically within 6 weeks.
- e. The typical electron microscopic finding is subepithelial electron dense "humps".

**B**

**D** 13. Which of the following statements about diabetic nephropathy is FALSE?

- a. It is a major cause of end-stage renal disease in the United States.
- b. Proteinuria usually precedes the development of renal insufficiency.
- c. The renal biopsy findings include mesangial nodules and glomerular basement membrane thickening.
- d. Most patients develop diabetic nephropathy years before the appearance of diabetic retinopathy.
- e. Aneurysms may form in the glomerular capillaries.

**D**

## QUESTIONS 14-24

Match each of the following clinical vignettes in questions 17 through 27 with the disease in a through e that it most closely fits. Each item in a through e may be used once, more than once or not at all.

- a. Focal segmental glomerulosclerosis
- b. Thrombotic microangiopathy
- c. Crescentic glomerulonephritis
- d. Membranous glomerulopathy
- e. Allergic interstitial nephritis

- E** 14. A 54 year-old man develops fever, cough and dyspnea. Chest x-ray shows a right lower lobe infiltrate suggestive of pneumonia and sputum cultures are positive for pneumococcus. The patient is treated with penicillin for four weeks, with resolution of the pulmonary infiltrates and fever. Two weeks into the course of therapy, he develops an erythematous rash over the chest, peripheral eosinophilia and rising serum creatinine. Urinalysis reveals many wbc with wbc casts and urinary eosinophils.
- B** 15. An outbreak of enterocolitis is traced to a fast-food restaurant in northern New Jersey. Thirty-three of the several hundred people consuming hamburgers in the restaurant over a 2-day period develop a diarrheal illness, including several cases of hemorrhagic colitis. One of the affected children develops acute renal failure with microangiopathic hemolytic anemia and thrombocytopenia.
- A** 16. A 16 year-old girl presented at age 4 with nephrotic syndrome. Renal biopsy performed at age 4 was reported to have shown minimal change disease. The patient initially responded to an 8-week course of steroid therapy with complete resolution of proteinuria. However, from the age of 10 to the age of 16, the patient developed multiple episodes of recurrent nephrotic syndrome, many of which were steroid resistant. In the past year, her creatinine has risen from 0.7 mg/dl to 1.7 mg/dl. A renal biopsy is performed.
- D** 17. A 45 year-old man with history of reflux in early childhood presents with proteinuria and renal insufficiency. The reflux was reportedly corrected surgically at age 3, without recurrence. An employment physical examination at age 45 discloses creatinine 2.6 mg/dl with urinary protein 5.5 grams/day and serum albumin 3.2 g/dl. Urinalysis reveals 3+ protein with inactive sediment.
- B** 18. A 38 year-old Black male without past medical history presents to the emergency room with headache, diplopia and nausea. He is found to have blood pressure (BP) 240/130, with papilledema and serum creatinine 5.2 mg/dl.
- D** 19. A 12 year old Cambodian boy develops edema. His pediatrician finds him to have urinary protein 6.5 g/day, serum albumin 3.2 g/dl, and serum cholesterol 400 mg/dl.

Multiple members of the immediate family have history of hepatitis B infection. Although the child has no history of acute hepatitis, he is found to have a positive hepatitis B surface antigen and mildly elevated liver function tests.

D 20. A 65 year old white woman with history of rheumatoid arthritis for over twenty years develops nephrotic syndrome with urinary protein over 8.0 grams per day. Her current medications include aspirin and gold salts.

A 21. A 32 year-old Black male intravenous drug abuser with AIDS develops edema and rapidly rising serum creatinine to 4.8 mg/dl over the course of 6 weeks. Urinary protein is 15 grams per day and urinalysis discloses many oval fat bodies and maltese crosses. Ultrasound shows the kidneys to be markedly enlarged (15 cm) and hyperechoic.

B 22. A previously healthy 20 year-old white female pregnant with twins develops hypertension, edema and proteinuria during her third trimester of pregnancy. Proteinuria and hypertension resolve following successful delivery by Cesarean section in the 36<sup>th</sup> week of pregnancy.

C 23. A 55 year-old white male develops chronic sinusitis, rash and hemoptysis. Chest x-ray discloses a cavitory lesion in the left lower lobe. His serum creatinine is 3.9 mg/dl with urinary protein 2.0 g/day. Urinalysis reveals many rbc and rbc casts. Serologic work-up includes negative ANA, negative anti-GBM antibody and positive anti-neutrophil cytoplasmic antibody (ANCA).

C 24. A 19 year-old white boy develops pulmonary-renal syndrome with hemoptysis and rapidly progressive renal failure. Serologies are pending while an emergency renal biopsy is performed. The major finding by immunofluorescence is linear staining of the glomerular basement membranes with antisera to IgG.

**Essay Question # 1-4:**

1. Two patients have chronic renal disease but have no symptoms of any disease and are otherwise in good shape.

	Patient A	Patient B
Na	140	140
Cl	100	110
HCO <sub>3</sub>	25	18
pH	7.40	7.30
Creatinine	3	3.0
Urine pH	5.2	5.2

What is the reason for the difference between them. What other serum or urine tests would document your conclusions.

2. How would you know that a patient was in steady state with respect to
- Glomerular filtration rate
  - Extracellular fluid volume
  - Free water content
  - Potassium Content

3. A patient with untreated heart failure is seen to have edema and on measurement, his plasma aldosterone level is high. Plasma electrolytes show that

Na 137, Cl 99; HCO<sub>3</sub> 26; K 4.0

He is given the diuretic furosemide and a few days later his plasma electrolytes show

Na 137; Cl 90; HCO<sub>3</sub> 32; K 3.0

- How come the plasma K and HCO<sub>3</sub> are normal despite the hyperaldosteronism
- Explain how they became abnormal after a few days of furosemide treatment.

4. A patient is admitted to the hospital with severe oliguria (Urine output 400 ml/day) and is found to have the following tests

Na	140
K	3.5
Cl	100
HCO <sub>3</sub>	25
BUN	42
Cr	1.4
Urine Na	14
Urine Creatinine	140
Urine Osmolality	800 mOsm

One week later, a nephrologist was called because the patient was still oliguric with a urine output of 400 ml/day. After repeating all the tests above, she concluded that the patient now has Acute Tubular Necrosis. How did the test results change to allow her to reach the diagnosis.

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What is the reason for the difference between them. What other serum or urine tests would document your conclusions.

There are two general classes of chronic renal diseases: glomerular and tubulo-interstitial diseases. In both patients A and B, the glomerular filtration rate is reduced to about one third of normal; in other words, only one third of the nephrons are filtering. Patient B has metabolic acidosis with a normal anion gap. Assuming that the acidosis is not produced by diarrhea or other intercurrent illness (we are told that they have no symptoms) then it is likely that the acidosis is produced by renal disease itself. Excretion of acid by each nephron is largely a reflection of the amount of  $\text{NH}_4^+$  produced by that nephron. Each nephron can increase its ammonia production by a factor of four or five. Hence, patient A maintains a normal acid base balance by tripling the ammonia production in each remaining nephron. Since patient B is acidotic, his remaining nephrons must not be able to do that. Therefore it is likely that patient A has a glomerular disease where the remaining nephrons have reasonably normal tubules while patient B has a tubulo-interstitial disease where the remaining nephrons are affected by tubular atrophy, inflammation or other process. The acidosis is frequently aggravated in these patients by the presence of hyporeninemic hypoaldosteronism frequently seen in such patients. In addition, most such patients are hyperkalemic which inhibits ammonia production.

Other serum studies that would be helpful is a serum K. It is usually high in tubulo-interstitial disease and normal in glomerular disease. K is high in tubulo-interstitial disease because of the tubular atrophy and also because acidosis increases release of K from cells. Finally, hypoaldosteronism also tends to cause hyperkalemia. Urinalysis in glomerular disease usually shows heavy proteinuria with casts while in tubulo-interstitial disease it is frequently unremarkable, with mild, if any proteinuria and few cells but usually no casts.

2. How would you know that a patient was in steady state with respect to
- Glomerular filtration rate
  - Extracellular fluid volume
  - Free water content
  - Potassium Content

The steady state is defined as that condition when the intake matches the output and therefore the content and concentration of the material at issue is constant.

A For GFR, the best test is to formally measure the creatinine clearance over a period of

amount of  $H^+$  secreted.

B Furosemide inhibits Na reabsorption in the thick ascending limb which leads to increased delivery of Na and also fluid to the collecting duct. The increased flow rate will stimulate K secretion by a collecting already primed by aldosterone to have more open K channels in the luminal membrane. The increased delivery of Na will result in enhanced Na transport by the already primed Na channels. This will lead to increased negativity of the collecting tubule. This will stimulate  $H^+$  secretion and incidentally also K secretion. Further, furosemide over a period of a few days could produce volume depletion, which increases the AII and aldosterone levels even further. Hence there will be more fluid and  $HCO_3^-$  reabsorption in the proximal tubule, allowing more of the  $H^+$  secreted in the collecting tubule to generate new  $HCO_3^-$  to add to the body fluids to produce alkalosis.

4. A patient is admitted to the hospital with severe oliguria (Urine output 400 ml/day) and is found to have the following tests

Na	140
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Urine Na	14
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Urine Osmolality	800 mOsm

One week later, a nephrologist was called because the patient was still oliguric with a urine output of 400 ml/day. After repeating all the tests above, she concluded that the patient now has Acute Tubular Necrosis. How did the test results change to allow her to reach the diagnosis.

The results suggest that the patient has acute renal failure because of oliguria and elevated serum creatinine. The fractional excretion of Na is very low (about 0.1%) suggesting that initially he had pre-renal azotemia. Additional evidence for pre-renal azotemia is the high urine osmolality in the setting of oliguria. One week later, the continued oliguria suggests continuation of the process; we would now expect the serum creatinine to be much higher. Since the nephrologist concluded that he had ATN, she must have found that his BUN and creatinine have increased and the BUN/Cr ratio had fallen from the initial 30 to something more like the normal ratio of 10-20. It is also very likely that his fractional excretion of Na would have now increased to a level of 1% or more. The continued oliguria would have resulted in hyperkalemia since the decreased urine flow would have limited this person's ability to excrete much K in the urine. We also would expect such a patient to have developed acidosis because of continued renal failure which would contribute to his hyperkalemia. Finally, the urine osmolality would now approach isotonicity since the medulla would have lost its ability to concentrate the urine.