Renal Board Review

Intensive Review of Internal Medicine
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Question 1

• In the United States, the single-most frequent cause of chronic renal failure is:
  – A. Hypertension
  – B. Polycystic Kidney Disease
  – C. Glomerulonephritis
  – D. Diabetes mellitus
  – E. Analgesic Abuse

Incidence of Diabetic ESRD is Increasing

Question 2

• A 42 year old woman presents to your office with a 4 week history of a petechial rash on her legs, diffuse non-specific abdominal pain, gross hematuria and edema. She relates a 2 year history of intermittent polyarthralgias. Physical examination is notable for mild periorbital edema, a BP of 164/88 mmHg, HR 66 bpm, afebrile. Her lungs and cardiovascular examination are normal. She has some mild abdominal tenderness without guarding centrally, but bowel sounds are normal. Rectal exam is normal. She has 3+ edema.

• Urinalysis shows a SG of 1.020, pH 5.0, 4+ blood, 4+ proteinuria, 1+ leukocytes, rest of the dipstick was negative. Urine sediment examination shows 15-20 dysmorphic red cells, and 1 RBC cast. Her electrolytes are normal, BUN was 36 mg/dL, creatinine 1.8 mg/dL. Serological examination shows: ANA negative, ASLO titer negative, ANCA and anti-GBM negative. Complements were normal. Skin biopsy showed a leukocytoclastic vasculitis. A renal biopsy was performed.

• The most likely finding on the renal biopsy is:
  – A.) A WHO class IV diffuse proliferative glomerulonephritis
  – B.) A minimal change lesion
  – C.) Linear staining on immunofluorescence
  – D.) Kimmelsteil-Wilson lesions with nodular glomerulosclerosis
  – E.) A mesangial proliferative lesion with IgA deposition on immunofluorescence
Pathology of IgAN/HSP nephritis

HSP nephritis
Clinical Features

Dermal
Purple, nonblanching, urticarial, purpuric papules may become confluent
Histology: leukocytoclastic vasculitis

GI
Abdominal pain (2/3rds of cases) may precede rash
Vomiting
Diarrhea
Periumbilical pain
Major complications (5%)
Intussusception
Bowel ischemia
Necrosis

Joints
Arthralgias and periarticular edema (2/3)
Knees, ankles, elbows, wrists

Glomerular Syndromes

- Nephritis: Hypertension, Azotemia, proteinuria, hematuria, RBC casts / dysmorphic RBCs
- Nephrosis: edema, proteinuria, hypoalbuminemia, lipid abnormalities
- RPGN: rapid renal failure, crescents on renal biopsy + nephritis
- Isolated urinary abnormalities: hematuria / proteinuria

Question 3

- 67 year old man - 1 week history of anorexia, nausea, lassitude, and pedal edema.
- Longstanding hypertension, well controlled with hydrochlorothiazide and amlodipine.
- Medications: HCTZ, amlodipine and ibuprofen for osteoarthritis of the hip for the past 3 months.
- Exam: BP 157/93mm, HR 72 bpm, Temp of 97.8°F, JVP 8 cm; normal cardiac and pulmonary examinations; and 2+ pitting edema. UA: SG 1.017, protein 4+, 1+ blood, glucose neg. Sediment: 2-4 erythrocytes and 15-20 leukocytes/hpf, and occasional granular casts.

- BUN 32 mg/dL; Cr 1.8 mg/dL; Na 137, K 4.4, Cl 95, Ca 9.2, Phos 7.8, UA 7.7 mg/dL; Alb 2.9 g/dL; HCT 29%. ANCA (-) Antinuclear (+) 1:40 titer, anti-dsDNA antibody level 0.

- 24 h protein excretion 7.7 g.
- Renal ultrasound showed normal sized kidneys bilaterally without obstruction.
- Three months previously his serum creatinine was 1.7 mg/dL.

- Renal 33% children, 63% adults
Hematuria, macroscopic / microscopic
Proteinuria
Azotemia

Question 3 cont’d

Question 3

- The nephrotic-range proteinuria and renal failure are most likely the result of:
  - A). Lupus nephritis
  - B). Multiple myeloma
  - C.) Systemic small vessel vasculitis
  - D.) Ibuprofen-induced nephrotic syndrome and interstitial nephritis
  - E.) Renal vein thrombosis secondary to membranous nephropathy
**NSAIDs and the Kidney**

- Prerenal azotemia
- Ischemic acute tubular necrosis
- Allergic interstitial nephritis (AIN)
- AIN plus minimal change nephropathy
- ARF plus bilateral flank pain
- Sodium and water retention
- Hyperkalemia
- CRF and papillary necrosis


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**Question 4**

A 22 year-old woman is admitted with a diagnosis of Goodpasture’s syndrome. This diagnosis is confirmed by an ELISA and Western blot analysis demonstrating anti-GBM antibodies. A preliminary reading of the renal biopsy confirms the diagnosis of anti-GBM nephritis. Her serum creatinine is 3.2 mg/dL. 2 weeks previously her serum creatinine was 0.7 mg/dL. Which of the following therapeutic options would be most appropriate for her:

- A.) Prednisone 60 mg/day for 1 month followed by a gradual weaning of her prednisone dose.
- B.) Pulse methylprednisone accompanied by daily plasmapheresis with exchange, followed by high dose oral prednisone coupled with cyclophosphamide, until her anti-GBM titer is undetectable.
- C.) Pulse methylprednisone followed by high dose oral prednisone coupled with cyclophosphamide, until her anti-GBM titer is undetectable.
- D.) Prednisone 60 mg/day plus cyclophosphamide 3 mg/Kg/day
- E.) Plasmapheresis alone

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**Goodpasture’s Syndrome**

- Uncommon: incidence 0.1 cases/million
- 1-2% of renal biopsy specimens
- Slight preponderance in males
- Age 1st to 9th decade
- More common in whites over African-American’s
- Year-round presentation, ? Spring and summer
- 50-75% have upper respiratory prodrome,
  - plus fever, rash, myalgias, malaise, headache, weight loss

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**Pathologic Features of Anti-GBM Nephritis**

**Goodpasture’s Syndrome**

- Renal presentation with RPGN
- Proteinuria but usually not nephrotic
- Hypertension uncommon
- US - normal size kidneys
- Renal function declines rapidly
Goodpasture’s Syndrome Treatment

- Treatment without methylprednisone and plasmapheresis
  - 89% progress to death or dialysis; only 10% improved
- Treatment with pulse steroids, plasmapheresis, and Cytoxan
  - standard-of-care
  - 50% improve
- Patients with serum creat of ≥7.0 respond to treatment
  - 75% with Scr < 7 respond, 8% with Scr > 7 respond
  - No improvement in 58 patients on dialysis

Goodpasture’s Syndrome Treatment

- Protocol
  - Pulse solumedrol 1 g QD x 3 d, 1-1.5 mg/Kg prednisone
  - Cyclophosphamide 3 mg/Kg/d (reduced dose in older patients, or if GFR < 10) > 2 months
  - Plasma exchange daily 4 L with albumin replacement (or FFP if pulmonary hemorrhage present) x 14 d or until ab dissapears

Question 5

- In all of the following conditions an increase in serum creatinine can be explained by a reduction in GFR EXCEPT
  - A.) Bilateral hydronephrosis
  - B.) Severe extracellular volume contraction caused by diarrhea
  - C.) Severe congestive heart failure
  - D.) Increase in serum creatinine 1 day post arteriogram
  - E.) Cimetidine treatment of peptic ulcer disease

Limitations of serum creatinine

- Creatinine - freely filtered, secreted, extra-renal degradation
  - secretion and extra-renal elimination increases as GFR falls
  - Scr dependent on muscle mass and meat intake
  - Sensitivity of creatinine as GFR measure approx 60%

Creatinine metabolism

- creatinine production proportional to muscle mass
  - males 20-25 mg/Kg/24h
  - females 15 to 20 mg/Kg/24h
- Expected creat excretion (male) = (28-0.2[age years])(weight[kg])
- Expected creat excretion (female) = (24-0.17[age years])(weight[kg])
- Secreted by organic cation exchanger
- Drugs that interfere with proximal secretion
  - Cimetidine
  - Trimethoprim
  - Dapsone
  - Probenecid

Question 6

- You are asked to consult on a 62 year old African-American male with acute on chronic renal insufficiency secondary to diabetes mellitus ascribed to contrast nephrotoxicity. Routine chemistry labs show a potassium of 8.2 mg/dL. All of the following would be changes seen on the EKG compatible with hyperkalemia, except:
  - A.) Peaked T waves
  - B.) Prolonged QRS
  - C.) Flattened p wave
  - D.) Sine-wave appearing QRS complex
  - E.) U wave
EKG changes in hyperkalemia

• Early: tenting of T waves “pinch-bottomed T waves”; precordial leads
• Prolonged P-R interval
• ST segment depression and lengthening of QRS
• P wave disappears, further widening of QRS
• Ventricular fibrillation

Question 7

• The most common type of kidney stone observed in the United States is:
  – A.) Cystine stone
  – B.) Triple phosphate stone
  – C.) Struvite stone
  – D.) Calcium oxalate stone
  – E.) Uric acid stone

EKG changes in Hyperkalemia

Nephrolithiasis

• 12% of US population affected
• Incidence rate (age 30-65)
  – Male: 3/1000/yr
  – Female: 1/1000/yr
• Calcium oxalate > 75%
  – Hypercalciuria, hyperoxaluria, hypocitruria, hyperuricosuria
• Infection stone/Magnesium ammonium phosphate/struvite/triple phosphate 7-15%
• Uric acid 2%
• Calcium phosphate 2%
• Cystine <1%

Question 8

• 48 year old male ESRD patient presents to the ED with a K= 7.8 mEq/L, HC03 of 22. His EKG shows peaked T waves. Recommended initial treatment include all of the following EXCEPT:
  – A.) Calcium gluconate 10 mls, IV
  – B.) Insulin 10 units and 1 amp of 50% dextrose
  – C.) Albuterol nebulizer (10-20 mg)
  – D.) IV bicarbonate 8.4%, 1 to 2 amps IV
  – E.) Emergent dialysis

Common Crystals

Source: www.medstat.med.utah.edu/WebPath
Changes in plasma K
8.4% bicarb, epinephrine, insulin/dextrose, or HD

Changes in plasma K during IV infusion of bicarbonate in HD patients

Question 9

A 42-year old white male 8 days post bone marrow transplantation on treatment with FK506 (tacrolimus), among many other medications is diagnosed with a type IV renal tubular acidosis. All of the following features would be compatible with this diagnosis except:

- A.) A urine pH of 5.0
- B.) The presence of hyperkalemia
- C.) A negative urine anion gap of -22
- D.) A serum bicarbonate of 18
- E.) A normal anion gap

Urine Anion Gap

- Urine anion gap
  - \( (\text{Na}^+) + (\text{K}^+) - (\text{Cl}^-) \)
  - unmeasured anions – unmeasured cations
  - Most cases of MA has negative value due to excretion of an unmeasured anion NH4+
  - Normal subjects, 20-40 meq NH4+ is excreted and anion gap = 0
  - Metabolic acidosis, NH4+ excretion increases and UAG = -20 to –50
  - In CRF or type 1 and 4 RTA, impaired H+ and NH4 excretion, UAG is positive

Renal Tubular Acidosis

- 3 types
- Type 1 (distal) RTA
  - Reduced H+ secretion by collecting tubule
  - Reduced NH4+ and titratable acid excretion
    - Defective H+–ATPase pump
    - Reduction in cortical Na+ resorption (voltage-dependent defect)
    - Increased membrane permeability, back diffusion of H+ (gradient defect)
  - Causes
    - Idiopathic
    - Autoimmune (SLE, RA etc), drugs and toxins (ampho B, Toluene, lithium)
    - Marked volume depletion

- Type 2 (proximal)
  - Proximal NaHCO3 reabsorption is reduced
  - Self limiting disorder, HCO3 14-20 mEq/L
  - Etiology
    - Idiopathic
    - Hereditary (cystinosis, Wilson’s disease)
    - Acquired (multiple myeloma, drugs (acetazolamide, outdated tetracycline, lead etc), amyloidosis, Sjogren’s
  - Diagnosis
    - Normal AG metabolic acidosis
    - Moderate acidosis (14-20)
    - Urine pH variable (> or < 5.3 depending on threshold)
    - Plasma K normal
  - Treatment
    - Bicarb replacement

Renal Tubular Acidosis
### Hyperkalemic Distal RTA Type IV

- Disturbance of distal nephron function
- Impaired excretion of H+ and K+
- Normal gap acidosis and hyperkalemia

<table>
<thead>
<tr>
<th>Type 1 RTA</th>
<th>Type 4 RTA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypokalemia</td>
<td>Hyperkalemia</td>
</tr>
<tr>
<td>NL renal fxn</td>
<td>CRI</td>
</tr>
<tr>
<td>U pH &gt; 5.5</td>
<td>U pH &lt; 5.5</td>
</tr>
<tr>
<td>Metabolic acidosis</td>
<td>Metabolic acidosis</td>
</tr>
<tr>
<td>Severe HC03 &lt; 15</td>
<td>Mild HC03 &gt; 15</td>
</tr>
</tbody>
</table>

### Causes of Type IV RTA

<table>
<thead>
<tr>
<th>Defect</th>
<th>Causes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mineralocorticoid Deficiency</td>
<td>Low renin low aldo</td>
</tr>
<tr>
<td></td>
<td>-- Diabetes mellitus</td>
</tr>
<tr>
<td></td>
<td>-- Drugs: NSAIDS, CsA, ß-blockers</td>
</tr>
<tr>
<td>High renin low aldo</td>
<td>-- Adrenal destruction</td>
</tr>
<tr>
<td></td>
<td>-- Congential enzyme defects</td>
</tr>
<tr>
<td></td>
<td>-- Drugs: ACEi, ARBs, heparin, ketoconazole</td>
</tr>
<tr>
<td>Abnormal cortical collecting duct</td>
<td>-- Absent or defective mineralocorticoid receptor</td>
</tr>
<tr>
<td></td>
<td>-- Drugs: spironolactone, amiloride, pentamidine, trimethoprim</td>
</tr>
<tr>
<td></td>
<td>-- Chronic tubulointerstitial disease</td>
</tr>
<tr>
<td></td>
<td>-- UTI, lupus nephritis, sickle cell neph</td>
</tr>
</tbody>
</table>

### RTA

<table>
<thead>
<tr>
<th>Type 1 (distal)</th>
<th>Type 2 (proximal)</th>
<th>Type 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basic Defect</td>
<td>Aldo deficiency or resistance</td>
<td></td>
</tr>
<tr>
<td>Serum bicarb</td>
<td>Maybe &lt; 10</td>
<td>14-20</td>
</tr>
<tr>
<td>Plasma K</td>
<td>Low or NL</td>
<td>Usually &gt; 15</td>
</tr>
<tr>
<td>Urine pH</td>
<td>&gt; 5.3</td>
<td>Elevated &gt;5.3</td>
</tr>
<tr>
<td>Other</td>
<td></td>
<td>Serum aldo level</td>
</tr>
<tr>
<td>Dose of HC03</td>
<td>1-2 mEq/d</td>
<td>10-15 mEq/d</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1-2 meq/d</td>
</tr>
</tbody>
</table>

### Question 10

- A 52 year old African-American female presents to the emergency room with unstable angina. She is noted to have a past medical history of mild chronic renal insufficiency (creatinine of 1.8 mg/dL). She is transferred to the coronary care unit and therapy for her unstable angina is initiated. A cardiac catheterization is planned for the next day. Risk factors that would predispose this woman to contrast nephrotoxicity include all of the following except:
  - A.) Diabetes mellitus
  - B.) Pre-existing renal insufficiency
  - C.) The volume of IV contrast utilized in the procedure
  - D.) Presence of extracellular volume contraction
  - E.) A history of coronary artery disease

### Question 11

- Her cardiologist asks you for an estimate of her risk of developing contrast nephrotoxicity. Which one of the following would be the closest estimate:
  - A.) 60%
  - B.) <5%
  - C.) 20%
  - D.) >80%
  - E.) >95%

### Contrast Nephrotoxicity

- ARF and oliguria within 24-48 hours
- Peak serum creatinine on days 3-5
- Low fractional excretion of sodium
- Benign sediment or granular casts
- Resolution usual within 1 week
- Risk factors: CRI, diabetic nephropathy, dose>120 cc, multiple myeloma, volume
- Prevention: hydration 75 cc 0.45% saline, non-ionic for high risk patients
Contrast Nephropathy

### Background
- 12% of hospital-acquired ARF due to contrast (Hou et al)
- Mortality of CN with Scr > 2.0, 48 h post angiography > 34%
- 0.7% of diagnostic cath patients develop CN
  - 10.9% with Scr > 1.2 mg/dL
- Overall Risk
  - CRI patients 10-30%, Diabetes mellitus 24-50%

### Risk Factors
- Pre-existing renal insufficiency
- Diabetes mellitus
- CHF
- Volume Depletion
- Dose of Contrast agent

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**Question 12**

A 42 year otherwise healthy white male runs the Boston Marathon in 4 hours and 4 minutes. He complains of severe body cramps immediately after the race and then after he returns to his hotel room. At night, on voiding, he notices that the volume is small and it is dark red in color. His spouse insists he goes to the emergency room, where a blood test shows that his serum creatinine is 4 mg/dL and his BUN is 18. His urine shows a positive dipstick for blood but virtually no red blood cells in the sediment. The next step in management should be:

- A.) 800 mg indomethacin 3 times a day and return if not improved.
- B.) Starting the patient on pulse methylprednisone 500 mg/day (for 3 consecutive days).
- C.) Immediate initiation of hemodialysis
- D.) Aggressive hydration with normal saline and mannitol
- E.) Intravenous furosemide to initiate a diuresis

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**Question 13**

All of the following are true regarding glomerulonephritis except:
- A.) Minimal change disease is the commonest form of nephrotic syndrome in children
- B.) ANCA-associated crescentic glomerulonephritis is invariably pauci-immune on immunofluorescent staining of the renal biopsy
- C.) Crescents are typically seen in the renal biopsy of patients with rapidly progressive glomerulonephritis
- D.) Serum complements are usually normal in patients with IgA nephritis
- E.) Oval fat bodies are never seen in the urinary sediments of patients with nephrotic syndrome

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**Features of Rhabdomyolysis**

- Muscle pain and dark urine “Coca-Cola” color
- Orthotoludine-positive urine without RBCs
- Elevated CPK and myoglobin
- Increased K, Phos, urate, decreased Ca
- Rapid increase in serum creatinine
- Mechanism: free radicals, ferrihemate, reduced nitric oxide
- Treatment: saline repletion, alkaline diuresis, mannitol. Dialysis once ARF established
### Causes of Rhabdomyolysis
- Excessive muscle activity
  - seizures, delerium tremens, sport
- Direct of ischemic muscle injury
  - trauma, compression syndrome, vascular occlusion
- Metabolic disorders
  - hypokalemia, hyponatremia, hypophosphatemia
- Drugs or toxins
  - ethanol, isopropyl alcohol, heroin, methadone
- Infections
  - tetanus, legionaires, influenza

### Question 14
A 60-year old man who has been previously in good health and on no medications develops the nephrotic syndrome. No systemic causes are identified and serologic work up is completely negative. The most likely histologic lesion of percutaneous renal biopsy is:
- A.) Light chain nephropathy
- B.) Membranous glomerulopathy
- C.) Myeloma kidney
- D.) Membranoproliferative glomerulonephritis
- E.) IgA nephropathy

### MN points
- Subepithelial ID
- Etiology unknown
- Secondary causes include Hep B, Hep C, Gold, penicillamine, NSAIDs, Toxins, Autoimmune diseases
- 2/3rds no cause found
- Epidemiology
  - <5% pediatric
  - 30% adults, 50% of older adults
  - Increased risk in HLA-DR3 (3-fold)

### Question 15
A 16-year old woman who presents with a history of a sore throat 2 weeks previously has edema, mild hypertension, hematuria and red cell casts on her urine sediment. Her complements are low. The most likely diagnosis is:
- A.) Minimal change disease
- B.) Post-infectious glomerulonephritis
- C.) IgA nephropathy
- D.) Acute interstitial nephritis
- E.) Light chain deposition disease

### MN points
- Idiopathic
  - Insidious onset
  - M>F 2-3:1
  - 80% NS at presentation
  - 20% asymptomatic non-nephrotic proteinuria
  - 50% have hematuria
  - HTN not common (30%)
  - Increased risk of thromboembolism (15-40%)
  - Insidious decline in GFR

### MN points
- Treatment
  - Non-specific
    - BP control, Lipids
    - ACEI, Dietary protein restriction (?)
  - Specific
    - Target for selected patients
      - Steroids and cytotoxic
        - Cytoxan + prednisone
        - Chlorambucil and prednisone
        - MMF
      - Cyclosporine
      - IVIG
Infectious agents and IC GN

- **Bacterial**
  - Gp A-beta strep
  - Staph aureus
  - Staph epi
  - Gram neg bacilli
  - Strep pneumoniae
  - Treponema pallidum
  - Salmonella typhi
  - Meningococcus
  - Leptospirosis

- **Viral**
  - Hep B and C
  - CMV
  - Enterovirus
  - Measles
  - Parvo virus
  - Oncovirus
  - Mumps virus
  - Rubella
  - Varicella

- **Parasitic**
  - Plasmodium malariae
  - Toxoplasma
  - Filaria
  - Schistosomia
  - Trichinella
  - Trypanosome

- **Rickettsial**
  - Scrub typhus

- **Fungal**
  - Coccidioides immites

PSGN points

- Follows pharyngeal and skin infection
- Nephritogenic strains M types Serotype 49 commonest
- Primarily disease of children, age 5-15, rare <2 y and > 40 y.
- Latent period 7-14 d pharyngeal, 14-28 d pyoderma
- Presentation: hematuria (70%), periorbital edema, weight gain, HTN, oliguria
- UA: proteinuria (usually < 2g/24h), RBCs, RBC casts, WCCs, WC casts
- FENA usually < 0.5% in acute phase
- Serology: Antistreptolysin ab (ASO), Antistreptokinase, antideoxyribosenuclease B, and antinicotyladenine dinucleotidase
  - Titers rise 10-14 d post strep pharyngitis, peak at 3-4 wks
  - No relationship with development of nephritis or its severity

Question 16

- Hemodialysis is of value in all of the following intoxications except:
  - A.) Methanol
  - B.) Lithium
  - C.) Theophylline
  - D.) Digoxin
  - E.) Ethylene glycol