Renal Board Review

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Question 1.

• Answer: A; Add chlorthalidone
Figure 1.—Risk of cardiovascular events by hypertensive status in subjects aged 35 to 64 years, Framingham Study, 36-year follow-up. Coronary disease includes clinical manifestations of coronary disease such as myocardial infarction, angina pectoris, sudden death, other coronary deaths, and coronary insufficiency syndrome; peripheral artery disease is manifested as intermittent claudication. The biennial age-adjusted rate is per 1000 persons at risk (from D'Agostino et al).
Treatment of Hypertension

• Make the diagnosis
  – Measure correctly
  – Ambulatory monitoring
  – End organ damage/CV risks

• Look for modifiable risk factors
  – Obesity, sedentary lifestyle, alcohol use, drugs, dietary factors

• Think about secondary causes
  – RAS, OSA, endocrine, coarctation, renal disease

• Pick your medication(s)
  – First line for AA, Caucasian, underlying conditions

• Treat to goal
  – Add synergistic agents, avoid side effects

Resistant hypertension:
Blood pressure that is uncontrolled on 3 medications from different classes, at optimal dose, one of which is a diuretic.

• On lisinopril, nifedipine, atenolol
• ADD thiazide (GFR > 30) or loop diuretic (GFR < 30)
Question 2.

- Answer: D; Lifestyle modifications
Lifestyle Modifications for HTN

• Make the diagnosis
  – Measure correctly
  – Ambulatory monitoring
  – End organ damage/CV risks

• Look for modifiable risk factors

• Think about secondary causes
  – RAS, OSA, endocrine, coarctation, renal disease

• Pick your medication(s)
  – First line for AA, Caucasian, underlying conditions

• Treat to goal
  – Add synergistic agents, avoid side effects

Modifiable Risk Factors for Hypertension

• Obesity
• Sedentary lifestyle
• Alcohol use
• Low potassium diet
• High sodium diet
## Lifestyle modifications in the management of hypertension

<table>
<thead>
<tr>
<th>Modification</th>
<th>Recommendation</th>
<th>Approximate systolic BP reduction, range*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight reduction</td>
<td>Maintain normal body weight (BMI, 18.5 to 24.9 kg/m²)</td>
<td>5 to 20 mmHg per 10 kg weight loss</td>
</tr>
<tr>
<td>Adopt DASH eating plan</td>
<td>Consume a diet rich in fruits, vegetables, and low-fat dairy products with a</td>
<td>8 to 14 mmHg</td>
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<tr>
<td></td>
<td>reduced content of saturated and total fat</td>
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<tr>
<td>Dietary sodium reduction</td>
<td>Reduce dietary sodium intake to no more than 100 meq/day (2.4 g sodium or 6</td>
<td>2 to 8 mmHg</td>
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<td></td>
<td>g sodium chloride)</td>
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<tr>
<td>Physical activity</td>
<td>Engage in regular aerobic physical activity such as brisk walking (at least 30</td>
<td>4 to 9 mmHg</td>
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<td>minutes per day, most days of the week)</td>
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</tr>
<tr>
<td>Moderation of alcohol</td>
<td>Limit consumption to no more than 2 drinks per day in most men and no more</td>
<td>2 to 4 mmHg</td>
</tr>
<tr>
<td>consumption</td>
<td>than 1 drink per day in women and lighter-weight persons</td>
<td></td>
</tr>
</tbody>
</table>

For overall cardiovascular risk reduction, stop smoking. The effects of implementing these modifications are dose and time dependent and could be higher for some individuals; they are not all additive.

BMI: body mass index; BP: blood pressure; DASH: Dietary Approaches to Stop Hypertension.

Question 3.

• Answer: D; Continue clinical observation
Manage HTN in a patient who is over age 60.

**BP Definitions:**

- **Normal**
  - <120/80 mm Hg

- **Prehypertension**
  - 121-139/80-89 mm Hg

- **Stage 1 HTN**
  - 140-159/90-99 mm Hg

- **Stage 2 HTN**
  - ≥ 160 systolic or ≥ 100 diastolic mm Hg

**JNC 8 Goal BPs:**

- <150/90 is goal BP in patients > 80 years old
- <140-90 in patients ≤ 60 years old
- Between 140 and 150 mm Hg systolic in patients 60-80 years old depending on their tolerance
- In general you should not let diastolic blood pressures go below 60 mm Hg or even 65 mm Hg with known CAD
Question 4.

- Answer: D: Plasma aldosterone-plasma renin activity ratio
Understand the differential diagnosis of resistant hypertension

**Problem List:**
- 42 yo man
- Resistant hypertension
- Mild hypokalemia

**Definition of Resistant HTN:**
- Blood pressure measurements consistently exceed goal on 3 antihypertensive medications, one of which is a diuretic
- BP controlled on ≥ to four medications
- 12.8% of adults being treated for HTN

**Differential Diagnosis:**
- Non-adherence to therapy
- White coat resistant hypertension
- Renal parenchymal disease
- Renal artery stenosis
- Pheochromocytoma
- **Primary hyperaldosteronism**
- Obstructive Sleep Apnea
- Drug- induced
- Volume overload
Primary Hyperaldosteronism:

60% of patients have NORMAL K level

- ALDOSTERONE HIGH
- RENIN LOW
- AR RATIO >25 is suggestive BUT NOT diagnostic
- Metabolic alkalosis and hypokalemia MAY OR MAY NOT be present

8 AM draw
- OFF spironolactone or eplerenone for 6 weeks
- Possibly off ACEI

NO CONFIRMATION test needed:
- Spontaneous hypokalemia
- Undetectable renin level
- Aldosterone >30 ng/dL
Question 5.

- Answer: D: Type B lactic acidosis
Diagnose type B lactic acidosis

**Problem List:**
- 78 year-old woman
- Prosthetic valve endocarditis
- Anion gap metabolic acidosis
- Significantly elevated lactate
- Normal blood pressures

**Type A Lactic Acidosis**
- Tissue hypoperfusion due to shock
- Reduced systolic blood pressure may be minimized by severe vasoconstriction
- Altered mental status
- Cool extremities
- Oligoanuria
- **Lactic acid level predicts mortality**

**Type B Lactic Acidosis**
- Normal systemic perfusion
- Impaired cellular metabolism or regional ischemia
- Metformin
- **Linezolid (IV, prolonged)**
- HIV medications
- Liver disease
- Malignancy (lymphoma)
- D-lactic acidosis (bacterial overgrowth)
- Thiamine deficiency
Question 6.

- Answer: C: Measure urine chloride level
Evaluate a Patient with Hypokalemic Metabolic Alkalosis

**URINE CHLORIDE < 15 (LOW)= Chloride Responsive (90%)**
- Low effective circulating volume
- Volume depleted (orthostatic, hypotensive)
- **NORMAL** increase in renin, angiotensin, aldosterone
- Distal tubule wastes H+ and K+ and holds onto Na+
- Urine chloride LOW <15
- Cannot replace K until volume is replaced (GIVE sodium CHLORIDE)

**URINE CHLORIDE >15 (HIGH) = Chloride Unresponsive (10%)**
- Hypertensive
- Hypervolemic
- **ABNORMAL** increase in aldosterone or renin
- Distal tubule wastes H+ and K+ to holds onto Na+
- Urine chloride HIGH >15
Question 7.

- Answer: B: Estimate GFR using the Chronic Kidney Disease-Epidemiology Collaboration equation (CKD-Epi)
Estimate the glomerular filtration rate in a low-risk, healthy person

**Equations**
- Preferred to estimate GFR
- Creatinine MUST be stable for 24-48 hours
- MDRD (Modification of Diet in Renal Disease) underestimates GFR
- Cockcroft-Gault overestimates GFR
- CKD-EPI (Chronic Kidney Disease Epidemiology): just right: better for GFR > 60

**24 hour measurement**
- Extremes in age
- Extremes in weight
- Pregnancy
- Cirrhosis
- Amputations

**Radionuclide Scanning**
- Most precise method
- Used for kidney donor evaluation if GFR is borderline
Question 8.

- Answer: B: Hypokalemic distal (type 1) renal tubular acidosis
Diagnose hypokalemic distal (type 1) renal tubular acidosis

<table>
<thead>
<tr>
<th></th>
<th>Type 1 RTA (distal)</th>
<th>Type 2 RTA (proximal)</th>
<th>Type 4 RTA (distal)</th>
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<tr>
<td>Chloride</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
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<tr>
<td>Bicarbonate</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
</tr>
<tr>
<td>Potassium</td>
<td>↓</td>
<td>NL</td>
<td>↑</td>
</tr>
<tr>
<td>Urine pH</td>
<td>High (&gt; 5.5)</td>
<td>Low (&lt;5.5)</td>
<td>Low (&lt;5.5)</td>
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<tr>
<td>Etiologies</td>
<td>Chronic hepatitis</td>
<td>Multiple Myeloma</td>
<td>Diabetes mellitus</td>
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<td><em>Amphotericin B</em></td>
<td>Metal poisoning</td>
<td>Sickle cell</td>
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<td></td>
<td>Toluene</td>
<td><em>Acetazolamide</em></td>
<td><em>Spironolactone</em></td>
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<td>Lithium</td>
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<td>Sjogren’s; SLE</td>
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<td>Associations</td>
<td><strong>Nephrolithiasis</strong></td>
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<tr>
<td></td>
<td>due to hypercalcuria</td>
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</tbody>
</table>
Question 9.

- Answer: B: Chlorthalidone
Manage hypercalciuria in a patient with nephrolithiasis

- **Hypercalciuria:**
  - \(>250\) mg/24 hours WOMEN
  - \(>300\) mg/24 hours MEN
  - \(>200\) mg/liter

- **WORSENED by:**
  - High sodium diet
  - High animal protein diet
  - Loop diuretics

- **DO NOT advise a calcium restricted diet,** as this increases GI absorption of oxalate, increasing oxaluria

- **DO ADVISE:**
  - Thiazide diuretic
  - Fluids > 2 liters/day
  - Low purine diet
  - Low sodium diet
Question 10.

• Answer: B; Celecoxib toxicity
Identify the cause of hyperkalemia

Problem List:
- 83 year-old woman
- HTN, CKD stage 3, total knee replacement
- Amlodipine, fondaparinux, celecoxib
- New hyperkalemia

Differential Diagnosis of Hyperkalemia:
- Pseudohyperkalemia
- Increased potassium release from cells
- Decrease potassium excretion from kidney

Renal effects of NSAIDS that causes hyperkalemia:
1) Lower renin secretion (mediated by local prostaglandin synthesis)
2) Lower angiotensin II- induced aldosterone release
3) INDOMETHACIN >> SULINDAC AND LOW DOSE ASPIRIN
Question 11.

• Answer: A; AL amyloidosis
Diagnose Multiple Myeloma as a cause of acute kidney injury

**Clinical Features of MM:**
- Anemia (NCNC) (80%)
- Bone pain (70%)
- Recurrent infections
  - 25% presenting
  - 75% during disease
- Renal complications (50%)
- Hypercalcemia (25%)
- Renal failure (25%)

**Renal Complications:**
- Tubular Damage
  - Adult Fanconi’s syndrome
  - RTA Proximal Type 2
- Cast Nephropathy *
  - Proteinaceous casts clog the tubules resulting in tubule atrophy
- Glomerulopathy
  - Light chain disease deposition
  - Resulting in albuminuria!
- Exquisite sensitivity to IV contrast!

*most common
Amyloidosis: In an apple-green nutshell

**Primary AL Amyloidosis**
- Monoclonal protein related to plasma cell dyscrasia
- SPEP/IFE, UPEP/IFE, free light chains
- Bone marrow positive for plasma cell proliferation
- Monoclonal proteins infiltrate tissues; heart, kidney, GI tract, pleura, nerves (peripheral and autonomic)
- Kidney involvement may result in nephrotic proteinuria (albumin)

**Secondary AA Amyloidosis**
- **Polyclonal protein** related to inflammatory state; rheumatologic or infectious
- Juvenile RA, anklyosing spondylitis, psoriatic arthritis, IBD
- Familial Mediterranean Fever (60% of cases in Turkey)
- NEGATIVE SPEP/IFE etc for monoclonal proteins
- Kidney disease may result in nephrotic proteinuria (albumin)

**Hereditary ATTR Amyloidosis**
- Mutation in the transthyretin gene making abnormal proteins that infiltrate organs
- Cardiac and neurologic involvement more common than renal involvement
- NEGATIVE SPEP/IFE etc for monoclonal proteins
- Rare to have kidney involvement
Question 12.

• Answer: A: Interstitial nephritis
Diagnose Acute Interstitial Nephritis

Clinical Presentation:

- Fever, rash, eosinophilia, and elevated creatinine (10%)
- UA: WBC, WBC casts
- NEGATIVE CULTURE (sterile pyuria)
- Eosinophiluria (sensitive but not specific)
- < 2 gm/24 hr proteinuria

Causes: Drugs, Infections, Illnesses

- Antibiotics (β-lactam, cephalosporins, quinolones, Bactrim, rifampin)
- NSAIDS * (nephrotic proteinuria) with minimal change disease on biopsy
- Thiazides
- Proton Pump Inhibitors
- Phenytoin
- Allopurinol
- 5-aminosalicylates
Question 13.

• Answer: D; Continued observation
Diagnose IgA nephropathy: The most common cause of nephritic syndrome

**Ig A Nephropathy**

- CONCOMMITANT pharyngitis
- Normal complements

**Post-Strep Gnitis**

- 7-10 days AFTER pharyngitis
- Antibodies to:
  - Streptolysin O
  - DNAse B
- Low complements (C3)

**DIFFERENTIAL (NL C3):**

- IgA nephropathy (25-30%)
- Pauci-immune glomerulonephritis (15-25%)
- Anti-GBM antibody disease (3%)

**DIFFERENTIAL (LOW C3):**

- Lupus nephritis (20-30%)
- Membranoproliferative Gnitis (MPGN) (6-10%)
- Post-strep Gnitis (4-8)
Presentation/Treatment of IgA Nephropathy

3 Presentations:
1. Synpharyngitic hematuria
2. Asymptomatic microscopic hematuria with proteinuria
3. Henoch-Schonlein purpura

Treatment:
• Acute disease:
  – Methylprednisolone
  – Cyclophosphamide
• Chronic disease:
  – Blood pressure control
  – Control of proteinuria
  – No benefit of tonsillectomy
Question 14.

• Answer E: Supportive Care
Manage Post-Infectious Glomerulonephritis (PIGN)

- MANY bacteria, viruses and parasites can cause PIGN
- Most common nephritogenic strains of strep and staph
- Rapid onset of hypertension, oliguria, erythrocyte casts, and edema, LOW C3

**MANAGEMENT is SUPPORTIVE:**
- Early treatment of the bacterial infection
- Diuretics for volume overload
- Antihypertensives for elevated BP
- Dialysis if necessary
- NO evidence for immunosuppression, steroids, plasmapheresis
Question 15.

- Answer: A: Cryoglobulinemia associated with Hepatitis C
Diagnose Hepatitis C virus associated glomerulonephritis

- Occurs in up to 20% of patients with chronic Hepatitis C
- Presents as membranoproliferative glomerulonephritis or mixed cryoglobulinemia (skin, kidney, and nerve involvement)
- 1/3 relapsing dz with progression to ESRD
- Low complement (C4)
- + Rheumatoid factor
- TREAT Hep C virus

EXTRA-HEPATIC MANIFESTATIONS OF HEPATITIS C INFECTION:

1. Membranoproliferative GNitis
2. Mixed Essential Cryoglobulinemia
3. Lichen Planus
   - (the 5 Ps)
4. Porphyria Cutanea Tarda
   - (vesicles, milia, photosensitivity)
Question 16.

- Answer: C; Hemoglobinuria
Evaluation of Red Urine

Hemoglobinuria due to Intravascular hemolysis:

- Microangiopathic hemolytic anemia
- Transfusion reactions
- Mechanical shear from valves
- Infections
  - (Clostridial sepsis, Malaria)
- Paroxysmal Nocturnal Hemoglobinuria (PNH)
- Hypotonic fluid infusions
- Exposure to compounds with high oxidant potential (copper poisoning, Wilson’s disease)
Question 17.

- Answer: B; HIV antibody test
Diagnose Focal Segmental Glomerulosclerosis:
the most common renal cause of nephrotic syndrome in US (36-80%)

**Primary Disease:**
Podocyte damage similar to minimal change dz

**Secondary Disease Associations:**
- Morbid obesity
- Heroin use
- HIV
- Vesicoureteral reflux

**Risk factors for progression to ESRD:**
- Black race
- >2 gm/24 hr proteinuria
- Low GFR
- BMI > 27
- Hypertension

**Clinical Manifestations:**
- Acute onset of nephrotic syndrome with hematuria, renal failure and hypertension in primary disease;
- Asymptomatic subnephrotic to nephrotic proteinuria in secondary disease

**Management:**
- Immunosuppression with steroids or calcineurin inhibitors in primary disease
- ACEI +/- ARB in primary and secondary disease
- BP goal < 125/75 mm Hg
Question 18.

- Answer: B: Membranous nephropathy
Diagnose Membranous Nephropathy: the second most common renal cause of nephrotic syndrome

**Primary disease:**
- Immune complexes of IgG react with antigens in the outer aspect of GBM
- Antibody to PLA2

**Secondary disease associations:**
- Malignancy
- Hep B and C
- NSAIDS

**Risk factors for progression to ESRD:**
- Male gender
- Age>50
- Persistent proteinuria > 4g/24 h over 6 months
- Declining GFR

**Clinical manifestations:**
- Nephrotic syndrome with preserved GFR
- Renal vein thrombosis
- Hypercoagulability

**Management:**
- ACE and/or ARB
- BP goal < 125/75 mm Hg
- Persistent proteinuria > 4g/24 hr
- Cyclophosphamide, corticosteroids, or calcineurin inhibitor with possible need for rituxan
Question 19.

- Answer: D; Fluid restriction
Fig. 1 - Diagnostic algorithm for hyponatremia: hyponatremia (serum [Na⁺] < 135 mmol/L). ECF = extracellular fluid.
Manage asymptomatic hyponatremia

Treatment algorithm for hyponatremia

Severe hypotonic hyponatremia (serum sodium < 125 mmol/L)

Symptomatic (Neurological signs and symptoms)
- Acute (<48 hours)
  - Emergency correction
    - Aim is to correct cerebral edema
    - Start 3% saline (1.2 mL/kg/h) until symptoms resolve, then 1.0 mL/kg/h (do not exceed >12 mEq/day)

Asymptomatic
  - Chronic (>48 hours)
    - Urgent correction
      - Use 3% saline (1 mL/kg/h) until symptoms resolve; thereafter correct at a rate of 0.5 mEq/L/h with 0.9% saline

Determine the ECF Volume status

Normovolemic
- Restrict water intake
- Give AVP receptor antagonists
- Treat the underlying causes
- Give AVP-receptor antagonists

Hypervolemic
- Restrict salt and water intake
- Give diuretics

Hypovolemic
- Restore ECF volume with 0.9% saline
- Treat the underlying causes
- Give AVP-receptor antagonists
- Treat underlying causes

Fig. 3 - Treatment algorithm for hyponatremia: severe hypotonic hyponatremia (serum sodium < 125 mmol/L). AVP = arginine vasopressin; ECF = extracellular fluid.
Question 20.

- Answer: B; Substitute labetalol for lisinopril
Manage HTN in a woman of childbearing age

**Normal physiology in pregnancy**
- Blood pressure lowers
- Plasma volume increases
- GFR increases
- Renal pelvis, calices, and ureters dilate
- Increased risk for pyelo
- Hyperventilation causes resp alkalosis with increased renal bicarb excretion

**Pearls in Pregnancy “20 weeks”:**
- Hypertension BEFORE 20th week indicates new dx of chronic hypertension
- Safe BP agents in pregnancy are *methyldopa and labetalol*: ACEI, ARBs and renin inhibitors are NOT safe
- Gestational hypertension develops AFTER 20 weeks: no proteinuria or end-organ damage
- Pre-eclampsia hypertension develops AFTER 20 weeks and is associated with proteinuria
- LOW dose aspirin reduces the risk of preeclampsia