Dear T2 Class,

Welcome to the Renal Block! In three short weeks we will cover a large amount of material that I hope you find as exciting and stimulating as I do. Nephrology covers a wide spectrum of physiology and pathology, including electrolytes, acid-base disorders, and intrinsic kidney diseases. In this syllabus, I have provided a general outline for the course, with suggested readings and overall objectives for the course. While each lecture or learning activity will also have their own objectives posted on tmedweb, which you will also be responsible for (i.e. fair game for the exam), if you can master all the following course objectives you will know more nephrology than most interns or residents! Each of the objectives is clinically important and essential for the practice of nephrology (many are also essential for the practice of internal medicine).

Some housekeeping issues: There is required attendance for all TBLs and PBLs. Doreen Barrett who is the coordinator for the course will be out for two weeks. This is also my first year as course director so I hope you will help me in seeing that the course runs smoothly by checking your email at least daily and emailing me with any questions or concerns that arise. I welcome any questions you may have. I find the questions from students to be the most challenging, and part of the fun of practicing medicine in an academic center. My door is always open to students.

Our book for the course will be *Renal: An Integrated Approach to Disease* by Paul G. Schmitz (2012). The book is in the bookstore and also on reserve at Matas. *Renal Pathophysiology: The Essentials*, by Rennke and Denker is also an excellent textbook (the textbook I used in med school) and acceptable if you already own it. The newest 4th edition now has pictures in color and is on reserve in Matas. Any required reading from either textbook has been made available on tmedweb. The Pathology CD-ROM (aka the Electronic Learning Module on tmedweb) is also a great resource for supplementary learning (a few chapters are required as part of a TBL).

I look forward to working with you all.

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Renal Pathophysiology Syllabus 2014

**WEEK 1 Contents:**

Introduction/Review of physiology
Electrolytes
Hypertension (including pharmacology on ACE inhibitors)
Introduction to renal pathology to prepare for Glomerular Diseases in week 2

**WEEK 2 Contents:**

Acid-Base Homeostasis
Application exercise: case studies on electrolytes and acid-base disorders
Acute Kidney Disease and Chronic Kidney Disease
Glomerular Diseases I
Continuation of renal pharmacology (diuretics)
Renal infectious disease

**WEEK 3 Contents:**

Glomerular Diseases II
Continuation of renal pharmacology (PBL)
Reviews/Study time
Exam
Course Objectives

Electrolytes and Water:
1. Understand mechanisms by which serum sodium concentration may increase or decrease. What is the pathophysiology of the major causes of hyponatremia and hypernatremia
2. Recognize that serum sodium is a reflection of water in comparison to the sodium content of the body, and that disorders of serum sodium concentration usually reflect disorders of excess water or water loss
3. Describe how the body compensates for volume loss
4. Understand how edema forms. Describe the mechanism of edema formation in nephrotic syndrome, and compare it with mechanisms of edema formation in congestive heart failure and cirrhosis
5. Recognize that there are no “normal values” for urine chemistries, rather expected values for a particular situation
6. Define polyuria. Differentiate between a solute diuresis and a water diuresis. Understand pathophysiology of impaired urinary diluting ability and impaired urinary concentrating ability
7. Understand how potassium is handled by the kidney, and the role of aldosterone in disorders of potassium homeostasis
8. Understand the kidney's role in calcium and phosphorus homeostasis, including the role of vitamin D and PTH. Recognize abnormalities in calcium and phosphorus metabolism in chronic kidney disease

Lectures: Disorders of Water, Disorders of Sodium, Disorders of Potassium, Calcium/Phosphorus Homeostasis
Other learning activities: PBL on Sodium and Water (10/9), Fluid and Electrolytes Case Studies (10/17)
Resources: Schmitz 2012 Chapters 10, 11, 12 (Pros: short, the basic information is there, the explanations are simplified, Cons: the explanations are a little superficial). Supplemental Reading (optional): Renal Pathophysiology The Essentials, 4th edition, 2014, by Rennke and Denker, chapters 2, 3, 4 (longer, but good explanations, book is on reserve in Matas, chapters will also be photocopied and placed on TMedWeb). CD-ROM questions and answers

Hypertension:
1. Understand the classification of essential and secondary hypertension
2. Understand approach to treatment of hypertension and the mechanism of action of various anti-hypertensive medications (e.g. effects of ACEi on glomerular hemodynamics, systemic blood pressure, and electrolytes)

Lectures: Hypertension by Dr. Alper, Pharmacology lectures
Other learning activities: Pharmacology PBL on Hypertension (10/21)
Resources: Schmitz 2012 Chapter 20
**Acid-Base Homeostasis:**

1. Be able to identify single acid-base disorders, and when there is more than one acid-base disorder. Know common clinical scenarios associated with acidosis and alkalosis, i.e. common causes of acidosis and alkalosis
2. When there is a metabolic acidosis, be able to calculate the anion gap and understand what is the significance of an anion gap. Be able to compare different types of metabolic acidosis, i.e. anion gap and non-anion gap metabolic acidosis
3. Understand compensatory mechanisms of acid/base derangement, and be able to use Winter’s formula

*Lectures:* Acid-Base Homeostasis  
*Other learning activities:* PBL on Acid–Base Case Studies (10/16), Fluid and Electrolyte Case Studies (10/17)  
*Resources:* Schmitz 2012 Chapter 14 (Chapter 13 reviews normal acid-base physiology). CD-ROM questions and answers

**Acute Kidney Injury and Chronic Kidney Disease:**

1. Know the three major categories of AKI: prerenal, intrarenal, and post-renal, and common causes of each type of AKI.  
   a. Intrarenal kidney disease can then be classified anatomically  
      i. Glomerular diseases: e.g. FSGS  
      ii. Tubular diseases: e.g. ATN  
      iii. Interstitial diseases: e.g. Acute Interstitial Nephritis (AIN)  
      iv. Vascular diseases: e.g. HUS/TTP  
2. Understand how changes in renal hemodynamics can affect GFR
3. Know the appropriate diagnostics tools (urinalysis, urine electrolytes, urine protein assessment, urine culture, kidney imaging, blood tests, physical exam, and history) in the evaluation of AKI, and be able to utilize them to develop a differential diagnosis for AKI
4. Define CKD and the stages of CKD
5. Identify common pathophysiologic disturbances that occur in CKD (e.g. symptoms of uremia)

*Lectures:* none (partial introduction in Kidney biopsy lectures by Dr. Kidd on 10/10)  
*Other learning activities:* TBL on Acute and Chronic Kidney Diseases (10/13)  
*Resources:* (within Dr. Krane’s objectives on tmedweb)
Glomerular Diseases (an intrinsic/intrarenal cause of AKI and CKD):
1. Compare and contrast the differences between nephrotic and nephritic syndrome
2. Know the major complications of nephrotic syndrome
3. Know and be able to classify the major glomerular diseases in terms of nephrotic or nephritic presentations
   a. Nephropathies
      i. Primary (renal limited as opposed to systemic) nephrotic (Minimal Change Disease, FSGS, Membranous)
      ii. Systemic nephrotic (DM, Amyloidosis/multiple myeloma, systemic lupus erythematosus type V)
   b. Nephritis (Nephritides)
      i. Nephritic glomerular diseases with low complement (post-infectious, MPGN, cryoglobulinemia, infective endocarditis, systemic lupus erythematosus)
      ii. Nephritic glomerular disease with normal complement (IgA, Alport’s syndrome, ANCA vasculitis, Goodpasture’s syndrome, TTP/HUS)
4. Correlate renal pathology to the various pathomechanisms of glomerular diseases (e.g. foot process effacement in minimal change disease)

Lectures: none (partial introduction in Kidney biopsy lectures by Dr. Kidd on 10/10)
Other learning activities: TBL on Glomerular Diseases (10/15 and 10/20)
Resources: (within Dr. Krane’s objectives on tmedweb)
<table>
<thead>
<tr>
<th>Test</th>
<th>Normal</th>
<th>Function</th>
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<tbody>
<tr>
<td>BUN</td>
<td>7-18 mg/dL</td>
<td>A marker for kidney function</td>
<td>Can rise in volume depletion, large protein meal, steroid use, GI bleed</td>
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<tr>
<td>Creatinine</td>
<td>0.6-1.2 mg/dL</td>
<td>A marker for kidney function</td>
<td>Varies with muscle mass, e.g. small women should have lower Cr than men</td>
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<tr>
<td>BUN:Cr ratio</td>
<td>10:1</td>
<td>Will be elevated in volume depleted states (or any situation when there is increase sodium reabsorption in the proximal tubule, which leads to increase urea reabsorption in the proximal tubule)</td>
<td>High catabolic state or high protein diet can elevated BUN, and low muscle mass will lead to low Cr, leading to elevated ratio independent of volume status</td>
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<tr>
<td>Sodium</td>
<td>135-145 mEq/L</td>
<td>Low value indicates water excess, high value indicates water deficit</td>
<td>Cannot be used to assess volume status</td>
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<tr>
<td>Potassium</td>
<td>3.5-5.0 mEq/L</td>
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<td>Can be artificially high in a hemolyzed sample</td>
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<tr>
<td>Bicarbonate</td>
<td>22-28 mEq/L</td>
<td>Low levels may indicate a metabolic acidosis or compensation from a primary respiratory alkalosis. High levels may indicated a metabolic alkalosis or a compensation from a chronic respiratory acidosis</td>
<td>Cannot determiner acid-base status from bicarb level alone, need pH from an atrial blood gas (ABG). Clinical history also very helpful</td>
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<tr>
<td>Corrected Serum Calcium</td>
<td>8.5 - 10.3 mg/dL</td>
<td>Corrected Calcium = 0.8 x (normal albumin – serum albumin) + [Ca^{2+}]</td>
<td>Calcium binds with albumin, in low albumin state the correction factor better estimates free ionized calcium</td>
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<tr>
<td>Serum Anion Gap</td>
<td>About 10-12 Cations = Anions Na⁺ = Cl⁻ + HCO₃⁻ + Albumin⁻ AG = Na⁻ - (Cl⁻ + HCO₃⁻) = the unmeasured anions, which is mostly Albumin</td>
<td>There is a correction factor for what is considered normal AG when there is low albumin. Expected AG = [Albumin] x 2.5 Small increase in AG may not always be identified, but large increases in AG (e.g. ≥ 20) indicates metabolic acidosis with increased organic anions</td>
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<tr>
<td>Measured serum osmolality</td>
<td>275-295 mOsm/kg</td>
<td>To determine if patient has a true hypoosmolal state in the setting of hyponatremia When serum Osm are normal and serum Na is low, this is pseudohyponatremia, seen with severe hyperlipidemia, multiple myeloma, or other state of high serum protein (due to artifact in the way sodium is measured by dilution in the lab)</td>
<td>In the setting of hyperglycemia (water shifts out of cells → hyponatremia) the serum osms will be high, indicating a HYPERosmolal state</td>
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<tr>
<td>Calculated serum osmolality</td>
<td>2 x Na + BUN/2.8 + glucose/18</td>
<td>Compare with measured serum osmolality when ingestion of a volatile alcohol is suspected (i.e. the osmolar gap)</td>
<td>If osmolar gap &gt;10 suspect: Alcohol Methanol Isopropyl alcohol Ethylene glycol</td>
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**Urine Studies:** The term “urine lytes” is not specific. If someone tells you to order “urine lytes”, you should ask them which ones for the particular patient scenario.

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<tr>
<td>Urine Na</td>
<td>DEPENDS...in volume contracted states the kidney should be preserving sodium and Urine Na should be &lt;20</td>
<td>Can be used to differentiate prerenal azotemia from acute tubular necrosis (ATN) Can also be used to determine if patient is Na+ avid in the setting of hyponatremia (hypovolemic hyponatremia)</td>
<td>In the setting of prerenal and a very concentrated urine the urine Na may be borderline (not low), here a FeNa can be helpful</td>
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<td>FeNa</td>
<td>( \frac{P_{Cr} \times U_{Na}}{P_{Na} \times U_{Cr}} \times 100 ) \n(&lt; 1% ) is consistent with prerenal azotemia \n( &gt;1% ) is consistent with ATN</td>
<td>Should not be used as the gold-standard for diagnosing prerenal, gold-standard is if Cr improves with hydration</td>
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<tr>
<td>Urine Osm</td>
<td>DEPENDS...in hypoosmolal state kidney should be excreting water, and urine Osm should be low...in hyperosmolal state kidney should be reabsorbing water, and urine Osm should be high In SIADH: hyponatremia with inappropriately high water reabsorption and inappropriately high urine Osm In Diabetes Insipidus: hypernatremia with inappropriately low water reabsorption and inappropriately low urine Osm</td>
<td>Reflection of the ADH level Max ADH ( \rightarrow ) water is reabsorbed ( \rightarrow ) max urine Osm are 900-1200 No ADH ( \rightarrow ) water is being excreted ( \rightarrow ) min urine Osm are 50-100</td>
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<tr>
<td>Urine Cl</td>
<td>DEPENDS...low in volume depleted states...high with diuretic use</td>
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<td>Urine K</td>
<td>DEPENDS</td>
<td>Usually checked in the evaluation of hypokalemia to determine if potassium losses are renal or extra-renal</td>
<td>In the setting of hypokalemia the kidney can limit daily potassium loss to 5-25 mEq. Can measure K in a 24 hr urine collection, or estimate it with a K/Cr ratio (be aware of units)</td>
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<tr>
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<tr>
<td>Urine Anion Gap</td>
<td>Urine (Na + K) – Urine Cl</td>
<td>Compares the major ions in the urine (note that bicarbonate is not a major urinary anion)</td>
<td>Cannot be used if there is also an AG metabolic acidosis because there may be 2 unmeasured ions in the urine</td>
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<td>NH4+ is the primary unmeasured cation, the excess Cl(^-) is being excreted with NH4+</td>
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<td></td>
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<td>UAG is an indirect assay of urinary NH4+</td>
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<td>Used in the setting of a non-AG metabolic acidosis to distinguish between a distal RTA and diarrhea. In the setting of acidosis, if UAG is very negative, this indicates renal acid excretion in the form of NH4+/kidney’s ability to excrete acid (not a renal tubular acidosis)</td>
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<tr>
<td>Urine albumin</td>
<td>Use with urine Creatinine to determine mg of albumin per gram of Cr (estimate urinary excretion of creatinine at a 1g of Cr/day)</td>
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<td>Microalbuminuria = 30-300 mg/day of urine albumin</td>
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<td>UAlbumin mcg/dL ÷ UCr mg/dL = Albumin mg/day (normal is &lt; 30mg/day)</td>
<td>Diabetics with microalbuminuria are more likely to have progression of renal disease and benefit from RAAS blockade</td>
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<td>A more sensitive test than urine total protein. Used in diabetics to detect early kidney disease, not used in patients with GRAMS of proteinuria</td>
<td>Will not detect proteinuria due to light chains (e.g. in Multiple Myeloma), need to send total urine protein</td>
</tr>
<tr>
<td>Urine protein/Cr ratio</td>
<td>Total urine protein = albumin + Tamm Horsfall (aka uromodulin, most abundant protein in normal urine) + other proteins (e.g. light chains)</td>
<td>UPCR = Urine protein mg/dL ÷ Urine Cr mg/dL</td>
<td>Can be falsely high or low based on patient’s muscle mass (low muscle mass = low Cr = high UPCR)</td>
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<td></td>
<td>Normal &lt; 150-200 mg/day &gt; 3.5 grams/day = nephrotic range</td>
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### 'Renal' Hormones

<table>
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<tr>
<th>Hormone</th>
<th>Produced by</th>
<th>Stimulated by</th>
<th>Action</th>
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</table>
| Renin   | Cells of the JGA | 1. Dec afferent arteriolar stretch  
2. Decrease NaCl delivery to the macula densa  
3. Hypotension and decreased sympathetic neural tone (baroreceptors) | Converts angiotensinogen to angiotensin I |
| Angiotensin II | Conversion of Ang I | | 1. Potent systemic vasoconstrictor  
2. Constricts afferent and efferent arterioles (EA > AA)  
3. Increases proximal Na+ reabsorption  
4. Stimulates production of Aldo |
| Aldosterone | Zona glomerulosa cells of the adrenal gland | 1. Ang II (low flow to glomerulus → activation of RAAS)  
2. Hyperkalemia | 1. Increases distal Na+ reabsorption  
2. Increases K+ secretion  
3. Increases H+ secretion |
| ADH (aka vasopressin, aka AVP) | Synthesized in the hypothalamus, secreted from the posterior pituitary | 1. Hyperosmolar state  
2. Volume depletion | In the kidney: Inserts Aquaporin channels in the distal nephron to allow WATER reabsorption without sodium  
(also increases peripheral vascular resistance) |
| ANP | Myocardial cell in the atria | Expansion of the ECF volume/Increase sodium load → atrial stretch | 1. Vasodilator  
2. Increases Na+ and water excretion |
Diuretics

<table>
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<tr>
<th>Drug Type/Name</th>
<th>Indication</th>
<th>Side Effects</th>
<th>Caution</th>
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<tbody>
<tr>
<td><strong>Carbonic anhydrase inhibitors</strong></td>
<td>- Edematous states with metabolic alkalosis</td>
<td>Bicarbonate wasting leads to metabolic acidosis</td>
<td>- Net diuresis is limited by distal Na reabsorption (not good for volume diuresis)</td>
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<tr>
<td>Acetazolamide</td>
<td>- Post-hypercapnic alkalosis</td>
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<td></td>
<td>- Glaucoma</td>
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<td></td>
<td>- Pseudotumor cerebri</td>
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<tr>
<td>Loop diuretics</td>
<td>- Edema</td>
<td>- Volume depletion</td>
<td>- Ototoxicity at high doses or when used with aminoglycosides</td>
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<tr>
<td>Furosemide</td>
<td>- CHF (also need low Na diet or frequent dosing)</td>
<td>- Hypokalemia</td>
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<tr>
<td>Bumetamide (inc bioavailability)</td>
<td>- Hyperkalemia</td>
<td>- Metabolic alkalosis</td>
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<tr>
<td>Ethycrinic acid (no sulfa moiety)</td>
<td>- Hypercalcemia</td>
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<tr>
<td>Torsemide (longer acting)</td>
<td>- Can also be used for SIADH (produces hypotonic urine)</td>
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| **Thiazides**  
Hydrochlorothiazide  
Chlorthalidone  
| -Long acting, good adjunct for HTN tx  
-Can be used with loop diuretics to increase diuresis  
-To decrease hypercalciuria in stone formers, increase calcium reabsorption in osteoporosis  
-Use to promote mild volume depletion and increase proximal reabsorption to limit losses in DI  
| -Volume depletion  
-Hyponatremia (limits the kidney’s ability to make maximally dilute urine)  
-Hypokalemia (increase distal Na delivery leads to K loss)  
-Hypercalcemia  
-Metabolic alkalosis  
| No longer 1st choice for essential HTN (now ACEi or CCB)  
Impotence  
Hyperlipidemia  
Hyperglycemia  
Gout |

| **K+ sparing diuretics**  
*Block Aldo:*  
Spironolactone  
Eplerenone  
*Blocks ENaC:*  
Amiloride  
Triamterene  
| To decrease potassium loss from other diuretics  
-To decrease potassium loss from other diuretics  
-Refractory edema in CHF or cirrhosis  
-Hyperaldosteronism  
| Hyperkalemia  
Hyperkalemia  
Gynecomastia |
