ARF!*  

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*Acute Renal Failure

Goals
- All of these are real cases from U of I....
- Focus on diagnosing and treating acute renal disease
- OK...so it is AKI (acute kidney injury) and not ARF. But the dog is so cute!

What constitutes AKI?
- Creatinine increase of 0.3mg/dl in 48 hours
- Or
- Creatinine of 1.5mg/dl above baseline.

Case
- 52 year old male presents with complaints of “feeling poorly”. He notes that he has had increasing swelling in his ankles over the past couple of months. His doctor placed him on a diuretic but to no avail. He notes (very proudly) that his urine bubbles when he pees.
- Exam remarkable for 3+ pitting edema.
BP 150/100
Weight is 140 lbs

What is causing his urine to bubble?

Urinalysis: How would you classify this urine (nephrotic, nephritic, other..)?
- 2+ protein
- 3+ blood
- 2+ leukocyte esterase

Nephritic Urine: “Active” sediment
- White cells
- Protein
- Red cells
- Casts
Nephrotic Urine
- Bland
- Oval fat bodies
- Fatty casts
- Maybe sloughed renal tubular cells

- Fat Bodies suggest glomerular disease except:
  - Polycystic kidney disease
  - Fat embolism syndrome

You get some labs back
- Creatinine = 1.4
- BUN = 21
- Rest of labs are normal.

Is he in renal failure?
- Creatinine = 1.4
- BUN = 21
- Age = 52
- Wt = 140 lb

- Est. Creatinine Clearance = \( \frac{[140 - \text{age(yr)}] \times \text{weight(kg)}}{72 \times \text{serum Cr(mg/dL)}} \)

- There are a bunch of equations. Choose one you like to get you in the ballpark.
A creatinine of 1.4mg/dl puts him in stage 3 renal failure
- Stage 1 GFR > 90ml/min with albuminuria
- Stage 2 GFR 60-89 ml/min persistent albuminuria
- Stage 3 GFR 30-59
- Stage 4 GFR 15-29
- Stage 5 GFR < 15

You send the patient home to follow up next week.

He returns to the ED in 2 months..
- Cr= 2.5
- Urine shows casts

What is it and what does it signify?
RBC Casts

- Pathognomonic for glomerulonephritis
- Also interstitial nephritis

Granular Cast

- Non-specific
- Chronic renal disease, exercise, glomerulonephritis

Oval Fat Bodies: Glomerular disease (leaking)

Fatty cast: Glomerular disease, Polycystic kidney disease
Renal tubular cell cast (Epithelial cell cast)

White cell cast

Waxy Cast: Non-specific
• Red cell casts: glomerulonephritis
• White cell casts: parenchymal infection, interstitial nephritis, occasionally glomerular disease
• Granular casts are non-specific → Chronic renal disease, exercise, glomerulonephritis
• Waxy casts: chronic renal disease → non-specific
• Renal tubular cell: ATN, glomerulonephritis

He goes on to dialysis and nobody is happy except the nephrologist

Next Case: The Return after Surgery....
• 55 year old diabetic female who presents to the ED after surgery noticing that she isn’t feeling the best. She had surgery for her gallbladder yesterday in an outpatient surgery center and is having decreasing amounts of urine output.
• She is mildly confused

Your first thought is urinary retention from narcotics.

• Or anticholinergics or alpha stimulants (e.g. pseudoephedrine) or prostate (?)
• So you put in a Foley/do a bladder scan = scant urine

<table>
<thead>
<tr>
<th>Lab test</th>
<th>Before surgery</th>
<th>Day 1 after surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium meq/L</td>
<td>138</td>
<td>140</td>
</tr>
<tr>
<td>Potassium meq/L</td>
<td>4.5</td>
<td>5.8</td>
</tr>
<tr>
<td>Chloride meq/L</td>
<td>103</td>
<td>105</td>
</tr>
<tr>
<td>HCO₃ meq/L</td>
<td>24</td>
<td>18</td>
</tr>
<tr>
<td>BUN mg/dL</td>
<td>15</td>
<td>29</td>
</tr>
<tr>
<td>Creatinine mg/dL</td>
<td>1.1</td>
<td>2.0</td>
</tr>
</tbody>
</table>

The surgical team comes in…one wants to give fluids, one wants to give furosemide, one wants do both….They have been up all night on call and are not happy.
You are called in to mediate:

- The BUN/Cr ratio is <20. This suggests that
  A. She is dehydrated
  B. She has a prerenal cause of her increased creatinine such as hypoperfusion
  C. Intrinsic kidney disease is more likely than a prerenal cause
  D. None of the above

Answer: C

- BUN/Cr ratio of <20 generally indicates an intrinsic renal cause of renal failure
- BUN/Cr ratio of >20 indicates a prerenal cause such as hypoperfusion (CHF, dehydration, etc.).

- Urine volumes indicate that your patient has become oliguric. What is the next step?
  A. Calculation of creatinine clearance.
  B. Arterial blood gases.
  C. CT scan of the abdomen.
  D. Fractional excretion of sodium.
Answer: D

• Oliguric Renal Failure: Check fractional excretion of sodium
• Careful if have pre-existing renal disease (e.g. chronic pre-renal disease—cirrhosis, etc.), diuretics
• The equation used to calculate FENa is:
  \[ \text{FENa (\%)} = \left( \frac{\text{Urine Na/Plasma Na}}{\text{Urine Cr/Plasma Cr}} \right) \times 100 \]
• If on diuretics, check fractional excretion of urea:
  – FEUrea being 50 to 60 percent in acute tubular necrosis (ATN)
  – Usually below 35 percent in prerenal disease

Most common causes of renal failure in inpatients.

• ATN – 45 percent
• Prerenal disease – 21 percent
• Acute superimposed on CKD – 13 percent (mostly due to ATN and prerenal disease)
• Urinary tract obstruction – 10 percent (most often older men with prostatic disease)
• Glomerulonephritis or vasculitis – 4 percent
• Acute Interstitial Nephritis – 2 percent
• Atheroemboli – 1 percent

And the following....
This is easy

<table>
<thead>
<tr>
<th>FENa</th>
<th>Prerenal</th>
<th>Renal</th>
<th>Explanation</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1%</td>
<td></td>
<td>&gt;2%</td>
<td>Kidney holding on to sodium appropriately</td>
</tr>
<tr>
<td>Urine Na</td>
<td>Low (&lt;20)</td>
<td>High (&gt;40)</td>
<td>Hold sodium to fix pre-renal state</td>
</tr>
<tr>
<td>BUN/Cr</td>
<td>&gt;20</td>
<td>&lt;20</td>
<td>Functioning kidney absorbing fluid trying to resolve pre-renal problem</td>
</tr>
</tbody>
</table>

- This calculation most useful in oliguric renal failure (urine output < 400 cc/day).
- What if FENa 1-2%? Not helpful
- Look at the other stuff.

May have low FeNa occasionally with...
- Early ATN\(\) prerenal
- ATN with underlying prerenal disease
  - Cirrhosis, CHF.
- 10% of those with non-oliguric ATN
- Occasionally with: glomerulonephritis, renal failure from heme or radiocontrast, interstitial nephritis

Case contd
- Mildly disoriented female in no acute distress. She has lower extremity and sacral edema.
- UA = Specific gravity of 1.020, pH 6, 3 RBCs/hpf, 2 WBCs/hpf, and muddy brown casts.
- Urine creatinine is 6.5 mg/dL and the urine sodium is 45 meq/L. You calculate the FENa which turns out to be >2%
Given the clinical course and urine findings, which of the following is the best diagnosis?

A. Acute tubular necrosis.
B. Acute interstitial nephritis.
C. Vasculitis.
D. Congestive heart failure.
E. Lactic acidosis.

Answer: A

• Acute tubular necrosis (ATN)
  – Major cause renal failure in hospitalized patients
  – Metabolic derangements in ATN;
    • progressive hyponatremia, hyperkalemia, and metabolic acidosis with a high anion gap.
  • ATN have an FENa is > 1% and a urine sodium is > 40 meq/L.
  • “Muddy” brown casts

You suspect that ATN is the result of:
A. Acetaminophen
B. Hypotension
C. Intrinsic renal infection
D. Cefotetan
Answer: B

• Causes of ATN
  – Hypoperfusion and renal hypoxia (shock, hypotension, CHF)

Remember drugs as a cause of increased creatinine/ATN:

• ACE or ARB
• NSAIDS
• Diuretics
• Antiretroviral
• Anything that will reduce renal perfusion (beta blockers, calcium channel blockers, etc.)
• Gold, Lithium, iron
• Tacrolimus
• Iron
• Anything that can cause rhabdomyolysis (coca, ethanol)
• Carbon monoxide
• PCP
• PCN
• Aminoglycosides

And get a good history.

The workup of renal failure is cookbook!

When you are presented with a patient with nephritis/nephrotic urine:

• 5 basic categories
  – Infectious
  – Immunologic
  – Endocrine
  – Malignancy
  – Other
Immunologic

- ANA: Lupus
- ANCA: Wegener’s, etc.
- Compliment levels: Post strep, lupus, Membranoproliferative glomerulonephritis, PG, etc.
- Anti-glomerular basement membrane: Goodpasture’s
- Cryoglobulins
- Clinical dx:
  - Henoch-Schönlein
  - TTP: Fever, fluctuating mental status, renal failure, thrombocytopenia, microangiopathic hemolytic anemia

Infectious

- ASO: Post streptococcal glomerulonephritis.
- Hepatitis B and C (up to 20% nephrotic syndrome)
- Sub-acute bacterial endocarditis
- Hemolytic-Uremic syndrome, shiga toxin
- HIV
- Legionella

Misc.

- Malignancy: Leukemia, lymphoma, myeloma, etc.
  - CXR
  - Screen for malignancy by age
  - Serum and urine protein electrophoresis
- Metabolic
  - Glucose: Rule out DM
  - Calcium: Rule out sarcoid
- Pregnancy (Toxemia)
- Hypertension including malignant
- Alport’s syndrome (hereditary)
- Etc.
Intravenous Contrast Material Exposure Is Not an Independent Risk Factor for Dialysis or Mortality

Radiology
December 2014
Volume 273, Issue 3

Game changer

- IV contrast does not increase adverse renal effects.
- 10,000 patients in two groups based on propensity score.
- Either got or did not get IV contrast.
Propensity scoring

• Both groups are just as likely to get an intervention (in this case CT) based on their illness.
• It just happens that one group got the intervention and the other didn’t.
• An example:
  – Two patients with a similar history of abdominal pain, same age, same intensity of pain, same smoking history, etc.
  – One gets a contrast CT and the other a plain CT (or no CT).

• No difference in acute kidney injury (Cr elevated >0.5mg/dl)
• No difference in mortality or dialysis
• Importantly, this was also true for patients with a Cr of >2mg/dl, those with CHF, those with DM.
• Feel more comfortable if really need that CT.

Any more recent evidence?

What does contrast do to the kidneys?

This study: retrospective

- 7201 who underwent contrast-enhanced CT
- 5499 who underwent unenhanced CT
- 5234 who did not undergo CT (control for other factors that might increase Cr.)
- Propensity scoring to match groups.
- Inclusion criteria: baseline creatinine of 0.4–4.0 mg/dL.

Inclusion Criteria

- Creatinine within 8 hours before CT, repeat within 72 hours after CT
- Exclusion:
  - Dialysis
  - Transplant
  - CT within 6 months before the study

Outcome measures

- Cr increase =/> 0.5mg/dl
- Or 25% over baseline

No difference in renal outcomes. Don’t go hog wild but it is OK to do a CT with contrast if necessary in folks with Cr< or = 4.0mg/dl

If you are thinking PE and you need to know and the creatinine is 2.2 or 3mg/dl, go for it!
We also now have a meta-analysis:

- Over 100,000 patients
- Acute kidney injury (odds ratio (OR) 0.94; 95% confidence interval [CI] 0.83 to 1.07), need for renal replacement therapy (OR 0.83; 95% CI 0.59 to 1.16), or all-cause mortality (OR 1.0; 95% CI 0.73 to 1.36).


Your next step is to:

- A. Give large dose furosemide to convert oliguric to non-oliguric renal failure
- B. Start “renal dose” dopamine to improve kidney perfusion
- C. Start hemodialysis
- D. Protein restriction
- E. Continue to match input and output. No other changes in therapy at this time

Answer: E

- Converting oliguric to non-oliguric renal failure may worsen outcomes.
- This patient does not yet need hemodialysis

Renal failure due to ATN typically lasts 7 – 21 days. The most common cause of death in patients with ATN is:

- A. Haemorrhage
- B. Dialysis
- C. Infection
- D. Transfusion reaction
- E. CHF secondary to fluid overload
Answer: C

• Generally infection though have multisystem dysfunction

Haemodialysis not indicated
– May worsen disease (recurrent hypotension, infection, complement activation in kidney)
• Match fluid intake and output
• Some conflicting data

In general the later you start dialysis the better.

Absolute indications for dialysis
• Persistent nausea and vomiting
• Pericarditis
• Fluid overload
• Uremic encephalopathy
• Accelerated hypertension
• Bleeding due to uremia,
Dialysis contd

- Electrolyte abnormalities
- Serum creatinine greater than 12 mg/dL,
- Malnutrition relative indication
- NKF ➔ GFR<10 or so... (unless clinically well)
- Clinical indications trump numbers all of the time.

But....

- Early initiation of dialysis leads to increased mortality in chronic renal failure...
- Wait until GFR is 5-7ml/min/1.73m²
- That doesn’t mean you shouldn’t involve nephrology.

Dialysis isn’t Benign

Hypotension with dialysis...

- Excessive ultrafiltration
- Clearance simultaneous with ultrafiltration
- Medullary volume loss (GI losses, decreased oral intake)
- Intravascular volume loss (tube and hemodialyser blood losses)
- Nondialytic volume loss (vascular access blood loss)
- Medication effects (antihypertensives, opiates)
- Decreased vascular tone (sepsis, food, diastolic temperature >37°C or <98.6°F)
- Cardiac dysfunction (LFT, ischemia, hypoxia, arrhythmia)
- Renal failure diastase (effusion, tamponade)
Dialysis disequilibrium

- Occurs at the end of dialysis
- Hypertension, nausea, vomiting
- Seizure and death.
- Probably from hypo-osmolarity, brain edema

Treatment
- Stop dialysis
- Mannitol

Air embolism

- Sx depend on how patient is positioned
  - Sitting → up internal jugular → increased intracranial pressure
  - Recumbent → to right ventricle → output → hypotension
- May hear churning in heart
- 100% O2
- Suck air out of ventricle
- Etc....
New Case

- 25 year old female returns to the ED after being discharged from the hospital. She is on home IV antibiotics for osteomyelitis after a skiing accident. She has recently begun to spike a fever.

- Fever, rash over the trunk and arms, and arthralgias.
- Exam: T 38.4 degrees C, No CVA tenderness.
- Lab: BUN 30 mg/dL, creatinine 2.8 mg/dL, WBC 5,700.

- Medications:
  - Methicillin
  - Ibuprofen
  - Morphine
- Labs: Cr = 3.5mg/dl; BUN = 25 mg/dl
- CBC shows mild eosinophilia
• All things being equal, what would you expect to find?
  – FENA > 2%, Urine Sodium < 20
  – FENA < 1%, Urine Sodium < 20
  – FENA > 2%, Urine sodium > 40
  – FENA < 1%, Urine sodium > 40

Answer: C

• Remember...her BUN/Cr < 20 therefore it is likely NOT pre-renal disease.
• Intrinsic kidney disease: FENA>2%, Urine sodium > 40mg/dl

UA

• Urinalysis: 1+ protein, few eosinophils, 3 RBCs/hpf.
• And these.....
White Cell Cast

- Of the following diagnoses, this patient’s condition is most consistent with:
  A. Acute tubular necrosis.
  B. Acute interstitial nephritis.
  C. Hypovolemia.
  D. Pyelonephritis.
  E. Nephrotic Syndrome

Answer: B

- Symptoms/Signs/Laboratory Findings in Acute Interstitial Nephritis
  - Fever
  - Rash (variable, may not be seen in all)
  - Acute rise in plasma creatinine
  - Active urine sediment that includes white cell casts. Note that only 3% of patients with interstitial nephritis have WBC casts (uptodate)
  - Eosinophilia and eosinophils in the urine (in most cases)
  - Renal tubular acidosis

- How long after drug exposure does interstitial nephritis generally begin?
  A. 2-3 days
  B. 10-14 days
  C. Several months
  D. A and B
  E. All of the above
Answer: E

- Rifampin can often cause interstitial nephritis on day one.
- 2-5 days if there has been a prior exposure.
- 10-14 days on first exposure to a drug.
- NSAIDS for months.

- Common Drugs Associated with Interstitial Nephritis
  - Penicillins
  - Aspirin
  - Ciprofloxacin and likely other fluoroquinolones
  - Allopurinol
  - NSAIDS
  - Some ACE inhibitors
  - Erythromycin

Helpful Tip

- Interstitial nephritis secondary to NSAIDS may occur without fever, rash or eosinophilia.

Treatment

- Stop drug
- Biopsy if need more (prednisone, cytotoxic drugs)
Quick....What laxative may cause acute calcinosis and renal failure?

• Oral or rectal sodium phosphate......