Introduction to AIN and HRS

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LBVA/UCI
8/14/2017

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- School of Medicine
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University of California Irvine Nephrology Training Program
The only nephrology fellowship program in OC and Long Beach!

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Unprecedented Improvements in UCI Nephrology fellowship

1. **UCIMC Call schedule:** Every 4th weekend (used to be every 2nd until Aug 2015)
2. **UCIMC consult service:** 2 fellows (used to be 1 until June 2015)
3. **Fellows office in 7th floor** next to ICU.
4. **VA weekday call coverage** on Tuesdays and Thursdays by research fellow
5. Meaningful productivity of research rotation
6. Coming soon: Phasing out sending fellows to UCLA Transplant one month a year
7. The most important features: BEST TEACHERS! World Class Nephrology Centers in UCIMC and Long Beach!

Learning Objectives

- Review acute interstitial nephritis (AIN) and hepatorenal syndrome (HRS)
- Recognize the clinical features
- Become familiar with diagnosis
- Review treatment options and outcomes
### Acute Kidney Injury

#### Inpatient/Hospital acquired

- **Pre-Renal**
  - Urine Volume: Decreased
  - Urine Sp. Gravity: > 1.020 (~1.010)
  - Urine Osmolality, mosm/kg: > 500 ** < 350
  - FE\textsubscript{Na} %: < 0.5% > 2%
  - FE\textsubscript{urea} %: < 35% > 35%
  - FE\textsubscript{uric acid} %: < 7% > 15%
  - Urine Sediment: None to Hyaline casts (bland)
  - U-creatinine: <100 mg/dL <50 mg/dL
  - Renal US: Normal
  - BUN/Crea ratio: >20 * <10
  - UrineCr./PlasmaCr.: >40 <20
  - U-Na: <20 mEq/L >40 mEq/L
  - Response: Responds intra-vascular volume expander

- **Intrinsic Renal**
  - Urine Volume: Variable
  - Urine Sp. Gravity: ~1.010
  - Urine Osmolality, mosm/kg: < 350
  - FE\textsubscript{Na} %: > 2%
  - FE\textsubscript{urea} %: > 35%
  - FE\textsubscript{uric acid} %: > 15%
  - Urine Sediment: Others, e.g. granular casts
  - U-creatinine: <50 mg/dL
  - Renal US: Variable (e.g. ATN)
  - BUN/Crea ratio: <10
  - UrineCr./PlasmaCr.: <20
  - U-Na: >40 mEq/L
  - Response: Usually no response to volume

#### Outpatient acquired

- **Postrenal**
  - Urine Volume: Decreased Variable
  - Urine Sp. Gravity: > 1.020 (~1.010)
  - Urine Osmolality, mosm/kg: > 500 ** < 350
  - FE\textsubscript{Na} %: < 0.5% > 2%
  - FE\textsubscript{urea} %: < 35% > 35%
  - FE\textsubscript{uric acid} %: < 7% > 15%
  - Urine Sediment: None to Hyaline casts (bland)

- **Intrinsic Renal**
  - Urine Volume: Variable
  - Urine Sp. Gravity: ~1.010
  - Urine Osmolality, mosm/kg: < 350
  - FE\textsubscript{Na} %: > 2%
  - FE\textsubscript{urea} %: > 35%
  - FE\textsubscript{uric acid} %: > 15%
  - Urine Sediment: Others, e.g. granular casts

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Clinical Case One

- 60 yo Caucasian Male with Type II DM, HTN, GERD, and Hyperlipidemia who was found to have a Cr of 5.4 (Baseline Cr 1.2 six months prior).

- ROS is negative.

- Home medications include
  - Lisinopril 40mg QD
  - Glipizide 5mg Tid
  - Omeprazole 20mg QD
  - Simvastatin 40mg QHS

Admission Labs

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<thead>
<tr>
<th>BMP</th>
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<td>K</td>
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<tr>
<td>Cl</td>
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<td>CO2</td>
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<td>Ca</td>
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<table>
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<tr>
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<td>Hgb</td>
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<td>Hct</td>
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<td>32.5</td>
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<tr>
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<td>MCV</td>
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<table>
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<td>Color</td>
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<td>SG</td>
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<td>pH</td>
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<td>Protein</td>
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<td>Ketones</td>
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<tr>
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<td>None</td>
</tr>
<tr>
<td>Blood</td>
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<td>Nitrite</td>
<td>None</td>
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<td>Glucose</td>
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<td>WBC</td>
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<td>RBC</td>
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**Cystatin C?**
### Additional studies

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
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<tbody>
<tr>
<td>Urine Cr</td>
<td>67.4 mg/dL</td>
</tr>
<tr>
<td>Urine Na</td>
<td>105 mEq/L</td>
</tr>
<tr>
<td>Urine Protein</td>
<td>77 mg/dL</td>
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<tr>
<td>FE~na</td>
<td>6%</td>
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<tr>
<td>Urine Eos</td>
<td>0%</td>
</tr>
<tr>
<td>Creatinine</td>
<td>41.6 mg/dL</td>
</tr>
<tr>
<td>Protein</td>
<td>46 mg/dL</td>
</tr>
<tr>
<td>Total Volume</td>
<td>3700 mL</td>
</tr>
<tr>
<td>24hr Urine Cr</td>
<td>1.5 g</td>
</tr>
<tr>
<td>24hr Urine Protein</td>
<td>1.7 g</td>
</tr>
</tbody>
</table>

**Urine Sediment:**
- Several WBCs, One non-dysmorphic RBC, 3 renal tubular epithelial cells/HPF

### Additional studies

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
</tr>
</thead>
<tbody>
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<td>HIV</td>
<td>Neg</td>
</tr>
<tr>
<td>HCV Ab</td>
<td>Neg</td>
</tr>
<tr>
<td>HBV Surface Ag</td>
<td>Neg</td>
</tr>
<tr>
<td>HBV Core Ab</td>
<td>Neg</td>
</tr>
<tr>
<td>RPR</td>
<td>NR</td>
</tr>
<tr>
<td>SPEP</td>
<td>Normal</td>
</tr>
<tr>
<td>UPEP</td>
<td>No Bence Jones Protein</td>
</tr>
<tr>
<td>ESR</td>
<td>10</td>
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<tr>
<td>HS-CRP</td>
<td>34.4</td>
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<tr>
<td>ANA</td>
<td>&lt;1:40</td>
</tr>
<tr>
<td>ANCA</td>
<td>&lt;1:20</td>
</tr>
<tr>
<td>c-ANCA</td>
<td>Neg</td>
</tr>
<tr>
<td>p-ANCA</td>
<td>Neg</td>
</tr>
<tr>
<td>C3</td>
<td>103</td>
</tr>
<tr>
<td>C4</td>
<td>27.5</td>
</tr>
<tr>
<td>Anti-GBM</td>
<td>&lt;1.3</td>
</tr>
</tbody>
</table>

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AIN: Diagnosis

- Best confirmed by renal biopsy
- Major histologic changes
  - Inflammatory interstitial infiltrate of T-lymphocytes and monocytes (fewer eosinophils, plasma cells, and neutrophils)
  - Interstitial edema
  - Glomerular and vascular sparing
Renal biopsy

Inflammatory infiltrates within the interstitium

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Back to our patient

- Pt was started on **prednisone 60mg** po qd and **omeprazole** was discontinued.
- Cr was improved from 5.2 to 2.9 after one week.
- Prednisone was decreased to 40mg qd after 1 month, and tapered off slowly over the next month. His cr came down to 1.5.
AIN: Clinical Presentation

- Nonspecific in clinical features
- Diverse in etiology
- Symptoms and signs of an allergic-type reaction:
  - Fever (27%)
  - Eosinophilia (23%)
  - Rash (15%)
  - Triad of rash, fever, and eosinophilia (10%)

- Time from drug exposure to development varies:
  - The onset ranges from 3-5 days with a second exposure, to as long as several wks with a first exposure.
  - The latent period may be as short as 1 day with rifampin or as long as 18 months with a NSAIDs.

The changing profile of acute interstitial nephritis

- A review of three series that totaled 128 pts
  - Drugs (71%)
  - Infection-related (15%)
  - Idiopathic (8%)
  - Tubulointerstitial nephritis and uveitis (TINU) syndrome (5%)
  - Sarcoidosis (1%)

Backer RJ; Pusey CD, Nephrol Dial Transplant 2004 Jan;19(1):8-11
**Etiology: medications**

- **Antibiotics:** 1/3 of these cases
  - Penicillins and Cephalosporins, Bactrim, Ciprofloxacin/quinolones, Rifampin
- **NSAIDs**
- **Proton pump inhibitors:** omeprazole and lansoprazole
- Cimetidine (rare cases reported)
- **Diuretics:** furosemide, bumetanide, thiazide
- Allopurinol
- Phenytoin
- Indinavir
- 5-aminosalicylates (mesalamine), Interferon alpha

**Etiology**

- **Infections**
  - Pneumonia with AIN: Legionella
  - Leptospirosis
  - CMV
  - Streptococcus

- **Autoimmune disorders:**
  - SLE
  - Sjogren’s
  - Sarcodiosis
  - Tubulointerstitial Nephritis and Uveitis Syndrome (TINU)
AIN: Laboratory Manifestations

- An acute rise in Creatinine (or Cystatin C)
- A urine sediment: white cell casts, sterile pyuria, microscopic hematuria.
- Eosinophilia and eosinophiluria
  - when eosinophils >1% of urinary white cells by Hansel's stain

Noninvasive diagnostic test: eosinophiluria

AIN: Diagnosis

- Best confirmed by renal biopsy

- Major histologic changes
  - Inflammatory interstitial infiltrate of T-lymphocytes and monocytes (fewer eosinophils, plasma cells, and neutrophils)
  - Interstitial edema
  - Glomerular and vascular sparing
The optimal therapy is unknown d/t a paucity of data in the literature.

Identify the cause and careful review of medication list. Withdraw the offending drug and treat underlying infection/disease.

With suspected drug-induced AIN, no further therapy is required if renal function begins to improve within a week after drug withdrawal.

Treatment

- A trial of corticosteroids (1 mg/kg of prednisone/day to a maximum of 40-60 mg for 6-12 weeks) can be considered.
- Several small retrospective studies have suggested that corticosteroid therapy improves clinical outcome; however, no prospective randomized controlled trials exist.
- For steroid-unresponsive or dependent cases, some anecdotal success with MMF and cyclosporine.

Interesting findings

- A retrospective analysis of 61 pts with biopsy proven AIN
- Only 8 pts (13%) had the classic triad of fever, rash and eosinophilia.
- Antibiotic in 34 cases
  - Cephalosporin in 15 cases
  - Quinolone in 12 cases
  - Penicillin in 7 cases
- NSAIDs in 23 cases
- Allopurinol in 1 case
- Ranitidine in 1 case
- Omeprazole in 1 case
- Pimozide in 1 case
Key Finding

Table 2 | Characteristics of Group 1 (steroid treatment) and Group 2 (no steroid treatment)

<table>
<thead>
<tr>
<th></th>
<th>Group 1 (n=52)</th>
<th>Group 2 (n=9)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>57.6 ± 17.7</td>
<td>58.1 ± 17.5</td>
<td>NS</td>
</tr>
<tr>
<td>Gender (M:F) (%)</td>
<td>41.5/58.5</td>
<td>77.8/22.2</td>
<td>NS</td>
</tr>
<tr>
<td>Baseline Scr (mg per 100 ml)</td>
<td>1.14 ± 0.4</td>
<td>1.14 ± 0.37</td>
<td>NS</td>
</tr>
<tr>
<td>Baseline eGFR (ml per min per 1.73 m²)</td>
<td>71 ± 26</td>
<td>70 ± 20</td>
<td>NS</td>
</tr>
<tr>
<td>Offending drug (antibiotics/NSAIDs/other) (%)</td>
<td>53.9/34.6/11.5</td>
<td>66.7/33.3/0</td>
<td>NS</td>
</tr>
<tr>
<td>Duration of the treatment (days)</td>
<td>13.4 ± 3.6</td>
<td>12.6 ± 4.3</td>
<td>NS</td>
</tr>
<tr>
<td>Highest Scr (mg per 100 ml)</td>
<td>3.0 ± 3.4</td>
<td>4.0 ± 3.3</td>
<td>NS</td>
</tr>
<tr>
<td>Proteinuria (mg/24h)</td>
<td>1.1 ± 1.2 (range 0-6)</td>
<td>0.6 ± 0.6 (range 0-2)</td>
<td>NS</td>
</tr>
<tr>
<td>eGFR (ml per min per 1.73 m²)</td>
<td>7.5 ± 3.5 (range 4-17.5)</td>
<td>7.5 ± 3.5 (range 4-17.5)</td>
<td>NS</td>
</tr>
<tr>
<td>Chronic diabetas</td>
<td>2.1 (13.4 %)</td>
<td>4.4 (44.4 %)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Final Scr (mg per 100 ml)</td>
<td>2.1 ± 2.1 (range 0.7-12.7)</td>
<td>3.7 ± 2.9 (range 0.7-6.9)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Follow-up (months)</td>
<td>19 ± 19 (range 6-60)</td>
<td>18 ± 18 (range 6-56)</td>
<td>NS</td>
</tr>
</tbody>
</table>

eGFR, estimated glomerular filtration rate; F, female; M, male; NS, not significant; NSAID, non-steroidal anti-inflammatory drug. Scr, serum creatinine.

AIN: Prognostic factor

- Clinical and histologic indicators of a decreased likelihood of recovery
- Prolonged renal failure (>3 wks), ? Severity
- AIN associated with NSAIDs use
- Histology
  - degree of interstitial fibrosis and tubular atrophy
  - diffuse vs patchy infiltrate
  - interstitial granulomas

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Take Home Messages: AIN

- A syndrome that is becoming both increasingly non-specific in clinical features and diverse in etiology
- Unexplained acute renal injury with normal sized kidneys (+/- increased echogenicity)
- ALWAYS get a thorough history on pt’s medications
- Consider steroid therapy in certain pts. (do it early)

Clinical Case Two:

- 58 y/o white male with Hep C cirrhosis, advanced recurrent HCC (with evidence of tumor thrombus in portal vein) s/p TACE x 2 (2014 and 2016), DM2, HTN, HL, who presents with severe abdominal distension due to ascites, anasarca with lower extremity edema, decreased urine output and AKI. His baseline Cr 2 wks. prior was 0.9, and current Cr is 4.8, BUN 70, Na 123, K 6.2, and Bicarb 17. His ascites is refractory to diuretics (lasix and aldactone). He underwent large volume paracentesis ~8L removed 2 weeks ago.
- Exam: BP 97/58 HR=82, JVP=12
  - Icteric, muscle wasting, tense ascites, 3+ pitting edema on LE
  - T Bili=9.7, INR=1.2; WBC=5.5; Hgb 9.4, albumin 2.0
  - Urine sediment nl; Urine Na=<10
Hepatorenal Syndrome (HRS)

- What is the most common cause of AKI in pts with cirrhosis?

A. Prerenal azotemia  
B. Acute tubular necrosis  
C. HRS

Definition of HRS

- Hepatorenal syndrome represents the end-stage of a sequence of reductions of renal perfusion induced by severe hepatic injury
  - Functional renal failure, with absence of histological changes
  - Development of diuretic resistant or refractory ascites
  - The Hallmark is renal vasoconstriction.
  - Worst prognosis of all complications of cirrhosis
Types of HRS

- **Type 1 HRS (AKI)**
  - Rapid deterioration in renal function within 2 wks. (double initial Cr > 2.5mg/dl)
  - Three-fourth with “second” hit:
    - SBP (20%), a large volume paracentesis (15%), GI bleed, and rapid diuresis.
  - One-fourth without precipitating factor
  - Survival in weeks (median 2 wks)

- **Type 2 HRS (CKD)**
  - Slowly progressive renal impairment
  - Spontaneous
  - Associated with refractory ascites in 75% (resistant to diuretics)
  - Survival in months (median 6 months)

Probability of survival: Type 1 vs Type 2

Alessandria et al, Hepatol 2005
Assessing kidney function in pts with cirrhosis

Q: Why is Cr falsely low in cirrhosis?

a). Decreased synthesis d/t lower hepatic production of creatine  
b). Malnutrition and less muscle mass  
c). Dilutional d/t the edematous state in end-stage liver disease leading to large distribution of Cr in the body  
d). Cr assays are subject to interference by chromogens, hyperbilirubinemia being the major one  
e). Complications such as variceal bleeding, spontaneous bacterial peritonitis or sepsis lead to increased Cr tubular excretion  
f). All of the above.
Endogenous vasoactive factors

The hallmark of HRS is intense renal vasoconstriction with predominant peripheral arterial vasodilation.

<table>
<thead>
<tr>
<th>Vasomotor Substances</th>
<th>Compensated Cirrhosis</th>
<th>Cirrhosis with Ascites</th>
<th>Hepatorenal Syndrome</th>
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<tr>
<td>Isoprostanes (F2α)</td>
<td>↔</td>
<td>↑</td>
<td>↑↑</td>
</tr>
</tbody>
</table>

Ascites and HRS as a Continuum

Clinical Aspects

Physiological Aspects

Portal hypertension

Splanchnic vasodilation

Renal vasoconstriction

Cystatin C?
Diagnosis and management of acute kidney injury in patients with cirrhosis: Revised consensus recommendations of the International Club of Ascites


Journal of Hepatology
Volume 62, Issue 4, Pages 968-974 (April 2015)

Diagnostic Criteria defined by the International Club of Ascites (ICA)

- Advanced hepatic failure and portal hypertension
- **Diagnosis of AKI according to ICA-AKI criteria**
  - an increase in Cr by >0.3 mg/dL within 48 hrs, or an increase from baseline by >50% within 7 days
  - No response after 2 consecutive days with **diuretic withdrawal** and **volume expansion with albumin**
  - 1g/kg of body weight (max 100 g/day)
- Absence of shock
- No current or recent use with nephrotoxic drugs.
- **No macroscopic signs of structural kidney injury**
  - Absence of proteinuria >500 mg/day, microhematuria (>50 RBC/hpf), and abnormal renal ultrasonography.

Journal of Hepatology 2015 62, 968-974
HRS is diagnosis of exclusion

- Hypotension (DDx→ pre-renal)
- Serum sodium < 130 mEq/L (hypervolemic hyponatremia)
- Urine sodium <10 mEq/L
- Urine volume <500 ml/day
- Urine Osm > Plasma Osm
- Bland urine sediment

Diagnostic Approach to AKI in Cirrhotics

AKI in a pt with cirrhosis

- ECF fluid losses; rapid/excessive diuretics
- Vomiting, diarrhea, hemorrhage, recent LVP / hemodynamic changes due to use of NSAIDS (or) ACEI/ARB
- Recent use of nephrotoxic medications
- Hypotension (sepsis, hemorrhage)
- Glomerular proteinuria & hematuria (i.e., dysmorphic RBCs and RBC cast)
- Imaging (USG, CT scan) shows hydronephrosis, urinary retention
- Patient has evidence of Portal Hypertension & fulfills HRS-AKI diagnostic criteria

YES → hold diuretics/offending medications
YES → Trial of intravascular volume expander (albumin)
YES → if renal function ↑ with trial, Diagnosis of prerenal is made
YES → Toxic or ischemic renal injury
YES → Glomerular disease
YES → Obstructive uropathy
YES → Diagnosis of HRS can be made
Treatment of HRS

Liver Transplantation: the only effective permanent tx.

Transjugular Intrahepatic Portosystemic Shunt (TIPS)
- For HRS type 2 and refractory ascites
- Reduce portal hypertension, increase effective arterial volume and reverse splanchnic vasodilatation
- Complications (Encephalopathy, Shunt stenosis, Hemolysis and Hyperbilirubinemia)

Complications (Encephalopathy, Shunt stenosis, Hemolysis and Hyperbilirubinemia)

Optimize Renal Perfusion:
- Hold Beta Blockers and diuretics
- [non-renal] vasoconstrictors combined with albumin

ICU-Treatment:
- Norepinephrine in combination with albumin with goal to raise MAP by 10mmHg
  - Meta-analysis, 154 pts, Type 1 HRS, N+A vs Terlipressin + A, similar results, N+A less side effects

Non-ICU Treatment:
- Terlipressin + Albumin if available
- Midodrine + Ocreotide + Albumin

HRS: Management

- Vasoconstrictors to increase MAP by 10-15 mmHg.
  - **Midodrine**: alpha 1-adrenergic agonist → systemic vasoconstrictor
    - 5mg tid up to a maximum of 15mg tid
  
  - **Octreotide**: analogue of somatostatin → inhibitor of vasodilation
    - 100mcg sc tid, with maximum 200mcg tid
  
  - **Terlipressin**: vasopressin analogues, V-1 receptor agonist → splanchnic vasoconstriction

A 60-yr-old man with alcoholic cirrhosis is admitted with SBP. Despite antibiotic therapy, he develops AKI (Cr increased from 0.6 to 1.8 mg/dl). Which ONE of the following therapies has been shown in a randomized, controlled trial to improve renal function in patients with hepatorenal syndrome?

A. Albumin and octreotide  
B. Fenoldopam and terlipressin  
C. Dopamine and octreotide  
D. Terlipressin and albumin  
E. Midodrine and octreotide
Terlipressin for hepatorenal syndrome

Systemic review of randomized trials of terlipressin in HRS

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Control</th>
<th>Relative risk (95% CI)</th>
<th>Relative risk (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Martin-Ulth, 2008</td>
<td>9/23</td>
<td>1/23</td>
<td>13.9%</td>
</tr>
<tr>
<td>Noet, 2008</td>
<td>21/26</td>
<td>5/26</td>
<td>38.6%</td>
</tr>
<tr>
<td>Sanval, 2008</td>
<td>19/56</td>
<td>7/56</td>
<td>59.5%</td>
</tr>
<tr>
<td>Scharpki, 2003</td>
<td>5/12</td>
<td>9/12</td>
<td>7.9%</td>
</tr>
<tr>
<td>Total</td>
<td>64/117</td>
<td>13/117</td>
<td>100.2%</td>
</tr>
</tbody>
</table>

Reversal of Hepatorenal syndrome

Ghadr et al., Hepatology 2010

Terlipressin

HRS: Effects of terlipressin and albumin on circulatory and renal function

<table>
<thead>
<tr>
<th>Pretreatment</th>
<th>End of treatment</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum creatinine (mg/dL)</td>
<td>3.9±0.7</td>
<td>1.5±0.2</td>
</tr>
<tr>
<td>Serum sodium (mEq/L)</td>
<td>122±1</td>
<td>131±2</td>
</tr>
<tr>
<td>Mean arterial pressure (mmHg)</td>
<td>68±2</td>
<td>80±4</td>
</tr>
<tr>
<td>Plasma renin activity (ng/mL/h)</td>
<td>23±12</td>
<td>3±2</td>
</tr>
<tr>
<td>Plasma aldosterone (ng/dL)</td>
<td>342±73</td>
<td>89±29</td>
</tr>
<tr>
<td>Plasma norepinephrine (pg/mL)</td>
<td>1,549±373</td>
<td>373±88</td>
</tr>
</tbody>
</table>

Uriz et al., J Hepatol 2000

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**Acute Kidney Injury (AKI)**

[a.k.a. Acute Renal Failure, ARF]

Kamyar Kalantar-Zadeh, MD, PhD, MPH
Professor of Medicine, Pediatrics, Public Health & Epidemiology
Division of Nephrology and Hypertension
Univ. California Irvine

<table>
<thead>
<tr>
<th>Key elements:</th>
<th>Normal blood range:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cr or Scr = serum creatinine</td>
<td>Cr or Scr =</td>
</tr>
<tr>
<td>BUN = blood urea nitrogen (SUN)</td>
<td>men ≤ 1.5 mg/dL</td>
</tr>
<tr>
<td>HCO₃⁻ = bicarbonate</td>
<td>women ≤ 1.3 mg/dL</td>
</tr>
<tr>
<td>Na = sodium</td>
<td>BUN = 5-25 mg/dL</td>
</tr>
<tr>
<td></td>
<td>HCO₃⁻ = 23-24 mEq/L</td>
</tr>
</tbody>
</table>
Drink a Glass of Water

Celebrate World Kidney Day with us!

On March 12, 2015, we invite everyone to drink a glass of water and give one too to celebrate their kidneys.

This is a symbolic gesture to remember that kidneys are vital organs and that they should be taken care of; it is a way to make people more conscious about their lifestyle choices. It is a conversation starter to raise awareness about the risks, dangers and burden of kidney disease and how to prevent and treat it.

Participating is easy. Take a picture of yourself drinking and giving a glass of water. Tweet it @worldkidneyday with the message: “Today I celebrate #worldkidneyday, I drink and give a #glassofwater because #supportkid.” Share it on our Facebook page! If you don’t have access to social media, you can send your picture by e-mail to info@worldkidneyday.org

Nutritional Needs and Guideline Support for AKI
Nutrient Needs of AKI Patients as Defined by ESPEN Guidelines*

Macronutrients

<table>
<thead>
<tr>
<th>Nutrient</th>
<th>Requirement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Energy (non-protein calories)</td>
<td>20–30 kcal/kg/d</td>
</tr>
<tr>
<td>Carbohydrates</td>
<td>3–5 (max. 7) g/kg/d</td>
</tr>
<tr>
<td>Fat</td>
<td>0.8–1.2 (max. 1.5) g/kg/d</td>
</tr>
</tbody>
</table>

Protein (Essential and Non-essential Amino Acids)

<table>
<thead>
<tr>
<th>Condition</th>
<th>Requirement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conservative therapy, mild catabolism (mild AKI on CKD)</td>
<td>0.6–0.8 (max. 1.0) g/kg/d</td>
</tr>
<tr>
<td>Extracorporeal therapy, moderate catabolism</td>
<td>1.0–1.5 g/kg/d</td>
</tr>
<tr>
<td>CCRT, severe hypercatabolism</td>
<td>Up to maximum 1.7 g/kg/d (or 2.0 or higher!)</td>
</tr>
</tbody>
</table>

*Adapted to catabolism levels and to individual needs in case of underweight or obesity.
*Adjust as necessary for obese patients.

Effect of AKI Requiring RRT on Outcome in Critically Ill Patients (N=19,067)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Estimate</th>
<th>P-value</th>
<th>Odds ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>SAPS II score</td>
<td>0.00798</td>
<td>0.166</td>
<td>1.08</td>
</tr>
<tr>
<td>Cardiopulmonary resuscitation</td>
<td>0.06160</td>
<td>0.004</td>
<td>1.86</td>
</tr>
<tr>
<td>Multiple vasoactive medication</td>
<td>0.02930</td>
<td>&lt;0.001</td>
<td>1.34</td>
</tr>
<tr>
<td>Mechanical ventilation</td>
<td>0.02930</td>
<td>&lt;0.001</td>
<td>1.34</td>
</tr>
<tr>
<td>Single vasoactive medication</td>
<td>0.01160</td>
<td>0.012</td>
<td>1.13</td>
</tr>
<tr>
<td>Treatment of complicated metabolic acidosis/alkalosis</td>
<td>0.00768</td>
<td>0.034</td>
<td>1.08</td>
</tr>
<tr>
<td>Care of drains</td>
<td>-0.00883</td>
<td>0.002</td>
<td>0.91</td>
</tr>
<tr>
<td>Enteral nutrition</td>
<td>-0.01480</td>
<td>&lt;0.001</td>
<td>0.86</td>
</tr>
</tbody>
</table>

Enteral Nutrition is Associated with Favorable Outcomes in AKI

SAPS, Simplified Acute Physiology Score.
Variables express the proportion of days on which this activity was performed. The odds ratios reflect the change in the risk of dying during the intensive care unit stay if the proportion of days with intervention increases by 10%.
Acute Renal Failure: Mechanisms

Renal Vascular: Stenosis, vasculitis

Volume ↓
Prerenal

Interstitial
damage

Acute Glomerulonephritis

Acute tubular damage

Post-renal Obstruction

A nephron and the blood vessels associated with it.

Case 1

- A 50-year-old male was brought to the ER complaining of vomiting for two weeks. There was no history of drug ingestion and no prior history of renal disease.
- Physical examination on admission revealed: BP 100/60 supine and 85/50 upright; pulse 120; wt 135 lbs. The rest of the physical examination was unremarkable.
- Lab data: BUN 100 mg/dl; Cr 3.7 mg/dl; Na 125 mEq/L; K 4.2 mEq/L; HCO3 30 mEq/L.
- Urinalysis was negative for protein and showed no RBC or casts.
Case 1

1.i. What is the most likely cause of renal failure?

A: ARF due to volume depletion
   (pre-renal azotemia)

B: ARF due to renal vascular dis.
   (renal artery stenosis,
    vasculitis,
    atheroembolic dis)

C: ARF due to acute glomerulonephritis (GN)

D: ARF due to acute tubular necrosis (ATN)

E: ARF due to acute interstitial nephritis (AIN)

F: ARF due to urinary tract obstruction, e.g., prostate
   hypertrophy (post-
   renal azotemia)

G: CKD with chronic renal insufficiency

Acute Renal Failure: Mechanisms

Renal Vascular: Stenosis, vasculitis

Prerenal Volume ↓

Acute Glomerulonephritis

Interstitial damage

Acute tubular damage

Post-renal Obstruction
Case 1
1.ii. What information obtained from the physical examination and laboratory data is helpful in establishing the diagnosis of ARF?

A: History of vomiting
B: Orthostatic changes in BP
C: Tachycardia consistent with volume depletion
D: The high BUN/Scr ratio
E: Elevated serum HCO₃
F: Lack of history of drug ingestion and previous renal disease and bland urine sediment.
G: All of the above

✓

Case 1
1.iii. What other laboratory data would be helpful?

A: Urine lytes and osmolality showing a pre-renal profile
B: Elevated Hct and uric acid levels
C: Both.
D: Neither

✓

C: Both.
Case 1
1.iv. What treatment is indicated and what is the expected effect on renal function?

A: Keep patient NPO and no IV fluid
B: Give high dose loop diuretics such as furosemide (Lasix)
C: Emergent dialysis treatment, because patient's renal function will not improve
D: Volume repletion with normal saline will likely improve renal function

It's Important To Keep Hydrated While On the Job

Keep hydrated
- Drink when thirsty
- Drink before feeling thirsty
- Drink two to three liters of water a day
- Drink more if you exercise

It's Important To Keep Hydrated While On the Job
Pre-Renal AKI: Some Causes

- **Hypovolemia**
  - Volume Loss – GI, renal, skin
  - Blood Loss – GI, MVA

- **Cardiac Causes (hemodynamic CRS)**
  - Acute cardiogenic shock
  - Chronic congestive heart failure

- **Liver Disease**

- **Nephrotic syndrome**

- **Renovascular**
  - Renal venous thrombosis

### Pre RENAL vs Intra Renal

<table>
<thead>
<tr>
<th></th>
<th>Pre-Renal (incl Hepato-renal)</th>
<th>Intrinsic Renal (incl ATN)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urine Volume</td>
<td>Decreased</td>
<td>Variable</td>
</tr>
<tr>
<td>Urine Sp. Gravity</td>
<td>&gt; 1.020</td>
<td>~1.010</td>
</tr>
<tr>
<td>Urine Osmolality, mosm/kg</td>
<td>&gt; 500 **</td>
<td>&lt; 300</td>
</tr>
<tr>
<td>FE(_{Na}), %</td>
<td>&lt; 0.5%</td>
<td>&gt; 2%</td>
</tr>
<tr>
<td>FE(_{urea}), %</td>
<td>&lt; 35%</td>
<td>&gt; 35%</td>
</tr>
<tr>
<td>FE(_{uric acid}), %</td>
<td>&lt; 7%</td>
<td>&gt; 15%</td>
</tr>
<tr>
<td>Urine Sediment</td>
<td>None to Hyaline casts (bland)</td>
<td>Others, e.g. granular casts</td>
</tr>
<tr>
<td>U-creatinine</td>
<td>&gt;100 mg/dL</td>
<td>&lt;50 mg/dL</td>
</tr>
<tr>
<td>Renal US</td>
<td>Normal</td>
<td>Variable, echo-gen. (ATN)</td>
</tr>
<tr>
<td>BUN/Crea ratio</td>
<td>&gt;20 *</td>
<td>&lt;10</td>
</tr>
<tr>
<td>UrineCr./PlasmaCr.</td>
<td>&gt;40</td>
<td>&lt;20</td>
</tr>
<tr>
<td>U-Na</td>
<td>&lt;10 mEq/L</td>
<td>&gt;40 mEq/L</td>
</tr>
<tr>
<td>Response</td>
<td>Responds intra-vascular volume expander</td>
<td>Usually no response to volume</td>
</tr>
</tbody>
</table>
Case 5

• A 30-year-old female noted dysuria and frequency and was given ampicillin for a presumed urinary tract infection. Two to 3 days after beginning the medication, she noted the onset of a diffuse skin rash and a fever to 101°F.

• Physical examination revealed: BP 130/80 supine and upright. There was an erythematous rash on the abdomen and extremities, but the physical examination was otherwise negative.

• Lab data: BUN 75 mg/dl; Cr 5.0 mg/dl; Na 140 mEq/L; K 5.0 mEq/L; HCO3 20 mEq/L. Urinalysis showed 2+ protein, many RBCs and WBCs, no RBC casts.

5.1. What is the most likely cause of renal failure?

A: ARF due to volume depletion (pre-renal azotemia)
B: ARF due to renal vascular dis. (renal artery stenosis, vasculitis, atheroembolic dis)
C: ARF due to acute glomerulonephritis (GN)
D: ARF due to acute tubular necrosis (ATN)
E: ARF due to acute interstitial nephritis (AIN)
F: ARF due to urinary tract obstruction, e.g., prostate hypertrophy (post-renal azotemia)
G: CKD with chronic renal insufficiency
Case 5

5.ii. What information in the history, physical examination and lab data is helpful in making a diagnosis of the cause of the renal disease?

A: Skin rash after starting ampicillin
B: Low-grade fever after starting ampicillin
C: Presence of skin rash on physical exam
D: Presence of WBCs and RBCs, but no casts
E: Moderate proteinuria (2+ protein)
F: Only A, B and C
G: All of the above

A: Skin rash after starting ampicillin
B: Low-grade fever after starting ampicillin
C: Presence of skin rash on physical exam
D: Presence of WBCs and RBCs, but no casts
E: Moderate proteinuria (2+ protein)
F: Only A, B and C
G: All of the above
Acute Interstitial Nephritis

Case 5
5.iii. What single laboratory test would be the most helpful in determining the cause of renal failure?

A: Eosinophiluria (eosinophils in the urine) esp. if > 5% [Hansel stain of urine]
B: Rectal examination
C: Chest X-ray
D: Only A and B
E: All of the above

A: Eosinophiluria (eosinophils in the urine) esp. if > 5% [Hansel stain of urine]
Case 5
5.iv. What treatment is indicated?

A: Withdrawal of ampicillin (+/- steroid)
B: Administer IV contrast
C: Replace ampicillin with aminoglycoside
D: Give high dose NSAID
E: All of the above

Acknowledgement

The Harold Simmons Center for Kidney Disease Research & Epidemiology

Investigators and Staff
- Elani Streja, MPH, PhD
- Connie M. Rhee, MD, MSc
- Hamid Moradi, MD
- Wei Ling Lau, MD
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- Foad Ahamdi, MD
- Paungpaga Lertdumrongluk, MD
- Saeedeh Rezakhani, MD
- Melissa Sochoo, MPH
- Bryan Shapiro, MPH
- Rochelle Begier, MPH
- Amanda Brown, RD
- Tracy Nakata
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- Google+: [https://plus.google.com/109239031645120656897](https://plus.google.com/109239031645120656897)
- Google Scholar: [https://scholar.google.com/citations?user=kYonxzoAAAAJ&hl=en](https://scholar.google.com/citations?user=kYonxzoAAAAJ&hl=en)