UPDATE IN ACUTE KIDNEY INJURY

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Disclosures

- Nothing to disclose

Case: Etiology of obstruction

- 35 yo male with a congenital solitary kidney
- Baseline Cr 1.2mg/dl
- Presents to ER in severe pain
- Ultrasound shows hydronephrosis
- Labs show a creatinine increase to 2.7mg/dl

Based on his age alone, what is the most likely etiology of the obstruction?

- A. Kidney stone
- B. Prostatic obstruction
- C. Retroperitoneal neoplastic disease
- D. Anatomic abnormality

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Most Common Causes of Obstruction by Age

- Children
  - *Anatomic abnormalities*
- Young Adults
  - *Kidney stones*
- Older Adults
  - *Prostatic obstruction*
  - *Retroperitoneal or pelvic neoplasms*
  - *Kidney stones*

Case: The "Negative" Urinalysis

- 65 yo female presents to her PCP feeling "unwell" for 3 weeks with poor PO intake
- Labs checked and Cr 3.7
- She is referred to the ER and admitted for AKI, started on IV fluids
- Amongst other workup, a urinalysis is performed and the dipstick is reported as "negative" with no blood, protein, leukocytes, or nitrites

Which of the following is NOT in your differential given this urinalysis?

- A. Myeloma cast nephropathy
- B. Dehydration due to poor PO intake
- C. Tumor lysis syndrome from a new lymphoma
- D. Rhabdomyolysis

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Bland urinalysis

- No RBCs, protein, or WBCs
- Often pre-renal or post-renal
- DO NOT consider glomerulonephritis or nephrotic syndrome if urine is bland
- Other considerations
  - *Myeloma cast nephropathy*
  - *Vascular ischemia without infarction*
  - *Tumor lysis*
  - *Acute phosphate nephropathy*
  - *Hypercalcemia*

Urinalysis: Proteinuria

- "Proteinuria" on a dipstick is really albuminuria
- Proteinuria DOES NOT rule out myeloma/light chain disease
- Proteinuria on a dipstick is completely dependent on the urine concentration so need to quantify if positive
- Traditionally "microalbuminuria", or <300mg/g albumin, was below the level the dipstick could detect, but that is no longer the case with better dipsticks and also depends on concentration

Urinalysis: Hematuria

- Hematuria without RBCs on sediment- think myoglobin/rhabdomyolysis!
- Can indicate a glomerulonephritis
- Some nephrotic syndromes have hematuria
- Foley placement will cause hematuria

Urinalysis: White Blood Cells

- AIN
- UTI/pyelonephritis
- Sterile pyuria
- Can be seen with GNs as well
- Can be seen with "dirty" urines, especially in women

Case: Use of the Protein:creatinine ratio

- 65 yo male with diabetes and microalbuminuria (last malb/cr 55mg/g) for foot amputation
- Develops AKI post-op, Cr from 0.9 to 3.3 over 3 days
- Pr/Cr checked as part of workup of AKI, ratio found to be ~4g
- 24h urine performed, found to have 1.2g/24 hours
- Why the discrepancy?

Why the discrepancy?

- A. We are measuring different types of proteins in the two assay
- B. The ratio is inaccurate while serum creatinine is rising
- C. In diabetics we should be using malb/cr, not pr/cr
- D. 24 hour collection was undercollected

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Protein:Creatinine Ratio in AKI

- Pr/Cr takes into account BOTH protein and creatinine
- AKI is NOT a steady state during the creatinine rise
- Thus, denominator of ratio is low and overestimates 24h excretion

Protein:Creatinine Ratio

- Works at the population level since the average daily creatinine excretion is 1g/day
- More limited at the patient level but good for tracking, although both Pr and Cr excretion variable during a day
- Very limited in AKI as creatinine excretion is not in a steady state

Case: Use of the fractional excretion of sodium (FeNa)

- 45 yo male alcoholic "found down"
- Appeared short of breath, got a PE protocol CT scan which was negative
- Admitted to hospital
- Baseline Cr 0.6
- Day 2 Cr 1.8
- Eating poorly but drinking water
- UOP 1200cc/day
- FeNa on Day 2 was 0.6%
- Aggressive fluids given for presumed prerenal azotemia
- Day 3 Cr 2.3, renal fellow looks at urine and sees muddy brown casts

Which of the following is NOT a cause for the low FeNa?

- A. He is dehydrated as well
- B. Poor solute intake with good UOP decreases the sodium concentration
- C. Contrast causes afferent arteriolar vasoconstriction
- D. Serum creatinine level is fluid in AKI

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FeNa

- (Una x SCr)/(SNa x UCr) x 100
- If <1% then prerenal
- Limitations
  - *ONLY applies to patients with low GFR and oliguria– if GFR normal and/or urine output normal, sodium excretion depends on dietary sodium intake*
  - *Serum creatinine level is fluid in AKI*
  - *Diuretic therapy can increase sodium even if prerenal*
  - *Other causes of AKI can induce a low FeNa*

Other causes of AKI with low FeNa

- ATN with some underlying ischemia or poor perfusion such as sepsis
- Contrast nephropathy
- Myoglobinuria
- Any cause of AKI where tubular function is preserved despite decreased glomerular function

Fractional excretion of urea (FeUrea)

- (UUN x SCr)/(SUN x PCr) x 100
- If <35% suggestive of prerenal
- Less sensitive than FeNa in patients NOT on diuretics
- More sensitive than FeNa in patients on diuretics
- Similar limitations to the FeNa

Case: Urine Electrolytes

- 23 yo female admitted for abdominal pain, thought to be irritable bowel syndrome in past
- Creatinine up from 0.7 baseline to 1.1 at admission
- Noted to have K 3.2 and bicarb 34
- Urine lytes show:
  - *Urine sodium: 70mmol/L*
  - *Urine chloride: <assay*
- After much questioning after seeing urine lytes, admits to surreptitious vomiting

Why are the urine sodium and chloride values so disparate?

- A. She ingested sodium bicarbonate tabs
- B. She also surreptitiously took lasix, raising the urine sodium
- C. Sodium is being excreted with the excess bicarbonate
- D. She has Bartter's syndrome

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Urine Electrolytes: Sodium

- Low urine sodium suggests a sodium-avid state
- Not considered as accurate as a FeNa as does not account for rate of water reabsorption and has same other limitations as the FeNa
- Lower limit of assay range differs at different hospitals!

Urine Electrolytes: Chloride

- Reabsorbed with sodium, usually low when sodium is low
- Helpful in volume depletion with alkalosis
  - *Bicarbonate is excreted as NaHCO3, thus urine sodium may not be less than assay*
  - *However, urine chloride will still be low indicating volume depletion*
  - *Usually the case if alkalosis is more severe than the volume depletion or else NaHCO3 will be reabsorbed proximally as well*

Case: Urine Sediment

- 85 yo male with dementia and baseline Cr 0.8 is admitted with confusion and diarrhea
- Cr at admit is 2.4
- Given IV fluids and creatinine goes down to 0.8 over 3 days
- You look back at the urine microscopy report from the day of admission

Which of the following is a likely finding?

- A. Muddy brown casts
- B. Hyaline casts
- C. Waxy casts
- D. RBC casts

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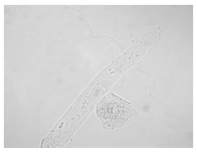
- A. Muddy brown casts
- B. **Hyaline casts**
- C. Waxy casts
- D. RBC casts

Urine Sediment: Casts

- Hyaline casts often seen with poor perfusion
- Waxy casts are seen with CKD
- Granular casts are very non-specific- ATN, poor perfusion, CKD
- WBC casts usually AIN or pyelonephritis but can be GN as well
- RBC casts usually GN

Urine Sediment: Casts

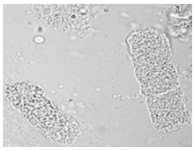
Hyaline cast



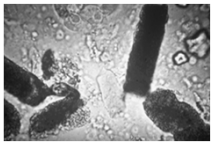
Waxy cast

Urine Sediment: Casts

Fine granular cast

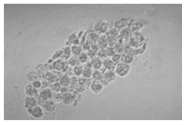


Muddy brown cast

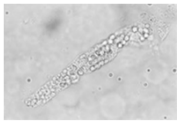


Urine Sediment: Casts

White cell cast



Red cell cast



Case: Glomerulonephritis and the urinalysis

- 74 yo female with hx of GERD, recent history of sinusitis, is found to have Cr 1.7mg/dl and sent to the ER for workup
- In days prior to the presentation was also eating and drinking less due to feeling unwell
- BP 149/66, HR 91, O2 sat 96%
- Exam otherwise unremarkable, no edema
- Creatinine in ER 1.9mg/dl
- ANCA level done due to the sinus and pulmonary complaints, found to be positive

Which of the following sets of urine results should prompt concern for a glomerulonephritis?

- A. Blood 2+, leukocyte esterase 2+, nitrite positive, protein 1+
- B. Blood negative, leukocyte esterase negative, protein 3+
- C. Blood 3+, leukocyte esterase trace, protein 3+, nitrite negative
- D. All negative results

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Urine findings in glomerulonephritis

- If don't see blood AND protein, VERY unlikely to be a glomerulonephritis
- Urine sediment sometimes reported as having RBC casts, but many times no RBC casts so does not rule out
- Can see leukocytes in a glomerulonephritis, does not rule out
- UTIs can have blood and protein but GNs should not have positive nitrites
- If AKI and urine sediment shows blood and protein, renal consult ASAP is necessary!

Symptoms that should prompt thinking of glomerulonephritis

- Any pulmonary or sinus symptoms and/or hemoptysis consider ANCA disease and anti-glomerular basement membrane disease (i.e. Goodpasture's syndrome), IgA can present this way as well
- Other GNs can present with an array of symptoms, usually some overlap with rheumatologic symptoms and/or infections

Case: AIN

- 66 yo male on multiple medications presents to his PCP with a rash and fever
- Found on labs to have Cr 2.5, send to ER for admission and workup
- Also noted to have a WBC differential with 7% eosinophilia
- ER physician presumes AIN

Which of the following would be the LEAST likely cause of this presentation?

- A. Ibuprofen
- B. Furosemide
- C. TMP/SMX
- D. Omeprazole

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Proton Pump Inhibitors and AIN

- Do NOT present as classical AIN
- Often late-onset after at least 4-6 months of the medication
- Rarely present with rash, fever, or eosinophilia
- May resolve with stopping the medication but will often require steroids

Urine Eosinophils

- Used to test for AIN but sensitivity and specificity are poor
- Sensitivity and specificity averages for ≥1% eosinophils on Hansel stain
  - *Sensitivity- 63-91%*
  - *Specificity- 85-93%*
- Other conditions with eosinophils
  - *Transplant rejection*
  - *Pyelonephritis/cystitis/prostatitis*
  - *RPGN*
  - *Atheroembolic disease*

Plasma Eosinophils

- Seen in 20-35% of cases of acute AIN in various studies
- Classic triad of rash, fever, and eosinophilia only in ~10% of cases

Case: Imaging in AKI

- 67 yo female presents to the ER with hypertensive emergency
- She has not seen an MD in 10 years and has never had kidney function tested
- Cr 3.7mg/dl

Which imaging modality can help you determine if this is acute or chronic?

- A. Nuclear scan
- B. Xray
- C. Renal ultrasound
- D. MRI

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- **C. Renal ultrasound**
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Renal Ultrasound in AKI

- Should order only if you think it will help with making a diagnosis
- R/o hydronephrosis
- Infiltrative disease if one or both kidneys are very large
- Cortical thinning and/or increased echogenicity
  - *Suggest underlying chronic disease*
- Disparate kidney sizes
  - *Atrophic kidney*
  - *Unilateral RAS*

Case: Contrast Nephropathy

- 57 yo female with diabetes and Cr 1.4mg/dl is admitted for SOB and pleuritic chest pain.
- You are worried about a PE and want to do a PE CT but are understandably concerned about her renal function

Which of the following is currently recommended for renal prophylaxis?

- A. Isotonic Saline
- B. Isotonic Bicarbonate
- C. N-Acetylcysteine
- D. Saline with furosemide to prevent volume overload

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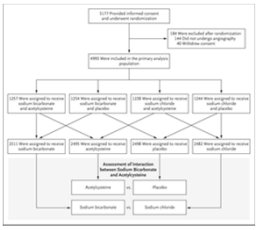
Contrast Nephropathy

- Higher risk: diabetes, myeloma, prior renal insufficiency, proteinuria
- Increase in Cr within 24-48 hours, peak 3-5 days, baseline in 6-10 days
- Usually non-oliguric
- Can see muddy brown casts
- FeNa often <1% with high specific gravity of urine

Prevention of contrast nephropathy

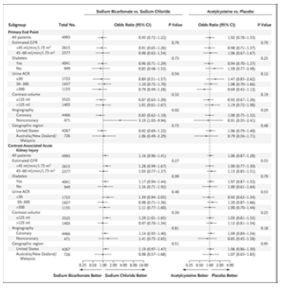
- This is highly debatable and many studies
- Isotonic saline may be better than 1/2NS
- Isotonic bicarb data is equivocal
- Saline WITH furosemide appears to cause a higher risk of CIN
- Data regarding N-acetylcysteine (NAC) equivocal despite many meta-analyses, most recent analyses appear to NOT show a benefit
- **Currently the most consistent recommendation is to give saline if no contraindications given it is cheapest with the least side effects, some studies do show benefit**

PRESERVE Trial



Weisbord SD et al. N Engl J Med 2018;378:603-614

PRESERVE Trial



Weisbord SD et al. N Engl J Med 2018;378:603-614

But what about AMACING? Is there benefit to saline?

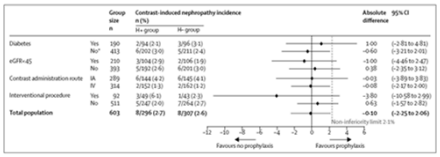


Figure 2: Incidence of contrast-induced nephropathy in the total study population and by patient subgroup
The dashed line indicates the non-inferiority margin of 2·1%. Error bars indicate two-sided 90% CIs. Bullets indicate the absolute difference (no hydration minus hydration) in proportion with contrast-induced nephropathy. eGFR=estimated glomerular filtration rate. IA=intra-arterial. IV=intravenous. *The no diabetes subgroup represents the guideline high-risk group with eGFR <60 mL per min/1·73 m² and two risk factors. p values for interaction: diabetics vs non-diabetics, p=0·5232; eGFR <45 vs eGFR ≥45, p=0·6040; intra-arterial vs intravenous contrast administration, p=0·9608; interventional vs diagnostic procedure, p=0·3289.

N Ijsaen EC et al, Lancet, 2017; 389. 1312-1322.

Why not follow AMACING and avoid prophylaxis?

- Randomized, controlled trial of "high risk" patients set up as non-inferiority trial of saline versus placebo
- However, group thought not to be high risk enough:
  - *GFR 30-59ml/min/1.73m2 but only 35% were <45ml/min/1.73m2*
  - *48% intraarterial contrast which is higher risk, only 6 in each group had AKI and none required dialysis*
  - *Only 2.7% overall had AKI which is lower than general risk in high risk group in most studies*

Case: NSAIDs and AKI

- 47 yo female with DM 1 and albuminuria but normal creatinine
- Prescribed ibuprofen 600mg QID for a rotator cuff injury
- 2 weeks later notices significant leg swelling and goes to PCP
- Cr 5.4mg/dl and UA with 3+ protein

Which of the following is NOT an affect of NSAIDs on the kidney?

- A. Decrease in afferent vasodilation to decrease GFR
- B. Interstitial nephritis
- C.Minimal change disease
- D. Membranous nephropathy
- E. Focal and segmental glomerulosclerosis

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NSAIDs

- Inhibits prostaglandin-mediated afferent vasodilation
- Causes an ischemic state by itself, or decreases threshold to other injury
- Other causes of AKI with NSAIDs:
  - *Acute interstitial nephritis*
  - *Minimal change disease*
  - *Membranous nephropathy*

Case: Diuretics and AKI

- 82 yo male admitted with baseline Cr 1.3mg/dl admitted with SOB
- PE CT done and shows PE
- 2 days later creatinine starts to trend upwards but UOP is still good
- You follow him and 2 days after that creatinine is 4.5mg/dl and UOP is 10cc/h

Which of the following is a true statement regarding diuretics and AKI?

- A. If he gets diuretics on day 4 and responds, this predicts better recovery
- B. He should not get diuretics on day 4 as this will further dehydrate the kidneys and do harm
- C. He should get diuretics on day 2 to prevent worsening AKI
- D. Diuretics should never be given in AKI

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Are Diuretics Useful?

- Diuretics should NOT be given prophylactically to prevent AKI
  - *126 patients given dopamine, saline, or furosemide for 48 hours around cardiac surgery*
  - *Patients given furosemide had more AKI*
- Diuretic responsiveness to oliguria does predict better recovery
  - *Shorter duration of oliguria and better UOP but may just be lest severe ATN*

Lassner et al, JASN, 2000. 11(1): 97

Case: COVID-19 and AKI

- 67 yo African-American male with HTN and DM, admitted to the hospital with shortness of breath and diagnosed with COVID
- Admitted to ICU and intubated
- Found to have progressive AKI with Cr up to 5.0 and oliguria
- Initiated on HD

Which of the following is NOT a likely cause of the COVID-19-associated AKI?

- A. ATN due to hypotension
- B. Direct toxic effect of the virus
- C. Collapsing glomerulopathy
- D. Acute interstitial nephritis
- E. Thrombotic microangiopathy

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- **D. Acute interstitial nephritis**
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COVID-19 and AKI

- Studies showing anywhere for 3-37% of hospitalized patients with COVID-19 develop AKI
- Almost all have ATN on biopsy
- Unclear if due to hemodynamics, cytokine release, or direct viral cytotoxicity
- Some cases of COVID vaccine and glomerular disease development
- Multiple case reports of African-Americans with AKI and biopsy showing collapsing glomerulopathy
  - *Potentially in the setting of an APOL1 mutation*

Disclosures

- Nothing to disclose

Thank you!