The Practical Guide to Acute Kidney Injury

Elise Barney, DO

Nephrologist

Clinical Assistant Professor, Medicine

University of Arizona College of Medicine

AZCOM / Midwestern University

Acute Renal Failure
Grey's Anatomy

- https://youtu.be/vGtP5nN936s

Objectives

- Define acute kidney injury (AKI) including stages
- List common causes of acute kidney injury
- Complete an initial workup for AKI, including pertinent history, laboratory and necessary imaging
- Describe the initial management of acute kidney injury and indications for emergent renal replacement therapy.

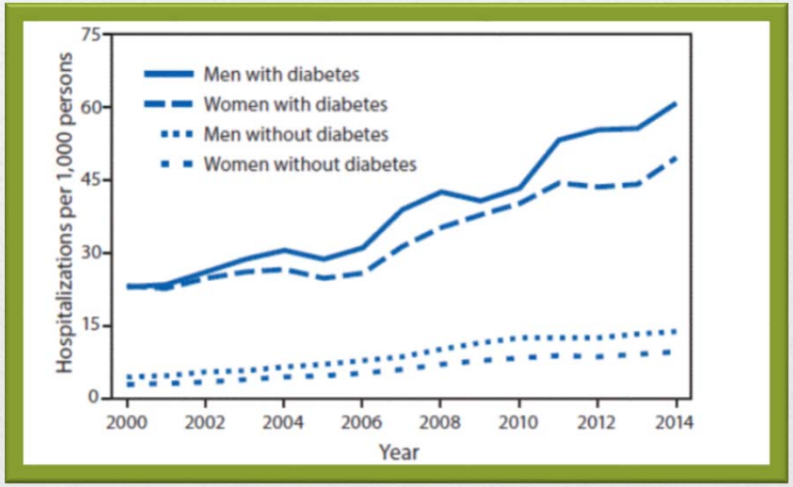
Acute Kidney Injury (AKI): Epidemiology

- On the rise!
  - Now exceeds the annual incidence of MI[1]
  - Hospitalizations for AKI increased by 139% in diabetics & 230% in non-diabetics from 2000-2014 (CDC)
  - Total hospitalizations for AKI ~ 4 million in 2014 from 954,000 in 2000 (CDC)
- 50% of all critically ill pts will experience acute kidney injury
- 30% of cancer patients during their disease course[2]
- Increases mortality for hospitalized pts
  - Up to **80%** mortality for dialysis-requiring AKI
  - Independent risk factor for mortality
- Risk factor for chronic kidney disease (CKD)
- Increased likelihood of long-term care[3]
- Higher healthcare costs

1. doi:10.1001/jama.2018.7160 , *2.* Perazella M and Rosner M. Acute kidney injury in patients with cancer. Oncology 2018; 32(7). *3.* Pavkov ME, Harding JL, Burrows NR. Trends in Hospitalizations for Acute Kidney Injury — United States, 2000–2014. MMWR Morb Mortal Wkly Rep 2018;67:289–293.

Risk Factors

- Diabetes, HTN, advanced age
- Pre-existing kidney disease



Pavkov ME, Harding JL, Burrows NR. Trends in Hospitalizations for Acute Kidney Injury — United States, 2000–2014. MMWR Morb Mortal Wkly Rep 2018;67:289–293. DOI: http://dx.doi.org/10.15585/mmwr.mm6710a2.

Acute Kidney Injury (AKI): Definitions

KDIGO (Kidney Disease: Improving Global Outcomes) 2012

- AKI is defined as any of the following :
- Increase in SCr by $\geq$ 0.3 mg/dl within 48 hours

OR…

- Increase in SCr to 1.5 times baseline (within the 7 days prior)

OR…

- Urine volume < 0.5 ml/kg/hr x 6 hours or more

RIFLE & AKIN Criteria

RIFLE Criteria	Change in Cr	Oliguria	Hospital Mortality	AKIN Criteria
RISK	1.5 – 2 x baseline	UO < 0.5 mL/kg/hr x ***> 6*** hrs	8.8 %	**STAGE 1** *Increase Cr* *≥0.3mg/dl* or ≥ 50% increase in < 48 hrs
INJURY	2-3 x baseline	UO < 0.5 mL/kg/hr x ***> 12*** hrs	11.4 %	**STAGE 2**
FAILURE	> 3 x baseline or Cr > 4 mg/dl	UO < 0.5 mL/kg/hr x ***> 24*** hrs ***or*** Anuria > 12 hrs	26.3 %	**STAGE 3** (including any pt requiring RRT)
LOSS OF FUNCTION	Need for RRT for > 4 wks			
ESRD	Need for RRT ≥ 3 mos			

AKI Biomarkers

- Serum creatinine
- Cystatin C
- TIMP-2 (Tissue Inhibitor of Metalloproteinase-2)
- IGFBP-7 (Insulin-like Growth Factor Binding Protein-7)
  - TIMP-2 & IGFBP-7 involved in G1 cell-cycle arrest in the earliest phases of injury to the kidney
  - Sapphire study concluded taken together, urinary TIMP-2 and IGFBP-7 levels were significantly superior to all previously described markers of AKI
  - Nephrocheck test: AKI risk score= [TIMP-2] x [IGFBP-7]
- Other markers: Neutrophil gelatinase-associated lipocalin (NGAL), Urinary angiotensinogen, Urinary microRNA, Interleukin-18 (IL-18), Kidney injury molecule 1 (KIM-1), Liver-type fatty acid–binding protein (L-FABP), Calprotectin

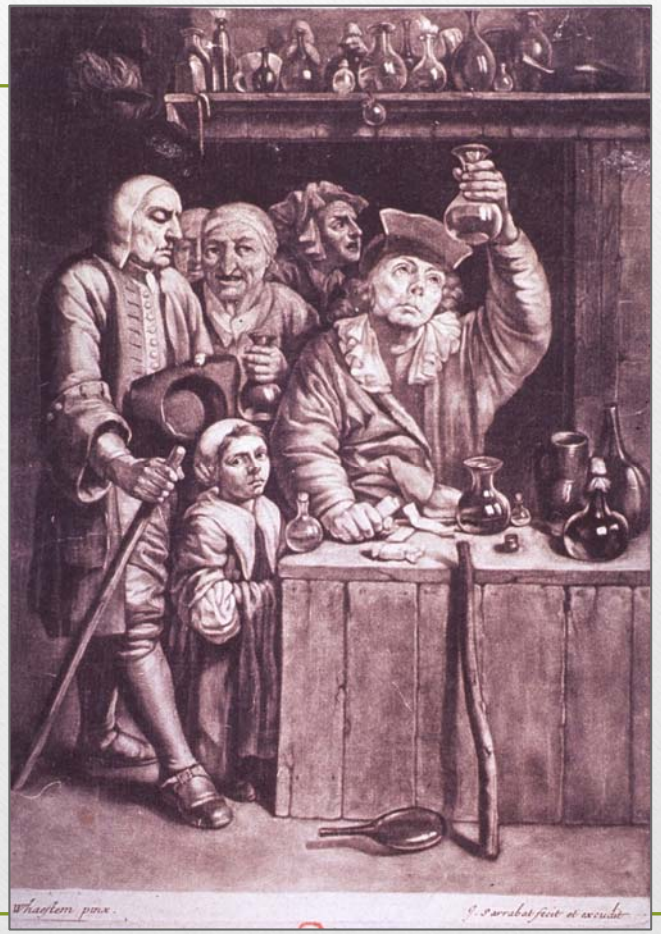
Kashani K et al. Discovery and validation of cell cycle arrest biomarkers in human acute kidney injury. Crit Care. 2013; 17(1):R25

NephroCheck

Acute Kidney Injury 101: Detective Work

AKI from Nephrologist Perspective

- 3 Keys to Diagnosis:
  - History, history, history!
  - Urine studies
  - Renal Ultrasound



Acute Kidney Injury by Etiology

Prerenal

- Intravascular volume depletion
- Cardiorenal syndrome
- Hepatorenal syndrome
- Bilateral RAS
- Burns
- Bleeding

Intrinsic

- Acute Tubular Necrosis (ATN)
- Contrast-induced
- Rhabdomyolysis
- Acute Glomerulonephritis
- Tumor lysis syndrome
- Nephrotoxins
- Acute Interstitial Nephritis (AIN)
- Atheroembolic renal disease
- Acute papillary necrosis

Post-Renal

- Kidney / Ureter:
  - Extrinsic compression ie tumor, Retroperitoneal fibrosis
  - Nephrolithiasis/Ureterolithiasis
  - Ureteral stricture
- Bladder:
  - BPH
  - Neurogenic bladder
  - Clot
  - Urethral stricture
  - Extrinsic compression ie tumor

Case 1

- You are a new intern at the VA and it's your first night on call. The night nurse on 4D pages you at midnight for a sleep med. She mentions "by the way your patient Mr. P. has not urinated all day". You look at the X-cover notes which state the patient is a 58 yr old man with hx HTN, admitted overnight with an ulcerative colitis flare. You go see the patient and he is sitting comfortably without complaints except bloody diarrhea which he says has been going on "awhile." His BP is 90/58, HR 115. I/O: 1875/100 urine (stool not recorded).

Labs from 4am:

- 140|110| 90 /105 Ca 9.1 Hg 9.1, MCV 86

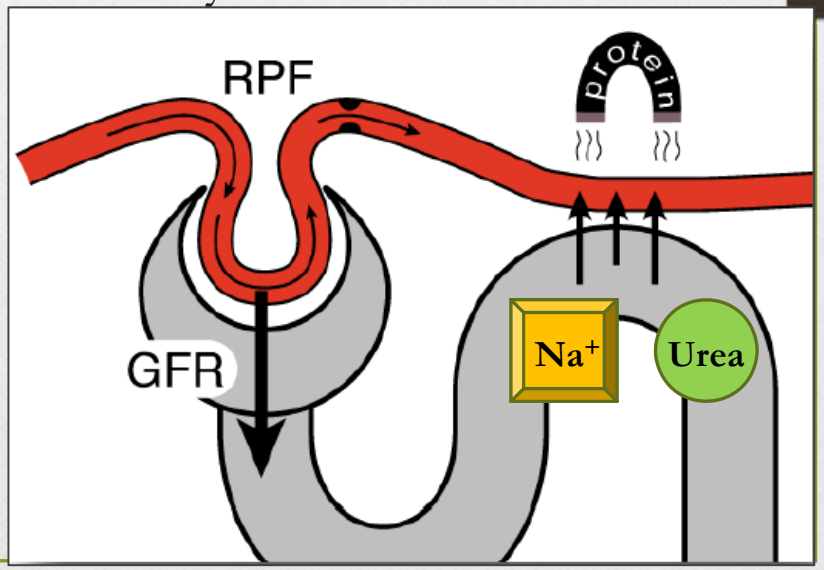
  4.8| 18| 3.17 \

Case 1: Management

- What diagnostics should you do next?
  - A) Check UA, urine studies
  - B) Check PVR and place Foley
  - C) Check orthostatics
  - D) Renal US
  - E) Recheck Hg, consider transfusion
  - F) All of the above
- What is the likely etiology?
- What are the "clues" here?

"Prerenal" AKI

- Caused by any decrease in renal perfusion or renal plasma flow
- Most common cause of community AKI
- BUN/Cr ratio > 20:1
- U_{Na} < 20



Hyaline Cast

The FE_{Na} Test

Use in the Differential Diagnosis of Acute Renal Failure

Carlos Hugo Espinel, MD

(*JAMA* 236:579-581, 1976)

- FeNa = excreted fraction of filtered Sodium
- The FeNa test was performed in 17 patients in the oliguric phase of acute renal failure
- Determined to distinguish between prerenal & ATN ($P < .001$):
  - Prerenal "azotemia" : FeNa < 1%
  - ATN : FeNa > 3%
- <u>Limitations:</u>
  - Most accurate in oliguria
  - Diuretics increase urinary Na excretion
  - Non-volume depleted states with low FeNa : acute glomerulonephritis, renal transplant rejection, contrast-induced nephropathy, hepatorenal, early ATN/sepsis, rhabdomyolysis
  - States with high FeNa: CKD, diuretics

$$FE_{Na} = \frac{\text{Na excreted}}{\text{Na filtered}} \times 100$$

$$FE_{Na} = \frac{U_{Na}\ (V)}{P_{Na}\ (GFR)} \times 100$$

$$FE_{Na} = \frac{U_{Na}\ (V)}{P_{Na}\ (C_{Cr})} \times 100$$

$$= \frac{U_{Na}\ (V)}{P_{Na}\left(\frac{U_{Cr}\ [V]}{P_{Cr}}\right)} \times 100 \qquad \text{thus,}$$

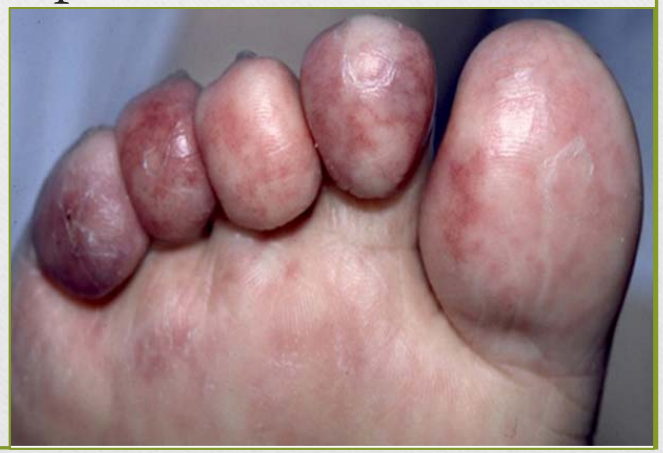
$$= \frac{U_{Na}\ (P_{Cr})}{P_{Na}\ (U_{Cr})} \times 100 \qquad \text{or}$$

$$\left(\frac{U}{P}\right)Na \Big/ \left(\frac{U}{P}\right)Cr \times 100,$$

where U and P represent concentrations in urine and plasma, respectively, and V, urinary flow in milliliters per minute. In the final expression, there is no urine flow (V) term.

Case 2

- A 70 yo man was diagnosed two days ago with acute MI and underwent percutaneous coronary intervention to reperfuse his LAD. Two days later his creatinine is noted to be elevated (despite being normal the day before) and he complains of a "rash" on his foot pictured below.



Case 2

- Which of the following would most likely be found in laboratory studies?
- A) Hyponatremia
- B) Hypokalemia
- C) Granular urine casts
- D) Urine leukocytes
- E) Eosinophiliuria and decreased complements

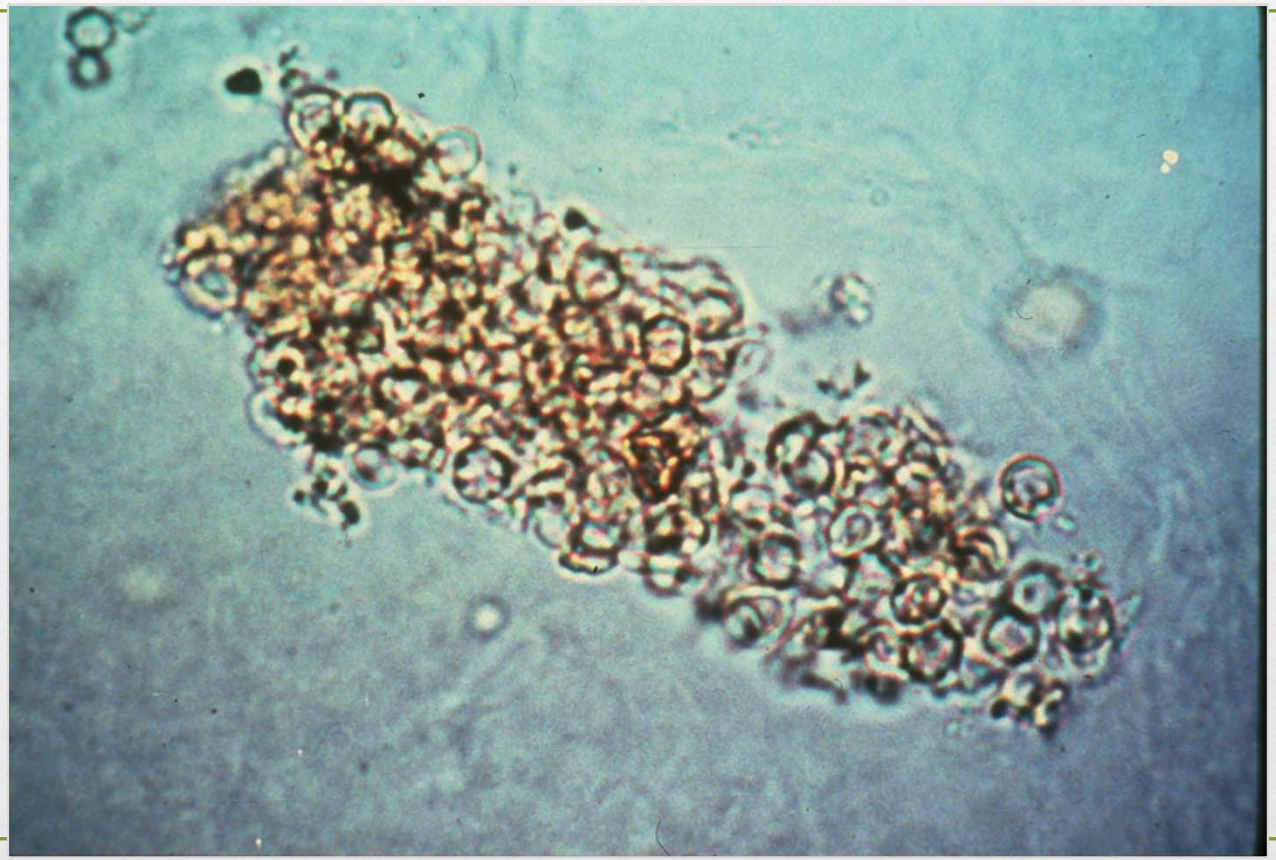
Intrinsic AKI

- Most common cause in hospitalized patients
- ATN #1 cause
- Oliguric vs non-oliguric
- Oliguric AKI more common in ATN than other etiologies
- Most important test is **URINALYSIS**

Intrinsic AKI: Diagnoses and Clues

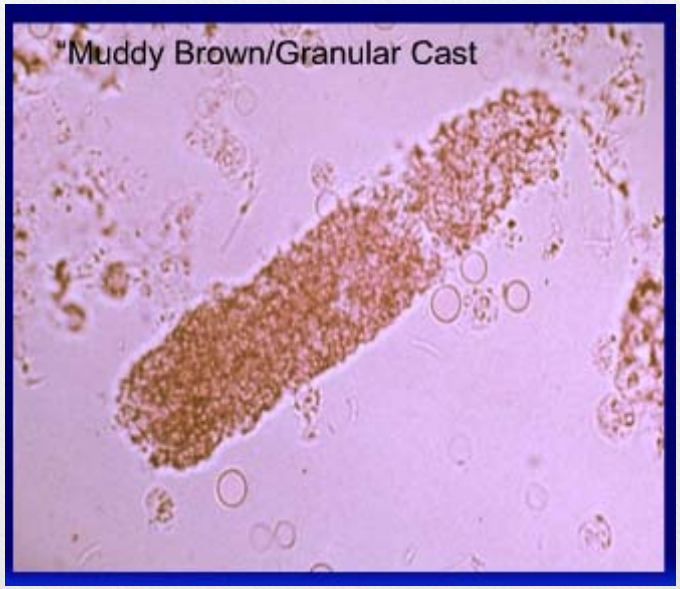
Etiology	Findings
ATN	Hypotension, muddy brown casts
Contrast-induced	Exposure iodinated contrast within past 72 hrs
Rhabdomyolysis	Elevated CK, Blood on UA (no RBC)
Glomerulonephritis	Protein, RBC, RBC casts on UA
Tumor lysis syndrome	Elevated uric acid, Phos, K; Hematological malignancy
Nephrotoxins	History of drug exposure
Acute Interstitial Nephritis	Rash, peripheral eosinophilia, urine Eos, history of drug exposure
Atheroembolic renal disease	Recent cardiac intervention, >70yo, urine Eos, livedo reticularis rash
Acute papillary necrosis	DM, SCC, Analgesic abuse; + Flank pain, gross hematuria
Malignant HTN	Severe uncontrolled HTN; Microhematuria
Renal vein thrombosis	Hypercoaguable state, + Renal Venous Doppler U/S

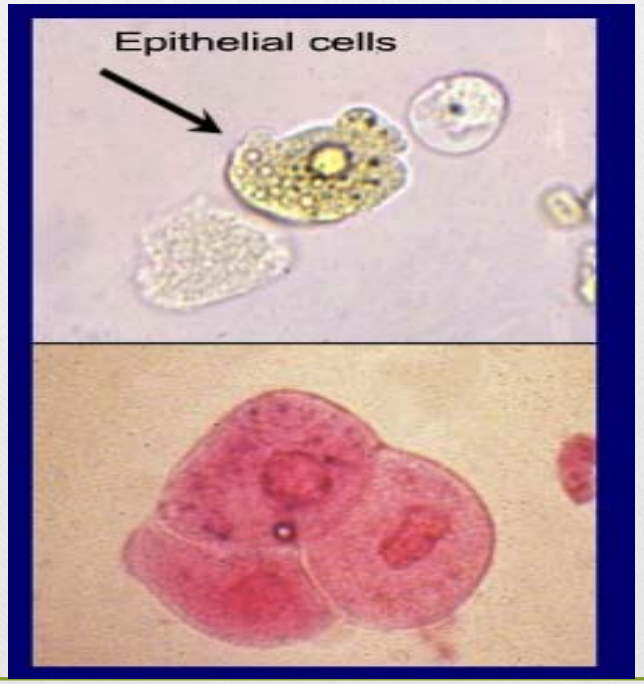
RBC Cast



Acute Tubular Necrosis

- Tubular hypoxia, inflammatory mediators, vasoconstriction → apoptosis and necrosis of tubule
- Renal tubular epithelial cells or muddy brown casts on UA





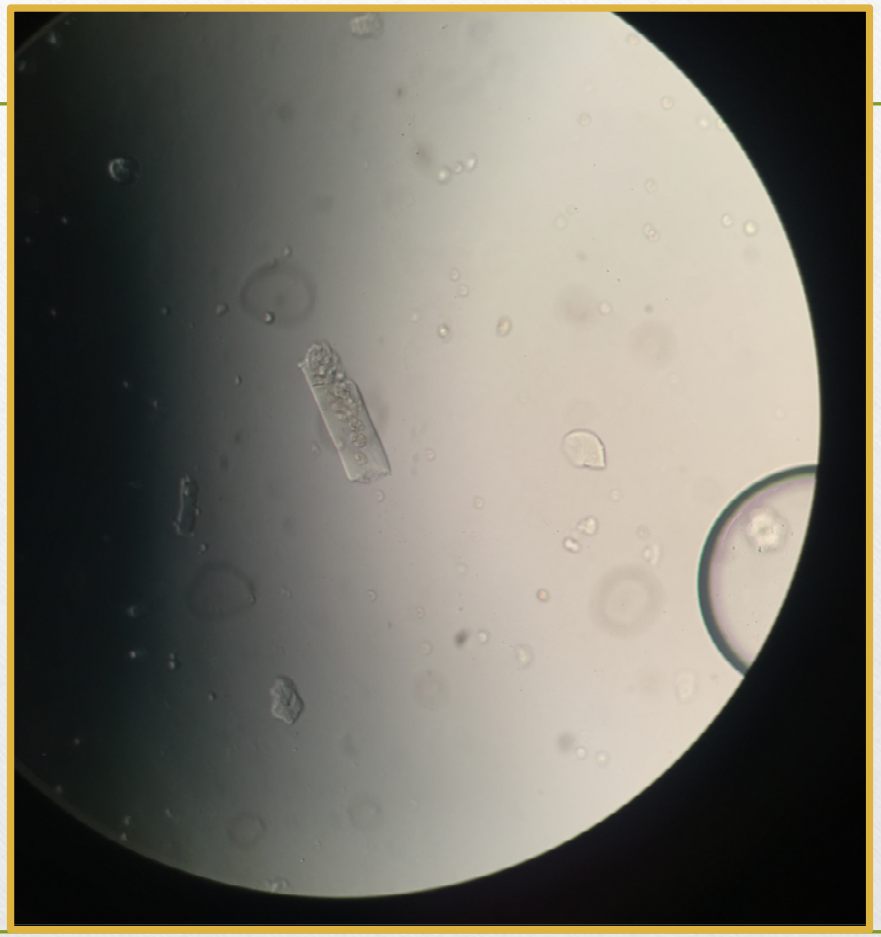
Acute Tubular Necrosis: Causes

- Sepsis/hypotension/shock
- Contrast-induced injury
- Ingestions: Ethylene glycol, cocaine, methamphetamines, synthetic cannibinoids
- Drugs/Nephrotoxins: Aminoglycosides, Amphotericin B, Cisplatin, high dose Vancomycin, Zolendronate, CNIs (Cyclosporine/Tacrolimus)

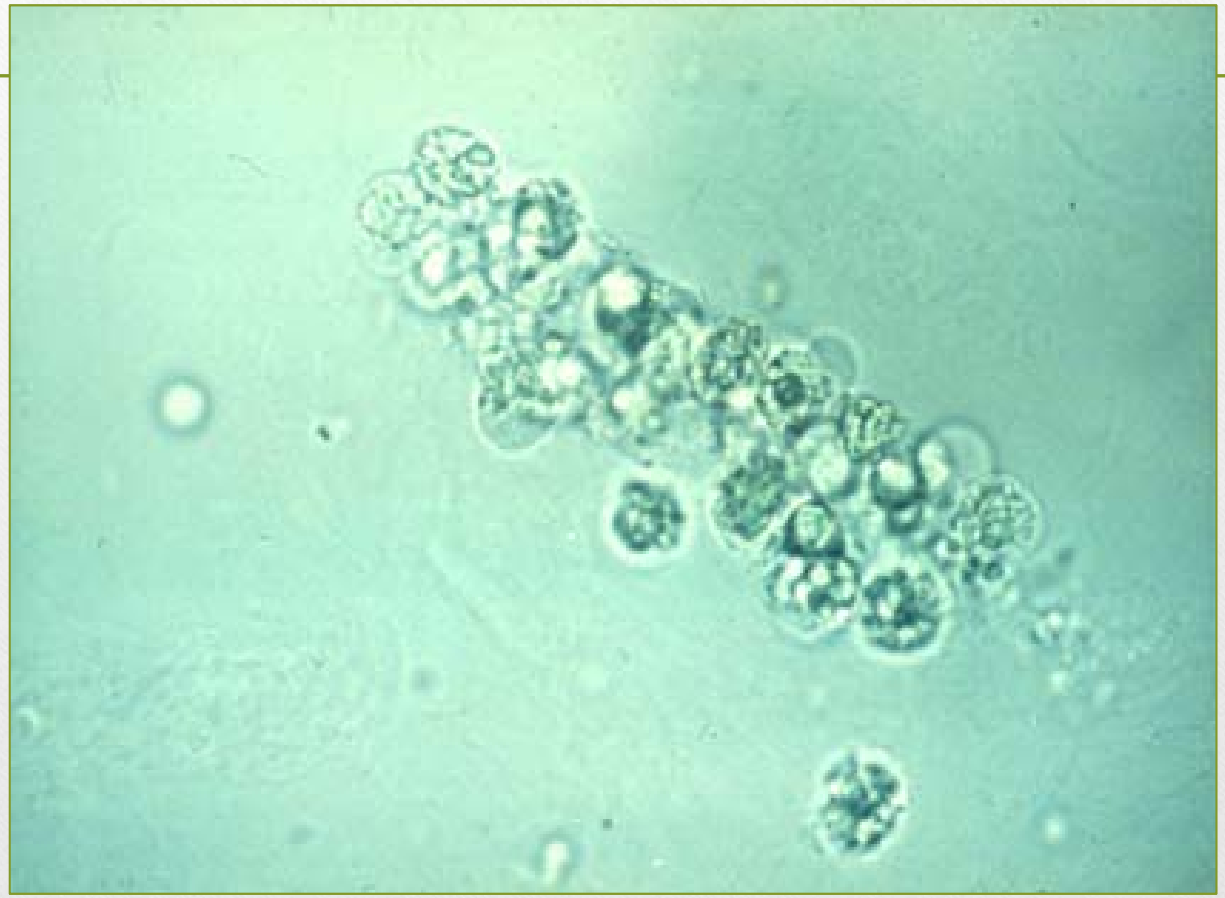
Case 3

- 50 year old man with hx HTN, admitted to VA overnight with "inability to urinate" and serum creatinine of 6. Denies N/V/D, change in BP or any other symptoms whatsoever. Home medications include Amlodipine. He denies NSAID use. He is given IVF overnight and remains anuric. You are on the Renal rotation and the next day you are consulted to see the patient. A Foley is inserted and 5 ml of urine is obtained which you spin in the lab and review:

What is your diagnosis?

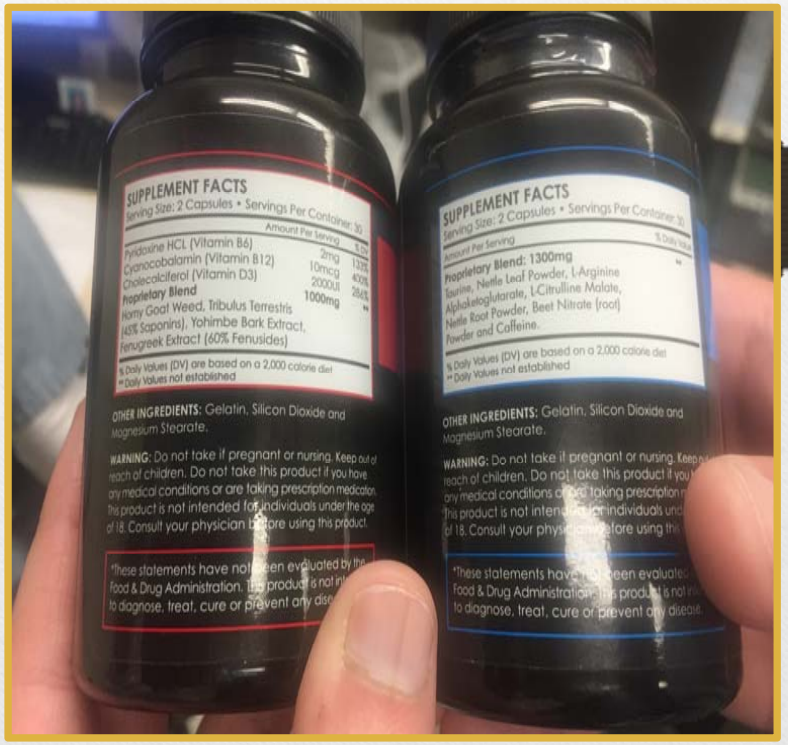


WBC Cast



Back to the patient…

- A follow up discussion with him reveals he ordered a performance-enhancing "natural" medicine online
  - His wife brings in the pill bottles
  - Kidney biopsy confirms **acute interstitial nephritis**



Acute Interstitial Nephritis

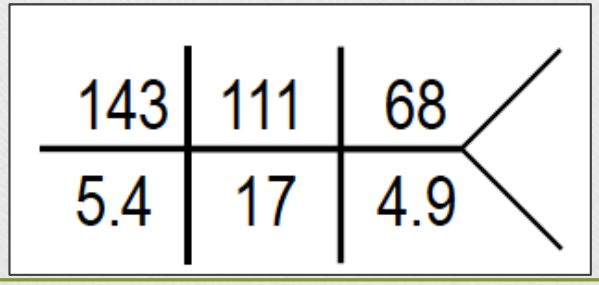
- Hypersensitivity-type reaction with interstitial infiltrate
- * 70% drug-induced / 15% Infectious and 6% Autoimmune
- Onset after 1st exposure: weeks
- Onset after 2nd exposure: 3-5 days
- Prototype drug: Rifampin – can occur after 1 day
- NSAIDs – can occur as long as 18 months
- Others: PPIs, PCN, Cephalosporins, Sulfas, Allopurinol, FQ, Phenytoin

OTC Nephrotoxins

- NSAIDs
- PPIs (potential)
- Vitamin C → Oxalate nephropathy
- Chromium
- Chapparal
- Willow bark
- Wormwood oil
- Contaminated spices

Case 4

- A 78 yo white man with a history of BPH has been self-treating a "sinusitis" for the last few days with over the counter medications. He finally relents and comes to the doctor for "some antibiotics." His PCP orders routine labs and sends him home. The patient receives a call that evening telling him to go straight to the ED. You are called by the ED with the following labs:



Case 4 Management

- What is your next step in management?
- A) Give him Kayexelate 30 gm x 1 now
- B) Stat CT abdomen/pelvis
- C) Check post-void residual
- D) Give him 2 liters IV NS bolus

Case 4 Management

- The bladder scan showed a post-void residual of 1100 cc and you place a Foley catheter. You round on the patient in the morning and he reports he is "doin' great doc, they've emptied this bag 5 times already!." You are not as happy as he is about this because you know he is *now* at risk for which of the following electrolyte abnormalities?
- A) Hypernatremia
- B) Acidosis
- C) Hypophosphatemia
- D) Hypomagnesemia
- E) Hypokalemia
- F) All of the above EXCEPT B

Post-Renal AKI

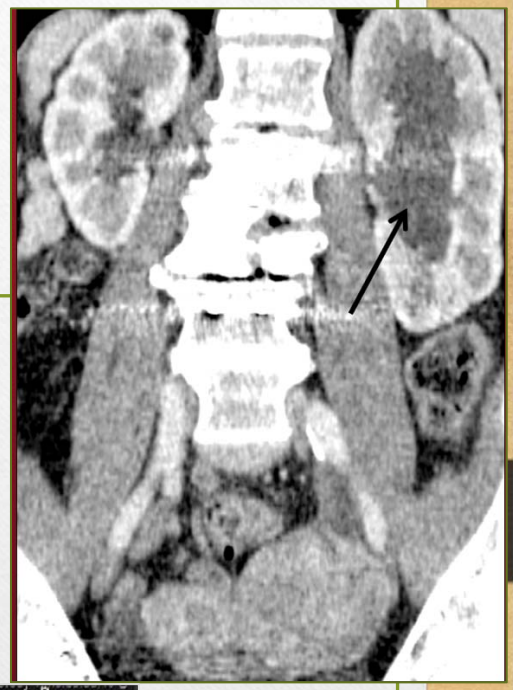
- Men: #1 cause BPH
- Women: #1 cause Cervical cancer
- Can be anatomic/physical or neuromuscular
  - Neurogenic Bladder Causes
    - Diabetes
    - MS, Parkinsons
    - Anticholinergics
    - Alpha-adrenergic agonists
    - Opiates, sedative hypnotics

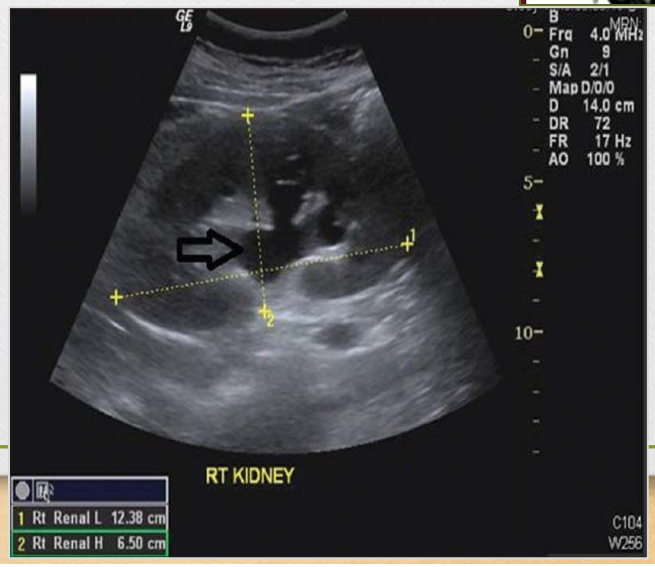
Post-Renal AKI Pitfalls

- Patients only oliguric/anuric with severe bilateral obstruction
- Frequency, nocturia and polyuria are sx of obstruction
- Concurrent volume depletion obstruction may not show hydronephrosis on US
- Patients early in the course of obstruction may not have developed hydronephrosis yet
- Large retroperitoneal tumors can encase the kidney and both cause the obstruction & prevent hydronephrosis.
- Retroperitoneal fibrosis can prevent hydronephrosis

Post-Renal Diagnosis

- Urinary hesitancy and dribbling
- Abdominal/bladder distention on exam
- Hyperkalemia out of proportion to AKI
- Elevated PVR > 100 ml
- Imaging: hydronephrosis





Management

- Specific treatments tailored to etiology
- Fluid and electrolyte management
- Remove nephrotoxins/NSAIDS
- Avoid hypotension / ICU: goal MAP > 65
- Dialysis if indicated

ORIGINAL ARTICLE

Balanced Crystalloids versus Saline in Critically Ill Adults

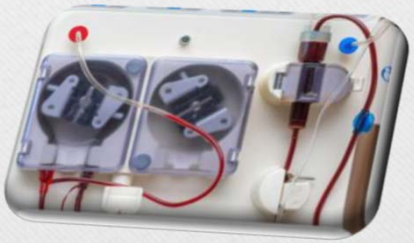
Matthew W. Semler, M.D., Wesley H. Self, M.D., M.P.H., Jonathan P. Wanderer, M.D., Jesse M. Ehrenfeld, M.D., M.P.H., Li Wang, M.S., Daniel W. Byrne, M.S., Joanna L. Stollings, Pharm.D., Avinash B. Kumar, M.D., Christopher G. Hughes, M.D., Antonio Hernandez, M.D., Oscar D. Guillamondegui, M.D., M.P.H., Addison K. May, M.D., et al., for the SMART Investigators and the Pragmatic Critical Care Research Group*

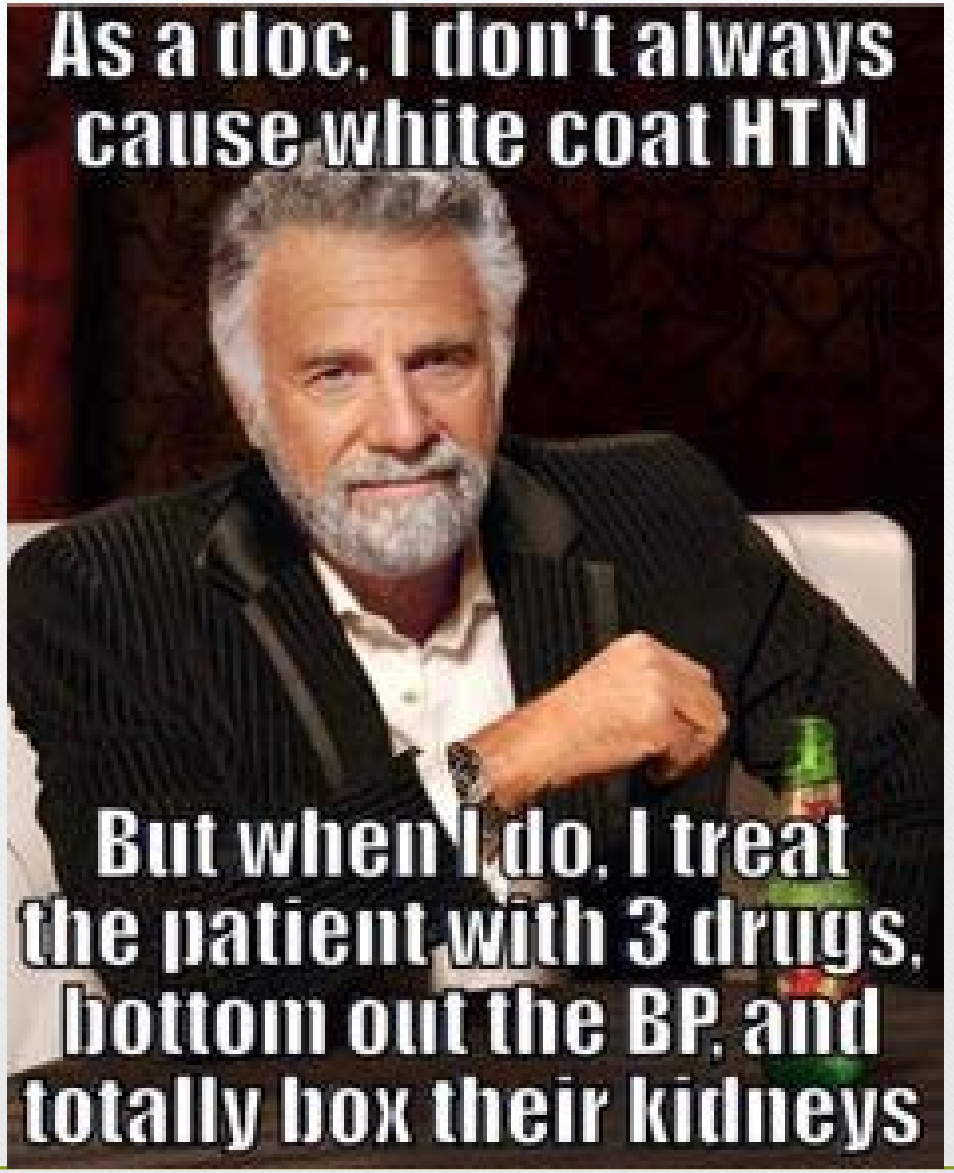
- Cluster-randomized, multiple-crossover trial in 5 ICUs at academic center, NEJM
- 15,802 adults received either saline (0.9% sodium chloride) or balanced crystalloids (lactated Ringer's solution or Plasma-Lyte A) for IVF administration
- The primary outcome was a major adverse kidney event within 30 days — death from any cause, new renal-replacement therapy (RRT), or persistent renal dysfunction
- Balanced crystalloids resulted in a lower rate of the composite outcome of death from any cause, new RRT, or persistent renal dysfunction than the use of saline

N Engl J Med 2018; 378:829-839

Indications for Dialysis: AEIOU

- Acidemia / Severe Acidosis
- Electrolyte: hyperkalemia
- Ingestion: Drug toxicity
- Overload of fluid
- Uremia



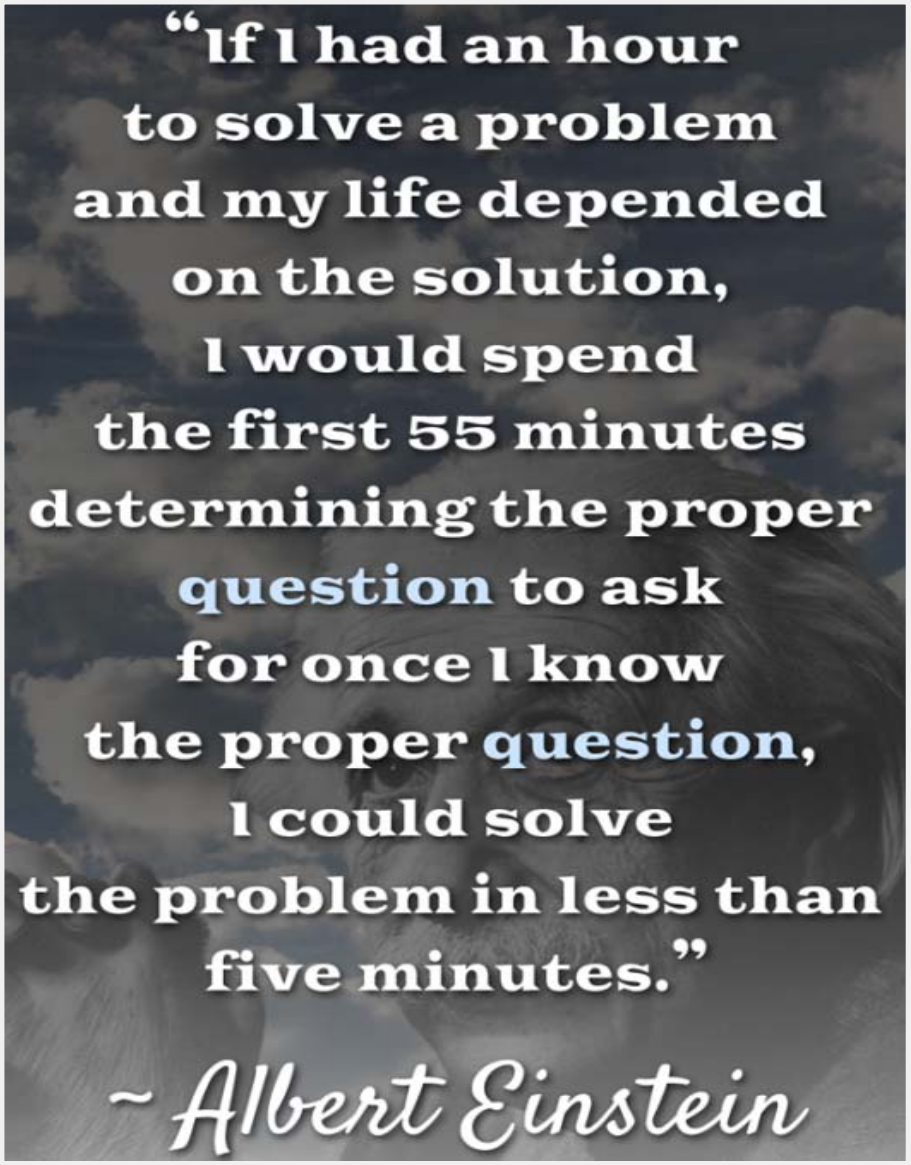

As a doc, I don't always cause white coat HTN
But when I do, I treat the patient with 3 drugs, bottom out the BP, and totally box their kidneys

Bonus: Case 5

A 57-year-old man with a history of diabetes mellitus and chronic kidney disease with a baseline creatinine of 1.8 mg/dL undergoes cardiac catheterization for acute myocardial infarction. He is subsequently diagnosed with acute kidney injury related to iodinated contrast. All of the following statements are true regarding his kidney injury EXCEPT:

- **A.** Fractional excretion of sodium will be low.
- **B.** His creatinine is likely to peak within 3–5 days.
- **C.** His diabetes mellitus predisposed him to develop contrast nephropathy.
- **D.** Transient tubule obstruction with precipitated iodinated contrast contributed to the development of his acute kidney injury.
- **E.** White blood cell casts are likely on microscopic examination of urinary sediment.

Questions?


"If I had an hour
to solve a problem
and my life depended
on the solution,
I would spend
the first 55 minutes
determining the proper
question to ask
for once I know
the proper question,
I could solve
the problem in less than
five minutes."
~ Albert Einstein