# Acute Kidney Injury

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# Objectives

1. Identify characteristics and relevant review of systems that may indicate a specific etiology of acute kidney injury including fevers and arthralgia.

2. Assess past medical history for risk factors and predisposing conditions including causative medications and toxin exposures.

3. Identify key physical exam findings that assess volume status (including orthostatic blood pressure measurement, jugular venous pressure, and presence of edema) and assess presence of uremic symptoms (including pericardial rub and asterixis).

4. Identify and interpret key laboratory and imaging tests and list indications, benefits, test characteristics, risks, and costs of testing:
   - Identify presence of acute kidney injury including patients with rising serum creatinine or decrease urine output.
   - Determine underlying etiology including urinalysis with microscopic evaluation, urine chemistries, chemistry panel, and renal ultrasound.

# Objectives (cont.)

5. Develop and prioritize a differential diagnosis including common and non-to-miss diagnoses:
   - Distinguish pre-renal, intra-renal, and post-renal causes:
     - Describe pre-renal causes including ineffective circulating volume.
     - Describe intra-renal causes including glomerular, tubular, interstitial, and vascular etiologies.
     - Describe post-renal causes including ureteral obstruction and bladder outlet obstruction.

6. Describe a rational and evidence-based approach to treating a patient with acute kidney injury:
   - Describe treatment of acute conditions including hyperkalemia and fluid deficit.
   - Describe treatment based on etiology including relieving obstruction in bladder outlet obstruction and withdrawal of causative medications in active interstitial nephritis.

7. Describe the long-term renal prognosis for patients with acute kidney injury.

8. List clinical interventions that may prevent acute kidney injury in patients at increased risk including discontinuation of causative medications, prevention of hypotension, and judicious use of iodinated contrast.

# Case 1: History

A 26-year-old male was admitted to the hospital complaining of generalized muscle soreness. He had completed the Boston Marathon three days prior to admission. He has become progressively anorexic and lethargic. He also noticed a decreasing amount of urine output over the past three days.

Medical history: No past medical history.

Social history: He denied alcohol and illicit drug use.

Meds: None. No supplements.

Allergies: None known

Family history: Unremarkable for renal disease.

# Case 1: Physical Exam

Well-developed, well-nourished male appearing lethargic

BP 135/70, HR 84, RR 20, 98.9F, weight 80 kg

HEENT – within normal limits

Cardiac – S1, S2 without S3, S4, murmur or rub

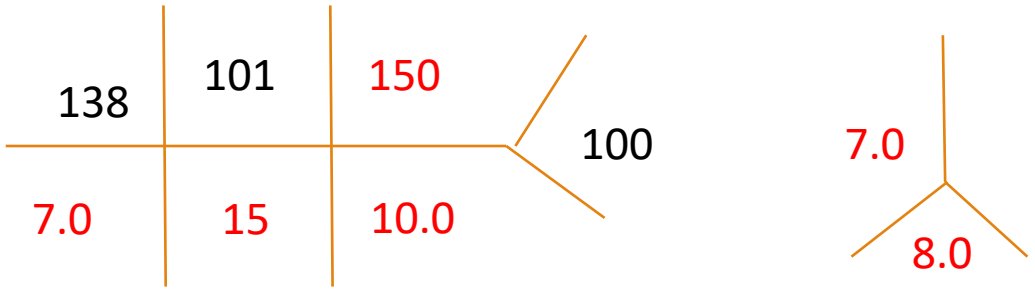
Pulmonary – clear to auscultation and percussion

Abdomen – Supple and non-tender, NABS

Extremities – ttp b/l with 2+ edema b/l

Neuro – no focal deficits. He was oriented to person, place and time, but was somnolent and had difficulty performing simple mathematical calculations.

# Case 1: Labs







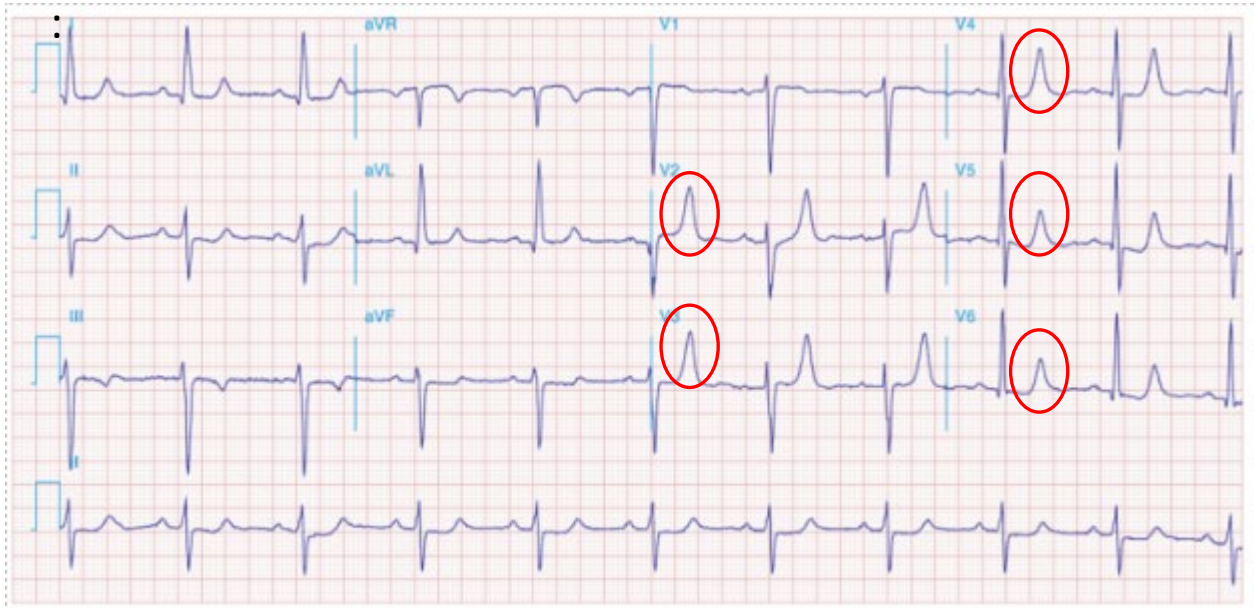
Serum albumin: 3.5
Arterial Blood Gas:  pH 7.35/28/105/15

Urinalysis: Specific gravity 1.015, pH 6.0, protein 2+, blood 4+, ketones (negative), glucose (negative) 2-5 RBC/HPF, 0-2 WBC/HPF
Na 35 meq/L, creatinine 56 mg/dl
UOSM 320.

# Case 1: Imaging

Renal ultrasound – right kidney 10.8 cm, left kidney 11.0 cm. Normal echogenicity without calculi or hydronephrosis.

EKG:




Source: J.L. Jameson, A.S. Fauci, D.L. Kasper, S.L. Hauser, D.L. Longo, J. Loscalzo: Harrison's Principles of Internal Medicine, 20th Edition
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# KDIGO 2012: AKI Definition

The KDIGO guidelines define AKI as follows :

1. Increase in serum creatinine by ≥0.3 mg/dL within 48 hours

or

2. Increase in serum creatinine to ≥1.5 times baseline, which is known or presumed to have occurred within the prior seven days

or

3. Urine volume <0.5 mL/kg/hour for six hours

The diagnostic criteria should only be applied after volume status has been optimized.

Urinary tract obstruction needs to be excluded if urine volume is used as a sole criteria.

Kidney International Supplements (2012) 2, 1

# AKI Stages

| Stage | Serum creatinine | Urine output |
|---|---|---|
| 1 | 1.5–1.9 times baseline<br>or<br>≥0.3 mg/dl (≥26.5 μmol/l) increase | <0.5 ml/kg/h for 6–12 h |
| 2 | 2.0–2.9 times baseline | <0.5 ml/kg/h for ≥12 h |
| 3 | 3 times baseline<br>or<br>≥4.0 mg/dl (≥353.6 μmol/l) increase<br>or<br>initiation of RRT<br>or<br>in patients <18 years a decrease in eGFR<br><35 ml/min/1.73 $m^2$ | <0.3 ml/kg/h for ≥24 h<br>or<br>anuria ≥12 h |

Kidney International Supplements (2012) 2, 1

# Pitfalls of serum Cr

- **AKI is not a steady state and hence cannot calculate estimated GFR using any of the available formulae.**

- **Serum creatinine lags behind the actual injury**

- **Serum Creatinine levels depend on:**

  **Clearance rate (changing in AKI)**

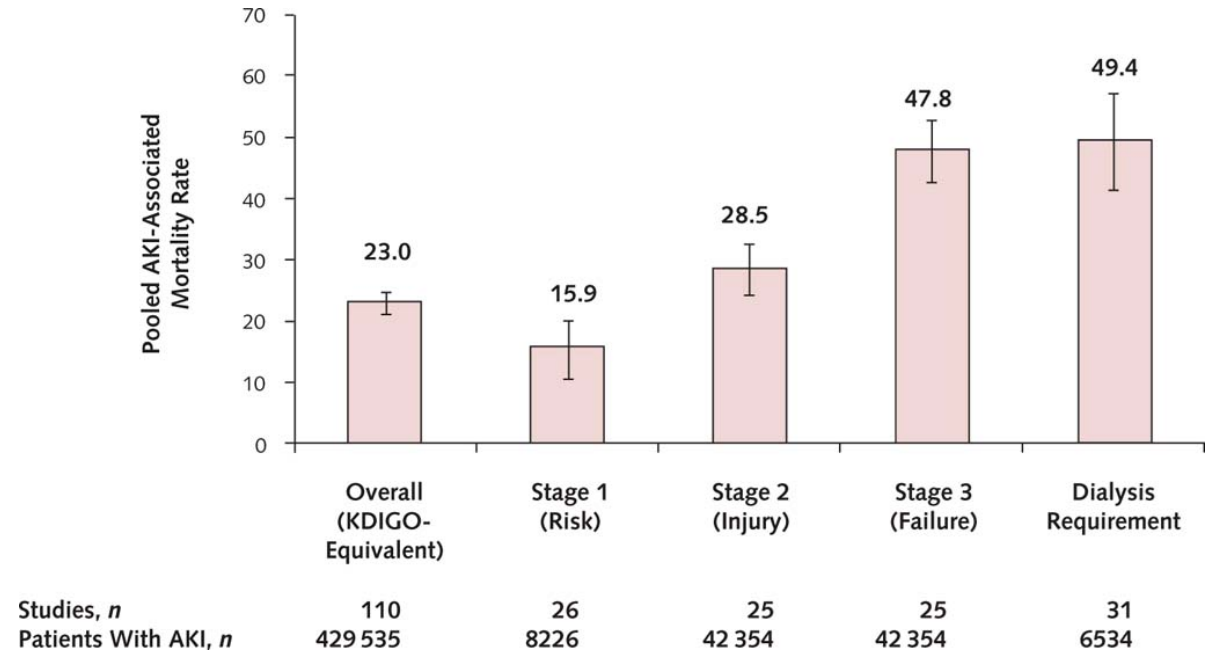
  **Rate of production (changing in AKI)**

  **Volume of distribution (changing in AKI)**

- **Creatinine produced predominantly by the muscles and hence, muscular people can have high serum creatinine and emaciated people with very low serum creatinine, not corresponding with the actual GFR.**

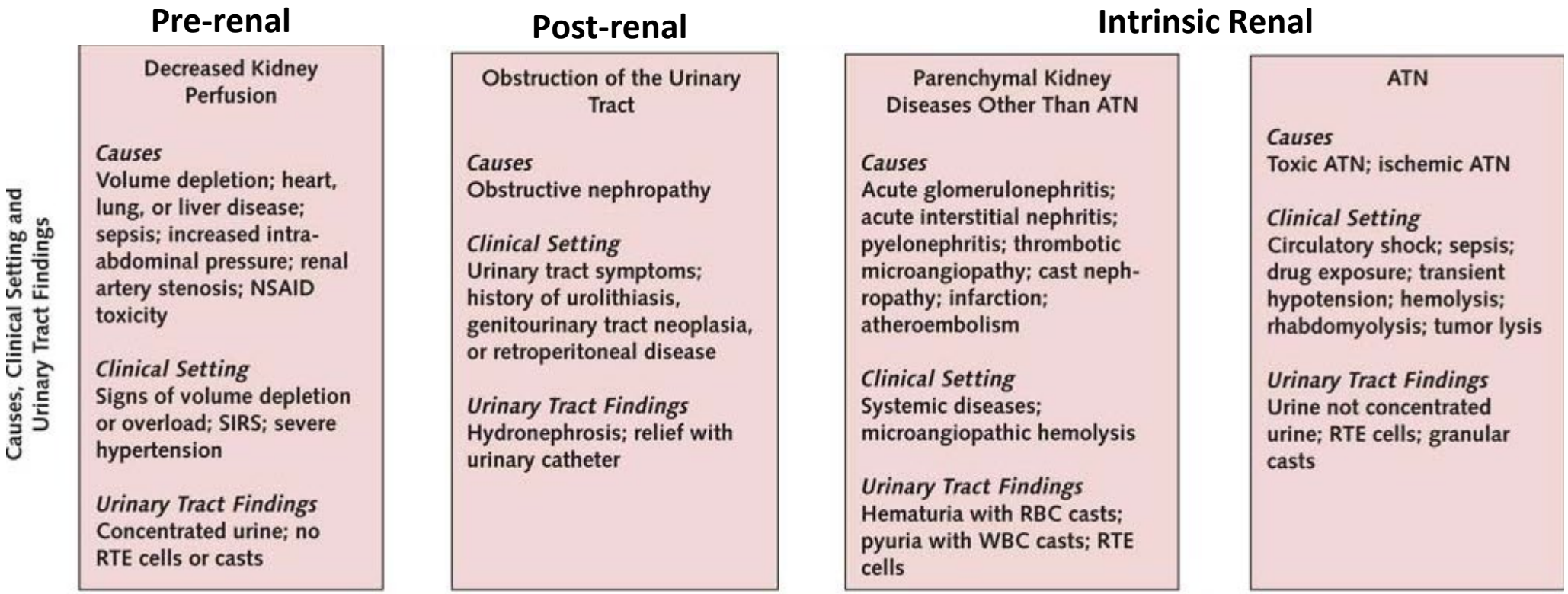
# AKI: Epidemiology

- Occurs in 20% of hospitalized patients
- 10% require dialysis
- Of those requiring dialysis, mortality is 50%




Andrew S. Levey, Matthew T. James. Acute Kidney Injury . Ann Intern Med.2017;167:ITC66 - ITC80. [Epub 7 November 2017]. doi: 10.7326/AITC201711070

# AKI: Etiologies

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# From H&P to Diagnosis

Detective work:

History of inciting events

Thorough chart review for in-hospital AKI

Is/Os, trends in BP/HR and weights, intra-op notes if available, medication/contrast exposure

Recent change in medications

Physical exam findings

Interpreting UA, urine and serum chemistries

Where applicable, using imaging studies (ultrasound, CT)

# From H&P to Diagnosis (cont.)

HPI: The presenting complaint will be your lead to get the pertinent history as in if patient presents with SOB, you are going to ask about orthopnea, PND, swelling in the legs, whether he is taking his medications as prescribed, low salt diet and so on…

Medications: Any recent changes or additions or over the counter medications including herbal supplements

FH: Pertinent to kidney problems

SH: occupation could be important in certain circumstances (any exposure to chemical substances), illicit drug use or alcohol abuse

Vitals: If patient is hemodynamically stable (BP normal or slightly on the high side, HR within normal range and no fevers or tachypnea), you are either dealing with an intrinsic or post-renal in most cases but you could be tricked with right heart failure patients who look otherwise normal..

# From H&P to Diagnosis (cont.)

Physical exam: extremely important in coming up with a differential, to mention a few examples…

Volume depletion: dry oral mucosa, decreased skin turgor

Heart failure: +ve JVD, crackles or diminished breath sounds bilaterally, tachypnea and accessory muscle usage if severely SOB, pedal edema (generally pretty impressive)….

Cirrhosis: jaundice, distended abdomen with fluid thrill…

Uremia: pericardial rub, scratch marks if patient has itching which could be one of the manifestations

Vasculitis: Skin rash or purpura

Pyelonephritis: CVA tenderness

Bladder distention: Suprapubic fullness (tough to interpret in obese patients)

# Urinalysis

Component Results

| Component | Value | Ref Range & Units |
|---|---|---|
| COLOR | YELLOW | YELLOW |
| CLARITY | CLEAR | CLEAR |
| PH | 6.0 | 4.5 - 8.0 |
| SPEC GRAVITY | 1.008 | 1.003 - 1.035 |
| PROTEIN | NEG | NEG |
| BLOOD | NEG | NEG |
| GLUCOSE | NEG | NEG |
| KETONES | NEG | NEG |
| BILIRUBIN | NEG | NEG |
| UROBILINOGEN | <2.0 | <2.0 MG/DL |
| NITRITE | NEG | NEG |
| LEUKOCYTES | NEG | NEG |
| RFLX MICROSCOPY | MICROSCOPIC NOT INDICATED | |
| RBC | MICROSCOPIC NOT INDICATED | 0 - 2 /HPF |
| WBC | MICROSCOPIC NOT INDICATED | 0 - 5 /HPF |
| REFLEX CULTURE | CULTURE NOT INDICATED | |

Bland UA in pre-renal. Kidneys are trying to convey that they are not the primary culprits and urging us to look beyond the kidneys….

# Urinalysis (cont.)

**Result Date - 11/24/2015**

Component Results

| Component | Value | Ref Range & Units |
|---|---|---|
| COLOR | YELLOW | YELLOW |
| CLARITY | HAZY ! | CLEAR |
| PH | 5.0 | 4.5 - 8.0 |
| SPEC GRAVITY | 1.010 | 1.003 - 1.035 |
| PROTEIN | 2+ ! | NEG |
| BLOOD | LARGE ! | NEG |
| GLUCOSE | NEG | NEG |
| KETONES | NEG | NEG |
| BILIRUBIN | NEG | NEG |
| UROBILINOGEN | <2.0 | <2.0 MG/DL |
| NITRITE | NEG | NEG |
| LEUKOCYTES | MOD ! | NEG |
| RFLX MICROSCOPY | MICROSCOPIC PERFORMED | |
| RBC | >180 ^ | 0 - 2 /HPF |
| WBC | 16 ^ | 0 - 5 /HPF |
| SQUAMOUS EPITHELIAL | 5 | 0 - 5 /HPF |
| MUCOUS | FEW | FEW |
| AMORPHOUS CRYSTAL | PRES | |

Urine is pretty active (rule out UTI for sure…)
Kidneys are begging for your attention.

# Urine Chemistry

| LAB VALUE | PRE-RENAL | INTRINSIC |
|---|---|---|
| Urine Specific Gravity | > 1.020 | < 1.010 |
| Urine Osmolality (mosm/kg) | > 500 | < 350 |
| Urine Na (mEq/L) | < 20 | > 40 |
| Fractional excretion of sodium, FeNa (%) | < 1 | > 1 |
| Fractional excretion of urea, FeUrea (%) | < 35 | > 35 |
| U/P Creatinine ratio | > 40 | < 20 |
| Serum BUN/Cr ratio | > 20:1 | < 10:1 |
| Furosemide Stress Test | UOP increases | No response |
| What do they reflect? | Intact tubular function | Impaired tubular function |

**As tubules are injured, sodium reabsorption is impaired, so urine Na is high.**

**As tubules are injured, urea reabsorption and creatinine secretion is impaired. So relatively less rise in serum BUN.**

**Intact tubules in prerenal, so non-oliguric patients respond to diuretics.**

# FeNa and FeUrea

Fractional excretion of sodium (FeNa) = $\frac{\text{UNa x SCr}}{\text{SNa x UCr}} \times 100$

FeNa = 4.5%

Fractional excretion of urea (FeUrea) = $\frac{\text{Uurea x SCr}}{\text{Surea x UCr}} \times 100$

FeNa <1 : pre-renal
FeNa >1 : intrinsic or post-renal

FeUrea <35 : pre-renal
FeUrea >35 : intrinsic or post-renal
*FeUrea more accurate in setting of diuretics.

Urine sodium <20: pre-renal
(decreased renal perfusion)

# Case 1: Diagnosis

What category of AKI?

- Intrinsic renal

What additional tests would help make the diagnosis?

- CK and urine myoglobin

What is the final diagnosis?

- Rhabdomyolysis

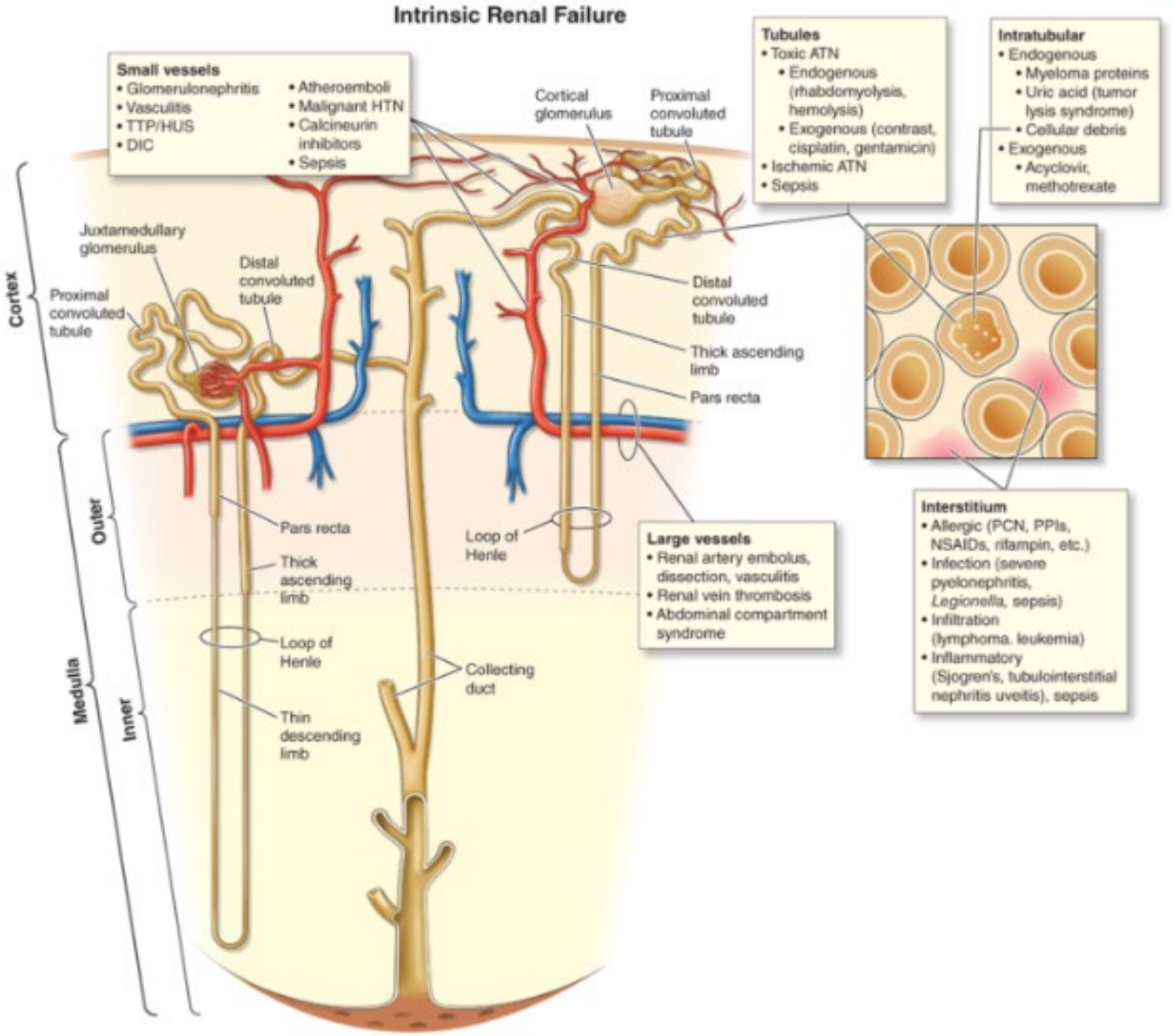
# AKI: Intrinsic Causes

Acute tubular necrosis (ATN):

Ischemic ATN:
- hypoperfusion
- sepsis

Toxic ATN:
- vancomycin
- aminoglycosides

Urinalysis: granular casts, renal tubular epithelial casts

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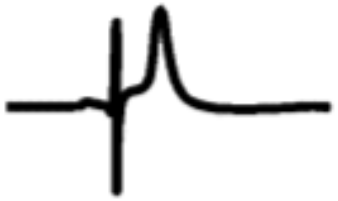
# Case 1: EKG Findings

| Serum potassium | Typical ECG appearance | Possible ECG abnormalities |
|---|---|---|
| Mild (5.5-6.5 mEq/L) |  | Peaked T waves<br>Prolonged PR segment |
| Moderate (6.5-8.0 mEq/L) |  | Loss of P wave<br>Prolonged QRS complex<br>ST-segment elevation<br>Ectopic beats and escape rhythms |
| Severe (>8.0 mEq/L) |  | Progressive widening of QRS complex<br>Sine wave<br>Ventricular fibrillation<br>Asystole<br>Axis deviations<br>Bundle branch blocks<br>Fascicular blocks |

# Hyperkalemia Management

| Action | Agent | Dose |
|---|---|---|
| **Stabilization of cardiac membrane** | Calcium gluconate (10%) | 10 ml over 10 min |
| **Shift of K Intracellularly** | 1. Short acting Insulin and Dextrose<br>2. Sodium bicarbonate<br>3. Albuterol | 1. 10 units IV push with 25-40 gm of Dextrose<br>2. 50 meq slow IV push or IV drip<br>3. 10-20 mg nebulizer treatments |
| **K Excretion**<br>Gut - can't be used in acute abdominal issues or major abdominal procedures | 1. Sodium polystyrene sulfate<br>2. Zirconium<br>3. Patiromer | 1. 15 to 30 mg Q 4-6 hrs as needed<br>2. 5-10 gm 3 x daily for first 2 days<br>3. 8.4 gm daily (more for chronic hyperkalemia management) |
| Kidneys – not effective if patient is anuric | 1. IV fluids<br>2. Lasix<br>3. Fluids + Lasix if euvolemic | 1. Bolus 500 or 1000 cc Normal saline<br>2. Depending on patient's kidney function<br>3. Give simultaneously |
| **Removing K by extracorporeal circuit** | Hemodialysis – takes time to get a dialysis catheter in and have the dialysis machine ready, treatment of choice for ESRD patients who already have a dialysis access in place. | Nephrology evaluation |

# Case 1: Other electrolyte abnormalities

1. Hyperkalemia

2. Hypocalcemia

3. Hyperphosphatemia

In Rhabdomyolysis or any form of cell lysis, there is release of potassium and phosphorus leading to high K and Phos. Calcium gets deposited in the cells leading to hypocalcemia.

Remember that advanced renal failure on any etiology can cause the above abnormalities as well, kidney is unable to get rid of K and Phos and hypocalcemia as there is lack of active form of vitamin D (1,25 hydroxy vitamin D).

# Renal Ultrasound Interpretation

Few findings that can help determine the chronicity of renal failure:

1. Increased echogenicity generally suggests scarring/fibrosis and so points more towards a chronic process.
2. Small kidneys (relative to vertebral height) point towards chronic process. Generally the right kidney is 0.3-0.5 cm smaller than the left kidney.

Ultrasound also helps you in ruling out post-renal etiology: Hydronephrosis seen in upper urinary tract obstruction and distended bladder in lower urinary tract obstruction. Sometimes you will need a CT for better delineation of hydronephrosis and diagnosing kidney stones.

# AKI Management

- Treatment of underlying etiology
  1. Volume repletion in volume depletion
  2. Treatment of heart failure
  3. Treatment of underlying infections
  4. Stopping offending medications
  5. Relieving obstruction.
- Track daily weights, BP and Inputs/outputs.
- Maintain mean arterial pressure (MAP > 60 mmHg).
- Dose medications to renal function – can be tricky.
- Avoid contrast studies and use least nephrotoxic medications when possible (should be the case in general).
- Management of electrolyte disturbances – hyperkalemia, metabolic acidosis, hyperphosphatemia.

# AKI: Indications for Dialysis

- General indications for dialysis: AEIOU still stand true to date.
- Acidosis
  - metabolic acidosis refractory to medical management
- Electrolytes
  - hyperkalemia refractory to treatment
- Intoxications with a dialyzable drug
    - salicylates, lithium, isopropanol, methanol, and ethylene glycol (SLIME)
- Overload
  - volume overload that does not respond to diuresis
- Uremia
  - elevated BUN with signs of uremia, such as uremic bleeding, encephalopathy, and pericarditis.

# AKI: Prognosis

- Depends on the severity of underlying illness.
- Most patients recover but "complete" recovery is not always the case even if serum creatinine reaches baseline.
- At risk for CKD with repeated AKI episodes.
- May take up to 3 months for patients to recover especially if they are become dialysis dependent from an acute insult.
- Mortality of > 50% in patients with AKI and multi-organ dysfunction.

# Case 2: History

74yo with hx of *hypertension, diabetes, heart failure* with *reduced ejection fraction of 30%,* and *benign prostatic hypertrophy* who is brought to the emergency room by his family with **lethargy, decreased oral intake, and fever for two days**. They note his temperature at home reached 101.0 F.

His current medications include carvedilol 12.5mg BID, **losartan 25mg daily**, **furosemide 40mg BID, metformin 1000mg BID, and tamsulosin 0.4mg daily**. His family reports he has been compliant with these medications.

# Case 2: Physical Exam

Older, frail appearing male

**BP 101/58, pulse 98, respirations 20**, temp 101.4F

HEENT notable for dry mucous membranes and poor dentition

Cardiac – borderline tachycardic, *+ S4 and 2/6 systolic murmur* heard best at the RUSB

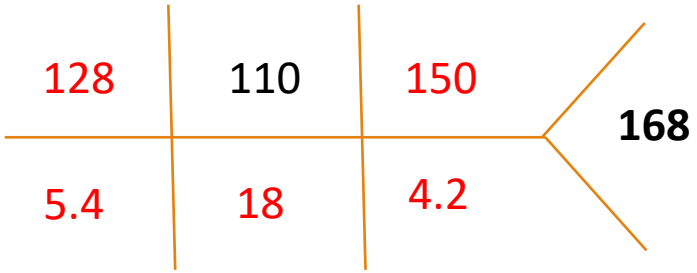
Pulmonary – clear to auscultation and percussion

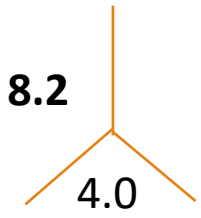
Abdomen – Supple and non-tender

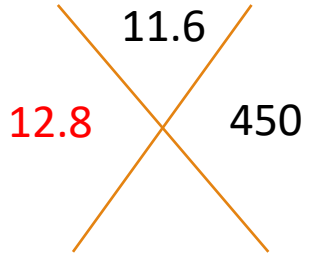
Extremities – **venous stasis changes noted with trace LEE b/l**

Neuro – **drowsy** but able to respond to questions. No focal deficits noted on exam

# Case 2: Labs




**Baseline Cr 1.8 mg/dl**

Serum albumin 3.7

Urinalysis: Specific gravity **1.6**, pH 5.8, **protein 1+, blood 1+, ketones 2+,** glucose (negative), 2-5 RBC/HPF, 10-20 WBC/HPF, + leukocyte esterase, + nitrates, + hyaline casts, 3+ bacteria

Urine chemistry:
Na 20 meq/L, creatinine 100 mg/dl, urea 400mg/dl

# Case 2: Diagnosis

What is the etiology of AKI?

- Pre-renal azotemia
  - Physical exam findings
  - UA consistent with UTI
  - Hyaline casts
  - FeNa 0.65%, FeUrea 11.5%

# Case 2: Treatment

IVF hydration

Stopping nephrotoxic agents:

- Losartan, furosemide

Renally dose medications

- Stop metformin

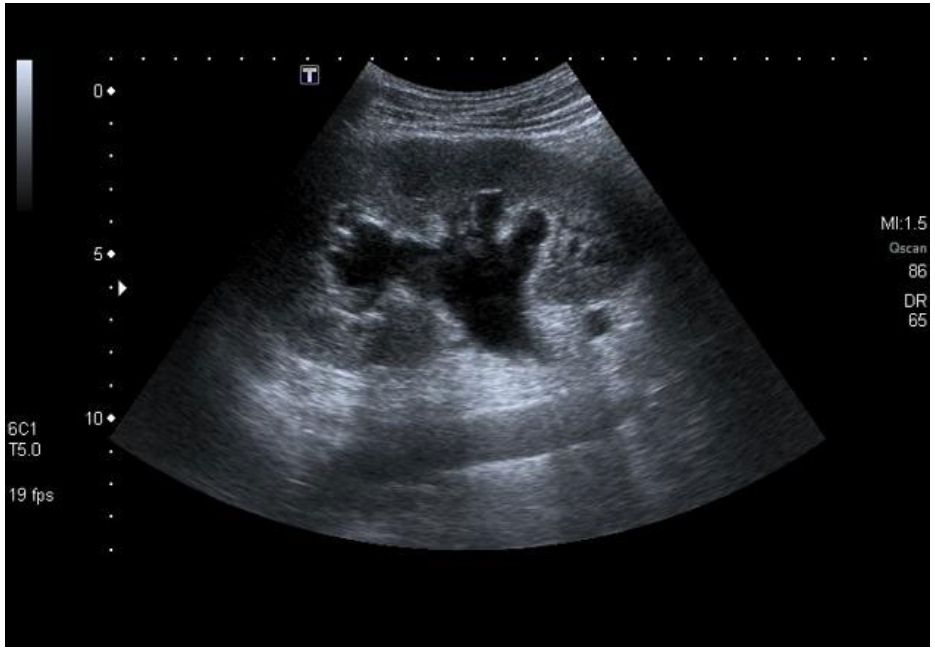
# Case 2: Continued

The patient is treated appropriately, his mental status improves, his fevers resolve, and his urine output increases. On **day three** of his hospital stay, the nurse notes that his *urine output has started to decline again*. His vitals have remained stable, a repeat urinalysis is negative, and his white blood cell count has normalized. His creatine improved from 4.2mg/dl to 2.0mg/dl but **is now 2.3mg/dl.**

# Case 2: Work-up

Bladder scan with post-void residual (PVR) =
**250 cc**

Renal ultrasound: Bilateral hydronephrosis




Refat A, Obstructive uropathy and urolithiasis on ultrasound. Case study, Radiopaedia.org (Accessed on 04 Sep 2024) https://doi.org/10.53347/rID-25562

# Case 2: Treatment (cont.)

Diagnosis:

- Obstructive nephropathy likely due to bladder outlet obstruction in setting of BPH.

Management:

- Place Foley catheter for bladder decompression.