# AKI: Clinical Pearls to Accompany Concept Map

**How Do We Define AKI?**

- Rapid increase in serum creatinine, decrease in urine output, or both
- Change in serum creatinine is generally easier to quantify in patients who do not have a foley catheter (i.e., most pediatric patients not in the ICU)
- An increase in creatinine of **50% above baseline** or an **absolute** increase of **0.3 mg/dl** are the most commonly used cutoffs for defining pediatric AKI
    - there are multiple classifications schemes which are overall more similar than they differ, and the minute details are more important for research purposes than from clinical care
    - the **take-home point** is that the **percentage change from baseline** matters the most -- an increase in creatinine from 0.2 mg/dL to 0.3 mg/dL represents the **same** loss of renal function as an increase from 1.0 mg/dL to 1.5 mg/dL
- General staging of acute kidney injury (slight differences in definition from each classification scheme)
    - Stage 1: Serum creatinine between 1.5 and 2 times baseline
    - Stage 2: Serum creatinine between 2 and 3 times baseline
    - Stage 3: Serum creatinine greater than 3 times baseline

**How Can We Estimate Renal Function Based on Serum Creatinine?**

- Use the **Bedside Schwartz Formula**: GFR = 0.413 * ht (in cm) / (SCr)
- Caution:
    - This is an estimation assuming **steady state** conditions, and renal function is **dynamic** in the setting of AKI (i.e., a doubling of serum creatinine in the acute setting represents transient total loss of renal function)
    - Healthy individuals can lose **up to 50% of renal functional capacity** without any associated change in GFR or creatinine (due to compensatory glomerular hyperfiltration)
    - Prerenal azotemia, if transient, may not result in true kidney *injury* (i.e., an irreversible and damaging process), but this is impossible to tell without (1) predicting the future or (2) performing a kidney biopsy

**Why Do We Care About AKI?**

- The conservative cutoff of an increase in creatinine by **50% above baseline** is used because even an increase this small has been a/w adverse outcomes, via multiple possible mechanisms:
    - Acidosis
    - Dyselectrolytemias (hyperkalemia, hyperphosphatemia, hypocalcemia) --> cardiac arrhythmias, impaired cellular functioning
    - Fluid overload / third spacing
    - Toxin accumulation --> neutrophil dysfunction
    - Sequelae of uremia (platelet dysfunction, encephalopathy, pericarditis)
- **Short-term** complications
    - Patients with Stage 2 AKI (Cr 2.0x baseline or greater) that does not resolve within 7 days have 47% hospital mortality and 1-year survival of only 77%
- **Long-term** complications
    - Single episode of kidney injury --> “recovery” due to hyperfiltration of remaining functional nephrons --> serum creatinine “normalizes” but pt is at elevated risk of developing CKD

**How Can We Think Through the Differential for Causes of AKI?**

- **Pre-renal**: any cause of decreased blood flow to the kidney
    - **Systemic hypoperfusion** (i.e., decreased effective arterial blood volume): hypovolemia (GI losses), hemorrhage, sepsis, anaphylaxis, decompensated heart failure, cirrhosis
    - **Localized decrease in renal blood flow**: renal artery stenosis or thrombosis, ACE inhibitor / ARB use on top of second cause of hypoperfusion, medium-to-large vessel vasculitis, intra-abdominal hypertension
- **Intrinsic renal**: disease of renal parenchyma
    - **Acute tubular necrosis** - results from prolonged ischemia or nephrotoxin exposure (drugs: vancomycin, zosyn, aminoglycosides, NSAIDs, iodinated contrast, antivirals [acyclovir, ganciclovir, cidofovir, etc], calcineurin inhibitors, cytotoxic chemotherapy vs other toxins: myoglobin, uric acid)
        - Classically w/ **muddy brown casts** on UA (but not necessarily)
    - **Acute interstitial nephritis** - immune reaction to certain drugs (NSAIDs, penicillins) and infections in those with a genetic predisposition
        - classically with **fever, rash,** and **eosinophiluria**
    - **Microvascular damage -** think small-vessel vasculitis (e.g., microscopic polyangiitis, granulomatosis with polyangiitis, Henoch-schonlein purpura, IgA nephritis) vs thrombotic microangiopathy (hemolytic-uremic syndrome, thrombotic thrombocytopenic purpura, disseminated intravascular coagulation, transplant-associated thrombotic microangiopathy)
    - **Glomerular disease** - typically glomerulonephritis more so than nephrosis - membanoproliferative GN, SLE nephritis, anti-GBM disease, IgAN
- **Post-renal**: any obstruction preventing urine outflow resulting in intra-glomerular HTN
    - **Tubular obstruction** - cast nephropathy as in myeloma, crystalline nephropathy (indinavir, acyclovir)
    - **Mechanical blockade** - posterior urethral valves, vesico-ureteral reflux, bilateral obstructing calculi (e.g., struvite staghorn calculi), cancer in urinary system or metastatic to abdomen with ureteral blockade

**What Tests Are Helpful? Which Are Less Helpful, and in What Cases?**

- Chem 10 - gives BUN:Cr ratio (>15 suggestive of pre-renal), acid/base status, electrolytes
- CBC - screen for infections, may give clues to etiology (e.g., lymphopenia --> SLE, anemia and thrombocytopenia --> HUS/TMA)
- UA with microscopy
    - Muddy brown casts - think ATN
    - Eosinophils - think AIN
    - Hematuria with RBC casts - think GN
    - Heavy proteinuria (urine protein:Cr ratio >2) - think nephrotic syndrome
- C3/C4 if concerned regarding GN (e.g., SLE causes classically hypocomplementemic GN)
- CK to rule out rhabdomyolysis
- Renal ultrasound to rule out hydronephrosis (post-renal cause) or scarring (is AKI occurring in the background of occult CKD?)
- What about FeNa?
    - So-called “fraction of excreted sodium”
    - (UNa x PCr) / (PNa x UCr)
    - Normalizes % of sodium excreted by relative ratio of urine to plasma creatinine
    - Can be helpful in distinguishing between pre-renal and intrinsic renal injury, but **only if measured prior to fluid administration**

        - In the setting of pre-renal azotemia, kidneys will be maximally sodium-avid --> FeNa < 1%
        - In the setting of intrinsic renal damage, kidneys will not be able to conserve Na properly --> FeNa > 2%

**How do we Manage AKI?**

- Unfortunately there is no specific therapy to reverse or treat renal injury
- Therapy focuses on identifying and reversing any active precipitants of renal damage:
    - **Correct hypovolemia** if present and aim for goal net even to slightly positive (assuming patient's overall fluid status can tolerate). This may include **blood transfusions** to restore Hgb > 7.0.
    - **Correct causes of third spacing** (i.e., reverse causes of effective arterial blood volume depletion -- manage sepsis, give albumin for profound hypoalbuminemia, decrease afterload and/or increase inotropy for acute decompensated heart failure)
    - **Minimize dose and duration of nephrotoxic medications** when possible (common culprits: NSAIDs, vancomycin, zosyn, iodinated contrast, aminoglycosides, antivirals [acyclovir, ganciclovir, cidofovir, etc], calcineurin inhibitors, cytotoxic chemotherapy)
    - **Identify possible urinary obstruction** and relieve obstruction as indicated (e.g., urologic surgery, stent placement)
- At the same time, be aware of complications:
    - **Acidosis** - consider $NaHCO_3$ bolus; if refractory, dialyze
    - **Hyperkalemia** - if K >6.5 and EKG changes, give calcium gluconate. Temporize with albuterol and/or insulin/glucose. Get rid of total body K burden via diuresis (loop diuretics preferred), Kayexalate (via decanting feeds and/or orally), and/or dialysis if severe and refractory.
    - **Fluid overload** - provide respiratory support as necessary and diurese as tolerated; again, if refractory, dialyze
    - **Uremia** - give DDAVP for uremic bleeding, dialyze for complications (encephalopathy, bleeding, pericarditis)

**References for Additional Reading**

Ronco C, Bellomo R, Kellum JA. Acute Kidney Injury. *Lancet* 2019; 394: 1949–64.