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Acute Kidney Injury in Children

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Learning Objectives

- Formulate a differential diagnosis for causes of acute kidney injury (AKI) based on clinical and laboratory findings.

- Describe the initial management of AKI and recall the indications for renal replacement therapy.

*Figures for this presentation, unless otherwise noted, were created by Brian Stotter, MD, FAAP on behalf of the AAP Section on Nephrology (SONp) Executive Committee.

A 38-week gestational age male infant is delivered via C-section for fetal distress. He requires PPV, intubation, and chest compressions in the delivery room.

APGARs are 3, 6, and 7 at 1, 5, and 10 minutes respectively. After resuscitation he remains hypotensive and requires IV fluids, packed RBCs, and is started on dopamine.

Image courtesy of Rebekah Bretz.

On day of life 2 he becomes oliguric, edematous, and poorly responds to a trial of furosemide. His birth weight was 3.2 kg and his current weight is 3.7 kg. His length is 50.8 cm. Labs are notable for hyperkalemia with potassium 6.7 mmol/L, BUN 13 mg/dL, and creatinine 1.4 mg/dL.

How would you assess his current kidney function?

How would you manage this patient?

Image courtesy of Rebekah Bretz.

Definitions of AKI

- Abrupt loss of renal function that results in the kidneys' inability to maintain homeostasis
- Anuria – no urine production
- Oliguria – urine production less than 0.5 mL/kg/hr or less than 300 mL/m^2/day
- Non-oliguria – urine production greater than 0.5 mL/kg/hr

Comparison of AKI Criteria

Table 1
Acute kidney injury classification criteria

pRIFLE Criteria[7]			AKIN Criteria[9]			KDIGO Criteria[13]		
Stage	**SCr-Based**	**Urine Output**	**Stage**	**SCr-Based**	**Urine Output**	**Stage**	**SCr-Based**	**Urine Output**
Risk	>25% eCCl decrease	<0.5 mL/kg/h for 8 h	I	SCr increase ≥0.3 mg/dL OR 150%–200% in ≤48 h	<0.5 mL/kg/h for 8 h	I	SCr increase ≥0.3 mg/dL in 48 h OR 1.5–1.9 times	<0.5 mL/kg/h for 6–12 h
Injury	>50% eCCl decrease	<0.5 mL/kg/h for 16 h	II	SCr increase 200%–300%	<0.5 mL/kg/h for 16 h	II	SCr increase 2.0–2.9 times	<0.5 mL/kg/h for 12 h
Failure	>75% eCCl decrease OR eCCl <35 mL/min/1.73 m^2	<0.5 mL/kg/h for 24 h OR <0.3 mL/kg/h for 12 h	III	SCr increase 200%–300% OR SCr >4.0 mg/dL	<0.5 mL/kg/h for 24 h OR <0.3 mL/kg/h for 12 h	III	SCr ≥3.0 increase OR SCr > 4.0 mg/dL OR if <18 y of age then eCCl <35 mL/min/1.73 m^2	<0.5 mL/kg/h for 24 h OR <0.3 mL/kg/h for 12 h

Abbreviations: AKIN, Acute Kidney Injury Network; eCCl, estimated creatinine clearance; KDIGO, Kidney Disease Improving Global Outcomes; pRIFLE, pediatric version of the RIFLE criteria (Risk, Injury, Failure, and 2 outcome criteria, Loss and End-Stage Kidney Disease); SCr, serum creatinine.

Fortenberry JD, Paden ML, Goldstein SL. Acute kidney injury in children: an update on diagnosis and treatment. *Pediatr Clin North Am.* 2013;60(3):669–688.

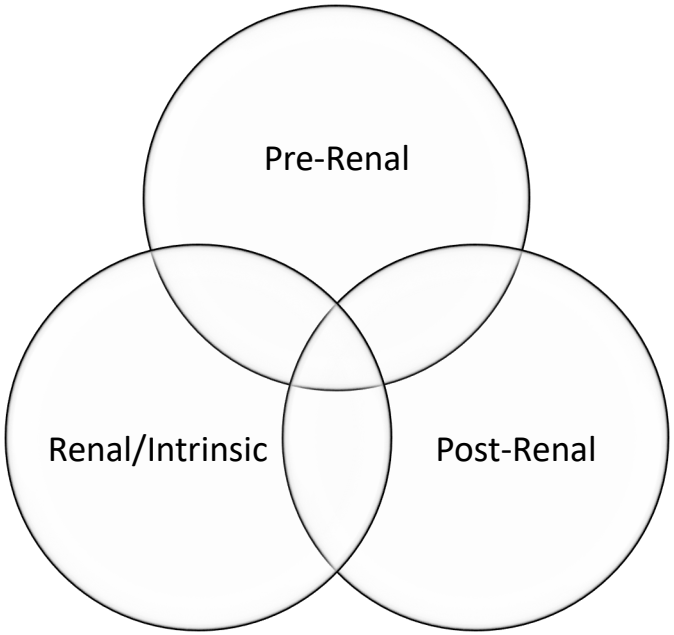
Who Gets AKI?

- Occurs in 0.39%–1% of all pediatric hospital admissions.
- 34.5% of admissions with AKI require ICU level care.
- Mortality rate 15.3% in all hospitalizations complicated by AKI, compared to 0.6% in non-AKI hospitalizations.
- Mortality rate 27.1% for children with AKI requiring renal replacement therapy, 32.8% for children requiring ICU-level care.
- Incidence of CKD (GFR <90 mL/min/1.73m^2) up to 6.5 years after AKI event approaches 28% (*BMC Nephrol.* 2014;15:184).

Who Gets AKI?

- The most common causes of AKI vary based on clinical setting.
  - Community – moderate/severe dehydration, glomerulonephritis, HUS
  - Hospital – sepsis, nephrotoxic medications, cardiac surgery, bone marrow or solid organ transplantation
    - 20%–40% of post-op cardiac patients develop some degree of AKI

Why Does AKI Occur?



- There can be overlap and multiple contributors for a single AKI event.
- What factors could have contributed to our newborn's AKI?

Pre-Renal

- Injury related to decreased renal perfusion
  - Hypovolemia (e.g. gastroenteritis, hemorrhage)
  - Hypotension (e.g. shock)
  - Hypoxia (e.g. birth asphyxia)
  - Hepatic failure/hepatorenal syndrome
  - Third spacing (e.g. hypoalbuminemia, nephrotic syndrome)
  - Cardiac dysfunction
  - Sepsis
  - Medications (e.g. NSAIDs)
  - Renovascular disease (e.g. thrombus)

Renal/Intrinsic

Glomerular	Vascular	Tubular/Interstitial
Post-infectious GN	TMA/HUS	ATN • Following pre-renal factors or nephrotoxic medications
IgA nephropathy	Vasculitis (HSP, IgA)	Interstitial nephritis • Drug allergy • Viral infection • Autoimmune • Pyelonephritis
SLE nephritis	Renal artery stenosis	
ANCA vasculitis		

Post-Renal

- Injury related to obstruction of urine flow
  - Congenital anomalies
    - PUV
    - UPJ and UVJ obstruction
  - Acquired
    - Stones
    - Tumors and masses

History/Physical Exam

- Is fluid overload present (big risk factor for mortality)?
- Is there hemodynamic instability (may suggest poor renal perfusion)?
- Any recent nephrotoxic medications or toxic exposures?
  - NSAIDs, aminoglycosides, chemotherapy
  - Contrast agents
- Is there a history of an abnormal voiding pattern?
- Any findings to suggest a systemic disease process?
  - Rash or joint pain (HSP, SLE nephritis, ANCA vasculitis)

Assessment

- Varies depending on clinical scenario and suspected cause(s)
- At a minimum
  - CBC, electrolytes, BUN, creatinine, calcium, phosphorus
  - Urinalysis with microscopy
    - Sediment may provide clues to etiology (e.g. RBC casts in glomerulonephritis, “muddy brown” casts in ATN)
- Urine indices (e.g. urine sodium) may help distinguish pre-renal AKI from ATN in oliguric patients
- Imaging
  - Renal/bladder ultrasound
  - CT/MRI as indicated

Fractional Excretion of Sodium

- Kidneys respond to low renal perfusion by increasing sodium reabsorption from the ultrafiltrate to restore volume.
- Fractional excretion of sodium (FE_{Na}) can be used to distinguish pre-renal AKI from ATN in **oliguric** AKI.
  - <1% in children or <3% in neonates/infants suggests pre-renal.
  - >1% in children or >3% in neonates/infants suggests ATN.

$$FE_{Na} = \frac{U_{Na} \times S_{Cr}}{U_{Cr} \times S_{Na}} \times 100\%$$

- FE_{Na} not valid if diuretics have been used (FE_{urea} can be used instead).

Practice

An 8-year-old boy has oliguric AKI from sepsis. His serum labs show sodium 126 mmol/L, potassium 5.8 mmol/L, chloride 102 mmol/L, bicarbonate 20 mmol/L, BUN 97 mg/dL, creatinine 3.5 mg/dL. His urine labs show a urine sodium 118 mmol/L, urine creatinine 41 mg/dL.

What is his FE_{Na}?

$$FE_{Na} = \frac{U_{Na} \times S_{Cr}}{U_{Cr} \times S_{Na}} \times 100\%$$

$$= \frac{(118)(3.5)}{(41)(126)} \times 100\%$$

$$FE_{Na} = 8.0\%$$

Management

- Treat or remove the underlying cause.
- Adjust current medication dosing based on estimated GFR (may be inaccurate in AKI).
  - Bedside Schwartz equation
    - eGFR (mL/min/1.73m^2) = 0.413 x height (cm)/S_{Cr}
- Optimize renal perfusion while minimizing fluid overload.

Management

- Electrolytes
  - Hyperkalemia
    - **Calcium gluconate** – stabilize cardiac membranes
    - No potassium-containing fluids
    - Cation exchange resin – sodium polystyrene sulfonate
    - Diuretics
    - For emergent hyperkalemia treatment, use albuterol or insulin + IV dextrose to promote intracellular K^+ shift
  - Hyperphosphatemia
    - Phosphate binders, especially if severe and associated with hypocalcemia (calcium carbonate)

Management

- Metabolic acidosis
  - Treat reversible causes and improve renal perfusion when possible (e.g. volume depletion, lactic acidosis).
  - May need renal replacement therapy for severe acidosis refractory to conservative management.
  - Caution: rapid correction of acidosis may lower ionized calcium and lead to symptomatic hypocalcemia.
- Hypertension
  - Diuretics often helpful for hypertension in AKI related to volume expansion and fluid overload.
  - Calcium channel blockers (e.g. amlodipine, isradipine) and beta blockers (e.g. labetalol) frequently used.
  - Avoid ACE inhibitors and ARBs, as these may worsen GFR.

Common Indications for Renal Replacement Therapy

- Fluid overload refractory to diuretics or associated with respiratory compromise
- Refractory hyperkalemia or metabolic acidosis
- Uremia (altered mental status, seizures, pericarditis, bleeding diathesis)
- AKI in the setting of a known dialyzable toxin (e.g. ethylene glycol)

Back to our patient…

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How would you assess his current kidney function?

How would you manage this patient?

Image courtesy of Rebekah Bretz.

How would you manage this patient?

- eGFR = 0.413 x height (cm)/S_{Cr} = (0.413 x 50.8)/1.4 = 15 mL/min/1.73m^2
- Adjust medication dosing to eGFR
- Avoid further nephrotoxic insults (medications, contrast)
- BSA is approx. 0.23 m^2, limit fluid to insensibles (300 mL/m^2/day = 69 mL/day) plus replacement for ongoing losses
- 24 hr fluid goal: net negative fluid balance (baby is above birth weight and edematous)
    - May consider an increased dose of furosemide or other diuretics
- For hyperkalemia, give calcium gluconate for cardioprotection (especially if EKG changes are present), remove potassium in IV fluids/TPN, consider sodium polystyrene sulfonate (cautious in neonates)

Image courtesy of Rebekah Bretz.

Further Reading

Fortenberry JD, Paden ML, Goldstein SL. Acute kidney injury in children: an update on diagnosis and treatment. *Pediatr Clin North Am.* 2013;60(3):669–688.

Goldstein SL and Zappitelli M. "Evaluation and Management of Acute Kidney Injury in Children." In *Pediatric Nephrology, 7th Edition.* Eds: Avner ED, Harmon WE, Niaudet P, Yoshikawa N, Emma F, and Goldstein SL. Heidelberg: Springer-Verlag Berlin Heidelberg, 2016.

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