

AKI Workup and Diagnostic Approach

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AKI Workup and Diagnostic Approach: Student Handout

Learning Objectives

By the end of this handout, you should be able to: - Classify AKI into prerenal, intrarenal, and postrenal causes - Interpret urine microscopy findings to differentiate AKI types - Perform systematic diagnostic evaluation of acute kidney injury - Recognize rapidly progressive glomerulonephritis and acute cortical necrosis as nephrologic emergencies - Apply the furosemide stress test for AKI risk stratification

Overview: What is Acute Kidney Injury?

Definition: Acute kidney injury represents a complex clinical syndrome with rapid deterioration in kidney function. Approximately 20% of hospitalized patients experience AKI, making it one of the most common serious complications in hospital medicine.

Key Concept: AKI exists on a spectrum with chronic kidney disease (CKD). The traditional distinction has evolved; we now recognize an intermediate category called “acute kidney disease” that bridges the acute-to-chronic transition, occurring between 7-90 days after initial injury.

Clinical Pearl: Many patients present with “acute-on-chronic” kidney disease (AKI superimposed on existing CKD), representing a particularly high-risk population requiring specialized management approaches.

The Diagnostic Framework: Three Categories

PRERENAL AKI (Reduced Kidney Perfusion)

Mechanism: Decreased blood flow to kidneys triggers activation of the renin-angiotensin-aldosterone system. The kidney attempts to preserve function through sodium and water retention.

Common causes: - Gastrointestinal losses (vomiting, diarrhea) - Hemorrhage or dehydration - Sepsis with distributive shock - Heart failure (reduced cardiac output) - Medications that alter renal hemodynamics (NSAIDs, ACE inhibitors in certain settings)

Key Laboratory Findings: | Test | Finding | Significance | |---|----|-----| | Fractional Excretion of Sodium (FENa) | <1% | Intact tubular sodium reabsorption | | Urine specific gravity | >1.020 | Concentrated urine | | Urine osmolality | >500 mOsm/kg | Preserved concentrating ability | | BUN:Creatinine ratio | >20:1 | Preferential urea reabsorption |

Urine Microscopy: Minimal abnormalities. May see occasional hyaline casts (composed of Tamm-Horsfall protein) indicating preserved tubular function. Absence of significant cellular elements supports functional rather than structural injury.

Important Caveat: FENa interpretation requires caution: - Only valid in oliguric patients (urine output <400 mL/day) - Recent diuretic use falsely elevates FENa despite prerenal physiology - Consider fractional excretion of urea instead if diuretics recently given

Clinical Pearl: Hyaline casts in concentrated urine from an oliguric patient represent a strong indicator of prerenal azotemia.

INTRARENAL AKI (Primary Kidney Damage)

Intrarenal AKI encompasses multiple distinct pathologic processes affecting different kidney compartments: glomeruli, tubules, and interstitium.

Acute Tubular Necrosis (ATN) Mechanisms:

1. **Ischemic ATN** (most common, ~50% of hospitalized AKI)
 - Results from prolonged hypotension or severe volume depletion
 - Damages tubular epithelial cell membrane
 - Causes tubular obstruction from cellular debris
 - Creates tubular leak of filtered glomerular filtrate
2. **Nephrotoxic ATN** (endogenous toxins)
 - **Hemoglobin-induced:** Massive intravascular hemolysis
 - **Myoglobin-induced:** Rhabdomyolysis (muscle breakdown)
 - **Light chains:** Plasma cell disorders (multiple myeloma)

Key Laboratory Findings: | Test | Finding | Significance | |---|----|-----| | Fractional Excretion of Sodium | >2% | Loss of tubular reabsorption | | Urine specific gravity | <1.015 | Loss of concentrating ability | | Urine osmolality | ~300 mOsm/kg | Isoosmotic with plasma |

Urine Microscopy—Diagnostic Features: - **Muddy brown granular casts** (pathognomonic) — result from tubular debris - Renal tubular epithelial cells (RTECs) and RTEC casts - Absence of RBC casts (which would suggest glomerular disease)

Clinical Pearl: “Muddy brown” casts represent the hallmark finding and should prompt recognition of ATN.

Rapidly Progressive Glomerulonephritis (RPGN) Clinical Urgency: This is a NEPHROLOGIC EMERGENCY requiring rapid diagnosis and treatment to preserve kidney function.

Pathophysiology: Severe glomerular injury causes crescent formation (proliferating cells in Bowman’s space), destroying filtration capacity within days.

Key Findings: - Rapidly rising creatinine (often doubling within days to weeks) - Active urinary sediment: RBCs, dysmorphic RBCs, RBC casts, proteinuria - May present with systemic symptoms (hemoptysis, arthralgia, rash)

Urine Microscopy: Shows numerous RBCs, RBC casts, and WBCs indicating active glomerular bleeding.

Classification (by immunofluorescence pattern): 1. **Anti-GBM disease** (linear IgG) — Goodpasture syndrome 2. **Immune complex RPGN** (granular staining) — lupus, post-infectious 3. **ANCA-associated vasculitis** (pauci-immune) — MPO-ANCA or PR3-ANCA

Diagnostic Evaluation: - ANCA panel (MPO, PR3 antibodies) - Anti-GBM antibodies - Complement levels (C3, C4) - Kidney biopsy for definitive diagnosis

Critical Point: Combination of rapidly rising creatinine + active sediment with RBC casts = emergency requiring immediate nephrology referral and biopsy within 24-48 hours.

Acute Interstitial Nephritis (AIN) Mechanism: Immune-mediated inflammatory response affecting the tubulointerstitium, most commonly from medications.

Common causative agents: - Antibiotics (amoxicillin, ciprofloxacin) — most common - Proton pump inhibitors (omeprazole) - NSAIDs - Diuretics - Allopurinol

Clinical Presentation: - May include fever, rash, eosinophilia (but absent in ~2/3 of cases) - AKI typically develops days to weeks after drug initiation - Usually nonoliguric (maintenance of urine output despite rising creatinine)

Urine Findings: - Mild proteinuria (usually <1 g/day) - Elevated WBCs (>5 cells/hpf, often 13-138 cells/ μ L) - White blood cell casts (supportive but not diagnostic) - **Note:** Urine eosinophils lack diagnostic utility (poor sensitivity/specificity)

Definitive Diagnosis: Kidney biopsy showing lymphoplasmacytic infiltration of interstitium with sparing of glomeruli.

Treatment: Early discontinuation of offending agent + corticosteroids (if started within 2-3 weeks, better outcomes).

Clinical Pearl: Classic triad of fever, rash, eosinophilia occurs in <10% of drug-induced AIN cases.

Light Chain Nephropathy Association: Multiple myeloma or other plasma cell disorders.

Mechanism: Overproduction of monoclonal light chains causes tubular obstruction and direct toxic injury.

Key Features: - AKI in setting of myeloma (confirmed by serum/urine protein electrophoresis) - Urine shows characteristic large, fractured casts with angular edges - Diagnosis requires kidney biopsy for pathologic confirmation

Urine Microscopy: Look for characteristic large casts with angular fracture patterns.

POSTRENAL AKI (Urinary Obstruction)

Mechanism: Mechanical blockade of urine flow at any level from renal pelvis to urethral meatus.

Common causes: - Nephrolithiasis (kidney stones) - Malignancy with urinary tract compression - Benign prostatic hyperplasia (in males) - Blood clots or papillary necrosis - Retroperitoneal fibrosis

Clinical Features: - Colicky flank pain (with stones) or silent obstruction - May have oliguria, anuria, or paradoxical polyuria (with partial obstruction) - Suprapubic distention or flank mass on examination

Diagnostic Approach: 1. **First-line:** Renal ultrasound (no radiation, rapid assessment for hydronephrosis) 2. **Important caveat:** Early obstruction (<24 hours) may show minimal dilatation on ultrasound 3. **Definitive:** CT scan without contrast for precise obstruction location (especially stone detection) 4. **Alternative:** MR urography for soft tissue evaluation (pregnant patients, retroperitoneal masses)

Urine Microscopy: Usually minimal abnormalities in pure obstruction; may show crystals, RBCs (stone trauma), or WBCs (concurrent infection).

Clinical Pearl: Retroperitoneal fibrosis can cause functional obstruction without classical hydronephrosis pattern on imaging.

Special Emergency Situations

Anuria (Urine Output <100 mL/24 hours)

Clinical Significance: Nephrologic emergency requiring immediate evaluation and intervention.

Differential Diagnosis Includes: - Bilateral renal artery stenosis/occlusion (consider in patients with severe atherosclerosis) - Bilateral renal vein thrombosis (nephrotic syndrome, severe dehydration) - Complete bilateral urinary obstruction (emergency decompression needed) - Acute cortical necrosis (ominous sign, poor prognosis)

Immediate Management: 1. Bladder catheterization to rule out lower urinary tract obstruction 2. Urgent imaging (renal US, CT angiography as indicated) 3. Emergency nephrology consultation 4. Prepare for possible emergent intervention or dialysis

Acute Cortical Necrosis

Severity: Most severe form of AKI; necrosis of renal cortex with medullary sparing.

Triggers: - Severe prolonged hypotension - Septic shock - Obstetric catastrophes (placental abruption, postpartum hemorrhage) - Severe dehydration in infants

Clinical Recognition: - Anuria or severe oliguria with gross hematuria - Flank pain - Chronic phase: characteristic “rim-like” calcification on imaging

Prognosis: Poor; most patients require chronic dialysis.

Special Topic: Contrast-Associated Acute Kidney Injury

Paradigm Shift: “Contrast-induced nephropathy” has been renamed “contrast-associated AKI” (CA-AKI) to reflect the understanding that multiple factors—not contrast alone—contribute to injury.

Risk Factors: - Chronic kidney disease - Diabetes mellitus - Volume depletion - Heart failure - Concurrent nephrotoxin exposure

Presentation: Non-oliguric ATN developing 24-72 hours post-contrast, with peak elevation 3-5 days.

Prevention Strategies: - **Most important:** Adequate hydration with isotonic crystalloid - Minimize contrast volume - Use iso-osmolar or low-osmolar agents - Avoid concurrent nephrotoxins when possible - N-acetylcysteine prophylaxis: controversial, minimal benefit in recent studies

The Furosemide Stress Test: A Functional Assessment Tool

Purpose: Predicts AKI progression and guides clinical decision-making by evaluating tubular function.

Principle: Furosemide requires active tubular secretion (not glomerular filtration) to work; response reflects tubular integrity.

Standardized Protocol: 1. Confirm adequate resuscitation (volume replete) before testing 2. Administer 1.0 mg/kg IV furosemide (loop diuretic-naive patients) 3. OR 1.5 mg/kg if prior furosemide exposure within 7 days 4. Measure urine output hourly for 2-6 hours 5. Interpret based on 2-hour urine volume

Clinical Interpretation: - **FST-responsive** (>200 mL in 2 hours): Low risk of progression; only 13.6% require RRT - **FST-nonresponsive** (<200 mL in 2 hours): High risk; 75-98% require renal replacement therapy

Diagnostic Performance: - Sensitivity: 81% for AKI progression prediction - Specificity: 88% for AKI progression prediction - Predicts: progression to Stage 3 AKI, need for RRT, and inpatient mortality

Clinical Application: Can identify patients with severe intrinsic renal failure in whom urine output becomes an unreliable perfusion marker, helping avoid futile fluid resuscitation.

Systematic Diagnostic Approach to AKI

Step 1: Clinical Assessment

- **Volume status:** Euvolemia? Dehydration? Edema/fluid overload?
- **Hemodynamics:** BP, orthostatics, perfusion signs
- **Recent medications:** NSAIDs, ACE inhibitors, diuretics, nephrotoxic drugs
- **Relevant history:** Prior renal disease? Diabetes? Systemic illness?

Step 2: Laboratory Evaluation (First-Tier)

- Complete metabolic panel (electrolytes, creatinine, BUN, calcium, phosphorus)
- Urinalysis (specific gravity, proteinuria, hematuria, WBCs)
- Urine microscopy (CRITICAL for differentiation)
- Complete blood count

Step 3: Urinalysis Interpretation

Matches the clinical context with microscopy findings to narrow differential: | Microscopy Pattern | Most Likely Diagnosis | Key Finding | |—|—|—| | Hyaline casts, no cells | Prerenal AKI | Preserved tubular function | | Muddy brown casts, RTECs | Acute tubular necrosis | Tubular damage | | RBC casts, dysmorphic RBCs | RPGN or GN | Glomerular bleeding | | WBC casts, WBCs | Acute interstitial nephritis | Tubulointerstitial inflammation | | Large fractured casts | Light chain disease | Associated with myeloma |

Step 4: Calculate Fractional Excretion (if appropriate)

FENa = (Urine Na × Plasma Cr) / (Plasma Na × Urine Cr) - FENa <1% suggests prerenal physiology - FENa >2% suggests intrinsic renal disease - Consider FEUrea if diuretics given

Step 5: Imaging (if indicated)

- **Renal ultrasound:** First-line for obstructive symptoms
- **CT without contrast:** For stone, obstruction detail
- **MR urography:** Soft tissue, pregnant patients

Step 6: Additional Tests Based on Clinical Context

- Urine and serum protein electrophoresis (light chain disease)
- ANCA/anti-GBM (RPGN)
- Complement levels (post-infectious GN)
- Creatine kinase (rhabdomyolysis)

Practice Questions

Question 1: A 65-year-old with CKD Stage 3b presents with AKI. Urinalysis shows muddy brown granular casts and renal tubular epithelial cells. BUN:Cr ratio is 15:1. FENa is 3.2%. What is the most likely diagnosis? A) Prerenal AKI B) Acute tubular necrosis C) Acute interstitial nephritis D) Rapidly progressive glomerulonephritis

Answer: B) Acute tubular necrosis. The muddy brown granular casts are pathognomonic for ATN, indicating tubular epithelial cell breakdown. The elevated FENa (>2%) confirms loss of tubular sodium reabsorption. While the lower BUN:Cr ratio initially suggests ATN (not prerenal), the casts are diagnostic.

Question 2: A 28-year-old presents with hemoptysis, arthralgia, hematuria, and rapidly rising creatinine (baseline 0.9, now 2.1 in 3 days). Urinalysis shows proteinuria and RBC casts. What is the most appropriate immediate next step? A) Start prednisone 1 mg/kg B) Urgent nephrology referral for kidney biopsy C) Ultrasound to rule out obstruction D) Measure FENa to assess tubular function

Answer: B) Urgent nephrology referral for kidney biopsy. The constellation of rapidly progressive AKI with active urinary sediment (RBC casts) and systemic symptoms (hemoptysis, arthralgia) suggests rapidly progressive glomerulonephritis—a nephrologic emergency. Biopsy is essential for diagnosis and guides immunosuppressive therapy. Delays >48 hours risk permanent kidney loss.

Question 3: A 58-year-old with hypertension and diabetes develops AKI after starting an ACE inhibitor for proteinuria. Urinalysis is bland; urinary specific gravity is 1.003. Which additional finding would most strongly suggest prerenal AKI rather than drug-induced interstitial nephritis? A) FENa of 0.6% B) Urine WBC casts C) Fever and rash D) Recent NSAID use

Answer: A) FENa of 0.6%. While the bland urinalysis and very dilute urine (low specific gravity) suggest prerenal physiology, an FENa <1% would be diagnostic for prerenal AKI. In this case, the ACE inhibitor likely worsened renal perfusion in a patient with underlying renovascular disease or advanced CKD. Options B and C would support AIN; option D compounds the problem but doesn't diagnose the mechanism.

Key Takeaways

1. **Classify first:** Prerenal, intrarenal, or postrenal—this shapes management
 2. **Urine microscopy is essential:** It's your primary diagnostic tool
 3. **RPGN is an emergency:** Rapidly rising creatinine + RBC casts = biopsy urgently
 4. **FENa has limitations:** Valid only in oliguria; interpret with clinical context
 5. **The furosemide stress test** helps predict progression and guides RRT timing
 6. **AKI and CKD overlap:** Consider acute-on-chronic disease patterns
 7. **Medications matter:** NSAIDs, ACE inhibitors, and antibiotics are common culprits
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See Also

Related Student Handouts

- AKI Biomarkers and Early Detection
- ATN Management
- Drug-Induced AKI
- Rhabdomyolysis
- Acute Interstitial Nephritis

Clinical Content (01-Clinical-Medicine/Nephrology)

- AKI Hub - Full Clinical Reference

- Kidney Biopsy Guide
- Essential Renal Laboratory Tests
- Acid-Base Disorders in AKI

Atomic Notes (ZK)

- CRRT Principles
- Cell Cycle Arrest Biomarkers in AKI
- Cardiorenal Syndrome

Butler-COM Resources

- Butler COM - Nephrology Deep Dive
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Related Clinical Notes

- Full AKI Workup Reference
 - Hyponatremia Management
 - Cardiorenal Syndrome
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