Acute Kidney Injury

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Background

- **Acute kidney injury (AKI)** is a clinical syndrome generally defined by a sudden reduction in kidney functions as evidenced by changes in laboratory values, serum creatinine (Scr), blood urea nitrogen (BUN), and urine output.

- **The Kidney Disease: Improving Global Outcomes (KDIGO) Clinical Practice Guidelines** were developed to provide one standardized definition of AKI

Background

- **KDIGO** defines **AKI** as being present if any of the following criteria is met:

1. **Increase in S_{cr} by at least 0.3 mg/dL (27 µmol/L) within 48 hours.**
2. **Increase in S_{cr} by at least 1.5 times baseline within the prior 7 days.**
3. **Decrease in urine volume to less than 0.5 mL/kg/h for 6 hours.**

Pathophysiology

- AKI can be categorized as:
- **Prerenal:** resulting from decreased renal perfusion in the setting of undamaged parenchymal tissue.
- **Intrinsic:** resulting from structural damage to the kidney, most commonly the tubule from an ischemic or toxic insult.
- **Postrenal:** resulting from obstruction of urine flow downstream from the kidney.

Prerenal - AKI

i. **Volume depletion:** hemorrhage, GI losses, renal losses (diuresis or diabetes insipidus), and skin losses (burns).

ii. **Decreased effective circulatory blood volume:** decreased cardiac output, pulmonary hypertension, hypotension, sepsis, liver failure.

iii. **Drugs:** NSAIDs, ACEIs, ARBs

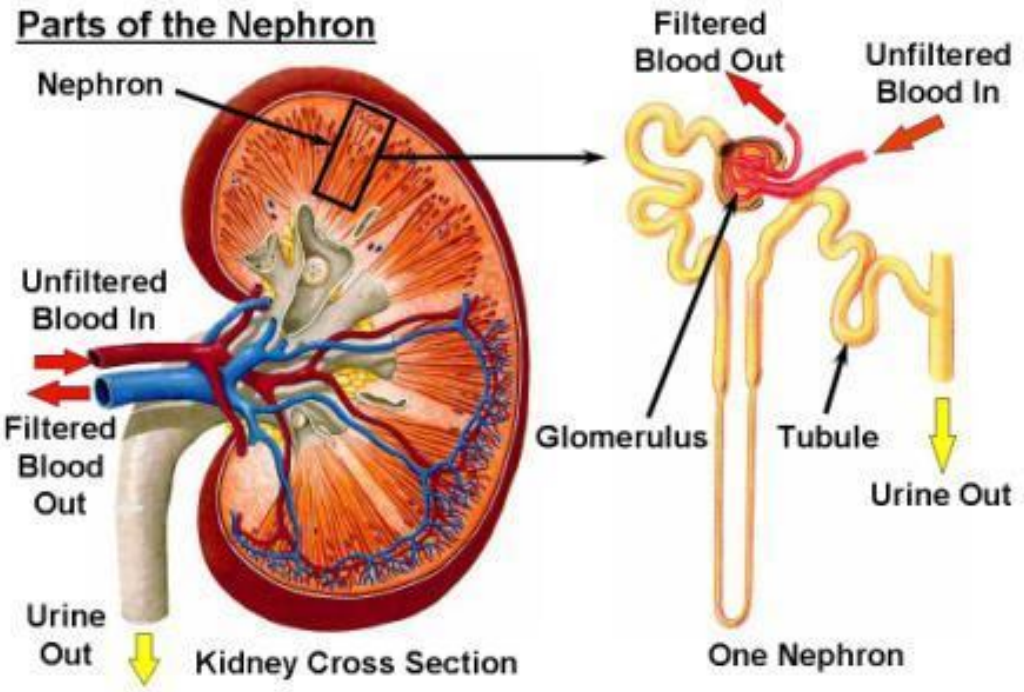
Intrinsic - AKI

i. **Vascular damage:** renal artery/vein thrombosis.

ii. **Glomerular damage:** Nephrotic glomerulopathies, autoimmune diseases.

iii. **Acute tubular necrosis:** Ischemic, hypotension, sepsis, nephrotoxic drugs, contrast dyes.

iv. **Acute interstitial nephritis:** NSAIDs, certain antibiotics, Infection.

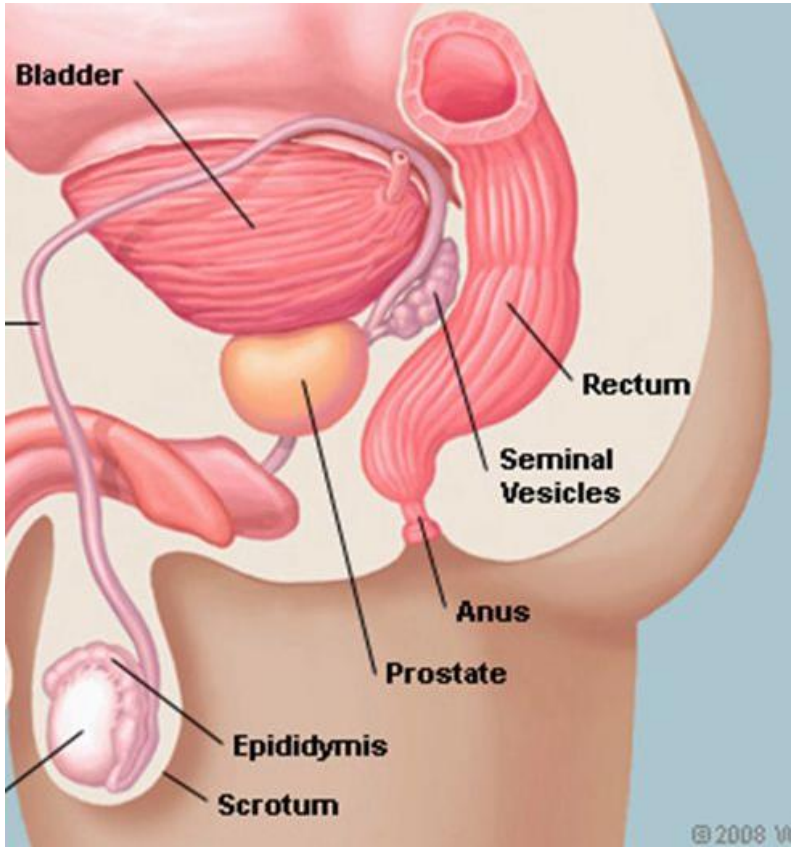


Postrenal - AKI

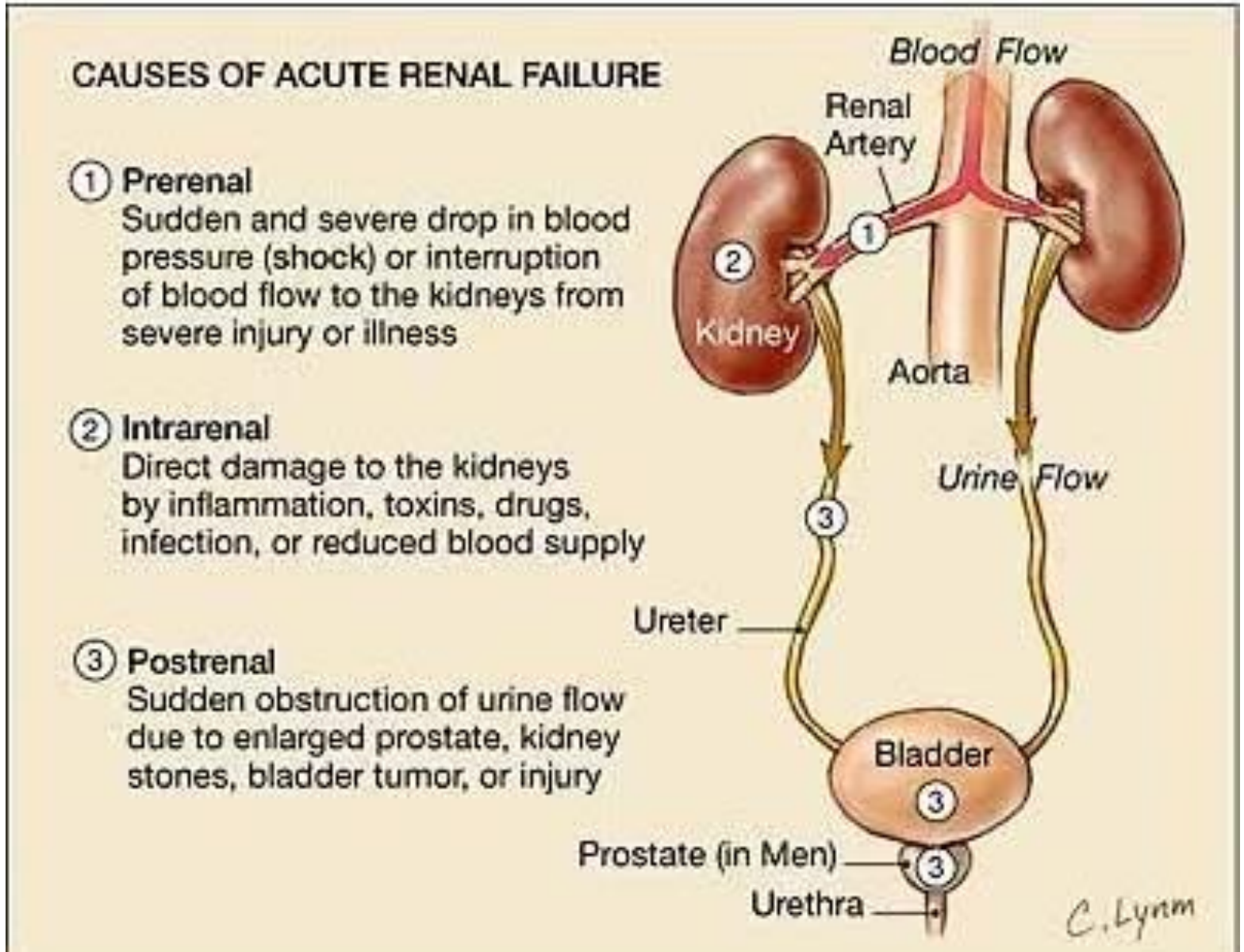
iv. **Bladder outlet obstruction:** benign prostatic hyperplasia, malignancy, anticholinergic drugs, displaced bladder catheter.

v. **Ureteral obstruction:** malignancy, nephrolithiasis.

vi. **Tubular obstruction:** nephrolithiasis, drugs



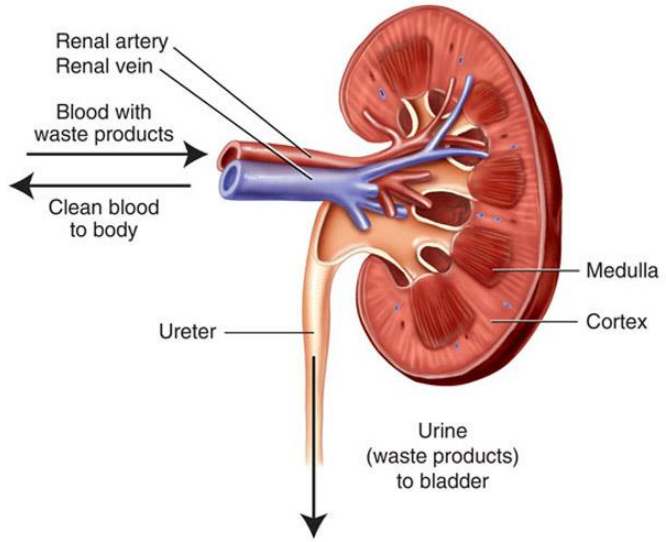
Acute renal failure



Clinical Presentation

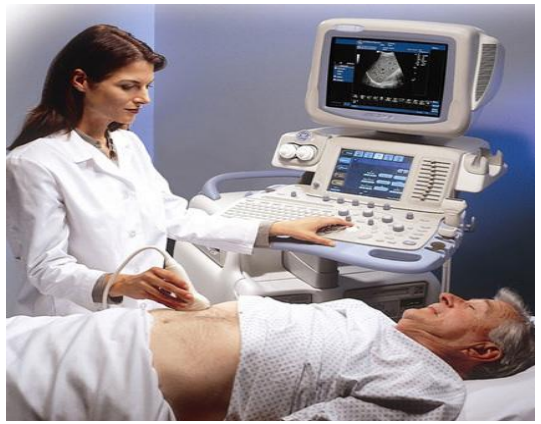
- Patient presentation varies widely and depends on the underlying cause.

- Signs and symptoms may include
  - **acute change in urinary habits**
  - **weight gain**
  - **flank pain**
  - **edema**
  - **colored or foamy urine**
  - **in volume depleted patients, orthostatic hypotension**



Diagnosis

- We do need:
  - Medical and medication histories
  - Physical examination
  - Assessment of laboratory values
  - Imaging studies sometimes may be important in the diagnosis of AKI



Diagnosis

- **Scr** cannot be used **alone to diagnose AKI** because it is **insensitive to rapid changes in glomerular filtration rate (GFR)** and therefore may not reflect current renal function.

- The use of **BUN** in AKI is very limited because **urea's production** and **renal clearance** are heavily influenced by **extrarenal factors** such as
  - **critical illness**
  - **volume status**
  - **protein intake**
  - **medications**

Diagnosis

- **Urine output measured** over a specified period of time allows for short-term assessment of kidney function, but its utility is limited to cases in which it is significantly decreased.

Diagnosis

- Calculation of the **fractional excretion of sodium (FE_{Na})** can help determine the **etiology of AKI**.

$$FE_{Na} = (U_{Na} \times S_{Cr} \times 100)/(U_{Cr} \times S_{Na})$$

U_{Na} = urine sodium

S_{Cr} = serum creatinine

U_{Cr} = urine creatinine

S_{Na} = serum sodium.

Diagnostic Parameters for Differentiating Causes of AKI

Laboratory Test	Prerenal AKI	Intrinsic AKI	Postrenal AKI
Urine sediment	Hyaline casts, may be normal	Granular casts, cellular debris	Cellular debris
Urinary RBC	None	2–4+	Variable
Urinary WBC	None	2–4+	1+
Urine Na (mEq/L or mmol/L)	<20	>40	>40
FE_{Na} (%)			Variable
Urine/serum osmolality			<1.5
Urine/S_{cr}			<20:1
Urine specific gravity	>1.018	<1.012	Variable

$$\text{Specific gravity} = \frac{\text{Weight of substance}}{\text{Weight of equal volume of water}}$$

Prevention

- **Goals of Prevention:** The goals are
  - to screen and identify patients at risk
  - monitor high-risk patients
  - implement prevention strategies when appropriate

General approach to prevention

Nonpharmacologic Therapies

- **Hydration** is routinely used to prevent contrast-induced nephropathy, a common cause of acute tubular necrosis in the inpatient setting.

- **KDIGO** guidelines recommend either **sodium bicarbonate** or **normal saline infusions**.

General approach to prevention

Nonpharmacologic Therapies

- **Sodium bicarbonate** regimen is
  - before the procedure
    - 154 mEq/L (154 mmol/L) infused at 3 mL/kg/h for 1 hour.
  - after the procedure
    - at 1 mL/kg/h for 6 hours.

- **Normal saline** regimen is 1 mL/kg/h for 12 hours pre- and post procedure.

General approach to prevention

Pharmacological Therapies

- **Ascorbic acid** (3 g orally pre- and 2 g orally twice daily for two doses post-procedure).

- **N-acetylcysteine** (600–1200 mg orally every 12 hours for 2–3 days [first two doses pre-contrast]) are antioxidant options for prevention of contrast-induced nephropathy.

Treatment of Acute Kidney Injury

- Goals of Treatment:
  - **minimizing the degree of insult to the kidney**
  - **reducing extra-renal complications**
  - **accelerating recovery of renal function**
  - **restoration of renal function to pre-AKI baseline which is the ultimate goal**

General approach to treatment

- Currently, there is no definitive therapy for AKI.
- **Supportive care** is the mainstay of AKI management regardless of etiology.

Nonpharmacologic Therapies

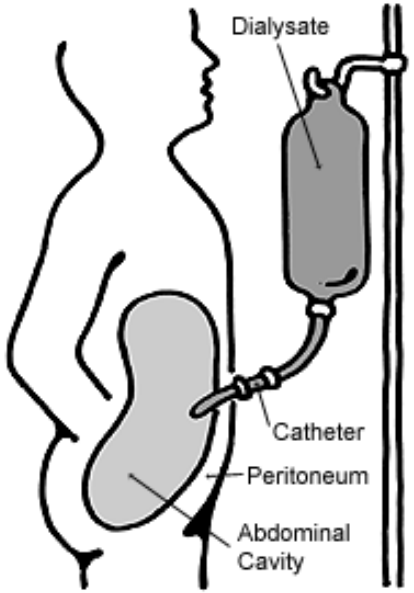
- **Supportive care** goals include maintenance of adequate **cardiac output** and **blood pressure** to optimize tissue perfusion while restoring renal function to pre-AKI baseline.

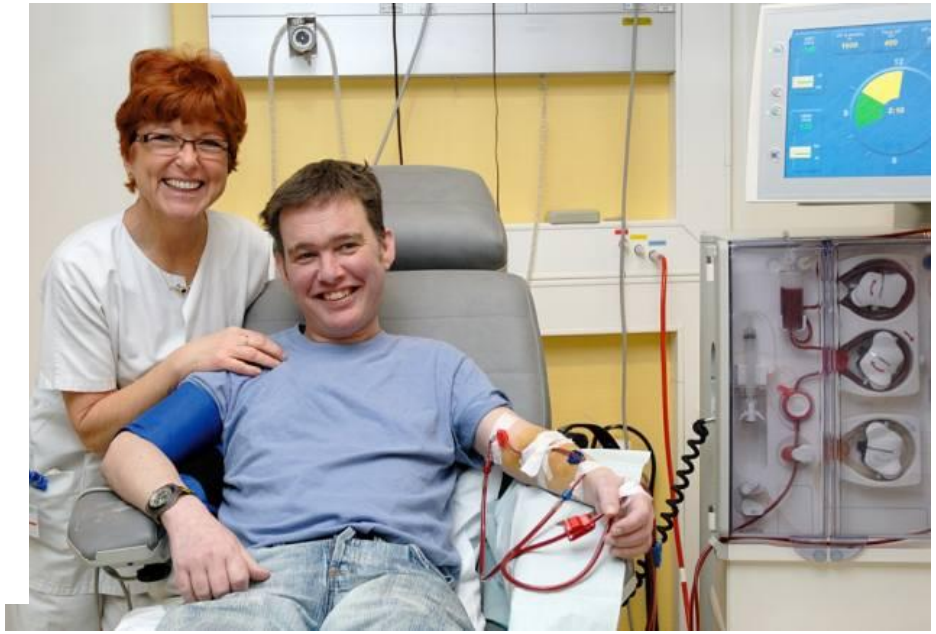
- Discontinue medications associated with diminished renal blood flow.

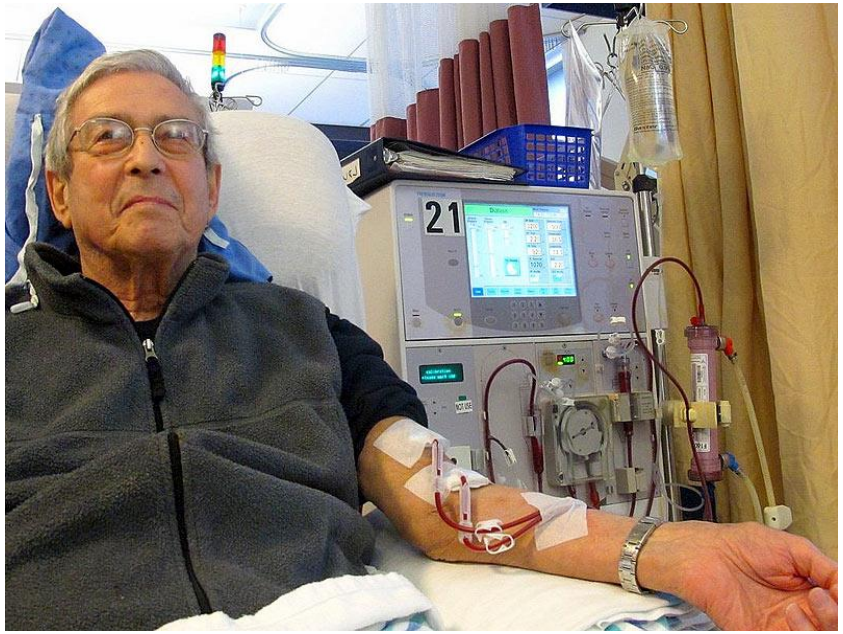
- Initiate appropriate fluid and electrolyte management. Avoid use of nephrotoxins.

Nonpharmacologic Therapies

- In severe AKI, **renal replacement therapy**, such as **hemodialysis** and **peritoneal dialysis**, maintains fluid and electrolyte balance while removing waste products.







Nonpharmacologic Therapies

Common Indications for Renal Replacement Therapy

Indication	Clinical Setting
Acid–base abnormalities	Metabolic acidosis resulting from the accumulation of organic and inorganic acids
Electrolyte imbalance	Hyperkalemia, hypermagnesemia
Intoxications	Salicylates, lithium, methanol, ethylene glycol, theophylline, phenobarbital
Overload of fluid	Postoperative fluid gain/overload
Uremia	Accumulation of uremic toxins

Pharmacologic Therapies

- Mannitol in AKI:
  - **increases renal blood flow**
  - **maintains filtration fraction**
  - **maintains oxygenation**

- Mannitol 20% is typically started at a dose of **12.5 to 25 g IV over 3 to 5 minutes**.

Pharmacologic Therapies

Disadvantages include IV administration

- hyperosmolality risk
- need monitoring for
  - urine output
  - serum electrolytes
  - serum osmolality

Because Mannitol can contribute to AKI.

Pharmacologic Therapies

- **Loop diuretics** effectively reduce **fluid overload** but can worsen AKI.
- Equipotent doses of loop diuretics (**furosemide**, **bumetanide**, **torsemide**) have similar efficacy.
- **Continuous infusions** of loop diuretics appear to
  - overcome **diuretic resistance**
  - to have **fewer adverse** effects than intermittent boluses

Pharmacologic Therapies

- Dose of loop diuretics come into two steps:

1. **IV loading dose** of **furosemide 40–80 mg**
2. **continuous infusion** of **furosemide 10–20 mg/h**

Pharmacologic Therapies

- Strategies are available to **overcome diuretic resistance**.
- **Administration of agents from different classes** may be synergistic when combined with loop diuretics such as diuretics that work at
  - the **distal convoluted tubule** (thiazides)
  - the **collecting duct** (amiloride, triamterene, and spironolactone)
- **Metolazone** is unlike other thiazides, it produces effective diuresis at **GFR less than 20 mL/min**.

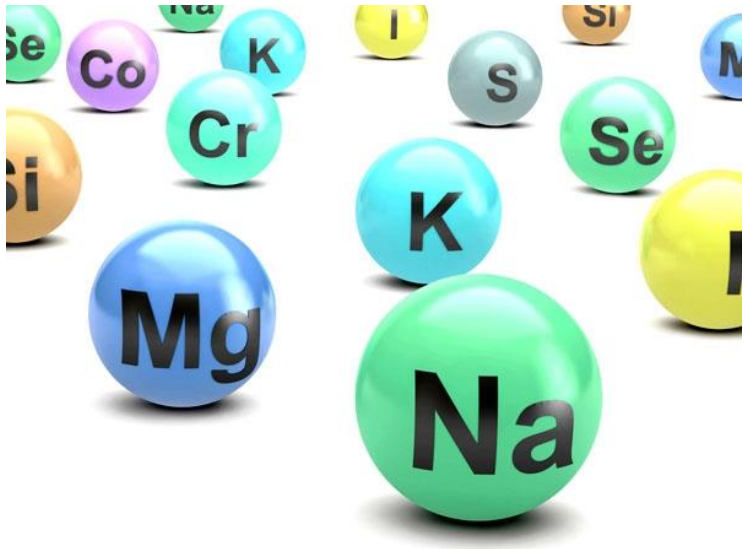
Causes of Diuretic Resistance	Potential Therapeutic Solutions
Excessive sodium intake (sources may be dietary, IV fluids, and drugs)	Remove sodium from nutritional sources and medications
Inadequate diuretic dose or inappropriate regimen	Increase dose, use continuous infusion or combination therapy
Reduced oral bioavailability (usually furosemide)	Use parenteral therapy; switch to oral torsemide or bumetanide
Nephrotic syndrome (loop diuretic protein binding in tubule lumen)	Increase dose, switch diuretics, use combination therapy
Reduced renal blood flow	
Drugs (NSAIDs, ACEIs, vasodilators)	Discontinue these drugs if possible
Hypotension	Intravascular volume expansion and/or vasopressors
Intravascular depletion	Intravascular volume expansion
Increased sodium resorption	
Nephron adaptation to chronic diuretic therapy	Combination diuretic therapy, sodium restriction
NSAID use	Discontinue NSAID
Heart failure	Treat the heart failure, increase diuretic dose, switch to better-absorbed loop diuretic
Cirrhosis	High-volume paracentesis
Acute tubular necrosis	Higher dose of diuretic, diuretic combination therapy; add low-dose dopamine

Electrolyte management

- **Serum electrolytes** should be **monitored daily**.
- **Hyperkalemia** is the most common and serious electrolyte abnormality in AKI.
- **Hypernatremia** and **fluid retention** commonly occur, requiring
  - **calculation of daily sodium intake**, including sodium contained in commonly administered antibiotic and antifungal agents.

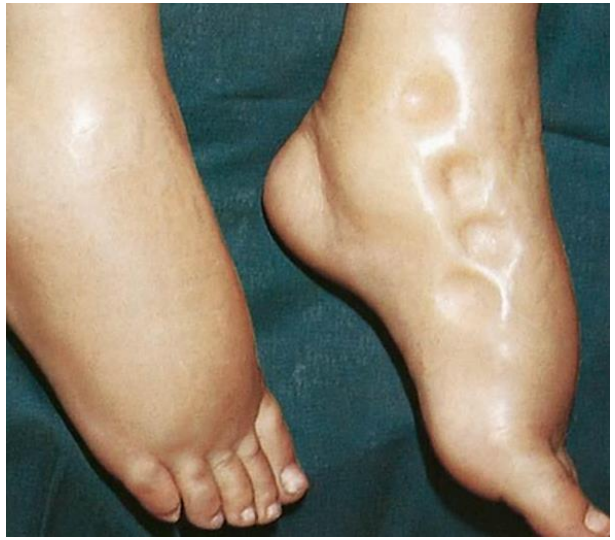
Electrolyte management

- **Phosphorus** and **magnesium** should be monitored, especially in patients with significant tissue destruction due to increased amounts of released phosphorus; **neither is efficiently removed by dialysis**.



Drug-Dosing considerations

- Drug therapy optimization in AKI is a **challenge**.



- Confounding variables include
  - **drug clearance**
  - **fluid accumulation**
  - **use of renal replacement therapy**

- **Volume of distribution** for water-soluble drugs is significantly increased due to edema.

Evaluation of therapeutic outcomes

- **General monitoring** of patient status is essential.

- **Therapeutic drug monitoring** should be done frequently because of
  - **changing volume status**
  - **changing renal function**
  - **renal replacement therapy**

TABLE 73–6 Key Monitoring Parameters for Patients With Established Acute Kidney Injury

Parameter	Frequency
Fluid ins/outs	Every shift
Patient weight	Daily
Hemodynamics (blood pressure, heart rate, mean arterial pressure, etc)	Every shift
Blood chemistries	
Sodium, potassium, chloride, bicarbonate, calcium, phosphate, magnesium	Daily
Blood urea nitrogen/serum creatinine	Daily
Drugs and their dosing regimens	Daily
Nutritional regimen	Daily
Blood glucose	Daily (minimum)
Serum concentration data for drugs	After regimen changes and after renal replacement therapy has been instituted
Times of administered doses	Daily
Doses relative to administration of renal replacement therapy	Daily
Urinalysis	
Calculate measured creatinine clearance	Every time measured urine collection performed
Calculate fractional excretion of sodium	Every time measured urine collection performed
Plans for renal replacement	Daily

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