Acute Kidney Injury (AKI)

- Acute renal failure (ARF) is an abrupt reduction (usually within a 48-h period) in kidney function (glomerular filtration rate (GFR) or creatinine clearance (CrCl)).
- This results in an accumulation of nitrogenous waste products and other toxins.
- Many patients become oliguric (low urine output) with subsequent salt and water retention.
- ARF has been replaced by acute kidney injury (AKI) to emphasize that the disorder exists along a wide continuum, ranging from mild renal dysfunction to the need for renal replacement therapies (RRTs), such as hemodialysis and peritoneal dialysis.

The clinical course of AKI:

AKI has three distinct phases

• Oliguric Phase: a progressive decrease in urine production after kidney injury

• Diuretic Phase: initial repair of the kidney insult with resultant diuresis of accumulate duremic toxins, waste products, and fluid

• Recovery Phase: return of kidney function depending on the severity of injury

Classification and causes

AKI can be categorized as

1-Pre-renal: resulting from decreased renal perfusion in the setting of undamaged parenchymal tissue.It is usually a consequence of

- Decreased intravascular volumes (hypovolemia) Examples of this include diarrhea and vomiting, burns and excessive use of diuretics. and/or
- decreased intravascular pressures(hypotension)

2- Intrinsic: resulting from structural damage to the kidney tubule from an ischemic or toxic insult.

- acute tubular necrosis (ATN) most commonly (in >80% of cases)
- Immune and inflammatory renal diseasethese are divided into glomerular causes (glomerulonephritis) and interstitial causes (interstitial nephritis). Rarely, acute pyelonephritis, which is an infection of renal parenchyma, usually as a consequence of ascending infection, can cause AKI.

3- Post-renal: resulting from obstruction of urine flow downstream from the kidney)these can be divided into causes within theureters(e.g. calculi or clots), a problem within the wall of ureter(malignancies, benign strictures) and external compression(e.g. retroperitoneal tumors). It is extremely unusualfor drugs to be responsible for post-renal AKI. Practololinducedretroperitoneal fibrosis resulting in bilateral uretericobstruction is a rare example.

Differentiating pre-renal from renal acute kidney injury

It is sometimes possible to distinguish between cases of prerenal and renal AKI through examination of biochemical markers. In renal AKI, the kidneys are generally unable to retain Na+ owing to tubular damage. This can be demonstrated by calculating the fractional excretion of sodium **(FENa)**; in practice this is not often done because it lacks sensitivity and specificity and may be difficult to interpret in the elderly who may have pre-existing concentrating defects.

$$\text{FENa} = \text{sodium clearance/creatinine clearance}$$

$$\text{FENa} = \frac{\text{urine sodium} \times \text{serum creatinine}}{\text{serum sodium} \times \text{urine creatinine}}$$

- If FENa<1%, this indicates pre-renal AKI with preserved tubular function;
- ifFENa>1% this is indicative of ATN.

Clinical manifestations

- The signs and symptoms of AKI are often non-specific.
- The patient may exhibit signs and symptoms of volume depletion or overload, depending upon the precipitating conditions, course of the disease and prior treatment.
- In those patients with volume depletion, a classic pathophysiological picture is likely to be present with tachycardia, posturalhypotension, and reduced skin turgor and cold extremities. The most common sign in AKI is oliguria,where urine production falls to less than 0.5 mL/kg/h forseveral hours.
- In those patients with volume overload, a classic pathophysiological picture is likely to be present with ankle swelling ,oedema,Jugular venous distension and ,pleural effusion
- Metabolic disturbances that accompany AKI; these include excess potassium, hydrogen ions (acidosis) and phosphate in blood. Most cases of AKI are first identified by an abnormal blood test, though some patients may have symptoms that are specifically attributable to AKI; these include nausea, vomiting, diarrhoea, gastro-intestinal haemorrhage, muscle cramps and a declining level of consciousness.

Common Diagnostic Procedures

•Urinary catheterization (insertion of a catheter into a patient's bladder; an increase in urine output may occur with post renal obstruction

•Renal ultrasound (uses sound waves to assess size, position, and abnormalities of the kidney; dilatation of the urinary tract can be seen with post renal ARF)

•Renal angiography (administration of intravenous contrast dye to assess the vasculature of the kidney)

•Retrograde pyelography (injection of contrast dye into the ureters to assess the kidney and collection system)

•Kidney biopsy (collection of a tissue sample of the kidney for the purpose of microscopic evaluation; may aid in the diagnosis of glomerular and interstitial diseases)

Laboratory Tests

- Hyperkalemia
- Metabolic acidosis
- Elevated serum creatinine concentration (normal range approximately 0.6 to 1.2 mg/dL [53 to 106 µmol/L].
- Elevated BUN concentration (normal range approximately 8to 25 mg/dL [2.9 to 8.9 mmol/L].
- Decreased creatinine clearance (normal 90 to 120mL/minute.
- BUN: creatinine ratio (elevated in prerenal ARF)
  Greater than 20:1 (prerenal ARF)
  Less than 20:1 (intrinsic or post renal ARF)

GENERAL APPROACH TO TREATMENT

✓ A primary goal of therapy is ameliorating any identifiable underlying causes of ARF such as hypovolemia, nephrotoxic drug administration, or ureter obstruction.

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

✓ There is no evidence that drug therapy hastens patient recovery in ARF, decreases length of hospitalization, or improves survival.[3]Therefore, options are limited to supportive therapy, such as fluid, electrolyte, and nutritional support, renal replacementtherapy (RRT)

Pharmacologic Therapy

❖ **Diuretics**

- Loop diuretics have not been shown to accelerate AKI recovery or improve patient outcome; however, diuretics can facilitate management of fluid overload. The most effective diuretics are mannitol and loop diuretics.
- Mannitol 20% is typically started at a dose of 12.5 to 25 g IV over 3 to 5 minutes. Disadvantages include IV administration, hyperosmolality risk, and need for monitoring because mannitol can contribute to AKI.

- Equipotent doses of loop diuretics furosemide, bumetanide, torsemide, and ethacrynic acid) have similar efficacy.
- **Ethacrynic** acidis less commonly used to treat ARF because ototoxicity(sometimes irreversible) is associated with its useso reserved for sulfa-allergic patients only.
- Continuous infusions of loop diuretics appear to overcome diuretic resistance and tohave fewer adverse effects than intermittent boluses.
- **Bumetanide** may be given to patients who are unresponsive or allergic to furosemide. The usual dosage, administered intravenously or intramuscularly inthe treatment of ARF, is 0.5 to 1.0 mg/day; however, some patients may requireup to 20 mg/day.
- An initial IV loading dose (equivalent to furosemide 40–80 mg) should be administered before starting a continuous infusion (equivalent to furosemide 10–20 mg/hour).
- Agents from different pharmacologic classes, such as diuretics that work at the distal convoluted tubule (thiazides) or the collecting duct (amiloride, triamterene, and spironolactone), may be synergistic when combined with loop diuretics.
- Metolazone is commonly used because, unlike other thiazides, it produces effective diuresis at GFR < 20 ml/min.

❖ Diuretic Resistance

- Patients with renal insufficiency often encounter a decreased response to loop diuretics often referred to as "diuretic resistance." Some common causes of diuretic resistance in ARF are excessive sodium intake, inadequate diuretic dose or inappropriate regimen, reduced bioavailability (from gastrointestinal edema), reduced renal blood flow (drugs, intravascular depletion), increased sodium reabsorption, and nephrotic syndrome (in nephrotic syndrome, diuretics bind to proteins in the renal tubule, reducing diuretic effects).
- ***Strategies to overcome diuretic resistance*** may include increasing the dose or the dosing frequency; continuous intravenous infusion of the diuretic; and concomitant administration of loop diuretics with diuretics that act at the distal convoluted tubule (thiazides) or the collecting duct (amiloride, triamterene, and spironolactone).

❖ Vasoactive Agents

1- Dopamine

Low-dose dopamine, in doses ranging from 0.5 to 3 mcg/kg per minute, predominantly stimulates dopamine-1 receptors,leading to renal vascular vasodilation and increased renal blood flow. While this effect has been substantiated in healthy,euvolemic individuals with normal kidney function, a lack of efficacy data exists in patients with ARF.[3]

- Dopamine has no role in **preventing or treating** AKI.[2] احد المصادر يقول

2- Fenoldopam

Fenoldopam is a selective dopamine-1 receptor agonist that is approved for short-term management of severe hypertension.Because it does not stimulate dopamine-2, α-adrenergic, and β-adrenergic receptors, fenoldopam causes vasodilation in therenal vasculature with potentially fewer non-renal effects thandopamine.

❖ **Calcium Channel Blockers**

After ischemic ARF, calcium channel blockers may protect against ARF by inhibiting vasoconstrictive responses of the afferent arterioles and increasing GFR. In addition, calcium antagonists may prevent damage from elevated intracellular calcium after hypoxic injury.

Treatment of hyperkalemia ❖

This is a particular problem in AKI, not only because urinaryexcretion is reduced but also because intracellular potassium may be released. Rapid rises in extracellular potassium are to be expected when there is tissue damage,as in burns, crush injuries and sepsis. Acidosis also aggravates hyperkalaemia by provoking potassium leakage from healthy cells. The condition may be life-threatening causing cardiac arrhythmias and, if untreated, can result in asystolic cardiac arrest.

- Dietary potassium should be restricted to less than 40 mmol/day and potassium supplements and potassium-sparing diuretics removed from the treatment schedule.
- Emergency treatment is necessary if the serum potassium level reaches7mmol/L (normal range 3.5–5.5 mmol/L) or if there are the progressive changes in the electrocardiogram (ECG) associated with hyperkalaemia. These include tall, peaked T waves, reduced P waves with increased QRS complexes that often presages cardiac arrest.

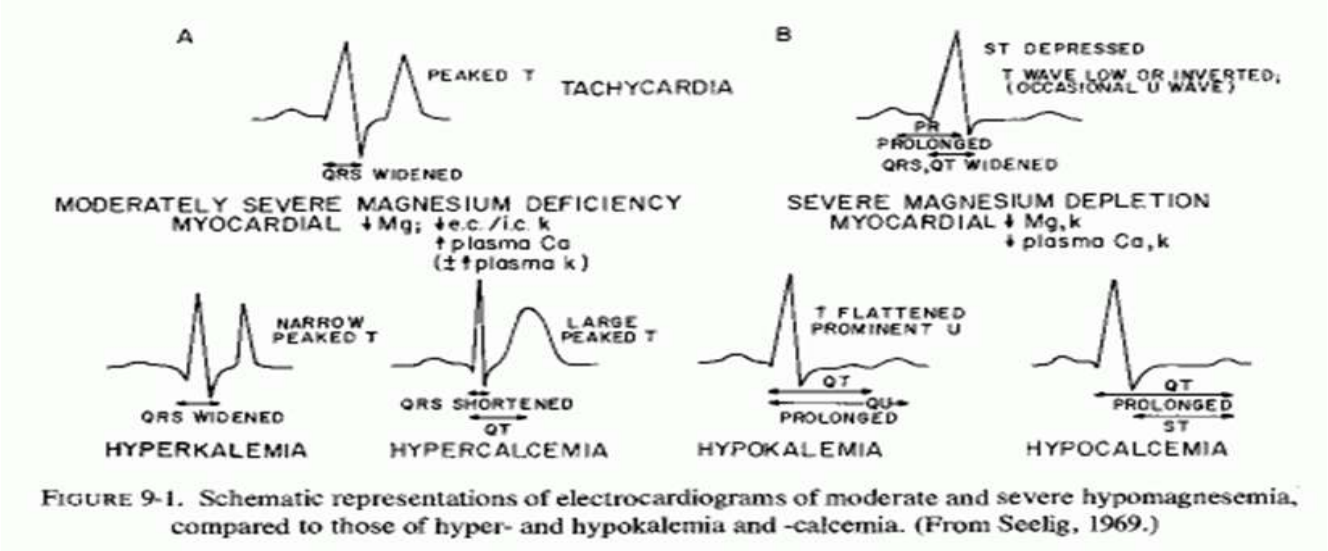
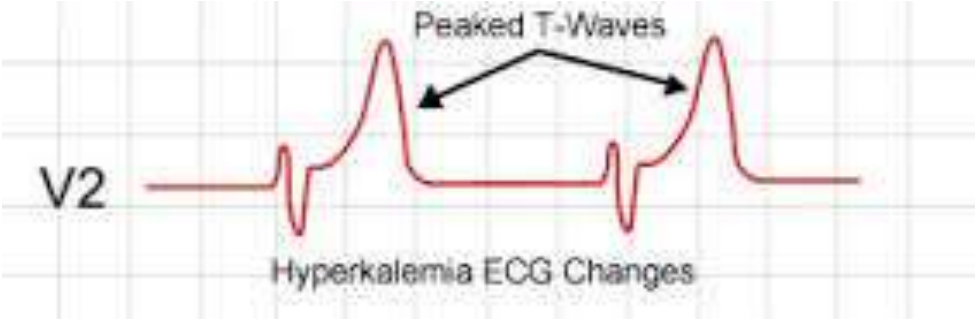


FIGURE 9-1. Schematic representations of electrocardiograms of moderate and severe hypomagnesemia, compared to those of hyper- and hypokalemia and -calcemia. (From Seelig, 1969.)



Emergency treatment of hyperkalemia consists of thefollowing:

1- 10-30 mL (2.25–6.75 mmol) of calcium gluconate 10%intravenously over 5–10 min; this improves myocardialstability but has no effect on the serum potassium levels.The protective effect begins in minutes but is short lived
(<1 h), although the dose can be repeated.
2- 50 mL of 50% glucose together with 8–12 units of solubleinsulin over 10 min. Endogenous insulin, stimulated bya glucose load or administered intravenously, stimulatesintracellular potassium uptake, thus removing it fromthe serum.
3-Nebulized salbutamol has also been used to lowerpotassium; however, this is not effective for all patientsand does not permanently lower potassium.

- **Treatment of acidosis**

The inability of the kidney to excrete hydrogen ions may result in a metabolic acidosis. This may contribute to hyperkalemia.It may be treated orally with sodium bicarbonate 1-6g/day in divided doses (though this is not appropriate for acute metabolic acidosis seen in AKI), or 50–100 mmol of bicarbonate ions (preferably as isotonic sodium bicarbonate 1.4 %or 1.26%, 250–500 mL over 15–60 min) intravenously may be used. The administration of bicarbonate in acidotic patients will also tend to reduce serum potassium concentrations.

- **Treatment of hypocalcaemia**

Calcium malabsorption, probably secondary to disordered vitamin D metabolism, can occur in AKI. Hypocalcaemia usually remains asymptomatic, as tetany of skeletal muscles or convulsions does not normally occur until serum concentrations are as low as 1.6–1.7 mmol/L (normal 2.20–2.55 mmol/L).Should it become necessary, oral calcium supplementation with calcium carbonate is usually adequate, and although vitamin D may be used to treat the hypocalcaemia of AKI, it rarely has to be added. Effervescent calcium tablets should be avoided as they contain a high sodium or potassium load.

- **Treatment of hyperphosphataemia**

As phosphate is normally excreted by the kidney, hyperphosphataemia can occur in AKI but rarely requires treatment.Should it become necessary to treat, phosphate-binding agents may be used to retain phosphate ions in the gut. The most commonly used agents are calcium containing such as calcium carbonate or calcium acetate and are given with food.

❖ **Treatment of hyponatremia**

(1) Moderate or asymptomatic hyponatremia may require only **fluid restriction**.
(2) Sodium chloride may be given for severe symptomatic hyponatremia (i.e., a serum sodium level below 120 mEq/L).
(a) Mechanism of action and therapeutic effect. Sodium chloride replaces and maintains sodium and chloride concentration, thereby increasing extracellular tonicity.
(b) Administration and dosage
(i) A 3% or 5% sodium chloride solution may be administered by slow IV infusion. The amount of solution needed is calculated from the following equation:
(Normal serum sodium level _ actual serum sodium level) total body water
(ii) Typically, 400 mL or less is administered.

❖ **Treatment of infection**

Patients with AKI are prone to infection and septicemia, whichcan ultimately cause death.Antibiotic therapy should be broad spectrum until a causative organism is identified.

❖ **Renal replacement therapy**

Renal replacement therapy is indicated in a patient with AKI when kidney function is so poor that life is at risk. However,it is desirable to introduce renal replacement therapy early in AKI, as complications and mortality are reduced if the serum urea level is kept below 35 mmol/L. Generally, replacement therapy is urgently indicated in AKI to:
1-Remove uraemic toxins when severe symptoms are apparent, for example, impaired consciousness, seizures, pericarditis, and rapidly developing peripheral neuropathy
2 .Remove fluid resistant to diuretics, for example,pulmonary oedema
3-Correct electrolyte and acid–base imbalances, for example,hyperkalemia >6.5 mmol/L or 5.5–6.5 where there are
ECG changes, increasing acidosis (pH < 7.1 or serum bicarbonate <10 mmol/L) despite bicarbonate therapy,or where bicarbonate is not tolerated because of fluid overload.

The common types of renal replacement therapy used in clinical practice are:

- haemodialysis
- haemofiltration
- haemodiafiltration
- Peritoneal dialysis

- Several continuous RRT (CRRT) variants have been developed including continuous hemofiltration, continuous hemodialysis, or a combination. CRRT gradually removes solute, resulting in better tolerability by critically ill patients. Disadvantages include limited availability of equipment, need for intensive nursing care, and the need toindividualize IV replacement, dialysate fluids, and drug therapy adjustments.

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