Acute Kidney Injury

- **Oliguria** means "reduced" urine volume less than that necessary to remove endogenous solute loads that are the end products of metabolism.
- **Oliguria** is defined as a urine output that is less than 1 mL/kg/h in infants, less than 0.5 mL/kg/h in children, and less than 400 mL daily in adults.

- **Acute Kidney Injury (AKI)**: is a condition in which the glomerular filtration rate is abruptly reduced, causing a sudden retention of endogenous and exogenous metabolites (urea, potassium, phosphate, sulfate, creatinine, administered drugs) that are normally cleared by the kidneys. The urine volume is usually low (<400 mL/day). If renal concentrating mechanisms are impaired, the daily urine volume may be normal or even high (*high-output or no oliguric renal failure*).

- Not all cases of acute kidney injury are characterized by oliguria. Renal failure that results from nephrotoxic injury, interstitial nephritis is frequently of the no oliguric type, and has a better prognosis.
- **Anuria**: (urine output completely shuts down or less than 50 ml/day) in acute kidney injury.
- Prerenal causes are usually reversible if treated promptly, but a delay in therapy may allow it to progress to a fixed intrinsic renal failure (e.g., acute tubular necrosis).

Table 1. Causes of acute kidney injury.

I. Prerenal

1. Dehydration
2. Vascular collapse due to sepsis, anti-Hypertension drug, third spacing.
3. Reduced cardiac output.
4. Functional–hemodynamic: NSAID, ACE inhibitor
5. Vascular: Atheroembolism**.**

II. Parenchymal (Intrarenal):

1. **Nonspecific**
   - ⇒ Acute tubular necrosis (ATN).
   - ⇒ Acute cortical necrosis

2. **Specific**
   - ⇒ Glomerulonephritis
   - ⇒ Interstitial nephritis
   - ⇒ Toxin, dye induced
   - ⇒ Hemolytic uremic syndrome.

III. Postrenal

- Mechanical obstruction of the urinary collecting system, including the renal pelvis, ureters, bladder, or urethra, results in obstructive uropathy or postrenal AKI.

1. **Stone in patients with solitary kidney.**
2. **Bilateral ureteral obstruction** (Stones, external pressure by tumor, ligation during pelvic surgery.
3. **Bladder Outlet Obstruction (BOO):**
   - ⇒ Benign prostatic hypertrophy (BPH): most common cause of **obstruction**).
   - ⇒ Urethral stricture).
   - ⇒ prostatic Cancer.
   - ⇒ bladder tumour
4. **Leak, posttraumatic.**
5. **Neurogenic bladder.**

PRERENAL KIDNEY INJURY

- ❖ The term *prerenal* denotes inadequate renal perfusion or lowered effective arterial circulation.
- ❖ The most common cause of this form of AKI is dehydration due to renal or extrarenal fluid losses from diarrhea, vomiting, excessive use of diuretics, and so on.
- ❖ Less common causes are septic shock, “third spacing” with extravascular fluid pooling (e.g., pancreatitis), and excessive use of antihypertensive drugs. Heart failure with reduced cardiac output also can reduce effective renal blood flow.
- ❖ Careful clinical assessment may identify primary condition responsible for the prerenal state, but many times several conditions can coexist.
- ❖ In the hospital setting, these circulatory abnormalities often are prolonged, leading to a more sustained injury (acute tubular necrosis).

Clinical Findings

A. Symptoms and Signs

- ❖ patients usually complain of thirst or of dizziness in the upright posture (orthostatic dizziness).
- ❖ There may be a history of overt fluid loss
- ❖ Physical examination frequently reveals decreased skin turgor, collapsed neck veins, dry mucous membranes, and, most importantly, excessive orthostatic or
- ❖ postural changes in blood pressure (defined as a systolic drop >20 or a diastolic drop >10 mm Hg) and pulse.

B. Laboratory Findings

1. Urine

- The urine volume is usually low.
- Accurate assessment may require bladder catheterization followed by hourly output measurements (which will also rule out lower urinary tract obstruction).
- Routine urinalysis usually shows a bland sediment.

2. Urine and blood chemistries:

⇒ The blood urea nitrogen– creatinine ratio, normally 10:1, is usually increased with prerenal renal failure.

3. Central venous pressure:

⇒ A low central venous pressure indicates hypovolemia.

4. Fluid challenge:

⇒ An increase in urine output in response to a **carefully** administered fluid challenge is both diagnostic and therapeutic in cases of prerenal renal failure.

⇒ Rapid intravenous administration of 300–500 mL of physiologic saline is the usual initial treatment.

⇒ Urine output is measured over the subsequent 1–3 hours. A urine volume increase of >50 mL/h is considered a favorable response that warrants continued intravenous infusion.

⇒ If the urine volume does not increase, the physician should carefully review the results of blood and urine chemistry tests, reassess the patient's fluid status, and repeat the physical examination to determine whether an additional fluid challenge (with or without furosemide) might be worthwhile.

Treatment

1. In states of dehydration, fluid losses must be rapidly corrected to treat oliguria. Inadequate fluid management may cause further renal hemodynamic deterioration and eventual renal tubular ischemia.
2. If oliguria and hypotension persist in a well-hydrated patient, vasopressor drugs are indicated in an effort to correct the hypotension associated with sepsis or cardiogenic shock.
3. Discontinuance of antihypertensive medications or diuretics can, by itself, cure the apparent acute kidney injury resulting from prerenal conditions.

INTRARENAL CAUSES

1. Specific intrarenal disease states:

- The most common causes of intrarenal acute kidney injury are acute or rapidly progressive glomerulonephritis, acute interstitial nephritis, toxic nephropathies, and hemolytic uremic syndrome.

Laboratory Findings

1. **Urine:** Urinalysis discloses variably active sediments:
2. **Blood test:** Components of serum complement are often diminished (due to activation and consumption). Rapidly progressive glomerulonephritis can be evaluated with tests for ANCA (antineutrophil cytoplasmic antibodies) and anti-GBM titers (anti-glomerular basement membrane antibodies).
3. **Renal biopsy.**

Treatment

1. Therapy is directed toward removing the underlying injurious constituent, for example, eradication of infection, removal of antigen, elimination of toxic materials and drugs, suppression of autoimmune mechanisms, removal of autoimmune antibodies, or a reduction in effector-inflammatory responses.
2. Immunotherapy may involve drugs (corticosteroids)
3. Temporary use of plasmapheresis.
4. Initiation of supportive dialysis may be required.

2. Nonspecific intrarenal states:

- RISK FACTOR:

1. Usually occur in hospital settings. Various morbid conditions leading to septic syndrome–like physiologic disturbances are often present.
2. Elderly patients, who are more prone to have this form of oliguric acute kidney injury, develop following hypotensive episodes.
3. Nephrotoxic drugs (e.g., aminoglycosides, NSAID, cisplatin.
4. Endogenous compounds (e.g., haemoglobin in haemolysis, myoglobin in rhabdomyolysis) are toxic or potentially toxic to the kidney.
5. Following exposure to radiocontrast agents, especially in patients with preexisting renal impairment, diabetes mellitus, or myeloma.

Fluid challenges

- There is no increase in urine volume following intravenous administration of mannitol or physiologic saline.
- Occasionally, following the use of furosemide or "renal doses" of dopamine (1–5 μg/kg/min), a low urine output is converted to a high fixed urine output. Although, traditionally, it was thought that by converting patients with oliguric AKI into no oliguric states by the above means translates into better prognosis, this does not appear to be evidence based.
- In fact, recent studies seem to suggest worse outcomes in those administered loop diuretics in the midst of AKI.

Treatment (General treatment of AKI)

❖ Serum potassium must be closely monitored to ensure early recognition of hyperkalemia. This condition can be treated with:

1. Intravenous sodium bicarbonate administration.
2. Intravenous glucose and insulin.
3. Intravenous calcium preparations to prevent cardiac irritability (usually given with electrocardiographic changes, e.g., peaked T waves, widening of QRS complexes).
4. Kayexalate, 25–50 g (with sorbitol).
5. Dialysis:

POSTRENAL AKI

- ❖ The conditions involve primarily the need for urologic diagnostic and therapeutic interventions.
- ❖ Postrenal causes of AKI are characterized by acute obstruction to urinary flow. Urinary tract obstruction increases intratubular pressure and thus decreases GFR.
- ❖ Following lower abdominal surgery, urethral or ureteral obstruction should be considered as a cause of AKI.
- ❖ The causes of bilateral ureteral obstruction:

1. Retroperitoneal neoplastic involvement, with masses or nodes.
2. Retroperitoneal fibrosis.
3. Renal pelvic or Ureteric stone.
4. Postsurgical or traumatic interruption.

- ❖ With a solitary kidney, ureteral stones can produce total urinary tract obstruction and acute kidney injury.

Clinical Findings

A. Symptoms and Signs

1. Pain and tenderness over the costovertebral angle often are present (obstruction).
2. If there has been an operative ureteral injury with associated urine extravasation, urine may leak through a wound.
3. Edema from overhydration may be noted.
4. Ileus is often present along with associated abdominal distention and vomiting.

B. Laboratory Findings: Urinalysis is usually not helpful.

C. IMAGING:

- ❖ Ultrasound examination often reveals a dilated upper collecting system with deformities characteristic of hydronephrosis.
- ❖ CT Scan without contrast usually diagnostic.

Treatment: relieve obstruction.

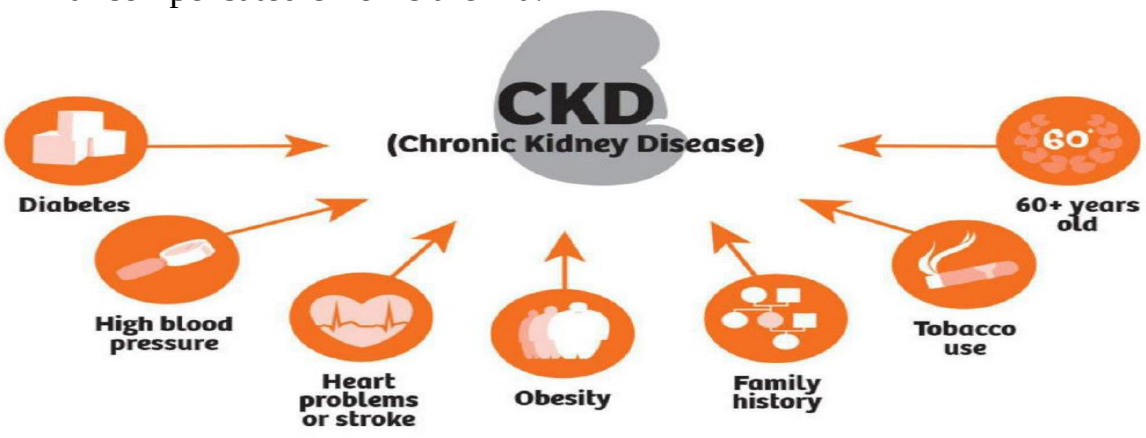
1. A large volume of urine obtained by catheterization may be both diagnostic and therapeutic for Bladder Outlet obstruction.
2. Cystoscopy and retrograde ureteral catheterization demonstrate ureteral obstruction.

Chronic Kidney Disease

- In chronic kidney disease (CKD), reduced clearance of certain solutes principally excreted by the kidney results in their retention in the body fluids. The solutes are end products of endogenous metabolism as well as exogenous substances (e.g., drugs).
- The most commonly measured indicators of renal failure are blood urea nitrogen and serum creatinine. The renal clearance of creatinine (as calculated from a 24-hour urine collection) is often used as a surrogate measure of glomerular filtration rate (GFR).
- In individual cases, it is often difficult to establish the duration of renal failure. Historical clues such as preceding hypertension or radiologic findings such as small, shrunken kidneys tend to indicate a more chronic process.
- Acute renal failure may progress to irreversible chronic renal failure.
- There are now numerous calculators that can estimate GFR (eGFR) based on the creatinine value, although not perfect.
- The use of dialysis and transplantation is expanding rapidly worldwide.

Etiology

- A variety of disorders are associated with CKD. Either a primary renal process (e.g., glomerulonephritis, pyelonephritis, congenital hypoplasia) or a secondary one (owing to a systemic process such as diabetes mellitus or lupus erythematosus) may be responsible.
- Once there is kidney injury, it is now felt that the initially adaptive hyperfiltration to undamaged nephron units produces further stress and injury to remnant kidney tissue, ultimately leading to worsening renal function and urinary abnormalities (i.e., proteinuria).
- The patient will show progression from one stage of CKD severity to the next.
- Superimposed physiologic alterations secondary to dehydration, infection, obstructive uropathy, or hypertension may put a borderline patient into uncompensated chronic uremia.



Clinical Findings

A. Symptoms and Signs

- With milder CKD, there may be no clinical symptoms.
- Symptoms such as pruritus, generalized malaise, lassitude, forgetfulness, loss of libido, nausea, and easy fatigability are frequent and nonfocal complaints in moderate to severe CKD.
- Growth failure is a primary complaint in preadolescent patients.
- Most patients with CKD have elevated blood pressure secondary to volume overload or from hyperreninemia.
- The pulse and respiratory rates are rapid as manifestations of anemia and metabolic acidosis.
- Clinical findings of uremic fetor, pericarditis, neurologic findings of asterixis, altered mentation, and peripheral neuropathy are present only with severe, stage V CKD.
- Palpable kidneys suggest polycystic disease.
- Ophthalmoscopic examination may show hypertensive or diabetic retinopathy.

Table 1. Stages of chronic kidney disease.

Stage	Description	eGFR (mL/min)	Potential complications of reduced GFR (in alphabetical order)
1	Kidney damage with normal or ↑ GFR	≥90	• Anemia, including functional iron deficiency • Blood pressure increases • Calcium absorption decreases • Dyslipidemia /heart failure/volume overload • Hyperkalemia • Hyperparathyroidism • Hyperphosphatemia • Left ventricular hypertrophy • Metabolic acidosis • Malnutrition potential (late)
2	Kidney damage with mild ↓ GFR	60–89	
3	Moderate ↓ GFR	30–59	
4	Severe ↓ GFR	15–29	
5	Kidney failure	<15 or dialysis	

B. History

- In 20% of cases, there is a family history of CKD.
- It is important to review drug usage and possible toxic exposures (e.g., lead).

C. Laboratory Findings

1. Urine composition:

- Proteinuria can be variable.
- urinalysis is nonspecific and inactive.

2. Blood testing:

1. Often seen is a picture of normocytic, normochromic anemia, the so-called **anemia of chronic disease**. With worsening renal function, iron deficiency may ensue.
2. Despite normal platelet counts, patients suffer from dysfunction (thrombasthenia), characterized by abnormal bleeding times.
3. Several abnormalities in serum electrolytes and mineral metabolism become manifest when the GFR drops below 30 mL/min (in the case of secondary hyperparathyroidism, impairment may begin with GFR < 60 mL/min).
4. Progressive reduction of body buffer stores and an inability to excrete titratable acids result in progressive metabolic acidosis characterized by reduced serum bicarbonate and compensatory respiratory hyperventilation.
5. The metabolic acidosis of uremia is associated with a normal anion gap, hyperchloremia, and normokalaemia. However, as renal dysfunction progresses, some patients may develop an anion gap acidosis (due to the buildup of organic anions).
6. Hyperkalemia is not usually seen unless the GFR is below 5 mL/min.
7. In moderate to severe CKD, multiple factors lead to an increase in serum phosphate and a decrease in serum calcium. The hyperphosphatemia develops as a consequence of reduced phosphate clearance by the kidney.
8. In addition, vitamin D activity is diminished because of reduced conversion of 25-OH vitamin D to the active form, 1,25-OH vitamin D in the kidney by the enzyme 1α- hydroxylase. These alterations lead to secondary hyperparathyroidism with skeletal changes of both osteomalacia and osteitis fibrosa cystica.
9. Uric acid levels are frequently elevated but rarely lead to calculi or gout during chronic uremia.

D. IMAGING:

- Patients with reduced renal function should not be routinely subjected to radiographic studies involving iodinated contrast (nephrotoxic).
- Renal sonograms are helpful in determining renal size (usually small) and cortical thickness (usually thin) and in localizing tissue for percutaneous renal biopsy.
- Patients with polycystic kidney disease will have variably large kidneys with evident cysts (on sonograms or abdominal CT scans).

E. Renal Biopsy

COMPLICATIONS

- Complications begin to develop as kidney disease progresses, most often when patients reach to eGFR is <60 mL/minute/1.73 m2 (stage 3). • Often, these complications go unrecognized or are inadequately managed during the earlier stages of CKD, leading to poor outcomes by the time a patient is in need of dialysis therapy.

1. **GROWTH RETARDATION** (a. Malnutrition, anemia b. Metabolic acidosis c. Bone disease d. Resistance to growth hormone e. Reduced levels of sex hormones)
2. **ANEMIA** a. Lack of erythropoietin b. Uremia c. Iron and folate deficiency d. Hyperparathyroidism causing myelofibrosis
3. **MINERAL & BONE DISORDER (CKD-MBD)** :(a. Decreased production of 1,25 DHD3 b. Reduced excretion of Phosphorus c. Stimulation of PTH d. Adynamic lesions e. Metabolic acidosis).
4. **Fluid, Electrolyte and Acid-Base Effects:** Fluid retention, Hyperkalemia, Hypocalcemia, Hyperphosphatemia, Metabolic acidosis.
5. **NEUROLOGICAL ABNORMALITIES**: Lethargy, Depressed sensorium, Seizures, Encephalopathy, hypotonia, truncal ataxia, peripheral neuropathy
6. **INFECTIONS.**
7. **BLEEDING TENDENCY.**
8. **GLUCOSE INTOLERANCE.**
9. **Cardiovascular:** HYPERTENSION, HYPERLIPIDEMIA, PERICARDITIS, LEFT VENTRICULAR DYSFUNCTION.
10. **Poor nutritional status.**
11. **Dermatologic:** Altered pigmentation, Pruritus.
12. **Gastrointestinal: Anorexia**, Nausea, vomiting, delayed gastric emptying, GI bleeding, Ulcers**.**
13. **Psychological:** Depression, Anxiety, Psychosis

Treatment

Conservative Treatment:

- Overall, management should be conservative until it becomes impossible for patients to continue their customary lifestyles.

A. Recent studies indicate some benefit of drugs to reduce progression of CKD.

1. The use of **angiotensin-converting enzyme inhibitors** (ACEI) and **angiotensin receptor blockers** (ARB) in slowing down renal decline has been well documented, especially in the diabetic population with significant proteinuria. With the addition of aldosterone antagonists to optimize blood pressure control, patients need to be followed closely for potential hyperkalemia.
2. **Lipid lowering agents** should be employed to lower the already accelerated risk of atherosclerotic disease in the ESRD population and can potentially retard the progression of renal dysfunction.

B. **Restriction of dietary protein** (0.8–1.0 g/kg/d), **potassium**, and **phosphorus** is recommended. As well, maintenance of close sodium balance in the diet is necessary so that patients become neither sodium expanded nor depleted. This is best done by the accurate and frequent monitoring of the patient's weight.

C. **Use of oral bicarbonate** (0.5–1 mEq/ kg/d) can be helpful when moderate acidemia occurs (aim for serum HCO3 level ≥ 23 mEq/L).

D. **Anemia** can be treated with recombinant erythropoietin given subcutaneously (aiming for hemoglobin levels between 11.0 and 12.0 g/dL).

E. **Prevention of possible uremic osteodystrophy and secondary hyperparathyroidism** requires close attention to calcium and phosphorus balance. Phosphate-retaining antacids and calcium or vitamin D supplements may be needed to maintain the balance. Cinacalcet can directly reduce parathyroid hormone secretion. If severe secondary hyperparathyroidism occurs, subtotal parathyroidectomy may be needed.

B. Dialysis:(renal replacement therapy)

1. Chronic Peritoneal Dialysis

2. Chronic Hemodialysis

- Indications for renal replacement therapy include the following:
  1. Severe metabolic acidosis
  2. Uncontrollable Hyperkalemia
  3. Pericarditis (risk of hemorrhage or tamponade)
  4. Uremic Encephalopathy
  5. Intractable volume overload
  6. Failure to thrive and malnutrition
  7. Intractable gastrointestinal symptoms (N, V, Bleeding)
- Chronic hemodialysis using semipermeable dialysis membranes is now widely performed.
- Treatment is intermittent—usually 3–5 hours three times weekly.
- Common problems with either type of chronic dialysis include infection, bone symptoms, technical accidents, persistent anemia, and psychological disorders. The excessive morbidity and mortality associated with atherosclerosis often occurs with long-term treatment.
- It is now recognized that occasionally uremic patients, despite dialysis, can develop wasting syndrome, cardiomyopathy, polyneuropathy, and secondary dialysis-amyloidosis so that kidney transplant must be urgently done. Routine bilateral nephrectomy should be avoided because it increases the transfusion requirements of dialysis patients.
- Despite these medical, psychological, social, and financial difficulties, most patients lead productive lives while receiving dialysis treatment.

C. Renal Transplantation

Thank You

2021-2022