# Renal Block

## Lecture One

## Acute Kidney injury


### Objectives:

- Introduction to the renal pathology
- Acute Kidney Injury
- Definition, Types, Clinical Overview, Causes
- Pathological findings
- Differential Diagnosis

This lecture doesn't focus on a single subject and it is mostly an introduction for renal pathology.

Before studying, you should know the Anatomy, Histology and Physiology of the renal system.

## First some important definitions for renal pathology:

**Oliguria**:

It is decreased urine output (less than 400cc /24h)

**Non-oliguria:**

Urine output is not decreased (greater than 400cc /24h).

**Anuria:**

It is no urine outflow (less than 50cc/24h).

**Azotemia:**

Elevated blood urea nitrogen (BUN) not from an intrinsic renal disease.

**Uremia:**

It is azotemia + clinical manifestations + systemic biochemical abnormalities.

Examples of **clinical manifestations** of uremia:

- Renal failure
- Anorexia (Loss of appetite for food)
- Dysgeusia (Distortion of the sense of taste)
- Nausea and vomiting
- Pruritis (Itch)
- Dyspnea.
- Pericarditis.
- Neuropathy.
- Lethargy (tiredness)

## What is acute kidney injury (acute renal failure)? ARF - Helpful Video

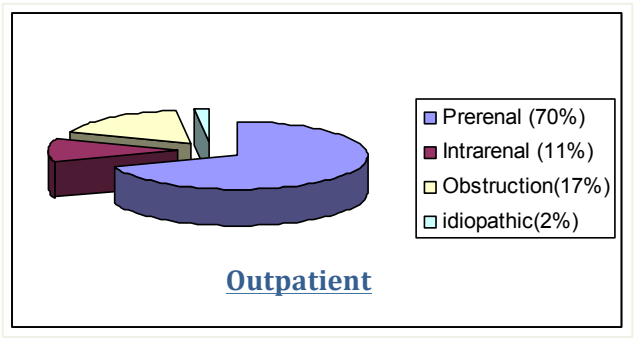
Acute kidney injury is defined as a sudden decline in renal function. (Within hours to days)

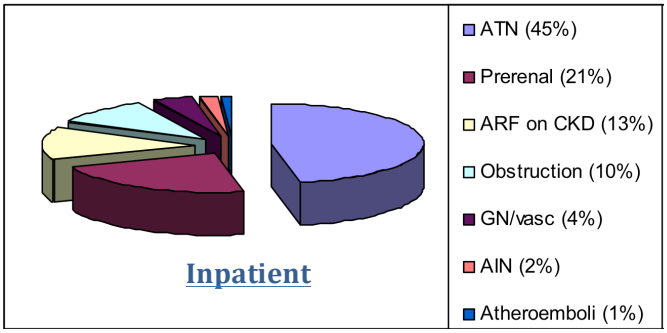
## What constitutes ARF?

- Acid-base disturbance.
- Increased Scr.
- Electrolyte and mineral disorders.
- Derangement of extracellular fluid balance.
- Accumulation of nitrogenous waste products.

## Etiology:

1. Outpatients: the most common cause is Prerenal.
2. Inpatients: the most common cause is Intrarenal.
3. Obstruction happens to both with approximately same percentage.



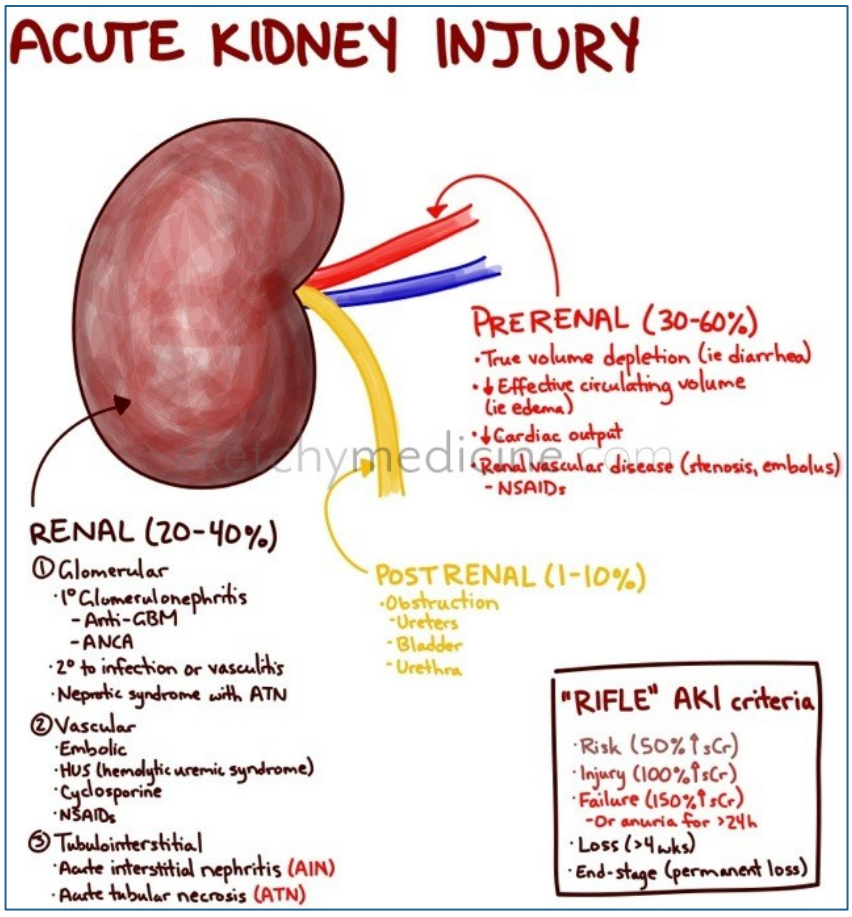
## Mortality of ARF:

Despite technical progress in the management of acute renal failure over the last 50 years, mortality rates seem to have remained around 50% (Must be treated immediately)

## Predictors of Dialysis in AKI: (غسيل الكلى)

- Oliguria:
  - Less than 400cc/24hr 85%will require dialysis
  - More than 400cc/24hr 30-40% will require dialysis. (But not as much)
- Mechanical ventilation.
- Acute myocardial infarction.
- Arrhythmia (K+ Level up).
- Hypoalbuminemia.
- ICU stay.
- Multisystem organ failure

## Causes of acute kidney injury:



## ➢ Prerenal[1] ARF:

Glomerular filtration rate is directly proportional to renal blood flow. Therefore, any condition that decreases renal blood flow would cause a decrease in **(GFR)** → **azotemia**

Decreased blood flow could be due to:

A. Hypotension:

Shock (septic, cardiogenic, hypovolemic)

B. Vascular pathology:

- Renal artery stenosis
- Abdominal aortic aneurysm may apply pressure on renal artery → decreasing blood flow to kidneys.
- Atheroemboli.
- Vasculitis.

C. Third spacing[2].

D. Volume depletion:

Loss of fluids, for example:

- GI losses: vomiting, diarrhea
- Skin losses: burns, sweat
- Renal losses: DKA, DI, Addison's, Na wasting

E. Drug induced:

NSAID, CsA, FK506, ACE, ARB

How?

AgII normally constricts efferent arterioles of the glomerular capsule → increased pressure in the glomerular capillaries → increase GFR.

If the patient is on angiotensin converting enzyme inhibitor (ACE I) there will be decreased AgII → decreased constriction of efferent arteriole → decreased pressure in glomerular capillaries → decreased GFR

- In prerenal azotemia there is decreased renal perfusion with *no damage* to the kidney parenchymal cells (in the beginning).
- There is a continuum from prerenal physiology to ischemic pathology
- In addition, decreased blood flow → Decrease in GFR → ischemia to the nephrons → necrosis of the kidney's cells after hours.

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[1] Before-Kidney.

[2] Fluid that isn't circulating (Something that got out from the blood flow) → might lead to edema

- Intrarenal ARF:

Happens from the kidney itself, due to one or more of the four elements, which are: tubules, glomeruli, blood vessels and interstitium.

Acute Tubular injury (necrosis):

It's characterized by damaged tubular epithelial cells and acute renal failure. Also, granular casts and tubular cells are observed in the urine, and it is the most common cause of acute renal failure.

How is it described based on Clinicopathological entity?

Pathologically:

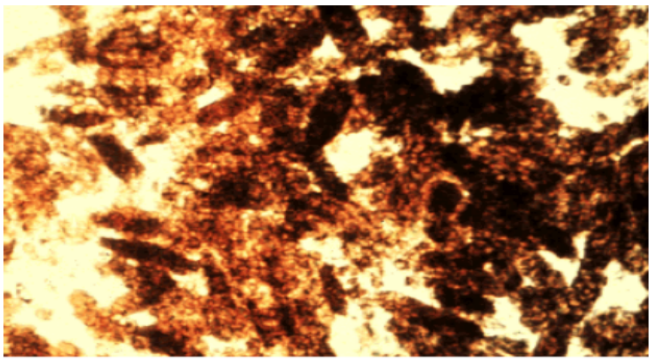
Destruction of tubular epithelial cell (Acute tubular necrosis)

Clinically:

Acute suppression of renal function (no urine or below 400 ml/24h)

**What are granular casts?**

Granular cast is a type of urinary cast. Urinary casts are cylindrical structures produced by the kidney and present in the urine in certain disease states. They form in the distal convoluted tubule and collecting ducts of nephrons, then dislodge and pass into the urine, where they can be detected by microscopy.



**Sediment in ATN** Urine sediment showing multiple, muddy brown granular casts. These findings are highly suggestive of acute tubular necrosis in a patient with acute renal failure. Courtesy of Harvard Medical School.

- Postrenal[3] ARF:
  - Results when urine flow is obstructed.
  - Examples include kidney stones, BPH (Benign Prostatic Hyperplasia), tumors, etc.

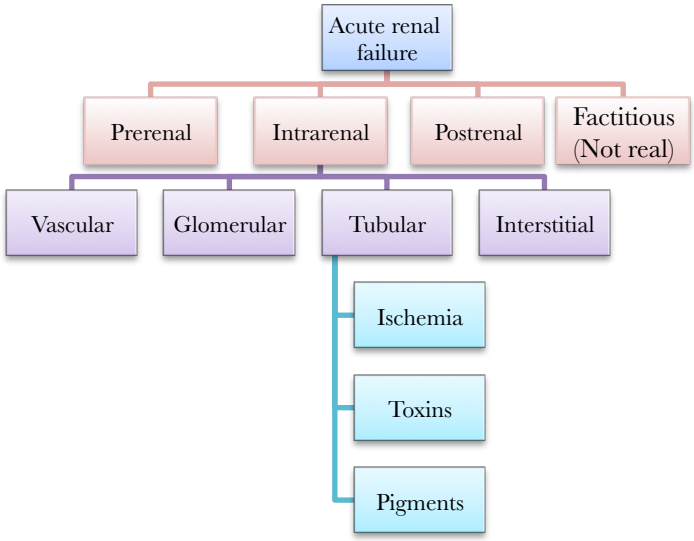
    How?

    When there is obstruction to urine flow → pressure will back up to the Bowman's space. → increase in the hydrostatic pressure in Bowman's space.

    The hydrostatic pressure of Bowman's space opposes GFR → the net result is decreased GFR.

[3] After-Kidney

## Acute tubular injury: (Robbins Pg. 537)




Ischemia:

Shock, sepsis, incompatible blood transfusion, thrombotic disease.

Tubular Toxins:

- Antimicrobials:

  Aminoglycosides, vancomycin, foscarnet, pentamidine, amphotericin B.
- Chemotherapeutics:

  Cisplatin, mitomycin C, ifosfamide.
- Immunotherapy:

  IVIG (Intravenous immunoglobulin).
- Complex Sugars:

  Maltose, sucrose, mannitol.
- Heavy metals.
- Sepsis, hypoxia.
- Radiocontrast agents.

**We have two types of toxins:**

A- Endogenous:

Produced by our own body. For example:

- Crush injury[4]:

  Caused by **Myoglobin,** which is found normally in skeletal muscles.

  How can it cause injury to the tubular cells?

  Crush injury (E.g. car accident or a wall falling on their leg) → rhabdomyolysis→ release of large amounts of myoglobin → accumulation of it in the kidney → acute kidney injury (renal failure).
- Hemoglobinopathy.

B- Exogenous:

- Drugs
- Radiocontrast dye
- Metals.

[4] Any injury that leads to crushing muscles

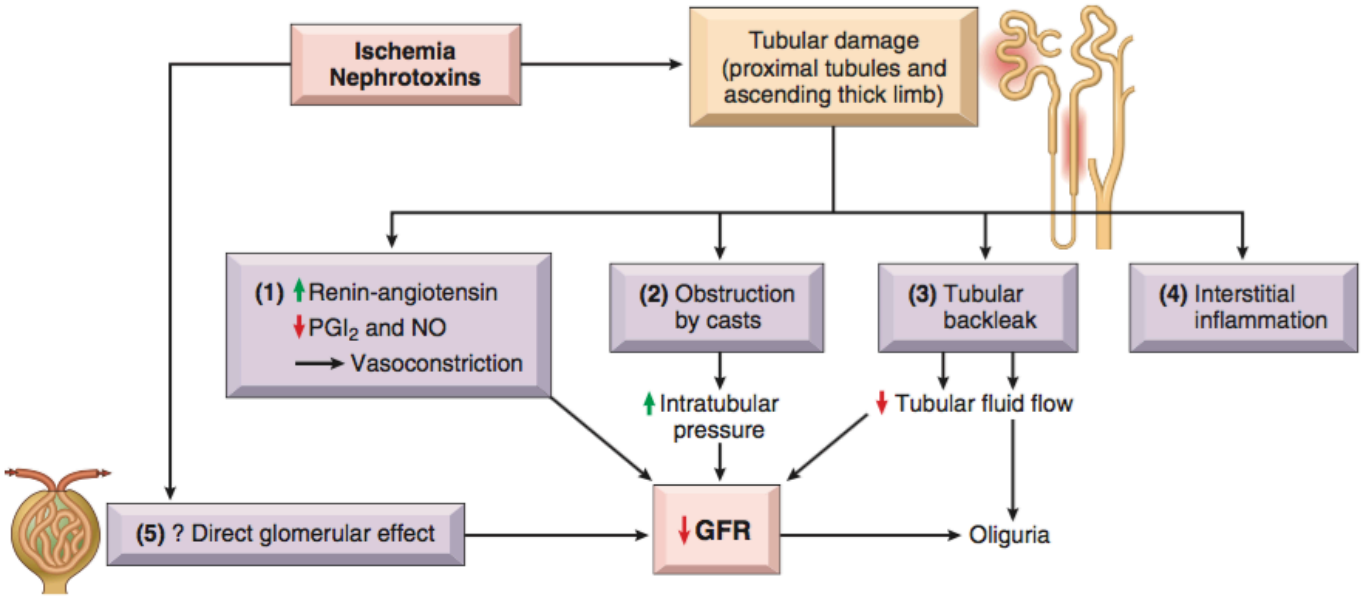



**Figure 13–17** Pathophysiologic mechanisms of acute kidney injury. Various injuries can directly damage tubules, which in turn decreases GFR by multiple mechanisms and also promotes vasoconstriction. Some injuries that cause tubular injury also directly decrease GFR by decreasing renal blood flow. NO, nitric oxide; $PGI_2$, prostaglandin $I_2$ (prostacyclin).
*(Modified from Lameire N, et al: JASN 12:S20-S32, 2001.)*

## Other causes for acute kidney injury include:

A. **RPGN** (Rapidly Progressive Glomerulonephritis):

   A syndrome defined by the loss of renal function over days to weeks due to acute glomerulonephritis.

B. Diffuse renal vascular diseases, such as microscopic polyangiitis and thrombotic microangiopathies.

C. Acute **drug induced** allergic interstitial nephritis.

   (Example: Ethylene glycol (antifreeze) is extremely toxic when ingested and can result not only in acute tubular necrosis but also in renal oxalosis with massive intratubular oxalate crystal deposition that can be visualized under polarized light)

## Congenital and Cystic Renal Diseases: (Not mentioned in the slides but in Dr. Rikabbi notes)

1. **Cystic renal dysplasia:**
   - Commonest cystic renal disease in children.
   - Caused by disorganized renal development.
   - Can be unilateral or bilateral.
   - Often associated with poorly formed ureter.
   - Rarely part of a syndrome.
2. **Autosomal dominant polycystic kidney disease:**
   - Progressive distention of kidney by enlarging cysts.
   - About 10% require dialysis/ transplantation.
   - 1-2 cases per 1000 live births. Usually present in adults.
   - Caused by mutation in two genes PKD1 (85% of cases: chromosome 16) and PKD2 (155 cases, chromosome 4) (also PKD3 in rare cases). 10% new mutations.
   - Maybe associated with cysts in liver, pancreas, spleen and cerebral/ coronary artery and aneurysms.
3. **Autosomal recessive polycystic kidney disease:**
   - Rare, 1 case per 20,000 live births.
   - Gene on chromosome 6.
   - Liver is always affected.
   - Large kidneys at birth (may cause death soon after birth due to renal failure).
4. **Medullary sponge kidney**
   - Dilated collecting ducts give "spongy" appearance.
   - 1 case per 5000 populations.
   - May present with renal infections in adult life.
   - No obvious genetic link.

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قال صلى الله عليه وسلم: (من سلك طريقًا يلتمس فيه علمًا سهّل الله له به طريقًا إلى الجنة).

دعواتنا لكم بالتوفيق.