Team Medicine

Acute Kidney Injury

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■ Important notes ■ doctor notes ■ Step up to medicine

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Kidney functions:

- Electrolyte homeostasis
- Excretion of certain hormones
- Maintain blood pressure
- Fluid homeostasis
- Excretion of waste products

In AKI kidneys fail to perform some of these functions, not all of them.

Acute Kidney Injury

- Deterioration of renal function over a period of hours to days, resulting in
  - the failure of the kidney to excrete nitrogenous waste products and
  - to maintain fluid and electrolyte homeostasis

Oliguria: <400 ml urine output in 24 hours.

Anuria: <100 ml urine output in 24 hours

- **An abrupt (within 48 hours) absolute increase in creatinine by 0.3 mg/dl (=26.4 µmol/l) or percentage increase of >50% from base line or urine output <0.5 ml/hour for 6 hours.**

Why the cutoff point is 0.3 mg/dl (=26.4 µmol/l)?
Because this is when the ***mortality risk*** starts

A patient with rise in creatinine by 26.44 µmol/l has an increase risk of mortality y 4.1

Infection is a common and serious complication of AKI (occurs in 50% to 60% of cases). The cause is probably multifactorial, but uremia itself is thought to impair immune functions. Examples include pneumonia, UTI, wound infection, and sepsis.

The most common cause of ***death (mortality)*** in AKI patients is infection (75% of all deaths), followed by cardiorespiratory complications.

Staging previously was based on RIFAL criteria, now it is 1,2,3. ***Mortality*** goes up with each stage

Stage	Creatinine criteria	Urine Output criteria
AKI stage I	1.5-2 times baseline **OR** 0.3 mg/dl increase from baseline (≥ 26.4 µmol/L)	<0.5 ml/kg/h for >6 h
AKI stage II	2-3 times baseline	<0.5 ml/kg/h for >12 h
AKI stage III	3 times baseline **OR** 0.5 mg/dl (44 µmol/L) increase if baseline>4mg/dl(≥ 354 µmol/L) **OR** Any renal replacement therapy given	<0.3 ml/kg/h for >24 h **OR** Anuria for >12 h

If we detect a high serum creatinine > 26.4 µmol/L , there're three possibilities:

1- **Acute kidney injury.**
2- **Chronic kidney injury.**
3- **Acute-on-chronic kidney injury.**

Then you differentiate based on History & presentation of the patient.

In other words

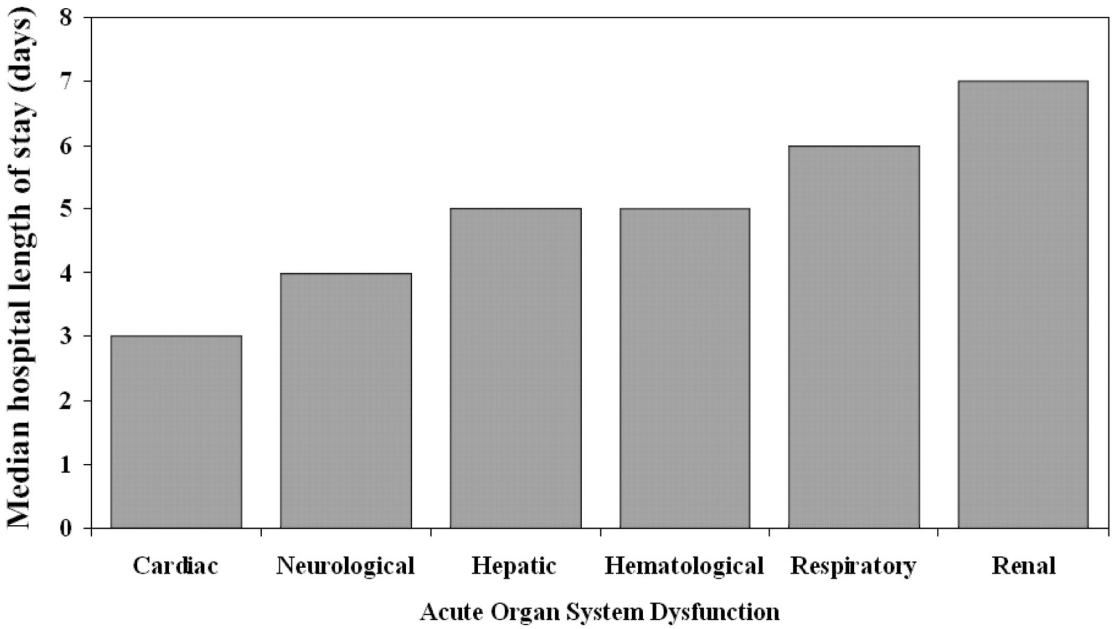
Whenever a patient has elevated Cr levels, the first thing to do is determine the patient's baseline Cr level, if possible. This helps deter- mine whether the patient has aKI, CKD, or chronic renal insufficiency/failure with superimposed aKI. (This condition is known as "acute on chronic" renal failure.)

Normal level of creatinine (Baseline) depends on:

- Age. - Gender. - Body built.

Epidemiology:

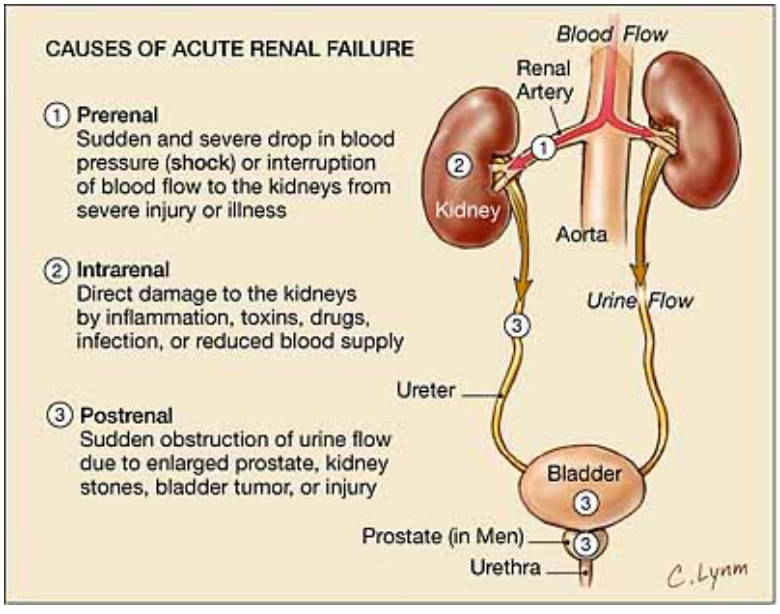
- It occurs in
  - 5%of all hospitalized patients and
  - 35% of those in intensive care units **(Because they're in shock, so the morbidity of AKI is higher.)**
  - Mortality is high:
    - up to 75–90% in patients with sepsis
    - 35–45% in those without



***Patients with renal problems tend to stay longer in hospitals, so the cost is going to be higher. 1bed per night costs around 1500 riyals**

So patient with AKI will have both high mortality rate and high cost for their management

Etiology of ARF:



Pre-renal AKI:

(Any abnormality affecting renal perfusion)

- **Volume depletion**
  - Renal losses (diuretics, polyuria)
  - GI losses (vomiting, diarrhea)
  - Cutaneous losses (burns, Stevens-Johnson syndrome)
  - Hemorrhage
  - Pancreatitis
- **Decreased cardiac output**
  - Heart failure
  - Pulmonary embolus
  - Acute myocardial infarction
  - Severe valvular heart disease
  - Abdominal compartment syndrome (tense ascites)

Post-renal AKI:

(Only Bilateral obstruction of two ureters, otherwise shouldn't be cause AKI unless if the patient has one kidney so the obstruction will results in AKI).

- **Ureteric obstruction**
  - Stone disease,
  - Tumor, inside lumen obstructing of outside compressing the lumen
  - Retroperitoneal Fibrosis,
  - Ligation during pelvic surgery
- **Bladder neck obstruction**
  - Benign prostatic hypertrophy [BPH]
  - Cancer of the prostate
  - **Neurogenic bladder**
  - Drugs(Tricyclic antidepressants, ganglion blockers,
  - Bladder tumor,
  - Stone disease, hemorrhage/clot)
- **Urethral obstruction** (strictures, tumor)

Urethral obstruction secondary to enlarged prostate (BPH) is the most common cause of Post renal AKI.

The basic three tests for postrenal failure:

1- physical examination-palpate the bladder
2- Ultrasound-look for obstruction, hydronephrosis
3- Catheter-look for large volume of urine

Renal of AKI:

If we suspect a renal cause of AKI, we should think of three structures that might be affected:
- Tubules. – Interstitium. – Glomeruli.

IMP: Doctor said: In this section, I Don't expect you to know exactly what is the etiology, but I expect you to know whether this is most likely tubular? Glomerular? Or interstitial?

How to differentiate?

WBCs + WBC casts → Interstitial
RBCs + RBC casts → Glomerular disease
Muddy brown urine → Acute Tubular Necrosis

Tubular injury
(Acute Tubular Necrosis)

- **Ischemia:**
  - Hypotension, sepsis, **prolonged pre-renal state**

- **Prolonged pre- renal state (Hypotension) will affect tubules causing ATN. The mechanism is the tubular cells will be sloughed away and accumulated in the tubules causing obstruction and resulting in Muddy brown urine which contains these tubular cells. "Muddy brown casts"**

- **Toxic**
  - Heme pigment (**rhabdomyolysis**, intravascular hemolysis)
  - Crystals (tumor lysis syndrome, seizures, ethylene glycol poisoning, megadose vitamin C, acyclovir, indinavir, methotrexate)
  - **Drugs** (aminoglycosides, lithium, amphotericin B, pentamidine, cisplatin, ifosfamide, **radiocontrast agents**)

- **Rhabdomyolsis → muscles breakdown lead to release of myoglobin, which will be directed to the tubules causing injury. Etiology of rhabdomyolysis can be statins and lipid lowering agents. Patient presents with muscle aches and pain.**
  Hallmark in urinalysis: positive heme but negative red blood cells.

- ***Radiocontrast agents*** → **either provoke rapid vasoconstriction of the vasa recta artery that supplies the renal tubules resulting in necrosis. Or direct toxicity. Or both**
  Treatment: stop the offending agent and rehydrate.

From step UP: Radiographic contrast media can cause ATN (typically veryrapidly)bycausing spasm of the afferent arteri- ole. It can be prevented with saline hydration.

- Diagnose by history, ↑ **FENa (>2%)**
- sediment with **coarse granular casts**, RTE cells
- Treatment is supportive care.
- 80% will recover, if initial insult can be reversed

Interstitial causes:

Box 1: Common causes* of acute interstitial nephritis[2,4,6]

Drugs
- Antimicrobials (ampicillin, ciprofloxacin, methicillin, penicillin, rifampicin, sulfonamides)
- Nonsteroidal anti-inflammatory drugs (acetylsalicylic acid, fenoprofen, ibuprofen, indomethacin, naproxen, phenylbutazone, piroxicam, tolmetin, zomepirac)
- Acid suppressors (omeprazole, pantoprazole, rabeprazole, cimetidine)
- Others (phenytoin, furosemide, allopurinol, phenindione)

Infections
- Direct infiltration (leptospirosis, cytomegalovirus, candidiasis)
- Reactive to systemic infections (streptococcal infection, diphtheria, *Hantavirus*)

Systemic diseases
- Metabolic diseases (urate nephropathy, hypercalcemic nephropathy, oxalate nephropathy)
- Immunologic reactions (transplant rejection, systemic lupus erythematosis, sarcoidosis, cryoglobulinemia)
- Neoplastic diseases (lymphoproliferative diseases)

Idiopathic causes

*These are the most common causes of acute interstitial nephritis, but this list is not exhaustive.

Box 2: Characteristics of acute interstitial nephritis
- Acute elevation in creatinine levels (not caused by pre- or post-renal etiologies)
- General malaise, nausea (caused by buildup of metabolites)
- Normal blood pressure, no edema (distinguishes acute interstitial nephritis from acute tubular necrosis)
- Polyuria and polydypsia (kidneys unable to concentrate urine)
- Maculopapular rash (may be an early indication of drug-induced acute interstitial nephritis)
- Proteinuria (caused by tubular damage)
- Pyuria (occurs in almost all cases)
- Hematuria (occurs in about 90% of cases)
- Eosinophiluria (occurs in 80% of cases of drug-induced acute interstitial nephritis)

- **In AKI due to interstitial nephritis, the urine will be full of WBCs casts.**

Glomerular causes:

- Anti–glomerular basement membrane (GBM) disease (in Goodpasture syndrome)

- Anti–neutrophil cytoplasmic antibody-associated glomerulonephritis (ANCA-associated GN) (in Wegener granulomatosis, Churg-Strauss syndrome, microscopic polyangiitis)
- Immune complex GN (in lupus, postinfectious, cryoglobulinemia, primary membranoproliferative glomerulonephritis)

Acute Glomerulonephritis

- Rare in the hospitalized patient
- Diagnose by history, hematuria, **RBC casts**, **proteinuria** (usually non-nephrotic range), low serum complement in post-infectious GN), RPGN often associated with anti-GBM or ANCA
- Usually will **need to perform renal biopsy**.
- **Signs and symptoms resulting of primary disease.**
- **Signs and symptoms resulting from loss of kidney function:**
  - decreased or no urine output, flank pain, edema, hypertension, or discolored urine
  - weakness and
  - easy fatiguability (from anemia)
  - anorexia,
  - vomiting, mental status changes or
  - Seizures
  - Edema
- **Asymptomatic**
  - elevations in the plasma creatinine
  - abnormalities on urinalysis
- **Systemic symptoms and findings:**
  - fever
  - arthralgias,
  - pulmonary lesions

AKI Diagnosis:

- Blood urea nitrogen and serum creatinine
- CBC, peripheral smear, and serology
- Urinalysis
- Urine electrolytes
- U/S kidneys
- Serology: ANA,ANCA, Anti DNA, HBV, HCV, Anti GBM, cryoglobulin, CK, urinary Myoglobulin

- **Urinalysis**
  - **Unremarkable in pre and post renal causes**
  - Hansel stain for Eosinophils. (eosinophils are high in interstitial nephritis)

- **How to differentiate between ATN & AIN & AGN ?**

Acute tubular necrosis	Acute interstitial nephritis	Acute glomerulionephritis
Muddy brown urine	**WBCs Casts**	**RBCs casts**

- **FENa < 1% (Pre-renal state)**
  - May be low in selected intrinsic cause
    - » Contrast nephropathy
    - » Acute GN
    - » Myoglobin induced ATN

If the urine Na is low, so the Fractional Excretion of Na (FENa) is also low and vice versa.

- **FENa > 1% (intrinsic cause of AKI)**

TABLE 3-3. Laboratory Tests Useful in the Diagnosis of Acute Renal Failure

Test	Favors Prerenal Disease	Favors ATN
BUN/P_{cr} ratio	>20:1	10–15:1
Rise in P_{cr}	Variable rate of rise with downward fluctuations in some patients	Progressive increase of ≥0.5 mg/dL per day, particularly in oliguric patients
Urinalysis	Normal or near normal; hyaline casts may be seen but are not an abnormal finding	Many granular casts with renal tubular epithelial cells and epithelial cell casts
U_{osm}	>500 mosmol/kg	<350 mosmol/kg
U_{Na}	<20 meq/L	>40 meq/L
FE_{Na}	<1 percent	>2 percent

Treatment of AKI:

- **Treating the underlying cause if it's due to pre-renal or post-renal causes**
- Optimization of hemodynamic and volume status
- Avoidance of further renal insults
- Optimization of nutrition
- If necessary, institution of renal replacement therapy

Indications for renal replacement therapy

- Symptoms of uremia (encephalopathy,...)
- Uremic pericarditis
- Refractory volume over load
- Refractory hyperkalemia
- Refractory metabolic acidosis

From step up: Order dialysis if symptomatic uremia, intractable acidemia, hyperkalemia, or
volume overload develop.

Correcting fluid imbalance.

a. If the patient is volume depleted, give IV fluids. However, many patients with AKI are volume overloaded (especially if they are oliguric or anuric), so diuresis may be necessary.

b. The goal is to strike a balance between correcting volume deficits and avoid- ing volume overload (while maintaining adequate urine output).

c. Monitor fluid balance by daily weight measurements (most accurate esti- mate) and intake–output records.

d. Be sure to take into account the patient's cardiac history when considering treatment options for fluid imbalances (i.e., do not give excessive fluid to a patient with CHF)

Case 1

- 75 years old female, known to have DM II and HTN Presented with nausea, vomiting and diarrhea for 3 days, Medication: Insulin, lisinopril, and her Serum Creatinine 205. On history, there's no evidence of previous high creatinine or chronic renal disease ? + patient had a normal Cr.

The patient has Acute Kidney Injury due to pre-renal cause which is volume depletion (diarrhea, vomiting). We treat her by IV fluids, if left untreated for a long time, it might lead to Acute tubular necrosis.

Also patient has DM2 and HTN so she is at high risk of chronic kidney disease as well.

- **What do you expect to find in urine analysis?**

  - **Normal +- Hyaline casts** which are devoid of contents (seen in prerenal failure).
- **What do you expect urinary Na, osmolality?**
  - **Urinary Na<10 (low)**
  - **Osmolality > 300 (high)**
  - **Fractional excretion of Na <1%**
  - **We might find proteinuria because she is diabetic NOT because of her recent condition.**
- **Treatment:**
  - **Rehydration**
  - **Take her off nephrotoxic medications if present**
  - **Monitor her kidney functions**

Case 2

- 16 years old Saudi male, after road traffic accident developed quadriplegia, Creatinine 32 few days ago, now 201. His urine output is 2 L/day. No history of vomiting or diarrhea, no new medication added. On examination: BP 123/73 mmHg, pulse 78 /min
  FiO2 saturation is 99% on room air ?

First, it's an Acute Kidney Injury because few days ago his creatinine level was normal. On examination, his BP is normal and there're no signs of volume loss, so we rule out pre-renal causes. No medication history and his presentations don't suggest a renal cause, so exclude it. Due to his quadriplegia, the patient got "Neurogenic bladder". Simply, the management is (Foley catheter).

Case 3

- 25 years old Saudi male sustained Road traffic accident this morning in ER was hypotensive and required 6 units of blood transfusion urine out put decreased significantly serum creatinine 285µmol/l?

What is your differential? Prerenal AKI or ATN.
What to do to differentiate? By Urinanalysis: Dark color and high Urine Na>10.

- Further information
  - Previously healthy
  - And urine output for the last 3 hours is <10 cc and dark colour
  - Physical examination
  - Asses volume status
  - Blood pressure
  - Pulse
  - JVP
  - Urine out put
  - Laboratory investigation:

- K 4.7, Bicarbonate 21, Cl 99, Na 137
- Urinary Na> 10, Urine osmolality < 350

Diagnosis: Acute Kidney Injury secondary to Acute tubular necrosis due to shock
What to do? Give fluids and blood and make sure his BP is back to normal.
Remove offending agent if present. And monitor the patient.

- Next day when you came to assess the patient you found him incubated and they told you he went into respiratory distress. BP 120/78mmHg
  - Urine output none for the last 3 hours
  Lab result as follow:
  - K 6.3
  - Creatinine 499µmol/l
  - Bicarbonate 12

This is because he developed pulmonary edema (because high fluids were given to the patient with no urine output)
Cr increased further
Bicarbonate is low so patient developed acidosis
Now we decided to dialyze him

Contrast nephropathy Versus Atheroembolic AKI:

Any contrast given IV will go to the kidneys and cause either direct toxicity to tubules or vasoconstriction leading to hypoxia to tubules.

Who develop contrast nephropathy? Patients at high risk: elderly, patients with chronic kidney disease, DM, and multiple myeloma…etc.

You have to tell the patients you are at high risk, rehydrate them, and follow up the Cr levels.

Lets say a patient is at high risk and we gave him IV contrast (if there is no alternative to avoid the contrast) → if patient develop signs and symptoms within 12-48 hours, this is Contrast nephropathy.

However, if patient develop symptoms and signs after a week, this is due to a thrombus and embolus formation "Thromboembolic".

So ask the patient when was the contrast given to differentiate.