Acute kidney injury

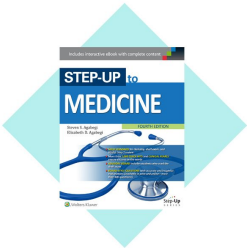
Objectives:

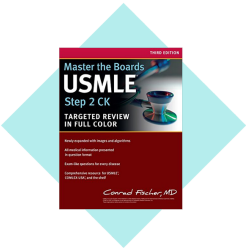
- Define Acute Kidney Injury
- Know the epidemiology of Acute Kidney Injury
- Know the etiology of Acute Kidney Injury
- Manage Acute Kidney Injury:
    - Diagnose Acute Kidney Injury
    - Treat Acute Kidney Injury

[Color index : Important | Notes | Extra]

Resources:

- 435 slide





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Acute Kidney Injury Definitions

Traditionally referred to as acute renal failure (ARF), it has many definitions.

1- Acute kidney injury definition: The old generic/descriptive definition is ARF

- 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**.
- **Olig**uria: **<400** ml urine output in 24 hours.
- **An**uria: **<100** ml urine output in 24 hours.

2- ARF(AKI) in one study was defined as:

- ➔ a 0.5 mg/dL increase in serum creatinine if the baseline serum creatinine was ≤1.9 mg/dL.
- ➔ Or an 1.0 mg/dL increase in serum creatinine if the baseline serum creatinine was 2.0 to 4.9 mg/dL.
- ➔ Or a 1.5 mg/dL increase in serum creatinine if the baseline serum creatinine was ≥5.0 mg/dl.

So you can see physician define a case as AKI, while someone else don't , that's why they set RIFLE criteria.

3- RIFLE criteria:

	GFR/Creatinine criteria	Urine Output criteria
Risk	Increase in creatinine x1.5 Or GFR decrease >25%	< 0.5 ml/kg/hr for 6 hrs
Injury	Increase in creatinine x 2 Or GFR decrease >50%	< 0.5 ml/kg/hr for 12 hrs
Failure	Increase in creatinine x 3 Or GFR decrease >75%	< 0.3 ml/kg/hr for 24 hrs or Anuria for 12 hrs
Loss	Persistent ARF = Complete loss of renal function > 4 weeks	
ESRD	End Stage Renal Disease > 3 months	

Then, they noticed there is a difference in defining GFR, so they set AKI stages

4- AKI stages:

Stage	Creatinine criteria	Urine Output
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 > 4 mg/dl(≥ 354 µmol/L) - OR Any renal replacement therapy given	<0.3 ml/kg/h for >24 h OR Anuria for >12 h

These values and stages are **based on** the difference of **mortality rate** which is shown below.

For example: patient presented with Cr 100 µmol/L, and his baseline was 70 µmol/L, what does he have? AKI stage I (note the difference was more than 26.4 µmol/L)

- **Acute kidney injury, mortality, length of stay, and costs in hospitalized patients:**
  19,982 pts admitted to academic medical centre in SF 9,205 pts with >1 creatinine results.

Rise in creatinine	Multivariable OR (hospital mortality)
≥ 0.3 mg/dl (26.4 µmol/L)	4.1
≥ 0.5 mg/dl (45 µmol/L)	6.5
≥ 1.0 mg/dl (90 µmol/L)	9.7
≥ 2.0 mg/dl (180 µmol/L)	16.4

You can notice that mortality rate increases when Creatinine is higher.

5- KDIGO Definition for AKI: the latest definition for AKI

An abrupt **within 48 hours**:

- ➔ **Absolute increase in creatinine by 0.3 mg/dl (26.4 µmol/l)**.
- ➔ Or **percentage increase of >50% from baseline.**
- ➔ Or **urine output <0.5 ml/hour for 6 hours.**

Epidemiology and impact of Acute Kidney Injury

It occurs in:

- 5% of all hospitalized patients.
- 35% of those in ICU. Due to hypotension, sepsis, septic shock as well as nephrotoxic medications they will develop AKI.

Mortality is high in:

- Up to 75–90% in patients with sepsis.
- 35–45% in those without sepsis.
  Hospitalized patient, not community. It's much lower in community

AKI impact:

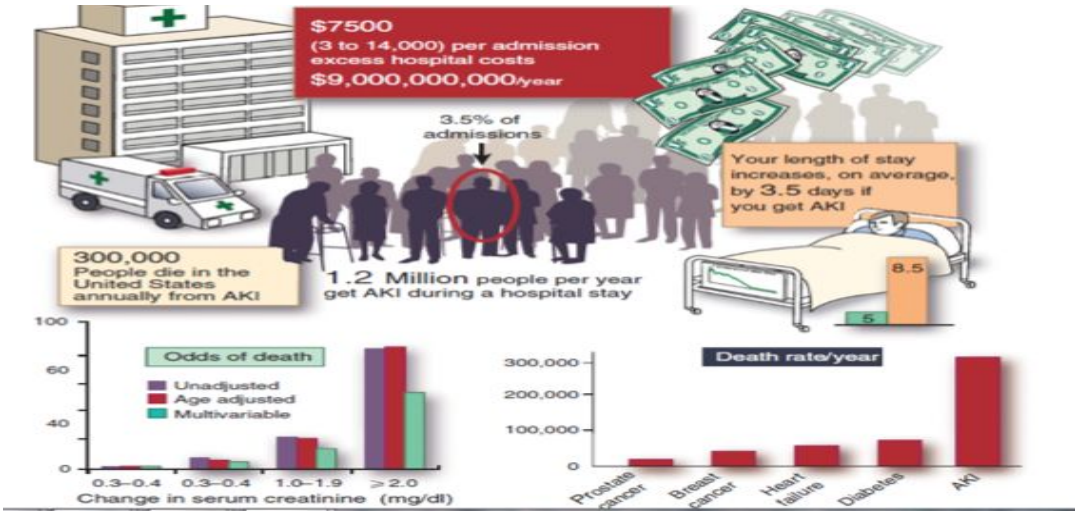
Correlation between AKI classification and outcome:
22,303 adult patients admitted to 22 ICUs in UK and Germany between 1989–1999 with ICU stay ≥24 hours.

	No AKI 65.6%	**AKI I** 19.1%	**AKI II** 3.8%	**AKI III** 12.5%
Mean age	60.5	62.1	60.4	61.1
ICU mortality	**10.7%**	**20.1%**	**25.9%**	**49.6%**
Hospital mortality	16.9%	29.9%	35.8%	57.9%
Length of stay in ICU (median)	2d	5d	8d	9d

Mortality rate increases with AKI stages.

- Risk of CKD: Increasing evidence that **episodes** of AKI leave **permanent** renal **damage**. In sepsis related AKI.
- AKI is **associated** with: increased risk of **CKD**, **Cardiovascular** event and increased **long-term mortality.**

AKI clinical outcomes:



AKI Mortality is much higher than cumulative risk of death for HF, DM, breast and prostate cancer!

Etiology of Acute Kidney Injury

Pre-renal	Renal	Rost-renal
- Volume depletion. - ↓ cardiac output.	- Acute Tubular necrosis ATN. - Acute interstitial nephritis AIN. - Acute Glomerulonephritis GN.	- Ureteric obstruction. - Bladder neck obstruction. - Urethral obstruction.
Clinical Consequences		
- Chronic Kidney disease. - End Stage Renal Disease ESRD.	- Hospitalization. - Mortality.	

Kidney is normal in pre and post-renal, unless it get affected due to maladaptation.

Pre-renal AKI: (most common cause of AKI)

- **Volume depletion:**
  - ➔ Renal losses (diuretics, polyuria)
  - ➔ GI losses (vomiting, diarrhea)
  - ➔ Cutaneous losses (burns, Stevens-Johnson syndrome)
  - ➔ Hemorrhage
  - ➔ Pancreatitis

  Patients present with dehydration, Low JVP, tachycardia, low BP, no edema.
  Treatment: Treat the underlying cause, IV fluid
- **Decreased cardiac output:**
  - ➔ Heart failure
  - ➔ Pulmonary embolus
  - ➔ Acute myocardial infarction
  - ➔ Severe valvular heart disease
  - ➔ Abdominal compartment syndrome (tense ascites)

  Patients present with edema
  Treatment: diuretics, drugs to elevate blood pressure

Post-renal AKI: (least common cause of AKI)

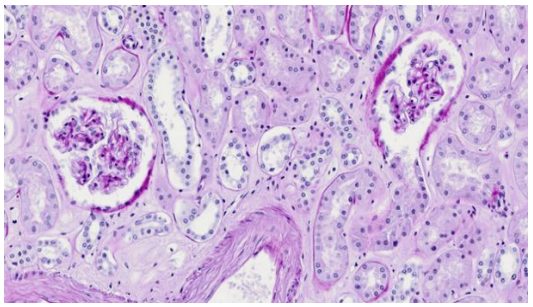
Dx: by US, Rx: treat the underlying cause.

Ureteric obstruction (**Uncommon**, it must be bilateral to cause renal failure)	Bladder neck obstruction	Urethral obstruction

- Stone disease
- Tumor
- Fibrosis
- Ligation during pelvic surgery.
Patients may present with anuria, flank pain, normal Vital signs, hematuria in case of tumor or stones
	- Benign prostatic hypertrophy (BPH)
	- Cancer of the prostate
	- Neurogenic bladder
	- Drugs:
	  - Tricyclic antidepressants
	  - Ganglion blockers
	- Bladder tumor
	- Stone disease
	- Hemorrhage or clot.
		- Secondary to enlarged prostate (BPH) is the most common cause of post-renal AKI
		- Strictures
		- Tumors

Renal AKI:

It can be Tubular, Interstitial or Glomerular



Normal kidney histology (1.tubules 2.glomerulus, and 3.interstitium.)

A) Tubular injury: Acute Tubular Necrosis (ATN)

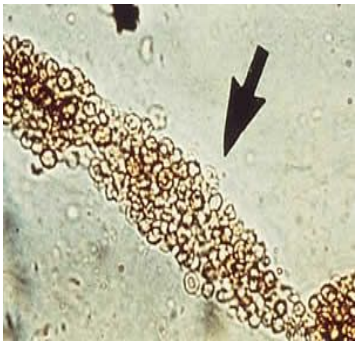
- **Ischemia** (most common cause):
  - ➔ Hypotension (pre-renal at first then it becomes renal)
  - ➔ Sepsis
  - ➔ Prolonged pre-renal state
  - ➔ **Atheroembolic ARF:**
    - Creatinine peaks 1-2 weeks post-procedure.
    - **Associated with:** Emboli of fragments of atherosclerotic plaque from aorta and other large arteries.
    - **Risk factors:** Commonly occur after intravascular procedures or cannulation (cardiac cath, CABG, AAA repair, etc.)
    - **Diagnose:** By history, physical findings (evidence of other embolic phenomena-CVA, ischemic digits, "blue toe" syndrome, etc), absent pulses, livedo reticularis, low serum C3 and C4, peripheral eosinophilia, eosinophiluria.
    - **Treatment:** Supportive treatment, poor prognosis.
- Nephro**toxins**: we don't think that specific causes are of highly importance in our level, so just read through it.

Heme pigment	Crystals	Drugs
- Rhabdomyolysis: skeletal muscle breakdown → release of muscle myoglobin into bloodstream → toxic to kidneys→ AKI - Intravascular hemolysis	- Tumor lysis syndrome - Seizures - Ethylene glycol poisoning - Megadose vitamin C - Acyclovir (insoluble in urine) - Indinavir - Methotrexate	- Aminoglycosides - Amphotericin B - Pentamidine - Lithium - Cisplatin - Ifosfamide - Radiocontrast agents

- **Diagnosis of ATN :** By history, FENa (>2%) "FENa = fractional excretion of Na" sediment with coarse granular casts.
- **Treatment of ATN** is supportive care:
  - ➔ Maintenance of euvolemia (with diuretics, IVF, as necessary).
  - ➔ Avoidance of hypotension.
  - ➔ Avoidance of nephrotoxic medications (including NSAIDs and ACE-I).
  - ➔ Dialysis, if necessary.

  80% will recover, if initial insult can be reversed.

Muddy brown granular casts of ATN



Comparison between prerenal and acute tubular necrosis:

	Pre renal	ATN
Urea/ Creatinine ration	>20:1	10-15:1
Urine	Normal	**Muddy brown casts**
Urine Osmolality	> 500	<350
Urine Na	<20	>20
Fractional excretion of Na	<1 %	> 1%

Fractional excretion of Na:

$$FENa = \frac{sodium\ urinary \times creatinine\ plasma}{sodium\ plasma \times creatinine\ urinary} \times 100 = \frac{UNa \times PCr}{PNa \times UCr} \times 100$$

- When FENa less than 1% → pre-renal state due to
  - ➢ Contrast nephropathy. exception of other nephrotoxins
  - ➢ Acute GN
  - ➢ Myoglobin induced ATN
- When FENa more than 1% → intrinsic induced ATN

B) Interstitial injury : Acute Interstitial Nephritis (AIN):

- **Causes of AIN:**
  - ➔ Drugs (most commonly cause) eg. allergic interstitial nephritis
  - ➔ Infection
  - ➔ Systemic diseases.
- **Diagnosis of AIN:**
  - ➔ History of systemic disease known to be associated with AIN
  - ➔ Skin rash
  - ➔ Esinophilia
  - ➔ WBC cast in urine
  - ➔ Eosinophiluria not common
  - ➔ Renal biopsy
- **Treatment of AIN:**
  - ➔ Remove offending agent
  - ➔ Conservative
  - ➔ May use steroids

C) Glomerular injury[1] [2]: Acute Glomerulonephritis:

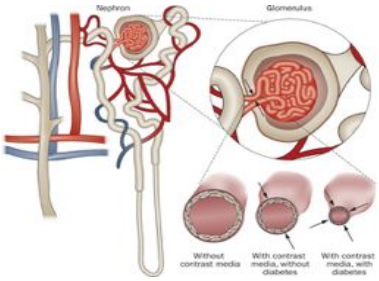
Mainly caused by **acute glomerulonephritis GN.** If the presentation is Rapidly progressive GN:

- **Anti-GBM antibody Immune complex:**
  - ➔ Post-infectious. (streptococcal infection)
  - ➔ Connective tissue disease
    - Lupus nephritis
    - Henoch-Schönlein purpura.
  - ➔ Membranoproliferative glomerulonephritis (MPGN)
- **Pauci-immune** (Vasculitis):
  - ➔ Wegener granulomatosis (WG)
  - ➔ Microscopic polyangiitis (MPA)
  - ➔ Churg-Strauss syndrome
- **Clinical feature:**
  - ➔ Symptoms and signs of systemic disease
  - ➔ Non specific: lower limb swelling, hematuria, frothy urine
  - ➔ Symptoms and signs of ESRD
- **Treatment:**
  - ➔ General: **supportive** therapy
  - ➔ Disease specific: Steroid - Immunosuppressive agents - Plasmapheresis

D)Other causes of renal AKI:

Contrast nephropathy:

- 12-24 hours post exposure, peaks in 3-5 days
- Non-oliguric, FENa <1%, even tho it's a nephrotoxin.
- **Risk Factors:** CKD, Older age, Hypovolemia ,DM,CHF
- **Prevention:** Alternative procedure if feasible
- **Treatment:**
  - 1/2 NS 1 cc/kg/hr 12 hours pre/post
  - N-acetyle cystein 600 BID pre/post (4 doses)
  - Monitoring of urine output, Creatinine and lytes



[1] More details in Glomerular diseases lecture

[2] 1-Anti–glomerular basement membrane (GBM) disease (Goodpasture syndrome).
2- Anti–neutrophil cytoplasmic antibody-associated glomerulonephritis (ANCA-associated GN):
(Wegener granulomatosis, Churg-Strauss syndrome, microscopic polyangiitis)
3- Immune complex GN (lupus, postinfectious, cryoglobulinemia, primary membranoproliferative glomerulonephritis)

Diagnosis of Acute Kidney Injury

Diagnostic approach in AKI:

- The first thing to do is to determine the **duration** of renal failure. **A baseline Creatinine** level provides this information.
- The second task is to **determine** whether AKI is due to **prerenal, renal, or postrenal** cause. This is done via a combination of **history,** physical **examination**, and **laboratory** findings.

Just go through this table quickly, if you don't have time for it skip it and check the lab findings.

In History and physical examination	Investigations
- Signs and symptoms resulting of <u>primary disease</u>: ❖ Signs of **volume depletion** and CHF suggest a **prerenal** etiology. ❖ Signs of an **allergic reaction** (rash) suggest acute **interstitial nephritis** (an intrinsic renal etiology). ❖ A **suprapubic mass, BPH**, or **bladder dysfunction** suggests a **postrenal** etiology. **- Signs and symptoms resulting from loss of kidney function:** ❖ Decreased or no urine output, flank pain, edema, hypertension or discolored urine ❖ Weakness ❖ Easy fatigability due to anemia ❖ Anorexia ❖ Vomiting, mental status changes or seizures **- Systemic symptoms:** ❖ Fever ❖ Arthralgias ❖ Pulmonary lesions **- Asymptomatic:** ➔ Elevations in the plasma creatinine. ➔ Abnormalities on urinalysis. **- Medication review** (look for **toxic drugs** in hx)	- **Blood urea nitrogen and serum creatinine ratio:** The best initial test is the BUN and creatinine. ➔ If the BUN:creatinine ratio is above 20:1 the etiology is either **prerenal or postrenal** damage of the kidney. ➔ **Intrinsic renal disease** has a ratio closer to 10:1. - CBC, peripheral smear and serology. - Urine electrolytes. - Urinalysis: unremarkable in pre and post renal causes. - Serology: ANA, ANCA, Anti DNA, HBV, HCV, Anti GBM, cryoglobulin, CK, urinary Myoglobin. - Urine chemistry (FENa, osmolality, urine Na+, urine Creatinine) - Renal ultrasound (to rule out obstruction) - **Renal sonogram is the best initial imaging test** without contrast. (Contrast should be avoided in renal insufficiency).

The lab findings of pre & post renal are the same , but there are other different findings you should pay attention to, such as:

Pre-renal	Post-renal
Clear history of hypoperfusion or hypotension	- Renal ultrasound to identify the area of obstruction commonly would show dilated collecting system (hydronephrosis). - Distended bladder or massive release of urine after inserting catheter.

★ This is very helpful to sum it all up.

Lab findings in AKI					
Etiology	**Pre-renal**	**Post-renal**	**Renal**		
Signs	Discussed in the Diagnosis of ARI		**ATN** **Hypovolemia , hypotension**	**AIN** **Skin rash**	**AGN** **Presentation of primary disease**
Urinalysis (urine sediment)	Hyaline casts	-	"Muddy brown" casts	WBCs casts, Eosinophils Hansel stain for Eosinophils	RBCs casts,RBCs
BUN/Cr ratio	> 20:1		< 20:1 (10:1)		
FENa	<1%		>2% - 3%		
Urine osmolality	>500 mOsm/kg		< 350 mOsm/kg	>350 variable	
Urine sodium	< 20 mEq/L		> 20 mEq/L	variable	

★ **Casts** are very **useful if found**, but they are rarely present.

Treatment of Acute Kidney Injury

Treatment		
Pre-renal	**Renal**	**Post-renal**
Treat underlying disorder - Give Normal Saline to maintain euvolemia and restore BP. - Important to stop antihypertensive medications. - Eliminate any offending agent NSAID or ACEI.	**Eliminate the underlying cause:** -Nephrotoxicity by drugs or Myoglobin released secondary to **rhabdomyolysis** -Ischemia **(most common)** **If oliguric a trial of diuretic (furosemide) may help to increase urine flow**	**Relieving the obstruction by catheter** You must secure an IV line in order to replace the fluid that the patient will urinate. If you did not do so, the patient would lose lots of fluids and would go into hypovolemic shock.

*Normal saline is not given for patients with ascites or edema.

Complications of AKI:

- ECF volume expansion → Pulmonary edema
- Metabolic:
  - ➔ Hyperkalemia.
  - ➔ Metabolic acidosis.
  - ➔ Hypocalcemia.
  - ➔ Hyponatremia
- Uremia
- Infections: a common & serious complications of AKI (occurs in 50% to 60% of cases)
  - ➔ Pneumonia
  - ➔ UTI
  - ➔ Wound infection
  - ➔ Sepsis.

Dialysis Triggers:

If there is a life-threatening symptom:

- Symptoms of uremia (uremic pericarditis, encephalopathy, etc.)
- Uremic pericarditis.
- Refractory volume overload
- Refractory hyperkalemia
- Refractory metabolic acidosis

Differentiating Acute Kidney Injury vs Chronic Kidney Disease:

	Acute	Chronic
History	Short: Days-week	Long: Month-years
Haemoglobin	Normal	Low
Renal size	Normal	Reduced Except diabetes and amyloidosis
Creatinine	Increase, Acute reversible	Chronic irreversible

Important cases from the doctor slides

First of all, whenever elevated creatinine is detected, you should identify whether it's acute, chronic or acute on top of chronic? Based on patient history. Then distinguish the cause (renal, pre or post-renal)

Case study 1:

50 years old Saudi male status post Right hemicolectomy 6 hours ago for colon cancer intra operative course complicated by bleeding and hypotension required 6 units of blood transfusion urine output decreased significantly serum creatinine 285µmol/L?

- **What other information you need to know?** Check patient's anaesthesia history.

- He is Previously healthy, And urine output for the last 3 hours is <10 cc and dark colour
- **PE:** Pulse 134/min tachycardia, BP 80/55 hypotensive, temperature 37°C normal, low JVP, normal CVS, respiratory and abdominal examination.
- **CBC:** Hb decreased, WBC increased.
- **Urinalysis:** Dark, low gravity (diluted urine indicate non-functional tubules) with protein and granular cast.

Test	Value	Normal values
Creatinine	350 µmol/L	62-115 µmol/L
Urea	29 mmol/L	2.5-6.4 mmol/L
Potassium	6.2 mmol/L	3.5-5.1 mmol/L
Sodium	137 mmol/L	135-145 mmol/L
Bicarbonate	16 mmol/L	22-26 mmol/L

- **What is your diagnosis?** Acute Kidney Injury
- **Where is the etiology?** Renal
- **Diagnosis:** Acute Kidney Injury secondary to Acute tubular necrosis due to shock
- **Treatment:** maintain the blood volume, avoid the cause, monitor the patient.

Case study 2:

75 years old female, known to have DM II & HTN, Presented with nausea, vomiting and diarrhea for 3 days, she is on Insulin and lisinopril.

- **PE**: Pulse 95/min normal, BP 112/67 mmHg normal, temperature 37°C normal, low JVP, dry mucus membrane.normal CVS, respiratory and abdominal examination.
- **CBC:** ↑ WBC, normal hemoglobin and platelet.
- **Urine dipstick:** Shows dark urine with protein.

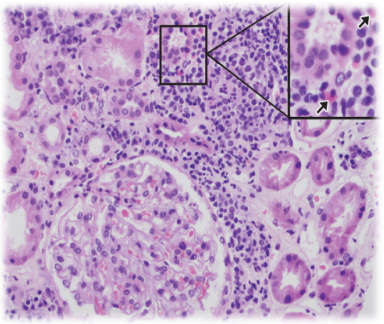
Test	Value	Normal values
Creatinine	154 µmol/L	62-115 µmol/L
Urea	23 mmol/L	2.5-6.4 mmol/L
Potassium	4.3 mmol/L	3.5-5.1 mmol/L
Sodium	137 mmol/L	135-145 mmol/L
Bicarbonate	20 mmol/L	22-26 mmol/L

- **What is your diagnosis?** Acute Kidney Injury.
- **What is the etiology of AKI?** Pre renal (dehydration)
- **What do you expect to find in urine analysis?** Normal
- **What do you expect urinary Na, osmolality?**

Urinary Na<10 ,Osmolality > 300 ,Fractional excretion of Na <1%

- **Treatment?** IV fluid

Case study 3:



19 years old girl known to have: Inflammatory bowel disease,
Referred for evaluation of high serum creatinine 320 µmol/l,
Creatinine (baseline 90 µmol/l) July 2015,
Creatinine (160 µmol/l) June 2017
PE: Pulse 95/min, BP 123/67 mmHg, temperature 37 C normal,normal JVP, normal CVS, respiratory and abdominal examination, maculopapular rash all over the body.
CBC: Normal Hb and platelet level, elevated WBC count mainly eosinophils.
Urinalysis: Dark urine with WBC casts

Test	Value	Normal values
Creatinine	123 µmol/L	62-115 µmol/L
Urea	10 mmol/L	2.5-6.4 mmol/L
Potassium	4.3 mmol/L	3.5-5.1 mmol/L
Sodium	137 mmol/L	135-145 mmol/
Bicarbonate	22 mmol/L	22-26 mmol/L

- **What is your diagnosis?** Acute Kidney Injury in top of chronic secondary to interstitial nephritis
- **What is the treatment of this condition?** Look for offending agent (most likely because of IBD) - Steroid

Case study 4:

19 years old Saudi male, status post road traffic accident seven months ago, bedridden, on folly's catheter, you have been called to see the patient because of high serum creatinine is 198 µmol/l
Baseline creatinine 45 µmol/l two days ago, Urine output 1.2 L/day
PE: Pulse 65/min normal, BP 124/67 mmHg, temperature 37.5°C. normal JVP, normal CVS, respiratory and abdominal examination.
CBC: Normal.
Urinalysis: Dark urine.

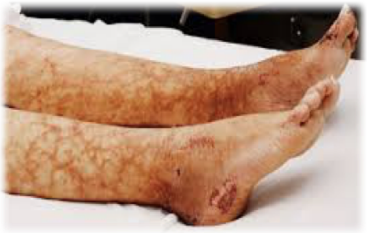
Test	Value	Normal values
Creatinine	198 µmol/L	62-115 µmol/L
Urea	16 mmol/L	2.5-6.4 mmol/L
Potassium	3.9 mmol/L	3.5-5.1 mmol/L
Sodium	137 mmol/L	135-145 mmol/
Bicarbonate	23 mmol/L	22-26 mmol/L

- **What is your diagnosis?** Acute Kidney Injury.
- **What is the etiology of AKI?** Post renal (obstruction) because of wrong catheter.
- **Treatment?** Remove the wrong catheter.

Case study 5:

76 years old man Known to have: Long standing diabetes and hypertension, Ischemic heart disease. Presented with acute chest pain and shortness of breath diagnosed to have Acute coronary syndrome, underwent cardiac catheterization

Baseline creatinine 120 , 12 days later creatinine has increased to 560 with oliguria



PE: Pulse 98/min normal,BP 146/67 mmHg HTN, temperature 37.5°C. Normal JVP, skin lesion over lower limbs and absent dorsalis pedis and posterior tibial arteries, black toes bilaterally, normal CVS, respiratory examination shows bilateral basal crackles, Abdominal examination: soft and lax.

Test	Value	Normal values
Creatinine	560 µmol/L	62-115 µmol/L
Urea	26 mmol/L	2.5-6.4 mmol/L
Potassium	5.7 mmol/L	3.5-5.1 mmol/L
Sodium	134 mmol/L	135-145 mmol/
Bicarbonate	13 mmol/L	22-26 mmol/L

- **What is your diagnosis?** Acute kidney injury in top of chronic
- **What your differential diagnosis?**
  - Atheroembolic disease
  - Contrast induced AKI (not after 12 days!) it could be correct if it's 2 days or less.

Case study 6:

34 years old man, Presented with lower limb swelling and SOB for 2 week and fatigue. Found to have high Cr.
PE: Pulse 88/min normal, BP 167/94 mmHg HTN. temperature 37.1°C, normal JVP, bilateral lower limb edema. Normal CVS, respiratory examination. abdominal examination soft and lax.
CBC: Normal,
Urinalysis: Yellow urine with RBC casts.

Test	Value	Normal values
Creatinine	245 µmol/L	62-115 µmol/L
Urea	17 mmol/L	2.5-6.4 mmol/L
Potassium	4.9 mmol/L	3.5-5.1 mmol/L
Sodium	139 mmol/L	135-145 mmol/
Bicarbonate	17 mmol/L	22-26 mmol/L

- **What is your diagnosis?** Renal Acute kidney injury: Most likely glomerulonephritis
- **How would you investigate this patient further?**
  - Blood urea nitrogen and serum creatinine.
  - CBC, peripheral smear, and serology.
  - Urinalysis, 24 hours urine collection for proteins.
  - Urine electrolytes.
  - U/S kidneys.
  - Serology: ANA,ANCA, Anti DNA, HBV, HCV, Anti GBM, cryoglobulin, CK, urinary Myoglobulin.
  - Kidney biopsy

Cases

1) A 76-year-old man presents to the emergency room. He had influenza and now presents with diffuse muscle pain and weakness. His past medical history is remarkable for osteoarthritis for which he takes ibuprofen, and hypercholesterolemia for which he takes lovastatin. Physical examination reveals blood pressure of 130/90 with no orthostatic change. The only other finding is diffuse muscle tenderness. Laboratory data include:
BUN: 30 mg/dL, Creatinine: 6 mg/dL, K: 6.0 mEq/L, Uric acid: 18 mg/dL, Ca: 6.5 mg/dL, PO4: 7.5 mg/dL
UA: large blood, 2+ protein. Microscopic study shows muddy brown casts and 0 to 2 rbc/hpf (red blood cells/high power field).
Which of the following is the most likely diagnosis?
a. Nonsteroidal anti-inflammatory drug-induced acute kidney injury (AKI)
b. Volume depletion
c. Rhabdomyolysis-induced acute kidney injury
d. Urinary tract obstruction
e. Hypertensive nephrosclerosis

2) A 73-year-old man undergoes abdominal aortic aneurysm repair. The patient develops hypotension to 80/50 for approximately 20 minutes during the procedure according to the anesthesia record. He received 4 units of packed red blood cells. Postoperatively, his blood pressure is 110/70, heart rate is 110, surgical wound is clean, and a Foley catheter is in place. Over the next 2 days his urine output slowly decreases. His creatinine on post-op day 3 is 3.5 mg/dL (baseline 1.2). His sodium is 140 mEq/L, K 4.6 mEq/L, and BUN 50 mg/dL. Hemoglobin and hematocrit are stable. Urinalysis shows occasional granular casts but otherwise is normal. Urine sodium is 50 mEq/L, urine osmolality is 290 mosmol/L, and urine creatinine is 35 mg/dL. The FeNa (fractional excretion of sodium) based on these data is 3.5.
What is the most likely cause of this patient's acute renal failure?
a. Acute interstitial nephritis
b. Acute glomerulonephritis
c. Acute tubular necrosis
d. Prerenal azotemia
e. Contrast induced nephropathy

3) A patient is admitted to the hospital with a nursing-home–acquired pneumonia. His blood pressure is normal and the extremities well perfused. Admission creatinine is 1.2 mg/dL. UA is clear. The patient is treated on the floor with piperacillin/tazobactam and improves clinically. On the fourth hospital day, the patient notes a nonpruritic rash over the abdomen. The creatinine has risen to 2.2 mg/dL. The urinalysis shows 2+ protein, 10 to 15 WBC/hpf, and no casts or RBCs.
Which of the following is the most likely diagnosis?
a. Prerenal azotemia because of intravascular volume depletion
b. Ischemia-induced acute tubular necrosis
c. Nephrotoxin-induced acute tubular necrosis
d. Acute interstitial nephritis
e. Postrenal azotemia because of obstructive uropathy
f. Postinfectious glomerulonephritis

4) A 62-year-old man is admitted with pneumonia and severe sepsis. Vasopressors are required to maintain peripheral perfusion, and mechanical ventilation is needed because of ARDS. Admission creatinine is 1.0 mg/dL but rises by the second hospital day to 2.2 mg/dL. Urine output is 300 cc/24 h. UA shows renal tubular epithelial cells and some muddy brown casts. The fractional excretion of sodium is 3.45.
Which of the following is the most likely diagnosis?
a. Prerenal azotemia because of intravascular volume depletion
b. Ischemia-induced acute tubular necrosis
c. Nephrotoxin-induced acute tubular necrosis
d. Acute interstitial nephritis
e. Postrenal azotemia because of obstructive uropathy
f. Postinfectious glomerulonephritis

5) A 76-year-old man is admitted with pneumonia. He has a history of diabetes mellitus. Admission creatinine is 1.2 mg/dL. He responds to ceftriaxone and azithromycin. He develops occasional urinary incontinence treated with anticholinergics, but his overall status improves and he is ready for discharge by the fifth hospital day. On that morning, however, he develops urinary hesitancy and slight suprapubic tenderness. The creatinine is found to be 3.0 mg/dL; UA is clear with no RBCs, WBCs, or protein.
Which of the following is the most likely diagnosis?
a. Prerenal azotemia because of intravascular volume depletion
b. Ischemia-induced acute tubular necrosis
c. Nephrotoxin-induced acute tubular necrosis
d. Acute interstitial nephritis
e. Postrenal azotemia because of obstructive uropathy
f. Postinfectious glomerulonephritis

Answers

1) C. Rhabdomyolysis-induced AKI is characterized by hyperkalemia, hyperphosphatemia, and hyperuricemia, all caused by release of intracellular muscle products. The high phosphorus level causes hypocalcemia. The BUN/creatinine ratio, normally 10/1, is reduced because of release of muscle creatine, which is converted to creatinine. The load of creatinine to be excreted by the failing kidney therefore exceeds the urea load, which is little changed. The presence of "blood" on the dipstick determination is caused by myoglobinuria. The dipstick registers red blood cells,hemoglobin (eg, from intravascular hemolysis), and myoglobin as "blood." Trauma, medications (especially statins), infectious processes (influenza, sepsis), and extreme muscular exertion (seizures, exertional heat stroke) are common causes. All nonsteroidal agents may cause decreased renal function. Usually this is attributed to decreased blood flow less commonly, to drug-induced interstitial nephritis. The laboratory abnormalities in this case do not suggest decreased blood flow or interstitial nephritis. However, stopping the ibuprofen would be prudent. The absence of orthostatic hypotension makes the diagnosis of volume depletion very unlikely. Nothing on history, physical examination, or electrolyte abnormalities suggests obstruction.
However, in a 76-year-old man, a renal sonogram to rule out occult obstruction would be reasonable. Hypertensive nephrosclerosis causes chronic rather than acute renal insufficiency and would not account or the electrolyte abnormalities.

2) C. This patient with known atherosclerotic disease and a minimally elevated baseline creatinine has suffered a brief period of hypotension and hence renal hypoperfusion. By calculating the fractional excretion of sodium (FeNa) using the data that have been provided (FeNa = Urine sodium X plasma creatinine X 100/plasma sodium X urine creatinine), one can feel more comfortable distinguishing between prerenal azotemia and acute tubular necrosis. If the FeNa is less than 1, the patient likely has prerenal azotemia. If it is over 2, it is more likely that the patient has acute tubular necrosis or some other intrinsic renal disease. The clinical scenario of this patient, along with the high FeNa and the granular (sometimes called "muddy brown") casts in the urine, all point toward acute tubular necrosis (ATN). Interstitial nephritis more commonly occurs in patients following exposure to certain medications and typically is associated with white blood cells (especially eosinophils) in the urine. This patient may have had recent exposure to a contrast agent, but that has not been mentioned.

Glomerulonephritis is unlikely due to the hypotension and the lack of red cell casts on the urinalysis.

3)D, 4)B and 5)E

Acute kidney injury in adults usually occurs during hospitalization for other illness. The history (in particular, exposure to nephrotoxins including intravenous contrast agents), physical examination (in particular, assessment of volume status and search for allergic manifestations such as skin rash), and urine studies will usually establish the diagnosis. The fractional excretion of sodium may demonstrate renal underperfusion if this is not clear from the clinical setting. If the kidneys are underperfused from volume depletion, third space losses, or poor cardiac output, the kidneys will retain salt and water, and the fractional excretion of sodium (FENa) will be low. In the cases presented here, the clinical setting suggests the diagnosis. Interstitial nephritis typically occurs as an allergic reaction to antibiotics, particularly beta-lactams and sulfa derivatives. So-called tubular proteinuria is modest (< 1g/24 h), albuminuria is minimal, and the nephrotic syndrome does not occur. Pyuria and eosinophiluria are usually present. The commonest cause of acute renal failure is acute tubular necrosis. The FENa is usually above two and muddy brown cases may be present on the urinalysis. Ischemia (often owing to sepsis) and nephrotoxins are the usual causes.

Obstructive uropathy can occur acutely, particularly in the setting of bladder outlet obstruction (BPH) or neurogenic bladder (as can occur in diabetes). The patient will often have difficulty voiding and the urinalysis will be unremarkable. Complete anuria or fluctuations from oliguria to polyuria also suggest the diagnosis. Bladder catheterization or renal sonography are diagnostic. Glomerulonephritis rarely occurs during hospitalization for unrelated acute illness.

Summary

	Pre-renal AKI most common cause of AKI	
Etiology	**Volume depletion**	**Decreased cardiac output**
Causes	Renal losses due to: - Diuretics. - Polyuria	Heart failure.
	GI losses due to: - Vomiting. - Diarrhea.	Pulmonary embolus.
	Cutaneous losses due to: - Burns. - Stevens-Johnson syndrome.	Acute myocardial infarction.
	Hemorrhage.	Severe valvular heart disease.
	Pancreatitis.	Abdominal compartment syndrome (tense ascites).
Presentation	Dehydration, tachycardia, Low JVP, Low BP, **No** edema.	Patient present with **edema.**
Treatment	Treat the underlying cause, IV fluid.	Diuretics, Drugs to elevate blood pressure.

	Post-renal AKI		
Etiology	**Ureteric obstruction** uncommon, because must be bilateral to cause renal failure	**Bladder neck obstruction**	**Urethral obstruction**
Causes	➔ Stone disease. ➔ Fibrosis. ➔ Ligation during pelvic surgery.	➔ Benign prostatic hypertrophy (BPH). ➔ Cancer of the prostate. ➔ Neurogenic bladder. ➔ Drugs: - Tricyclic antidepressants. - Ganglion blockers. ➔ Bladder tumor. ➔ Stone disease ➔ Hemorrhage or clot.	➔ Strictures ➔ Tumors ➔ 2nd to enlarged prostate (BPH) is the most common cause of Post-renal AKI
Presentation	Patient may present with anuria, flank pain, normal Vital signs. Hematuria in case of tumor or stones	-	-
Diagnosis	Ultrasound		
Treatment	Treat the underlying cause		

	Renal AKI			
Etiology	**Tubular injury:**		**Interstitial:**	**Glomerular:**
	(Acute tubular necrosis ATN)		**Acute Interstitial Nephritis (AIN)** most commonly caused by drugs	**Acute Glomerulonephritis:** **Mainly GN causes AKI if the presentation is Rapidly progressive GN**
	Ischemia most common cause	**Nephrotoxin**		
Causes	**1)Hypotension** (pre-renal at first then it becomes renal) **2)Sepsis.** **3)Prolonged pre-renal state.**	**1)Heme pigment:** ➔ Rhabdomyolysis ➔ Intravascular hemolysis **2) Crystals:** ➔ Tumor lysis syndrome ➔ Seizures ➔ Ethylene glycol poisoning ➔ Megadose vitamin C ➔ Acyclovir ➔ Indinavir ➔ Methotrexate **3)Drugs:** ➔ Aminoglycosides ➔ Amphotericin B ➔ Pentamidine ➔ Lithium ➔ Cisplatin ➔ Ifosfamide ➔ Radiocontrast agents	**1)Drugs** **2)Infection** **3)Systemic diseases.**	**1)Anti-GBM antibody Immune complex:** ➔ Post-infectious. ➔ MPGN. ➔ Connective tissue disease: A) Lupus nephritis. B) Henoch-Schönlein C) C)purpura. **2) Pauci-immune:** ➔ Wegener granulomatosis (WG) ➔ Microscopic polyangiitis (MPA) ➔ Churg-Strauss syndrome
Clinical feature Or Diagnosis	➔ By history ➔ FENa (>2%) ➔ Sediment with coarse granular casts.		➔ Hx of systemic disease known to be associated with AIN. ➔ Skin rash. ➔ Esinophilia. ➔ WBC cast (urine). ➔ Eosinophilia not common. ➔ Renal biopsy.	Clinical feature: 1) Symptoms and signs of systemic disease. 2) Non specific: ➔ Lower limb swelling ➔ Hematuria ➔ Frothy urine 3) Symptoms and signs of ESRD.
Treatment	**Supportive care:** ➔ Maintenance of euvolemia (with diuretics, IVF as necessary). ➔ Avoidance of hypotension. ➔ Avoidance of nephrotoxic medications (including NSAIDs and ACE-I). ➔ Dialysis, if necessary: ➔ 80% will recover, if initial insult can be reversed.		➔ Remove offending agent ➔ Conservative ➔ May use steroids	1) General “supportive” 2) Disease specific: ➔ Steroid ➔ Immunosuppressive agents ➔ Plasmapheresis

	Other causes of renal AKI		
	Contrast nephropathy	**Rhabdomyolysis:** **ATN → Nephrotoxin**	**Atheroembolic ARF:** **ATN → Ischemia**
Definition	➔ 12-24 hours post exposure, peaks in 3-5 days ➔ Non-oliguric ➔ FENa <1%!!	Skeletal muscle breakdown → Release of muscle myoglobin → Bloodstream → Toxic to kidneys → AKI	➔ Creatinine peaks 1-2 weeks post-procedure. ➔ Associated with emboli of fragments of atherosclerotic plaque from aorta and other large arteries.
Risk factors	➔ CKD ➔ Older age ➔ Hypovolemia ➔ DM ➔ CHF	Skeletal muscle breakdown caused by: ➔ Trauma ➔ Crush injuries ➔ Burns ➔ Prolonged immobility ➔ Seizures ➔ Snake bite ➔ Limb ischemia occasionally after - IABP - Cardiopulmonary bypass	Commonly occurs after intravascular procedures or cannulation: ➔ cardiac cath ➔ CABG ➔ AAA repair, etc.
Diagnosis	-	➔ Serum creatine phosphokinase (CPK) usually > 10,000 ➔ Urine dipstick (+) for blood without RBCs on microscopy ➔ Pigmented granular casts ➔ HypErkalemia ➔ HypOcalcemia ➔ HypEruricemia	by history, physical findings (evidence of other embolic phenomena-CVA, ischemic digits, “blue toe” syndrome, etc), absent pulses, livedo reticularis, low serum C3 and C4, peripheral eosinophilia, eosinophiluria.
Treatment	**Rx:** ➔ 1/2 NS 1 cc/kg/hr 12 hours pre/post ➔ N-acetyle cystein 600 BID pre/post (4 doses) **Prevention:** Alternative procedure if feasible	➔ IV uids ➔ mannitol (osmotic diuretic) ➔ bicarbonate (drives K back into cells).	➔ **Supportive** treatment ➔ **Poor prognosis**