

Approach to Acute Kidney Injury Med 341

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October 2019



Objective

- At the end of this tutorial you will be able to:
 - Define Acute Kidney Injury (AKI)
 - Discuss the epidemiology of AKI
 - Discuss the etiology of AKI
 - Describe the management of AKI
 - Diagnose AKI
 - Treat AKI

Learning methods

☐ Lecture/material review

Interactive case scenarios

Acute Kidney Injury (AKI)

- 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

Acute renal failure (definition)

- ARF in one study was defined as:
 - as a 0.5 mg/dL increase in serum creatinine if the baseline serum creatinine was ≤1.9 mg/dL,
 - an 1.0 mg/dL increase in serum creatinine if the baseline serum creatinine was 2.0 to 4.9 mg/dL, and
 - a 1.5 mg/dL increase in serum creatinine if the baseline serum creatinine was ≥5.0 mg/dl

Acute kidney injury RIFLE definition

	GFR/Creatinine criteria	Urine Output criteria	
R isk	Increase in creatinine x1.5 Or GFR decrease >25%	UO < .5ml/kg/hr for 6hrs	
<i>I</i> njury	Increase in creatinine x 2 Or GFR decrease >50%	UO < .5ml/kg/hr for 12hrs	
F ailure	Increase in creatinine x 3 Or GFR decrease >75%	UO < .3ml/kg/hr for 24 hrs or Anuria for 12hrs	
L oss	Persistent ARF = complete loss of renal function > 4 weeks		
E SRD	End Stage Renal Disease > 3 months		

Am J Kidney Dis. 2005 Dec;46(6):1038-48

AKIN definition:

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

Mehta R et al. Crit Care 2007;11(2):R31 Ostermann et al. Critical Care 2008 **12**:R144

Definition:

"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

Chertow et al. JASN 2005; 16:3365-3370

Acute kidney injury

KDIGO Definition:

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

Acute kidney injury

Incidence:

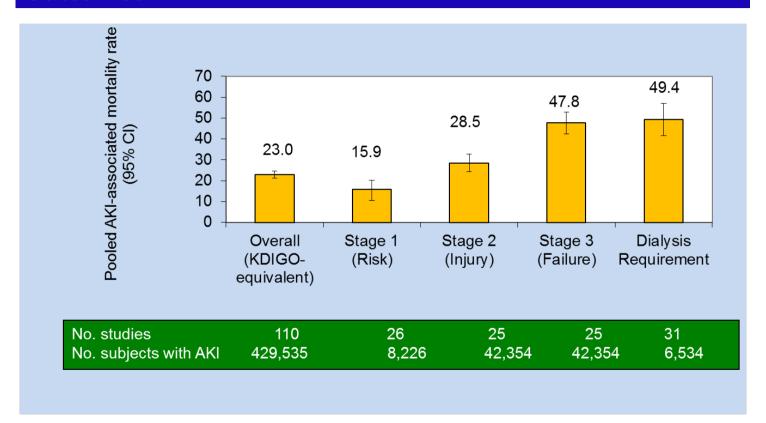


Epidemiology

- It occurs in
 - 5% of all hospitalized patients and
 - -35% of those in intensive care units
- Mortality is high:
 - up to 75–90% in patients with sepsis
 - 35–45% in those without

Acute kidney injury

Outcome:



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	AKII	AKI II	AKI III
	65.6%	19.1%	3.8%	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)	2 d	5 d	8 d	9 d

Ostermann et al, Critical Care 2008;12:R144

CKD risk

Risk of CKD

Increasing evidence that episodes of AKI leave permanent renal damage

Long-term prognosis after AKI requiring RRT"

- 206 ICU patients with RRT for AKI
- □ Single centre in Geneva
- □ 90 day survival: 46%
- ☐ 3 years post ICU:
 - 60/206 (29.1%): alive
 - 25/60 (41.7%): new CKD
 - 9/60 (15%): ESRD, on dialysis

Triverio et al. NDT 2009

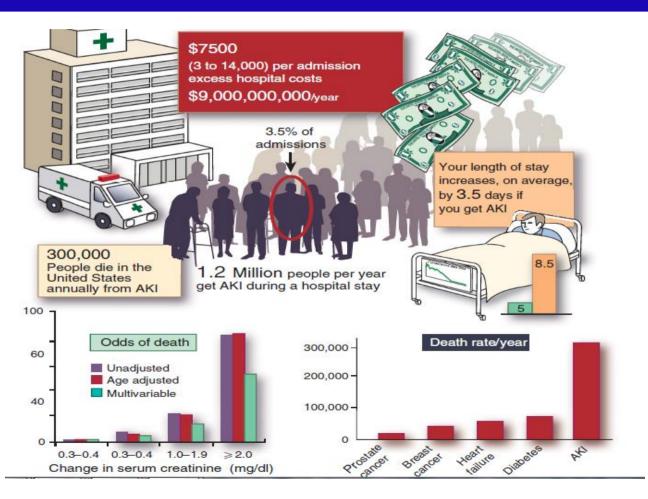
Impact

"Long-term risk of mortality and other adverse outcomes after AKI: A systematic review and meta-analysis"

- 48 studies, 47,017 patients with AKI (varying criteria)
 Length of follow-up: 6 months 17 years
- AKI associated with: increased risk of CKD increased risk of CV event increased long-term mortality

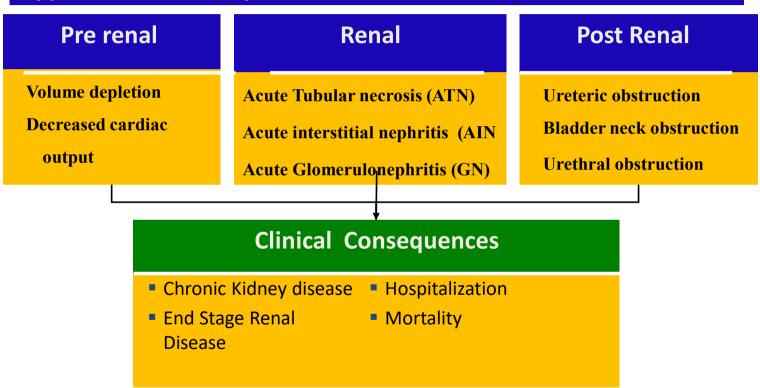
Coca S et al, Am J Kidney D, June 2009

Clinical outcome:

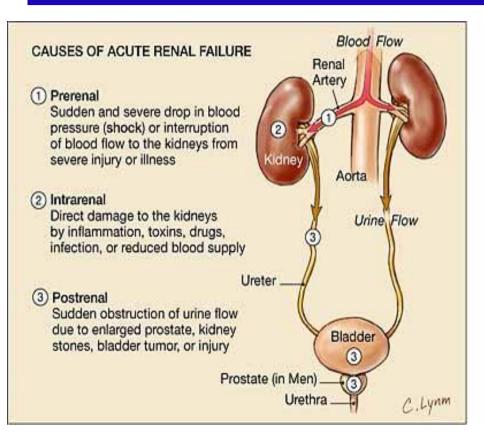


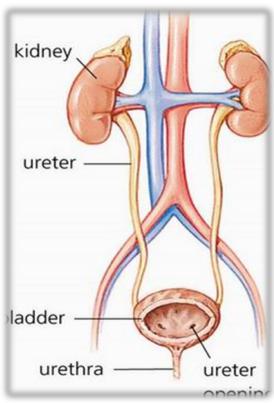
Acute kidney injury

Types and consequences:



Etiology of ARF





Scenario 1

50 years old Saudi male s/p Right hemicoloectomy 6 hours ago for colon cancer intra operative course complicated by bleeding and hypotension required 6 units of blood transfusion urine out put decreased significantly serum creatinine 285µmol/l?

- How would you approach this patient?
- What other information you need to know?

Scenario 1

- Previously healthy
- And urine output for the last 3 hours is <10 cc and dark colour

Scenario 1

Vital Signs	Result	Normal Range
Pulse	134/min	60-100/min
Blood pressure	80/55 mmHg	130/80 mmHg
Temperature	37.0°C	36.6-37.2°C

Jugular venous pressure was low, cold periphery,

Cardiovascular examination:

Normal first and second heart sound no added sound or murmurs.

Respiratory system examination:

Lungs are clear to percussion and auscultation

Abdominal examination:

No tenderness, liver and spleen were not palpable.

Scenario 1

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	22-26 mmol/l

Scenario 1

Complete blood count (CBC)	Result	Normal reference ranges
Hemoglobin	70 g/L	Male: 135-175 g/L (13.5-17.5 g/dl) Female: 120-155 g/L (12-15.5 g/dl)
White cell count	12 x 10* 9/L	4.5-11.0 x 10* 9/L
Platelet count	198 x 10*9/L	140-450 x 10* 9/L

	Result	Normal values
Color	Dark	Amber yellow
Character	clear	clear
PH	6.0 acidic	4.8-8.0
Specific gravity	1.003	1.015-1.025
Protein	+2	(-)
Glucose	(-)	(-)
Red blood cells	1-2 /hpf	(-)
Hemoglobin	Negative	(-)
Pus cells (WBC)	1-2 /hpf	(-)
Epithelial cells	(-)	(-)
Amorphus phosphate	(-)	(-)
Bacteria	(-)	(-)
Granular cast	seen	(-)

Scenario 1

- What is your diagnosis?
 - Acute Kidney Injury
- Where is the etiology?
- Renal?
 - ATN (acute tubular necrosis)
 - AIN (acute interstitial nephritis)
 - GN (glomerulonephritis)
- Diagnosis:
 - Acute Kidney Injury secondary to Acute tubular necrosis due to shock

Acute Tubular Necrosis (ATN)

Ischemia:

Hypotension, sepsis, prolonged pre-renal state

Totoxic

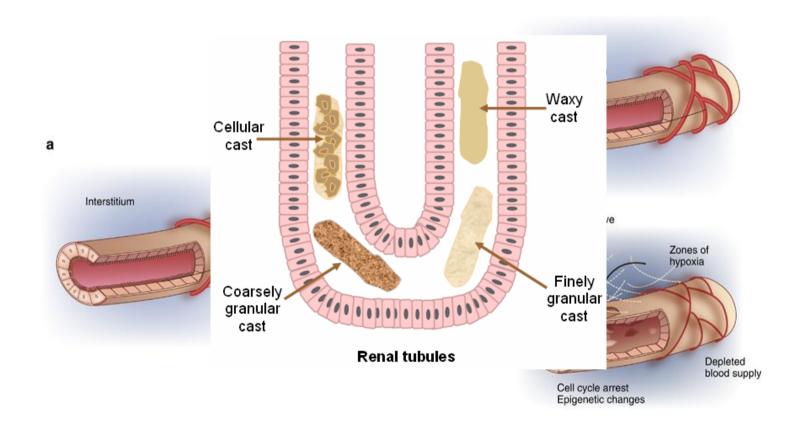
- Heme pigment (rhabdomyolysis, intravascular hemolysis)
- Crystals (tumor lysis syndrome, seizures, ethylene glycol poisoning, megadose vitamin C, acyclovir, indinavir, methotrexate)
- Drugs (aminoglycosides, lithium, amphotericin B, pentamidine, cisplatin, ifosfamide, radiocontrast agents)

<u>Diagnose by history, \uparrow FE_{Na} (>2%)</u> sediment with coarse granular casts,

Treatment 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

Acute tubular necrosis



Acute Kidney Injury Pre renal vs ATN

	Pre renal	Acute Tubular necrosis (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%

$$FENa = \frac{UNa \times PCr}{PNa \times UCr}$$

FENa < 1% (Pre-renal state)

- Contrast nephropathy
- Acute GN
- •Myoglobin induced ATN

FENa > 1% (intrinsic cause of AKI)

Scenario 1

Indication for dialysis in acute kidney injury setting:

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

Scenario 2

75 years old female, known to have:

- DM II
- HTN
- Presented with nausea, vomiting and diarrhea for 3 days
- Medication: Insulin, lisinopril,

Scenario 2

Vital Signs	Result	Normal Range
Pulse	95/min	60-100/min
Blood pressure	112/67 mmHg	130/80 mmHg
Temperature	37.0°C	36.6-37.2°C

Jugular venous pressure was low, dry mucus membrane

Cardiovascular examination:

Normal first and second heart sound no added sound or murmurs.

Respiratory system examination:

Lungs are clear to percussion and auscultation

Abdominal examination:

No tenderness, liver and spleen were not palpable.

Scenario 2

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	22-26 mmol/l

Acute vs Chronic

	Acute	Chronic
History	Short (days-week)	Long (month-years)
Haemoglobin	Normal	Low
Renal size	Normal	Reduced
Serum Creatinine	Acute reversible increase	Chronic irreversible

Scenario 2

Complete blood count (CBC)	Result	Normal reference ranges
Hemoglobin	134 g/L	Male: 135-175 g/L (13.5-17.5 g/dl) Female: 120-155 g/L (12-15.5 g/dl)
White cell count	12 x 10* 9/L	4.5-11.0 x 10* 9/L
Platelet count	198 x 10*9/L	140-450 x 10* 9/L

	Result	Normal values
Color	Dark yellow	Amber yellow
Character	clear	clear
PH	6.0 acidic	4.8-8.0
Specific gravity	1.025	1.015-1.025
Protein	+1	(-)
Glucose	(-)	(-)
Red blood cells	1-2 /hpf	(-)
Hemoglobin	Negative	(-)
Pus cells (WBC)	1-2 /hpf	(-)
Epithelial cells	(-)	(-)
Amorphus phosphate	(-)	(-)
Bacteria	(-)	(-)
Granular cast	(-)	(-)

Scenario 2

- What is your diagnosis?
 - Acute Kidney Injury.
- What is the etiology of AKI?
 - Pre renal (dehydration)
- What do you expect to fined in urine analysis?
 - Normal
- What do you expect urinary Na, osmolality?
 - Urinary Na<10</p>
 - Osmolality > 300
 - Fractional excretion of Na <1%

Scenario 3

19 years old girl

known to have:

- Inflammatory bowel disease
- Referred for evaluation of high
- serum creatinine 320
- Creatinine (base line 90) July 2015
- Creatinine (160) June 2017

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Scenario 3

Vital Signs	Result	Normal Range
Pulse	95/min	60-100/min
Blood pressure	123/67 mmHg	130/80 mmHg
Temperature	37.0°C	36.6-37.2°C

Jugular venous pressure was normal, maculopapular rash all over the body Cardiovascular examination:

Normal first and second heart sound no added sound or murmurs.

Respiratory system examination:

Lungs are clear to percussion and auscultation

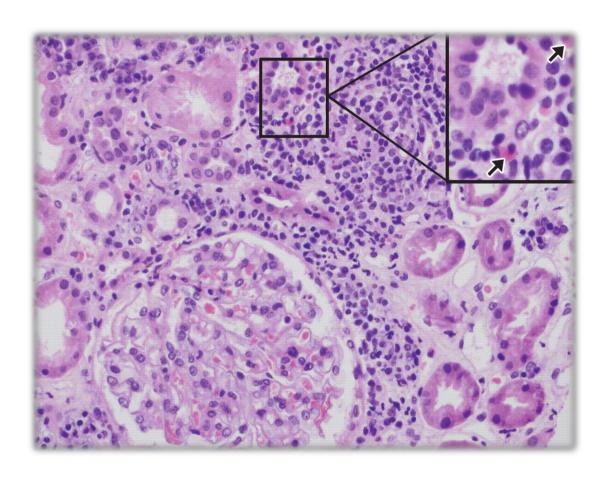
Abdominal examination:

No tenderness, liver and spleen were not palpable.

Complete blood count (CBC)	Result	Normal reference ranges
Hemoglobin	146 g/L	Male: 135-175 g/L (13.5-17.5 g/dl) Female: 120-155 g/L (12-15.5 g/dl)
White cell count	13 x 10* 9/L esinophilia	4.5-11.0 x 10* 9/L
Platelet count	198 x 10*9/L	140-450 x 10* 9/L

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/L
Bicarbonate	22	22-26 mmol/l

	Result	Normal values
Color	Dark yellow	Amber yellow
Character	clear	clear
PH	6.0 acidic	4.8-8.0
Specific gravity	1.025	1.015-1.025
Protein	+1	(-)
Glucose	(-)	(-)
Red blood cells	1-2 /hpf	(-)
Hemoglobin	Negative	(-)
Pus cells (WBC)	30-40 /hpf	(-)
Epithelial cells	(-)	(-)
Amorphus phosphate	(-)	(-)
Bacteria	(-)	(-)
Granular cast	WBC cast	(-)



Scenario 3

What is your diagnosis?

Acute Kidney Injury secondary to interstitial nephritis

What is the treatment of this condition?

- Look for offending agent
- Steroid

Acute Interstitial Nephritis (AIN)

Causes of AIN:

- Drugs:
- Infection:
- Systemic diseases:

Diagnosis of AIN:

- History of systemic disease known to be associated with AIN
- Skin rash
- Esinophilia
- WBC cast (urine)
- Esinophiluria
- Renal biopsy

Treatment of AIN:

- D/c offending agent
- Conservative
- May use steroids

Scenario 4

- 19 years old Saudi male,
 - s/p road traffic accident 7 months ago,bedridden, on folly's catheter

- you have been called to see because of
- high serum creatinine is 198 μmol/l
- Baseline craetinine 45 μmol/l 2 days ago
- Urine out put 1.2 litter/day

What is next?

Scenario 4

Vital Signs	Result	Normal Range
Pulse	65/min	60-100/min
Blood pressure	124/67 mmHg	130/80 mmHg
Temperature	37.5°C	36.6-37.2°C

Jugular venous pressure was normal,

Cardiovascular examination:

Normal first and second heart sound no added sound or murmurs.

Respiratory system examination:

Lungs are clear to percussion and auscultation

Abdominal examination:

no tenderness liver and spleen were not palpable.

Complete blood count (CBC)	Result	Normal reference ranges
Hemoglobin	146 g/L	Male: 135-175 g/L (13.5-17.5 g/dl) Female: 120-155 g/L (12-15.5 g/dl)
White cell count	9 x 10* 9/L	4.5-11.0 x 10* 9/L
Platelet count	178 x 10*9/L	140-450 x 10* 9/L

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/L
Bicarbonate	23	22-26 mmol/l

	Result	Normal values
Color	Dark	Amber yellow
Character	clear	clear
PH	6.0 acidic	4.8-8.0
Specific gravity	1.021	1.015-1.025
Protein	(-)	(-)
Glucose	(-)	(-)
Red blood cells	0 /hpf	(-)
Hemoglobin	Negative	(-)
Pus cells (WBC)	0 /hpf	(-)
Epithelial cells	(-)	(-)
Amorphus phosphate	(-)	(-)
Bacteria	(-)	(-)
Granular cast	(-)	(-)





Causes

Pre renal	Post Renal
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)	Ureteric obstruction Stone disease, Tumor, 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)

Causes

	Renal		
	(ATN)	(AIN)	(GN)
Symptoms	??????	??????	????
Signs	Hypovolemia , hypotension	Skin rash,	Presentation of primary disease
Urine	Muddy brown casts	WBC casts Eosinophils	RBC casts
Urine Osmolality	<350	Variable >350	>350 variable
Urine Na	<20	variable	variable

Acute Tubular necrosis (ATN) Acute interstitial nephritis (AIN) Acute Glomerulonephritis (GN)

Acute Glomerulonephritis (GN)

Causes:

Mainly GN causes AKI if the presentation is Rapidly progressive GN:

Anti-GBM antibody Immune complex

- Post-infectious
- Connective tissue disease:
 - Lupus nephritis Henoch-Schönlein purpura
- MPGN

Pauci-immune

- 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
- Disease specific:
 - Steroid
 - Immunosuppresive agents
 - Plasmapheresis

Scenario 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, 2 days later creatinine has increased to 560 with oliguria

Scenario 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

Scenario 5

Vital Signs	Result	Normal Range
Pulse	98/min	60-100/min
Blood pressure	146/67 mmHg	130/80 mmHg
Temperature	37.5°C	36.6-37.2°C

Jugular venous pressure was normal, skin lesion over lower limbs and absent dorsalis pedia and posterior tibial arteries, black toes bilateraly Cardiovascular examination:

Normal first and second heart sound no added sound or murmurs.

Respiratory system examination:

bilateral basal crackles

Abdominal examination:

soft and lax, liver and spleen were not palpable.



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/L
Bicarbonate	13	22-26 mmol/l

Scenario 5

What is your diagnosis?

Acute kidney injury

What your differential diagnosis?

Athero embolic disease

Contrast induced AKI

Athero embolic AKI

- 1-2 weeks post procedure, creatinine peaks
- Commonly occur after intravascular procedures or cannulation (cardiac cath, CABG, AAA repair, etc.)
- •Associated with emboli of fragments of atherosclerotic plaque

- •Diagnose by history,
 physical findings (evidence of
 other embolic phenomena-CVA, ischemic digits, "blue
 toe" syndrome, absent pulses,
 livedo reticularis,
 low serum C3 and C4,
 peripheral eosinophilia,
 Eosinophiluria
- Treatment is supportive
- ■In general prognosis is poor

Contrast induced AKI

12-24 hours post exposure,

Creatinine peaks in 3-5 days

- Non-oliguric, FE Na <1%!!
- Risk Factors:
 - ■CKD,
 - Older age
 - •Hypovolemia ,DM,CHF

- **■**Treatment /Prevention:
- **Alternative procedure if feasible**
- 1/2 NS 1 cc/kg/hr 12 hours pre/post
- N-acetyle cystein 600 BID pre/post (4 doses)
- Monitoring of urine out put
- Creatinine and lytes

Scenario 6

34 years old man

Presented with lower limb swelling and SOB for 2 week and fatique

Found to have high creatinine

Scenario 6

Vital Signs	Result	Normal Range
Pulse	88/min	60-100/min
Blood pressure	167/94 mmHg	130/80 mmHg
Temperature	37.1°C	36.6-37.2°C

Jugular venous pressure was normal, bilateral lower limb edema Cardiovascular examination:

Normal first and second heart sound no added sound or murmurs.

Respiratory system examination:

Lungs are clear to percussion and auscultation

Abdominal examination:

soft and lax, liver and spleen were not palpable

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/L
Bicarbonate	17	22-26 mmol/l

Complete blood count (CBC)	Result	Normal reference ranges
Hemoglobin	146 g/L	Male: 135-175 g/L (13.5-17.5 g/dl) Female: 120-155 g/L (12-15.5 g/dl)
White cell count	9 x 10* 9/L	4.5-11.0 x 10* 9/L
Platelet count	178 x 10*9/L	140-450 x 10* 9/L

	Result	Normal values
Color	yellow	Amber yellow
Character	clear	clear
PH	6.0 acidic	4.8-8.0
Specific gravity	1.021	1.015-1.025
Protein	(+++)	(-)
Glucose	(-)	(-)
Red blood cells	11 /hpf	(-)
Hemoglobin	Negative	(-)
Pus cells (WBC)	1-2 /hpf	(-)
Epithelial cells	(-)	(-)
Amorphus phosphate	(-)	(-)
Bacteria	(-)	(-)
RBC cast	(+)	(-)

Scenario 6

What is your diagnosis?

Acute kidney injury

Renal: 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

Summary

- Acute kidney injury is a syndrome characterised by the rapid loss of the kidney's excretory function
- Acute kidney injury is common and serious health problem which carry high mortality and morbidity
- Acute kidney injury is amenable to prevention, early detection and treatment