Acute Kidney Injury

Objectives:

- 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

Done by:

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Revised by:

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Lecturer: Dr. Mohammed Al-Ghonaim
Same 436 lecture Slides: Yes

Resources:

- Doctor’s slides - Team 436 - Doctor’s notes - Master the Boards - Step-Up to Medicine
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

**AKI RIFLE definition**

<table>
<thead>
<tr>
<th>GFR/Creatinine criteria</th>
<th>Urine Output criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Risk</strong></td>
<td></td>
</tr>
<tr>
<td>Increase in creatinine x1.5</td>
<td>UO &lt; .5ml/kg/hr for 6hrs</td>
</tr>
<tr>
<td>Or GFR decrease &gt;25%</td>
<td></td>
</tr>
<tr>
<td><strong>Injury</strong></td>
<td></td>
</tr>
<tr>
<td>Increase in creatinine x 2</td>
<td>UO &lt; .5ml/kg/hr for 12hrs</td>
</tr>
<tr>
<td>Or GFR decrease &gt;50%</td>
<td></td>
</tr>
<tr>
<td><strong>Failure</strong></td>
<td></td>
</tr>
<tr>
<td>Increase in creatinine x 3</td>
<td>UO &lt; .3ml/kg/hr for 24 hrs or Anuria for 12hrs</td>
</tr>
<tr>
<td>Or GFR decrease &gt;75%</td>
<td></td>
</tr>
<tr>
<td><strong>Loss</strong></td>
<td>Persistent ARF = complete loss of renal function &gt; 4 weeks</td>
</tr>
<tr>
<td>ESRD</td>
<td>End Stage Renal Disease &gt; 3 months</td>
</tr>
</tbody>
</table>

This just means there were different definitions. Not used anymore.

The kidney’s degree of deterioration in function depends on the degree of kidney failure... If you have severe kidney failure, you will have obvious deterioration of the kidney function, if you have very mild you may not see the deterioration. Also lifespan erythropoietin functions and others needs time to decrease and as we now the lifespan of RBC is 100 to 120 days.
### AKI Stages

<table>
<thead>
<tr>
<th>Stage</th>
<th>Creatinine Criteria</th>
<th>Urine Output</th>
</tr>
</thead>
<tbody>
<tr>
<td>AKI stage I</td>
<td>• 1.5-2 times baseline</td>
<td>• &lt;0.5 ml/kg/h for &gt;6 h</td>
</tr>
<tr>
<td></td>
<td>• OR 0.3 mg/dl increase from baseline (≥ 26.4 μmol/L)</td>
<td></td>
</tr>
<tr>
<td>AKI stage II</td>
<td>• 2-3 times baseline</td>
<td>• &lt;0.5 ml/kg/h for &gt;12 h</td>
</tr>
<tr>
<td>AKI stage III</td>
<td>• 3 times baseline</td>
<td>• &lt;0.3 ml/kg/h for &gt;24 h OR</td>
</tr>
<tr>
<td></td>
<td>• OR 0.5 mg/dl (44 μmol/L) increase if baseline &gt; 4mg/dl (≥ 354 μmol/L)</td>
<td>• Anuria for &gt;12 h</td>
</tr>
<tr>
<td></td>
<td>• OR Any renal replacement therapy given</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• &lt;0.3 ml/kg/h for &gt;24 h</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Anuria for &gt;12 h</td>
<td></td>
</tr>
</tbody>
</table>

**“Acute kidney injury, mortality, length of stay, and costs in hospitalized patients”**

For Creatinine to rise and urine output to decrease after the insult, they take time. But it’s the best that we have. (No early markers)

This is the universal criteria.

26.4 μmol/L was chosen due to its association with increased mortality and to also to achieve standardization.

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  

**KDIGO 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/kg/hour for 6 hours

This is the latest definition

They may come up with a new definition include a marker such as troponin for the MI in the future and we will follow it then

pts admitted to academic medical centre in SF 9,205 pts with >1 creatinine 19,982 results
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

AKI Impact

AKI Incidence

The percentages refer to AKI due to sepsis in hospital. NOT prerenal AKI (e.g., dehydration: hydrate, treat and they’ll be fine.) they aren’t in this category.

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

<table>
<thead>
<tr>
<th>AKI Classification</th>
<th>No AKI</th>
<th>AKI I</th>
<th>AKI II</th>
<th>AKI III</th>
</tr>
</thead>
<tbody>
<tr>
<td>No AKI</td>
<td>65.6%</td>
<td>19.1%</td>
<td>3.8%</td>
<td>12.5%</td>
</tr>
<tr>
<td>Mean age</td>
<td>60.5</td>
<td>62.1</td>
<td>60.4</td>
<td>61.1</td>
</tr>
<tr>
<td>ICU mortality</td>
<td>10.7%</td>
<td>20.1% doubled</td>
<td>25.9%</td>
<td>49.6%</td>
</tr>
<tr>
<td>Hospital mortality</td>
<td>16.9%</td>
<td>29.9%</td>
<td>35.8%</td>
<td>57.9%</td>
</tr>
<tr>
<td>Length of stay in ICU (median)</td>
<td>2 d</td>
<td>5 d</td>
<td>8 d</td>
<td>9 d</td>
</tr>
</tbody>
</table>

No need to memorize. serum creatinine level increases with the higher stage of AKI = higher mortality rate + longer hospital stay which will cost. For one dialysis session it costs 5000 to 6000 thousands.

“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

No studies.

AKI Outcomes

As you can see on the graph, the mortality rate of AKI is higher than the sum of all the cancers mentioned in the graph.
Acute Kidney Injury

**CKD risk**

- 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

Pre renal: It means something related to the heart which will lead to low perfusion or inside blood vessels like hemorrhage>low BP>low perfusion

Post renal: It means something related to the kidneys directly

Urine analysis:
- Osmolarity is high
- Specific gravity is high
- Na is low no water or urea reabsorption

**Etiology of AKI**

<table>
<thead>
<tr>
<th>Pre renal</th>
<th>Renal</th>
<th>Post Renal</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Volume depletion</td>
<td>- Acute Tubular necrosis (ATN)</td>
<td>- Ureteric obstruction</td>
</tr>
<tr>
<td>- Decreased cardiac output</td>
<td>- Acute interstitial nephritis (AIN)</td>
<td>- Bladder neck obstruction</td>
</tr>
<tr>
<td></td>
<td>- Acute Glomerulonephritis (GN)</td>
<td>- Urethral obstruction</td>
</tr>
</tbody>
</table>

**Clinical Consequences**
- Hospitalization
- Mortality
- Chronic Kidney disease
- End Stage Renal Disease

So it means the kidney is still functioning
Shock=kidney perfusion is decreased, the kidney should reabsorb Na⁺ because it wants to reserve every bit to save the kidney, and of course as we know that water will follow, so the urine will concentrated (why)? because all the water was reabsorbed in the kidney and no water was excreted in urine. -The pt with pre-renal AKI present with: nausea, vomiting, diarrhea, SOB, sometimes shock (which will decrease blood volume) > (decreased renal perfusion)
-in examination: ↓BP, tachycardia, JVP ↓ (if volume depletion) + lower limb edema (if HF), urea↑, JVP↑ creatinine↑ (the urea and creatinine will increase irrespective of the cause, prerenal, renal or post). -Tx: restore the volume (IV or blood if needed) in HF give diuretics and drugs to increase BP. -In urinalysis: I don’t see RBC,WBC,PROTEIN. Urine Analysis will be normal and the urine is concentrated.
# Etiology of AKI

<table>
<thead>
<tr>
<th>Pre renal</th>
<th>Post Renal</th>
</tr>
</thead>
<tbody>
<tr>
<td>➔ Volume depletion</td>
<td>➔ Ureteric obstruction</td>
</tr>
<tr>
<td>➔ Renal losses (diuretics, polyuria)</td>
<td>➔ Stone disease, Presents with flank pain, hematuria Do Ultrasound to rule out stones. Unlikely to affect both kidneys</td>
</tr>
<tr>
<td>➔ GI losses (vomiting, diarrhea)</td>
<td>➔ Tumor, e.g. lymphoma. (Treat with nephrostomy tube to relieve the obstruction temporarily until treated.)</td>
</tr>
<tr>
<td>➔ Cutaneous losses (burns, Stevens-Johnson syndrome)</td>
<td>➔ Fibrosis, e.g. retroperitoneal fibrosis (rare) (would compress both kidneys. Associated with migraine meds.)</td>
</tr>
<tr>
<td>➔ Hemorrhage</td>
<td>➔ Ligation during pelvic surgery</td>
</tr>
<tr>
<td>➔ Pancreatitis, Presents with abdominal pain</td>
<td>➔ Bladder neck obstruction</td>
</tr>
<tr>
<td>➔ Decreased cardiac output</td>
<td>➔ Benign prostatic hypertrophy [BPH] BPH: Sudden dribbling then anuria, otherwise healthy looking pt</td>
</tr>
<tr>
<td>➔ Heart failure, Presents with SOB</td>
<td>➔ Cancer of the prostate</td>
</tr>
<tr>
<td>➔ Pulmonary embolus</td>
<td>➔ Neurogenic bladder</td>
</tr>
<tr>
<td>➔ Acute myocardial infarction</td>
<td>➔ Drugs (Tricyclic antidepressants, ganglion blockers)</td>
</tr>
<tr>
<td>➔ Severe valvular heart disease</td>
<td>➔ Bladder tumor,</td>
</tr>
<tr>
<td>➔ Abdominal compartment syndrome</td>
<td>➔ Stone disease, hemorrhage/clot)</td>
</tr>
<tr>
<td>➔ (tense ascites)</td>
<td>➔ Urethral obstruction (strictures, tumor) (The catheter won’t bypass the bladder or ureters problems)</td>
</tr>
</tbody>
</table>

Presentation of PRErenal pt: low BP, signs of dryness (dry mucous membranes), low JVP (except HF: low BP, high JVP)

Ureteric obstruction is commonly missed so we put a foley catheter, if the obstruction is not relieved it means the obstruction is probably higher> do ultrasound to rule out obstruction or sometimes we do nephrostomy tube to relieve the obstruction and then treat the underlying cause.
Renal (ATN) | (AIN) | (GN)  
---|---|---
**Symptoms** | Oliguric, anuric (depends on the aetiology). (2) | (raised BUN and Creatinine) with: Fever, rash, arthralgias.(3) | Presentation is variable.  
**Signs** | Hypovolemia, hypotension | Skin rash, ........ | Presentation of primary disease  
**Urine** | Muddy brown casts(1), Granular casts, epithelial casts/tubular casts. | WBC casts, Eosinophils, RBC. | RBC casts, dysmorphic RBC, WBC casts, fatty casts.  
**Urine Osmolality** | <350 Diluted urine | Variable >350 | >350 variable  
**Urine Na** | >20 High | variable | variable  

(1) Due to ischemia the tubular cells will slough away and get imbedded into Tamm-Horsfall proteins (gelatinous, normally found, from proximal convoluted tubules) passed in the urine and give the muddy brown appearance.  

(2) Supposedly a pt with untreated ATN would develop polyuria, because the blood and water is still filtered. BUT due to Tubuloglomerular feedback (simply if the tubules are damaged, the glomeruli switches off) that’s why the pt becomes oliguric/anuric if ATN is present. Otherwise in 1 hour the pt will die of polyurea.  

(3) All of these features occur simultaneously in only 10% of patients. (rarely)
### Acute Tubular Necrosis (ATN)

<table>
<thead>
<tr>
<th>Causes</th>
<th>Diagnosis</th>
<th>Treatment</th>
</tr>
</thead>
</table>
| **Ischemia:** most common cause of ATN  
- Hypotension, sepsis, prolonged prerenal 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, NSAIDs) takes 5-10 days. Dose dependent (the more administered the sicker the pt)  
  - Contrast induced usually within 2 days | • Diagnose by history, ↑ FENa (>2%) sediment with coarse granular casts, | Treatment is supportive care:  
  - Maintenance of euvoelema (with diuretics e.g. in HF, IVF as necessary)  
  - Avoidance of hypotension  
  - Avoidance of nephrotoxic medications (including NSAIDs and ACE-I)  
  - Dialysis, if necessary |  
*FENa < 1% (Prerenal state)*  
- Contrast nephropathy  
- Acute GN  
- Myoglobin induced ATN  
*FENa > 1% (intrinsic cause of AKI)* |

### Comparison Between Prerenal and Acute Tubular Necrosis:

- **Pt** is hypotensive + high urine Na = Kidneys are affected.  
If you leave hypotensive pts (prerenal AKI) untreated for a while, they will develop ATN (renal AKI).

<table>
<thead>
<tr>
<th>Urea/ Creatinine ratio (4)</th>
<th>Pre renal</th>
<th>Acute Tubular necrosis (ATN)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;20:1</td>
<td>kidsneys are still intact, responding physiologically to low perfusion by preserving volume through reabsorbing water and Na</td>
<td>10-15:1</td>
</tr>
<tr>
<td>Urine Osmolality</td>
<td>Normal</td>
<td>Muddy brown casts</td>
</tr>
<tr>
<td>High = concentrated urine &gt; 500</td>
<td>&lt;350</td>
<td></td>
</tr>
<tr>
<td>Urine Na</td>
<td>Low &lt;20</td>
<td>&gt;20</td>
</tr>
<tr>
<td>Fractional excretion of Na</td>
<td>&lt;1 %</td>
<td>&gt; 1%</td>
</tr>
</tbody>
</table>

(4) It’s not accurate to assess. The urea will be reabsorbed with water and Na, that’s why it’s higher than creatinine.

Oliguria is always found in prerenal failure  
Bland urine sediment prerenal (no cellular damage)  
Differentiate clinically between prerenal and ATN: ATN is associated with prolonged hypotension, high urine Na, low osmolality and diluted urine.

#### FENa

FENa = \( \frac{\text{sodium urinary} \times \text{creatinine plasma}}{\text{sodium plasma} \times \text{creatinine urine}} \times 100 = \frac{\text{UNa} \times \text{Pc}}{\text{PNa} \times \text{UCr}} \times 100 \)

FENa is another way of assessing Na. FENa is most useful if oliguria is present.
### Acute Interstitial Nephritis AIN

<table>
<thead>
<tr>
<th>Causes</th>
<th>Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Drugs 70%: penicillin, sulfa drugs, phenytoin, rifampin, quinolones, allopurinol, proton pump inhibitors.</td>
<td>- History of systemic disease known to be associated with AIN</td>
</tr>
<tr>
<td>- Infection:</td>
<td>- Skin rash</td>
</tr>
<tr>
<td>- Systemic diseases:</td>
<td>- Esinophilia</td>
</tr>
<tr>
<td></td>
<td>- WBC cast (urine)</td>
</tr>
<tr>
<td></td>
<td>- Esinophiluria</td>
</tr>
<tr>
<td></td>
<td>- Renal biopsy</td>
</tr>
</tbody>
</table>

**symptoms and signs of systemic disease**
- lower limb swelling
- hematuria
- frothy urine

**symptoms and signs of ESRD**

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

### Acute Glomerulonephritis:

- Mainly GN causes AKI If the presentation is Rapidly progressive GN:

  Hallmark here is RBC, RBC cast, proteinuria
  You need to do serology

<table>
<thead>
<tr>
<th>Causes</th>
<th>Clinical feature</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Anti-GBM antibody Immune complex:</td>
<td>➔ Symptoms and signs of systemic disease</td>
</tr>
<tr>
<td>➔ Post-infectious. (streptococcal infection)</td>
<td>➔ Non specific: lower limb swelling, hematuria, frothy urine</td>
</tr>
<tr>
<td>➔ Connective tissue disease:</td>
<td>➔ Symptoms and signs of ESRD</td>
</tr>
<tr>
<td>1-Lupus nephritis.</td>
<td></td>
</tr>
<tr>
<td>2--Henoch-Schönlein purpura.</td>
<td></td>
</tr>
<tr>
<td>➔ Membranoproliferative glomerulonephritis (MPGN)</td>
<td></td>
</tr>
<tr>
<td>- Paucl-immune (Vasculitis):</td>
<td></td>
</tr>
<tr>
<td>➔ Wegener granulomatosis (WG)</td>
<td></td>
</tr>
<tr>
<td>➔ Microscopic polyangiitis (MPA)</td>
<td></td>
</tr>
<tr>
<td>➔ Churg-Strauss syndrome</td>
<td></td>
</tr>
</tbody>
</table>

**treatment**
- General
- Disease specific: Steroid - Immunosuppressive agents - Plasmapheresis
**Diagnostic approach in AKI:**

- The **first** thing to do is to determine the duration of renal failure. A baseline Creatinine level provides this information. (Acute, chronic, acute on top of chronic)
- 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.

<table>
<thead>
<tr>
<th>Contrast nephropathy:</th>
<th>Atheroembolic ARF:</th>
</tr>
</thead>
<tbody>
<tr>
<td>● 12-24 hours post exposure, peaks in 3-5 days <strong>immediate</strong></td>
<td>★ Creatinine peaks 1-2 weeks post-procedure.</td>
</tr>
<tr>
<td>● Non-oliguric, FENa &lt;1%, even tho it’s a nephrotoxin.</td>
<td>★ <strong>Associated with:</strong> Emboli of fragments of atherosclerotic plaque from aorta and other large arteries.</td>
</tr>
<tr>
<td>● Risk Factors: CKD, Older age, Hypovolemia, DM, CHF</td>
<td>★ <strong>Risk factors:</strong> Commonly occur after intravascular procedures or cannulation (cardiac cath, CABG, AAA repair, etc.)</td>
</tr>
<tr>
<td>● Prevention: Alternative procedure if feasible</td>
<td>★ <strong>Diagnose:</strong> 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.</td>
</tr>
<tr>
<td>● Treatment:</td>
<td>★ <strong>Treatment:</strong> Supportive treatment, poor prognosis.</td>
</tr>
<tr>
<td>-1/2 NS 1 cc/kg/hr 12 hours pre/post</td>
<td></td>
</tr>
<tr>
<td>-N-acetyl cysteine 600 BID pre/post (4 doses)</td>
<td></td>
</tr>
<tr>
<td>-Monitoring of urine output, Creatinine and proteins</td>
<td></td>
</tr>
</tbody>
</table>

- Asymptomatic: **Contrast toxicity happens rapidly within hours causing the afferent arterioles to spasm leading to reduced renal perfusion.**

**Other causes of renal AKI:**

- **Contrast nephropathy:**
  - 12-24 hours post exposure, peaks in 3-5 days **immediate**
  - 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-acetyl cysteine 600 BID pre/post (4 doses)
  - Monitoring of urine output, Creatinine and proteins

- **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.

**In History and physical examination**

- Signs and symptoms resulting from primary disease:
  - 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)

**Investigations**

- 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, HB V, 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).
Treatment of AKI:

**Pre-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.

**Post-renal**
- 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.

**Renal**
- 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

Complication 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.
**Differentiating Acute Kidney Injury vs Chronic Kidney Disease:**

<table>
<thead>
<tr>
<th></th>
<th>Acute</th>
<th>Chronic</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>History</strong></td>
<td>Short (days-week)</td>
<td>Long (month-years)</td>
</tr>
<tr>
<td><strong>Haemoglobin</strong></td>
<td>Normal (except in cases of anemia/bleeding)</td>
<td>Low</td>
</tr>
<tr>
<td><strong>Renal size</strong></td>
<td>Normal (or hydronephrosis)</td>
<td>Reduced (except in diabetes and amyloidosis the kidney size would remain normal)</td>
</tr>
<tr>
<td><strong>Serum Creatinine</strong></td>
<td>Acute reversible increase</td>
<td>Chronic irreversible</td>
</tr>
</tbody>
</table>

**Indication for dialysis in acute kidney injury setting:**
- Symptoms of uremia (encephalopathy,...)
- Uremic pericarditis
- Refractory volume overload
- Refractory hyperkalemia
- Refractory metabolic acidosis
  - Not responding to lasix
  - Not responding to bicarbonate

**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

E.g. Anuric pt with high creatinine and metabolic acidosis= supportive dialysis
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 (in shock), temperature 37°C, low JVP, normal CVS, respiratory and abdominal examination.
- CBC: Hb decreased due to bleeding, WBC increased.
- Urinalysis: Dark, low gravity with protein and granular cast.

<table>
<thead>
<tr>
<th>Test</th>
<th>Value</th>
<th>Normal values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Creatinine</td>
<td>250 µmol/L</td>
<td>62-115 µmol/L</td>
</tr>
<tr>
<td>Urea</td>
<td>29 mmol/L</td>
<td>2.5-6.4 mmol/L</td>
</tr>
<tr>
<td>Potassium</td>
<td>6.2 mmol/L</td>
<td>3.5-5.1 mmol/L</td>
</tr>
<tr>
<td>Sodium</td>
<td>137 mmol/L</td>
<td>135-145 mmol/L</td>
</tr>
<tr>
<td>Bicarbonate</td>
<td>16 mmol/L</td>
<td>22-26 mmol/L</td>
</tr>
</tbody>
</table>

First decide is it: acute, chronic, acute on top of chronic. By checking the pt’s history + Creatinine baseline pre op and compare to post op. In this case the pt is acute

Prerenal: Possible b/c of bleeding and hypotension.
Renal:
GN: based on history (unlikely, not within hours).
AIN: based on history (unlikely).
(No RBC or pus cells = unlikely for GN and AIN)
ATN: possible! (Happens over minutes-hours)+ granular cast.
Postrenal: based on history: tachycardia, hypotensive, low JVP, blood transfusion. = unlikely.
High K and Creatinine = metabolic acidosis
To differentiate between prerenal and renal, check urine Na and specific gravity.
Specific gravity is LOW (diluted urine), indication of non-functioning kidneys = renal AKI.

- **What is your diagnosis?** Acute Kidney Injury
- **Where is the etiology?** Renal (6 units of blood is not simple, so it result in ischemia to the tubules)
- **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, BP 112/67 mmHg, temperature 37°C, low JVP, dry mucus membrane, normal CVS, respiratory and abdominal examination.

- **CBC:** ↑WBC, normal hemoglobin and platelet.
  **Urine dipstick:** Shows dark urine with protein (due to diabetes)

  Acute, chronic, acute on top of chronic? Check baseline + history. (being diabetic/HTN doesn’t necessarily mean having high Creatinine)
  This pt is acute.
  **Prerenal:** likely, based on history. (vomiting, diarrhea, dryness) and physical exam.
  Renal: unlikely for GN and AIN (history + no RBC or pus cells)
  Postrenal: unlikely based on history.
  Urine Na would be low and osmolality is high (concentrated urine) = kidney is functioning. (Not ATN).

  - Stop lisinopril which is antihypertensive b/c it has intralglomerular hemodynamic effect stop it for few days and resume.
  - Renal Size in ultrasound is normal in acute whereas in chronic is reduced except two diseases (DM and Amyloidosis). In rare cases we do biopsy if there is fibrosis = chronic.

<table>
<thead>
<tr>
<th>Test</th>
<th>Value</th>
<th>Normal values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Creatinine</td>
<td>154 µmol/L</td>
<td>62-115 µmol/L</td>
</tr>
<tr>
<td>Urea</td>
<td>23 mmol/L</td>
<td>2.5-6.4 mmol/L</td>
</tr>
<tr>
<td>Potassium</td>
<td>4.3 mmol/L</td>
<td>3.5-5.1 mmol/L</td>
</tr>
<tr>
<td>Sodium</td>
<td>137 mmol/L</td>
<td>135-145 mmol/L</td>
</tr>
<tr>
<td>Bicarbonate</td>
<td>20 mmol/L</td>
<td>22-26 mmol/L</td>
</tr>
</tbody>
</table>
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% the kidney is still functioning, concentrated urine.

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 (normal) , temperature 37 C.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

<table>
<thead>
<tr>
<th>Test</th>
<th>Value</th>
<th>Normal values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Creatinine</td>
<td>123 µmol/L</td>
<td>62-115 µmol/L</td>
</tr>
<tr>
<td>Urea</td>
<td>10 mmol/L</td>
<td>2.5-6.4 mmol/L</td>
</tr>
<tr>
<td>Potassium</td>
<td>4.3 mmol/L</td>
<td>3.5-5.1 mmol/L</td>
</tr>
<tr>
<td>Sodium</td>
<td>137 mmol/L</td>
<td>135-145 mmol/</td>
</tr>
<tr>
<td>Bicarbonate</td>
<td>22 mmol/L</td>
<td>22-26 mmol/L</td>
</tr>
</tbody>
</table>

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, BP 124/67 mmHg, temperature 37.5°C, normal JVP, normal CVS, respiratory and abdominal examination.

CBC: Normal.

Urinalysis: Dark urine.

Postrenal: unlikely based on history (young, bedridden, in hospital) and urine output with Foley catheter. Due to usage of wrong catheter the urine output went from 2.5L/day, to 1.2L/day and the rest overflowed.
### Test Results

<table>
<thead>
<tr>
<th>Test</th>
<th>Value</th>
<th>Normal values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Creatinine</td>
<td>198 µmol/L</td>
<td>62-115 µmol/L</td>
</tr>
<tr>
<td>Urea</td>
<td>16 mmol/L</td>
<td>2.5-6.4 mmol/L</td>
</tr>
<tr>
<td>Potassium</td>
<td>3.9 mmol/L</td>
<td>3.5-5.1 mmol/L</td>
</tr>
<tr>
<td>Sodium</td>
<td>137 mmol/L</td>
<td>135-145 mmol/L</td>
</tr>
<tr>
<td>Bicarbonate</td>
<td>23 mmol/L</td>
<td>22-26 mmol/L</td>
</tr>
</tbody>
</table>

- **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. Insert Foley 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,BP 146/67 mmHg, 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.

<table>
<thead>
<tr>
<th>Test</th>
<th>Value</th>
<th>Normal values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Creatinine</td>
<td>560 µmol/L</td>
<td>62-115 µmol/L</td>
</tr>
<tr>
<td>Urea</td>
<td>26 mmol/L</td>
<td>2.5-6.4 mmol/L</td>
</tr>
<tr>
<td>Potassium</td>
<td>5.7 mmol/L</td>
<td>3.5-5.1 mmol/L</td>
</tr>
<tr>
<td>Sodium</td>
<td>134 mmol/L</td>
<td>135-145 mmol/L</td>
</tr>
<tr>
<td>Bicarbonate</td>
<td>13 mmol/L</td>
<td>22-26 mmol/L</td>
</tr>
</tbody>
</table>

Cath (contrast) damages the kidney by 2 mechanisms: 1-Vasoconstriction (same as prerenal:low Na & high osmolality. Treated by hydration. Could go into AKI.) 2-direct toxicity to tubule behave like renal (ATN like) (sometimes the damage is minimum, will plateau then come down after few days. Or may need dialysis.)

Case5: Acute on top of chronic based on baseline(120).

**If 1-2 weeks after cath** presented with Livedo reticularis (obstruction of the small venules that could develop into gangrene) it’s atherscloric emboli. Biopsy of one of the purplish skin lesions is the most accurate diagnostic test. It shows cholesterol crystals.
• What is your diagnosis? Acute kidney injury in top of chronic
• What your differential diagnosis?
  - Atheroembolic disease (not common, unpredictable, poor prognosis)
  - 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, BP 167/94 mmHg, 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.

<table>
<thead>
<tr>
<th>Test</th>
<th>Value</th>
<th>Normal values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Creatinine</td>
<td>245 µmol/L</td>
<td>62-115 µmol/L</td>
</tr>
<tr>
<td>Urea</td>
<td>17 mmol/L</td>
<td>2.5-6.4 mmol/L</td>
</tr>
<tr>
<td>Potassium</td>
<td>4.9 mmol/L</td>
<td>3.5-5.1 mmol/L</td>
</tr>
<tr>
<td>Sodium</td>
<td>139 mmol/L</td>
<td>135-145 mmol/L</td>
</tr>
<tr>
<td>Bicarbonate</td>
<td>17 mmol/L</td>
<td>22-26 mmol/L</td>
</tr>
</tbody>
</table>

• 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

Young and lower limb edema: most likely nephrotic syndrome.
Lots of protein and RBCs in the urine: most likely GN.
### Acute kidney injury (AKI)

**KDIGO 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

<table>
<thead>
<tr>
<th>Types</th>
<th>Pre-renal</th>
<th>Post-renal</th>
<th>Renal</th>
</tr>
</thead>
</table>
| **Etiology** | - Volume depletion  
- Decreased cardiac output | - Ureteric obstruction  
- Bladder neck obstruction  
- Urethral obstruction | - Acute Tubular necrosis (ATN)  
- Acute interstitial nephritis (AIN)  
- Acute Glomerulonephritis (GN) |

<table>
<thead>
<tr>
<th>Signs and Symptoms</th>
<th>Pre-renal</th>
<th>Post-renal</th>
<th>Renal</th>
</tr>
</thead>
</table>
| **Nausea, diarrhea, Vomiting, SOB and Low JVP** | Initially normal, may present with pain and anuria | ATN  
Hypovolemia, hypotension | AIN  
Skin rash |
| | | | AGN  
Presentation of primary disease |

<table>
<thead>
<tr>
<th>Lab findings</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Urine</strong></td>
<td><strong>Hyaline casts</strong></td>
<td><strong>Benign; blood and protein are negative, may or may not see RBC, WBC</strong></td>
<td><strong>Muddy brown cast</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><strong>WBCs casts, Eosinophils Hunsel stain for eosinophils</strong></td>
</tr>
<tr>
<td><strong>BUN/Cr</strong></td>
<td>&gt; 20:1</td>
<td></td>
<td>&lt; 20:1 (10:1)</td>
</tr>
<tr>
<td><strong>FENa</strong></td>
<td>&lt;1%</td>
<td></td>
<td>&gt;2% - 3%</td>
</tr>
<tr>
<td><strong>Urine osmolarity</strong></td>
<td>&gt; 500 mOsm/kg</td>
<td></td>
<td>&lt; 350</td>
</tr>
<tr>
<td><strong>Urine Na</strong></td>
<td>&lt; 20 mEq/L</td>
<td>&gt; 20</td>
<td>Variable</td>
</tr>
</tbody>
</table>

**Treatment**

- Treat underlying disorder.
- Relieving the obstruction by catheter.
- Eliminate the underlying cause.
1/A 55 year old male patient is admitted with a massive GI bleed. The patient is at risk for what type of acute kidney injury?

A) Post-renal  
B) Renal  
C) Pre-renal  
D) Intrinsic renal

2/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

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) Nephrotoxin-induced acute tubular necrosis  
C) Acute interstitial nephritis  
D) Postinfectious glomerulonephritis

4/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) Postinfectious glomerulonephritis  
C) Postrenal azotemia because of obstructive uropathy  
D) Acute interstitial nephritis

Answers: 1/C, 2/B, 3/C, 4/C