PRERENAL AND FUNCTIONAL ACUTE RENAL FAILURE

• Congestive Heart Failure and Nonsteroidal Anti-Inflammatory Drug Use
Case 1

• A.W. is a 71-year-old white man who had a ST-segment elevation myocardial infarction (STEMI) 2 months ago. His ejection fraction is currently 15% (normal, 50%–60%).

• He presents today for his 2-month follow-up clinic appointment complaining of shortness of breath, dyspnea on exertion, and inability to produce much urine.

• His medical history
  significant for longstanding hypertension, coronary artery disease, osteoarthritis, and recent-onset heart failure (HF) after his MI.

• His home medications
  furosemide 40 mg every day,
  enalapril 5 mg daily,
  metoprolol XL 100 mg daily
  digoxin 0.125 mg daily,
  atorvastatin 40 mg QD,
  naproxen sodium 550 mg twice daily (BID).

  Note: all of which are taken orally (PO) With the exception of naproxen,

  A.W. often forgets to take his medications.
• **Physical examination**
  - Reveals lower leg 3+ pitting edema
  - Pulmonary crackles and wheezes,
  - Positive jugular venous distention
  - S3 heart sound.

• **Vital signs**
  - Significant for a blood pressure (BP) of 198/97 mm Hg
  - Weight gain of 4 kg since his last visit 2 months ago. Last month
  - BUN and SrCr were 23 (normal, 5–20) and 1.2 mg/Dl (normal, 0.5–1.2), respectively.

• [SI units: BUN, 8.2 mmol/L (normal, 1.8–7.1); SrCr, 106 mol/L (normal, 44.2–106)]

• **What are A.W.'s risk factors for ARF?**
  1. **CHF with poor cardiac output** (ejection fraction, 15%, meaning very low) that resulted from his STEMI.

    CHF is a major cause of functional ARF.

  11. *(NSAID), such as naproxen,* are often overlooked as causes of ARF.

    NSAID ↓ prostaglandin synthesis, compensatory vasodilation ↓ renal perfusion.

• **Indomethacin** is associated with the highest risk of NSAIDs-induced renal ischemia, whereas **aspirin appears to have the lowest risk.**

• **Sulindac is the safest one used in acute renal failure**
• All of the following should be assessed daily in a patient with ARF, except?

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
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</thead>
<tbody>
<tr>
<td>I.</td>
<td>Liver aminotransferases</td>
</tr>
<tr>
<td>II.</td>
<td>Serum creatinine</td>
</tr>
<tr>
<td>III.</td>
<td>Weight</td>
</tr>
<tr>
<td>IV.</td>
<td>Medication dosages</td>
</tr>
<tr>
<td>V.</td>
<td>Urine output</td>
</tr>
</tbody>
</table>

Which one of the following represents the most likely cause (type) of acute renal failure in this patient?

A. Prerenal.
B. Intrinsic.
C. Postrenal.
D. Functional
A.W.’s cardiologist obtains a stat digoxin level, electrolyt panel, urinalysis, and urine electrolyte panel.

- **The digoxin level is reported as “not detectable”** (target, 0.5–0.8 ng/mL).

- **Other significant lab values**

<table>
<thead>
<tr>
<th>Serum Laboratory Values</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Na⁺ of 140 mEq/L</td>
<td>(normal, 133–145)</td>
</tr>
<tr>
<td>creatinine of 1.5 mg/dL</td>
<td>(normal, 0.5–1.2)</td>
</tr>
<tr>
<td>BUN 56 mg/dL</td>
<td>(normal, 5–20)</td>
</tr>
</tbody>
</table>

  **Urine Analysis**

<table>
<thead>
<tr>
<th>Urine Analysis</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>urinary osmolality of 622 mOsm/kg</td>
<td>(normal, 300–500 mOsm/kg)</td>
</tr>
<tr>
<td>specific gravity of 1.092</td>
<td>(normal, 1.010–1.020)</td>
</tr>
</tbody>
</table>

  **Urine Electrolytes**

<table>
<thead>
<tr>
<th>Urine Electrolytes</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Na⁺ of 12 mEq/L</td>
<td>(normal, 20–40)</td>
</tr>
<tr>
<td>creatinine of 87 mg/dL</td>
<td></td>
</tr>
</tbody>
</table>

[SI units: sodium, 140 mmol/L (normal, 135–145); BUN, 20 mmol/L (normal, 1.8–7.2); SrCr, 132.6 mol/L (normal, 44.2–106); urine Cr, 7691 mol/L]

**What laboratory findings suggest functional ARF?**

**Table 30-2: Urinary Indices in Acute Renal Failure**

<table>
<thead>
<tr>
<th>Component</th>
<th>Purred Aeren</th>
<th>Acute tubular necrosis</th>
<th>Postrenal obstruction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urine Na⁺ (mEq/L)</td>
<td>&lt;20</td>
<td>&gt;40</td>
<td>&gt;40</td>
</tr>
<tr>
<td>Fe²⁺</td>
<td>&lt;15%</td>
<td>&gt;2%</td>
<td>&gt;2%</td>
</tr>
<tr>
<td>Urine plasma creatinine</td>
<td>&gt;40</td>
<td>&lt;20</td>
<td>&lt;20</td>
</tr>
<tr>
<td>Specific gravity</td>
<td>&gt;1.10</td>
<td>&lt;1.00</td>
<td>Variable</td>
</tr>
<tr>
<td>Urine osmolality (mOsm/kg)</td>
<td>1200–1,200</td>
<td>&lt;300</td>
<td>&lt;300</td>
</tr>
</tbody>
</table>

**Classic laboratory findings associated with poor renal perfusion**
Case 2

- G.B. is a 53-year-old white woman with hypertension, coronary artery disease, peripheral vascular disease, and diabetes

**Medication**
- hydrochlorothiazide 25 mg PO daily
- atorvastatin 10 mg PO daily,
- aspirin 81 mg PO daily,
- NPH insulin 30 U subcutaneously Q morning and 15 U subcutaneously Q evening.

- At last week’s clinic visit, she had two consecutive BP readings of 187/96 and 193/95 mm Hg, respectively, measured 20 minutes apart.
- At that time, G.B.’s primary care physician discontinued her hydrochlorothiazide and started her on lisinopril 5 mg PO daily.

- She returns to the clinic today for her 1-week follow-up appointment complaining of dizziness, very little urine production over the past week, and swelling in her ankles.

- Her BP is 98/43 mm Hg. A stat serum electrolyte panel is significant for a BUN of 62 mg/dL (normal, 5–20) and an SrCr of 6.1 mg/dL (normal, 0.5–1.2).
Why is G.B. experiencing ARF? 2- what are the risk factors for this patient?

- Inhibition of the RAA system in patients with compromised renal blood flow is a common cause of functional ARF.
- The administration of ACE inhibitors directly inhibits the formation of AT II, which is necessary for efferent arteriole vasoconstriction.
Are there other factors that predispose patients to ACE inhibitor-induced ARF?

In addition to the above situation,

**First**, conditions of sodium and water depletion (e.g., dehydration, overdiuresis, poor fluid intake, low-sodium diet) can increase the dependency of the efferent arteriole on AT II. ARF can be averted by withholding the ACE inhibitor (or diuretic, or both) for a day and repleting the intravascular fluid volume with a saline-containing fluid (e.g., normal saline or 0.45% saline).

**Second**, ACE inhibitors can decrease the mean arterial pressure to such a degree that renal perfusion cannot be sustained.

**Finally**, ACE inhibitors may precipitate ARF in patients who are taking concomitant drugs with renal afferent arteriole vasoconstricting effects, most notably cyclosporine and NSAIDs.

**INTRINSIC ACUTE RENAL FAILURE**

**Acute Glomerulopathies**

**Poststreptococcal Glomerulonephritis**
Case 3

B.M. is an 18-year-old male college freshman in otherwise good health who recently developed strep throat. He received a 10-day course of amoxicillin, which cleared the infection. He returns to the student health center after completing his 10-day course complaining of “puffy eyes,” swelling in his legs, a cough productive of clear sputum, and decreased urine output that appears “tea-colored.” Other than the amoxicillin, he is not on any medication.

- Baseline records from a routine physical examination 2 months ago revealed a serum BUN and creatinine of 10 mg/dL and 0.8 mg/dL (normal, 5–20 and 0.5–1.2), respectively, and a BP of 120/80 mm Hg.
Today, the physical examination is significant for a BP of 176/95 mm Hg, 2+ peripheral edema, and bilateral pulmonary rales.

The urinalysis is significant for gross hematuria, nephritic-range proteinuria, RBC and WBC casts, and epithelial cells. B.M.’s SrCr has increased to 7.1 mg/dL. Based on the history, physical examination, and laboratory findings [SI units: BUN, 3.6 mmol/L (normal, 1.8–7.1); SrCr, 70.7 and 627.6 mol/L, respectively (normal, 44.2–106)],

what is the most likely cause of ARF in this patient?
Answer:

- B.M.'s recent history of a streptococcal infection with the development of ARF suggests poststreptococcal glomerulonephritis (PSGN).
- The pertinent positive physical findings include periorbital edema, and peripheral edema; tea-colored urine, hypertension, and decreased urine output.
- Pertinent laboratory data in B.M. include elevated SrCr, and urinalysis positive for hematuria, proteinuria, WBC casts, and epithelial cells.
- Oliguria is common in PSGN but anuria is rare.

Are there other tests that can be used to confirm this diagnosis?

Given that B.M. has received a 10-day course of amoxicillin, it is unlikely that throat cultures for the nephritogenic group a hemolytic streptococcal stain will be positive.

- The antistreptolysin O (ASO), an tiyaluronidase (AHase), antideoxyribonuclease B (ANDase B), and anticotyladeninedinucleotidase (NADase) antibody titers can be measured clinically.

- The streptozyme test, which can be used clinically for rapid screening purposes.
INTRINSIC ACUTE RENAL FAILURE

Acute Tubular Necrosis

Radiocontrast Media–Induced Acute Tubular Necrosis

Case 4

K.S., a 74-year-old man, presents to the emergency department complaining of chest pain. He has advanced coronary artery disease and has been taken to laboratory for a percutaneous coronary intervention. Immediately before the procedure, K.S. is given io-hexol (contrast) PO to enhance visualization of his cardiac arteries.

His medical history
advanced type 2 diabetes mellitus, with retinopathy, peripheral vascular disease, and advanced coronary artery disease.

LABS
His admission BUN is 37 mg/dL (normal, 5–20) and SScr is 1.5 mg/dL (normal, 0.5–1.2). Two days later, pertinent laboratory findings include a BUN and SScr of 60 and 2.0 mg/dL, respectively, and his urine output is 700 mL/day.
Why did K.S. develop ARF?

Answer

- **Radiocontrast media** administration is one of the most common causes of drug-induced ATN.

- It is generally considered when the SrCr increases by >0.5 g/dL over 2 to 5 days.

- Contrast-induced nephropathy (CIN) usually presents as a non-oliguric ATN.

- The mechanisms by which radio contrast media induce ARF are complex.
• Initially, the radio contrast medium produces renal vasodilation and an osmotic diuresis. This, however, is followed by intense vasoconstriction in the medullary portion of the kidney, which has been demonstrated by significant (decrease) in medullary Po2 after contrast administration.

• Consequently, disequilibrium exists between O2 supply and demand creating ischemic ATN.

What are the risk factors for CIN*?

<table>
<thead>
<tr>
<th>Table 30-4</th>
<th>Proven Risk Factors for Developing Radiocontrast Media–Induced Acute Tubular Necrosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetic nephropathy</td>
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<tr>
<td>Chronic kidney disease</td>
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<tr>
<td>Severe heart failure</td>
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<tr>
<td>Volume depletion and hypotension</td>
<td></td>
</tr>
<tr>
<td>Dosage and frequency of contrast administration</td>
<td></td>
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</tbody>
</table>

Others drugs? Examples?

* CIN: Contrast induced necrosis
Aminoglycoside-Induced Acute Tubular Necrosis

Case 5

F.D. is a 44-year-old man admitted with gram negative bacteremia. He receives 4 days of parenteral aminoglycoside therapy and develops acute tubular necrosis (ATN). Antibiotic therapy is adjusted on the basis of culture and sensitivity results.
Which one of the following is the urinalysis most likely to show?

A. BUN/SCr ratio greater than 20:1; urine Na less than 10 mOsm/L; fractional excretion of sodium (FENa) less than 1%; specific gravity more than 1.018; hyaline casts.

B. BUN/SCr ratio greater than 20:1; urine Na more than 20 mOsm/L; FENa more than 3%; specific gravity 1.010; no casts visible

C. BUN/SCr ratio 10–15:1; urine Na more than 40 mOsm/L; FENa more than 1%; specific gravity less than 1.015; muddy casts

D. BUN/SCr ratio 10–15:1; urine Na less than 10 mOsm/L; FENa less than 1%; specific gravity more than 1.018; muddy

Table 1. Classifications of Acute Kidney Injury

<table>
<thead>
<tr>
<th>Prerenal and Functional</th>
<th>Intrinsic (ATN and AIN)</th>
<th>Postrenal</th>
</tr>
</thead>
<tbody>
<tr>
<td>History/presentation</td>
<td></td>
<td>Kidney stones BPH Cancers</td>
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<tr>
<td></td>
<td>Volume depletion</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Renal artery stenosis</td>
<td></td>
</tr>
<tr>
<td></td>
<td>CHF</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Hypercalcemia</td>
<td></td>
</tr>
<tr>
<td></td>
<td>NSAID/ACEI use</td>
<td></td>
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<tr>
<td></td>
<td>Cyclosporin</td>
<td></td>
</tr>
<tr>
<td>Physical examination</td>
<td></td>
<td>Distended bladder Enlarged prostate</td>
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<tr>
<td></td>
<td>Hypotension</td>
<td></td>
</tr>
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<td></td>
<td>Dehydration</td>
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<td></td>
<td>Petchia if thrombotic</td>
<td></td>
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<tr>
<td></td>
<td>Aortic</td>
<td></td>
</tr>
<tr>
<td>Serum BUN/SCr ratio</td>
<td>&gt; 20:1</td>
<td>15:1</td>
</tr>
<tr>
<td>Urine concentrated?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td>Low urine Na (&lt; 20 mEq/L)</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td>Low FENa (&lt; 1)</td>
<td>No</td>
</tr>
<tr>
<td>High urine osmolality</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Urine sediment</td>
<td>Normal</td>
<td>Muddy, brown granular casts Variable, may be normal</td>
</tr>
<tr>
<td></td>
<td>Muddy, brown granular casts</td>
<td></td>
</tr>
<tr>
<td>Urinary WBC</td>
<td>Negative</td>
<td>2–4+</td>
</tr>
<tr>
<td>Urinary RBC</td>
<td>Negative</td>
<td>2–4+</td>
</tr>
<tr>
<td>Protein</td>
<td>Negative</td>
<td>1+</td>
</tr>
<tr>
<td>Negative</td>
<td>Variable</td>
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</tbody>
</table>
ACEI = angiotensin-converting enzyme inhibitor; ATN = acute tubular necrosis; AIN = acute interstitial nephritis; BPH = benign prostatic hypertrophy; BUN = blood urea nitrogen; CHF = congestive heart failure; FENa = fractional excretion of sodium; GFR = glomerular filtration rate; NSAID = nonsteroidal anti-inflammatory drug; Scr = serum creatinine; RBC = red blood cell (count); WBC = white blood cell (count).
Which one of the following is the urinalysis most likely to show?

A. BUN/SCr ratio greater than 20:1; urine Na less than 10 mOsm/L; fractional excretion of sodium (FENa) less than 1%; specific gravity more than 1.018; hyaline casts.

B. BUN/SCr ratio greater than 20:1; urine Na more than 20 mOsm/L; FENa more than 3%; specific gravity 1.010; no casts visible

C. BUN/SCr ratio 10–15:1; urine Na more than 40 mOsm/L; FENa more than 1%; specific gravity less than 1.015; muddy casts

D. BUN/SCr ratio 10–15:1; urine Na less than 10 mOsm/L; FENa less than 1%; specific gravity more than 1.018; muddy casts

Case 6

H.H. is a 43-year-old, 80-kg man being treated for gram-negative septic shock. He was admitted to the hospital 6 days ago, but he has spent the last 3 days intubated in the medical respiratory ICU because of hypotension, respiratory failure, and altered mental status.

Since admission, H.H. has received ceftriaxone 2 g/day and gentamicin 140 mg IV Q 8 hr.
Admission laboratory results were significant for the following: BUN, 13 mg/dL (normal, 5–20); SrCr, 0.9 mg/dL (normal, 0.5–1.2); and WBC count, 23,500 cells/mm³ (normal, 4,000–9,000) with a left shift (90% polymorphonuclear leukocytes [PMN] and 12% bands)

Serial blood, urine, and sputum cultures were positive for Acinetobacter baumanii sensitive to ceftriaxone and gentamicin. In addition to the previously listed antibiotics,

his current medication regimen

norepinephrine IV 18 mcg/minute
pancuronium 0.02 mg/kg IV Q 3 hr,
famotidine 20 mg IV Q 12 hr,
lorazepam IV 2 mg/hour
• Today (hospital day 7) H.H.’s vital signs
  • temperature, 101.5°F (38.6°C); BP, 90/40 mm Hg; pulse, 135 beats/minute; and respiration, 20 breaths/minute.
  
  Significant laboratory values are as follows: BUN, 67 mg/dL; SrCr, 5.4 mg/dL; and WBC count, 16,700 cells/mm³ with continued left shift.

Over the last 2 days, H.H.’s urine output has steadily declined, and today it is 700 mL/24 hours (normal, 1,500–2,500).

Urine electrolytes were obtained and reveal Na+, 55 mEq/L (normal, 20–40) and creatinine, 26 mg/dL (normal, 50–100).

A urinalysis revealed many WBC (normal, 0–5), 3% RBC casts (normal, 0%–1%), brush-border cells (normal, negative), and granular casts (normal, negative) with an osmolality of 250 mOsm/kg (normal, 400–600).

Serum gentamicin concentrations obtained with the last dose reveal a peak of 15 mg/dL (target, 6–10) and a trough of 9.1 mg/dL (target, <2.0).
what is the likely source of H.H.’s ARF?

Answer:

✓ The source of ARF _______ multifactorial(Table 30-1).

• **First**, H.H. is experiencing diminished renal perfusion from profound hypotension and septic shock.

• As a result, he is receiving high-dose norepinephrine, a potent vasopressor.

Consequently, the combination of these variables reduces renal perfusion further, resulting in prolonged renal ischemia.
Second received 1 week of gentamicin a well-known nephrotoxic antibiotic

- Table 30-5. The risk factors for developing aminoglycoside nephrotoxicity are listed
- The latest gentamicin trough concentration (traditional dosing 3 times daily)
- Given the laboratory data (Table 30-2) and the clinical course of prolonged hypotension, vasopressor, and aminoglycoside administration, nonoliguric ATN is the most likely diagnosis.

Table 30-5 Risk Factors for Developing Aminoglycoside Nephrotoxicity

<table>
<thead>
<tr>
<th>Patient Factors</th>
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</thead>
<tbody>
<tr>
<td>Elderly</td>
</tr>
<tr>
<td>Underlying renal disease</td>
</tr>
<tr>
<td>Dehydration</td>
</tr>
<tr>
<td>Hypotension and shock syndromes</td>
</tr>
<tr>
<td>Hepatorenal syndrome</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Aminoglycoside Factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aminoglycoside choice: gentamicin &gt; tobramycin &gt; amikacin</td>
</tr>
<tr>
<td>Therapy &gt; 3 days</td>
</tr>
<tr>
<td>Multiple daily dosing</td>
</tr>
<tr>
<td>Serum trough &gt; 2 mg/L</td>
</tr>
<tr>
<td>Recent aminoglycoside therapy</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Concomitant Drug Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amphotericin B</td>
</tr>
<tr>
<td>Cisplatinum</td>
</tr>
<tr>
<td>Cyclosporine</td>
</tr>
<tr>
<td>Foscarnet</td>
</tr>
<tr>
<td>Furosemide</td>
</tr>
<tr>
<td>Radiographic contrast media</td>
</tr>
<tr>
<td>Vancomycin</td>
</tr>
</tbody>
</table>
MCQ

- Drugs that increases Aminoglycosides toxicity includes the following ?
1. Cyclosporine
2. amphotericin B
3. Diuretics
4. Vancomycin
5. All of the Above

- The rational approach to aminoglycoside nephrotoxicity is:
  1- use the less nephrotoxic aminoglycoside amikacin then tobramycin then gentamicin.
  2- therapy is less than 3 days.
  3- using once daily dose.
  4- serum tough < 2 mg/L.
  4- Between each aminoglycoside therapy and another therapy is at least 3 months.
How does aminoglycoside-induced ATN present, and what are the mechanisms of toxicity?

- H.H. illustrates the typical presentation of aminoglycoside-induced nephrotoxicity.

- Generally, the onset occurs after 5 to 7 days of treatment and presents as a hypo-osmolar, nonoliguric renal failure with a slow rise in SrCr.

- Because of the tubular necrosis that occurs, the urinalysis is often positive for low-molecular-weight proteins, tubular cellular casts, epithelial cells, WBC, and brush-border cells.

- The mechanism of aminoglycoside-induced ATN is complex. Approximately 5% of filtered aminoglycoside is actively reabsorbed by the proximal tubule cells.

- These agents are poly cationic and bind to the negatively charged brush-border cells within the tubule lumen. Once attached, these agents undergo pinocytosis and enter the intracellular space, setting off complex biochemical events that result in the formation of myeloid bodies.

- With continued formation of myeloid bodies, the brush-border cells swell and burst, releasing large concentrations of aminoglycoside and lysosomal enzymes into the tubule lumen, which cause tubular destruction.

- The following rank order of nephrotoxicity has been collated from human and animal data: neomycin > gentamicin = tobramycin = amikacin = netilmicin > streptomycin.
Extended-Interval Dosing
Is “extended-interval” aminoglycoside dosing less nephrotoxic than multiple daily dosing regimens?

- Extended-interval aminoglycoside dosing entails the administration of one large daily aminoglycoside dose.

- Aminoglycoside nephrotoxicity is a function of drug exposure, and it might be minimized with extended-interval dosing because of saturable uptake kinetics in the proximal tubule. That is, only a maximal amount of aminoglycoside is transported into the tubule cell,
- no matter how much aminoglycoside is present in the tubule.

- In summary, extended-interval aminoglycoside dosing appears to result in similar or greater efficacy, with similar or reduced toxicity.
- the typical extended interval inpatients with normal renal function is dosing every 24 hours, the interval may have to be prolonged to several days in patients with renal failure.
Complete the following statement

Aminoglycosides follow ............... kinetics in the proximal tubule

Answer (saturable)

True or false?

Extended dosing strategy in aminoglycosides is less nephrotoxic than multiple daily dosing?

Justify?
POSTRENAL ACUTE RENAL FAILURE

Case 7

- T.C., a 48-year-old man, presents to the emergency department
- complaining of sharp flank pain radiating to the groin, gross hematuria, and dysuria.
- He states that these symptoms have been present for 4 hours and that they are similar to previous episodes of calcium nephrolithiasis he has experienced.
• Serum chemistries are ordered and are significant only for a BUN of 34 mg/dL (normal, 5–20) and an SrCr of 1.5 mg/dL (normal, 0.5–1.2), which are up from his baseline values of 15 and 0.9 mg/dL, respectively.

• A urine sample was obtained and visualized with microscopy. It was determined that T.C. passed a kidney stone, based on the large amount of calcium oxalate crystals found in the urinary sediment.

• On questioning, he admits that he has not been drinking much fluid over the past week owing to a busy work schedule, and his urine volume has been markedly lower than usual.

What are the common subjective and objective data that suggest nephrolithiasis, and how can this be prevented from occurring in the future?
T.C. illustrates the classic presentation of nephrolithiasis: acute, severe flank pain that radiates to the groin. It is usually accompanied by gross or microscopic hematuria, dysuria, or frequency. Of symptomatic calculi, 90% pass spontaneously, as in T.C.’s case, and invasive surgical treatment is not necessary.

The risk factors
- 1-age within the fourth decade
- 2-decreased fluid intake and urine output.

mechanisms can prevent stone formation?
- 2-Dietary modifications remain controversial
- 3-fast walking
- 4-effervescent

**Summery**

- a high calcium intake
- increases the risk of nephrolithiasis
- only in patients with absorptive hypercalciuria and not in normal subjects
Drug-Induced Nephrolithiasis

Can drugs crystallize in the urine and cause ARF?

- Risk factors that predispose patients to crystalluria include:

  1. Severe volume contraction,
  2. Underlying renal dysfunction, or
  3. Acidotic or alkalotic urinary pH.

- In conditions of renal hypoperfusion, high concentrations of drug become stagnant in the tubule lumen.

- Drugs that are weak acids (e.g., methotrexate, sulfonamides) precipitate in acidic urine; drugs that are weak bases (e.g., indinavir, other protease inhibitors) precipitate in alkaline urine.
1. ___ failure is caused by obstruction of urine flow. (urethral obstruction by enlarged prostate or tumor; ureteral or kidney pelvis obstruction by calculi)
   A. Prerenal.
   B. Intrinsic.
   C. Postrenal.
   D. Functional

2. Acute renal failure is generally identified by oliguria (urine output ___ mL/day).

3. The cause of ___ failure is impaired blood supply to the kidney (Fluid Volume Deficit, hemorrhage, heart failure, shock)
   A. Prerenal.
   B. Intrinsic.
   C. Postrenal.
   D. Functional

• 4. _______ renal Failure is a rapid decline in renal function with an abrupt onset

• 5. which diagnostic test would be monitored to evaluate glomerulat filtration rate and renal function?
   A. Sreum creatinine and BUN
   B. Urinalysis
   C. Kidney biopsy
   D. creatinine cleatance
6.................failure is caused by Acute damage to renal tissue and nephrons or acute tubular necrosis: abrupt decline in tubular and glomerular function due to either prolonged ischemia and/or exposure to nephrotoxins. (Acute glomerulonephritis, malignant hypertension, ischemia; nephrotoxic drugs or substances; red blood cell destruction; muscle tissue breakdown due to trauma, heatstroke

A. Prerenal.
B. Intrinsic.
C. Postrenal.
D. Functional

• True or false?
  ➢ High fluid intake is a risk factor for developing nephrolithiasis?
  ➢ Aminoglycoside peak level consider to be a risk a factor for nephrotoxicity?
  ➢ Age and high urine output is a risk factor for nephrolithiasis?
  ➢ Acidic PH of the urine is risk factor for developing crystalluria?
  ➢ The streptozyme test, which can be used clinically for rapid screening of PSGN?
  ➢ Oliguria is common in PSGN but anuria is rare.?
  ➢ High calcium intake increases the risk of hypercalciuria in all patients?
  ➢ Contrast-induced nephropathy (CIN) usually presents as an oliguric ATN?
Chronic Renal failure

DIABETIC NEPHROPATHY
• M.R. is a 32-year-old, Native American woman (weight, 63kg) with a 15-year history of type 1 diabetes mellitus.

• She presents to the diabetes clinic with a 1-week history of nausea, vomiting, and general malaise.

• She has been noncompliant with regular appointments and her blood glucose has generally remained >200 mg/dL on prior evaluations, with a hemoglobin A1C of 9.1% (goal, <7%) 2 months ago.

• M.R. has been treated for peptic ulcer disease for the past 6 months.

➢ laboratory values:

• serum sodium (Na), 143 mEq/L (normal, 135–147 mEq/L); potassium (K), 5.3 mEq/L (normal, 3.5–5.0 mEq/L);

• chloride (Cl), 106 mEq/L (normal, 95–105 mEq/L);

• CO2 content, 18 mEq/L (normal, 22–28 mEq/L);

• SrCr, 2.9 mg/dL (normal, 0.6–1.2 mg/dL);

• BUN, 63 mg/dL (normal, 8–18 mg/dL);

• and random blood glucose, 220 mg/dL (normal, 140 mg/dL).
Additional laboratory studies

show serum phosphate, 7.6 mg/dL (goal, 3.5–4.6 mg/dL);
calcium (Ca), 8.8 mg/dL (goal, 8.4–9.5 mg/dL);
magnesium (Mg), 2.8 mEq/L (normal, 1.6–2.4 mEq/L);
and uric acid, 8.8 mg/dL (normal, 2.0–7.0 mg/dL).

Hematologic studies show hematocrit (Hct), 26% (normal, 36%–46%);
hemoglobin (Hgb), 8.7 g/dL (normal, 12–16 mg/dL);
and white blood cell (WBC) count, 9,600/mm³ (normal, 3,200–9,800/mm³).
Red blood cell (RBC) indices are normal.
Platelet count is 175,000/mm³ (normal, 130,000–400,000/mm³).
M.R.’s reticulocyte count is 2.0% (normal, 0.1%–2.4%).
Her urinalysis (UA) showed 4+ proteinuria, later quantified as a urinary albumin of 700 mg/24hrs (normal, <30 mg/day).

Physical examination

• a BP of 155/102 mmHg, mild pulmonary congestion, and 2+ pedal edema.
What subjective and objective data in M.R. are consistent with a diagnosis of advanced kidney disease?

**Answer:**

**Subjective:**
- Nausea, vomiting, and malaise may be a consequence of the accumulation of uremic toxins.
- Noncompliant with regular appointments and her blood glucose

**Objective**

I. M.R.’s abnormal values for Sr Cr, BUN, serum potassium, magnesium, phosphate, uric acid, CO2 content, hemoglobin, and hematocrit are all consistent with kidney disease and its associated complications.

II. Proteinuria.

III. Physical examination revealed a BP of 155/102 mmHg, mild pulmonary congestion, and 2+ pedal edema and type 1 diabetes mellitus.

IV. Metabolic acidosis results from impaired synthesis of ammonia by the kidney.

V. -- Anemia associated with CKD is caused primarily by decreased erythropoietin production by the kidneys. (Low Hb)
2. What is the cause of M.R.’s advanced kidney disease? And what risk factor and pathogenesis?

The cause .........................> diabetic nephropathy (is a disease of kidney due to diabetes).

- The exact mechanisms diabetic nephropathy are not clearly defined; however, several RISK factors for the development and progression of kidney damage.

- These include:
  • elevated BP
  • plasma glucose
  • glycosylated hemoglobin
  • Cholesterol
  • Smoking
  • advanced age
  • male gender
  • high protein intake.

Pathogenesis:
1. Insulin deficiency.
2. Increased ketone bodies.
3. Advanced glycosylation end products (AGE).

Q- Mention risk factors for developing diabetic nephropathy?

Q- Describe the pathogenesis of developing diabetic nephropathy?
3. What is the significance of M.R.’s albuminuria?

**Albuminuria**, the earliest sign of kidney involvement in patients with diabetes mellitus, correlates with the rate of progression of kidney disease. The presence indicates irreversible kidney damage.

What happen to GFR if there’s proteinuria? (GFR decline)

Annual testing for the presence of microalbuminuria is indicated in diabetic patients.

5. How to Assess M.R.’s sodium and water balance. What interventions may be used to address this problem?

Since this patient in late stage of CKD, commonly retain water. So M.R.’s has elevated BP, 2+pedal edema, mild pulmonary congestion, FENa (increased as glomerular and tubular adaptive processes develop).

Note:– Expansion of blood volume, if not controlled, can cause peripheral edema, heart failure, and pulmonary edema.
6. M.R. has a serum potassium concentration of 5.3 mEq/L. Describe the mechanisms by which potassium imbalance occurs in patients such as M.R. who have progressive CKD?

I. diminished renal potassium excretion,
II. redistribution of potassium into the extracellular fluid owing to metabolic acidosis
III. excessive potassium intake
IV. Additional factors include
   • metabolic or respiratory acidosis.
   (Acidotic conditions can cause a redistribution of intracellular potassium to the extracellular fluid.)
   • Potassium-sparing diuretics such as
     - spironolactone (Aldactone)
     - triamterene (Dyrenium),
     - amiloride (Midamor should be avoided in patients with severe CKD because they decrease tubular secretion of potassium.

9. What other electrolyte and metabolic disturbances are exhibited by M.R.?

- The mild degree of hypermagnesemia seen in M.R.

- M.R.’s hyperphosphatemia

- M.R. also has mild hyperuricemia.

Higher concentrations of hypermagnesemia can lead to:
- nausea, vomiting, and confusion

The risk of hypermagnesemia can be reduced:
--by avoiding magnesium-containing antacids and laxatives
10. What findings in M.R. are consistent with the diagnosis of anemia of CKD, and what is the etiology of this disorder?

M.R.’s hemoglobin of 8.7 g/dL and hematocrit of 26% are substantially lower than the normal range for premenopausal females (hemoglobin, 12–16 g/dL; hematocrit, 36%–46%) indicating that she has anemia.

- Etiology?
  caused by a decreased production of erythropoietin (EPO),

(EPO), is a glycoprotein that stimulates red blood cell production in the bone marrow and is released in response to hypoxia.

• Define the following
  ➢ Micoalbuminurea?
  ➢ Albuminurea (Macroalbuminurea)?
H.B. is a 65-year-old white man with stage 5 CKD who has just started chronic HD. He comes in today for his third HD session (dialysis scheduled three times per week, 4-hour duration).

He has a history of hypertension, which has been poorly controlled over the past 4 months (BP ranges 150–190/85–105 mmHg), and he has experienced shortness of breath and a significant weight gain over the past month. His pertinent medical history includes hypertension for the past 14 years.
H.B.’s current medications include metoprolol 50 mg BID, furosemide 80 mg BID, calcium carbonate 500 mg TID with meals, Nephrocaps 1 PO QD.

H.B.’s most recent predialysis BP was 175/98 mmHg, and his postdialysis BP was 158/90 mmHg.

A recent ECG showed evidence of LVH.

Serum sodium (Na), 140 mEq/L (normal, 135–147 mEq/L);
Potassium (K), 5.1 mEq/L (normal, 3.5–5.0 mEq/L);
Chloride (Cl), 101 mEq/L (normal, 95–105 mEq/L);
CO₂ content, 23 mEq/L (normal, 22–28 mEq/L);
SrCr, 8.8 mg/dL (normal, 0.6–1.2 mg/dL);
BUN, 84 mg/dL (normal, 8–18 mg/dL);
Phosphate, 5.2 mg/dL (normal, 2.5–5.0 mg/dL);
Ca, 8.6 mg/dL (normal, 8.8–10.4 mg/dL);
Serum albumin, 3.0 g/dL (normal, 4.0–6.0 g/dL);
Cholesterol (nonfasting), 345 mg/dL (normal, <200 mg/dL);
Triglycerides, 285 mg/dL (normal, <200 mg/dL);
Hct, 27% (normal, 39%–49%);
and Hgb, 9.0 g/dL (normal, 13–16 g/dL).

H.B. has a urine output of 50 mL/day.
13- What conditions evident in H.B. put him at increased risk of cardiovascular complications and mortality?

- H.B. has uncontrolled hypertension that is not being adequately managed with his current drug therapy or hemodialysis.
16. D.B. is a 42-year-old white woman who has a 24-year history of type 1 diabetes mellitus with complications of diabetic nephropathy, retinopathy, and neuropathy.

She has hypothyroidism and was diagnosed with stage 5 CKD 4 years ago. She started HD three times weekly at that time.

**Her current medications**

- levothyroxine 0.1 mg/day,
- metoclopramide (Reglan) 10 mg TID before meals,
- insulin aspart 10 U with meals,
- insulin glargine 25 U QHS, docusate 100 mg QD, OsCal 500 mg PO TID with meals,
- EPO 5,000 U IV twice weekly, iron sucrose 100 mg IV (TIW),
- paricalcitol 1 mcg IV three times per week (TIW), and Nephrocaps 1 capsule QD.

At a recent clinic visit, findings on **physical examination** included a BP of 128/84 mmHg, diabetic retinopathic changes with laser scars bilaterally, and diminished sensation bilaterally below the knees.
Her laboratory values were as follows: normal serum electrolytes;
a random blood glucose of 175 mg/dL (normal, 140 mg/dL);
BUN, 45 mg/dL (normal, 8–18 mg/dL);
SrCr, 8.9 mg/dL (normal, 0.6–1.2 mg/dL);
Hgb, 10 g/dL (goal, >11 g/dL);
WBC count, 6,200/mm³ (normal, 3,200–9,800/mm³);
Ca, 8.5 mg/dL (normal, 8.4–9.5 mg/dL);
phosphate, 6.8 mg/dL (normal, 2.5–5.0 mg/dL);
intact parathyroid hormone (iPTH), 450 pg/mL (normal, 5–65 pg/mL);
total serum protein, 5.0 g/dL (normal, 6.0–8.0 g/dL);
serum albumin, 3.1 g/dL (normal, 4.0–6.0 g/dL);
and uric acid, 8.9 mg/dL (normal, 2.0–7.0 mg/dL).

*Describe the etiology of D.B.’s abnormal bone, calcium, phosphorus, and PTH findings.*
Etiology

Renal osteodystrophy (ROD) is the term used to describe bone abnormality due to CKD

- Hyperphosphatemia
- Hypocalcemia
- Hyperparathyroidism
- decreased production of active vitamin D

and resistance to vitamin D therapy are all frequent problems in CKD that can lead to the secondary complication of ROD.

Endocrine Abnormalities Caused by Uremia

18. Does D.B.’s hypothyroidism have any relationship to her CKD? What other endocrine abnormalities are associated with uremia?

- the kidney is involved in all aspects of peripheral hormone metabolism.
- patients with CKD include Thyroidal and gonadal dysfunction.
- In children with kidney disease, growth retardation occurs despite normal or elevated growth hormone.
- T4 is not converted to T3 (PTH)
Altered Glucose and Insulin Metabolism

19 * Other than the obvious effect of D.B.’s diabetes mellitus on blood glucose, are there any effects of kidney disease itself on glucose metabolism?

- *Pseudodiabetes* .

* NOTE: ALL HORMONE IN THE BODY ARE HYPERGLYCEMIC EXCEPT INSULIN IS HYPOGLYCEMIC *

Gastrointestinal Complications

20. One month before her current clinic visit, D.B. complained of nausea and vomiting of partially digested food. Metoclopramide (Reglan) was begun at that time. Could D.B.’s nausea and vomiting have been caused by her kidney failure? Was the appropriate therapy selected?

- Gastrointestinal abnormalities are extremely common in patients with CKD caused by uremia .

- *Metoclopramide* is prokinetic recommended to relieve these Symptoms .

- *dialysis is the preferred therapy* .
Bleeding

21. During her clinic visit, D.B. reports that her bowel movements have become black and tarry in appearance. A rectal examination reveals guaiac-positive stools. Is GI bleeding related to kidney failure?

• D.B. should be evaluated for peptic ulcer disease and lower GI bleeding.
• Uremic patients are at risk for bleeding from mucosal surfaces such as the stomach.

Neurologic Complications
S.H., a 64-year-old, 72-kg, black man, went to his primary care physician because of weakness, nausea, lethargy, decreased exercise tolerance, and general malaise that has developed over the past few weeks.

S.H. had not been seen by a physician for >10 years.

His medical history was unremarkable, except he recalls being told approximately 5 years ago that he had borderline hypertension. He was taking no medications.

The physician's examination revealed a BP of 168/92 mmHg, and funduscopic examination showed grade III hypertensive changes.

On neurologic examination, S.H. was slightly confused, appeared somnolent, and had diminished sensation to pinprick in both lower extremities; asterixis was present. Examination of the skin showed pallor and excoriations across the abdomen, legs, and arms.

- Pertinent laboratory values were as follows:
  - Hct, 20% (normal, 39%–49%);
  - Hgb, 6.7 g/dL (normal, 13–16 g/dL);
  - WBC count, 9,100/mm³ (normal, 3,200–9,800/mm³);
  - serum Na, 135 mEq/L (normal, 135–147 mEq/L);
  - K, 5.8 mEq/L (normal, 3.5–5.0 mEq/L);
  - Cl, 109 mEq/L (normal, 95–105 mEq/L);
  - CO₂ content, 16 mEq/L (normal, 22–28 mEq/L);
  - random blood glucose, 121 mg/dL (normal, <140 mg/dL);
  - BUN, 199 mg/dL (normal, 8–18 mg/dL);
  - SrCr, 19.8 mg/dL (normal, 0.6–1.2 mg/dL);
  - Ca, 8.5 mg/dL (normal, 8.8–10.4 mg/dL);
  - phosphate, 11.1 mg/dL (normal, 2.5–5.0 mg/dL);
  - intact PTH, 830 pg/mL (normal, 5–65 pg/mL);
  - uric acid, 11.9 mg/dL (normal, 2.0–7.0 mg/dL);
  - and albumin, 3.0 g/dL (normal, 4.0–6.0 g/dL).

Renal ultrasonography revealed no obstruction and small kidneys bilaterally. Subsequent kidney biopsy showed chronic glomerular scarring. S.H. was diagnosed with stage 5 CKD, likely caused by chronic, untreated hypertension.
What is the likely explanation for S.H.’s altered mental status? What treatment, if any, is indicated for his neurologic findings?

- **Uremic encephalopathy** → Symptoms generally occur when the eGFR is <10% of normal.
- S.H.’s altered neurologic function is most likely caused by uremia.
- **CAUSES:**
  - Uremic toxin
  - Increase calcium entrance to CNS cell and neurons

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**Dermatologic Complications**

*Why does S.H. have excoriations on his skin? What therapy would be useful?*

_**Uremic pruritus**_
True or false

I. Most common etiology for patient with CKD is DM and hypertension?
II. GFR (30-15 ml/min) is considered to be ESRD?
III. Hyperphosphatemia Hypercalcemia Hyperparathyroidism decreased production of active vitamin .... = (ROD)
IV. Uremic patients are at risk for bleeding from mucosal surfaces such as the stomach?
V. All hormone in the body are hyperglycemic except insulin is hypoglycemic?