Hemodialysis in the Poisoned Patient
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ABSTRACT:

**Audience:** This classic team based learning (cTBL) didactic is aimed for emergency medicine residents and fourth year medical students entering emergency medicine.

**Introduction:** Over one million visits per year to United States (US) emergency departments (ED) are related to poisonings.1 Extracorporeal treatment (ECTR), specifically hemodialysis (HD), is one potential method to enhance elimination of certain drugs and their toxic metabolites.2-12 While HD may be life-saving in certain poisonings, it may have no effect on others and it carries associated risks and costs. It is essential that emergency physicians know the indications for HD in the poisoned patient. This cTBL reviews many poisonings which may be managed by HD.

**Objectives:** By the end of this cTBL, the learner will: 1) recognize laboratory abnormalities related to toxic alcohol ingestion; 2) calculate an anion gap and osmolal gap; 3) know the characteristics of drugs that are good candidates for HD; 4) discuss the management of patients with toxic alcohol ingestions; 5) discuss the management of patients with salicylate overdose; 6) know the indications for HD in patients with overdoses of antiepileptic drugs; 7) discuss the management of patients with lithium toxicity.

**Method:** This didactic session is a cTBL (classic team based learning).

**Topics:** Toxic alcohols, methanol, ethylene glycol, osmolal gap, anion gap acidosis, osmolality, lithium, dialysis, poisonings, toxicology, extracorporeal treatment, carbamazepine, valproic acid, phenytoin, overdose, salicylates, aspirin, fomepizole.
Linked objectives, methods and results:
The learner demonstrates knowledge of laboratory abnormalities and the anion gap and osmolal gap formulas (objectives 1 and 2) during the readiness assessment tests. The learner then shows how to use these formulas (objective 2) during case #1 in the group application exercise (GAE). The learner manages a theoretical patient with a toxic alcohol ingestion (objective 4), salicylate ingestion (objective 5), lithium (objective 7), and anti-epileptics (objective 6) during the group application exercise. The learner confirms knowledge of the characteristics of dialyzable drugs during the readiness assessment test and again in the post-test. The learner demonstrates knowledge of the indications for HD in overdose patients during the group application exercise and post-test.

Recommended pre-reading for instructor:
The instructor should be familiar with all answers and explanations for this exercise. The instructor may also benefit from reading the following paper:

The following are the various consensus statements and extracorporeal treatments in poisonings (EXTRIP) guidelines referenced in each of the exercises. The instructor should be aware of these and might review them:
If the instructor is unfamiliar with toxic alcohols and salicylates, they could consider reading any textbook chapter on toxic alcohols and salicylates, such as:


Other useful papers:

**Learner Responsible Content (LRC):**

The learner may read any textbook chapters on toxic alcohols and salicylate overdose, such as:

References/suggestions for further reading:


Hemodialysis in the Poisoned Patient: individual Readiness Assessment Test (iRAT)

1. What chemical properties favor a substance being dialyzable?

<table>
<thead>
<tr>
<th>Property</th>
<th>Circle one</th>
</tr>
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<tbody>
<tr>
<td>Molecular Weight</td>
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</tr>
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</tr>
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2. Name at least two complications of dialysis:

3. In an overdose setting, name at least four drugs that are good candidates for dialysis:

4. Please complete the following table: Key: AG = Anion Gap, OG = Osmolal Gap

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<thead>
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</table>
5. What lab tests do you need to order to calculate an osmolal gap?

6. Besides the toxic alcohols above, name at least four other causes for an elevated osmolal gap.

7. What is the formula for calculating an anion gap?

8. Name at least six causes for an elevated anion gap:
Hemodialysis in the Poisoned Patient: group Readiness Assessment Test (gRAT)

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6. Besides the toxic alcohols above, name at least four other causes for an elevated osmolal gap.

7. What is the formula for calculating an anion gap?

8. Name at least six causes for an elevated anion gap:
LEARNER MATERIALS

Hemodialysis in the Poisoned Patient: Group Application Exercise (GAE)

Case #1: She’s glowing!
A 26-year-old woman presents to the emergency department with altered mental status. Her (ex-?) boyfriend states that he broke up with her last night and she texted him stating that she was going to drink antifreeze. He went to check on her today and found her unconscious, so he called 911. The patient is obtunded. Her vital signs are: heart rate (HR) 148, blood pressure (BP) 140/70, respiratory rate (RR) 24, temperature (T) 35.1°C. She is intubated.

Her labs are as follows:
Na⁺=147 mEq/L
K⁺= 7.7 mEq/L
Cl⁻ = 105 mEq/L
HCO₃⁻ = <5 mEq/L
Blood Urea Nitrogen (BUN) = 18 mg/dL
Creatinine (Cr) = 2.4 mg/dL
Glucose = 137 mg/dL
Ca²⁺ = 8.3 mg/dL
Lactate = 3.6 mmol/L
Ethanol = Not detected
Acetaminophen < 5.0 mcg/ml
Salicylate <4 mg/dL
Osmolality = 338 mOsm/kg
ABG (arterial blood gas): pH 6.75 / pCO₂ 23.7/ HCO₃ 3.3/ pO₂ 582.9

1. What is her anion gap?

2. What is the formula for calculating an osmolal gap?

3. What is her osmolal gap?
4. Is she a candidate for gastric decontamination? Why/why not?

5. What antidote should be given? Dose?

6. How does the antidote work?

7. Should you start dialysis on this patient? Do you need other tests back to decide?

8. What are the complications of ethylene glycol ingestion?

9. What other poisoning with potential retinal toxicity can be treated with the antidote in 5? What is the dose?

10. What are the indications for dialysis for the toxin in 9 (Hint, there is a paper by Roberts DM, et al. as part of the EXTRIP group)?
Case #2: Anyone else hear that ringing??!

A 45-year-old male presents to the emergency department complaining of nausea, vomiting, tinnitus, and generalized weakness. Of note, the patient was seen one week ago in the ED for rib fracture he sustained while falling off of his motorcycle. His vital signs are as follows: HR 120 beats/min, RR 30 breaths/min, BP 110/70 mmHg, T=38.5°C, O₂ saturation 95% RA.

His labs are as follows:
Na⁺: 140 mEq/L
K⁺: 3.3 mEq/L
Cl⁻: 105 mEq/L
HCO₃⁻: 16 mEq/L
BUN: 20 mg/dL
Cr: 1.1 mg/dL
Glucose: 75 mg/dL

1. In addition to an ABG, what additional laboratory studies would you like to order?

2. Your ABG returns with a pH value of 7.46, pCO₂ = 25 mmHg, HCO₃ = 16 mEq/L. Additionally, your serum salicylate level is 75 mg/dL. Your patient states that he has been taking aspirin to control the pain from his rib fracture. What are some of the signs and symptoms associated with salicylate toxicity:

3. What is the treatment?

4. What are the indications for dialysis? (Hint: EXTRIP)
Case #3: Oh Limey!
A 45-year-old female with bipolar disorder presents to the emergency department. She states that her mania has been getting worse and her psychiatrist adjusted her medications two weeks ago. She started developing nausea, vomiting, and diarrhea 5 days ago. Now, she is starting to feel worsening agitation, dizziness, and tremors.

1. What medication was probably adjusted?

2. What is the normal serum concentration of this drug?

3. What signs and symptoms can occur with toxicity from this drug?

4. What is the treatment, and what are the indications for dialysis in overdose?
Case #4: Can’t fight the seizure...but we can try
A 30-year-old male with epilepsy went on vacation and forgot to bring his medications. After returning home, he took all of his medications in order to “catch up.” He is feeling confused and lethargic. He can’t remember the name of the antiepileptic drug that he is taking. You mention valproic acid, phenytoin, and carbamazepine. He says, “It’s definitely one of those!”

What symptoms would you expect for each and what are the indications for dialysis for each?

<table>
<thead>
<tr>
<th>Anti-epileptic drug</th>
<th>Symptoms in overdose</th>
<th>Treatment</th>
<th>Indications for dialysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phenytoin</td>
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<tr>
<td>Carbamazepine</td>
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<td>Valproic Acid</td>
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</tr>
</tbody>
</table>
Hemodialysis in the Poisoned Patient:
Brief Wrap Up

*Please find the associated Powerpoint to use for going over the answers.*

Also, there is a Kahoot post-test: [https://play.kahoot.it/#/k/4ca1-486f-b6a8-32ed4b62b623](https://play.kahoot.it/#/k/4ca1-486f-b6a8-32ed4b62b623) or you may use the following paper post-test:

1. Which of the following properties of a drug makes it more dialyzable?
   a. High tissue binding
   b. Large volume of distribution
   c. Small molecular weight
   d. Poor water solubility

2. Which of the following drugs is a good candidate for hemodialysis in overdose?
   a. Digoxin
   b. Lidocaine
   c. Theophylline
   d. Warfarin

3. Which of the following does isopropanol ingestion cause?
   a. Elevated anion gap
   b. Elevated osmolal gap
   c. Both

4. Which of the following is a feared complication of ethylene glycol overdose?
   a. Blindness
   b. Tinnitus
   c. Hepatotoxicity
   d. Renal failure

5. What is the most appropriate antidote for early ethylene glycol or methanol ingestion?
   a. Fomepizole
   b. Hemodialysis
   c. L-carnitine
   d. N-acetylcysteine
6. Which of the following is an indication for hemodialysis in salicylate poisoning?
   a. Hypoxemia
   b. Respiratory alkalosis
   c. Salicylate level > 40 mg/dL
   d. Tinnitus

7. Which drug in overdose can cause hyperammonemia and cerebral edema?
   a. Carbamazepine
   b. Lithium
   c. Phenytoin
   d. Valproic Acid
INSTRUCTOR MATERIALS

Answer keys to all exercises with explanations, are on the following pages.

Learners: please do not proceed.
1. Traditionally, what properties of toxins make them appropriate for hemodialysis?

Molecular Weight
Small

Volume of Distribution
Small

Tissue/protein binding
Poor

**Explanations:**

*Low molecular weight:* Traditionally, molecules amenable to dialysis are small in molecular weight (due to pore size), but recent advances with larger pore size of dialysis membranes are allowing for larger (but still <500 Daltons).

*Low volume of distribution:* Relatively more drug found in the vascular space (average volume of distribution of a person is 0.6L/kg).

*Water soluble:* Lower volume of distribution.

*Low tissue and protein binding:* However, some highly protein bound drugs have lower protein binding at toxic levels (higher saturation of protein bound molecules; therefore, a higher percentage of free drug in the serum).

**Other features of effectively dialyzed toxins:**

- Compelling indication for dialysis should be present (secondary to low but real frequency of complications)
- High water solubility
- Poor or impaired endogenous clearance
- Clinical benefit of hemodialysis has been demonstrated

2. What are some complications of dialysis?^7^

Complications of dialysis include:

- Complications related to catheter placement
- Bleeding, infection, thrombosis

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https://doi.org/10.21980/J88568
INSTRUCTOR MATERIALS

- Complications related to sites specific catheters: retroperitoneal hemorrhage (femoral), pneumothorax (subclavian), carotid arterial cannulation (internal jugular)
- Difficulty maintaining hemodynamic stability (blood pressure fluctuations)
- Use of heparin
- Cost: Dialysis nurse, nephrologist, setting up machine
- Air embolism

3. **In an overdose setting, which toxins are good candidates for dialysis?**\(^5,10,11\)
   (The **bolded** drugs are more commonly dialyzed.)
   Aminoglycosides, aminophylline, atenolol, carbamazepine, carisoprodol, chloral hydrate, disopyramide, ethchlovynol, **ethylene glycol**, isopropanol, **lithium**, meprobamate, **methanol**, methotrexate, mushroom, paraquat, phenobarbital, phenothiazine, phenytoin, salicylates, theophylline, trichloroethanol, **valproic acid**

4. **Please complete the following table:**
   Anion Gap (AG)
   Osmolal Gap (OG)

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<thead>
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<td>Methanol</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Windshield washer fluid</td>
<td>Formaldehyde Formic Acid</td>
</tr>
<tr>
<td>Ethylene Glycol</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Antifreeze</td>
<td>Glycolic Acid Oxalic Acid</td>
</tr>
<tr>
<td>Isopropanol</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Rubbing Alcohol</td>
<td>Acetone</td>
</tr>
</tbody>
</table>

5. **What labs do you need to order to calculate an osmolal gap?**\(^13\)
   Sodium, BUN, glucose, ethanol (EtOH), serum osmolality

https://doi.org/10.21980/J88568
6. **Besides the toxic alcohols above, what are other causes for an elevated osmolal gap?**
   Alcoholic ketoacidosis (AKA), renal failure, diabetic ketoacidosis (DKA), shock, mannitol, toxic alcohols, severe lactic acidosis, pseudohyponatremia, levothyroxine/lithium (high doses), activated charcoal.

7. **Anion Gap formula:**
   Anion Gap = Sodium - (Chloride + Bicarbonate)

8. **Name at least six causes for an elevated anion gap.**
Hemodialysis in the Poisoned Patient: Group Application Exercise (GAE) Key

Case #1: She’s glowing!
A 26-year-old woman presents to the emergency department with altered mental status. Her (ex-?) boyfriend states that he broke up with her last night and she texted him stating that she was going to drink antifreeze. He went to check on her today and found her unconscious, so he called 911. The patient is obtunded. Her vital signs are: HR 148/min, BP 140/70, RR 24, T 35.1. She is intubated.

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Lactate = 3.6 mmol/L
Ethanol = Not detected
Acetaminophen < 5.0 mcg/ml
Salicylate <4 mg/dL
Osmolality = 338 mOsm/kg
ABG: pH 6.75 / pCO₂ 23.7/ HCO₃ 3.3/ pO₂ 582.9

1. **What is her anion gap?**
   Anion Gap (AG): Na – (Cl + HCO₃)
   147 – (105 + <5)
   AG = > 37

2. **What is the formula for calculating an osmolal gap?**
   \[ \text{Osm}_{\text{Meas}} - \text{Osm}_{\text{Calc}} = \frac{2(\text{Na}) + (\text{BUN})/2.8 + \text{Gluc}/18 + \text{EtOH}/4.6}{2} \]

3. **What is her osmolal gap?**

   Osm(Meas) – Osm(Calc)
   338 – [2(Na) + (BUN)/2.8 + Gluc/18 + EtOH/4.6]
   338 – [294 + 6.4 + 7.6 + 0]
   338 – 308
   
   OG = 30 mOsm/kg

   The proper conversion factor for Ethanol is an area of continued debate. The conversion factor here is 4.6 (one-tenth of ethanol’s molecular weight), but there is good evidence that in reality a better conversion factor might be as low as 3.7, while 4.2 is also fairly commonly used. We use 4.6 in this equation.

4. **Is she a candidate for gastric decontamination? Why/why not?**

   No: Ethylene glycol is rapidly absorbed and does not bind well to activated charcoal. It has been several hours since her ingestion.

5. **What antidote should be given?**

   Fomepizole 15mg/kg IV
   Also consider ethanol 0.8 g/kg (less desirable)

6. **How does the antidote work?**

   Fomepizole is a competitive Alcohol Dehydrogenase (ADH) Inhibitor, which is the first step in the metabolism of ethylene glycol. Therefore, it may not be as effective in this case, since it has been several hours since the ingestion and all ethylene glycol may be metabolized.
7. **Should you start dialysis on this patient? Do you need other tests back to decide?**
   Yes, you have sufficient cause to start dialysis and you do not need to wait for an ethylene glycol level; it won’t come back in time. The patient is significantly acidemic and needs dialysis to clear the active metabolites (fomepizole will not clear the metabolites that have already formed). The patient has a suspected ethylene glycol ingestion, plus a pH<7.3 and should therefore be dialyzed.

8. **What are the complications of ethylene glycol ingestion?**
   - Renal insufficiency/failure
   - Hypocalcemia secondary to crystal formation (depletes calcium levels)
   - Cranial neuropathies
   - Severe acidemia: cardiopulmonary complications/ARDS (acute respiratory distress syndrome)

https://doi.org/10.21980/J88S68
9. **What other poisoning with potential retinal toxicity can be treated with the antidote in 5? What is the dose?**
   Methanol, same dose (fomepizole 15mg/kg)

10. **What are the indications for dialysis for the toxin in 9 (Hint, there is a paper by Roberts DM, et al. as part of the EXTRIP group)?**
    Coma, seizures, new vision defects, metabolic acidosis (blood pH<7.15), persistent metabolic acidosis despite supportive measures and antidote, serum anion gap >24 mmol/L, serum methanol concentrations >500mg/L if fomepizole not available; >700mg/L if fomepizole therapy available.

Case #2: Anyone else hear that ringing??!

A 45-year-old male presents to the emergency department complaining of nausea, vomiting, tinnitus, and generalized weakness. Of note, the patient was seen one week ago in the ED for rib fracture he sustained while falling off of his motorcycle. His vital signs are as follows: HR 120 beats/min, RR 30 breaths/min, BP 110/70, T=38.5°C, O₂ saturation 95% RA.

His labs are as follows:
- Na⁺: 140 mEq/L
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- Cl⁻: 105 mEq/L
- HCO₃⁻: 16 mEq/L
- BUN: 20 mg/dL
- Cr: 1.1 mg/dL
- Glucose: 75 mg/dL

1. What additional laboratory studies would you like to order?
   - Blood cultures (this may look like sepsis from pneumonia)
   - Salicylate level
   - Lactate
   - Urinalysis

2. Your ABG returns with a pH value of 7.46, pCO₂ = 25 mmHg, HCO₃⁻ = 16 mEq/L. Additionally, your serum salicylate level is 75 mg/dL. Your patient states that he has been taking aspirin to control the pain from his rib fracture. What are some of the symptoms associated with salicylate toxicity?¹⁸-²⁰
   - CNS: Tinnitus, confusion, agitation, lethargy, coma, seizure, syndrome of inappropriate antidiuretic hormone (SIADH)
   - GI: Nausea, vomiting, abdominal pain, gastritis, decreased motility
   - CV: Tachycardia (2/2 Hypovolemia and hyperpyrexia)
   - Pulm: ARDS, tachypnea
   - Heme: Prolonged PT, platelet dysfunction
   - Acid/base: Respiratory alkalosis, metabolic acidosis, respiratory acidosis, hypokalemia, hyponatremia or hypernatremia,
INSTRUCTOR MATERIALS

**Metabolic:** Hyperthermia, hyper- or hypoglycemia, hypoglycorrhachia, ketonemia, ketonuria

3. **What is the treatment?**
   - Consider multidose activated charcoal (MDAC)
   - IV fluids
   - Urine alkalinization ("ion trapping") is indicated for ASA level >40 mg/dL (1-2 mEq/kg sodium bicarbonate by IV bolus 3 amps NaHCO3 + 40mEq KCl in 1L D5W for goal urine pH 7.5, serum pH 7.45-7.55).
   - Consider hemodialysis

4. **What are the indications for dialysis?**
   - Salicylate 100 mg/dL (or 90 mg/dL with impaired renal function)
   - Altered mental status
   - Hypoxemia

   If standard therapy fails, consider HD in the following:
   - Salicylate >90 mg/dL (or 80mg/dL with impaired renal function)
   - pH 7.20 or lower
Case #3: Oh Limey!
A 45-year-old female with bipolar disorder presents to the emergency department. She states that her mania has been getting worse and her psychiatrist adjusted her medications two weeks ago. She started developing nausea, vomiting, and diarrhea five days ago. Now, she is starting to feel worsening agitation, dizziness, and tremors.

1. **What medication was probably adjusted?**
   Lithium

2. **What is the normal serum concentration of this drug**
   0.8 - 1.2 mEq/L

3. **What symptoms can occur in toxicity?**
   **Cardiovascular:** Wandering atrial pacemaker, sinus bradycardia, ST-segment elevation, unmasking Brugada syndrome, prolonged QT
   **Neurologic:** Lethargy, ataxia, confusion, agitation, tremors, fasciculations, myoclonic jerks, hyperreflexia, seizures
   **GI:** Nausea, vomiting, diarrhea, ileus

4. **Treatment?**
   Supportive
   Consider dialysis if:
   - Li$^+$ >4.0 mEq/L (with impaired kidney function)
   - Decreased level of consciousness, seizures, or dysrhythmias
   - Li$^+$>5.0mEq/L
   Expected time to reduce Li$^+$<1.0mEq/L with optimal management is >36 hours
Case #4: Can’t fight the seizure…but we can try

A 30-year-old male with epilepsy went on vacation and forgot to bring his medications. After returning home, he took all of his medications in order to “catch up.” He is not feeling well. He can’t remember the name of the anti-epileptic drug that he is taking. You mention valproic acid, phenytoin, and carbamazepine. He says, “It’s definitely one of those!”

What symptoms would you expect for each and what are the indications for dialysis for each?²,⁸,⁹

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<th>Symptoms in overdose</th>
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<tbody>
<tr>
<td>Phenytoin</td>
<td>Multidirectional nystagmus, Dizziness, Nausea, vomiting, Ataxia, Coma, Respiratory depression, Agitation, Irritability, Slurred speech, Hypotension, Cardiac arrest</td>
<td>Supportive Consider charcoal</td>
<td>-Reasonable in selected cases of severe phenytoin poisoning -Prolonged coma -Incapacitating ataxia -Do not perform based on the dose ingested -Do not perform solely based on serum concentrations</td>
</tr>
<tr>
<td>Carbamazepine</td>
<td>Movement disorders, Altered mental status, Seizures, Respiratory depression, Tachycardia, Hypotension, Anticholinergic effects, Myocardial depression, Conduction disturbances, QRS widening,</td>
<td>Hypertonic sodium bicarbonate (QRS widening) Multiple-dose activated charcoal Consider dialysis</td>
<td>-Intractable seizures -Life threatening dysrhythmias -Prolonged coma or respiratory depression requiring mechanical ventilation -Significant toxicity with rising concentrations</td>
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<td><strong>Bundle branch blocks, Brugada type patterns, AV blocks (Atrioventricular blocks), PVCs (Premature ventricular contractions)</strong></td>
</tr>
<tr>
<td><strong>Valproic Acid</strong></td>
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Hemodialysis in the Poisoned Patient: 
Brief Wrap Up Key

1. Which of the following properties of a drug makes it more dialyzable?
   a. High tissue binding
   b. Large volume of distribution
   c. **Small molecular weight**
   d. Poor water solubility

   See RAT key, explanation to question 1

2. Which of the following drugs is a good candidate for hemodialysis in overdose?
   a. Digoxin
   b. Lidocaine
   c. **Theophylline**
   d. Warfarin

   See RAT key, explanation to question 3.

3. Which of the following does isopropanol ingestion cause?
   a. Elevated anion gap
   b. **Elevated osmolal gap**
   c. Both

   See RAT key, explanation to question 4.

4. Which of the following is a feared complication of ethylene glycol overdose?
   a. Blindness
   b. Tinnitus
   c. Hepatotoxicity
   d. **Renal failure**

   See GAE Case #1, explanation to G

5. What is the most appropriate antidote for early ethylene glycol or methanol ingestion?
   a. **Fomepizole**
   b. Hemodialysis
   c. L-carnitine
   d. N-acetylcysteine
See GAE Case #1, explanation to E&F

6. Which of the following is an indication for hemodialysis in salicylate poisoning?
   a. Hypoxemia
   b. Respiratory alkalosis
   c. Salicylate level > 40 mg/dL
   d. Tinnitus

See GAE Case #2, explanation to D

7. Which drug in overdose can cause hyperammonemia and cerebral edema?
   a. Carbamazepine
   b. Lithium
   c. Phenytoin
   d. Valproic Acid

See GAE Case #4, explanation