

# Pharmacology/Toxicology Case Studies



- + 132 Pages
- + 60 Case Studies
- + Each case includes multiple questions followed by a detailed explanation

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# Acknowledgments

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## PHARMACOLOGY/TOXICOLOGY CASE STUDY #1

History: A 14-year-old female is brought to your emergency department by her parents after she admitted to ingesting a total of ten, 250 milligram amoxicillin tablets four hours ago after an argument at home that resulted in loss of her phone privileges. Her parents are concerned that she was trying to kill herself. She denies any co-ingestion and has no symptoms. There are no other prescription medications in the home.

PMH: None.

Physical Examination:

T: 99°F      HR: 100 bpm      RR: 16 breaths per minute      BP: 100/70 mm Hg

General: The patient is tearful, but otherwise in no distress.  
The remainder of the physical exam is completely normal.

### QUESTIONS CASE STUDY #4

1. What testing, if any, should be obtained?
2. Should activated charcoal be administered?
3. Are there other treatments that should be considered?

## CASE STUDY #1: GENERAL APPROACH TO TOXIC INGESTIONS

1. Acetaminophen levels should be obtained in all cases of reported or suspected poisoning, regardless of history and physical exam. Acetaminophen is readily available and patients can initially present without signs or symptoms even with toxic levels. Dose history should not be used to make management decisions because studies have found no correlation between the amount of acetaminophen reportedly ingested and the serum concentration measured. The patient's four hour acetaminophen level in this patient was 85 ug/mL. A pregnancy test should be performed in all females of childbearing age, as women may attempt suicide due to an unwanted pregnancy.

The role of routine urine drug screening in the evaluation of patients presenting to the emergency department with psychiatric-related complaints is controversial. ACEP's Clinical Policy: Critical Issues in the Diagnosis and Management of the Adult Psychiatric Patient in the Emergency Department, published in January 2006, makes a level C recommendation that routine urine screening for drugs of abuse in alert, awake, cooperative patients does not affect ED management and need not be performed as part of the ED assessment. Often, this testing is requested by the receiving psychiatric facility for admission purposes, long-term care planning or diagnosis. In these cases, it may be reasonable to obtain this testing in the emergency department; however this testing should not delay patient evaluation or transfer. These recommendations relate to the management of adult psychiatric patients; pediatric patients are excluded.

2. Previously, activated charcoal was not routinely recommended in treatment of ingestions that occurred greater than one hour prior to presentation; however newer data regarding acetaminophen ingestions suggests that the half-life of this drug in the stomach is markedly increased in overdose settings and that there may be some therapeutic benefit to its administration past the traditional one hour mark. Other circumstances that may warrant charcoal administration past the one hour mark include massive overdoses, poisoning with sustained release preparations and ingestion of agents that slow gastrointestinal motility. or acetaminophen, activated charcoal may offer some benefit when used up to four hours post ingestion.
3. The patient does not require treatment with N-acetylcysteine because her four hour acetaminophen level falls below the toxicity line on the Rumack-Matthew nomogram. Based on recommendations from the American Academy of Clinical Toxicology, this patient does not meet criteria for gastric lavage as she meets neither of two criteria for this intervention: ingestion of a potentially life-threatening amount of a poison and presentation within 60 minutes of ingestion. For similar reasons, this patient will not benefit from whole bowel irrigation. Home administration of ipecac syrup is no longer recommended by the American Academy of Pediatrics and its routine use in the emergency department is discouraged by the American Academy of Clinical Toxicology.

## PHARMACOLOGY/TOXICOLOGY CASE STUDY #2

History: A 40-year-old male presents to your emergency department after falling into a vat of chromic acid. The patient arrives via EMS with a dry cough and is actively vomiting. He is complaining of chest pain and shortness of breath.

PMH: Asthma.

Medications: Albuterol inhaler as needed.

Physical Examination:

T: 98.6°F    HR: 115 bpm    RR: 29 breaths per minute    BP: 176/94 mm Hg

General: He is awake and alert.

HEENT: Normal.

Pulmonary: Diffuse wheezing, poor air exchange.

CV: Tachycardic, regular rhythm without murmur, normal perfusion.

Extremities: Diffuse skin ulcers in exposed areas.

### QUESTIONS CASE STUDY #2

1. What would be your initial approach to this patient?
2. What complications may be associated with this type of exposure?
3. What therapy is indicated?

## CASE STUDY #2: CHROMIC ACID EXPOSURE

1. Decontamination should accompany stabilization of the airway, breathing and circulation. The patient should have all clothing removed and copious aqueous irrigation performed.
2. Chromic acid is a strong acid that contains the hexavalent ( $\text{CrVI}^3$ ), or most hazardous, form of chromium. Acute skin exposure may cause burns and chronic exposure may result in skin and nasal ulcer formation. These skin ulcers are round or oval growths with reddish edges and necrotic centers and are often referred to as “chrome holes” or “chrome sores”. Chromic acid inhalation may be associated with upper respiratory irritation and bronchospasm, manifested by cough, chest pain and dyspnea. Pulmonary congestion visible on radiographs, interstitial pneumonia and delayed, non-cardiogenic edema have been reported. Systemic effects include renal failure secondary to acute renal tubular acidosis, hemolysis and liver damage.
3. Initially, the focus should be decontamination, including removal of contaminated clothing and a deluge, or heavy downpour safety shower. Fluid and electrolyte balance should be maintained, especially in the case of large skin and mucosal lesions which can lead to significant fluid losses. The efficacy of activated charcoal has not been demonstrated. Ascorbic acid (vitamin C) has been recommended for cases of ingestion and skin exposure to reduce absorption of chromium by oxidizing it from the hexavalent to trivalent form, which does not cross cell membranes as rapidly. This intervention must be performed within two hours of exposure. Beta agonist therapy is indicated for bronchospasm. Patients should be observed for the development of renal failure, non-cardiogenic pulmonary edema and liver failure. Hemodialysis, exchange transfusion and chelation therapy are ineffective.

The Poison Control Center should be called for advice on antidotes and for assistance with management of poisoning/exposure to unfamiliar chemicals.

Prevention of exposure to chromium, particularly respiratory exposure, is critical as chromium has a demonstrated carcinogenic potential.

### PHARMACOLOGY/TOXICOLOGY CASE STUDY #3

History: A 30-year-old white male presents to your emergency department after ingesting "white powder" from a bag that was given to him by his friend. He has developed weakness, vomiting and diarrhea.

PMH: None.

Physical Examination:

T: 100.4°F    HR: 120 bpm    RR: 20 breaths per minute    BP: 90/60 mm Hg

General: He is awake and alert, but actively vomiting and having diarrhea.

Pulmonary: Clear to auscultation.

CV: Tachycardic without murmur, normal perfusion.

Neurologic: GCS 15. Cranial nerves II-XII intact. Remaining neurologic exam is nonfocal.

### QUESTIONS CASE STUDY #3

1. From what type of poisoning is this patient suffering and what are the typical signs and symptoms?
2. What initial therapy, if any, should be instituted?

### CASE STUDY #3: ARSENIC POISONING

1. This patient is suffering from arsenic poisoning. Arsenic is a naturally occurring metalloid element. Acute poisoning predominantly affects the gastrointestinal system, causing nausea, vomiting, abdominal pain and diarrhea. Affected individuals may have a garlic odor to their breath or stool. Resultant dehydration heralds cardiovascular instability, which occurs rapidly and progresses from sinus tachycardia to orthostatic hypotension with possible shock and death, depending on the amount and form of arsenic ingested. Patients may develop severe encephalopathy with delirium, confusion, seizures and coma. Other acute complications include rhabdomyolysis and acute renal failure.

Although a symmetrical sensorimotor peripheral polyneuropathy may develop 1-3 weeks following ingestion, some patients may develop symptoms within 24 hours. Sensory symptoms usually occur first with patients complaining of “pins and needles” or electrical shock-like pains in the lower extremities. Early examination may demonstrate isolated, diminished or absent vibratory sense. Motor weakness may later develop and can sometimes mimic Guillain-Barré syndrome. Reversible pancytopenia and hepatitis can occur within one week after the initial illness. Dermatologic lesions, a dry, hacking cough and Mees lines (horizontal 1-2 mm white lines on the nails) can also develop after severe acute and chronic exposures.

2. The white powder was rapidly identified as arsenic and a spot urine arsenic level was sent for confirmation of ingestion. Blood and urine were sent to the lab for determination of arsenic levels. Acute arsenic toxicity is life threatening and necessitates aggressive treatment.

Initial management should be focused on stabilizing the airway, breathing and circulation. The patient should receive 2 large bore IV's and be placed on a cardiac monitor with continuous pulse oximetry. Hypotension should be treated with crystalloid fluids; however, pressor agents may be required. Fluid status should be carefully monitored, as cerebral and pulmonary edema may occur. Potassium, calcium and magnesium concentrations should be maintained in the normal range and urine output should be maintained. Ventricular dysrhythmias may occur. Ventricular tachycardia and ventricular fibrillation are treated with lidocaine and electrical defibrillation. Because arsenic is associated with prolongation of the QTc, agents that prolong the QTc should be avoided (class IA, IC and III antidysrhythmic agents). Bicarbonate therapy may be effective.

Chelation therapy should be initiated as soon as possible with Unithiol (DMPS, a water-soluble analog of dimercaperol), dimercaperol (BAL, second choice if unithiol not immediately available) or DMSA (oral succimer), under the direction of a medical toxicologist.

Activated charcoal is sometimes used for ingestions that present within one hour, but its efficacy has not been proven.



## PHARMACOLOGY/TOXICOLOGY CASE STUDY #4

History: A 12-month-old male presents to your emergency department after ingesting a watch battery, which was left out on the counter. He has been drooling since the incident and refusing his bottle.

PMH: None.

### Physical Examination:

T: 98.6°F      HR: 137 bpm      RR: 32 breaths per minute      BP: 100/62 mm Hg

General: He is awake, alert and calm in appearance.

HEENT: Drooling from mouth.

Pulmonary: Clear to auscultation.

CV: Regular rate and rhythm without murmur, normal perfusion.

Extremities: Normal.

## QUESTIONS CASE STUDY #1

1. What is the initial approach to this patient?
2. What complications may be associated with these types of batteries?
3. On x-ray, the battery is located in the esophagus at the level of the aortic arch. What therapy is indicated?

## CASE STUDY #4: BUTTON BATTERY INGESTION

1. Any patient presenting with possible foreign body ingestion should have a complete assessment of his airway and respiratory status, including pulse oximetry readings when indicated. The child should remain in the upright position and NPO. Both anteroposterior and lateral radiographs should be obtained, imaging from the nasopharynx to the anus to localize the position of the foreign body.
2. Complications may occur for several reasons, including electrical discharge, pressure necrosis, obstruction and leakage of battery contents. Electrical discharge is the most important mechanism in most clinically significant cases. Discharged batteries still retain enough voltage and storage capability to generate an external current; however newer batteries are associated with a greater potential for tissue damage. The larger the battery the more likely an esophageal obstruction will occur. Esophageal perforation and aspiration have also been reported. In the majority of cases, 89% in one series, the battery will pass spontaneously without complication. Systemic absorption of heavy metals from broken or fragmented batteries is a common concern but has been rarely reported. Mercury batteries may pose a particular hazard if they break.
3. This battery requires emergent removal because of its location in the esophagus. Esophageal injury from button batteries has been reported in less than two hours. Endoscopy is the removal method of choice. Foley catheters have been recommended for removal of esophageal foreign bodies, but their use carries an added risk of aspiration. Magnetized probes are an alternative in skilled hands.

Risks are lower after entry into stomach but not absent. For button batteries in the stomach, monitoring of stool content or follow up x-ray in one week is recommended. Parents should be educated about concerning symptoms, including abdominal pain and vomiting.

## PHARMACOLOGY/TOXICOLOGY CASE STUDY #5

**History:** A 19-month-old male presents to your emergency department with his parents after ingesting 35 mL of phenytoin suspension. Parents relate that he appears to be “wobbly” and “sleepy”. He has had no vomiting and no seizure activity.

**PMH:** Brain aneurysm, seizure disorder, feeding disorder.

**Physical Examination:**

T: 100.4°F    HR: 132 bpm    RR: 30 breaths per minute    BP: 110/70 mm Hg

**General:** He appears very sleepy but is arousable and has an intact gag reflex.

**HEENT:** Examination reveals horizontal and vertical nystagmus. Mouth examination reveals gingival hyperplasia.

**Pulmonary:** Clear to auscultation.

**CV:** Regular rate and rhythm without murmur, capillary refill normal.

**Neurologic:** GCS = 15, cranial nerves II-XII intact. Truncal ataxia is present. Hyperreflexia present, all DTR's.

### QUESTIONS CASE STUDY #5

1. What are the usual signs of acute phenytoin toxicity?
2. What initial therapy should be instituted?
3. What are the signs and symptoms of chronic phenytoin toxicity?

## CASE STUDY #5: PHENYTOIN POISONING

1. CNS effects are the most common symptoms of acute phenytoin ingestion. The minimum oral toxic dose is 20 mg/kg. Mild to moderate intoxication causes horizontal nystagmus, ataxia, ophthalmoplegia, dysarthria, hyperreflexia, hyperglycemia, irritability and altered mental status. Severe intoxication causes stupor, coma and respiratory arrest. While phenytoin toxicity can produce paradoxical seizures, this finding should prompt a search for other causes as this is a rare finding. Death from phenytoin poisoning is also rare.

Serum phenytoin levels can be obtained and it is generally recommended that repeated levels are determined because of potential for slowed absorption. The therapeutic range is 10-20 mg/L. At levels under 10 mg/L, systemic manifestations are rare. At levels 10-20 mg/L, mild nystagmus may be present. At levels between 20-30 mg/L nystagmus is common, and ataxia may occur. At levels between 30-40 mg/L patients often develop ataxia and slurred speech. At levels between 40-50 mg/L patients may develop lethargy, confusion and combativeness. At levels above 50 mg/L patients also develop choreoathetoid movements and opisthotonic posturing. Survival has been reported in three patients with levels greater than 100 mg/L. Although cardiovascular effects occur after rapid intravenous administration of phenytoin, due to the propylene glycol excipient, these effects do not occur after chronic or acute oral exposures

In some instances, the patient's serum phenytoin level may seem discordant with their symptoms. In these situations, a serum albumin level might be helpful as higher free phenytoin concentrations are seen in the setting of hypoalbuminemia. Because it is the free phenytoin concentration that determines toxicity, but the total level that is reported, hypoalbuminemic patients may exhibit significant symptoms in the setting of only mildly elevated levels. Free phenytoin concentrations can be obtained; however they are generally not measured unless there is clinical uncertainty of the diagnosis.

2. Initial management is focused on stabilizing the airway, breathing and circulation. Patients with ataxia should have precautions taken to prevent injury from fall. Since the child has a seizure disorder, it is important not to drop the anticonvulsant level to a subtherapeutic range. If seizures occur, treat in the usual way and search for other causes. In the appropriate situation, activated charcoal may be administered. If the level is very high and the patient has significant symptoms, multi-dose activated charcoal can be given to enhance phenytoin elimination but is not necessary and may increase aspiration risk in symptomatic patients. Physicians should weigh the benefits of multidose activated charcoal in patients in need of chronic phenytoin therapy for seizure control.
3. Patients on long term phenytoin therapy can develop gingival hyperplasia, which is the most common adverse effect in adults and children. Chronic phenytoin

toxicity may result in phenytoin encephalopathy. Other adverse effects include hyperglycemia secondary to impaired insulin secretion, hypothyroidism, osteomalacia, aplastic anemia, malignant lymphoma, hemorrhagic disease of the newborn (responsive to vitamin K), and megaloblastic anemia secondary to decreased folate absorption and altered folate metabolism (responsive to folic acid).

## PHARMACOLOGY/TOXICOLOGY CASE STUDY #6

**History:** A 19-year-old female presents to your emergency department after ingesting a large amount of rubbing alcohol following a fight with her boyfriend. She appears very sleepy and complains of generalized weakness. She now denies suicidal ideation and has no plan to injure herself. She denies any co-ingestion and the paramedics found no other pills or substances in the house.

**PMH:** None.

**SH:** No previous suicide attempts or history of depression.

**Physical Examination:**

T: 99.4°F      HR: 78 bpm      RR: 18 breaths per minute      BP: 90/60 mm Hg

**General:** Lethargic.

**HEENT:** Acetone odor on the breath, otherwise normal.

**Pulmonary:** Clear to auscultation.

**CV:** Regular rate and rhythm without murmur, capillary refill 4 seconds.

**Neurologic:** GCS 14. Cranial nerves II-XII intact. Ataxia is present. All deep tendon reflexes are depressed. Strength is 3/5 all flexors and extensors of bilateral upper and lower extremities.

### QUESTIONS CASE STUDY # 6

1. What substance did the patient ingest?
2. What are the usual signs of acute toxicity?
3. What initial therapy should be instituted?
4. What are the characteristic laboratory findings?

## CASE STUDY #6: ISOPROPANOL POISONING

1. This patient ingested isopropyl alcohol. Rubbing alcohol contains approximately 70% isopropanol. It is also found in solvents, antifreeze and disinfectants. The primary reason people ingest this substance is to become intoxicated (for instance, as an inexpensive ethanol substitute in alcoholics) or to harm themselves.
2. The major effects of acute isopropanol ingestion are on the central nervous system, mimicking the inebriation caused by ethanol, and gastrointestinal systems. The usual signs and symptoms include CNS depression, slurred speech, ataxia, lethargy, weakness, nausea and headache. Abdominal pain, gastritis, hypotension and apnea can also occur. Uncommon adverse effects include hemolytic anemia, hypothermia, renal tubular acidosis and rhabdomyolysis. Death from isopropyl alcohol use is rare but can occur secondary to coma with untreated airway compromise, injury resultant from ataxia or stupor, or rarely, hypotension caused by vasodilation and possible myocardial depression after massive overdose. Some sources give an estimated lethal dose of 250 mL in adults; however with treatment, adults and children have survived much larger ingestions.
3. Initial management should be focused on stabilizing the airway, breathing and circulation. If exposure is by the cutaneous route, skin decontamination should be extensive as significant absorption and toxicity can occur, especially in infants. It is important to ensure that no methanol or ethylene glycol were co-ingested. Serum isopropanol levels are mostly used to substantiate the diagnosis and treatment is supportive. Levels greater than 100 mg/dL can cause a decreased level of consciousness. This patient requires intravenous access and volume resuscitation. Hypoglycemia should be corrected. There is no role for gastrointestinal decontamination due to rapid absorption and favorable outcomes with supportive care alone. Active charcoal can adsorb isopropyl alcohol; however massive doses must be used and are impractical given the fact that most patients will have CNS depression and recover with supportive care alone. Rarely, hemodialysis is needed for massive ingestions. It effectively removes isopropyl alcohol and acetone from the circulation. Indications for hemodialysis include isopropanol levels exceeding 400-500 mg/dL, renal failure, hypotension and coma in patients unresponsive to supportive care (intravenous fluids or vasopressors). Since the primary metabolite (acetone) is less toxic than the parent compound, there is no indication for ADH inhibition with fomepizole or ethanol.
4. It is crucial to differentiate isopropyl alcohol poisoning from that of ethylene glycol or methanol, as the latter are more dangerous. Characteristic laboratory findings include euglycemia, ketosis, little or no acidosis and increased osmolality. Isopropanol is metabolized by alcohol dehydrogenase to acetone, which can worsen CNS depressant effects and accounts for the marked ketosis seen in these patients. Isopropanol can be distinguished from methanol and ethylene glycol because it does not produce an elevated anion gap metabolic acidosis.

## PHARMACOLOGY/TOXICOLOGY CASE STUDY #7

**History:** A 17-year-old male presents to your emergency department after accidentally ingesting a large amount of methanol because he thought it was Gatorade<sup>®</sup>. He is not suicidal. He denies any co-ingestion, and the paramedics did not find any pills or substances in the house. The ingestion occurred approximately four hours prior to the call to EMS. He is currently complaining of blurred vision and nausea.

**PMH:** None.

**SH:** No previous suicide attempts or history of depression.

**Physical Examination:**

T: 99.4°F      HR: 120 bpm      RR: 24 breaths per minute      BP: 110/60 mm Hg

**General:** He is awake and alert.

**HEENT:** Examination reveals dilated pupils with sluggish light reaction and poor accommodation.

**Pulmonary:** Clear to auscultation.

**CV:** Regular rate and rhythm without murmur, capillary refill slightly prolonged.

**Neurologic:** GCS = 14. Cranial nerves II-XII intact.

### QUESTIONS CASE STUDY #7

1. What are the usual signs of acute toxicity?
2. Which initial therapies should be instituted?
3. What are the characteristic laboratory findings?



## Case Study #7: Methanol Poisoning

1. Methanol can be found in multiple industrial products, including antifreeze, solvents, disinfectants, de-icing solutions, windshield wiper fluid, and fuels. Exposure by ingestion is associated with the most negative effects, while cutaneous and inhalational exposures rarely cause toxicity. The primary reason people ingest this substance is to become intoxicated (for instance, as an ethanol substitute in alcoholics) or to harm themselves. Accidental poisonings can occur and affect multiple people in the setting of improper distillation of moonshine. The initial effects of methanol are inebriation and gastrointestinal discomfort. Due to metabolism of the parent alcohol to formic acid, a potent and specific neurotoxin, patients develop edema of the optic nerve with resultant visual changes, and ultimately, permanent blindness. Ischemic or hemorrhagic injury to the basal ganglia has been reported. Seizures, coma and death are possible. An afferent papillary defect is an ominous sign in methanol poisoning. A fundoscopic exam may reveal disc hyperemia and papilledema.
2. Initial management should be focused on stabilizing the airway, breathing and circulation. Methanol itself is of limited toxicity, but its metabolites produce toxicity. If methanol exposure is suspected, a stat blood level should be obtained. In any patient who has ingested more than a sip, has a metabolic acidosis and/or an osmolal gap, ADH inhibiting therapy with ethanol or fomepizole should be started **immediately**. The agent of choice is generally institution specific but a knowledge of each is important.

Ethanol, in sufficient concentrations, (greater than 100 mg/dL), competitively inhibits the formation of the toxic metabolites, as it has a greater affinity for ADH than methanol. This allows the unchanged parent alcohol (methanol) to be excreted by the pulmonary and renal routes. The loading dose is 15 ml/kg of 5% ethanol followed by a maintenance infusion of 2-4 ml/kg/hr. Ideally, the blood ethanol level should be maintained between 100-150 mg/dL. Treatment can be discontinued when methanol levels are below 20 mg/dL.

Fomepizole also has higher affinity for alcohol dehydrogenase than methanol and as such acts similar to ethanol to prevent the formation of toxic metabolites. It is becoming the antidote of choice in most institutions. Fomepizole is administered as follows: 15 mg/kg IV loading dose over 30 minutes, followed by maintenance doses. Maintenance doses are administered as follows: 10 mg/kg IV q12h for 48 hours, then 15 mg/kg IV q12h until methanol level is < 20 mg/dL. The acid-base status must be followed carefully and bicarbonate therapy may be required. After ADH blocking therapy, the elimination of methanol via the pulmonary and renal routes becomes first order and is drastically slowed (t 1/2 of approx 48 - 54 hours). Because of this, non-emergent hemodialysis is generally performed to remove methanol and avoid the excess cost associated with prolonged hospital stays and prolonged use of ADH inhibitors. Cofactor therapy with folic acid is sometimes used to expedite elimination of formic acid, which is

partially dependent on tetrahydrofolate.

3. Characteristic laboratory findings include an elevated anion gap metabolic acidosis and an osmolal gap.

## PHARMACOLOGY/TOXICOLOGY CASE STUDY #8

**History:** An 18-year-old male presents to your emergency department after ingesting an unknown quantity of lysergic acid diethylamide (LSD). His friends brought him in because he was “acting goofy.” He is not currently suicidal and has no plan to hurt himself. He claims not to have taken any other substances.

**PMH:** None.

**SH:** No previous suicide attempts and no history of depression.

### Physical Examination:

T: 100.4°F    HR: 124 bpm    RR: 18 breaths per minute    BP: 150/90 mm Hg

**General:** Agitated and actively hallucinating. The skin is moist and pale.

**HEENT:** Pupils are 4 mm bilaterally with sluggish light reaction. No nystagmus.

**Pulmonary:** Clear to auscultation.

**CV:** Regular rate and rhythm without murmur.

**Abdomen:** Soft and nontender with hyperactive bowel sounds.

**Neurologic:** GCS 14. Cranial nerves II-XII intact. Fine tremor.

## QUESTIONS CASE STUDY #8

1. What are the usual signs of acute toxicity?
2. How is the diagnosis confirmed and which initial therapy should be instituted?
3. What are the characteristic laboratory findings?

## Case Study #8: LSD Poisoning

1. Lysergic acid diethylamine (LSD) and similar hallucinogens are known by some as "enactogens" (to touch within). Despite much research, the exact mechanism of action is unknown. The major effects from an acute LSD ingestion include hallucinations and mild sympathetic effects. The usual sympathetic signs include hypertension, tachycardia, hyperthermia, mydriasis, bruxism, diaphoresis, tremor and decreased attention span, which, similar to hallucinations, seem to be dose-related. Paranoia and panic can occur at any dose. The toxic dose is variable and might be only slightly greater than the recreational dose. The desired enactogenic effects generally do not increase with increasing doses. Psychedelic agents rarely produce life-threatening problems. Morbidity and mortality from LSD are extremely rare and result from associated trauma or from intense sympathomimetic stimulation, including severe hyperthermia, seizure, intracranial hemorrhage, cardiac arrhythmias, rhabdomyolysis and myoglobinuria, renal failure, hepatic necrosis and disseminated intravascular coagulopathy.
2. The diagnosis is made by history and physical examination. Specific drug levels are not widely available or useful in the emergency department. Amphetamine derivatives in this class may cross-react with urine toxicology screening for amphetamines; however LSD and other non-amphetamine hallucinogens will not be reported on urine toxicology screens. Initial management should focus on stabilizing the airway, breathing and circulation. Supportive care is usually all that is required. Even if a psychedelic agent is suspected, the patient with altered mental status should receive dextrose, oxygen, thiamine and, if respiratory depression, naloxone. As always, other etiologies must also be considered in the differential diagnosis. The patient should optimally be placed in a quiet, but well-observed location with minimal stimuli and a calm support person. Reassurance and parenteral administration of benzodiazepines will usually adequately treat patients having a "bad trip" (i.e. who are fearful, crying, paranoid) and those with agitation, dysphoria and the signs of sympathetic excess. Hyperthermia must be aggressively treated with hydration, active external cooling and muscle relaxants ranging from benzodiazepines to paralytic agents, depending on the severity.
3. The laboratory findings are usually normal. CPK and urine should be obtained in patients with severe signs and symptoms to rule out rhabdomyolysis and myoglobinuria.

## PHARMACOLOGY/TOXICOLOGY CASE STUDY #9

History: A 17 month old male presents to your emergency department with his parents after he was found eating small pellets in the neighbors' basement. The child is asymptomatic. The patient's mother thinks the product is "some kind of super rat killer".

PMH: None.

### Physical Examination:

T: 99.4°F      HR: 110 bpm      RR: 18 breaths per minute      BP: 90/40 mmHg

General: Alert male in no acute distress.

HEENT: No pellet fragments in mouth. Handling secretions.

Pulmonary: Clear to auscultation.

CV: Regular rate and rhythm without murmur.

Abdomen: Soft, nontender.

Neurologic: No focal deficits.

## QUESTIONS CASE STUDY #9

1. What type of chemical did this child ingest and what is its mechanism of action?
2. What are the usual signs of acute toxicity?
3. What initial therapy should be instituted?
4. What other chemicals are used as rodenticides?

## CASE STUDY #9: SUPERWARFARIN POISONING

1. The most common rodenticides available today are the “superwarfarins,” brodifacoum, diphacinone, bromadiolone, chlorophacinone, difenacoum, pindone and valone. The most common is brodifacoum. These substances have intense and long-lasting anticoagulant effects and act by inhibiting the vitamin K dependent clotting factors (II, VII, IX, X) for weeks to months. Because they look similar to oats and grain and have a sweet taste, children can mistake them for food. Significant toxicity due to transcutaneous absorption of liquid preparations has been reported.
2. Because peak effects do not occur for two to three days (owing to the long half lives of factors IX and X), patients are usually asymptomatic after ingestion. Chronic use or delayed presentation can be manifested with signs of easy bleeding (such as petechiae under a blood pressure cuff, mucosal bleeding, hematuria), but can rarely present with more severe, potentially life-threatening bleeding.
3. Usually no initial treatment or laboratory tests are required after accidental pediatric ingestion. Vitamin K should not be administered, as it will make determination of toxicity impossible. Unless the child has underlying disease or abnormal clotting, baseline coagulation studies are not required. However, the child should be referred for daily prothrombin time values for three days. If they remain normal, no other treatment is required. In adult populations, baseline coagulation studies, CBC, type and cross could be considered depending on the clinical situation. A normal PT/INR 48 hours after ingestion excludes clinically significant ingestion. Commercially available Brodifacoum levels can be obtained at two laboratories in the United States and are mainly useful to diagnose repeated ingestions in patients whose PT/INR is failing to decrease appropriately, or is increasing despite oral vitamin K therapy (as sometimes seen in patients with underlying psychiatric issues).
4. One newer agent that has emerged as a potentially dangerous rodenticide is bromethalin, which was developed to combat increasing resistance of rats to the superwarfarins. This rodenticide acts as a potent and specific neurotoxin, uncoupling CNS mitochondrial oxidative phosphorylation and ultimately leading to cerebral edema, elevated ICP, seizures, coma and death. Multidose activated charcoal can be used to adsorb this toxicant. Other treatment strategies include dexamethasone and mannitol (useful during the absorptive phase) and supportive care. Other agents used in the past as rodenticides include zinc phosphide (still available in the Southwestern US), red squill, strychnine, arsenic and thallium.

## PHARMACOLOGY/TOXICOLOGY CASE STUDY #10

**History:** A 3-year-old presents to your emergency department after he was noted to have found two blue-green speckled white tablets and promptly ate them before his grandmother could take them away. Grandmother identified the pills as Clinitest® tablets. The ingestion occurred 20 minutes prior to arrival in the ED. Grandma is a diabetic but denies that the child ingested any other medications. The child vomited twice after the ingestion and has been drooling and having difficulty swallowing. The child refuses to drink, and when grandma looked in the mouth she saw red and white spots.

**PMH:** None.

### Physical Examination:

T: 99.4°F    HR: 128 bpm    RR: 31 breaths per minute    BP: 100/65 mm Hg

**General:** He is pale, agitated and crying.

**HEENT:** Examination reveals second degree burns to the oropharynx.

**Pulmonary:** Clear to auscultation.

**CV:** Regular rate and rhythm without murmur.

**Abdomen:** Soft and nontender.

**Neurologic:** GCS = 15. Cranial nerves II-XII intact.

## QUESTIONS CASE STUDY #10

1. Should gastric lavage be performed in this patient?
2. Does this child have signs and symptoms which suggest an esophageal injury?
3. What further testing does this child require?
4. Should this child be given steroids?

## CASE STUDY #10: CAUSTIC INGESTIONS

1. Emesis and gastric lavage are absolutely contraindicated in this patient. Emesis should be avoided because of the potential for re-exposure of the airway to the caustic agent, which may result in edema and airway compromise. Emesis may also result in bleeding or rupture of already-damaged tissues. The insertion of an orogastric or nasogastric tube into the stomach for gastric lavage may also result in perforation. There is no benefit to gastric decontamination since the caustic agents usually produce their damage immediately on contact and there is little to no systemic toxicity associated with the majority of these agents. pH-neutralizing solutions, such as dilute vinegar or bicarbonate are not recommended because of the theoretical possibility of heat injury secondary to neutralization reactions.
2. Although the literature is controversial regarding children who ingest caustic agents and do not develop oropharyngeal lesions, this child has signs and symptoms which suggest an esophageal injury. Gaudreault et al conducted a retrospective study which showed that 12.5% of asymptomatic children had grade 2 lesions and one of these children developed a stricture. Crain et al found that 50% of patients with two or more of the symptoms of drooling, stridor or vomiting had significant esophageal injury. None of the patients who had fewer than two of these symptoms had significant injury. Gorman et al found in their prospective series no constellation of signs and symptoms which could identify all patients with significant injury. In this series, vomiting was found to be the most sensitive indicator of injury. Other studies have concluded that the presence of oropharyngeal burns should increase suspicion for an esophageal injury, but the absence of oropharyngeal lesions does not exclude the possibility of an esophageal injury. Other clinical manifestations include dysphagia, drooling, pain (substernal, throat, or abdominal) and hematemesis.
3. This child requires endoscopy by a qualified specialist to identify any esophageal injuries. Early endoscopy identifies the injury, severity and the prognosis. Flexible endoscopy is preferred and is generally well tolerated with a low complication rate. Contraindications to endoscopy include burns involving the larynx, respiratory distress and severe agitation. These patients are usually followed with serial endoscopies to monitor healing of the lesions. Indications for endoscopy after caustic ingestion include those who are symptomatic, suicidal, ingest a large volume or ingest industrial strength caustics. Patients who meet all of the following criteria may not require endoscopy: accidental ingestion of household product, asymptomatic, not more than a sip/taste.
4. Corticosteroids are no longer recommended for reduction of esophageal and gastric scarring because are ineffective and can mask inflammation associated with perforation and because they may increase the risk of sepsis.



## PHARMACOLOGY/TOXICOLOGY CASE STUDY #11

History: A 20-year-old girl presents to your emergency department via EMS after she was found lying in the street naked. She reports that she went to a party but cannot recall any events after her arrival there. She denies any intentional ingestion.

PMH: None.

Physical Examination:

T: 99.4°F      HR: 65 bpm      RR: 12 breaths per minute      BP: 120/80 mm Hg

General: Agitated and crying.

HEENT: Examination is normal.

Pulmonary: Clear to auscultation.

CV: Bradycardia without murmur.

Abdomen: Soft and nontender.

Neurologic: GCS 15. Cranial nerves II-XII intact.

### QUESTIONS CASE STUDY #11

1. What is the most likely exposure?
2. What are the common signs and symptoms associated with this exposure?
3. What laboratory tests should be obtained?
4. What treatment is required?

## CASE STUDY #11: GHB EXPOSURE

1. This patient's presentation is highly concerning for drug facilitated sexual assault (DFSA). One of the most common agents involved in DFSA is gamma hydroxybutyrate, or GHB. GHB is a naturally-occurring metabolite of GABA that can cross the blood brain barrier, leading to CNS depression. Properties of GHB that make it attractive for DFSA include its rapid onset (clinical effects seen within 15 – 20 minutes), amnestic effects and rapid clearance from the body leading to difficult detection.
2. GHB is associated with dose-related sedation and respiratory depression similar to other sedative hypnotic agents. Coma is common. Hypotension, bradycardia and hypothermia can also occur. Patients generally awaken abruptly and are amnestic to the event. Although uncommon, agitation, seizure and death can result.
3. GHB is not detected on a routine urine toxicology screen. If lab confirmation is required, gas chromatography and mass spectroscopy must be performed (this can take 1-2 weeks). In cases of DFSA, first-catch urine and blood specimens should be collected as early as possible and care should be taken to preserve proper chain of custody. One should consider other exposures and test accordingly (e.g. carbon monoxide). Evaluation of this patient should include the same routine testing that would be performed in all poisoned patients (urine pregnancy, ECG, finger stick blood glucose, acetaminophen level).
4. The priority in treatment is stabilizing the airway, breathing and circulation. There is a high incidence of emesis in cases of GHB ingestion; intubation may be required for airway support. Patients should be treated with the standard agents used for altered mental status and undergo the same measures that would be offered to rape victims. Supportive care is all that is usually required.

## PHARMACOLOGY/TOXICOLOGY CASE STUDY #12

**History:** A 13-year-old female presents to your emergency department with her parents. She returned home after a party and has been complaining of dizziness, headache, palpitations and a feeling of chest tightness. She claims to have taken no drugs, but says that she ate at the party. She vomited twice at home and now feels very hungry.

**PMH:** None.

**Physical Examination:**

T: 99.4°F    HR: 110 bpm    RR: 19 breaths per minute    BP: 153/86 mm Hg

**General:** Pale, agitated and crying. She is very anxious.

**HEENT:** Examination is normal.

**Pulmonary:** Clear to auscultation.

**CV:** Tachycardic without murmur.

**Abdomen:** Soft and nontender.

**Neurologic:** GCS 15. Cranial nerves II-XII intact.

### QUESTIONS CASE STUDY #12

1. What are the effects of marijuana?
2. How should this patient be managed?
3. What other agents should be considered?

## CASE STUDY #12: MARIJUANA EXPOSURE

1. The effects of marijuana are primarily due to delta-9-tetrahydrocannabinol, also known as THC. Intoxication occurs within minutes if marijuana is inhaled and within hours if ingested and lasts 3-4 hours. THC intoxication includes both psychiatric and physical signs and symptoms. Although most patients feel euphoric (“high”), first time users and susceptible individuals can experience paranoia, anxiety and panic. Users may exhibit rapidly-changing emotions, irrelevant thought disturbed association, increased awareness of stimuli, altered concepts of space and time (perceived time is faster than clock time), impaired judgment, and speech changes (rapid, impaired, flighty). Other symptoms include increased appetite and thirst, nausea, dizziness, dysesthesias, somnolence and restlessness. Physical examination may show tachycardia, hypertension, tachypnea, ataxia, tremor, dry mucous membranes, and injected conjunctivae.
2. Most patients do not require medical intervention. The patient should be placed in a calm, supportive environment. In cases of severe agitation, benzodiazepines can be administered.
3. Marijuana intoxication should be differentiated from primary mental disorders as well as other agents that produce altered perception, including alcohol, sedatives, hallucinogens, phencyclidine (PCP), cocaine and anticholinergics. Marijuana intoxication can be distinguished from alcohol because these individuals often lack the aggressive behavior, diminished appetite, nystagmus and ataxia seen in alcohol intoxication. Differentiating marijuana from other drugs of abuse is more difficult and some individuals may combine other drugs with marijuana. PCP typically presents with miosis, nystagmus (horizontal, vertical and rotatory), hypertension, tachycardia, ataxia and CNS agitation. Cocaine and amphetamines produce a more classic sympathomimetic presentation. Although anticholinergic agents can produce delirium, the skin is dry and flushed with decreased GI motility and urinary retention.

## PHARMACOLOGY/TOXICOLOGY CASE STUDY #13

**History:** A 17-year-old male presents to your emergency department after accepting a “dare” from his friends to eat ten mushrooms that were picked in the Pacific Northwest. The patient states that he ate only one and was asymptomatic until approximately seven hours after ingestion. He now has severe vomiting and diarrhea. The patient brought one of the mushrooms with him which is identified as an *Amanita phalloides* mushroom.

**PMH:** None.

**Physical Examination:**

T: 99.4°F      HR: 120 bpm      RR: 17 breaths per minute      BP: 100/60 mm Hg

**General:** Pale.

**HEENT:** Examination is normal. Mucous membranes are dry.

**Pulmonary:** Clear to auscultation.

**CV:** Tachycardic without murmur.

**Abdomen:** Soft and nontender.

**Neurologic:** GCS = 15, cranial nerves II-XII intact.

**Skin:** Pale with a 5 second capillary refill.

### QUESTIONS CASE STUDY #13

1. What are the phases of this type of ingestion and their major toxicities?
2. What type of mushroom causes the majority of mushroom fatalities in North America?
3. What management strategies should be used?

## CASE STUDY #13: AMANITA PHALLOIDES

1. There are three phases of amatoxin poisoning. A key differentiating factor is that patients typically are asymptomatic for the first 6-12 hours. Phase I begins 6-24 hours after ingestion and is manifested by gastrointestinal symptoms, including nausea, vomiting, severe abdominal cramps and watery diarrhea (which may become grossly bloody). This phase can cause significant dehydration and metabolic acidosis, electrolyte abnormalities, hypoglycemia and shock. Phase 2 occurs 18-36 hours after ingestion and is characterized by a falsely reassuring period of improvement and sometimes recovery. During this period, elevation of the liver enzymes is common. Similar to cases of iron poisoning, clinicians must beware not to mistake this phase for resolution of a milder illness, such as gastroenteritis. Phase 3 occurs 2-4 days after ingestion and is characterized by hepatic, and ultimately, multisystem organ failure. Death generally occurs 6-16 days after ingestion.
2. Cyclopeptide-containing mushrooms account for 90% of all mushroom fatalities in North America. Amatoxins are a group of cyclopeptides found in various Amanita species, including Amanita phalloides.
3. The mortality rate for amatoxin poisoning is approximately 10-15% with intensive care. The first phase is managed with aggressive fluid and electrolyte replacement and supportive care and usually leads to a transient improvement during phase 2. A regime of supportive care, fluid and electrolyte replacement, high-dose penicillin G, dexamethasone and thiocetic acid has been used, but there is no proven effective therapy.

The patient's friends should be notified and their health and safety ensured.

## PHARMACOLOGY/TOXICOLOGY CASE STUDY #14

History: A 47-year-old female presents to your emergency department 30 minutes after a suicide attempt in which she ingested 2000 mg of sustained-release diltiazem. She insists there were no other ingested medications. The patient has experienced no vomiting.

PMH: None.

### Physical Examination:

T: 99.4°F      HR: 90 bpm      RR: 17 breaths per minute      BP: 120/70 mm Hg

General: Alert and oriented.

HEENT: Examination is normal.

Pulmonary: Clear to auscultation.

CV: Regular rate and rhythm without murmur.

Abdomen: Soft and nontender.

Neurologic: GCS 15. Cranial nerves II-XII intact.

Skin: Pale with a normal capillary refill.

## QUESTIONS CASE STUDY #14

1. What are the complications which may be associated with this type of overdose?
2. What type of gastrointestinal decontamination, if any, is indicated?
3. What management strategies should be used?

## CASE STUDY #14: CALCIUM CHANNEL BLOCKER POISONING

1. Cardiovascular toxicity predominates as a cause of morbidity and mortality after calcium channel blocker overdose. The primary signs are bradycardia and hypotension. Varying degrees of AV block, sinus arrest with junctional escape rhythm, idioventricular rhythm and asystole can also be seen. In addition, patients may experience nausea and vomiting, altered mental status, metabolic acidosis (likely secondary to hypotension), hyperglycemia (secondary to blockade of insulin release), seizures and coma.

Poisoning by the non-dihydropyridine (non-DHP) class of calcium channel blockers (versus poisoning by the dihydropyridine class), is generally considered to be more dangerous. Whereas the dihydropyridine class of calcium channel blockers exert their effects specifically on the L-type calcium channels in the vascular smooth muscle, non-DHP calcium channel blockers affect primarily the cardiac L-type calcium channels. The only two non-DHP calcium channel blockers used clinically include verapamil and diltiazem. In massive ingestions, the specificity of these classes can be lost.

2. Activated charcoal may be considered if the patient is protecting their airway and may be of benefit past the traditional one hour mark, especially in sustained release ingestions. Because calcium channel blocker poisoning is associated with a high mortality, gastric lavage should be considered in the appropriate setting however the clinician should be aware that vomiting is a powerful vagal stimulus that can make bradycardia worse. For large ingestions of sustained-release preparations, whole bowel irrigation can be considered.
3. Initial management includes support of the airway, breathing and circulation. Intravenous access, supplemental oxygen, cardiac monitoring and continuous pulse oximetry should be instituted immediately. Bradycardia may initially be treated with atropine, but multiple doses risk anticholinergic poisoning and isoproterenol or pacing may be considered. Hypotension should initially be treated with a fluid bolus. Calcium has traditionally been used and the serum calcium should not be raised to higher than 14 mg/dL. More severely poisoned patients may require addition of catecholamines to accelerate the heart rate, enhance AV conduction and restore tone to peripheral vessels. Isoproterenol and dopamine have been used. Glucagon has also been reported to be effective. Insulin and amrinone have also been used.

Initial treatment of hypotension includes bolus administration of crystalloid fluid, and epinephrine. Atropine can be used but is very short acting is generally not sufficient in moderate to severe poisoning. Cardiac pacing may be required but may not capture.

Administration of calcium can help to improve cardiac contractility by increasing its intracellular availability; however it has variable effects on peripheral



vasodilation and SA and AV node conduction. Calcium can be given as either calcium gluconate or calcium chloride. Calcium levels should be monitored when using repeated doses because lethal iatrogenic overdose has been rarely reported.

High dose insulin-Euglycemia (HIE) has had a powerful impact on treatment of calcium channel blocker poisoning and is quickly becoming a mainstay of therapy. For this therapy, regular insulin is given as a bolus of 1 unit/kg and is followed by an infusion rate of 0.5–1.0 unit/kg/hr. The infusion is titrated to effect, rarely up to 10 units/kg/hr. Calcium channel blockers commonly produce hyperglycemia by multiple mechanisms, including the induction of systemic insulin resistance and blockage of insulin release while maintaining intact stress hormone responses and glucogenic capacity. Although hypoglycemia is rare, supplemental glucose should be given. One suggestion for glucose supplementation is to start an infusion of D10 0.45% NS at 80% maintenance rate simultaneously with the high-dose insulin drip. Blood glucose levels should be checked every 20 minutes for the first hour, and once per hour thereafter. Hypokalemia is another potential adverse effect, so serum potassium levels should be monitored hourly and corrected as needed.

Glucagon has both inotropic and chronotropic effects and can be used in calcium channel blocker poisoning. Phosphodiesterase inhibitors (such as inamrinone) have been used to treat depressed myocardial contractility but may exacerbate hypotension.

Intravenous lipid emulsion therapy (Intralipid®) has emerged as a promising treatment for multiple medications, including calcium channel blockers.

## PHARMACOLOGY/TOXICOLOGY CASE STUDY #15

**History:** A 3-year-old child presents to your emergency department with his parents after ingesting an unknown quantity of furosemide (Lasix®) approximately 90 minutes ago. The most the child could have ingested is 10 mL. The child's older sibling has a history of congenital heart disease. The child did not ingest any other medications. The child has had no vomiting, diarrhea or change in behavior since the ingestion. The child has wet a "large" number of diapers.

**PMH:** None.

**Physical Examination:**

T: 99.4°F      HR: 142 bpm      RR: 32 breaths per minute      BP: 78/49 mm Hg

**General:** Alert and oriented.

**HEENT:** Examination is normal.

**Pulmonary:** Clear to auscultation.

**CV:** Regular rate and rhythm without murmur.

**Abdomen:** Soft and nontender.

**Neurologic:** GCS is 15. Cranial nerves II-XII intact.

**Skin:** Normal capillary refill.

### QUESTIONS CASE STUDY #15

1. What type of decontamination is indicated?
2. What are the complications which may be associated with this type of overdose?
3. What management strategies should be used?

## CASE STUDY #15: FUROSEMIDE EXPOSURE

1. This patient requires no decontamination; however activated charcoal can be administered in the setting of diuretic poisoning if the conditions are right (alert, early presenter).
2. Adverse effects from chronic use or misuse (in sports or dieting) of diuretics is more common than acute poisoning. Overdoses are usually benign and serious outcomes have not been reported. The loop diuretics, such as furosemide, ethacrynic acid and bumetanide act at the ascending limb of the nephron. The major complications associated with this type of an overdose include dehydration and electrolyte imbalance, such as hypokalemia, hypercalcemia, hypomagnesemia and hyponatremia. Various dysrhythmias, weakness, hyporeflexia, tetany and lethargy may ensue if the electrolyte abnormalities are severe. Nausea, vomiting and diarrhea are common after an acute overdose. An unusual complication which may occur is CNS depression.
3. There are no antidotes for diuretic poisoning. Management should focus on stabilization of the airway, breathing and circulation. Particular attention should be paid to fluid and electrolyte correction. Rapid correction of hyponatremia in patients with seizure and coma can be performed with hypertonic saline; however correction of hyponatremia should be cautious in chronic abusers to avoid osmotic demyelination syndrome. Continuous cardiac monitoring is recommended until the serum potassium is corrected.

## PHARMACOLOGY/TOXICOLOGY CASE STUDY #16

**History:** An 83-year-old woman presents to your emergency department with altered mental status. The family states that she has been having increasing problems with her memory over the last several months. The daughter found her in her room when she didn't come down for breakfast. Her blood pressure prescription is missing seven more tablets than it should.

**PMH:** Hypertension.

**Medications:** Clonidine.

**Physical Examination:**

T: 96.4°F      HR: 60 bpm      RR: 9 breaths per minute      BP: 80/40 mm Hg

**General:** Confused and somnolent.

**HEENT:** Miosis.

**Pulmonary:** Clear to auscultation.

**CV:** Bradycardic without murmur.

**Abdomen:** Soft and nontender.

**Neurologic:** Cranial nerves II-XII intact. Hyporeflexic. Muscle strength is markedly decreased.

### QUESTIONS CASE STUDY #16

1. What are signs and symptoms of a clonidine overdose?
2. What type of decontamination may be used in these patients? Are there specific antidotes available?
3. How should the hypotension be managed?
4. How should the patient's respiratory status be managed?
5. Are there special considerations that should be given in the diagnosis and management of patients suspected of poisoning with transdermal preparations?

## CASE STUDY #16: CLONIDINE POISONING

1. Clonidine is a centrally acting alpha-2 adrenergic receptor agonist. Stimulation of these receptors in the rostral ventrolateral medulla leads to decreased sympathetic outflow as manifested by reduced plasma norepinephrine. This effect leads to a decrease in heart rate and cardiac output. Overdose with clonidine may be life-threatening. The classic toxidrome includes central nervous system depression, bradycardia, hypotension, respiratory depression and miosis. Altered mental status is the most common finding. Other findings can include hypotonia, hyporeflexia, pallor, dry mucous membranes and hypothermia. These findings can mimic opioid intoxication and make distinction between the two conditions difficult. Partial peripheral adrenergic stimulatory effects can produce transient hypertension, which rarely requires treatment. Other symptoms less frequently displayed include diarrhea and seizures. Bradycardia is usually sinus, although sinus arrest has been described. AV block higher than first degree should prompt a search for poisoning from other cardioactive agents.
2. Activated charcoal is recommended to adsorb clonidine when the conditions are appropriate; however this patient does not have a secure airway at this time. It is recommended for use up to two hours post ingestion. No true antidote for clonidine poisoning exists; however naloxone has been used with varying success. Based on case reports, intravenous doses up to 10 mg to reverse CNS depression and apnea have been used, but this effect may be transient.
3. Hypotension usually occurs within one to three hours after the ingestion and may persist for 24 hours. Initial therapy should include intravenous fluids and Trendelenburg positioning. Bradycardia is usually mild but may respond to atropine. Dopamine may be beneficial if hypotension fails to respond to any of the previous.
4. The respiratory depression seen in clonidine overdose may respond transiently to tactile stimulation and is one of the features of this condition that may distinguish it from opioid overdose. If necessary, patient's respiratory compromise should be managed by intubation and mechanical ventilation.
5. Clonidine patch preparations contain total doses of 2.5, 5 and 7.5 mg, three-fourths of which may remain after seven days of use. Therefore, patients suspected of poisoning with this system should be observed for symptoms for at least twenty-four hours and physical examination should include a full body search for hidden patches. Serious overdose has been reported when transdermal patches were ingested.

## PHARMACOLOGY/TOXICOLOGY CASE STUDY #17

History: A 33-year-old woman presents with a fever and diarrhea. She is very tearful and admits to having taken 20 enalapril approximately 30 minutes ago. She claims she is not currently suicidal and ingested no other medications. She took her father's medication.

PMH: None.

### Physical Examination:

T: 100.8°F    HR: 100 bpm    RR: 18 breaths per minute    BP: 80/40 mm Hg

General: Awake and alert.

HEENT: Examination is normal.

Pulmonary: Clear to auscultation.

CV: Regular rate and rhythm without murmur.

Abdomen: Soft and nontender.

Neurologic: Cranial nerves II-XII intact. Muscle strength is normal.

## QUESTIONS CASE STUDY #17

1. What are signs and symptoms of an angiotensin-converting enzyme inhibitor overdose?
2. How should the hypotension be managed?
3. How do the angiotensin-converting enzyme inhibitors work?

## **CASE STUDY #17: ACE INHIBITOR POISONING**

1. Overdoses of ACE inhibitors rarely produce severe toxicity. Symptoms of poisoning can include hypotension, diarrhea, glomerulopathy, hyperkalemia, cough, rash, angioedema and drug fever.
2. The hypotension should be managed with supine positioning, intravenous fluids. Vasopressors are rarely required.
3. All of the ACE inhibitors have a common 2-methyl propranolol-L-proline moiety which blocks the active site of angiotensin converting enzyme. This inhibition prevents conversion of angiotensin I to angiotensin II in the lung, plasma and vascular endothelium. Because the formation of angiotensin II, the most potent endogenous vasoconstrictor, is inhibited by ACE inhibitors, decreased total peripheral resistance and decreased blood pressure result.

## PHARMACOLOGY/TOXICOLOGY CASE STUDY #18

History: A 33-year-old chef presents to your emergency department with vomiting. He prepared a meal using the mushroom *Gyromitra esculenta*, but later learned that they are toxic. He ate only a small amount.

PMH: None.

Physical Examination:

T: 98.6°F      HR: 80 bpm      RR: 18 breaths per minute      BP: 120/76 mm Hg

General: Awake and alert.

HEENT: Examination is normal.

Pulmonary: Clear to auscultation.

CV: Regular rate and rhythm without murmur.

Abdomen: Soft and nontender.

Neurologic: Cranial nerves II-XII intact. Muscle strength is normal.

### QUESTIONS CASE STUDY #18

1. What are signs and symptoms of a *Gyromitra esculenta* overdose?
2. What is the mortality for this type of ingestion? Are there special therapies?
3. How does this toxin work?



## CASE STUDY #18: GYROMITRA ESCULENTA POISONING

1. The signs and symptoms of gyrometra esculenta poisoning begin approximately six to ten hours after ingestion and include nausea, vomiting, seizures, abdominal pain and generalized weakness. Symptoms can progress to hepatorenal failure. The primary site of toxicity is the CNS.
2. The mortality for this type of ingestion is 15-40%. Pyridoxine, in doses of 25 mg/kg, is the antidote for seizures. This particular mushroom, also known as the “false morel,” is unusual in that it is edible in the western United States, but poisonous in other areas. Certain cooking methods may eliminate the toxin, but inhalation of the fumes may result in poisoning. Because of this “dual” personality, it is recommended that none of these mushrooms be ingested.

If the food was served to others, they should be notified and their well-being ensured. If the food was served in a public health setting, public health should be notified.

3. These types of mushrooms contain gyromitrin, which through a variety of chemical reactions yields a hydralazine moiety. This hydralazine moiety reacts with pyridoxine, which results in inhibition of pyridoxal phosphate-related enzymatic reactions.

## PHARMACOLOGY/TOXICOLOGY CASE STUDY #19

**History:** A 33-year-old male factory worker presents to your emergency department from work with complaints of muscle twitching, facial grimacing and a seizure. The company has recently acquired a new factory and he was in the process of cleaning up some white powder when he developed symptoms. A phone call to the previous owners identified the substance as strychnine, which had been placed to eliminate the rats in the building.

**PMH:** None.

**Physical Examination:**

T: 98.6°F      HR: 80 bpm      RR: 18 breaths per minute      BP: 120/76 mm Hg

**General:** Awake and alert.

**HEENT:** Examination is normal.

**Pulmonary:** Clear to auscultation.

**CV:** Regular rate and rhythm without murmur.

**Abdomen:** Soft and nontender.

**Neurologic:** Cranial nerves II-XII intact. Intermittent opisthotonos.

### QUESTIONS CASE STUDY #19

1. What is strychnine and where is it found today?
2. What are signs and symptoms of strychnine poisoning?
3. What types of interventions are indicated?
4. How does this toxin work?

## CASE STUDY#19: STRYCHNINE POISONING

1. Strychnine is a naturally occurring chemical derived from the seeds inside the fruit of the tree *Strychnos nux vomica*, also known as the Strychnine tree. It was first used as a rodenticide in 16<sup>th</sup> century Germany. Medical uses in the United States included treatment of indigestion and constipation; however due to the number of fatalities that resulted from its use, it was discontinued from over-the-counter medications in 1962. The majority of cases today occur when strychnine is used as a cutting agent in illicit drug distribution.
2. The signs and symptoms of strychnine poisoning usually occur within ten to 20 minutes of ingestion, but can be delayed if absorption occurs by another route (inhalation, injection, transdermal). Prodromal symptoms can include mydriasis, hypervigilance, anxiety, hyperreflexia, clonus, and stiffness of the facial and neck muscles. Later, CNS stimulatory effects, including muscle twitching, extensor spasm and opisthotonos can occur, mimicking generalized tonic clonic seizure activity. Apparent seizure activity in strychnine poisoning can be differentiated in that the patient retains a normal level of consciousness during the episode and lacks the characteristic post ictal period associated with true seizures. Strychnine poisoning is the clinical condition that most closely mimics generalized tetanus. These clinical effects can appear to wax and wane, with periods of relaxation occurring every few minutes. Death is most commonly due to involvement of the diaphragmatic and thoracic musculature. Prognosis is favorable if the patient survives the initial five hours of symptoms; however hyperthermia, significant lactic acidosis, rhabdomyolysis and compartment syndrome can occur.
3. Early interventions include skin decontamination and control of airway, breathing and circulation. Some sources suggest that non-depolarizing muscle relaxants, such as rocuronium, should be used preferentially to avoid the transient increased muscle tone associated succinylcholine. Activated charcoal may be used once the airway is protected. Any manipulation may trigger opisthotonos or muscle spasm activity; therefore, it is important to keep the patient in a calm environment. The extensor spasm, opisthotonos and seizures may be initially controlled with high-dose benzodiazepines, but may require phenobarbital. General anesthesia and/or neuromuscular blockade may be required if muscle spasms and seizures are not controlled and is the best method to control hyperthermia and acidosis. Adequate pain control is essential. It may be necessary to electively intubate the patient in order to achieve adequate pain control and muscle relaxation. Urine output should be maintained to prevent or treat common complications such as rhabdomyolysis, renal failure and acidosis.
4. Strychnine competitively antagonizes glycine, an inhibitory neurotransmitter in the central nervous system, at the postsynaptic spinal cord motor neuron. There, it prevents glycine's inhibitory mechanisms, leading to fierce muscle contractions.

## PHARMACOLOGY/TOXICOLOGY CASE STUDY #20

**History:** A 33-year-old male presents to your emergency department with severe, nonbloody diarrhea and vomiting two hours after eating dinner at a local fish restaurant. Associated symptoms include watery eyes, myalgias, arthralgias and numbness of the tongue, lips and throat. The patient states that his entrée consisted of red snapper that was well-done and had no unusual smell or taste.

**PMH:** None.

**Physical Examination:**

T: 98.6°F      HR: 80 bpm      RR: 18 breaths per minute      BP: 90/60 mm Hg

**General:** He is awake and alert.

**HEENT:** Examination is normal.

**Pulmonary:** Clear to auscultation.

**CV:** Regular rate and rhythm without murmur.

**Abdomen:** Soft and nontender.

**Neurologic:** Cranial nerves II-XII intact. The patient has reversal of temperature discrimination (cold feels hot).

### QUESTIONS CASE STUDY #20

1. What is the most likely etiology of the symptoms?
2. What types of interventions are indicated?
3. What types of symptoms are associated with this type of ingestion?
4. What, if any, food preparation strategies can help prevent transmission of ciguatera to humans? Are there characteristics of living, raw or prepared fish that might help to warn the patient that the fish might be affected?
5. What type of counseling should these patients be given?

## CASE STUDY #20: CIGUATERA POISONING

1. This patient is suffering from ciguatera poisoning, a fish-related foodborne illness caused by several distinct marine toxins, the most well-known of which is called ciguatoxin. Ciguatera fish poisoning is most common in the spring or summer and accounts for more than half of the fish-related food poisoning in the United States. It is commonly reported in Hawaii and Florida (90% of all cases).
2. Initial management should focus on stabilization of the airway, breathing and circulation of the patient (although rare, deaths have resulted from respiratory paralysis, seizures and inadequate ALS support). Intravenous access should be obtained and attention paid to volume resuscitation and electrolyte repletion. Some series suggest that intravenous mannitol, if given within the first 48 hours, may be associated with a decrease in neurologic and muscular dysfunction; Neurologic symptoms can occur as early as three hours after ingestion but onset can be delayed for as long as 72 hours. A unique manifestation of ciguatera poisoning is reversal of temperature discrimination and is highly suggestive of ciguatera fish as the source of the illness. Heart block, hypotension, bradycardia and orthostatic hypotension have also been reported.

The public health department should be notified.

3. Large fish (barracuda, sea bass, parrot fish, red snapper, grouper) become vectors of this type of poisoning after they ingest dinoflagellates that produce the toxin (either directly or via the consumption of smaller fish). The toxin becomes increasingly concentrated in the flesh, adipose and viscera of larger fish. When these larger fish are ingested by humans, symptoms occur.
4. Because ciguatoxin is a heat-stable, acid resistant neurotoxin, there are no food preparation strategies (such as cooking, freezing, etc.) that will decrease transmission. Fish seem to be unaffected after consuming this toxin. There are also no physical characteristics of raw or cooked fish (such as unusual smell, taste, texture, color change, etc.) that might warn a person that it has been infected.
5. One classic feature of ciguatera is return or worsening of symptoms after ingestion of fish, nuts, alcohol or caffeine, which can recur for six months after poisoning. Patients should be counseled to refrain from consuming these things for six months. Additionally, symptoms associated with future attacks of ciguatera may be more severe.

## PHARMACOLOGY/TOXICOLOGY CASE STUDY #21

**History:** An 18-year-old college student presents to your emergency department two hours after dinner with his parents with a complaint of burning sensation of the mouth, difficulty swallowing, headache and a rash. He has vomited several times and had two episodes of diarrhea. The patient states that his entrée consisted of well-done mahi-mahi. His parents, who had different entrees, are unaffected.

**PMH:** None

**Physical Examination:**

T: 98.6°F      HR: 121 bpm      RR: 16 breaths per minute      BP: 120/72 mm Hg

**General:** Awake and alert.

**HEENT:** Examination is normal.

**Pulmonary:** Clear to auscultation.

**CV:** Regular rate and rhythm without murmur.

**Abdomen:** Soft and nontender.

**Neurologic:** Cranial nerves II-XII intact.

**Skin:** Intense, diffuse erythema of the face, neck and upper torso.

### QUESTIONS CASE STUDY #21

1. What is the most likely etiology of the symptoms?
2. How does poisoning occur?
3. What types of symptoms are associated with this type of ingestion?
4. How can a diagnosis be made?
5. What treatment, if any, is indicated?
6. Can this type of poisoning be prevented?
7. Are there characteristics of living, raw or prepared fish that might help to warn the patient that the fish might be affected?

## CASE STUDY #21: SCOMBROID POISONING

1. This patient is suffering from scombroid poisoning, which is the most common seafood-related disease in the United States. It is associated with bacterial infection of dark meat fish of the Scombridae family, such as tuna, mackerel, skipjack and bonito, which can occur with improper handling and storage practices. Other fish associated with scombroid poisoning include anchovies, herring, mahi-mahi, salmon, sardines, swordfish and trout.
2. Certain bacteria, including *Vibrio* species, *Morganella morgagni*, *E. coli*, *Proteus*, *Salmonella sp.*, *Shigella sp.* and *Klebsiella pneumoniae* proliferate on the surface of improperly handled fish. These organisms contain histidine decarboxylase, an enzyme that converts histidine (found in high concentrations in the muscle of the fish) to histamine, saurine and other heat-stable substances. Saurine has been suggested as the agent responsible for scombroid poisoning.
3. Symptoms associated with scombroid poisoning usually occur minutes to several hours after ingestion (usually begin within one hour). Initially, the patient may develop numbness, tingling, perioral dyesthesia, dysphagia, headache, palpitations, significant tachycardia and a peculiar rash or “flush” that is characterized by an intense diffuse erythema of the face, neck and upper torso. Rarely, pruritus, urticaria, angioedema or bronchospasm ensues. Other symptoms may include nausea, vomiting, dizziness, palpitations, abdominal pain and diarrhea. Scombroid is not associated with any long term complications.
4. The diagnosis is a clinical one. Elevated serum or urine histamine levels occur, but are not clinically useful or practical. Because these symptoms mimic an IgE mediated allergy, scombroid poisoning is often misdiagnosed as a fish allergy and is therefore underreported.
5. The symptoms of scombroid poisoning typically resolve within twelve hours, even in the absence of treatment. Supportive care, including H1 antihistamines, intravenous rehydration, antiemetics and pain control may be beneficial in some cases. Use of H2 antihistamines has been reported. The presence of bronchospasm or angioedema may necessitate the use of epinephrine and beta agonists.
6. Proper handling and storage of fish implicated in scombroid poisoning is essential to its prevention. There are no food preparation strategies (such as cooking, freezing, etc.) that will decrease scombroid transmission.
7. Affected fish have been reported to have a salty, peppery or bubbly taste. There are no changes in smell, texture or color that might warn a person that a fish been affected.

## PHARMACOLOGY/TOXICOLOGY CASE STUDY #22

**History:** A 27-year-old woman presents to your emergency department after she was found in her apartment unresponsive following a call from a concerned friend. She was “barely” breathing and the paramedics placed her on 100% oxygen and assisted her ventilations. An intravenous line was started and the patient received glucose, thiamine and naloxone without response.

**PMH:** Depression.  
**Medications:** Chloral hydrate.

### Physical Examination:

**T:** 98.6°F      **HR:** 150 bpm      **RR:** 24 breaths per minute      **BP:** 130/86 mm Hg  
**General:** She is in a deep coma. The smell of pears is present.  
**HEENT:** Examination is normal.  
**Pulmonary:** Clear to auscultation.  
**CV:** Tachycardic without murmur.  
**Abdomen:** Soft and nontender. Bowel sounds diminished.  
**Neurologic:** Corneal reflexes are present. Deep tendon reflexes are diminished, plantar extension is present.

## QUESTIONS CASE STUDY #22

1. What is the most likely etiology of the symptoms?
2. What types of symptoms are associated with this type of an overdose?
3. What laboratory studies are indicated?
4. What treatment is indicated?
5. What other agents may be seen on plain films?



## CASE STUDY #22: CHLORAL HYDRATE POISONING

1. Chloral hydrate poisoning.
2. Chloral hydrate is a sedative-hypnotic agent used in the treatment of anxiety and insomnia. Its use has also been reported in drug-facilitated sexual assault. Sedative-hypnotic agents produce central nervous system depression and can cause respiratory arrest, coma and aspiration. Common signs seen in overdose include drowsiness, ataxia, nystagmus and stupor. Hypothermia can also occur, which, in combination with deep coma can cause the patient to appear dead or to be suffering from brain death. Depression of cardiac contractility and decreased venous tone can lead to hypotension. Chloral hydrate is metabolized to trichloroethanol which is also a CNS depressant and can sensitize the myocardium to catecholamines, resulting in ventricular dysrhythmias. A pear-like scent may be noted on the breath after ingestion.
3. Laboratory studies should focus on the identification of coingestants (acetaminophen, salicylate) and excluding other conditions that may produce coma such as infection, metabolic derangements, neurologic and psychiatric illness. In general, quantitative measurement is not useful.
4. Support of airway, breathing and circulation should be performed in the usual manner. Activated charcoal can be administered in the right clinical setting. Due to the potential to induce tachydysrhythmias, patients should undergo continuous cardiac monitoring for 18-24 hours. Propranolol and esmolol can be used to treat tachycardia.
5. Plain radiographs are only useful to confirm ingestion of certain materials and possibly to monitor the efficacy of whole bowel irrigation. The absence of signs on a plain radiograph cannot be used to exclude ingestion. Pills should not be laid directly on an x-ray plate to determine opacity as this technique leads to false positives secondary to an air-contrast effect. Agents visible on plain films can be remembered using the mnemonic "CHIPES", which represents Chloral hydrate/Calcium carbonate; Heavy metals; Iodine/Iron; Phenothiazine/Potassium; Enteric coated (highly variable); Sustained release (highly variable). Other sometimes visible agents include tricyclic antidepressants, sodium chloride, acetazolamide, bismuth subsalicylate and busulfan.

## PHARMACOLOGY/TOXICOLOGY CASE STUDY #23

History: A patient is transferred to your emergency department from a local psychiatric facility following the ingestion of a Betadine® solution. He states that he drank approximately one-half of the bottle.

PMH: Paranoid schizophrenia

Medications: Haloperidol

Physical Examination:

T: 98.6°F    HR: 82 bpm    RR: 20 breaths per minute    BP: 128/78 mm Hg

General: Awake and alert.

HEENT: Examination is normal except for brownish discoloration of the tongue.

Pulmonary: Clear to auscultation.

CV: Regular rate and rhythm without murmur.

Abdomen: Soft and nontender, bowel sounds were normal.

Neurologic: Normal deep tendon reflexes and normal muscle strength.

### QUESTIONS CASE STUDY #23

1. What is in Betadine® solution?
2. What types of symptoms are associated with this type of ingestion?
3. What treatment is indicated?

## CASE STUDY #23: BETADINE POISONING

1. Betadine® solution consists of iodine linked to polyvinylpyrrolidone.
2. Symptoms are largely related to the corrosive effects and may consist of vomiting, diarrhea, abdominal pain, gastrointestinal bleeding, anuria and vasomotor collapse. Absorption of topical preparations of iodophor can result in significant systemic toxicity. Acid-base disturbances may occur as well as markedly elevated iodine levels. Electrolyte abnormalities have also been reported after topical absorption of iodophors.
3. The management is generally supportive and includes airway support, fluid rehydration and correction of electrolyte abnormalities as needed. If a corrosive esophageal injury is suspected, endoscopy should be performed. Although rarely indicated, the use of starch or sodium thiosulfate may be considered in symptomatic patients to convert iodine to iodide. Its use via the intravenous route is not indicated.

## PHARMACOLOGY/TOXICOLOGY CASE STUDY #24

**History:** A 17-year-old male presents to your emergency department with his parents. Mom is concerned because the child has been very aggressive, anxious and paranoid over the last week. Mom says that he is an “intense” athlete and that the coach has convinced him he can become a professional athlete.

**PMH:** None.

### Physical Examination:

T: 98.6°F    HR: 70 bpm    RR: 14 breaths per minute    BP: 140/82 mm Hg

**General:** Calm but hostile. Alert and oriented.

**HEENT:** Examination is normal. Sclera icteric.

**Pulmonary:** Clear to auscultation.

**CV:** Regular rate and rhythm without murmur.

**Abdomen:** Soft and nontender, bowel sounds were normal.

**Neurologic:** Normal deep tendon reflexes and normal muscle strength.

**Musculoskeletal:** He has very well defined muscles.

**Skin:** Acne.

## QUESTIONS CASE STUDY #24

1. What medical concerns do you have?
2. What symptoms are associated with this type of medication use?
3. What other treatment may athletes use to “enhance” performance?

## **CASE STUDY #24: ANABOLIC STEROID ABUSE**

1. You suspect that this teenager may be abusing anabolic steroids.
2. Symptoms which may be associated with the abuse of anabolic steroids are very diverse. In males' testicular atrophy, reduction in sperm counts and alteration in sperm morphology, baldness, or development of breasts can occur. Females can get growth of facial hair, male pattern baldness, changes or cessation of menstrual cycle, or deepened voice. Adolescents may get stunted growth due to premature epiphyseal closure and be may more susceptible for ligament or cartilage damage. Psychologic manifestations may include aggression, anxiety, irritability, paranoia and mania. Hepatic dysfunction may occur and is manifested by cholestatic hepatitis. Hyperlipidemia with elevated LDL and lower HDL can occur. Severe acne can also be seen.
3. Athletes may also take human growth hormone to enhance body growth and increase strength. The use of red cell transfusions to increase oxygen-carrying capacity has been reported. Others have used recombinant human erythropoietin to increase red cell production. Other substances such as creatine, ephedrine, or herbal preparations may be used to enhance workouts.

## PHARMACOLOGY/TOXICOLOGY CASE STUDY #25

**History:** A 2-year-old female presents to your emergency department with her parents after ingesting an unknown quantity of her mother's levothyroxine seven days ago. The child did not vomit and has been acting fine until today. The child has been very agitated, sweating and "not acting right." In addition, the child has had diarrhea and vomiting for the last six hours.

**PMH:** None.

**Physical Examination:**

T: 101.8°F    HR: 170 bpm    RR: 30 breaths per minute    BP: 72/40 mm Hg

**General:** Agitated. Will not sit still.

**HEENT:** Examination is normal.

**Pulmonary:** Clear to auscultation.

**CV:** Tachycardic without murmur.

**Abdomen:** Soft and nontender. Bowel sounds normal.

**Neurologic:** Normal deep tendon reflexes and normal muscle strength.

## QUESTIONS CASE STUDY #25

1. What concerns do you have?
2. What symptoms are associated with this type of medication use?
3. What interventions should be performed for this child?

## CASE STUDY #25: LEVOTHYROXINE POISONING

1. You suspect that this child has developed hyperthyroidism from the ingestion of the levothyroxine.
2. Mild to moderate intoxication can cause tachycardia, flushing, GI symptoms such as vomiting and diarrhea, headache, agitation, anxiety, confusion, or psychosis. Severe intoxication can cause tachy-arrhythmias, hyperthermia, hypotension, and seizures.
3. Children with ingestions of T<sub>4</sub> compounds will usually be asymptomatic at the time of ingestion and develop manifestations approximately 2-5 days after the exposure when the T<sub>4</sub> is converted to the more active T<sub>3</sub>. Patients who ingest T<sub>3</sub> compounds will usually develop symptoms within 6-24 hours. No decontamination is indicated in this patient because the ingestion occurred one week ago. At this time, the child requires cardiac monitoring, and the administration of beta-adrenergic antagonists; propranolol is the agent of choice. The child should be admitted for observation until the symptoms abate. In severe ingestions propylthiouracil can be used to block the peripheral conversion of T<sub>4</sub> to T<sub>3</sub>. Providing appropriate discharge instructions is of paramount importance for levothyroxine ingestions. Because manifestations of poisoning can be delayed several days, patients should be counseled to watch for signs of thyrotoxicosis (nausea, vomiting, tremor, irritability, diarrhea) and should have daily heart rate and blood pressure checks for 14 days (can be performed at the pediatrician's office). They should be told to return to the emergency department if any abnormalities occur.

## PHARMACOLOGY/TOXICOLOGY CASE STUDY #26

**History:** A 16-year-old female was angry with her mother and ingested a large amount of the mother's medication, 30 minutes ago. She now presents to your emergency department with her mother requesting treatment. Mom has rheumatoid arthritis and has been placed on methotrexate. She ingested no other medications and is not currently suicidal.

**PMH:** None.

**Physical Examination:**

T: 98.8°F      HR: 92 bpm      RR: 16 breaths per minute      BP: 110/65 mm Hg

**General:** Alert, tearful and very remorseful.

**HEENT:** Examination is normal.

**Pulmonary:** Clear to auscultation.

**CV:** Regular rate and rhythm without murmur.

**Abdomen:** Soft and nontender, bowel sounds were normal.

**Neurologic:** Normal deep tendon reflexes and normal muscle strength.

### QUESTIONS CASE STUDY #26

1. What medical concerns do you have?
2. What symptoms are associated with this type of medication use?
3. What interventions should be performed?



## CASE STUDY #26: METHOTREXATE OVERDOSE

1. Methotrexate overdose may result in a wide variety of toxic effects. This patient requires careful monitoring and aggressive treatment.
2. Toxic side effects include gastrointestinal (nausea, vomiting, intestinal bleeding, stomatitis, mucositis, esophagitis), hematologic (leukopenia, anemia, thrombocytopenia), hepatic (transaminitis, cirrhosis, hyperbilirubinemia), pulmonary (acute lung injury) neurologic (hemiparesis, seizures, dysreflexia, encephalopathy, coma) and renal (acute tubular necrosis).
3. Leucovorin is a metabolically functional folic acid and can bypass the antifolate effects of methotrexate. It should be given within 1 hour of ingestion if possible. It should be given IV and the dose should equal or be greater than the dose of methotrexate. If dose is unknown then can give 75mg or 10mg/m<sup>2</sup>/dose in children. Then 12 mg is repeated every 6 hours for 4 doses. Methotrexate levels can then be obtained to guide therapy. There are no contraindications for leucovorin use and adverse side effects includes allergic reaction and possible hypercalcemia. Sodium bicarbonate and fluids can be used to help prevent nephrotoxicity. Activated charcoal can be used if patient is protecting their airway and the ingestion is within 1 hour.

## PHARMACOLOGY/TOXICOLOGY CASE STUDY #27

**History:** A 78-year-old male presents to your emergency department from his chemotherapy appointment for evaluation of a complication. He has been receiving intravenous chemotherapy at home and is scheduled for central line placement in two days. Today while the nurse was infusing his chemotherapy, the doxorubicin dose infiltrated. The nurse brought him to the Emergency Department for treatment.

**PMH:** Non-Hodgkins Lymphoma, hypertension  
**Medications:** CHOP chemotherapeutic regimen, ondansetron, decadron, prochlorperazine, mesna, lisinopril

**Physical Examination:**

T: 98.8°F      HR: 82 bpm      RR: 16 breaths per minute      BP: 110/65 mm Hg

**General:** Awake and alert.

**HEENT:** Examination is normal.

**Pulmonary:** Clear to auscultation.

**CV:** Regular rate and rhythm without murmur.

**Abdomen:** Soft and nontender, bowel sounds were normal.

**Neurologic:** Normal deep tendon reflexes and normal muscle strength.

**Skin:** The site is red, swollen and tender.

### QUESTIONS CASE STUDY #27

1. What types of factors influence the outcome of this type of injury?
2. What therapy should be initiated?

## CASE STUDY #27: EXTRAVASATION INJURY

1. Extravasation injury is much more likely to occur in patients with (1) poor vascular integrity and blood flow, (2) limited venous and lymphatic drainage, and (3) use of sites which are over joints. Factors associated with a poor outcome from this type of injury include (1) exposure in areas with little subcutaneous tissue, i.e. the dorsum of the hand, (2) high concentrations of extravasant, (3) increased volume and duration of contact with the tissues, and (4) type of agent. The vesicant agents such as doxorubicin tend to result in more significant local tissue destruction.
2. The treatment of extravasation injuries is controversial and available information is based upon animal studies, limited case reports and small studies. There are no controlled studies to validate the use of pharmacologic or nonpharmacologic techniques (e.g. application of ice or heat). As soon as an extravasation is suspected, the infusion should be halted and the extremity should be elevated. Venous access should be maintained and as much of the agent as possible should be aspirated from the line. Ice should be applied up to four times a day for 20 minutes to prevent cell injury by reducing the cellular metabolic rate. Local infiltration of hyaluronidase should be considered. Surgery should be immediately consulted for extravasations where there is a high likelihood of necrosis. This type of injury requires an immediate surgical consultation. After the area of necrotic skin evolves to the point where it can be delineated from healthy tissue, surgical debridement may be indicated.

## PHARMACOLOGY/TOXICOLOGY CASE STUDY #28

**History:** A 29-year-old comatose male arrives to your Emergency Department via EMS, after having two seizures at home. The paramedics state that en route to the hospital he had a generalized tonic clonic seizure that lasted 25 seconds. According to family members, he has no prior history of seizures.

**PMH:** Suicide attempt (tried to cut wrists) four days ago.

**Meds:** Unknown

### Physical Examination:

T: 101.1°F    HR: 140 bpm    RR: 22 breaths per minute    BP: 180/99 mm Hg

**General:** Comatose.

**HEENT:** Pupils 6 mm bilaterally and sluggishly reactive to light. There is no scleral edema or hemorrhage. No gag reflex.

**Pulmonary:** Clear to auscultation bilaterally.

**CV:** Regular rhythm, tachycardic.

**Abdomen:** Hypoactive bowel sounds. Soft, nontender. Palpable bladder.

The cardiac monitor shows sinus tachycardia.

## QUESTIONS CASE STUDY #28

1. What immediate diagnostic and therapeutic measures should be indicated at the bedside?
2. What is your differential diagnosis in this case?
3. What substance ingestions should be considered?
4. What therapeutic trial may help confirm the diagnosis?
5. How quickly should you expect a response to this treatment?

## CASE STUDY #28: ANTICHOLINERGIC POISONING

1. This patient should have his airway, breathing and circulation secured. Intravenous access, continuous cardiac monitoring and pulse oximetry should be initiated. A bedside glucose should be obtained (this patient's initial blood glucose reading was 134 mg/dL). A trial of naloxone was attempted with no response. The clinician should consider empiric administration of glucose and thiamine.
2. Physical exam implies autonomic nervous system dysfunction: tachycardia, mydriasis, hyperpyrexia, dry skin and mucous membranes, ileus and urinary retention. These symptoms fit a picture of cholinergic blockade. The anticholinergic toxidrome is differentiated from the sympathomimetic toxidrome by the presence of dry skin and absence of bowel sounds. The most useful place to check for dry skin is in the patient's axilla. The anticholinergic syndrome is a clinical diagnosis. One must also consider the possibility of head trauma.
3. Antihistamines  
Tricyclic antidepressants  
Belladonna alkaloids  
Antispasmodics  
Antiparkinsonian drugs  
Ophthalmic preparations  
Antipsychotics  
Various plants (Jimson weed)  
Numerous OTC medications (sleep aids, cold preparations)  
Atropine  
Scopolamine  
Street drugs (e.g. heroin "cut" with scopolamine)
4. A therapeutic trial of physostigmine may help to confirm the diagnosis and avoid invasive diagnostic workup; however benefits are generally outweighed by the risks associated with its use. Physostigmine is an anti-cholinesterase that antagonizes the enzyme cholinesterase, which breaks down acetylcholine at the receptor site. Physostigmine therefore helps to overcome the competitive antagonism of acetylcholine caused by the ingested substance. Physostigmine is a tertiary amine. It is non-ionized and lipophilic, so it crosses the blood-brain barrier to reverse central and peripheral toxic effects. Its use is controversial and should be reserved for severe toxicity with both central and peripheral symptoms, such as severe agitation or refractory seizures. Because there are case reports of asystole when used for reversal of symptoms caused by TCA poisoning, its use is contraindicated in this condition. If used in non-TCA related anticholinergic toxicity, an ECG should be obtained to ensure that the patient has no QRS prolongation and the medication should be given slowly while the patient is on continuous cardiac monitoring to detect arrhythmias.

5. Almost immediately. The clinician should; however, keep in mind that the patient's response may be delayed or masked by the presence of other coingestants. The duration of action of physostigmine is short, so most anticholinergic drug effects last longer than physostigmine.

## PHARMACOLOGY/TOXICOLOGY CASE STUDY #29

**History:** A 16-year-old female presents to the Emergency Department via private vehicle barely responsive to painful stimuli. An hour ago, she informed her sister that she had “taken all of Mom’s diazepam,” which her sister estimates to have been about 20 tablets (5 mg), and washed them down with “a bottle of vodka.” The reason for the delay in arrival was that she refused to be transported, so her sister waited until she “passed out” to put her into the car and drive her to the Emergency Department.

**Physical Examination:**

T: 98.8°F    HR: 78 bpm    RR: 6 breaths per minute    BP: 126/86 mm Hg

**General:** Groans in response to painful stimuli. There are no signs of trauma.

**HEENT:** Pupils are mid-position, equal and sluggishly reactive. She has a diminished gag reflex.

**Pulmonary:** Clear to auscultation.

**CV:** Regular rate and rhythm.

**Neurologic:** Neurological exam is without focal deficit.

### QUESTIONS CASE STUDY #29

1. What is most likely responsible for this patient’s respiratory depression?
2. Would you administer flumazenil to this patient?
3. What is the dose of flumazenil?

## CASE STUDY #29: BENZODIAZEPINE POISONING

1. The patient's respiratory depression is most likely the result of the ethanol co-ingestant. Oral benzodiazepine poisoning alone rarely causes respiratory compromise, and these patients instead often present with CNS depression and normal vital signs. Most intentional overdoses involve a co-ingestant, with ethanol being the most common.
2. The use of flumazenil in acute overdose is controversial. The cited benefit of this antidote is the potential to avoid the need for invasive procedures such as lumbar puncture. The patient's age and access to diazepam at home might raise concerns about the possibility of a chronic component of use in this teenager, so this should be considered carefully prior to administration of flumazenil.

Although it is not indicated in an undifferentiated overdose patient, flumazenil may be considered in a confirmed acute benzodiazepine overdose in a patient known not to be a regular benzodiazepine user. Flumazenil administration is not contraindicated in the presence of alcohol. Indiscriminate use may force a chronic benzodiazepine user into severe withdrawal. Contraindications to flumazenil administration include:

- a. History of chronic benzodiazepines use
- b. History of seizure disorder
- c. Concomitant ingestion of tricyclic antidepressants or other agents known to have proconvulsant properties

The most common use of flumazenil is for the reversal of iatrogenic conscious sedation.

3. The initial dose of flumazenil is 0.2 mg given intravenously. When using flumazenil in attempt to reverse the effects of acute overdose, patients who do not respond to an initial dose should be given subsequent doses of 0.3 mg, followed by 0.5 mg. This can be repeated until a total dose of 1 mg is reached. Relapse of CNS depression may be seen in large ingestions or in patients with hepatic dysfunction leading to prolonged half-lives by decreasing benzodiazepine metabolism. Additionally, the half-life of flumazenil is short. In these cases, patients may be given additional doses of 0.2 mg at one minute intervals (maximum total dose 1 mg). Use of continuous infusions has been reported (0.25 to 1 mg/hr).



## PHARMACOLOGY/TOXICOLOGY CASE STUDY #30

**History:** A 34-year-old female presents to your Emergency Department via EMS. Her husband states he found her sleeping when he returned home from a business trip and became concerned when he was unable to awaken her. She has been treated for depression recently. There was an empty bottle of amitriptyline (prescription filled two weeks ago) and an empty bottle of diazepam (prescription filled today) near the bedside.

**Physical Examination:**

T: 100.1°F    HR: 118 bpm    RR: 8 breaths per minute    BP: 90/60 mm Hg

**General:** There are no signs of trauma.

**HEENT:** Mucous membranes are dry. There is no gag reflex. Pupils are dilated bilaterally and sluggishly reactive.

**Pulmonary:** Clear to auscultation.

**CV:** An irregular, tachycardic heart rhythm.

**Abdomen:** Soft with diminished bowel sounds.

**Skin:** Warm and dry.

**Neurologic:** Decreased level of consciousness. Slurred speech, responds to pain.

Initial EKG shows sinus tachycardia with prolonged QT interval and QRS duration of 0.16 msec.

### QUESTIONS CASE #30

1. What are characteristic findings of TCA ingestion?
2. What drugs are contraindicated in this case?
3. What treatment would you institute in this case?

### **CASE STUDY #30: CYCLIC ANTIDEPRESSANT POISONING**

1. Patients with cyclic antidepressant (CA) toxicity present with signs and symptoms of anticholinergic toxidrome and usually have decreased level of consciousness. They also may develop seizures and, due to its sodium channel blocker properties, may develop cardiovascular toxicity (prolonged QT, prolonged QRS, hypotension, ventricular arrhythmias). CA toxicity should be considered in all patients with a decreased level of consciousness and prolonged QRS complex.
2. Both physostigmine and flumazenil are contraindicated in the treatment of TCA toxicity. Also contraindicated are type IA, IC, II and IV antidysrhythmics.
3. Initial treatment should focus on assessment of airway and breathing. Endotracheal intubation should be performed in patients with signs of respiratory depression. There is no evidence that gastrointestinal decontamination is indicated. The prolonged QRS interval should be immediately treated with an intravenous bolus of sodium bicarbonate until it narrows or to keep the serum pH 7.45-7.50. The treatment of choice for hypotension, unresponsive to fluids is also bicarbonate. If the cause of the hypotension is a loss of vascular tone, a direct acting alpha-adrenergic agonist such as norepinephrine may be considered. If the hypotension is secondary to a loss of inotropy, dobutamine may be beneficial. Seizures are treated with benzodiazepines.

## PHARMACOLOGY/TOXICOLOGY CASE STUDY #31

**History:** A 3-year-old girl is rushed into the Emergency Department carried by her frantic mother. The mother states that the child just consumed “a bottle of heart pills.” The mother and the patient were apparently visiting the patient’s grandmother this afternoon, when the mother discovered her daughter playing in the bedroom with an open bottle of pills. The bottle was labeled “digoxin 0.25 mg tablets,” and there were 10 left. The Grandmother estimated that there were probably 40 pills in the bottle this morning when she took her usual dose. Since the child had been playing alone for some time, the ingestion could have occurred anytime within the past 90 minutes.

**Physical Examination:**

T: 99.4°F      HR: 40 bpm      RR: 30 breaths per minute      BP: 98/52 mm Hg

Weight      33 pounds (15 kg)

**General:** Age appropriate, lethargic female, whimpering and whining in the bed. Responds irritably to any stimuli. There are no signs of trauma.

**Pulmonary:** Clear to auscultation.

**CV:** Bradycardic, regular rhythm.

Initial EKG shows sinus bradycardia with first degree AV block.

Bedside glucose: 84

### QUESTIONS CASE STUDY #31

1. What tests would be appropriate in this case?
2. What therapy would you recommend and how much would you give?
3. What therapy for hyperkalemia should be avoided in this case?

## CASE STUDY #31: DIGITALIS POISONING

1. After securing the patient's airway, breathing and circulation, and initiating intravenous access, continuous cardiac monitoring and pulse oximetry, an ECG would be the initial test of choice. In digitalis poisoning, immediate management is determined by history of significant ingestion, clinical signs of digitalis toxicity and ECG changes, NOT on the laboratory values. During IV placement, blood samples should be obtained and sent to the lab to determine the patient's digitalis level, serum potassium, renal function and other tests as indicated by the clinical scenario (e.g. pregnancy testing in females of childbearing age and screening for coingestants in cases of overdose or unreliable patients). While some sources recommend management based on serum digoxin level, the patient's clinical condition and ECG changes are considered the first decision point in the management algorithm. The clinician should be aware that serum digoxin levels are not reliable until approximately 6 hours after last ingestion and that prior to this time they will appear elevated secondary to incomplete drug distribution.
2. This patient's clinical condition precludes the administration of activated charcoal, although most sources recommend its use up to two hours after acute ingestion in patients with a secure airway. There is no role for activated charcoal in chronic digoxin poisoning. Based on this patient's clinical condition and history that includes good evidence for a potentially lethal ingestion (greater than 1 mg of digoxin in a child), the treatment of choice is digoxin-specific antibody (Fab) fragments. Derived from immunized sheep, digoxin-specific antibody fragments are the Fab portion of IgG antibodies that bind free digoxin in the serum so it can be renally excreted. There is one commercially available preparation of digoxin-specific antibody. There are several formulas available to assist the clinician in calculating the proper dose of antidote which are available in most references and on the manufacturer's website. Consultation with a medical toxicologist or a clinician experienced in the management of digoxin poisoning is recommended. Indications for its use include life-threatening arrhythmia, signs and symptoms of organ hypoperfusion and potassium level greater than 5.5 mEq/L. Some sources recommend its administration in acute ingestions with steady state levels greater than 10 ng/mL, chronic ingestions with steady state levels greater than 4 ng/mL, and acute ingestions of greater than 10 mg in adults and 4 mg in children. Caution should be used when administering digoxin-specific antibody fragments as they can unmask the condition for which digoxin was initially prescribed (e.g. atrial fibrillation with rapid ventricular response and heart failure). Signs and symptoms should improve within thirty minutes of antidote administration.
3. Based on two case reports by Bower et al in the early 1900's, the use of calcium in digoxin-poisoned patients with hyperkalemia has been considered dangerous due to a theoretical propensity to precipitate fatal ventricular fibrillation, or stone heart syndrome, by increasing intracellular calcium. The temporal relationship of digoxin administration to calcium administration, the patient's potassium levels

and the reasons for calcium administration were not well documented in these case reports. Although the physiology behind the “stone heart theory” makes sense, a recent thirty year medline review and multiple animal studies have been unable to substantiate the idea that calcium administration in digoxin poisoned patients and/or mild-moderate hypercalcemia are dangerous. Still, most sources recommend avoidance of calcium administration in these hyperkalemic, digoxin poisoned patients. Additionally, potassium lowering treatments should be used judiciously in these patients because hypokalemia can precipitate digoxin-induced arrhythmias.

## PHARMACOLOGY/TOXICOLOGY CASE STUDY #32

**History:** A 16-year-old woman presents to your emergency department with her boyfriend. She admits to having taken 25 acetaminophen tablets (500 mg each) approximately three hours prior to arrival. She has had three episodes of emesis in the past 30 minutes.

**Physical Examination:**

T: 98.6°F      HR: 80 bpm      RR: 16 breaths per minute      BP: 110/60 mm Hg

**General:** Alert and oriented.

**HEENT:** Pupils 3 mm bilaterally and reactive.

**Pulmonary:** Clear to auscultation.

**CV:** Regular rate and rhythm, without murmur.

**Abdomen:** Soft, nontender, no masses palpable.

**Neurologic:** GCS 15.

### QUESTIONS CASE STUDY #32

1. Should treatment with gastric lavage be used this patient? What treatment, if any, would you administer? What testing, if any, should be ordered?
2. The patient's acetaminophen level at four hours post-ingestion is 224 mcg/ml. What treatment, if any, is indicated now? How would you give it?
3. If administered on the patient's initial presentation, would charcoal interfere with the activity of the antidote?

## CASE STUDY #32: ACETAMINOPHEN POISONING

1. No. Gastric lavage is not indicated in cases of isolated acetaminophen overdose because of the efficacy of N-acetyl cysteine for treatment. Activated charcoal effectively adsorbs acetaminophen and its administration is generally recommended for up to four hours post ingestion, but its ability to influence outcome has not yet been proven.

An acetaminophen (APAP) level should be checked four hours after ingestion. There is little value to stat acetaminophen levels in these patients, except possibly to substantiate their claim of acetaminophen ingestion.

Based on the Rumack-Matthew nomogram, a level equal to or greater than 150 mg/dL at four hours is considered a potentially toxic dose and should be treated with N-acetyl cysteine (NAC).

2. The patient should be given N-acetyl cysteine (NAC) by either the oral or intravenous route. The protocol for oral NAC is 72 hours in length and is administered with a loading dose of 140 mg/kg followed by 70 mg/kg every four hours for seventeen doses. More recently, intravenous NAC has been used in the United States and its protocol is 21 hours in length. Intravenous NAC is administered with a loading dose of 150 mg/kg IV over fifteen to 60 minutes. After the loading dose, an infusion of 12.5 mg/kg/hr is continued for four hours, after which 6.25 mg/kg/hr is administered for sixteen hours. Starting NAC anytime within the first eight hours appears to be equally effective. Antiemetics (e.g. ondansetron) may be needed.
3. Theoretically, the administration of activated charcoal could interfere with gastric absorption of NAC. However, in practice, this effect is probably clinically insignificant, and charcoal can be administered in patients who will receive NAC.

## PHARMACOLOGY/TOXICOLOGY CASE STUDY #33

**History:** A father returns to your Emergency Department with his 3-year-old daughter, stating, "she's worse." She had been evaluated about 12 hours earlier, at which time she had presented with three episodes of vomiting. Physical examination at that time was unremarkable, and the patient was discharged as "gastroenteritis" with routine instructions for vomiting. The patient's father reports that she seemed fine and had no further emesis until about an hour ago. At that time, she began to complain of severe abdominal pain. Over the next 45 minutes, she became more lethargic and now she is difficult to arouse. In response to your astute questioning about recent ingestions, he relates that she was found playing with an empty bottle of her mother's prenatal vitamins about an hour before her initial vomiting began.

### Physical Examination:

T: 100 °F      HR: 144 bpm      RR: 30 breaths per minute      BP: 45/palp

Weight: 44 pounds (20 kg)

General: Pale, diaphoretic and barely responsive to stimuli.

Pulmonary: Clear to auscultation bilaterally.

CV: Regular rate and rhythm with no murmur. Capillary refill 5 seconds.

Abdomen: Mild, diffuse tenderness without peritoneal signs.

Neurologic: The patient is somnolent. No focal deficits.

### Laboratory Studies

ABG: 7.12 | 90 | 22 | 9

CBC: WBC = 18,300; Hgb = 8.9; Hct = 26

Electrolytes: Na=135; Cl=98; K=4.5; HCO<sub>3</sub>=8

Glucose: 54

BUN: 38

### Questions Case Study #33

1. Ingestion of what substance must be suspected here?
2. What would account for the patient's apparent improvement before her earlier discharge?
3. What lab tests are indicated in this case?
4. What therapy would you initiate, and when would you initiate it?



## Case Study #33: Iron Poisoning

1. Iron.
2. An understanding of the phases of iron poisoning will shed light on this patient's presentation, as it is typical of iron poisoning cases. Most sources divide iron poisoning into 5 phases, which are often overlapping. The first phase, called the "gastrointestinal phase", is usually present from approximately 30 minutes to six hours post ingestion. Abdominal symptoms, such as vomiting, diarrhea and pain predominate during this time. Death in this phase is rare, but when it occurs it is due to hypovolemic shock. Most patients do not progress beyond this phase. The second phase, called the "latent phase", is usually seen from approximately six hours to 24 hours post ingestion. During this time, circulating free iron is redistributed into the reticuloendothelial systems. This phase may be transient or may not occur at all; if it occurs it may last up to 12 hours. This second phase can be mistaken for resolution of gastroenteritis symptoms or resolution of iron poisoning, having devastating consequences. In this case, the patient likely experienced the first phase of toxicity at home and had transitioned to the second phase by the time she arrived to the emergency department. The patient's second presentation to the emergency department was during the third stage, which is characterized by metabolic acidosis and shock. The fourth stage of iron poisoning, which occurs twelve to 96 hours post ingestion, is characterized by hepatotoxicity and hepatic necrosis. During this phase, many patients die of liver failure. The fifth phase occurs two to eight weeks post ingestion and is manifested by bowel obstruction, which occurs classically at the gastric outlet, the area of the gastrointestinal tract where the iron pills tend to aggregate, causing mucosal injury that eventually leads to scarring and stricture formation.
3. In addition to the usual battery of tests for a patient in shock (i.e. CBC, electrolytes, BUN, glucose, ABGs, type and cross, etc.), a serum iron concentration (SIC) should be obtained. This test can be useful to confirm the diagnosis of iron ingestion but the result should be interpreted with caution. Failure to obtain samples at the correct time after ingestion can lead to falsely low levels and an underappreciation of the severity of illness. This happens because the serum iron concentration is a measure of free iron in the blood, which is rapidly cleared from the serum. For immediate release preparations, the best estimate is achieved when the SIC is drawn between four and six hours post ingestion. Because of this, the clinician should know that there is no test that is superior to the clinical status of the patient for determining the severity of an iron ingestion. Multiple sources provide tables to show the relationship between SIC and clinical toxicity, with serious systemic toxicity appearing at concentrations greater than 500 mcg/dL. It should also be noted that a KUB film may demonstrate iron tablets in the GI tract, which would further support your initial diagnostic impression and may influence the decision to perform GI decontamination.

4. The patient's hypotension should be treated immediately with an IV fluid challenge of 20 ml/kg of normal saline. There is no indication for activated charcoal, since ingested iron is not adsorbed by charcoal. If iron tablets are seen on x-ray, the patient should also receive whole bowel irrigation with polyethylene glycol electrolyte (PEG) lavage solution at 20-40 mL/kg/hour for young children and 1.5 to 2 L/hour for teenagers and adults until all of the pills are removed or until the patient's KUB demonstrates removal of all of the pills. Patients with severe symptoms (shock, lethargy/coma), anion gap metabolic acidosis, peak SIC >500 mcg/dL, significant numbers of pills on plain films and worsening clinical condition despite maximal therapy should receive deferoxamine (DFO), the intravenous chelating agent used to treat iron poisoning. This medication works by complexing with ferric (Fe<sup>3+</sup>) iron to form the water-soluble ferrioxamine, which is excreted by the kidneys and causes the urine to turn the classic "vin rose" color. This drug is administered at a dose of 15 mg/kg/hr continuous infusion (adult and pediatric dosing). There are no established guidelines for length of dosing and administration of this medication should be done in concert with your local poison center or a physician experienced in the management of severe iron poisoning. The deferoxamine challenge test, once advocated to confirm the diagnosis of iron poisoning, is no longer recommended. This test involves administering an intramuscular dose of deferoxamine and waiting to observe whether the patient's urine changes to a "vin rosé" color, indicating the presence of iron poisoning. Despite having severe iron poisoning, some patients fail to show vin rosé colored urine and have been prematurely sent home.

A search for GI bleeding should also be explored since the patient has low hemoglobin. Iron is a corrosive that can result in GI bleeding.

## PHARMACOLOGY/TOXICOLOGY CASE STUDY #34

**History:** A very anxious 27-year-old man presents to your Emergency Department with the chief complaint that he is “having a stroke.” He reports that, after some heavy drinking last night, he awoke with a headache and nausea. When he tried to eat some breakfast (about eight hours prior to ED arrival), he vomited. Because he continued to feel nauseated, he took two of his wife's 10 mg prochlorperazine tablets, left over from a “bout of the flu” she had experienced last month. He took another 10 mg tablet about four hours later. Now he feels as if his neck “is getting paralyzed.”

**Physical Examination:**

T: 98.6°F    HR: 78 bpm    RR: 12 breaths per minute    BP: 120/70 mm Hg

**General:** Anxious appearing male in no acute distress.

**Neurologic:** Normal, except that his neck is held in extreme extension and his facial muscles seem to tighten in an involuntary grimace.

### QUESTIONS CASE STUDY #34

1. Is this a stroke or an allergic reaction to prochlorperazine?
2. How would you treat this patient?

## CASE STUDY #34: ACUTE DYSTONIC REACTION

1. Neither. This patient is experiencing acute dystonia, an extra-pyramidal side effect of phenothiazines, a class of drugs to which prochlorperazine belongs. It is an idiosyncratic reaction to the medication and is not usually dose related. Neuroleptics, antiemetics, and antidepressants are the most common causes of dystonic reactions; alcohol and cocaine can increase the risk. Oculogyric crisis (deviation of eyes in all directions), akathisia, protrusion of the tongue, trismus, forced jaw opening, difficulty in speaking, facial grimacing, opisthotonos, and torticollis are physical exam findings associated with acute dystonic reaction. Mental status is unaffected and vital signs are usually normal. Laryngeal spasm can occur and the airway may need to be supported. Diagnosis is usually clinical with history, physical, and the resolution of symptoms with treatment.
2. The immediate treatment is 25-50 mg of diphenhydramine (Benadryl®) I.V., and/or 2 mg benztropine mesylate (Cogentin®) I.M. His symptoms should resolve within about 10-30 minutes. Multiple doses may be needed. The oral route is surprisingly ineffective.

## PHARMACOLOGY/TOXICOLOGY CASE STUDY #35

**History:** A 52-year-old female presents to your Emergency Department by squad with diminished level of consciousness and seizure activity. On arrival she has spontaneous respirations and “moaning”, incomprehensible speech. Family reports that the patient is diabetic and had been changed from oral hypoglycemic agents to insulin about nine months previously. She usually has seizures when her blood sugar “gets too low.”

**PMH:** Diabetes.

**En Route:** The patient had generalized tonic clonic seizure activity on EMS arrival IV, O<sub>2</sub>, monitor were established. Initial blood glucose was 18 mg/dL. One ampule of D50 was given intravenously.

**On arrival:** Blood glucose level rechecked and found to be 26 mg/dL. The patient was given an additional ampule of D50.

**Physical Examination:**

T: 98.4°F      HR: 84 bpm      RR: 16 breaths per minute      BP: 132/68mm Hg

**General:** The patient quickly responded after the second dose of dextrose and is now fully oriented. She appears to be postictal.

**Pulmonary:** Clear to auscultation.

**CV:** Regular rate and rhythm without murmur.

**Abdomen:** Multiple contusions over anterior abdomen at the site of insulin injection.

**Neurologic:** No focal deficits.

Cardiac monitor shows sinus rhythm.

Approximately 30 minutes after arrival, the patient again becomes unresponsive. A STAT blood sugar is 30. Patient improves with two ampules D50 followed by initiation of a D10 drip.

### QUESTIONS CASE STUDY #35

1. What historical information should be elicited?
2. What could account for her profound, persistent hypoglycemia?
3. What laboratory studies, if any, should be ordered?
4. How is an anion gap calculated and what is its significance?
5. How would you manage this patient?

## CASE STUDY #35: ORAL HYPOGLYCEMIC POISONING

1. The interview with the patient's husband was illuminating. Multiple similar episodes had occurred in the recent past. Her family doctor practiced at a different facility; no records were available for review. PMH was also significant for schizophrenia, and noncompliance with antipsychotic medications. She refused to allow family members to administer or monitor insulin. Her husband reported that she had prescriptions for NPH and Regular insulin, glipizide (supposedly discontinued) and haloperidol.
2. Poor dietary intake; increased physical activity; infection; excessive insulin administration; overdose of oral hypoglycemic agents; possible drug interactions; alcoholism; insulinoma, hepatic failure.
3. Frequent blood glucose monitoring, BUN, creatinine, electrolytes, ABG, consider a CT scan of the head and a toxicology screen including an acetaminophen level.
4. Anion Gap (AG) =  $\text{Na}^+ - (\text{Cl}^- + \text{HCO}_3^-)$

Normal = 8 - 12

The presence of an elevated anion gap acidosis suggests the presence of unmeasured anions in the blood.

Lactic acidosis, which will produce an elevated anion gap, can be seen in metformin overdose but is not seen in glipizide overdose.

5. The patient should be admitted to ICU on a dextrose infusion, with frequent BS monitoring. Other causes of hypoglycemia should be considered. Full toxicological profile should be performed. Serum glucose should be maintained to 90-100 mg/dL for at least the first 12 hours.

Octreotide can be used in addition to dextrose for hypoglycemia. Octreotide suppresses insulin by antagonizing pancreatic insulin release.

If the patient is unable to tolerate octreotide due to allergy and hypoglycemia continues despite dextrose, diazoxide can be used.

All oral hypoglycemic overdoses or hypoglycemia secondary to oral hypoglycemic drugs should be admitted, due to the long half life of these agents and risk for prolonged hypoglycemia.

## PHARMACOLOGY/TOXICOLOGY CASE STUDY #36

History: A 27 year old male presents to your emergency department for evaluation of palpitations, chest tightness and dizziness that started approximately thirty minutes after smoking crack cocaine. He describes himself as a casual user and states he has never had these symptoms. He denies recent ingestion of other drugs.

PMH: None.

Medications: None.

SH: Smokes crack cocaine 1-2 times per month. Drinks 4-6 cans of beer most nights.

### Physical Examination

T: 99.2°F    HR: 118 bpm    RR: 17 breaths per minute    BP: 223/109mm Hg

General: Anxious-appearing male in no acute distress.

HEENT: PEERL at 4mm, no nystagmus. Injected sclera bilaterally

Pulmonary: Clear to auscultation.

CV: Tachycardic, regular rhythm. No murmurs.

Abdomen: Soft, nontender.

Skin: Diaphoretic.

### QUESTIONS CASE STUDY #36:

1. What signs and symptoms are commonly seen following acute cocaine intoxication?
2. What type of diagnostic testing, if any, is indicated?
3. What therapeutic treatment, if any, is indicated?

## CASE STUDY #36: COCAINE-RELATED CHEST PAIN

1. Pleasurable effects of acute cocaine intoxication include euphoria, increased alertness, sociability and energy. Adverse effects include agitation, paranoia, panic, psychosis, hallucinations and impulsivity. Cardiopulmonary symptoms are common and effects include hypertension, tachycardia, chest pain, palpitations, cough, shortness of breath and wheezing.
2. Due to the ability of cocaine to cause coronary artery vasoconstriction and spasm, patients who present with acute chest pain after use should be presumed to have myocardial ischemia until proven otherwise. In this patient, continuous cardiac monitoring and pulse oximetry and EKG should be instituted. Serum troponins are specific for cardiac damage; however other markers, such as CPK, CK-MB and myoglobin may be increased secondary to increased psychomotor activity, rhabdomyolysis and skeletal muscle injury, clouding the diagnostic picture. There is no evidence that preexisting coronary artery disease is required for the development of cocaine-induced myocardial ischemia, although chronic use does contribute to accelerated atherosclerosis and possibly increased risk of acute coronary syndrome in these patients. Even young individuals can suffer from myocardial ischemia in the setting of acute cocaine intoxication.
3. Treatment of ACS in cocaine-related chest pain includes aspirin and early administration of benzodiazepines for anxiety, heart rate and blood pressure control (from which this patient would benefit). Agents with beta-receptor antagonizing properties should be avoided in these patients. Nitroglycerin or oral calcium channel blockers are recommended for patients with ischemic chest pain and ECG changes.

Every cocaine-associated chest pain victim should have a differential diagnosis including aortic dissection, pneumothorax and cardiac ischemia. Aortic dissection should be excluded prior to initiation of thrombolytic therapy. Acute coronary syndromes and aortic dissection may co-exist in cocaine users.



## PHARMACOLOGY/TOXICOLOGY CASE STUDY #37

History: A 5 year old female is brought to the Emergency Department by her mother and grandmother. While the women were visiting in the kitchen, the child was playing in the living room and found a pill bottle on top of the TV. The mother found the girl sitting on the floor with the pills spilled out around her. There were pill fragments in her mouth and some in her hand. They were brought immediately to the Emergency Department.

The pill bottle was brought in and the label identified the contents as Metformin.

Physical examination is unremarkable and the patient's vital signs are normal.

### QUESTIONS CASE STUDY #37

1. What diagnostic tests should be considered?
2. What are signs and symptoms could this child present with and when do symptoms usually occur in metformin poisoning?
2. What other considerations must not be overlooked?
4. What is the treatment and disposition for this patient?

## **CASE STUDY #37: ORAL HYPOGLYCEMIC POISONING**

1. Obtain blood glucose on this patient upon arrival. Chemistries should also be obtained, and with Metformin, a venous blood gas should be considered.
2. Signs and symptoms of hypoglycemia can be seen including agitation, confusion, seizures, coma, tachycardia, or diaphoresis. Metformin decreases hepatic glucose production and intestinal absorption, and increases peripheral utilization of glucose. Acute hypoglycemia is not usually seen in a metformin overdose. Lactic acidosis can occur with Metformin overdose but usually presents in patients with advanced age or renal insufficiency.
3. Multiple drug ingestion - consult Poison Control Center. Consider child abuse or neglect - consider consulting with a Children Services Agency.
4. This patient needs frequent blood glucose monitoring and should be admitted for at least 24 hours observation. In severe metformin overdosis, hemodialysis can be used for elimination of metformin and treatment of lactic acidosis.

## PHARMACOLOGY/TOXICOLOGY CASE STUDY #38

**History:** A 32-year-old, right hand dominant male presents to your emergency department at 1:00 a.m. complaining of a burn to his right hand and fingers. The patient states that approximately 12 hours ago he was working at a local factory that manufactures TV tubes. While spraying the TV tubes, his right glove developed a small leak. He noticed burning in his right hand, immediately took the glove off and washed his hands with soap and water for 20 minutes as directed by his supervisor. Since the burning had resolved, he finished his shift without difficulty. Throughout the night, he noticed increased burning and pain. Now he complains of intense pain on the dorsal surface of his right hand and fingers.

**Physical Examination:**

T: 99.8°F    HR: 92 bpm    RR: 14 breaths per minute    BP: 132/86 mm Hg

**General:** Age appropriate male in obvious discomfort.

**Pulmonary:** Clear to auscultation.

**CV:** Regular rate and rhythm without murmur.

**Extremity:** Examination of the right hand reveals intact skin with minimal erythema and significant tenderness on an approximately 3 x 3 cm area on the dorsum of the hand and proximal fingers. There are no blisters or evidence of second or third degree burn. No soft tissue swelling. Remainder of his bilateral upper extremity exam is unremarkable. Neurovascular exam intact bilaterally.

### QUESTIONS CASE STUDY #38

1. What steps should be taken to determine the appropriate treatment when a patient presents after exposure to an unknown chemical?
2. Why are hydrofluoric acid burns unique?
3. What laboratory test should be ordered?
4. How do hydrofluoric acid burns usually present?
5. What is the proper treatment?

## Case Study #38: Hydrofluoric (HF) Acid Exposure

1. All chemical exposures must be accurately identified. Because the patient is unable to identify the chemical he was working with, the factory or the supervisor of the company should be contacted.

Since the factory is closed for Labor Day, you wake up the supervisor at 2:00 a.m. The supervisor informs you that the patient was working with 20% hydrofluoric acid.

2. Hydrofluoric acid is a highly corrosive inorganic acid that produces injuries by both coagulation and liquefaction necrosis. Initially, the hydrogen ions denature proteins and cause a corrosive burn that is similar to other acid burns. Additionally, the fluoride ions penetrate the tissues and alter cellular metabolism, causing direct cellular toxicity. The fluoride ion penetrates into the deep tissues and complexes with calcium and magnesium to form salts. This continues until the fluoride is precipitated with calcium and magnesium. Hydrofluoric acid is the only acid that causes liquefaction necrosis.
3. It is important to remember that hydrofluoric acid burns not only cause skin injury, but also a potentially fatal systemic reaction. Burns of  $\geq 1\%$  body surface area or inhalation of fumes from  $\geq 60\%$  hydrofluoric acid concentration may result in hypocalcemia, so an electrolyte panel, including a serum calcium level, should be obtained. Hypocalcemia may stimulate an efflux of potassium ions from cells causing hyperkalemia, so an electrocardiogram should also be considered. Electrolyte abnormalities and direct cardiotoxic effects of fluoride ions contribute to the development of cardiac arrhythmias.
4. The hallmark of a hydrofluoric acid dermal burn is pain disproportionate to physical findings. Dermal exposure to concentrated hydrofluoric acid produces lesions that may be immediately and intensely painful; however the onset of lesions and pain may be delayed with more dilute solutions. Exposure to solutions containing greater than 50% HF produces immediate burning, erythema and tissue damage. Exposure to 20-50% results in pain and erythema, which may be delayed from one to eight hours. Exposure to solutions containing less than 20% results in erythema and pain delayed up to 24 hours after exposure. It is not unusual for some patients to seek medical treatment 18 to 24 hours after exposure. This delay in treatment can lead to severe tissue destruction. Always consider hydrofluoric acid burns in patients who present with severe hand pain.
5. Dry chemicals should be brushed off of the patient and immediately followed by a deluge shower. Keeping the hand warm and treating pain will help increase local circulation, therefore increasing the local supply of calcium and magnesium. Large surface burns require the same fluid therapy as thermal burns. Procedures directed at complexing fluoride ions are indicated after irrigation. One method of complexation is the application of a topical calcium gluconate gel,

2.5%, to the affected area. The earlier the initiation of this therapy after exposure, the more rapid the resolution of symptoms may occur. The gel must have access to the burn, so cloth or thick necrotic coagulum should be removed. This gel should be massaged into the skin until the pain has subsided for 15 minutes. It is recommended that 2 pairs of gloves be worn by personnel applying the gel in order to prevent hand burns due to exposure. One alternative for burns confined to the hands is to place the gel in a glove and then insert the patient's hand into the glove. The calcium from the gel will complex with free fluoride ions and help prevent further toxicity. Several companies manufacture the calcium gluconate gel and often patients suffering industrial exposure may arrive with it in hand. Alternatively, this gel may be made by adding 10 grams of USP calcium gluconate powder to 5 ounces (140 grams) of water soluble surgical lubricant. In severe cases or in cases of treatment failure with calcium gluconate gel, burned skin may be infiltrated with 5% calcium gluconate. (Scarring may be produced by use of concentrations greater than 5 %.) The usual recommendation is that injections be limited to 0.5 ml per square centimeter of involved tissue. This method cannot be used safely with burns on the digits. Resolution of pain suggests treatment is successful and can be stopped. If pain is not adequately controlled after one hour of more conservative therapies, or if there are large burns or burns caused by highly concentrated acid, intraarterial and intravenous infusions of calcium gluconate can be performed. Consultation with your local poison center or a physician experienced in the advanced management of hydrofluoric acid burns is recommended. There are no studies that compare these two modalities head-to-head. Hospitalization is indicated for patients with burn areas exceeding 50-100 cm<sup>2</sup>. ICU care is probably necessary when an area exceeding 100-150 cm<sup>2</sup> is involved. Addition of calcium gluconate to IV fluids (20 ml of a 10% solution added to the initial liter) to prevent hypocalcemia is suggested.

## PHARMACOLOGY/TOXICOLOGY CASE STUDY #39

**History:** An 80-year-old female who presents to the Emergency Department complaining of dizziness, anxiety and agitation. Her family informed the ambulance personnel that this was not her baseline mental status.

**PMH:** Congestive heart failure, arthritis and a psychiatric disorder.

**Medications:** Lithium, digoxin, furosemide, isosorbide dinitrate

**Physical Examination:**

T: 98.8°F      HR: 83 bpm      RR: 20 breaths per minute      BP: 110/84 mm Hg

**General:** Elderly white female in no acute distress. She is disoriented and unable to follow simple commands.

**HEENT:** No nystagmus.

**Pulmonary:** Clear to auscultation.

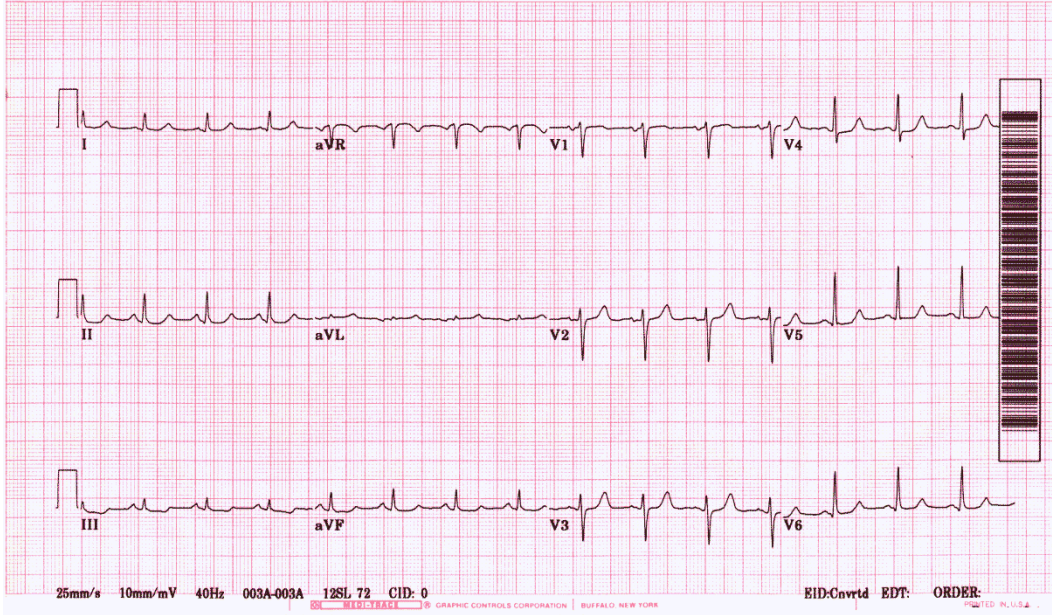
**CV:** Regular rate and rhythm without murmur.

An electrocardiogram was done because of her age and complaint of dizziness and was compared with a previous electrocardiogram from several months earlier.

### QUESTIONS CASE STUDY #39

1. How would one interpret the electrocardiogram?
2. What laboratory or ancillary information would be of help with this patient?
3. What are you concerned about?

64 yr		Vent. rate	89	BPM
Female	Caucasian	PR interval	128	ms
62in	150lb	QRS duration	88	ms
Room:SDS03		QT/QTc	376/457	ms
Loc:1	Option:24	P-R-T axes	76 56 17	



## CASE STUDY #39: DIGITALIS POISONING

1. The electrocardiogram demonstrates digitalis effect. The digitalis effect is characterized by sagging, horizontal or down sloping ST segment depressions seen predominantly in the anterior precordial leads (V1-V3) associated with slightly inverted or biphasic T waves. It is a sign that a patient is digitalized and does not indicate toxicity.
2. This patient should have an ECG obtained and blood should be sent to the lab to determine renal function, electrolytes, digoxin level, lithium level. Electrolytes were ordered as well as a digoxin and lithium level, which revealed a potassium level of 4.9, a digoxin level of 5.8 and a lithium level of 2.1. These numbers suggested that the patient was not only lithium toxic, but had a potentially toxic digoxin level; the ECG from her current ED evaluation was of concern because of the potential for ischemic changes, but also changes that may have been induced by digoxin and/or lithium.
3. Digoxin poisoning can cause multiple arrhythmias, which are related to increased automaticity and excessive increase in parasympathetic tone (bradycardia). The most common arrhythmia is PVCs, which can occur in isolation or as bigeminy. Although not pathognomonic, a patient who demonstrates bidirectional ventricular tachycardia should be presumed to have digoxin poisoning until proven otherwise.

Because of the patient's age and her abnormal mental status, the clinician should be aware of the potential ischemic effects as noted on the ECG.

Another cause of potential cardiovascular disturbances in this patient is elevated lithium level. Lithium may cause sinus bradycardia, non-specific ST abnormalities and ventricular ectopy with associated neurologic complaints of ataxia, confusion, neuromuscular irritability and even coma.

This patient represents a complicated medical situation. She has underlying cardiac and psychiatric diseases and is on a multitude of medications, which may affect not only her clinical status but also her EKG.

This patient was admitted to the telemetry unit of the cardiac care facility and subsequently had a negative cardiovascular course: cardiac enzymes were unremarkable and her ECG reverted to a normal sinus rhythm with non-specific ST changes following correction of her digoxin and lithium levels. Her mental status improved with decreasing anxiety and agitation and return to her baseline.



## PHARMACOLOGY/TOXICOLOGY CASE STUDY #40

**History:** A 21-year-old female presents to the Emergency Department with a three-hour history of epigastric and right-upper abdominal pain associated with nausea and vomiting. She denies any history of similar episodes in the past and also had no complaints of chest pain, fever or shortness of breath, frequency or dysuria. The patient denies sick contacts, although she did have a recent upper respiratory infection for which she was given antibiotics.

**Medications:** None.

**Allergies:** Penicillin.

**Physical Examination:**

T: 98.8°F      HR: 94 bpm      RR: 20 breaths per minute      BP: 136/98 mm Hg

**General:** Age appropriate, anxious patient with a flat affect in moderate discomfort.

**Pulmonary:** Clear to auscultation.

**CV:** Regular rate and rhythm without murmur.

**Abdomen:** Normal bowel sounds. Tenderness in epigastrium and right upper quadrant with guarding.

**Back:** No costovertebral tenderness.

**Rectal:** Rectal exam was non-tender and guaiac negative.

While in the ED, the patient had one episode of green emesis, which was tested for occult blood and found to be negative.

### QUESTIONS CASE STUDY #40

1. What further information may be helpful in taking care of this patient?
2. What laboratory studies and/or radiographic testing would you utilize, if any?

## CASE STUDY #40: DRUG-INDUCED PANCREATITIS

1. In this patient, it may be useful to inquire about a history of alcohol abuse in addition to any past medical history of pancreatitis, peptic ulcer disease, gallbladder disease, nephrolithiasis or abdominal surgeries, including appendicitis.
2. Ancillary diagnostic testing may include a KUB looking for signs of obstruction, gall stones or nephrolithiasis. Laboratory studies could include electrolytes, BUN, creatinine, glucose, CBC with differential, amylase, lipase, LFTs and a urinalysis with urine pregnancy test.

Upon further questioning pertinent to patient's history as above, the patient had been given erythromycin for an upper respiratory infection. She claimed that she never took the medication as directed and in fact, the night before her symptoms presented, she had an argument with her husband and subsequently ingested 20 tablets of erythromycin (250 mg).

This case represented an ingestion of erythromycin with secondary development of acute pancreatitis. Mrs. Smith had unremarkable radiographs, urinalysis and LFTs, but had a lipase of 512 U/L and an amylase of 1,033 U/L. Erythromycin, in particular oral preparations, may cause a number of side effects most frequently related to the GI tract, such as abdominal cramping, although nausea, vomiting and diarrhea may occur. Administration of more than 4 grams per day can cause tinnitus and ototoxicity.

In this case, the acute ingestion of a multitude of erythromycin tablets led to the secondary development of the patient's acute pancreatitis. Drugs are estimated to be responsible for approximately 2% of acute pancreatitis. Drug-induced pancreatitis is usually mild. Other drugs that are associated with pancreatitis include acetaminophen, azathioprine, cisplatin, tetracycline, sulfonamides, valproic acid, estrogens, furosemide, corticosteroids, octreotide, and salicylates. Of the top 100 drugs prescribed in the United States, 44 have been implicated in drug-induced pancreatitis. Treatment includes standard therapy for acute pancreatitis as well as the need for psychiatric consultation because of the patient's inappropriate reaction to her domestic problems.

## PHARMACOLOGY/TOXICOLOGY CASE STUDY #41

**History:** A 12-year-old female was brought to the Emergency Department by her family with the complaint that their daughter had exhibited gross twitching of her upper and lower extremities, her eyes rolling back in her head with drooling from her mouth and urinary incontinence. This activity was noted on two occasions within the last half hour and each episode lasted for approximately 2-3 minutes. The mother stated that the patient has never exhibited any similar activity. The mother states that the patient recently was very upset after having failed a major exam in mathematics. The father reports he found an empty pill bottle at home which had contained approximately forty 100 mg tablets of theophylline.

**PMH:** Asthma.  
**Medications:** Theophylline.

### Physical Examination:

T: 99.3°F    HR: 130 bpm    RR: 30 breaths per minute    BP: 140/98 mm Hg

**General:** Lethargic white female without any seizure activity.

**HEENT:** Pupils 4mm, equal and reactive to light bilaterally. No nystagmus.

**Pulmonary:** Clear to auscultation.

**CV:** Tachycardic, regular rhythm.

**Abdomen:** Unremarkable.

**Neurologic:** Diffuse hyperreflexia (3+) with down going Babinski bilaterally.

## QUESTIONS CASE STUDY #41

1. What are your immediate concerns with this patient? What lab work, x-rays or ancillary measures would you request?
2. Based upon the above history, physical and laboratory results, what further treatment(s) would you initiate for this patient?

## CASE STUDY #41: THEOPHYLLINE POISONING

1. Your immediate concern should be finding the etiology for the patient's seizures and controlling/preventing any recurrent seizures. Immediate laboratory tests should include electrolytes, glucose, BUN, creatinine, LFTs, U/A, CBC with differential, stat theophylline level and toxicology screen including acetaminophen level. Radiographic examination should include portable CXR, KUB and a head CT. A lumbar puncture should be considered for the evaluation of new seizures. Laboratory investigation was remarkable only for a theophylline level of 70 mg/L, CXR/KUB were negative.
2. Based on the history, physical and laboratory results, this patient has theophylline poisoning. There are 2 groups of theophylline intoxication:

Acute overdose – Patients usually have GI symptoms including vomiting, tremor, anxiety, tachycardia. Hypokalemia, hypophosphatemia, hyperglycemia and metabolic acidosis can be seen. With serum levels greater than 90mg/L you can see hypotension, ventricular arrhythmias and seizures. Symptoms can be delayed with sustained release preparation.

Chronic intoxication – Patients do not have GI symptoms as commonly. Metabolic effects like hypokalemia and hyperglycemia are less commonly seen in chronic intoxication. Severe side effects, such as seizures, occur at much lower levels and are usually seen around 40mg/L or higher. Chronic intoxication can occur with excessive doses in a period of 24 hours or longer, or if illness or drugs delay the hepatic metabolism of theophylline.

Initial treatment includes airway, breathing, and circulation. Activated charcoal should be administered after the airway is managed in this patient. Multiple doses should be considered and whole bowel irrigation should be considered if a sustained release preparation was ingested. Seizures should be controlled with benzodiazepines or phenobarbital; however, theophylline seizures can be resistant to treatment. Hypotension, tachycardia, and ventricular arrhythmias are likely the result of excessive beta-adrenergic stimulation and can be treated with propranolol or esmolol. However, caution should be used when giving beta-blockers to asthma patients. Theophylline can be removed with hemodialysis or charcoal hemoperfusion; these should be considered in acute intoxication with levels greater than 80mg/L, chronic intoxication with levels greater than 40mg/L, or persistent symptoms such as seizures, hypotension, or dysrhythmias. Multiple doses of activated charcoal can be used but is most effective with levels less than 100mg/L in acute intoxications.

## PHARMACOLOGY/TOXICOLOGY CASE STUDY #42

**History:** A 71-year-old male presents to the emergency department with reports of “feeling a little run down.” His son and daughter-in-law, with whom he lives, states that he has been confused with an unsteady gait, incomprehensible speech and unusual behavior for approximately three days. He has also been very irritable and other times seemed to be breathing very rapidly and deeply. This is apparently very unusual behavior for him because he generally lives semi-independently. They deny a history of any fall or injury, or any recent or remote history of head trauma. The patient denies any pain complaints and is unaware of any change in his sleep patterns, dietary, bowel or urinary habits. He does report, “I can't get my balance,” although he denies any syncopal or near syncopal episodes, fall or head injury.

**PMH:** Arthritis and “nerves.”

**Medications:** Multivitamin, hydrochlorothiazide, simvastatin, aspirin.

**SH:** Frequent alcohol use with last drink 4 days ago.

**Physical Examination:**

T: 100.6°F    HR: 100 bpm    RR: 30 breaths per minute    BP: 142/74 mm Hg

**General:** Elderly elderly, awake, alert male who is slightly tachypneic.

**HEENT:** No trauma. Face is flushed. Mucous membranes are dry. His speech is slurred but there is no facial droop. PEERL.

**Pulmonary:** Clear to auscultation

**CV:** Regular rate and rhythm.

**Abdomen:** Soft, non-tender with normal bowel sounds.

**Neurologic:** Symmetric motor strength testing in the upper and lower extremities. There is no clonus and Babinskis are down going bilaterally. Cranial nerves intact. He does appear to have ataxia with a coarse tremor, however, and he was not ambulated secondary to his unsteadiness.

Cardiac monitor shows normal sinus rhythm.

### QUESTIONS CASE #42

1. What is the differential diagnosis for this patient with acute neurologic symptoms including ataxia and confusion?
2. What physical exam findings would suggest a toxicologic cause of his symptoms?
3. What laboratory tests would assist you in the diagnosis of this patient?
4. What is your working diagnosis on this patient?
5. What therapeutic course should be pursued?

## Case Study #42: Chronic Salicylate Poisoning

1. An acute neurologic event such as a TIA or a cerebral vascular accident should be considered. Also, the metabolic causes for acute dementia should be considered. Toxicologic considerations should include: acute alcohol toxicity, alcohol withdrawal or drug overdose of routine medications, particularly aspirin. Head trauma should also be considered.
2. The patient's vital signs are unusual in that he has a low-grade temperature of 100.6°F and tachypnea without cardiopulmonary symptoms. Physical examination should include careful observation of the depth of a patient's respirations, as hyperpnea can increase minute ventilation, causing hyperventilation with a normal respiratory rate. Furthermore, his acute ataxia, coarse tremor and mental status changes are also suggestive of a toxicologic disorder.
3. Arterial or venous blood gas testing and serum electrolytes will help you determine the presence of an anion gap metabolic acidosis. A serum salicylate level will help determine the cause of the increased anion gap acidosis. A serum salicylate level should be obtained.

Arterial blood gas on room air revealed a pH of 7.35, pCO<sub>2</sub> of 15.9, pO<sub>2</sub> of 100 and HCO<sub>3</sub><sup>-</sup> of 9.8. Serum electrolytes reveal sodium 148, potassium 4.7, chloride of 109, CO<sub>2</sub> of 15.8. BUN 50, creatinine 2.1. Calculated anion gap is 23. CT scan of the brain was negative. The patient's initial ECG showed sinus tachycardia without evidence of ischemia or infarction and his troponin was negative. Urinalysis dips were positive for blood with no RBCs. Serum toxicology screen was negative for acetaminophen and alcohol. His salicylate level was 69.9 mg/dL.

4. Chronic salicylate poisoning.
5. GI decontamination should not be initiated, as this patient is suffering from chronic toxicity. Urinary alkalization should be initiated as this will enhance renal excretion of salicylates by ion trapping. The patient should be referred to an institution with the ability to perform hemodialysis. Dialysis not only removes the salicylates but will also correct the electrolyte and metabolic abnormalities that have occurred. Dialysis should be considered for salicylate toxicity in patients with:

- (1) Salicylate levels greater than 80 - 100 mg/dL in acute poisoning
- (2) Salicylate levels greater than 40 - 60 mg/dL in chronic poisoning
- (3) Seizure or cerebral edema
- (4) Renal failure that prevents elimination of salicylate
- (5) Severe acid/base or electrolyte abnormalities
- (6) Fluid overload that prevents bicarbonate administration
- (7) Non-cardiogenic pulmonary edema
- (8) Clinical deterioration despite appropriate and aggressive medical therapy.

## PHARMACOLOGY/TOXICOLOGY CASE STUDY #43

**History:** A 15-year-old male presents to your Emergency Department with his parents at 7:30 p.m. after he was found “huffing” spray paint in the shed out back. The patient’s parents appear angry and worried. The patient denies complaints and admits that over the last several weeks he has been buying spray paint at the local hardware store so he can “get high”.

**PMH:** None.

**Medications:** None.

**SH:** Denies alcohol and illicit drug use. Occasionally smokes cigarettes.

### Physical Examination:

**T:** 98.2°F      **HR:** 85 bpm      **RR:** 14 breaths per minute      **BP:** 122/64 mm Hg

**General:** Age appropriate, male in no acute distress.

**HEENT:** No evidence of trauma. Pupils 3 millimeters bilaterally and equally reactive to light.

**Pulmonary:** Clear to auscultation.

**CV:** Regular rate and rhythm.

**Abdomen:** Unremarkable.

**Skin:** Blue paint marks in the perioral area and also on the nose.

**Neurologic:** Unremarkable.

### QUESTIONS CASE #43

1. What clinical effects can result from inhalant abuse?
2. What laboratory testing, if any, should be ordered for this patient?
3. What is the difference between huffing, bagging and sniffing?
4. What is sudden sniffing death syndrome and what is the mechanism by which death can result?
5. What secondary poisonings can result from hydrocarbon abuse?

## CASE STUDY #43: INHALANT ABUSE

1. Initial effects from an acute inhalant intoxication are similar to alcohol intoxication. The person may feel drowsy, lightheaded and have a loss of inhibition. Hallucinations can occur. Long term effects include depression, mood changes, weight loss, inattentiveness, lack of coordination, irritability, weakness. Chronic abuse can cause permanent neurological damage with diminished cognitive function and memory impairment. Chronic abuse can also damage the liver, kidneys, heart or lungs.
2. A good history and physical should be sufficient. If the patient had a recent exposure to the inhalant an ECG may be considered.
3. Huffing is when a chemically soaked rag is held to the face or stuffed in the mouth and the substance is inhaled. Sniffing can be done directly from containers. The term bagging is used when substances are sprayed or deposited into a plastic or paper bag and the vapors are inhaled.
4. Sudden sniffing death syndrome can occur after a single inhalant use and is usually produced by highly concentrated chemicals in solvents or aerosols. And irregular heart rhythm is induced and rapid fatal heart failure occurs. This can occur within minutes of a prolonged inhalation. Death can also occur from asphyxiation, suffocation (usually occurs with bagging), choking from aspiration, or fatal injury from impaired judgment.
5. Methylene chloride → carboxyhemoglobinemia, mimics carbon monoxide poisoning  
Amyl nitrite → methemoglobinemia  
Gasoline may contain lead, methanol and benzene



## PHARMACOLOGY/TOXICOLOGY CASE STUDY #44

**History:** A 27 year old woman is stopped by airport security after a flight attendant reported suspicious behavior on the plane. She presents to you for medical clearance. The flight attendant became concerned when she noted that the patient appeared anxious and diaphoretic and did not eat for the entire duration of a twelve hour flight from Colombia. The patient is reporting vomiting, obstipation and abdominal pain.

**PMH:** None.

### Physical Examination:

T: 99.7°F    HR: 115 bpm    RR: 16 breaths per minute    BP: 142/94 mm Hg

**General:** Anxious appearing female in no acute distress.

**HEENT:** PEERL at 5 mm bilaterally.

**CV:** Tachycardic, no murmurs.

**Pulmonary:** Clear to auscultation.

**Abdominal:** Decreased bowel sounds. Diffusely tender to palpation, no peritoneal signs.

**Skin:** Moist.

## QUESTIONS CASE STUDY #44

1. This patient's behavior on the plane and presentation are concerning for what?
2. What diagnostic testing, if any, would be useful in this situation?
3. What management strategy would you employ once the diagnosis is confirmed?

## CASE STUDY #44: INTERNAL CONCEALMENT

1. The behavior exhibited by the patient on the plane is highly concerning for body packing, a form of internal drug concealment in which a person swallows a large number of drug-filled packages, for the purpose of smuggling. Internal concealment of drugs was first reported in 1973 and continues to be a major problem, with heroin and cocaine being the most commonly involved substances. Packets are sometimes also inserted into the vagina or rectum. Airport personnel are trained to identify people who may be smuggling drugs (“mules”). Suspicious behavior includes not eating or drinking on the plane, abnormal behavior when going through customs and overt signs of drug toxicity. Body packers ingest large amounts drug (50 – 100 packages, up to 1.5 kg of drug). In contrast to body packers, who ingest packets that have been prepared using sophisticated, multi-step processes designed to avoid package rupture and therefore, lost drug, body stuffers are individuals who swallow loosely wrapped packages (for example, plastic bag, aluminum foil, condoms) of drugs in attempt to escape the police.
2. This represents one clinical setting that urine drug testing may be useful. Positive urine drug testing may help confirm packet rupture; however false positives can occur if the external surface of the packet was contaminated. Other testing includes plain films of the abdomen (sensitivity of 75 – 95%), although some authors suggest that computed tomography has a higher sensitivity.
3. Previously, surgical intervention was used for all body packers to prevent death; however gastrointestinal decontamination is now the cornerstone of management. Use of whole bowel irrigation is commonly accepted and use of cathartics (non-oil based medications such as magnesium citrate) are sometimes recommended. Enemas and manual disimpaction should be avoided as they may precipitate packet rupture. Prompt surgical intervention is the treatment for individuals suffering from packet rupture.

## PHARMACOLOGY/TOXICOLOGY CASE STUDY #45

History: A 14-month-old female presents to the Emergency Department after an ingestion of furniture polish. Her mother relates that she coughed immediately following the ingestion and has developed progressive respiratory distress and altered mental status.

PMH: None.

### Physical Examination:

T: 98.2°F      HR: 183 bpm      RR: 88 breaths per minute      BP: 100/54 mm Hg  
General: Pale child in mild distress.  
HEENT: Normocephalic, pupils equal but sluggish.  
Pulmonary: Diffuse wheezing bilaterally, poor air exchange.  
CV: Regular rate and rhythm.  
Abdomen: Soft, nontender.

## QUESTIONS CASE STUDY #45

1. What complication is developing from the furniture polish ingestion?
2. What should be the management strategy?
3. What diagnostic tests should be ordered?

## CASE STUDY #45: HYDROCARBON POISONING

1. Hydrocarbons such as furniture polish are used as solvents, degreasers, fuels, and lubricants. Pulmonary aspiration causes injury to the lung and systemic intoxication can occur after ingestion, inhalation or skin absorption. In this case, the patient is developing aspiration and parenchymal lung injury which can cause respiratory distress, tachypnea, retractions, wheezing, rales, hypoxia, and hypercarbia. Coughing is usually the first symptom. Aspiration symptoms will begin within 6 hours. After 6 hours it is very unlikely pneumonitis will occur. Systemic symptoms can occur, however aliphatic hydrocarbons and simple petroleum distillates such as furniture polish, gasoline, or kerosene are poorly absorbed in the GI tract. If systemic intoxication occurs, ataxia, lethargy, headache, syncope, coma, cardiac arrhythmias, or respiratory arrest may occur. Camphor and carbon tetrachloride can cause serious systemic side effects.
2. Basic support and ABCs are the initial treatment. Respiratory involvement usually progresses over the first 24 hours. Children can die from respiratory failure with intractable hypoxia. Administer supplemental oxygen and treat bronchospasms. Cyanosis with increased oxygen requirements will necessitate, in most cases, the use of high PEEP, to enhance oxygenation. Alternatives to the barotrauma, which may result from the use of high PEEP, include the use of high frequency ventilation. Extra corporeal membrane oxygenation may also be indicated in children with severe respiratory disease. Corticosteroids and antibiotics have not been shown to be beneficial. Children who present after ingestion and remain asymptomatic after 6 hours from ingestion may be discharged.
3. Continuous pulse oximetry and ABGs should be monitored. A chest x-ray should be obtained and may be abnormal initially or not develop abnormalities until hours later. Fine, mottled densities in the perihilar and mid-lung areas may occur and later develop into areas of consolidation.

If systemic toxicity is suspected, than electrolytes, BUN, Cr, LFTs, and EKG should be monitored. Although hydrocarbon aspiration can cause fevers and lung injury, antibiotics should be avoided unless there is convincing evidence of infection.

## PHARMACOLOGY/TOXICOLOGY CASE STUDY #46

**History:** A 6-month-old female presents to the Emergency Department in the winter via EMS for evaluation of vomiting and lethargy. The paramedics report that the infant's family has been ill with flu-like symptoms. The child has had no fever, diarrhea or URI symptoms.

**PMH:** None.

**Physical Examination:**

T: 98.2°F    HR: 135 bpm    RR: 64 breaths per minute    BP: 92/64 mm Hg

**General:** The child is very lethargic and pale.

**HEENT:** The pupils are equal and reactive to light. The fontanelle is soft and sunken.

**Pulmonary:** Clear to auscultation.

**CV:** Regular rate and rhythm.

**Neurologic:** No focal deficits.

Initial blood glucose level is 90.

### QUESTIONS CASE STUDY #46

1. What are you concerned about?
2. What diagnostic testing would you order?
3. What therapy would you consider?
4. Which patients would you consider admitting?

## CASE STUDY #46: CARBON MONOXIDE POISONING

1. Carbon monoxide (CO) poisoning should be suspected based on the historical information and physical examination. Exogenous sources of CO include furnaces, car exhaust fumes, wood-burning stoves, smoke from fires, home water heaters, gas-powered engines and pool heaters. The signs and symptoms of CO poisoning can mimic other diseases and include headache, nausea, non-specific dizziness, generalized weakness and difficulty concentrating. More severe presentations of CO poisoning include confusion, lethargy, chest pain, syncope and coma.
2. Co-oximetry can be used to confirm the diagnosis. Carboxyhemoglobin levels can be used to guide therapy, but the levels do not consistently correspond to the severity of the exposure. This patient's carboxyhemoglobin level was 39 percent.
3. All of these patients should receive 100% oxygen as soon as possible. 100% oxygen decreases the half-life of carbon monoxide from 6 hours to 60-90 minutes. Since this child has an altered mental status and a carboxyhemoglobin level of 39%, the Emergency Department physician should consider treatment with hyperbaric oxygen (HBO). The use of HBO significantly reduces the half-life of the carboxyhemoglobin to about 20-30 minutes and some studies have shown it to reduce the risk of delayed neurologic sequelae from lipid peroxidation. Hyperbaric oxygen should be considered in any patient with loss of consciousness, carboxyhemoglobin greater than 25, neurologic symptoms, cardiovascular instability, altered mental status.
4. Patients who continue to be symptomatic after treatment with oxygen should be admitted. Treatment should be aimed at reducing the carboxyhemoglobin level to less than 5%.

## PHARMACOLOGY/TOXICOLOGY CASE STUDY #47

**History:** A 3-year-old presents to the emergency department with her mother, who reports that she found and ingested an entire tube of Orajel<sup>®</sup>. The mother reports watching her for 20 minutes after the ingestion and then putting her down for a nap. Several minutes later, she heard a weak cry from the room and when she checked on her, she was blue. Paramedics report that the child became progressively blue en route, despite supplemental oxygen administration. The child has had no fever, vomiting, diarrhea or respiratory distress.

**PMH:** None.

**Physical Examination:**

T: 96.1°F      HR: 131 bpm      RR: 25 breaths per minute      BP: 113/57 mm Hg

**General:** Active child in no acute distress.

**HEENT:** Normocephalic. Pupils equal and reactive to light.

**Pulmonary:** Clear to auscultation.

**CV:** Regular rate and rhythm.

**Abdomen:** Soft, no tenderness, no masses.

**Neurologic:** Normal.

**Skin:** Blue.

Cardiac monitor shows sinus tachycardia.

Pulse oximeter: 85% with good wave form.

### QUESTIONS CASE STUDY #47

1. What is the diagnosis?
2. How can the correct diagnosis be suspected and confirmed?
3. What therapy should be initiated?
4. What etiologies are there for this diagnosis?

## CASE STUDY #47: Methemoglobinemia

1. Methemoglobinemia secondary to benzocaine ingestion.
2. The diagnosis should be considered in any individual who is cyanotic, has a normal cardiopulmonary examination and is unresponsive to oxygen therapy. The diagnosis may be confirmed by drawing a blood sample, which will reveal the characteristic chocolate brown color and a normal pO<sub>2</sub>. The arterial pO<sub>2</sub> is not a measure of the hemoglobin oxygen saturation or oxygen content of the blood, but rather measures the partial pressure of the oxygen dissolved in the blood. Pulse oximetry is not accurate when the blood contains methemoglobin. It takes only 1.5g/dL of methemoglobin to produce detectable cyanosis. Individuals with hereditary defects tend to tolerate levels better than normal individuals with acute methemoglobinemia. The methemoglobinemia results in impaired oxygen delivery to tissue. This makes individuals with pre-existing congestive heart failure, anemia or COPD particularly vulnerable to this disease process. In previously healthy individuals, methemoglobin concentrations of 10-20% usually result in cyanosis without other clinical manifestations. At 20-50%, patients may experience dizziness, headache and exertional dyspnea. Levels of 50% are associated with lethargy and levels of 70% may be associated with death.
3. For most patients with mild methemoglobinemia, no therapy is indicated except withdrawal of the offending agent, oxygen and monitoring. The reversion rate is about 15%/hour. Patients with symptoms should be given oxygen. Patients with mental status changes, ischemic chest pain or abnormal vital signs should be treated. The most widely accepted treatment is 1-2 mg/kg of 1% methylene blue solution given IV over 5 minutes. Improvement should be noted within one hour of administration. If cyanosis has not disappeared within one hour, a second dose should be given. Administration of methylene blue is controversial in patients with G-6-PD deficiency because it can cause hemolysis.
4. An increase in the concentration of methemoglobin can result from a number of different causes. The individual may have the presence of an inherited abnormal hemoglobin structure which makes his or her hemoglobin more susceptible to oxidation stress. Neonates and persons with congenital methemoglobin reductase deficiency or G6PD deficiency or impaired ability to regenerate normal Hgb are more likely to accumulate methemoglobin after oxidant exposure. The patient may be exposed to a substance which poses an oxidant stress to the hemoglobin oxidative capacity. Commonly encountered oxidant compounds include nitrites, nitrates, local anesthetics like benzocaine, nitroglycerin, chloroquine, dapsone, primaquine, sulfonamides, trimethoprim, aniline dyes, aminophenol, bromates, and chlorates.



## PHARMACOLOGY/TOXICOLOGY CASE STUDY #48

**History:** A hysterical mom presents to the emergency department at 4:00 a.m. because she just opened her mail and her 1-year-old daughter (whom she brought with her) has a lead level of 30. The clinic was not open to tell her what to do. The patient has had no symptoms, including no altered mental status and no vomiting or diarrhea. The test was done at the clinic as part of her routine screening examination.

**PMH:** None.

**Physical Examination:**

T: 98.6°F    HR: 120 bpm    RR: 30 breaths per minute    BP: 100/59 mm Hg

**General:** Alert child in no acute distress.

**HEENT:** Normocephalic, normal.

**Pulmonary:** Clear to auscultation.

**CV:** Regular rate and rhythm.

**Neurologic:** Normal.

### QUESTIONS CASE STUDY #48

1. What therapy should be initiated for this child?
2. What are the indications for the use of dimercaprol?
3. What other interventions besides medications would be indicated with an elevated lead level?
4. What are other lead therapies and associated side effects?

## CASE STUDY #48: LEAD POISONING

1. The CDC recommends treatment for children with levels of 45mcg/dL or higher. Patient with blood lead levels between 25-44 mcg/dL need a medical evaluation and aggressive environmental intervention, but should not routinely receive chelation therapy. This patient should be referred back to the primary care physician for further follow up and management.
2. Dimercaprol is used in conjunction with Calcium EDTA in severe lead poisoning when encephalopathy is present or levels are greater than 70 mcg/dL. Its use accelerates removing lead from the RBCs and CNS and increases urinary excretion of lead. Dimercaprol (BAL) can be used initially and then followed 4 hours later by Calcium EDTA and BAL. Adverse effects of Dimercaprol include pain, hypertension, nausea, vomiting, headache, myalgias, rhinorrhea, lacrimations, burning sensation, fever (especially in children), CNS depression, and possible seizures. It is mixed with peanut oil and should not be used in patients with peanut allergies.
3. More important than chelation treatment is elimination of the environmental exposure, whatever the source.
4. Oral Succimer, a water soluble analog of dimercaprol, enhances urinary excretion of lead. This drug has the advantage of oral administration. Adverse effects include mild gastrointestinal, malaise and an occasional elevation of the liver enzymes, rashes, and rare cases of mild neutropenia.

Calcium EDTA, mobilizes lead from the soft tissues and from a fraction of larger stores in bone. Cessation of EDTA chelation can cause an upward rebound in blood lead levels due to equilibration of lead levels from bone to soft tissues. Nephrotoxicity can be an adverse effect. In lead encephalopathy, rapid or high volumes of calcium EDTA may increase intracranial pressure; therefore careful monitoring is warranted.

## PHARMACOLOGY/TOXICOLOGY CASE STUDY #49

History: An approximately twenty-something year old female presents to the emergency department via EMS after she collapsed outside a bar. Because she was unresponsive and apenic, a bystander administered CPR. No other history available.

PMH: Unknown.

### Physical Examination:

T: 98.9°F    HR: 100 bpm    RR: 5 breaths per minute    BP: 75/57 mm Hg

General: Obtunded, will moan to painful stimuli.

HEENT: Normocephalic, atraumatic. Pupils miotic but equal.

Pulmonary: Clear to auscultation.

CV: Regular rate and rhythm.

Abdomen: Normal

Neurologic: GCS = 8 (E1V2M5).

### QUESTIONS CASE STUDY #49

1. What medication, if any, would you administer?
2. What other ingestions should you be concerned about?
3. What is the classic presentation for this type of ingestion?

## CASE STUDY #49: OPIATE POISONING

1. In this scenario, the best medication to administer is naloxone. Naloxone is a pure opioid antagonist that competitively blocks mu, delta and kappa opioid receptors.

The first dose of 2 mg results in a reversal of the patient's respiratory depression and she opens her eyes. Because this patient is able to protect her airway once given naloxone, but is still sleepy, her clinical status precludes administration of activated charcoal.

Drugs which may be reversed by naloxone include morphine, heroin, codeine, hydrocodone and methadone. Naloxone is administered in doses 0.4-2.0 mg IV, IM, subcutaneously or endotracheally. Up to 10 mg can be administered if there is no response to the initial dose. After intravenous administration, effects are usually observed in 1-2 minutes. Different narcotics exhibit different sensitivities to naloxone reversal. Fentanyl and propoxyphene may require large doses of naloxone for reversal. Since the duration of the effect of naloxone is shorter than most opioids, these patients require careful monitoring for recurrence of toxicity. Patients who are successfully treated with naloxone may require an IV infusion of this medication to maintain arousal at a level that prevents intubation and other aggressive supportive measures. The clinician should be aware that overly aggressive reversal of opiates in dependent individuals can precipitate aggression and discomfort.

2. These patients should also be evaluated for the possibility of coingestants, including acetaminophen and salicylate, since opiates are commonly mixed with these agents.
3. The classic presentation of an opiate poisoning usually consists of the triad of CNS depression, respiratory depression and miosis. Hypotension can also occur. In suspected cases, the diagnosis may be confirmed by administering naloxone.

## PHARMACOLOGY/TOXICOLOGY CASE STUDY #50

**History:** A 6-year-old white male presents to the emergency department with his parents after accidentally ingesting one nadolol tablet. One hour following the ingestion, the child became dizzy and vomited. Because the child appeared to be very sleepy, the parents brought him in for evaluation.

**PMH:** None.

**Physical Examination:**

T: 98.6°F      HR: 100 bpm      RR: 22 breaths per minute      BP: 100/60 mm Hg  
General: Sleepy, but easily aroused.  
HEENT: Normocephalic, pupils equal and reactive to light.  
Pulmonary: Clear to auscultation.  
CV: Regular rate and rhythm.  
Neurologic: Unremarkable.

### QUESTIONS CASE STUDY #50

1. What are the most common clinical effects associated with  $\beta$ -blocker overdoses?
2. What management should be instituted if the patient's heart rate is 40 bpm?
3. What is the mechanism by which  $\beta$ -blockers cause toxicity?

## CASE STUDY #50: BETA-BLOCKER POISONING

1. The most common signs associated with beta-blocker overdoses are bradycardia and hypotension. More severe cases can result in AV block, cardiogenic shock and asystole. Although many patients present with reports of intentional or accidental overdose, others present reporting vague symptoms such as “weakness” and “dizziness”. Because there is no obvious toxidrome associated with beta-blocker overdose, the diagnosis can be difficult, especially in chronic or acute on chronic presentations.

Because of their membrane stabilizing activity, propranolol, acebutalol and sotalol may be associated with QRS widening and resultant ventricular dysrhythmias. CNS toxicity, including delirium, drowsiness, coma and seizure can occur with lipophilic beta-blockers, such as propranolol, carvedilol and nebivolol, which have the ability to cross the blood brain barrier. It should be noted, then, that these mental status changes can occur independently of changes in heart rate and blood pressure.

Rare effects include hypoglycemia and bronchospasm.

2. Immediate therapy includes stabilizing the airway, breathing and circulation. Intravenous access, supplemental oxygen, cardiac monitoring and continuous pulse oximetry should be instituted immediately. Symptomatic hypoglycemia should be treated in the usual fashion and benzodiazepines should be used to halt seizures. Activated charcoal may be considered in the first hour, but has not been proven effective.

Initial treatment measures include bolus administration of crystalloid fluid, atropine and glucagon. Atropine is very short acting so it may be necessary to begin an infusion; however in moderate to severe poisoning this therapy is generally not sufficient. Some sources recommend that atropine be given before vagal stimulus such as endotracheal intubation. Glucagon does not depend on  $\beta$ -receptors for its actions and has both inotropic and chronotropic effects. Glucagon is given as a 5 to 10 mg intravenous bolus. An effect should be observed within one to three minutes, with a peak response at five to seven minutes. Bolus doses can be repeated and if an increase in heart rate or blood pressure is achieved, an infusion is started at a rate of 5 to 10 mg/hour.

Additional interventions include use of catecholamines and calcium. Most sources recommend use of epinephrine or norepinephrine, although dobutamine, isoproterenol have been used. Calcium is thought to be of use to increase the available intracellular calcium, thus increasing contractility and can be given as either calcium gluconate or calcium chloride. Calcium levels should be monitored when using repeated doses because lethal iatrogenic overdose has been reported.

High dose insulin-euglycemia (HIE) has had a powerful impact on treatment of  $\beta$ -blocker poisoning. For this therapy, regular insulin is given as a bolus of 1 unit/kg and is followed by an infusion rate of 0.5–1.0 unit/kg/hr. The infusion is titrated to effect. Although hypoglycemia is considered rare, supplemental glucose should be given. One suggestion for glucose supplementation is to start an infusion of D10 0.45% NS at 80% maintenance rate simultaneously with the high-dose insulin drip. Blood glucose levels should be checked every 20 minutes for the first hour, and once per hour thereafter. Hypokalemia is another potential adverse effect, so serum potassium levels should be monitored.

Intravenous lipid emulsion therapy, known as Intralipid®, has recently emerged as a promising treatment for multiple medications, including beta blockers.

3. The primary mechanism of  $\beta$ -blocker poisoning is by excessive  $\beta$ -adrenergic blockade on cardiac myocytes, which leads to decreased intracellular CAMP. This results in negative inotropic, chronotropic and dromotropic effects on the heart and peripheral vasoconstriction. Propranolol and sotalol may also have quinidine-like effects as these drugs act on fast sodium channels in the myocardium, creating a membrane-stabilizing effect.

## PHARMACOLOGY/TOXICOLOGY CASE STUDY #51

History: A 24-year-old male presents to your Emergency Department via EMS after snorting crystal methamphetamine for the past two days. He says that everything is moving very “fast.” He has had no fever, vomiting or diarrhea. He had a seizure en route.

PMH: None.

### Physical Examination:

T: 100.1 °F    HR: 134 bpm    RR: 18 breaths per minute    BP: 142/96 mm Hg  
General: Alert, but agitated male who is actively pacing around the room.  
HEENT: Normocephalic, pupils dilated bilaterally.  
Pulmonary: Clear to auscultation.  
CV: Regular rate and rhythm.  
Neurologic: No focal deficits.  
Skin: Diaphoretic.

## QUESTIONS CASE STUDY #51

1. What is the classic presentation for a sympathetic or sympathomimetic overdose?
2. How is it different from an anticholinergic overdose?
3. What agents can cause a sympathetic toxidrome?
4. What treatment would you recommend for this patient?



## CASE STUDY #51: SYMPATHOMIMETIC POISONING

1. The classic presentation includes tachycardia, mydriasis, hypertension, hyperthermia, diaphoresis, seizures and CNS stimulation. Ingestions usually result in increased alertness, decreased fatigability, anorexia, insomnia and hyperkinesia. These patients present with adrenergic central nervous system predominance: anxious, irritable and talkative. More severe cases may present with psychotic features.
2. Anticholinergic symptoms include warm, dry, flushed skin, mydriasis, delirium, tachycardia, urinary retention. Hot as a hare, dry as a bone, red as a beet, mad as a hatter, seizing like a squirrel is the typical anticholinergic toxidrome. In contrast, sympathomimetics produce diaphoresis.
3. Dextroamphetamine, methylphenidate (Ritalin) used in ADHD and narcolepsy, methamphetamine (speed), MDMA (ecstasy), amphetamine related drugs in several weight loss medications, ephedrine/pseudoephedrine, LSD, caffeine, theophylline and cocaine may cause toxidrome.
4. The initial resuscitation focuses on ABC's. Benzodiazepines should be the initial treatment and most patients will respond well with a decrease in agitation, a decrease in the pulse and blood pressure and a decrease in the patient's risk of seizure. Activated charcoal can be given if patient is able to protect his/her airway and if within 60 minutes of ingestion. Hypertension not responsive to benzodiazepines should be treated with IV vasodilators such as nitroprusside. If additional therapy is needed for tachyarrhythmias than propranolol or esmolol can be used.

## PHARMACOLOGY/TOXICOLOGY CASE STUDY #52

**History:** A 48 year old male presents to your Emergency Department complaining of abdominal pain and intractable vomiting and diarrhea for approximately two hours duration. The patient reports that he was working in his garden earlier that morning and spilled chemicals all over an ungloved hand. He kept working and did not wash them off. Associated symptoms include weakness and “twitching” of his arms.

**PMH:** None.

### Physical Examination:

T: 99 °F      HR: 165 bpm      RR: 8 breaths per minute      BP: 172/95 mm Hg

**General:** Pale and agitated male in no acute distress.

**HEENT:** Miotic pupils. Clear drainage noted from bilateral eyes. Mucous membranes moist.

**Pulmonary:** Diffuse rales and wheeze.

**CV:** Regular rate and rhythm.

**Neurologic:** Cranial nerves II-XII intact. Lower extremities are symmetrically weak, 3/5 all flexors and extensors. Upper extremities are symmetrically weak, 4/5 all flexors and extensors. Intermittent fasciculations noted in the bilateral lower extremities. Sensory exam is normal. There is no clonus or hyperreflexia.

## QUESTIONS CASE STUDY #52

1. What are possible agents to cause this type of toxicity?
2. What are characteristic findings with this type of toxicity?
3. Why is this patient tachycardic?
4. What is the treatment?
5. If this patient requires intubation, are there medications that should be avoided?
6. How do these agents cause their toxicity?

## CASE STUDY #52: ORGANOPHOSPHATE POISONING

1. This presentation is consistent with acute cholinergic poisoning, most likely caused by either organophosphate (OP) or carbamate insecticide poisoning. These compounds are potent acetylcholinesterase inhibitors that, although structurally different, are often discussed together given their similar clinical presentations and management. These substances have been used as insecticides for many years in the United States and Worldwide. Specific examples of carbamates include aldicarb and methicarb. Specific examples of OP's include malathion, parathion and diazinon. Other uses of these substances include reversal of neuromuscular blockade, treatment of glaucoma, Alzheimer's Disease and myasthenia gravis, commercial veterinary products and as "nerve gases" for chemical warfare.
2. The accumulation of acetylcholine results in a classic cholinergic syndrome. The muscarinic signs associated with this syndrome are commonly remembered by using one of two mnemonics: **SLUDGE-BBB**, which represents salivation, lacrimation, urinary incontinence, defecation, GI cramps and emesis, Bronchospasm, Bronchorrhea and Bradycardia or **DUMBELS**, which represents defecation, urination, miosis, bradycardia/bronchorrhea/bronchospasm, emesis, lacrimation and salivation. It should be noted that none of the nicotinic and CNS effects of these substances are represented with these mnemonics. Nicotinic effects include fasciculations, and motor weakness or paralysis. CNS effects include central respiratory depression, altered mental status and seizures.
3. There are several possible reasons to explain this patient's tachycardia. Hypovolemia secondary to GI losses or developing respiratory distress are possibilities. Additionally, tachycardia (as well as mydriasis) can be seen because sympathetic ganglia also contain nicotinic receptors.
4. Initial management consists of decontamination and protection of health care providers from exposure. Decontamination includes removal of all clothes and washing the skin; the patient's clothing should be thrown away because the clothing can absorb these substances and re-exposure can occur despite thorough washing of fabrics. Initial priorities should focus on the ABC's. GI decontamination methods are of questionable value, although most sources recommend activated charcoal for ingestions presenting within one hour. Specific agents and antidotes which may be indicated include atropine and pralidoxime (2-PAM). Atropine may be used to reverse the muscarinic (not nicotinic) effects. The dose is 1 - 2 mg IV with doubling of each subsequent dose every five minutes until bronchorrhea resolves. Use of hundreds of milligrams of atropine in OP poisoning has been reported to be required to achieve this effect. Resolution of bradycardia or miosis and presence of tachycardia and mydriasis should NOT be used as an endpoint for atropine administration as these can be present despite significant toxicity. Pralidoxime and other oximes (eg. HI-6 and Obidoxime) act by regenerating acetylcholinesterase activity at all sites, including nicotinic receptors.

Use of these compounds represents an area of controversy owing to conflicting reports of clinical outcomes with its use. If used, this drug may be administered immediately to reverse muscle weakness and fasciculations and should always be given with atropine to prevent the muscle weakness that can result from transient acetylcholinesterase inhibition as oximes attach to the enzyme. Current World Health Organization recommendations for intravenous bolus therapy are at least 30 mg/kg in adults, and 25 to 50 mg/kg for children, based upon the severity of symptoms. Slow administration over a period of thirty minutes is recommended as rapid administration has been associated with cardiac arrest. Oximes are most effective when administered within the first 24 hours.

5. Depolarizing neuromuscular blocking agents (succinylcholine) should be avoided due to a potential for prolonged neuromuscular blockade in OP poisoned patients. This is because these agents are metabolized by acetylcholinesterase. As an alternative, nondepolarizing agents (rocuronium) can be used but large doses may be required due to competitive inhibition at the neuromuscular junction.
6. Organophosphate insecticides inhibit acetylcholinesterase which allows the excess accumulation of acetylcholine at muscarinic, nicotinic and CNS receptors.

## PHARMACOLOGY/TOXICOLOGY CASE STUDY #53

**History:** An elderly man presents to your Emergency Department from a nursing home for evaluation of diarrhea, crampy abdominal pain, hallucinations and seizure, all of which began this morning. The patient was admitted to the nursing home the day prior due to inability to care for himself after the recent death of his wife.

**PMH:** Several past admissions for liver disease.

### Physical Examination:

T: 100 °F      HR: 122 bpm      RR: 21 breaths per minute      BP: 163/96 mm Hg

**General:** Thin, pale elderly male who is very listless.

**HEENT:** Pupils dilated, equal and reactive.

**Pulmonary:** Clear to auscultation.

**CV:** Tachycardic, regular rhythm.

**Neurologic:** Fine tremor noted. Cranial nerves II-XII intact. No focal deficits.

**Skin:** Diaphoretic.

## QUESTIONS CASE STUDY #53

1. What is your concern and the most likely diagnosis?
2. What are medications that may cause this type of presentation?
3. What are other symptoms which might be present?

### **CASE STUDY #53: ALCOHOL WITHDRAWAL**

1. You should be concerned that this man is suffering from a withdrawal syndrome. The most likely etiologic agent would be alcohol withdrawal given this patient's history of multiple admissions for liver failure.
2. Other agents which may be responsible for the development of a withdrawal syndrome include sudden cessation of the use of barbiturates, benzodiazepene, narcotics and chloral hydrate.
3. Alcohol withdrawal syndrome usually develops 6-24 hours after the reduction of ethanol intake and lasts for two to seven days. Mild withdrawal is characterized by nausea, anorexia, tachycardia, hypertension and hyperreflexion. Major withdrawal is characterized by pronounced anxiety, insomnia, irritability, hypertension, decreased seizure threshold, auditory and visual hallucinations and finally, delirium. Delirium tremens is a life threatening syndrome and consists of tachycardia, diaphoresis, hyperthermia, and delirium and is caused by sympathetic nervous system over-activity. It is usually seen 48-72 hours after stopping ETOH. If untreated can cause significant morbidity and mortality.

## PHARMACOLOGY/TOXICOLOGY CASE STUDY #54

History: A 3-year-old child presents to the Emergency Department with her mother after sudden onset vomiting, shortness of breath, and “not acting right.” The mother reports that the child had found some apricot pits while grandma was cooking and chewed and swallowed “a lot” of them. No history of fever or head trauma.

PMH: None.

### Physical Examination:

T: 99 °F      HR: 190 bpm      RR: 38 breaths per minute      BP: 60/40 mm Hg

General: Pale, lethargic child.

HEENT: Normocephalic, atraumatic.

Neck: Supple, full range of motion.

Pulmonary: Clear to auscultation.

CV: Tachycardic, regular rhythm, no murmur.

Neurologic: Hypotonia. Moving all extremities.

## QUESTIONS CASE STUDY #54

1. What is the diagnosis and what other substances may result in exposure to this substance?
2. How does this agent cause its toxicity?
3. What is the usual presentation of patients affected by this problem?
4. How does the treatment work?

## CASE STUDY #54: CYANIDE POISONING

1. The diagnosis is cyanide toxicity and other sources for exposure include laboratories, the jewelry industry, plastic manufacturing, fires (combustion by-product), natural sources such as amygdalin (apricot pits, cassava) and prolonged sodium nitroprusside infusion.
2. Cyanide is a cellular toxin that uncouples oxidative phosphorylation by binding with cytochrome c oxidase, and inhibiting the aerobic utilization of oxygen.
3. Initial symptoms include headache, nausea, dyspnea, and confusion. Syncope, seizures, coma, and cardiovascular collapse progress rapidly, especially after heavy exposure. The smell of bitter almond suggests cyanide poisoning. Lab evaluation will show metabolic acidosis, with lactate levels commonly greater than 10.
4. Treatment is indicated for clinical suspicion of cyanide poisoning or bitter almond odor and symptoms. The patient should be decontaminated and supportive care initiated, including airway and circulatory support. Care should be taken to minimize the provider's exposure. The cyanide antidote kit consists of 3 components: amyl nitrite pearls, sodium nitrite and sodium thiosulfate. One pearl of amyl nitrite should be administered every 2 minutes and is a temporizing measure until intravenous access can be attained for the purpose of sodium nitrite administration. The dose of sodium nitrite is 300 mg intravenously, given over three minutes for an adult and 6 mg/kg intravenously in children, not to exceed 300mg. Amyl and sodium nitrite induce methemoglobin, which directly binds cyanide with greater affinity than cytochrome oxidase. Sodium nitrite should be avoided in patients with coexistent carbon monoxide poisoning due to the reduced oxygen carrying capacity of blood. Sodium thiosulfate potentiates the ubiquitous enzyme rhodanase which catalyzes the conversion of cyanide to thiocyanate, which is renally excreted. It should be administered in a dose of 12.5 grams intravenously. Hydroxycobalamin is a newer antidote that combines with cyanide to form cyanocobalamin (vitamin B-12), which is excreted in the urine.



## PHARMACOLOGY/TOXICOLOGY CASE STUDY #55

History: A 20-year-old male presents to the Emergency Department with a friend after drinking one quart of antifreeze solution in a suicide attempt. The patient denies co-ingestants and denies abdominal pain, nausea and vomiting.

PMH: None.

### Physical Examination:

T: 98.9 °F    HR: 90 bpm    RR: 30 breaths per minute    BP: 120/80 mm Hg

General: Intoxicated male in no acute distress.

HEENT: PERRL.

Pulmonary: Clear to auscultation.

CV: Regular rate and rhythm.

Neurologic: Oriented to person only. Cranial nerves II-XII intact. No focal deficits.

## QUESTIONS CASE STUDY #55

1. This patient is suffering from what type of poisoning?
2. What is the classic clinical presentation?
3. What is the treatment?

## CASE STUDY #55: ETHYLENE GLYCOL POISONING

1. Ethylene glycol toxicity
2. During the first 3-4 hours these patients usually present with acute intoxication symptoms similar to ethanol; nausea and vomiting may be present. The osmolar gap is increased. After 4-12 hours, the patient will develop a progressive anion gap acidosis, with hyperventilation, seizures, coma, dysrhythmias, pulmonary edema, cerebral edema and hypocalcemia. Oxalate crystals can also be found in the urine. Renal failure can be seen but is usually reversible.
3. Initial treatment includes three goals for patients with ethylene glycol toxicity: correction of metabolic acidosis, ADH blockade and removal of the parent alcohol and its metabolites. Primary focus should be on supportive care, which includes the administration of bicarbonate. Ethanol or fomepizole should be used to prevent future production of the toxic metabolites by competitive inhibition of alcohol dehydrogenase.

Indications for treatment include, ethylene glycol levels >20 mg/dl or suspected ethylene glycol ingestion with 2 or more of the following: osmolar gap greater than 10mOsm/l not accounted for by ethanol or other alcohols, serum bicarb less than 20mEq/L, pH less than 7.3, or presence of oxalate crystals in the urine. The goal is to maintain an ethanol concentration >100 mg/dl. Fomepizole blocks the metabolism of methanol and ethylene glycol and prevents formation of toxic metabolites. It is a pregnancy category C drug. Potential advantages of the use of fomepizole over ethanol include ease of use, predictable pharmacokinetics, improved patient safety profiles and standardized and less complicated dosing regimens. The main disadvantage is cost. The dose is 15 mg/kg followed by 10 mg/kg every 12 hours for 4 doses. After 5 doses, the dose increases to 15 mg/kg every 12 hours until the ethylene glycol concentration is undetectable or less than 20 mg/dL and the patient is asymptomatic with a normal arterial pH. Pyridoxine, thiamine and folate should be administered to enhance the conversion of glyoxylic acid to non-toxic products.

Hemodialysis efficiently removes ethylene glycol and its metabolites. Indications include suspected ethylene glycol poisoning and unresponsive to therapy, renal failure, concentrations greater than 50mg/dL and symptomatic and severe metabolic acidosis. Patients should still receive treatment with ethanol or fomepizole due to rebound elevation of ethylene glycol after dialysis.

## PHARMACOLOGY/TOXICOLOGY CASE STUDY #56

History: A 20-year-old female presents to the Emergency Department after ingesting over 50 tablets of Tylenol Extra Strength® eight hours prior to arrival in a suicide attempt. She denies coingestants and complains of nausea.

PMH: None.

### Physical Examination:

T: 99 °F      HR: 90 bpm      RR: 12 breaths per minute      BP: 120/72 mm Hg

General: Tearful female in no acute distress.

HEENT: Pupils 4 mm and reactive, moist mucus membranes.

Pulmonary: Clear to auscultation.

CV: Tachycardic with regular rhythm.

Abdomen: Normal bowel sounds, nontender to palpation.

Neurologic: Unremarkable.

### QUESTIONS CASE STUDY #56

1. What is the most important historical information that should be obtained?
2. What diagnostic testing, if any, would you perform?
3. What treatment, if any, should be initiated immediately?
4. What is the appropriate disposition of this patient?
5. Explain the mechanism of toxicity of acetaminophen.

## CASE STUDY #56: ACETAMINOPHEN POISONING

1. The presence of coingestants and confirmation of the time of ingestion is the most important historical information to obtain. The time of ingestion should be determined so that accurate plotting of the level on the Rumack-Matthew nomogram can be accomplished to determine the risk of toxicity. Tylenol Extra Strength® contains 500 mg of acetaminophen (APAP) per tablet; however there is no reliable way to predict toxicity based on the patient's report of the quantity ingested.
2. The only initial laboratory tests that should be obtained are a serum APAP level and a pregnancy test. Because the Rumack-Matthew nomogram does not risk stratify patients based on levels obtained prior to four hours after ingestion, obtaining acetaminophen levels prior to this time is not useful except possibly to substantiate a claim of overdose. One may consider ordering baseline LFTs and PT/PTT if the APAP level is in the toxic range, but this early after the ingestion, one would expect those to be normal if the patient has no underlying disease. A toxicology screen would not be useful because the patient is relatively asymptomatic and has a normal exam.
3. Because the ingestion occurred eight hours earlier, N-acetylcysteine (loading dose 140 mg/kg) should be administered prior to the laboratory results. The antidote is most effective if administered within the first 8-10 hours. If the level is non-toxic, further doses are not indicated. If the patient presents prior to the eight hour mark, there is no known advantage to administering NAC before the level returns. In this patient, the eight hour level is 250 mcg/ml.
4. Because the patient's eight hour acetaminophen level places her in the "probable hepatotoxicity" category, she should be admitted for the full course of NAC. Suicide precautions should be continued as an inpatient.
5. Hepatic metabolism of acetaminophen occurs via the cytochrome p450 system and produces a highly reactive metabolite called *N*-acetyl-*p*-benzoquinone imine, (NAPQI). In therapeutic doses, approximately 4% of APAP is metabolized via the P450 system and the resultant NAPQI is detoxified by the glutathione stores in the liver. In the presence of toxic doses, the amount of acetaminophen metabolized by the cytochrome p450 system increases, subsequently depleting glutathione stores and leading to an increased amount of NAPQI. NAPQI acts to cause toxicity by binding to the hepatocyte and resulting in cell death.

## PHARMACOLOGY/TOXICOLOGY CASE STUDY #57

**History:** A 12-year-old female presents to the emergency department reporting a history of ingesting twenty-six 81 mg aspirin tablets approximately three hours prior to arrival. The patient comes to the emergency department after four episodes of nausea and vomiting. Patient denies any other ingestions.

**Physical Examination:**

T: 99.9°F      HR: 140 bpm      RR: 30 breaths per minute      BP: 110/62 mm Hg

**General:** Alert female, tearful and vomiting.

**Neck:** Supple.

**Pulmonary:** Clear to auscultation.

**CV:** Tachycardic, regular rhythm.

**Abdomen:** Soft, non-tender.

**Neurologic:** Unremarkable.

### QUESTIONS CASE STUDY #57

1. What laboratory studies are indicated?
2. What laboratory abnormalities would you expect to find?
3. What initial treatment, if any, is indicated before the laboratory results return?
4. What are the indications for hemodialysis in salicylate poisoning?
5. Explain how urinary and serum alkalinization works.
6. If the patient was admitted and suddenly became short of breath and more tachypneic, what would you recommend?
7. What is oil of wintergreen?

## Case Study #57: Acute Salicylate Poisoning

1. A salicylate level, acetaminophen level, ABG or VBG, electrolytes, BUN/Cr, urine pregnancy test are indicated.
2. Elevated salicylate levels and an anion gap metabolic acidosis would be expected. The patient's blood gas would be expected to show both a metabolic acidosis and a respiratory alkalosis, both of which are primary disorders in salicylate poisoning. In this patient, the salicylate level is 64 mg/dL and the acetaminophen level is <10 mg/dL.
3. The patient should receive IV fluids and antiemetics, preferably ones that do not lower the seizure threshold. If the vomiting is controlled and the airway is protected, a dose of activated charcoal should be administered. Serum and urinary alkalization should also be initiated prior to laboratory confirmation. Alkalinization is performed by administering a 1-2 meq/kg bolus of sodium bicarbonate, followed by a bicarbonate drip. The drip is made by adding 3 amps of sodium bicarbonate to 1 liter of D<sub>5</sub>W and infusing at 1.5-2 times maintenance rate with a goal of increasing the urine pH to 7.5-8.0 (difficult), serum pH to 7.45-7.55, and maintaining urine output at 1-2 mL/kg/hr. It is important to remember that the sodium bicarbonate should be added to D5W, and not normal or half-normal saline as this would result in a hypertonic solution and possible harm to the patient.
4. Indications for hemodialysis in salicylate poisoning include salicylate levels greater than 100 mg/dL in acute poisoning and greater than 40 - 60 mg/dL in chronic poisoning, renal failure that prevents salicylate excretion, cerebral edema, non-cardiogenic pulmonary edema, fluid overload that prevents bicarbonate administration, seizure, severe acid-base or electrolyte imbalance and clinical deterioration despite appropriate, aggressive medical therapy. Hemodialysis should also be considered in individuals who require intubation for respiratory depression secondary to co-ingestants.
5. Alkalinization of the serum promotes formation of the ionized form of salicylate through the Henderson-Hasselbach equation. The ionized form of salicylate cannot cross the blood brain barrier, this prevents more drug from entering the CNS where it can cause cerebral edema and be converted to the ionized form and become trapped. Alkalinization of the urine causes formation of a larger amount of drug in the ionized form. The ionized form cannot be reabsorbed by the kidney, and is therefore excreted in the urine.
6. A chest x-ray and a repeat salicylate level and ABG should be obtained. One possible explanation is that the patient may be developing non-cardiogenic pulmonary edema (characteristic of salicylate poisoning). Another possible explanation for delayed elevations in salicylate levels is the formation of a

concretion, or bezoar, in the stomach. This is most common with sustained release preparations and can have devastating effects if unrecognized. If this is suspected, whole bowel irrigation is recommended.

7. Oil of Wintergreen, or methylsalicylate, is a natural product of many species of plants. It is sold as a rubefacient and is for external use only; however it smells and tastes good and is tempting to children. In fact, this product was once put into flavored tobaccos and confectionery products. One teaspoon contains the equivalent of approximately 7 grams of aspirin, or the equivalent of 21.7 tablets, and ingestion of as little as four milliliters can be fatal in a child.

## PHARMACOLOGY/TOXICOLOGY CASE STUDY #58

**History:** A 13-year-old female who is 37 weeks pregnant presents to your emergency department via EMS after ingesting 70 prenatal iron tablets two hours ago in a suicide attempt. EMS reports arriving at the scene approximately one hour after ingestion and administering ipecac. The tablets contained 325 mg of ferrous sulfate. The patient complains of three episodes of emesis and diarrhea.

**PMH:** None.

### Physical Examination:

T: 98.6°F      HR: 110 bpm      RR: 12 breaths per minute      BP: 100/65 mm Hg  
Weight: 65 kg  
General: Alert female in no distress  
HEENT: Mucus membranes moist. Pupils equal.  
Pulmonary: Clear to auscultation.  
CV: Tachycardic with regular rhythm and no murmurs.  
Abdomen: Soft, mildly tender in epigastrium.  
Rectal: Heme negative.  
Neurologic: Normal.

### QUESTIONS CASE STUDY #58

1. Did this patient take a toxic dose of iron?
2. Do you agree with the decision to administer ipecac? If not, is there a more desirable way to perform gastrointestinal decontamination in this case?
3. What laboratory studies, if any, do you recommend?
4. Do you recommend chelation in this patient? If yes, how would you administer the chelator and at what dose? If the urine does not change color, should treatment be continued?
5. Is the fetus at high risk of becoming iron toxic?
6. What are the most common symptoms of iron poisoning?
7. Is iron detected on a routine toxic screen?
8. If an iron level is unavailable, are there any other laboratory findings that suggest an elevated iron level (>300)?



### Case Study #58: Iron Poisoning

1. Yes. For all poisonings of iron-containing vitamins, it is important to calculate the amount of elemental iron ingested. Ferrous sulfate contains 20% elemental iron, so this patient ingested  $325 \text{ mg} \times 70 \times 0.2 = 4550 \text{ mg}$ . The total amount/kg is  $4550/65 = 70 \text{ mg/kg}$ . Because the toxic dose is 40 mg/kg, this patient has a potentially severe ingestion. Doses of 60-180 mg/kg have been associated with death.
2. Generally, there is no role for ipecac syrup administration. This is reflected by the position statement by the American Academy of Pediatrics on ipecac syrup. The American Academy of Medical Toxicology does not recommend emergency department administration of ipecac syrup but has no formal position on home use, though it is also not routinely recommended. Further, because the most sensitive indicator of iron poisoning is vomiting, ipecac administration may confuse potentially useful physical exam findings. If this patient had not already vomited or if iron tablets were seen in the stomach on x-ray, gastric lavage would have been the initial decontamination procedure of choice. This technique can be employed in patients who present early enough for this procedure to be initiated within one hour of ingestion. If the patient remained symptomatic, if tablets were noted past the pylorus, or if the patient presented past the one hour mark, whole bowel irrigation should be performed.
3. Laboratory studies that should be obtained include a serum iron concentration, electrolytes if the patient has had several episodes of vomiting and a complete blood count if there is suspicion of any bleeding. The most valuable time to assess serum iron concentration is four to six hours after ingestion. Total iron binding capacity (TIBC) is useless! While theoretically useful, the TIBC in iron poisoning is often unreliable, falsely elevated, and does not correlate with symptoms.

This patient's serum iron concentration is 400 mcg/dL.

Na 137, K 3.4 C1 109, CO<sub>2</sub> 18, BUN 5, Cr 0.7 glucose 383

WBC 17.8 H/H 13.1/36.8 acetaminophen is <10, salicylate <5 mg/dL.

4. The most important indication for deferoxamine is symptoms of iron poisoning. Most patients become significantly symptomatic with levels over 300 mcg/dL. Patients with severe symptoms (shock, lethargy/coma), anion gap metabolic acidosis, peak SIC >500 mcg/dL, significant numbers of pills on plain films and worsening clinical condition despite maximal therapy should receive deferoxamine (DFO), the intravenous chelating agent used to treat iron poisoning. Deferoxamine can be administered IV or IM. This medication works by complexing with ferric (Fe<sup>3+</sup>) iron, creating the complex ferrioxamine, which is excreted in the urine. Intravenous administration is generally safe if the rate is  $\leq 5 \text{ mg/kg/hr}$ ; however in adults, if that rate is chosen, they will receive very large doses of deferoxamine in 24 hours (25.2 grams). The recommended daily dose should not exceed 6-10 grams, so one can give 6 gm/24 hours or 250 mg/hr, which is approximately 3.5 mg/kg/hr. Another option is to start with 15 mg/kg/hr if the

patient is very ill and decrease the dose after 1-2 hours. Larger doses are often used to start because prolonged dosing of DFO can cause adverse effects such as ARDS.

Free iron may be present without the formation of the classic “vin rose” urine color change. If the patient remains symptomatic with elevated iron levels, treatment should continue even if there is no urine color change after the first dose of DFO.

5. No, because the placenta has an active mechanism for iron to cross. It occurs by active endocytosis. So if the mother has high iron levels, it is rare for the fetus to develop elevated iron levels. DFO probably does not cross the placenta, so pregnant patients should be treated no differently than non-pregnant, except for use of serial x-rays. Fetal monitoring should also be performed in pregnant patients with iron poisoning. If the fetus is viable and the mother is very ill or if fetal distress is noted, early delivery should be considered.
6. Gastrointestinal (nausea, vomiting, diarrhea). Any child that presents with sudden onset of GI symptoms should be questioned about iron availability in the household.
7. No.
8. Serum glucose >150, WBC >15,000 and acidosis all suggest a serum iron concentration greater than 300 mcg/dL. If an iron level is available and there are no other indications, those laboratories do not need to be routinely obtained.

## PHARMACOLOGY/TOXICOLOGY CASE STUDY #59

**History:** A 7-year-old male arrives to the Emergency Department with her parents after she was found playing in her room with an open bottle of topiramate 25 mg tabs. The parents noted that there were three pills missing. The medication belongs to the patient's mother, which she takes for migraine prophylaxis.

**PMH:** ADHD

**Medications:** Methylphenidate, clonidine.

**Physical Examination:**

**T:** 98.7°F      **HR:** 130 bpm      **RR:** 12 breaths per minute      **BP:** 92/54 mm Hg

**General:** Sleepy appearing child resting comfortably on the bed.

**HEENT:** Pupils are 3 mm and equally reactive to light. No nystagmus.

**CV:** Tachycardic, regular rate and rhythm.

**Pulmonary:** Clear to auscultation.

**Abdomen:** Soft, nontender.

**Skin:** Warm and dry.

## QUESTIONS CASE STUDY #59

1. What are the main adverse of this medication when taken in overdose?
2. How are these adverse events managed?

## CASE STUDY #59: TOPIRAMATE POISONING

1. Poisoning with newer anticonvulsants is becoming more common. Because several newer anticonvulsants have been developed with more favorable side effect profiles, and because of their multiple off label uses, such as in migraine prophylaxis and bipolar disorder, emergency physicians are likely to encounter an increasing number of overdoses with these medications. Overdose of topiramate can cause sedation and coma, rarely requiring ventilator support. Another potential adverse effect is seizures and status epilepticus. At least one fatality has been reported. Because this medication is a carbonic anhydrase-inhibiting diuretic, it can cause metabolic acidosis, which can be severe in overdose. Acidosis may be associated with irritability, hyperventilation and mental status changes. Less common adverse events reported include increased incidence of nephrolithiasis and secondary angle closure glaucoma (even in pediatric patients).
2. For patients with acute overdose, activated charcoal may decrease gastrointestinal absorption. Seizures are treated with benzodiazepines and supportive care. Severe acidosis should be treated with cautious administration of sodium bicarbonate. Excretion of topiramate is primarily renal and hemodialysis could be used for severe cases such as refractory acidosis and status epilepticus.

## PHARMACOLOGY/TOXICOLOGY CASE STUDY #60

**History:** A 53 year-old-female presents to the emergency department with her neighbor who is concerned that she has been disoriented for the past week. The patient is unable to provide any history except to say that she is having mild cramping abdominal pain. The neighbor relates that the patient's entire family was ill the week prior to symptom onset with a diarrheal illness that lasted for 5 days.

**PMH:** Hypertension, stage I kidney disease, bipolar disorder, anxiety  
**Medications:** Hydrochlorothiazide, enalaprilat, lithium, clonazepam prn

### Physical Examination:

T: 97.9°F      HR: 108 bpm      RR 14 breaths per minute      BP: 125/76 mmHg

**General:** Disheveled female in no acute distress. Oriented to person only.

**HEENT:** Pupils equal, round and reactive to light. Mucous membranes tacky.

**CV:** Tachycardic, regular rhythm. No murmurs.

**Pulmonary:** Clear to auscultation.

**Abdomen:** Normal bowel signs. Soft, with mild, diffuse tenderness. No guarding or rebound.

**Neurologic:** Cranial nerves II – XII intact. Motor testing is 4/5 diffusely, but symmetric. Gait examination reveals ataxia. No clonus or hyperreflexia.

**ED course:** the patient underwent a full laboratory evaluation that showed a creatinine of 2.1 (baseline 1.4) and a lithium level of 14 mg/dL.

She was admitted for lithium toxicity, which was thought to result from worsening renal dysfunction after an episode of gastroenteritis.

## QUESTIONS CASE STUDY #60

1. Describe common laboratory and physical exam findings in patients with chronic and acute lithium poisoning.
2. What are indications for hemodialysis in lithium toxicity? Are there different indications depending on whether the presentation is the result of acute versus chronic exposure?

## CASE STUDY #60: LITHIUM POISONING

1. Chronic lithium exposures can present with systemic symptoms such as lethargy, muscular weakness, slurred speech, ataxia, tremor, and myoclonic jerks. Severe intoxication can cause delirium, coma, convulsions, and hyperthermia. Patients with chronic lithium poisoning can also develop nephrogenic diabetes insipidus. Lithium levels may be only slightly above normal. Other laboratory findings can include leukocytosis. The ECG may show T wave flattening or inversion, QT prolongation, ST depression in lateral leads, and sinus bradycardia.

Acute lithium exposures commonly present with nausea and vomiting. Systemic symptoms are delayed for several hours while lithium distributes into tissues since it can take lithium about 6-8 hours to be completely absorbed. Initial lithium levels will be high in an acute intoxication and may fall once it is absorbed into the tissues. Other labs to obtain include electrolytes and renal function tests.

2. Lithium excretion is exclusively by the kidneys. Hemodialysis should be used for patients with severe symptoms such as abnormal mental status and seizures, for patients who cannot excrete lithium due to renal disease and patients who cannot tolerate aggressive fluid resuscitations (ex. heart failure). Treatment should be based on clinical presentation and not laboratory values.