17.0, Toxicologic Disorders

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18.0, Traumatic Disorders

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Appendix 1, Procedures and Skills

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Appendix 2, Other Components

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16. A 15-year-old boy is found unresponsive at a party. There is no history of trauma. Vital signs are blood pressure 100/60, pulse rate 40, respiratory rate 12, and temperature 36°C (98.6°F). Physical examination is remarkable for the absence of a gag reflex with some vomit present in his mouth, normal-sized and reactive pupils, bradycardia, and a GCS score of 3. The cardiac monitor reveals narrow-complex sinus bradycardia; blood glucose is normal, and there is no response to naloxone. The patient is intubated for airway protection; CT scan of the brain is normal. Serum ethanol level drawn on arrival is 20 mg/dL. The patient remains comatose for the next 5 hours but then suddenly awakens, pulls his endotracheal tube out, and attempts to leave. Which of the following agents induces toxicity that is most consistent with this presentation?

A. Carisoprodol
B. Flunitrazepam
C. GHB
D. MDMA
E. Oxycodone, sustained release

50. A 40-year-old man passed out while using a gas-powered cement cutter in his garage with the doors closed. His wife called 911; paramedics placed him on oxygen with a nonrebreather mask and transported him to the emergency department. On arrival he says he has only nausea and a mild headache. A venous blood COHb level of 20% confirms carbon monoxide poisoning; detailed neurologic examination is normal. The hospital's hyperbaric oxygen chamber is available. What is the rationale for using it to treat this patient?

A. To correct the presumed associated metabolic alkalosis more rapidly
B. To decrease the COHb level more rapidly
C. To decrease the likelihood of death
D. To decrease the likelihood of delayed neurologic sequelae
E. To prevent the development of cardiac dysrhythmias

86. In which of the following situations of known methanol ingestion are both administration of fomepizole (4-methylpyrazole) and performance of hemodialysis most indicated?

A. pH/Pco₂ 7.10/10; methanol level 0 mg/dL; ethanol level 0 mg/dL
B. pH/Pco₂ 7.10/10; methanol level 10 mg/dL; ethanol level 300 mg/dL
C. pH/Pco₂ 7.10/10; methanol level 30 mg/dL; ethanol level 30 mg/dL
D. pH/Pco₂ 7.40/40; methanol level 50 mg/dL; ethanol level 10 mg/dL
E. pH/Pco₂ 7.40/40; methanol level 200 mg/dL; ethanol level 300 mg/dL
107. A 65-year-old man with a severely depressed level of consciousness is brought to the emergency department by his grandson, who admits that his grandfather has been making moonshine. Laboratory testing reveals a glucose level of 80 mg/dL, an ethanol level of 40 mg/dL, and a hemoglobin of 8 g/dL. Wrist drop is found on physical examination. Which of the following statements regarding the cause of his alteration in mental status is correct?

A. Adults are generally thought to be at higher risk of CNS toxicity than children
B. Has a known physiological role at low levels
C. Is associated with a motor neuropathy more commonly than a sensory one
D. Most important route of exposure in occupational settings is typically ingestion
E. Withdrawal from the agent can be life threatening

121. Which of the following statements regarding warfarin is correct?

A. Cimetidine antagonizes the effect of warfarin
B. Clarithromycin antagonizes the effect of warfarin
C. Concerns about the risks of increased thrombogenesis soon after initiation of warfarin therapy are largely theoretical
D. Warfarin-induced skin necrosis is the most common complication of warfarin treatment
E. Warfarin-induced skin necrosis typically occurs soon after warfarin therapy is started

136. A 47-year-old man with bipolar disorder presents with confusion, tremulousness, and hyperreflexia. Regarding the agent that the patient is most likely poisoned from, which of the following is correct?

A. Activated charcoal is effective at decreasing the serum half-life
B. Chronic toxicity is usually the result of renal failure or intravascular volume depletion
C. CNS symptoms correlate well with serum levels
D. Diabetes mellitus is a complication of long-term therapy
E. It is associated with neuroleptic malignant syndrome
153. With regard to salicylate poisoning, which of the following is correct?
   A. A negative plain radiograph excludes the presence of enteric-coated or sustained-release aspirin in the gastrointestinal tract
   B. Ensuring hypoventilation after intubation is critical in management
   C. Reversible sensorineuronal hearing loss correlates with serum salicylate levels
   D. The Done nomogram is essential in guiding therapy
   E. Urinary pH is a determinant of mortality

165. Which of the following statements regarding rapid urine drugs of abuse panels is correct?
   A. A positive amphetamine screen is specific for methamphetamine
   B. A positive test confirms intoxication
   C. Generally more helpful clinically in adults than in children
   D. Medically indicated for most patients who present to the emergency department with suicidal ingestions
   E. Rarely contribute significantly to the evaluation, management, or outcome of emergency department patients

177. A 33-year-old woman presents 7 hours after ingesting, according to her boyfriend, “about 30” Extra-Strength Tylenol tablets. She is asymptomatic. Acetaminophen level testing is ordered, but results will not be available for 2 hours. Which of the following treatment strategies is most appropriate?
   A. Administer activated charcoal
   B. Administer the initial dose of N-acetyl-l-cysteine
   C. Cancel the test, and request psychiatry consultation
   D. Perform gastric lavage, and administer activated charcoal
   E. Take no action pending test results

192. A 30-year-old man presents after accidentally spilling household rust remover on his leg. He had no pain initially but has since developed persistent pain. Signs of skin damage are minimal. If the patient is suffering systemic toxicity, which of the following laboratory abnormalities would be expected?
   A. Alkalemia
   B. Hypercalcemia
   C. Hyperkalemia
   D. Hypermagnesemia
   E. Hyponatremia
204. Which of the following metabolic complications is most likely to occur in the setting of both therapeutic use and overdose of valproic acid?
   A. Elevated ammonia
   B. Elevated calcium
   C. Elevated carnitine
   D. Low sodium
   E. Metabolic alkalosis

217. A 28-year-old man presents complaining of withdrawal symptoms. He is yawning and sneezing; physical examination reveals mydriasis and piloerection. Which of the following statements regarding this withdrawal syndrome is correct?
   A. Altered level of consciousness is typical
   B. Buprenorphine administration is contraindicated
   C. Clonidine is an effective treatment
   D. Convulsions occasionally occur
   E. Inpatient therapy is required

225. Both neuroleptic malignant syndrome and serotonin syndrome:
   A. Are characterized by autonomic instability and neuromuscular abnormalities
   B. Are characterized by hyperreflexia and clonus
   C. Have specific tests to confirm the diagnosis
   D. Occur soon after initiating drug administration
   E. Typically occur after overdose

236. A 2-year-old boy is brought to the emergency department by his parents immediately after he was discovered "eating a few of his grandmother's pills." The grandmother, who is visiting from out of town, keeps her pills in an unlabeled, multicompartment plastic container that organizes her medications by the day of the week. The parents think the boy ingested 1 day's worth of pills. He is asymptomatic. Which of the following is the best next step?
   A. Administer activated charcoal along with a flavoring agent
   B. Feed the child syrup of ipecac to induce emesis
   C. Have the child ingest sorbitol to induce osmotic catharsis
   D. Initiate whole-bowel irrigation with polyethylene-glycol
   E. Perform gastric lavage with room temperature isotonic saline
A 10-month-old boy is brought in by his parents after he turned blue at home. The mother says he has been fussy recently, which she presumed to be caused by teething; she has been treating him with an over-the-counter topical teething gel. On examination, the boy has marked cyanosis, including the perioral area and nail beds. Vital signs reveal a mild degree of tachypnea and tachycardia. Room air oxygen saturation is 88% and does not improve on high-flow oxygen. His lungs are clear; work of breathing is normal, as are heart tones. Which of the following treatments is most likely to be successful in treating this child's cyanosis?

A. Botulinum antitoxin  
B. Deferoxamine  
C. Methylene blue  
D. Prostaglandin E1  
E. Sodium bicarbonate
274. A 15-year-old boy is brought to the emergency department by ambulance after being found unresponsive in his bedroom. Near him was the empty bottle of his mother's chronic pain pills, amitriptyline. Which pharmacologic effect of the medication is most responsible for the ECG changes seen in Figure 38?
   A. α-Adrenergic receptor inhibition
   B. Antihistaminic effects
   C. GABA-A receptor antagonism
   D. Potassium channel blockade
   E. Sodium channel blockade

![Figure 38](image)

379. Which of the following statements regarding the use of ketamine for procedural sedation and analgesia is correct?
   A. Advantages include the maintenance of protective airway reflexes and the absence of cardiovascular effects
   B. Concurrent use of benzodiazepines to prevent emergence reactions does not significantly prolong clinical recovery time
   C. Development of intense myoclonic jerking movements indicates the presence of a latent seizure disorder and should be treated with a benzodiazepine
   D. Induces dissociation between the cortical and limbic systems, resulting in amnesia, sedation, and analgesia
   E. Laryngospasm is rare, but when it occurs an emergent surgical rescue airway is often needed
γ-Hydroxybutyric acid, or GHB, is a naturally occurring analog of γ-aminobutyric acid (GABA), the major inhibitory neurotransmitter in the CNS. Side effects limited its use as a general anesthetic, but based on possible positive effects on muscle mass, it was marketed to bodybuilders. Recognition of its euphoria-inducing property at low doses led to recreational abuse and subsequent complications. Two precursors of GHB that, when ingested, are converted to GHB include γ-butyrolactone (GBL) and 1,4-Butanediol. Both of the precursors have legitimate industrial purposes but, along with GHB, remain drugs of abuse. GHB and its precursors are often ingested with other agents, as in this case, such as ethanol. Along with flunitrazepam, a benzodiazepine, GHB and its precursors are used for substance-induced rape because of their ability to rapidly induce coma. Because GHB is a CNS depressant, its use can lead to ataxia, sedation, respiratory depression, coma, apnea, and rarely, death. Non–hemodynamically compromising sinus bradycardia and mild hypothermia are common. Most characteristic, and actually quite specific for GHB, is rapid recovery of consciousness from a severely depressed CNS state. Management is supportive, with particular attention to airway and aspiration precautions. Naloxone is not effective in treating the CNS depression. A patient with a pure benzodiazepine poisoning, such as with flunitrazepam (known more commonly as Rohypnol), can appear clinically identical to one poisoned with GHB, but the rapid awakening from a comatose state will not occur. The same is true for a barbiturate poisoning, but barbiturate abuse is not as common now as it was 30 years ago. Carisoprodol is a sedative-hypnotic agent marketed as a muscle relaxant (Soma, for example) that is increasingly recreationally abused. It is converted in the body to meprobamate, a sedative that has also been abused. Sedation and coma can be expected after ingestion of an excessive amount. The sedation or coma can be impossible to distinguish from other sedative-hypnotics such as benzodiazepines, although a characteristic myoclonus is occasionally found. Similar to benzodiazepines, rapid awakening is not a feature of toxicity. The sustained-release formulation of oxycodone (OxyContin, for example), is an opioid that has become a common drug of abuse. Users typically crush the tablets, effectively destroying the sustained-release matrix, and then ingest, insufflate, or inject the drug. As with most other opioids, miosis is typical, and response to naloxone is expected (which is not the case with this patient). MDMA ("Ecstasy") is a synthetic derivative of methamphetamine that has sympathomimetic properties; agitation, tachycardia, and hyperthermia would be typical of toxicity.
Carbon monoxide (CO), an odorless, colorless gas produced by incomplete combustion of carbon-containing material, remains the leading toxicologic cause of morbidity and mortality in the United States. By avidly binding to hemoglobin, which causes a functional anemia and shifts the oxygen dissociation curve leftward, tissues are delivered less oxygen. Such binding allows for measurement of carboxyhemoglobin (COHb) levels (as accurate on venous sampling as arterial), the most useful diagnostic test in suspected CO poisonings. As a result of endogenous heme degradation, normal COHb levels range from 1% to 2%, while individuals who smoke have levels ranging from 5% to 10%. However, binding of CO to hemoglobin alone fails to explain all of the adverse effects seen with CO poisoning. Delivery of CO gas (not COHb) intracellularly and binding to heme proteins other than hemoglobin (myoglobin and cytochrome oxidase) might be crucial in the pathophysiology. Inactivation of cytochrome oxidase can initiate a cascade of events that, combined with cardiovascular effects of hypotension, might ultimately lead to lipid peroxidation of the brain. Hyperbaric oxygen (HBO), by various mechanisms, might interrupt or prevent this cascade, which is likely responsible for delayed neurologic sequelae. These sequelae include memory changes, cortical blindness, and parkinsonism. They might not be present during initial evaluation and, in fact, might not manifest for 2 to 40 days after exposure. Decreasing the risk of developing these delayed neurologic sequelae (which can be subtle and detectable only on detailed neuropsychiatric testing) is the basis for the primary and still controversial treatment rationale for HBO therapy in CO poisoning. Unfortunately, no consistently reliable clinical markers are yet available to predict who is at risk for developing delayed neurologic sequelae. No evidence exists that HBO therapy reduces mortality or decreases the risk of ventricular dysrhythmias, neither of which will occur in this recovering patient. HBO therapy more rapidly decreases COHb levels and more rapidly corrects the typical metabolic acidosis associated with CO poisoning than does normobaric oxygen. However, that is not the major rationale for treating this patient with HBO therapy. In fact, in the best study to date on HBO treatment for CO poisoning, in which some decrease in delayed neurologic sequelae was demonstrated, average levels of COHb before placement in the chamber were only 6%.
The conversion of methanol, itself nontoxic, to formic acid occurs in two separate enzymatic reactions beginning with alcohol dehydrogenase (AD) and followed by formaldehyde dehydrogenase. Formic acid is what causes the potentially severe metabolic acidosis as well as retinal toxicity. Ethanol has been traditionally administered to compete with methanol for metabolism by AD and is thought to be highly effective at a goal serum level of 100 mg/dL. There are problems with ethanol administration: intravenous preparations are often not available, and maintaining adequate serum concentrations can be difficult and requires serial measurements of ethanol levels, its intoxicating properties, and its potential for hepatic injury and hypoglycemia. Although no prospective study exists documenting the efficacy of ethanol for the treatment of methanol poisoning, it does work and should be administered if fomepizole is unavailable. Fomepizole is an inhibitor of AD that has been shown to be safe and effective in the treatment of methanol poisoning. It lacks the previously stated disadvantages of ethanol administration. Its main disadvantage is high cost. In the absence of substantial accumulation of formic acid, as evidenced by the absence of acidosis, hemodialysis is actually not mandatory as in situations D and E. In situations of high methanol levels without acidosis, hemodialysis might still be done at some point (not necessarily immediately) because of the very long half-life of methanol (54 hours in one study). Hemodialysis would prevent prolonged hospitalization and repeated doses of fomepizole, which are administered every 12 hours (more frequently with hemodialysis because some is dialyzed off). Hemodialysis effectively removes both the parent compound methanol and its toxic metabolite formic acid and is mandatory in methanol-poisoned patients with significant acidosis, such as in situations A, B, and C. In situation B, the patient has ingested ethanol in a quantity to effectively compete for metabolism of methanol. Specifically, since acidosis and therefore metabolism of methanol have occurred already, much of the ethanol must have been ingested at a later time. Initially, hemodialysis alone could be performed on this patient. Situation A would be the unusual situation in which all methanol has been metabolized, precluding the need for an agent to inhibit metabolism. This leaves C as the most appropriate answer.
107. The answer is C, Is associated with a motor neuropathy more commonly than a sensory one.
(Flomenbaum [Goldfrank's], 1148, 1311, 1313; Tintinalli, 1147-1148)

This patient is most likely suffering from lead encephalopathy. Illegally "moonshine" whiskey is often produced using lead-containing radiators; this remains a significant etiology of the relatively rare cases of severe lead poisoning. Various occupations expose individuals to lead, the highest risk group being those involved in the burning, cutting, or welding of lead. In such occupational settings, although ingestion can inadvertently occur, the most important route of exposure is inhalation. Lead has no known physiological role, so the presence of lead in humans represents environmental contamination. By various mechanisms, lead interrupts heme synthesis; at high levels associated with lead encephalopathy, it results in anemia, as found in this patient. Unlike the vast majority of toxic agents, lead predominantly causes a motor neuropathy rather than a sensory one. This can classically manifest as a wrist drop. As a presumed result of an immature blood-brain barrier and ongoing neurodevelopment, children are thought to be more susceptible than adults to the CNS effects of lead. The major treatment for significant lead poisoning, which can be confirmed with a whole blood lead level, is identifying and curtailing the exposure and initiating chelation therapy. Withdrawal from ethanol without appropriate treatment can be life threatening, but at a level of only 40 mg/dL, ethanol does not explain this patient's severely depressed level of consciousness.

121. The answer is E, Warfarin-induced skin necrosis typically occurs soon after warfarin therapy is started.
(Flomenbaum [Goldfrank's], 635; Tintinalli 1355-1356)

By blocking activation of vitamin K, warfarin interferes with the action of the vitamin K-dependent clotting factors II, VII, IX, and X, as well as the anticoagulant factors protein C and protein S. The early hypercoagulability that occurs after initiation of warfarin therapy results from the shorter half-lives of proteins C and S, compared with the procoagulant vitamin K-dependent clotting factors. The initial increased risk of thrombogenesis is, in fact, not just theoretical but has been demonstrated to be real and is one of the reasons that heparin is concomitantly started at the initiation of therapy. The initial increased risk of thrombogenesis also relates to the associated skin necrosis, which, if it occurs, will typically be early (3-8 days) after beginning warfarin. It is caused by thrombosis of small cutaneous vessels and occurs primarily in those with protein C deficiency. It is far less common than bleeding, the primary complication of warfarin therapy. Warfarin-induced skin necrosis is treated by discontinuing warfarin and administering heparin and vitamin K. Screening for protein C and S deficiencies should also be done. Many drug interactions occur with warfarin, are often related to the cytochrome P-450 enzymes involved in its metabolism, and should be considered when prescribing medications to individuals already taking warfarin. Cimetidine and clarithromycin are examples of drugs that inhibit the metabolism of warfarin and therefore are capable of potentiating rather than antagonizing its effects.
136. The answer is B, Chronic toxicity is usually the result of renal failure or intravascular volume depletion.

(Florence [Goldfrank's], 1054-1056, 1075; Tintinalli, 1046, 1048-1051)

This patient is manifesting some of the classic signs (confusion, tremor, hyperreflexia) of lithium poisoning. Although lithium has been used for other purposes, it is primarily used for the treatment of bipolar disorder. It is thought that the majority of patients chronically treated with lithium will at some point develop toxicity. The drug has a narrow therapeutic range, and many adverse drug reactions and interactions can occur. Adverse effects include hypothyroidism and nephrogenic diabetes insipidus (not diabetes mellitus). An adverse drug interaction is precipitation of serotonin syndrome (not neuroleptic malignant syndrome, which is associated with dopamine antagonists or withdrawal from dopamine agonists) when lithium is combined with other serotonergic agents. Lithium is eliminated entirely by renal excretion and is reabsorbed at the proximal tubule as sodium is. Any diminished excretion or enhanced reabsorption therefore can result in toxicity. In fact, in the vast majority of cases of chronic toxicity, the precipitant is renal failure or intravascular volume depletion. Activated charcoal is ineffective at adsorbing lithium but may be administered to bind coingestants. Sodium polystyrene sulfonate (Kayexalate) is effective not only at adsorbing lithium and preventing absorption but also at enhancing elimination once it is absorbed. The clinical efficacy of using it to treat lithium poisoning remains unproven, however. Serial measurements of serum levels are helpful in managing patients with toxicity, but the levels do not correlate well with CNS symptoms because of delayed uptake and elimination by the brain.
Salicylates remain a small but significant cause of death in poisonings. After absorption, aspirin is hydrolyzed to salicylic acid (salicylate). Activated charcoal can effectively adsorb aspirin and help prevent absorption. Although a positive plain radiograph can potentially identify the presence of enteric-coated or sustained-release aspirin in the gastrointestinal tract, a negative film cannot exclude its presence. Salicylate poisoning is characterized by various symptoms, signs, and laboratory abnormalities. Reversible sensorineuronal hearing loss is one of these, and it correlates with salicylate levels. Although there is a correlation, it must be kept in mind that the description of actual tinnitus is by no means 100% sensitive. A primary respiratory alkalosis (not just in response to the metabolic acidosis) also characterizes salicylate poisoning. In the unusual situation in which an individual with salicylate poisoning requires endotracheal intubation, it is critically important to maintain this hyperventilation and match the individual's minute ventilation. Failure to do so will result in the immediate development of respiratory acidosis and serum acidemia. Brain salicylate concentrations have been shown to directly correlate with mortality, and for a given serum salicylate concentration, brain salicylate concentrations will be substantially higher in the presence of serum acidemia. Therefore, everything possible should be done to avoid serum acidemia, including administering sodium bicarbonate. Bicarbonate administration can also be used to induce a urinary alkalization and enhance the elimination of salicylate. Although this alkalization will elevate urine pH and enhance elimination, urinary pH has not been shown to be a determinant of mortality. Although the Done nomogram was created to assist in the management of salicylate poisonings, clinical signs and symptoms combined with serial salicylate levels are far superior in guiding management, including the need for hemodialysis (an effective method to remove salicylate).
The answer is E. Rarely contribute significantly to the evaluation, management, or outcome of emergency department patients.

(Flomenbaum [Goldfrank's], 88, 93, 103-104, 106; Tintinalli, 1016)

Urine drugs of abuse panels have been shown to rarely contribute significantly to the evaluation, management, and outcome of emergency department patients. Clinical signs and symptoms of intoxication combined with routine laboratory testing are infinitely more helpful than rapid urine drugs of abuse panels. The tests themselves are generally not designed to test for clinical intoxication with an agent, but rather detect the presence of recent exposure. Although each test has a threshold limit of detection (usually quite low, and different among tests), the tests should be interpreted qualitatively. This is in contrast to ethanol serum or breathalyzer tests that yield quantitative information (ie, ethanol level) that can be useful to correlate clinically (ie, a level of 300 mg/dL could certainly explain why a patient is comatose). Rapid urine drugs of abuse tests often include testing for amphetamines as a class, barbiturates, benzoylecgonine (cocaine metabolite), benzodiazepines, opiates, phencyclidine, and tetrahydrocannabinol (THC). The test for amphetamines detects the amphetamine base structure and therefore might test positive (not really a “false” positive) for many substances with that structure (amphetamine, ephedrine, methamphetamine, pseudoephedrine, phenylpropanolamine). Therefore, testing positive for amphetamines as a class by no means confirms methamphetamine exposure. Only further testing such as with thin-layer chromatography and/or gas chromatography can confirm this. The test for benzoylecgonine, in contrast, is quite specific for recent cocaine exposure, but again only confirms recent exposure. Likewise, the barbiturate test is also quite specific for recent exposure to a barbiturate. The benzodiazepine screen tests for a specific metabolite of only certain benzodiazepines. Therefore, a negative test does not exclude the presence of an agent without that metabolite (eg, lorazepam). The opiate screen is directed toward detecting the morphine structure. Many synthetic opioids (agonists at the opioid receptor) will not be detected, such as fentanyl, meperidine, methadone, propoxyphene, and tramadol. Obviously, opioid intoxication should be detected and treated based purely on clinical findings rather than awaiting a drug screen, which as demonstrated, will miss many opioids. The phencyclidine test has been removed by some institutions because this agent currently is rarely used. Dextromethorphan is a classic agent that often produces a false-positive with this test. Rapid urine drug testing is much more likely to be helpful in children, where the presence of any positive test will have a clear explanation (eg, patient on phenobarbital for convulsions with positive barbiturate screen) or reveal the presence of an agent that obviously should not be present (cocaine-positive in an agitated child). Even in children, however, clinical signs and symptoms should supersede reliance on drug screens, and comprehensive testing is much more likely to be helpful than rapid urine screens. Although psychiatric colleagues might request that the test be performed routinely in patients who present after suicidal ingestion, it is rarely medically needed.
Very few clinically applicable studies show benefit of gastrointestinal (GI) decontamination, and it is recognized that it is unlikely to affect the outcome of many patients who present to the emergency department after an overdose. One reason for this is that many overdose patients present 2 hours or more after ingestion, a time at which decontamination will have minimal effect: much of the toxin will have been absorbed or moved into the intestine. However, there are situations in which GI decontamination can be quite effective and should be performed. One such situation is early after the ingestion of a potentially toxic quantity of acetaminophen (APAP). In the first study to demonstrate a real emergency department–based patient benefit of decontamination, charcoal administration to patients who had ingested acetaminophen was shown to decrease the number of patients who required the antidote, N-acetyl-L-cysteine (NAC). Although not a perfect study (and mortality rate was not affected), it did demonstrate that activated charcoal administration spared some patients the need for NAC therapy and hospitalization. Charcoal adsorbs to APAP; if administered soon after ingestion, it can effectively decrease absorption. Even in large doses, however, APAP is rapidly absorbed, reaching peak serum levels within 2 hours. Although delayed administration of charcoal (>2 hours postingestion) sometimes is reasonable to bind potentially dangerous coingestants, it is not needed in this case, 7 hours after an isolated, witnessed ingestion. In the first day after an APAP overdose, a patient can be asymptomatic or exhibit nonspecific symptoms and signs, including anorexia, nausea, vomiting, and malaise. What makes APAP poisoning unique is that the potential risk of developing liver failure can be completely prevented by the timely administration of NAC. Also unique to this poisoning is that laboratory evaluation (APAP level), not clinical status, completely guides initial therapy. When initiated within 8 hours of an acute APAP ingestion, NAC is nearly 100% effective in preventing hepatotoxicity. Because there is no benefit of administering NAC 0 to 4 hours versus 4 to 8 hours after an acute ingestion, waiting for the APAP level without empiric NAC therapy is usually indicated. However, in this patient, who by history ingested a potentially toxic quantity of APAP and in whom test results will not be back in time to initiate NAC therapy within 8 hours, the correct answer is to administer the first dose of NAC pending test results. When the APAP level is known, it should be plotted on the nomogram to determine if additional NAC therapy is necessary.
This patient was exposed to hydrofluoric acid, an agent commonly found in rust removers. It is used for a variety of other purposes, including etching and frosting glass, making semiconductors, tanning, and cleaning stone and brick. Exposures occur by a variety of routes, including dermal, inhalational, ocular, and oral. Hydrofluoric acid is capable of deeply penetrating tissue, and local tissue injury might not be obvious initially or might appear insignificant. However, persistent pain (which can seem out of proportion to the visible skin injury) indicates ongoing toxicity from the fluoride ion. Hydrofluoric acid is unique in its potential to cause systemic life-threatening toxicity, characterized by certain electrolyte abnormalities and sudden-onset dysrhythmias. The concentration of hydrofluoric acid (>20% is always potentially serious), route of exposure (oral and inhalational should always be considered potentially fatal), and surface area and volume exposed to can be helpful in assessing severity. The timing of pain onset can also give an idea of the concentration: a sooner onset is associated with higher concentrations. Fortunately, most hydrofluoric acid exposures are insignificant and characterized by small dermal exposures of low concentration. Most household rust removers, as in the case described, have concentrations of only 6% to 12%, which explains why the onset of pain can be delayed up to 24 hours. Systemic toxicity is characterized by acidosis, hypocalcemia, and hypomagnesemia, followed by hyperkalemia and sudden-onset dysrhythmias. Acidemia occurs from release of the hydrogen ion and tissue damage. The fluoride ion can bind calcium and magnesium, which can lead to significant hypocalcemia and hypomagnesemia. The delayed onset of hyperkalemia is attributed to tissue destruction and direct fluoride effects on potassium efflux. Effects on sodium have not been described. Hypocalcemia, hypomagnesemia, hyperkalemia, and the direct effects of the fluoride ion are all implicated in the production of dysrhythmias. Management of dermal hydrofluoric acid exposures involves immediate copious irrigation; when necessary, specific treatments are aimed at both neutralizing and treating the systemic effects of the fluoride ion. Calcium gluconate therapy by the topical, subcutaneous/intradermal injection, intraarterial, and intravenous regional perfusion routes has been described. Because of its caustic properties, calcium chloride should never be administered subcutaneously or intradermally. Other treatments have included magnesium and additional therapies beyond calcium aimed at the hyperkalemia.
Valproic acid has many indications, including the treatment of seizure disorders, bipolar disorder, and migraines. Various metabolic complications have been reported after overdose, including metabolic acidosis, hypernatremia, hypocalcemia, low carnitine levels, and elevated ammonia levels. Elevated ammonia also is a complication of therapeutic use: more than one third of patients on chronic therapy have ammonia levels greater than 60 micromol/L. Hyperammonemia can result in significant mental status disturbances; checking for it might reveal the etiology of significant depression of consciousness in an individual whose serum valproic acid level does not explain it. The mechanism responsible involves depletion of carnitine and interference with the urea cycle leading to hyperammonemia. Although hepatitis can be a complication of valproic acid treatment, hyperammonemia occurs typically in the absence of any hepatotoxicity, so measures such as the AST will be normal. Carnitine supplementation appears to be beneficial in treatment. Renal failure and coincident urea elevation are rare manifestations of acute toxicity.

Neuroleptic malignant syndrome (NMS) and serotonin syndrome are both iatrogenic disorders stemming from the administration of certain medications. NMS occurs from the administration of dopamine antagonists or occasionally from abrupt withdrawal of dopamine agonists. Serotonin syndrome results from stimulation of specific serotonin receptors by certain serotoninergic agents. Unlike NMS, which can occur unpredictably anytime after the agent is used, serotonin syndrome is typically precipitated soon after the initiation of a serotoninergic agent or, more typically, after the addition of a second serotoninergic agent. Although overdose of the offending agent(s) has been occasionally associated with either disorder, neither condition typically occurs after an overdose. A wide spectrum of presentations exists for both conditions, but both are classically characterized by autonomic instability (blood pressure and heart rate variability, diaphoresis, hyperthermia), altered level of consciousness (agitation, coma, confusion), and neuromuscular abnormalities (rigidity). Rigidity is classically more severe (often referred to as "lead pipe") in NMS, while in serotonin syndrome it has been described as worse in the lower extremities. Additionally, both hyperreflexia and clonus can coexist in serotonin syndrome, which is not typical of NMS. A detailed drug exposure history, physical examination, and exclusion of other similarly appearing processes are essential because there is no specific confirmatory laboratory testing for either disorder. Stopping the offending agent (or in the case of dopamine agonists, restarting the agent) and aggressive supportive care (which often involves sedation and rapid cooling measures) are the mainstays of treatment. Occasionally intubation and paralysis are also necessary. Various dopamine agonists such as bromocriptine and amantadine have been used for NMS, while serotoninergic antagonists such as cyproheptadine have been used for serotonin syndrome.
236. **The answer is A, Administer activated charcoal along with a flavoring agent.**

(Shannon [2005 LLSA article], 186-191; Strange, 559-565)

Several different management strategies can be used to address an unknown ingestion. These include gastric emptying with induced emesis or gastric lavage, administration of an adsorbent (e.g., activated charcoal), and catharsis to speed elimination of a potential poison from the gastrointestinal tract. Of these management strategies, the one with the best overall effect for the unknown medication ingestion is the administration of activated charcoal. When administered within 1 hour of ingestion, activated charcoal is thought to reduce toxin absorption by as much as 75%. The substances for which activated charcoal has minimal clinical effect are not typically seen in pills and include alcohols, hydrocarbons, metals, and minerals. Gastric emptying by both gastric lavage and the administration of syrup of ipecac is relatively contraindicated primarily because of unproven efficacy, concerns about safety, and delays in the more important administration of activated charcoal. Syrup of ipecac should be avoided in cases of calcium-channel blocker, β-blocker, and digitalis ingestions because of the risk of vagally mediated severe bradycardia. These medications are commonly prescribed to the elderly. Catharsis with sorbitol, and particularly with polyethylene-glycol, is primarily indicated for substances poorly adsorbed to activated charcoal, such as iron and lithium. Calling the grandmother’s pharmacy to identify her medications and then developing a management plan based on this information would also be a reasonable first step if it could be done rapidly.
245. **The answer is C, Methylene blue.**

(Tintinalli, 1169-1172, 1239-1240; Wollson [Harwood-Nuss'], 1606-1609)

Cyanosis, a bluish discoloration of the skin, can be secondary to an increased amount of deoxygenated (reduced) hemoglobin in the blood or to the presence of abnormal pigments such as methemoglobin and sulfohemoglobin within the red blood cells. Cyanosis is further classified as either central or peripheral. Central cyanosis affects both the skin and mucous membranes. It occurs when there is at least 5 g of deoxygenated hemoglobin or 1.5 g/dL of methemoglobin in the circulation. Central cyanosis is associated with hypoxemia due to right-to-left shunt, ventilation mismatch, and hemoglobin abnormalities. In contrast, peripheral cyanosis is due to reduced circulation in the peripheral vascular beds and is associated with low cardiac output states, arterial or venous obstruction, or cold extremities. Peripheral cyanosis can be localized or generalized. Methemoglobinemia from drugs is usually due to overdose—either accidental or with suicidal intent—and has been associated with phenazopyridine, phenacetin, sulfonamides, and benzocaine, an ingredient in many common teething gels. Oxidative metabolism in the red blood cells produces small amounts of methemoglobin. The erythrocytes maintain a low methemoglobin level (<1%) either by reducing the methemoglobin back to normal hemoglobin as soon as it is formed or by reducing oxidant compounds before they react with hemoglobin to create methemoglobin. These agents inflict a large oxidant stress on the red blood cells, which are then unable to maintain the methemoglobin levels below 1%. Of the choices listed, methylene blue is the treatment most likely to reverse cyanosis due to methemoglobinemia. Methylene blue accelerates the use of a normally minor reduction pathway of NADPH-methemoglobin reductase. This reduces the oxidized heme back to the normal oxygen-carrying capacity. Hypoxia due to respiratory depression from botulism would not be expected to manifest with tachypnea and a normal work of breathing. Therefore, botulinum antitoxin is not the best choice. Deferoxamine is used to treat iron ingestions. The clinical features of iron ingestion are typically gastrointestinal with bleeding and then liver failure; cyanosis is not a characteristic finding. Prostaglandin E1 is used to temporize congenital cardiac disorders for which the child's systemic circulation is dependent on a patent ductus arteriosus. When the ductus arteriosus closes during the first weeks of life, these children develop profound, life-threatening shock. Just like the child in this case, children with ductal-dependent lesions often have hypoxia that is unresponsive to high-flow oxygen therapy; this is called a failed hypoxia test. In this case, the child has an abnormal response to oxygen, but it is due to the abnormal hemoglobin and not a structural cardiovascular problem. Sodium bicarbonate is used to treat conditions such as salicylate ingestions, which do not characteristically present with cyanosis.
Tricyclic antidepressants (TCAs) have been used for many years in the treatment of depression, behavior disorders, and chronic pain syndrome. The use of TCAs in children and adolescents has been increasing significantly; in this age group, TCAs are the most commonly ingested agents in drug-related deaths. TCAs have many pharmacologic effects that result in their significant toxicity. The α-adrenergic receptor inhibition produces peripheral vasodilation that results in orthostatic hypotension, often associated with reflex tachycardia. Pupillary constriction is also the result of inhibition of the α-adrenergic receptors; however, on clinical examination, the patient with TCA toxicity can have normal or dilated pupils due to the antimuscarinic effect also caused by this class of medication. The antihistaminic effects of TCAs result in CNS changes of sedation and coma. Antagonism of the GABA-A receptors results in seizures through mechanisms that are not clearly defined. Treatment of the seizures that occur in patients with TCA overdose is with benzodiazepines and barbiturates, both potent GABA-A agonists. The potassium channels affect cardiac muscle repolarization, and blockade of these channels leads to QT prolongation seen in TCA toxicity. In this ECG, the QT interval is not significantly prolonged, as noted by the normal QTc. The blockade of the sodium channels of the heart leads to decreased contractility and a prolongation of the action potential of the cardiac cells. This quinidine-like effect is seen on the ECG as a prolonged PR interval and QRS complex and can cause right axis deviation. Findings of either of these effects indicate significant cardiac toxicity and mandate immediate treatment. In this ECG, the patient has a prolonged QRS complex (>0.10) and a prolonged PR interval (P wave seen best in lead I here). Right axis deviation is not always seen in TCA toxicity, as in this case. Bradycardia, as seen here, is an even more ominous sign when associated with a prolonged QRS complex. Blockade of the sodium channels can be reversed in part by alkalinization of the serum with a sodium bicarbonate drip to get the serum pH to 7.5 to 7.55. This will also increase the concentration of serum sodium, which might increase the extracellular sodium gradient and increase movement of sodium into the cells.
The answer is D. Induces dissociation between the cortical and limbic systems, resulting in amnesia, sedation, and analgesia.

(Blackburn 2005 LISA article, 803-823)

Ketamine has emerged as one of the leading agents for procedural sedation in pediatric patients. It is a synthetic derivative of phencyclidine and a dissociative anesthetic agent. The dissociative properties block the higher cortical functions from detecting auditory, visual, or painful stimuli. Clinically this manifests as analgesia, amnesia, and sedation. One of the major advantages of ketamine is that spontaneous respirations and airway tone are preserved. It also causes bronchodilation and increased salivation and secretions. Although ketamine is often characterized as not having cardiovascular effects, it does in fact cause catecholamine release, which increases heart rate, blood pressure, and cardiac output. Ketamine is highly lipid soluble and has a rapid onset of action (<1 minute intravenously and 5 minutes intramuscularly) with a duration of action of 15 minutes and 30 to 120 minutes, respectively. The concurrent administration of benzodiazepines prolongs recovery by at least 30%. Current dosing recommendations for ketamine are 1.5 mg/kg IV and 5 to 5 mg/kg IM. The use of an anticholinergic agent such as atropine or glycopyrrolate is recommended to decrease salivation and secretions. The major side effects of ketamine use include emergence reactions and laryngospasm. Emergence reactions are more common in children older than 10 years and adults and are characterized by hallucinations. Other risk factors for the development of emergence reaction include rapid intravenous administration, excessive noise or stimulation during recovery, and a history of frequent dreaming. In high-risk patients and settings, the concurrent administration of benzodiazepines is recommended to blunt the emergence phenomenon. Laryngospasm is the most serious complication associated with ketamine use. It is rare and typically transient and usually does not require intubation or a surgical airway. Muscle rigidity and hypertonicity are fairly common; occasionally myoclonic jerking is seen, but it has never been noted to be associated with EEG changes.