Chapter 17

TOXICOLOGICAL CONDITIONS

Saralyn R. Williams
Matthew D. Sztajnkrycer
R. Jason Thurman

Jimsonweed. Jimsonweed seed pod with dried seeds. (Photo contributor: Matthew D. Sztajnkrycer, MD, PhD.)

AMPHETAMINE TOXICITY

Clinical Summary

Amphetamines as a class may be abused by ingestion, insufflation ("snorting"), parenteral injection, and smoking. "Ice" refers to a pure preparation of methamphetamine hydrochloride in a large crystalline form. Designer amphetamines include 3,4-methylenedioxymethamphetamine (MDMA, "ecstasy"), paramethoxyamphetamine (PMA), and synthetic cathinones (ingredients in "bath salts"). While the central nervous system (CNS) targets of these compounds are serotonergic and dopaminergic pathways, the clinical presentation is manifested as a sympathomimetic toxidrome.

Although clinically indistinguishable from cocaine toxicity, the duration of effects is appreciably longer. The most common cardiovascular manifestations of toxicity are tachycardia and hypertension, although myocardial ischemia has been reported. Despite the cardiovascular effects, CNS toxicity is the primary reason most amphetamine users present for medical care. Presentations may range from increased anxiety to life-threatening agitated delirium with hyperthermia. Visual and tactile hallucinations and psychoses are common. Poor dentition is common among chronic users ("meth mouth"), and appears multifactorial in nature.

Management and Disposition

Treatment focuses upon the signs and symptoms of toxicity. As with other causes of sympathomimetic toxicity, initial management includes control of the agitation to prevent other complications (eg, rhabdomyolysis). Benzodiazepines are the first-line therapy for agitation; large repeated doses may be required. Severe hyperthermia requires evaporative cooling techniques. Hypertonic sodium may be useful for MDMA-associated cerebral edema and seizures.

Pearls

1. In addition to the medical complications associated with methamphetamine use, the manufacture of methamphetamine is associated with exposure to a number of toxic chemicals and risk for severe burns.
2. The hyperthermia associated with acute amphetamine poisoning may result in end-organ damage similar to patients with heat-stroke-like illness.
3. MDMA may result in syndrome of inappropriate antidiuretic hormone (SIADH) with subsequent hyponatremia and cerebral edema.

FIGURE 17.1 ■ **"Ice" Methamphetamine.** An example of the "ice" form of amphetamines with a pipe. (Photo contributor: US Drug Enforcement Administration.)

FIGURE 17.2 ■ **Ecstasy.** Examples of the candy-like appearance of ecstasy tablets. (Photo contributor: US Drug Enforcement Administration.)

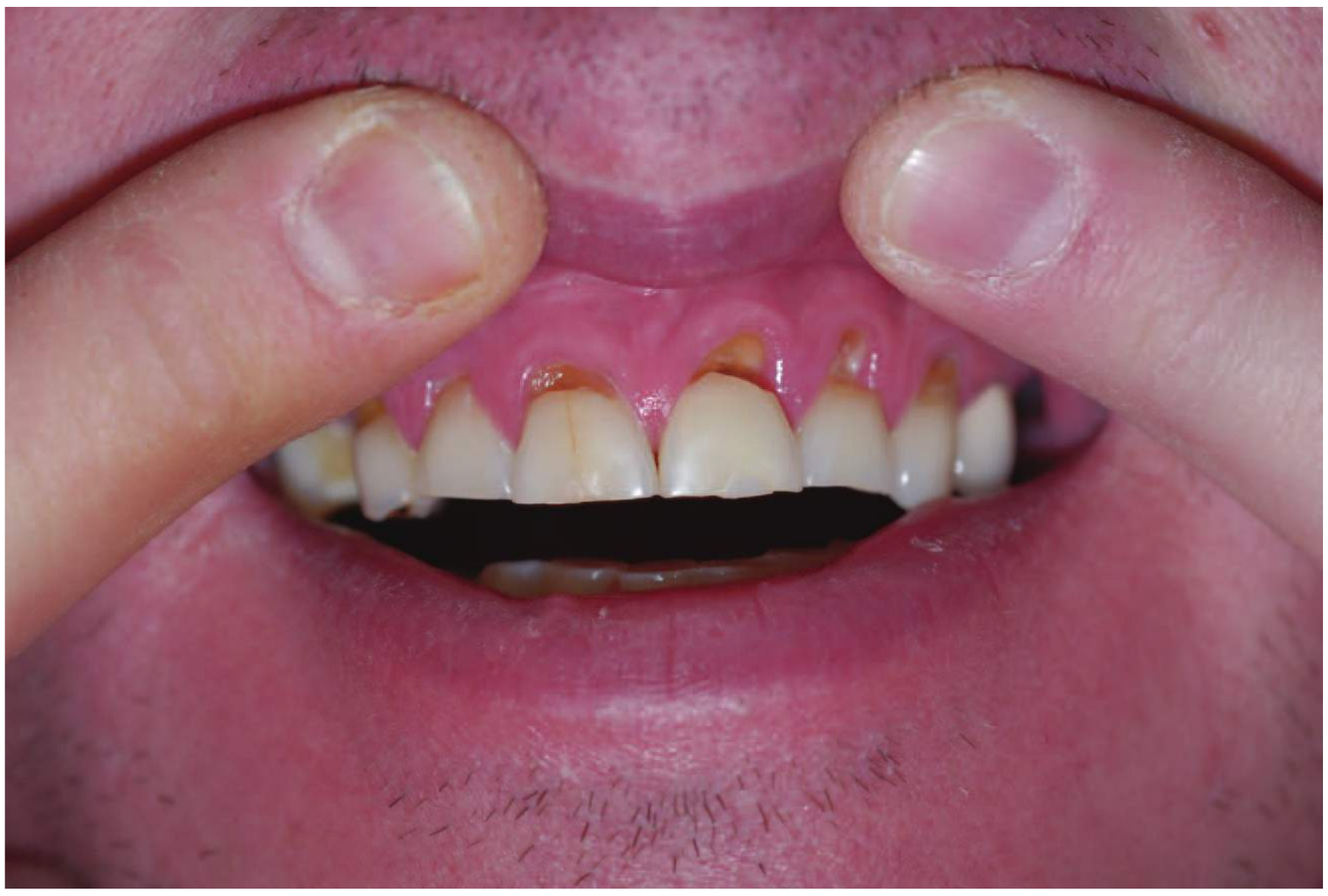

FIGURE 17.3 ■ **Early "Meth Mouth."** "Meth mouth," the extensive and accelerated dental caries associated with chronic methamphetamine abuse. (Photo contributor: R. Jason Thurman, MD.)

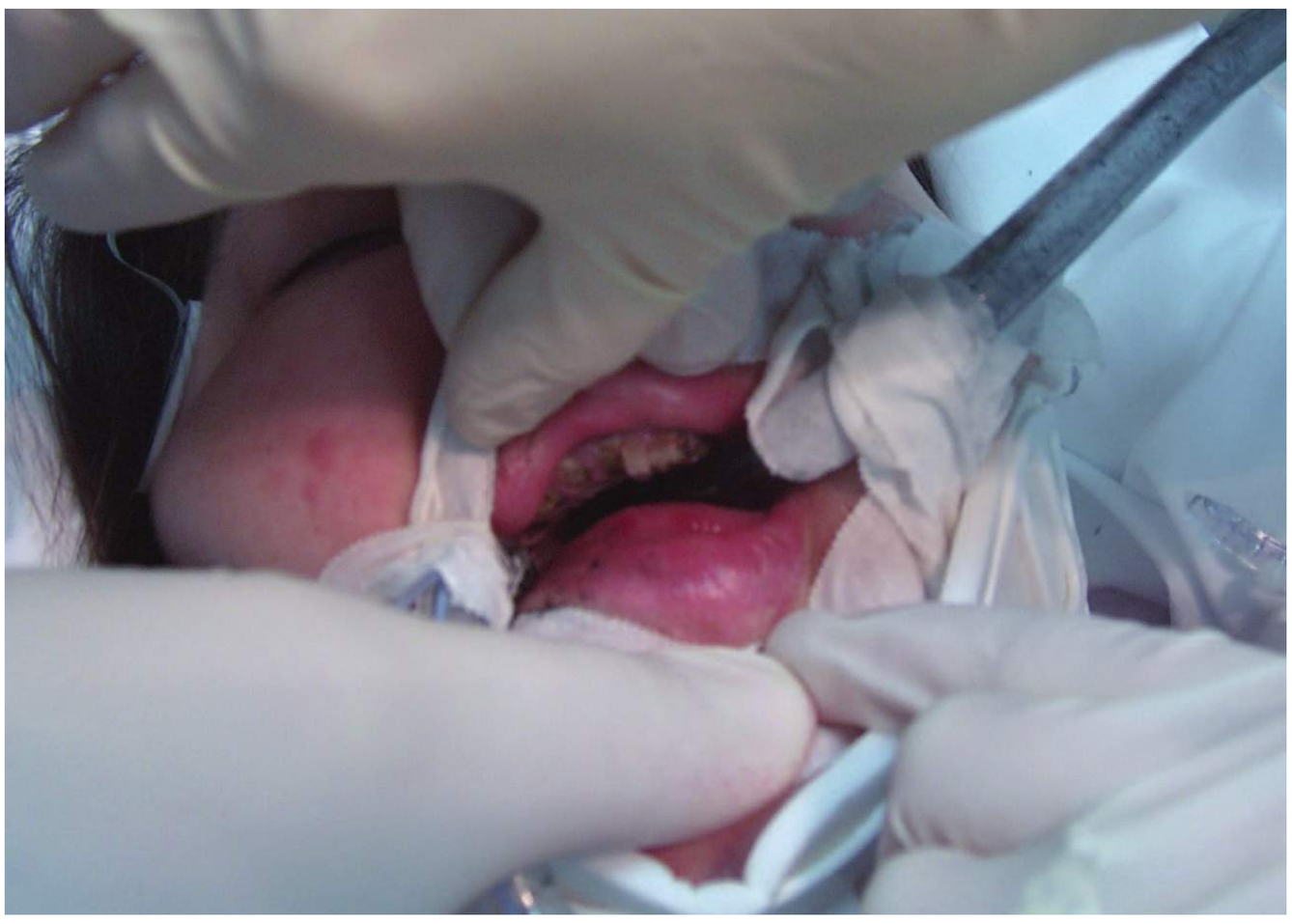

FIGURE 17.4 ■ **Advanced "Meth Mouth."** Note the severe dental decay in this chronic methamphetamine abuser. (Photo contributor: Carson Harris, MD.)

NEW DESIGNER DRUGS: "BATH SALTS" AND "SPICE"

Clinical Summary

The cathinones are derivatives of a naturally occurring phenethylamines found in the leaves of the Catha edulis (khat) plant. Some of these compounds include mephedrone, methylone, and methylenedioxypyrovalerone (MDPV). Adverse effects of these compounds include cardiac, psychiatric, and neurologic signs and symptoms, similar to effects seen with other sympathomimetics.

Synthetic cannabinoids have been promoted as "spice" or "incense" products that contain a substance usually labeled as "JWH" followed by a number. The designation reflects the original synthesis by John W. Huffman, an organic chemist at Clemson University. These compounds have full agonist effects at the cannabinoid receptors, in contrast with tetrahydrocannabinol (THC), which demonstrates only partial agonism. While cannabinoids such as marijuana do not typically result in sympathomimetic effects, the synthetic cannabinoids may also cause acute sympathomimetic toxicity including seizures and tachydysrhythmias.

FIGURE 17.5 ■ **Khat Plant**. The leaves of the khat plant (Catha edulis) are chewed for the stimulant effects. The leaves must be fresh in order for cathinone to be present. (Photo contributor: US Drug Enforcement Administration.)

FIGURE 17.6 ■ **Bath Salts.** Examples of typical packaging for bath salts. (Photo contributor: US Drug Enforcement Administration.)

Forensic analysis of these products has demonstrated significant variability in types and amounts of active products over time, both between and within marketed brands. As a result, individuals may experience different clinical effects with different exposures to the same product.

Management and Disposition

Patients under the influence of one of the synthetic compounds should be approached and managed similar to other acute sympathomimetic poisonings.

Pearls

1. The ingredients in "bath salts" are not detected by routine testing for amphetamines as a class.
2. Agitation, psychosis, and seizures are common clinical effects of synthetic cannabinoid use.

FIGURE 17.7 ■ **Synthetic Cannabinoids—"Spice."** Examples of the packaging of synthetic cannabinoids which are labeled "not for human consumption." (Photo contributor: John G. Benitez, MD, MPH.)

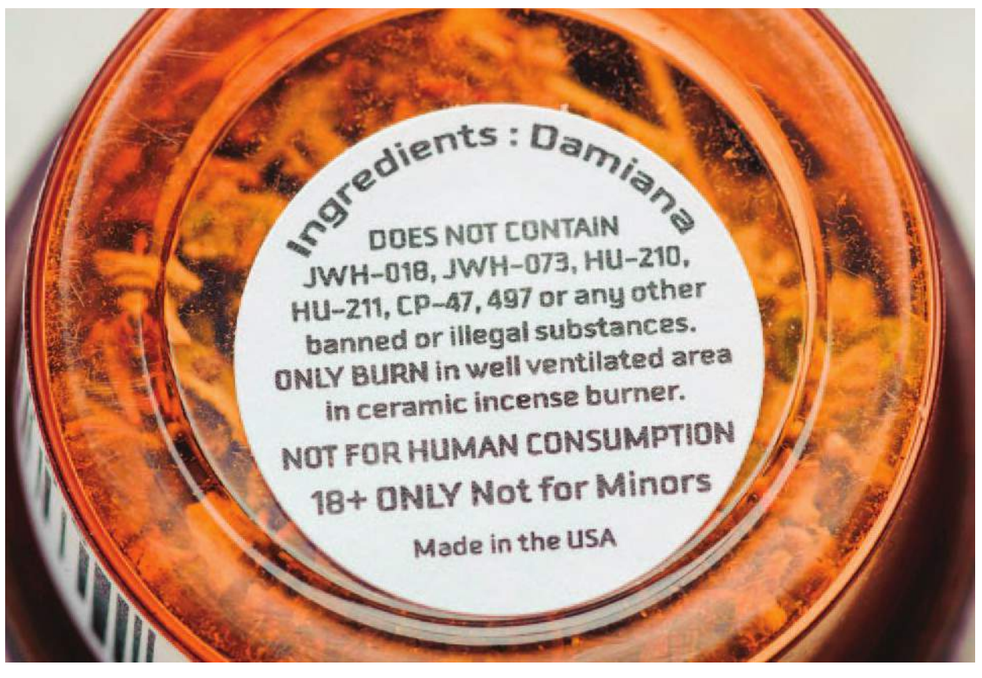

FIGURE 17.8 ■ **Synthetic Cannabinoids Disclaimer.** Close-up of the language used to suggest that the contents do not contain illegal substances. (Photo contributor: John G. Benitez, MD, MPH.)

Clinical Summary

Cocaine is a natural alkaloid derived from the leaves of Erythroxylum coca. Cocaine hydrochloride (powder cocaine) is a crystalline white powder. "Crack," the free-base of cocaine hydrochloride, is an off-white substance named both for its rock-like appearance ("rock") and due to the sound it makes when heated. In contrast to powder cocaine, crack may be smoked as it vaporizes instead of burning.

Cocaine intoxication manifests as a sympathomimetic toxidrome, with tachycardia, hypertension, diaphoresis, mydriasis, delirium, and hyperthermia. Increased muscular activity may result in rhabdomyolysis. Numerous neurological complications have been reported after cocaine use, including subarachnoid hemorrhage, intracerebral hemorrhage, cerebral infarction, and seizures.

Cardiovascular toxicity, including acute myocardial infarction, is well described after cocaine use. Dysrhythmias, including supraventricular tachycardia, atrial fibrillation and flutter, ventricular tachycardia, ventricular fibrillation, and torsades de pointes have been reported. Cocaine is a sodium channel blocker and may cause QRS widening on the electrocardiogram (ECG). Aortic dissection and rupture have been associated with cocaine use.

Pulmonary effects of cocaine use include reactive airway disease exacerbation, pneumothorax, pneumomediastinum, and cardiogenic and noncardiogenic pulmonary edema (NCPE). "Crack-lung" refers to an acute pulmonary syndrome of dyspnea, hypoxia, and diffuse pulmonary alveolar infiltrates.

Management and Disposition

Treatment is primarily supportive, and focuses upon the signs and symptoms of toxicity. No specific antidote exists. Cardiac monitoring is indicated for symptomatic patients. Initial management focuses upon control of agitation and hyperthermia, and prevention of complications (eg, rhabdomyolysis). The use of neuroleptic agents is relatively contraindicated for cocaine-associated psychomotor agitation due to the negative effects of these agents on thermoregulation, seizure threshold, and the potential for dysrhythmias. Benzodiazepines are the first line of therapy for agitation. They also appear beneficial in the management of cocaine-associated chest pain. Sodium bicarbonate administration should be considered for QRS widening in the setting of acute cocaine poisoning.

FIGURE 17.10 ■ **Drug Paraphernalia.** Crack pipe sequestered in the rectum during a patient's arrest, resulting in laceration of the hemorrhoidal venous plexus and massive hemorrhage. (Photo contributor: Matthew D. Sztajnkrycer, MD, PhD.)

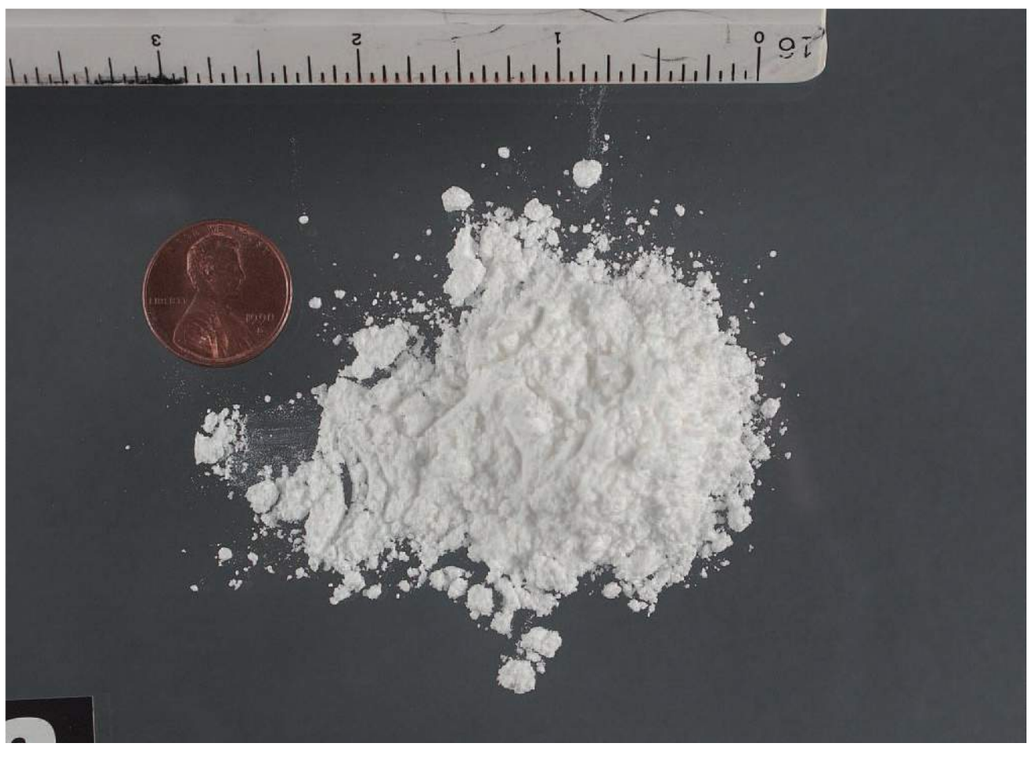

FIGURE 17.9 ■ **Cocaine Powder.** Cocaine powder. (Photo contributor: US Drug Enforcement Administration.)

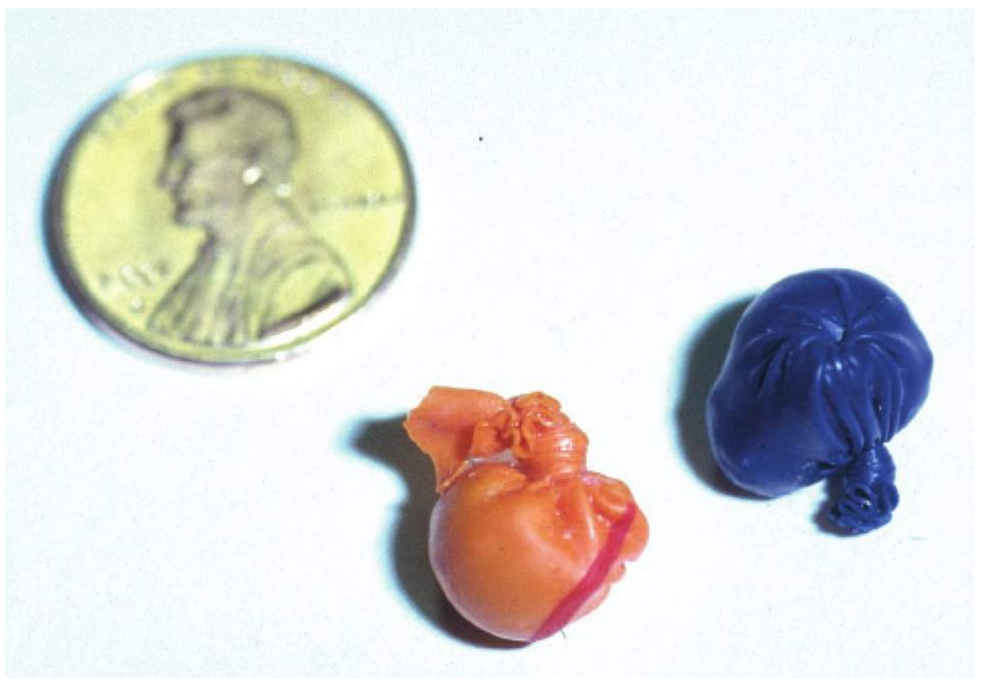

FIGURE 17.11 ■ **Cocaine Body-Packing.** Cocaine-filled balloon packets from the stool of a cocaine "body-packer" (penny used for scale). Radiopaque packets are often visible on KUB radiograph. Severe toxicity may result in the event of a ruptured packet. (Photo contributor: Alan B. Storrow, MD.)

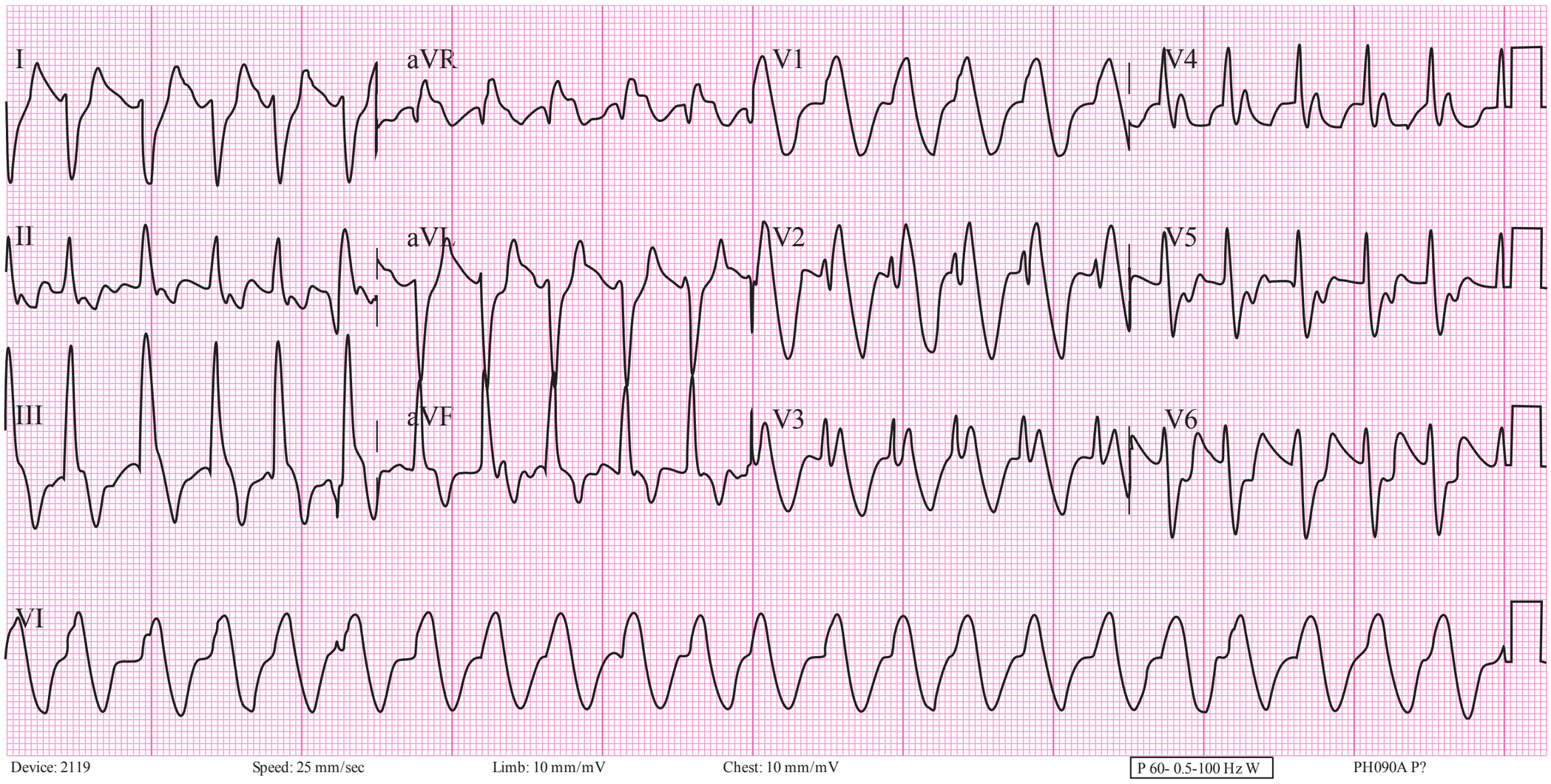

FIGURE 17.12 ■ **Cocaine Cardiotoxicity.** The initial 12-lead EKG of a patient with acute cocaine and cocaethylene poisoning demonstrating with wide complex rhythm from the sodium channel blocking effects. His initial serum pH was 6.8. (Photo contributors: Thomas Babcock, MD and Laurie Lawrence, MD.)

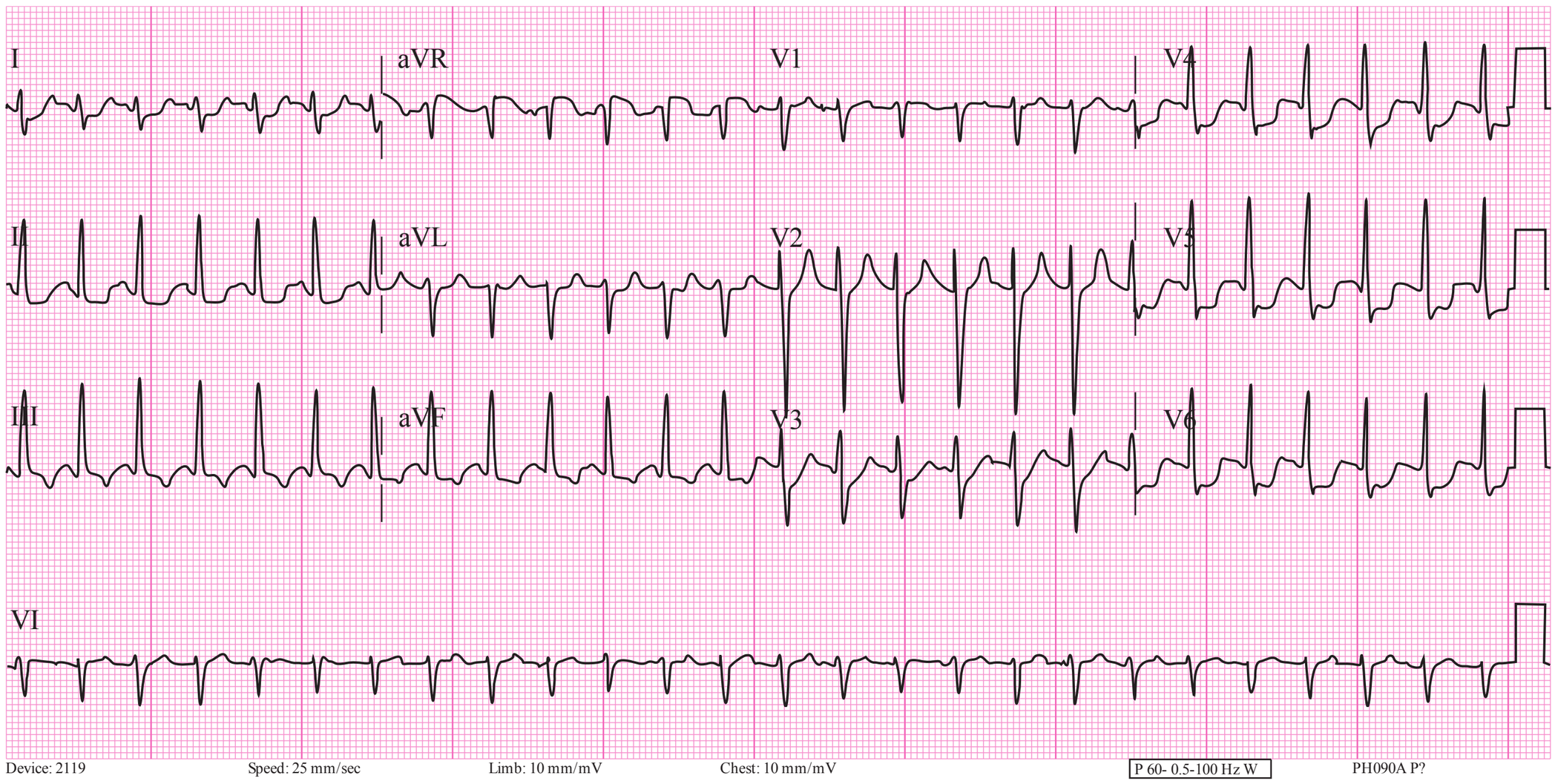

FIGURE 17.13 ■ **Treated Cocaine Cardiotoxicity.** The 12-lead EKG of the same patient in Fig. 17.12, 68 minutes later after aggressive treatment with sodium bicarbonate to a serum pH of 7.26. (Photo contributors: Thomas Babcock, MD and Laurie Lawrence, MD.)

Pearls

1. The use of β-blockers is contraindicated in the management of cocaine-associated chest pain and myocardial ischemia due to the potential for vasospasm and hypertensive crisis ("unopposed α-effect").
2. Although the risk of myocardial infarction is greatest immediately after use, myocardial ischemia may occur up to 6 weeks after last use.
3. Cocaethylene may form in vivo after the use of cocaine and ethanol. Cocaethylene is more cardiotoxic than cocaine and has a longer half-life.
4. The rupture of a cocaine packet in a body-packer may result in fatal toxicity. Emergent surgical intervention may be considered for immediate removal of the packets.

FIGURE 17.14 ■ **Cocaine-Induced Rhabdomyolysis.** Rhabdomyolysis is a common clinical finding in patients with severe cocaine poisoning. (Photo contributor: Mohamud Daya, MD.)

ANTICHOLINERGIC (ANTIMUSCARINIC) TOXIDROME

Clinical Summary

The anticholinergic toxidrome is well described by the mnemonic: hot as a hare, blind as a bat, mad as a hatter, red as a beet, and dry as a bone. As the etiology reflects central and peripheral muscarinic receptor blockade, it is more accurately termed an antimuscarinic toxidrome. A centrally mediated delirium may occur, which is typically not violent but is associated with mumbling speech and persistent "picking" behaviors. Other manifestations include hyperthermia, mydriasis, dry mucus membranes and axillae, tachycardia, decreased gastrointestinal (GI) motility, and urinary retention.

Many xenobiotics are antimuscarinic. One of the more common is diphenhydramine. Tricyclic antidepressants, (TCAs) phenothiazines, cyclobenzaprine, carbamazepine, atropine, scopolamine, glycopyrrolate, and belladonna alkaloids all have antimuscarinic properties. Plants such as jimson weed contain belladonna alkaloids and may be used recreationally.

Management and Disposition

Initial assessments of the vital signs and the duration of the QRS on ECG are critical. Since many antimuscarinic xenobiotics are also sodium channel blockers, QRS interval should be monitored. Hyperthermia occasionally occurs and is treated with evaporative cooling. Most of these patients require only supportive care, with the administration of benzodiazepines for agitation. A Foley catheter may be needed for treatment of the urinary retention. Occasionally, physostigmine is used as a diagnostic reversal agent for antimuscarinic poisoning, but its risks versus benefits must be considered. The half-life of physostigmine is only about 20 minutes.

Pearls

1. The antihistamine diphenhydramine has sodium channel–blocking properties and may cause significant QRS widening.
2. Physostigmine crosses the blood-brain barrier, so an improvement in antimuscarinic delirium can be elicited with administration of the drug.
3. Glycopyrrolate is an antimuscarinic that does not cross the blood-brain barrier, so delirium does not occur.
4. Many features of anticholinergic toxidrome can mimic a sympathomimetic one—moist axillae on exam may help differentiate the two clinically as the anticholinergic toxidrome prevents sweating, while the sympathomimetic toxidrome promotes it.

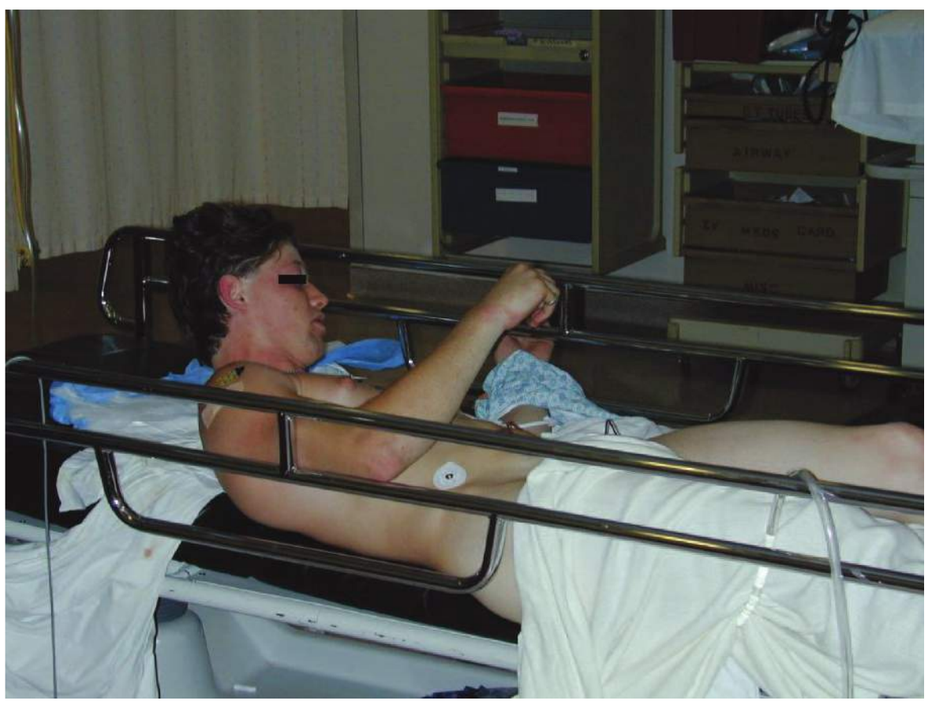

FIGURE 17.16 ■ **Anticholinergic Delirium.** Anticholinergic delirium is manifested by agitation, confusion, and a "picking" behavior. (Photo contributor: Matthew D. Sztajnkrycer, MD, PhD.)

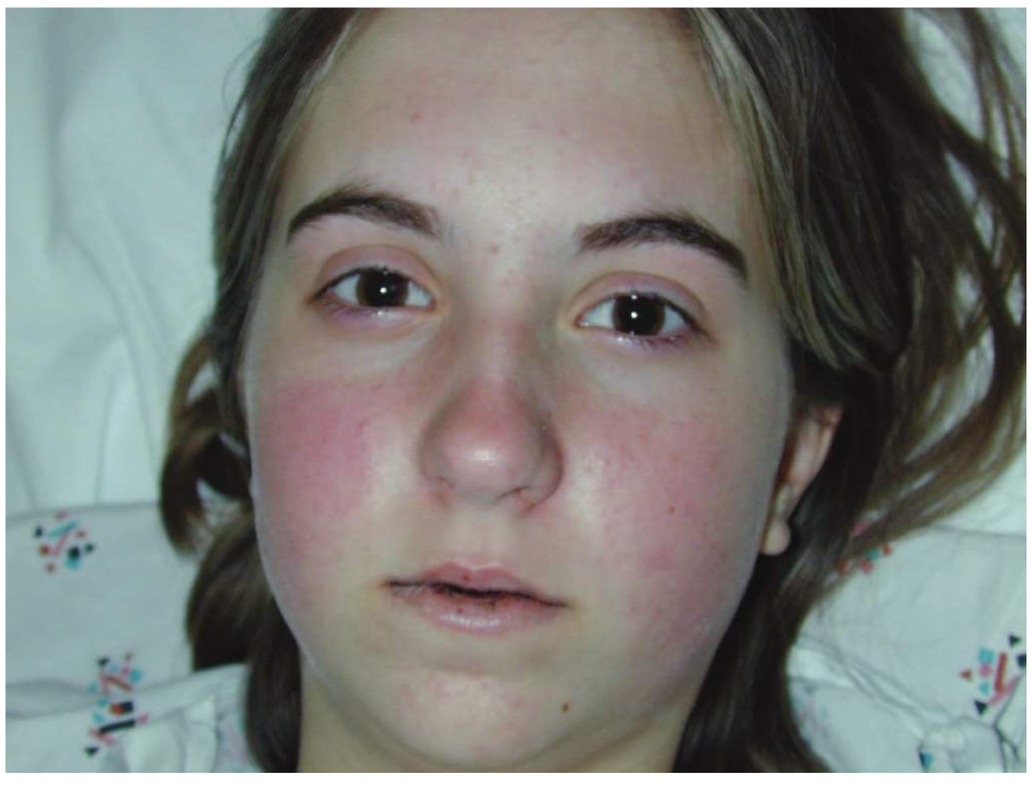

FIGURE 17.15 ■ **Anticholinergic Mydriasis.** Mydriasis and flushing are some of the characteristic findings of anticholinergic toxidrome. (Photo contributor: Matthew D. Sztajnkrycer, MD, PhD.)

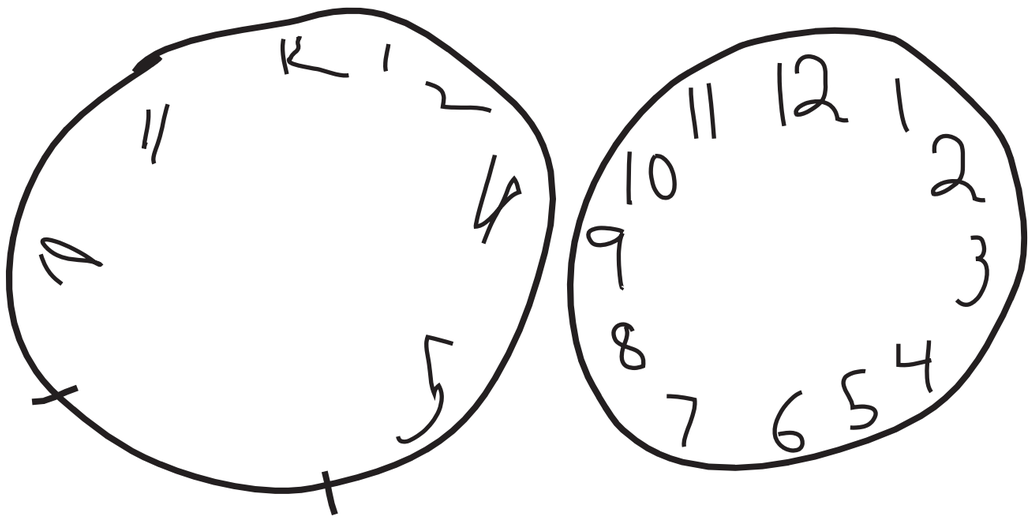

FIGURE 17.17 ■ **Anticholinergic Delirium.** Prior to treatment with physostigmine, a patient suffering acute anticholinergic delirium drew the clock on the left. Following physostigmine administration, the patient drew the clock on the right. (Photo contributor: Division of Medical Toxicology, University of California, San Diego.)

Clinical Summary

Acetylcholine (Ach) is a neurotransmitter of both the central and peripheral nervous systems and is the neurotransmitter for both muscarinic and nicotinic receptors. Inhibition of acetylcholinesterase increases Ach in the synapse. This results in a clinical syndrome producing both muscarinic and nicotinic effects. One mnemonic for the muscarinic effects is "DUMBBEL(L)S": diarrhea, urination, miosis, bronchorrhea, bradycardia, emesis, lacrimation, salivation. Nicotinic effects may include fasciculations, paralysis, and occasionally mydriasis and tachycardia.

The most common cholinergic poisoning occurs after exposure to anticholinesterase insecticides. These include organic phosphorus (OP) compounds and carbamates. OP compounds bind to acetylcholinesterase, and after a period of time, this bond "ages" and becomes permanent. Carbamates are reversible binders of acetylcholinesterase and tend not to cross the blood-brain barrier.

Management and Disposition

The initial management of patients with acute cholinergic poisoning includes decontamination of clothing and skin. The airway should be secured early in the resuscitation as most patients have difficulty oxygenating and ventilating due to bronchorrhea and muscle weakness. Succinylcholine should be avoided as a paralytic agent in cholinergic crisis because succinylcholine requires acetylcholinesterase for its metabolism. Atropine is the initial therapeutic agent and dosing is doubled until the pulmonary secretions are dried. Pralidoxime is administered as early as possible for those patients with acute OP poisoning but would not be of benefit to those patients who have known carbamate poisoning. Seizures should be aggressively treated with benzodiazepines.

Pearls

1. Patients developing central antimuscarinic toxicity during treatment with atropine who still require atropinization for secretion management may be treated with glycopyrrolate. Glycopyrrolate will not treat the central cholinergic effects as it does not cross the blood-brain barrier, but likewise will not cause central antimuscarinic toxicity.
2. The nicotinic clinical findings of cholinergic toxicity can be remembered by the days of the week: MTWtHF: mydriasis, tachycardia, weakness, hypertension, and fasciculations.
3. Nerve agents such as sarin, tabun, and soman are OP compounds and are readily absorbed through inhalational and dermal routes.
4. The pharmaceutical agents physostigmine, neostigmine, and pyridostigmine are carbamates; of these, only physostigmine crosses the blood-brain barrier.

FIGURE 17.18 ■ **Cholinergic Miosis.** Significant miosis seen in a patient with acute cholinergic poisoning. The patient had ingested a pesticide. (Photo contributor: Shannon Langston, MD.)

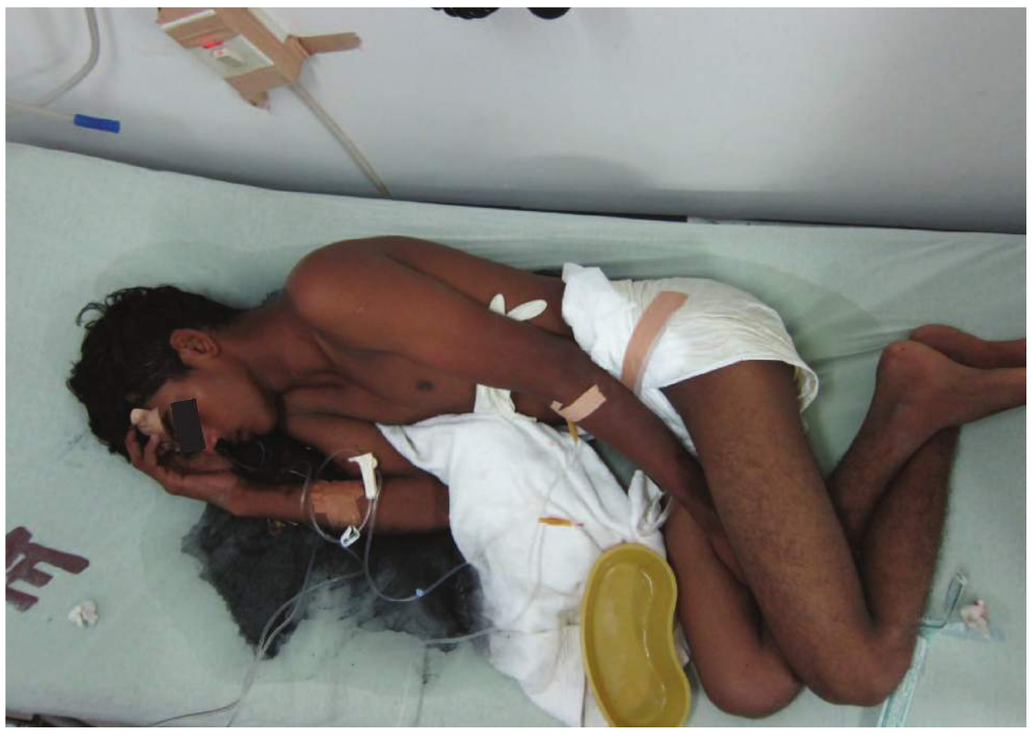

FIGURE 17.19 ■ **Cholinergic Toxidrome.** This patient is manifesting profound muscarinic effects from acute cholinergic poisoning, with intractable vomiting and diarrhea as prominent clinical features. (Photo contributor: Shannon Langston, MD.)

FIGURE 17.20 ■ **Atropine Therapy.** This picture demonstrates the use of several vials of atropine that were required to dry the secretions of a patient with severe acute cholinergic toxicity. Multiple repeat atropine doses are commonly needed to treat cholinergic poisoning. (Photo contributor: Shannon Langston, MD.)

Clinical Summary

Opium is derived from the poppy plant, Papaver somniferum. Opiates are naturally occurring drugs derived from opium and include morphine, codeine, and paregoric. The term opioid refers to drugs with opium-like activity. Heroin is a bitter-tasting white powder; however, most street-grade heroin varies in color from white to dark brown. Mexican "black tar" heroin may be sticky like roofing tar or hard like coal, and appears dark brown to black in color. Diversion and abuse of legal narcotic agents is a common practice that is resulting in increased number of opioid deaths. For example, time-released preparations can be abused by chewing the tablets, snorting crushed tablets, or dissolving and parenterally administering the tablets, bypassing the sustained release mechanism. Significant mucosal necrosis may occur from the repeated snorting of crushed opioid tablets.

The classic opioid toxidrome is a clinical triad of coma, respiratory depression, and miosis. However, opioid-related CNS depression can range from mild sedation to coma. Normal or dilated pupils may occur after overdose of meperidine or pentazocine, or in the setting of CNS hypoxia. Death is typically due to respiratory depression. NCPE is associated with the use of certain opioids, including heroin, methadone, and morphine.

Management and Disposition

Care of these patients focuses upon airway management and antidotal therapy. Whole-bowel irrigation has been advocated after ingestion of sustained release formulations, or in the setting of body-packing and body-stuffing. In the latter, abdominal x-rays are indicated to look for evidence of foreign bodies. Chest radiographs are indicated for signs and symptoms of NCPE. Rhabdomyolysis and cerebral hypoxia may occur after prolonged periods of respiratory and CNS depression. Naloxone is the antidote of choice for significant opioid toxicity. In administering naloxone, care should be taken not to precipitate acute opioid withdrawal. Naloxone drips are indicated with longer acting opioids to avoid rebound respiratory depression from unopposed effects when the initial naloxone dose wears off.

FIGURE 17.22 ■ **Black Tar Heroin.** Black tar heroin has a different appearance and texture than the South American and Asian heroin. Because it has a "gummier" texture, it is usually injected or smoked. Black tar heroin is associated with wound botulism. (Photo contributor: US Drug Enforcement Administration.)

FIGURE 17.21 ■ **Asian Heroin.** Asian heroin tends to be available in a powder form. (Photo contributor: US Drug Enforcement Administration.)

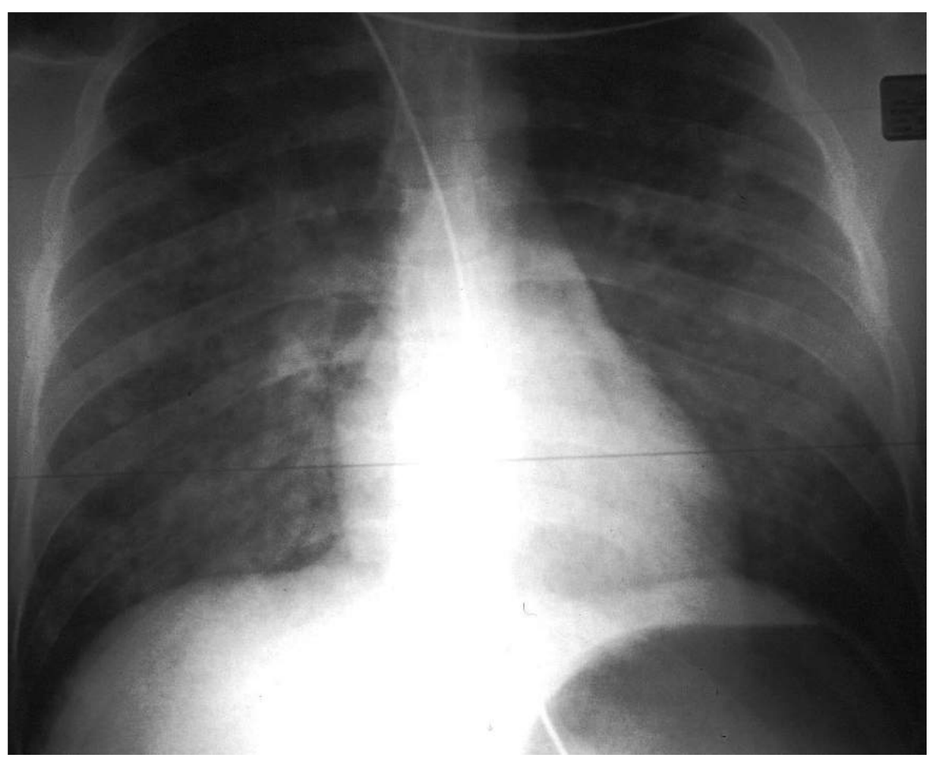

FIGURE 17.23 ■ **Heroin-Related Noncardiogenic Pulmonary Edema.** Noncardiogenic pulmonary edema may occur in the setting of opioid poisoning. The radiograph demonstrates the bilateral airspace opacities and the normal-sized cardiac silhouette. (Photo contributor: Division of Medical Toxicology, University of California, San Diego.)

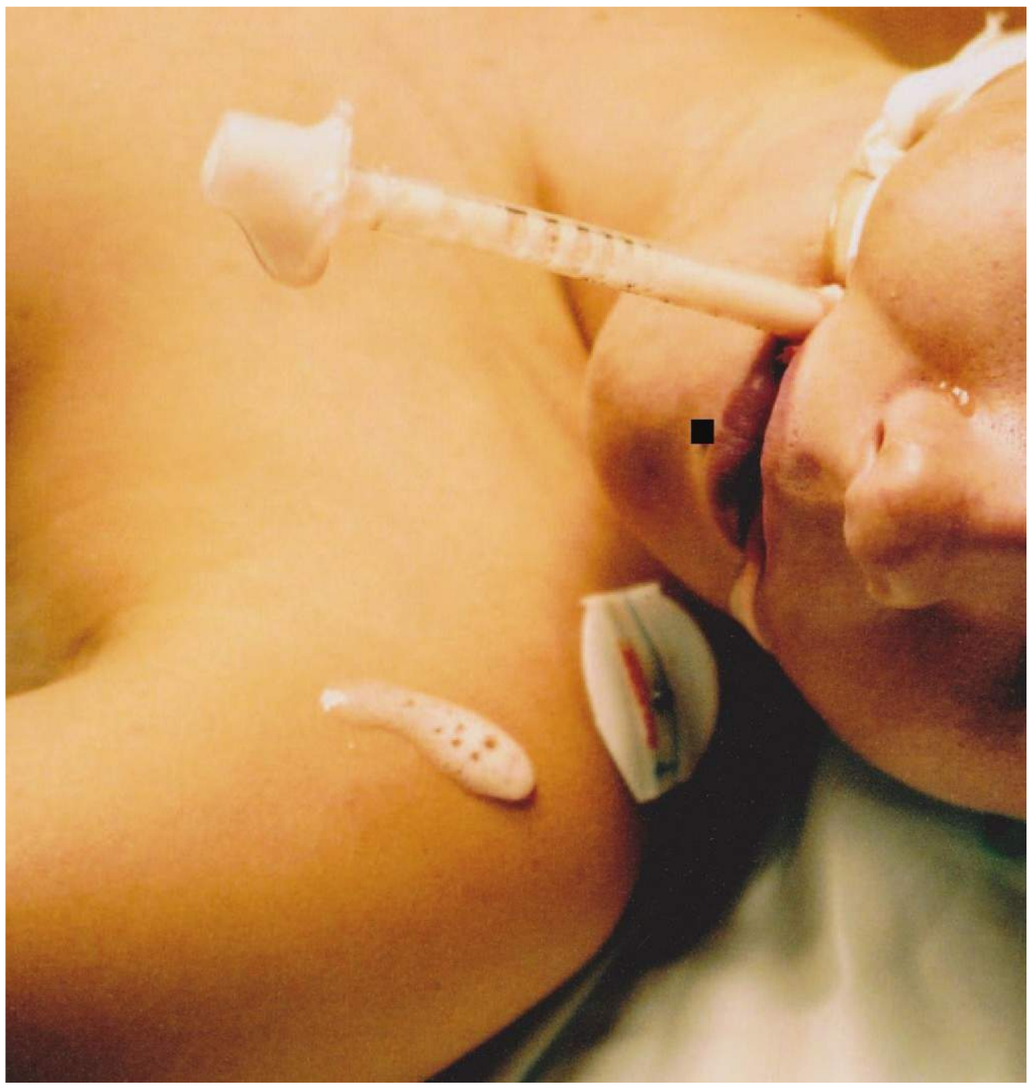

FIGURE 17.24 ■ **Opioid-Induced Noncardiogenic Pulmonary Edema.** Copious frothy expectorant is flowing from the endotracheal tube in this patient with severe opioid-induced noncardiogenic pulmonary edema. (Photo contributor: Matthew D. Sztajnkrycer, MD, PhD.)

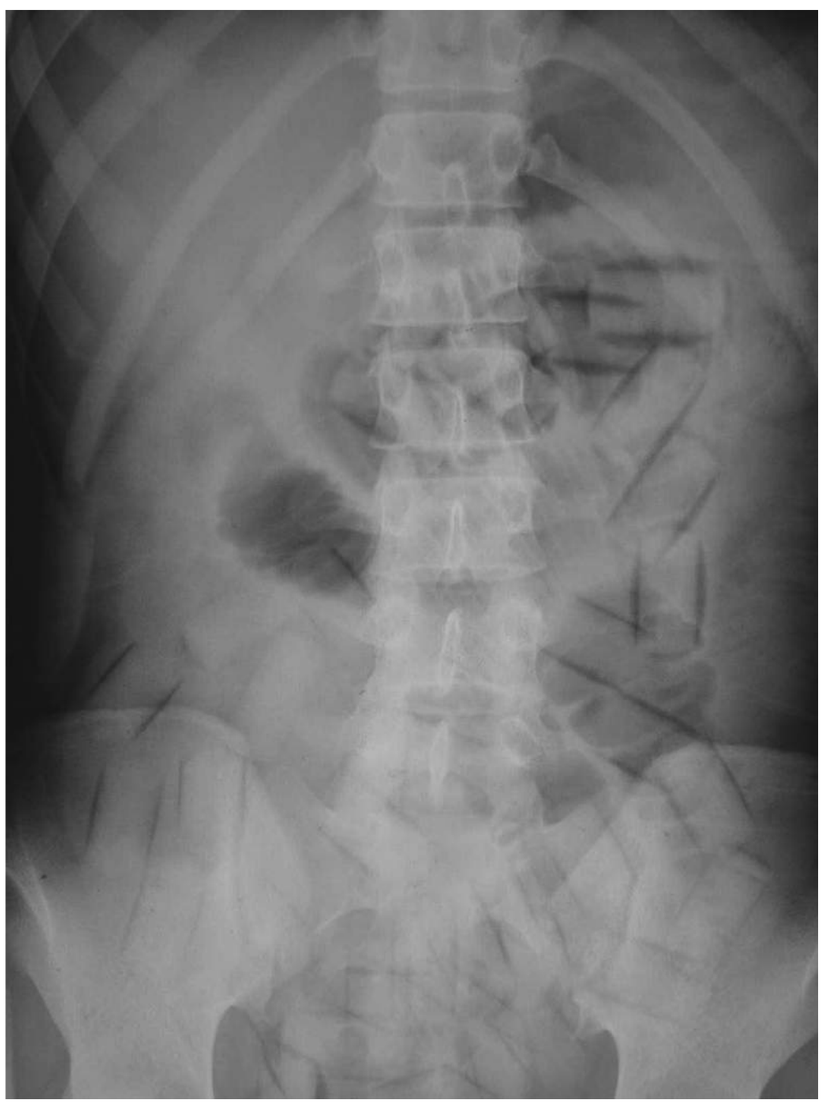

FIGURE 17.25 ■ **Heroin Body-Packing.** KUB radiograph of a "packer" demonstrating the presence of radiopaque foreign bodies. Rupture of a packet may result in severe opioid toxicity. (Photo contributor: Jason Chu, MD.)

Pearls

1. The presence of adulterants such as scopolamine or clenbuterol may mask or alter the appearance of the classic opioid toxidrome and may result in more significant toxicity than the primary drug.
2. Recurrent toxicity and life-threatening respiratory depression may occur following short-term reversal with naloxone administration, especially in body-stuffers or after ingestion of sustained release formulations.
3. The use of naloxone in the setting of tramadol toxicity is relatively contraindicated due to the occurrence of seizures.
4. The use of black tar heroin has been associated with wound botulism.
5. Poisoning from α_2 agonists like clonidine mimics acute opioid poisoning.

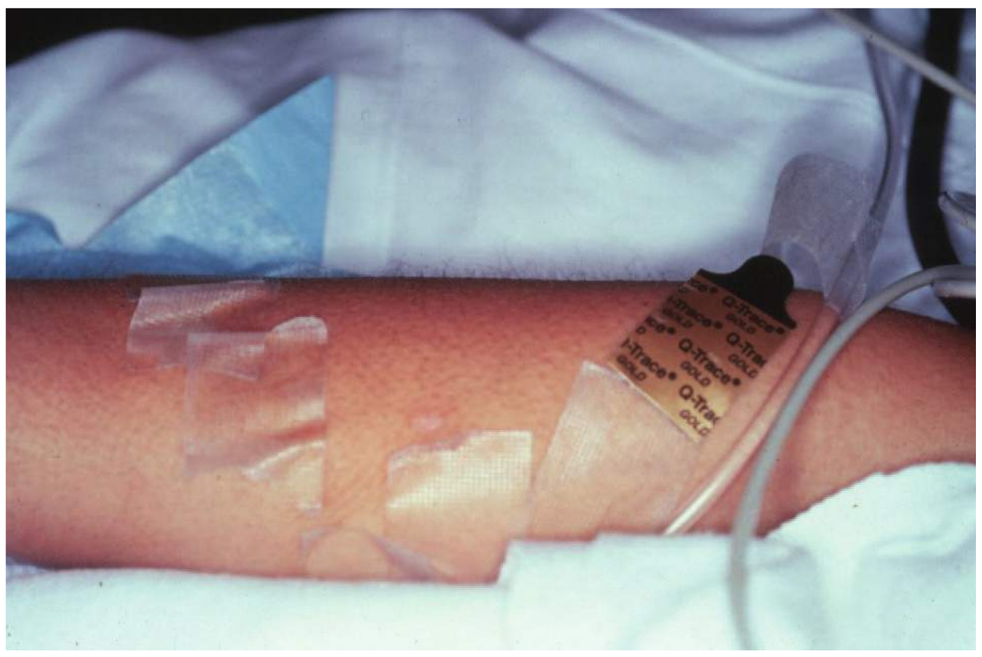

FIGURE 17.26 ■ **Piloerection.** Piloerection may be noted with acute opioid withdrawal. (Photo contributor: Division of Medical Toxicology, University of California, San Diego.)

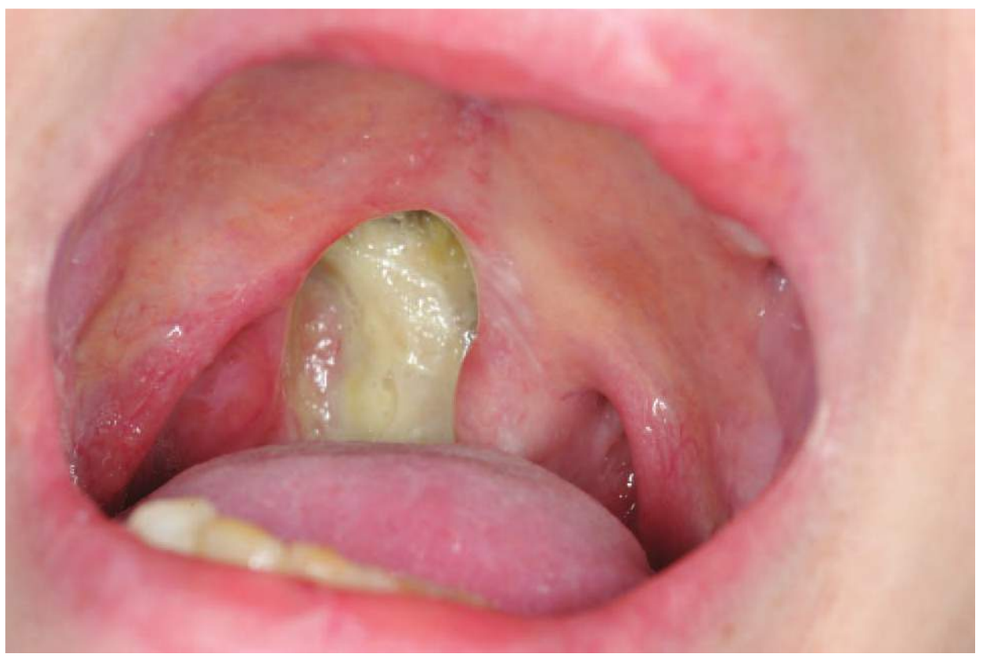

FIGURE 17.27 ■ **Opioid Mucosal Necrosis.** In this patient, significant necrosis of the soft palate in seen. The necrosis occurred secondary to repeated opioid abuse by snorting crushed oxycodone tablets. (Photo contributor: Lawrence B. Stack, MD.)

ACETAMINOPHEN POISONING

Clinical Summary

Acetaminophen is a widely available analgesic and antipyretic agent. It is commonly found in combination with opioids, decongestants, antihistamines, and other over-the-counter and prescription products. Patients may complain of nausea and vomiting shortly after a toxic ingestion, but may also be asymptomatic. Signs and symptoms of acute liver injury typically occur within 36 hours after acute ingestion. Occasionally, patients present to the emergency department after developing evidence of hepatotoxicity, not realizing that the large ingestion of an acetaminophen-based product is the etiology.

In the overdose setting, acetaminophen exerts its toxic effects via a metabolite that is created via the P-450 enzyme system. The metabolite causes centrilobular necrosis of the liver which may lead to fulminant hepatic failure. Renal failure may also occur. Fatalities from hepatic failure usually occur 3 to 5 days after the ingestion. Treatment includes the administration of N-acetylcysteine (NAC), which can prevent acetaminophen-induced hepatotoxicity if initiated within 8 hours of the acute ingestion.

Management and Disposition

Activated charcoal may be considered in patients who present within 2 hours of acetaminophen overdose. A serum acetaminophen level drawn at 4 hours after a single acute ingestion can be plotted on the Rumack-Matthew nomogram to determine the need for treatment. If the serum level is at or above the treatment line, the patient should be treated with a standard course of oral or intravenously administered NAC. Patients who require administration of NAC should be admitted to the hospital.

Pearls

1. Acetaminophen is a common agent in many over-the-counter medications. Patients who overdose on these medications require routine checking of a serum acetaminophen level to identify those who may need treatment with NAC.
2. The formulation of oral NAC is available in a 20% solution. The 20% solution comprises 20 g of NAC per 100 mL of solution. For the average 70-kg adult, the initial oral loading dose of 140 mg/kg would be 9.8 g, or approximately 50 mL of the 20% solution.
3. To enhance palatability, oral NAC can be diluted into a beverage of choice and served in a cup with a lid and straw.
4. Massive ingestions of acetaminophen may result in an anion gap metabolic acidosis.

FIGURE 17.28 ■ **Acetaminophen Overdose.** Multiple acetaminophen-containing pills are seen in the vomit of an overdose patient. The patient had ingested the pills a few hours prior to presentation in a suicide attempt. (Photo contributor: Alan B. Storrow, MD.)

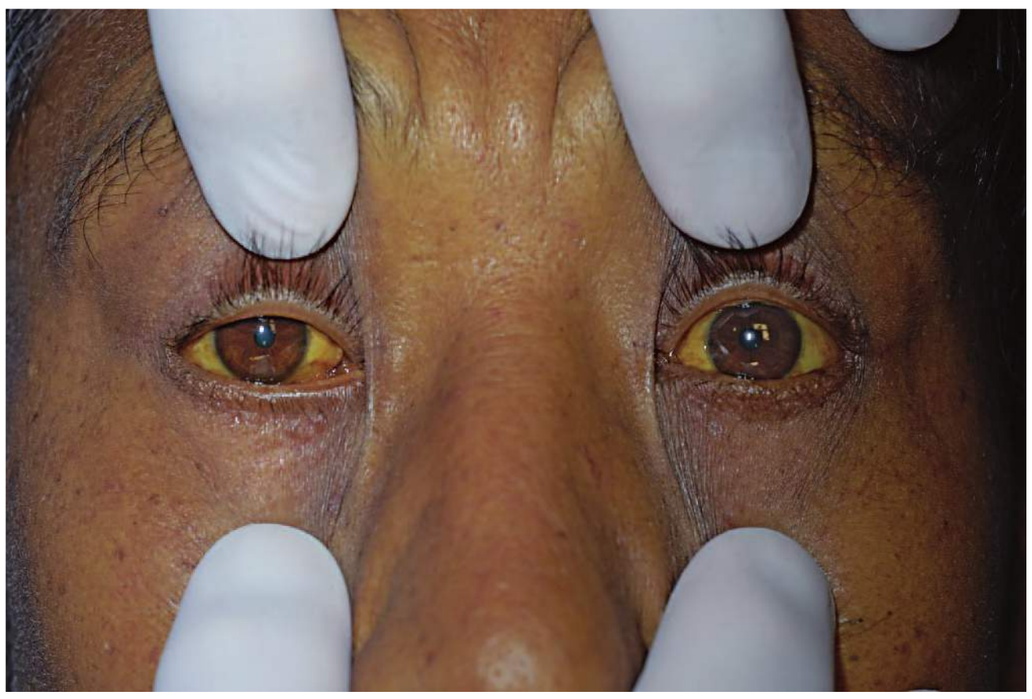

FIGURE 17.29 ■ **Acute liver failure.** This patient developed hepatic failure with marked jaundice as a result of an intentional acetaminophen overdose. (Photo contributor: R. Jason Thurman, MD.)

SALICYLATE POISONING

Clinical Summary

Salicylates are a common cause of analgesic poisoning. Acute ingestions of large quantities of aspirin may have delayed absorption due to the formulation of the drug or the formation of bezoars. Poisoning may occur with chronic ingestions as well, particularly in older patients.

Early effects after ingestion include GI irritation which may lead to nausea and vomiting. Classically, salicylate-poisoned patients present with a mixed acid-base picture. Central stimulation of the respiratory drive results in a primary respiratory alkalosis. As a result of disrupted energy mechanics and decreased adenosine triphosphate (ATP) production, metabolic acidosis and lactate accumulation occur. The initial pH of the patient's serum may be acidemic or alkalemic depending on the predominant acid-base disorder at the time of blood sampling. Ketonuria may also be noted. Hyperthermia occurs due to the generation and release of heat secondary to uncoupling of oxidative phosphorylation. Coma and seizures indicate severe nervous system toxicity and are associated with poor outcomes. Increased capillary permeability may result in NCPE and cerebral edema.

Management and Disposition

Fluid resuscitation to replace volume depletion is paramount early in the presentation. Since salicylate is a weak acid, alkalinizing the serum to a pH between 7.45 and 7.55 range traps the salicylate in an ionized form, decreasing entry into the CNS. Similarly, urinary alkalinization prevents tubular reabsorption, thereby enhancing the renal elimination of the salicylic acid. Because of the underlying metabolic acidosis and bicarbonate-induced hypokalemia, potassium replacement is usually needed in order to alkalinize the urine. Hemodialysis should be considered for deterioration in the acid-base status of the patient, renal failure, NCPE, or cerebral edema. A rapidly rising serum salicylate concentration is another consideration for dialysis. Patients with chronic ingestions may meet clinical criteria for extracorporeal elimination even with serum salicylate levels in the 40 to 50 mg/dL range. Admission should be strongly considered for any toxic salicylate ingestion.

Pearls

1. Oil of wintergreen is typically 98% methylsalicylate (1400 mg/mL). One teaspoon (5 mL) provides the equivalent 7000 mg of salicylic acid.
2. If a patient with severe salicylism must be intubated, careful attention should be made to mimic the minute ventilation of the nonparalyzed patient. If a respiratory acidosis is allowed to occur, the patient will become severely acidemic which allows the salicylate to further distribute into the tissues and poison the mitochondria.

FIGURE 17.30 ■ **Aspirin Bezoar.** Pill bezoar found in the GI tract of a patient who ingested approximately 750 enteric-coated aspirin tablets. At the time of death, approximately 13 hours after ingestion, the serum salicylate level was 128 mg/dL. More than 300 partially digested pills remained in the GI tract on postmortem. (Photo contributor: Jared M. Orrock, MD.)

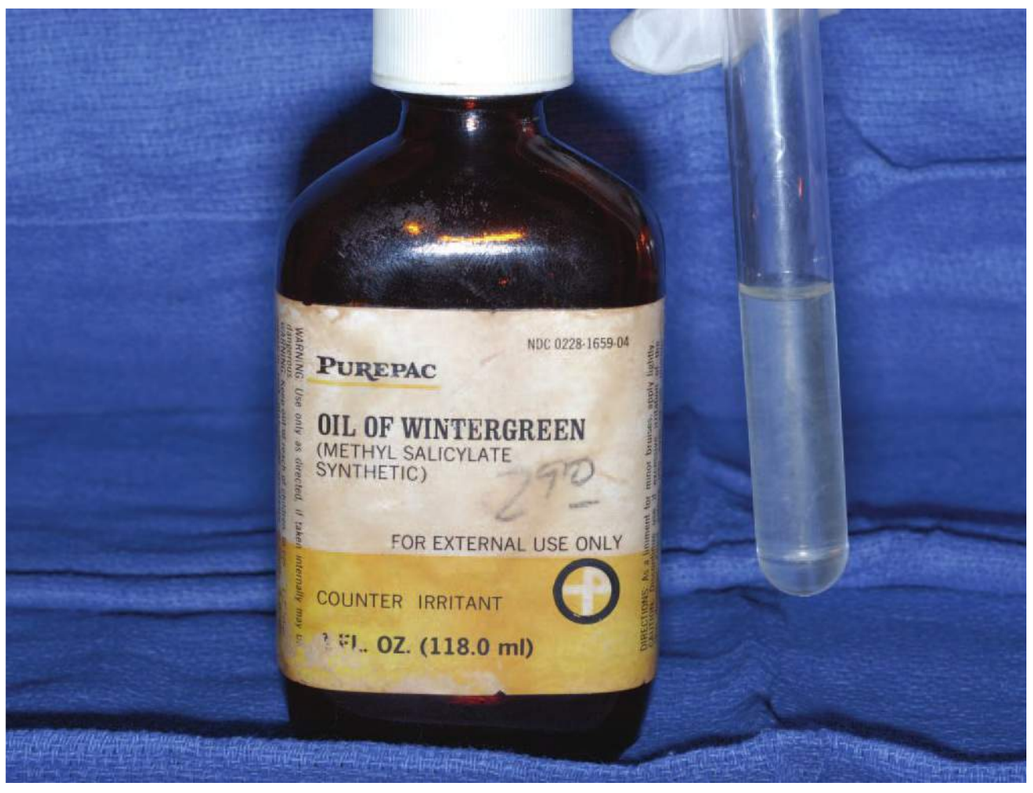

FIGURE 17.31 ■ **Oil of Wintergreen.** Severe salicylism may occur from ingestion of products that contain a high concentration of oil of wintergreen (methylsalicylate). This bottle of oil of wintergreen is a 98% solution, which contains the equivalent of 7000 mg of salicylate per teaspoon. (Photo contributor: R. Jason Thurman, MD.)

3. While acetazolamide administration results in alkalinization of the urine, the excretion of the bicarbonate into the urine comes at the expense of promoting acidemia, which could further drive the salicylate into the CNS and enhance toxicity.
4. The agent diflunisal will cause markedly elevated serum salicylate levels in the absence of other clinical or biochemical indicators of toxicity.

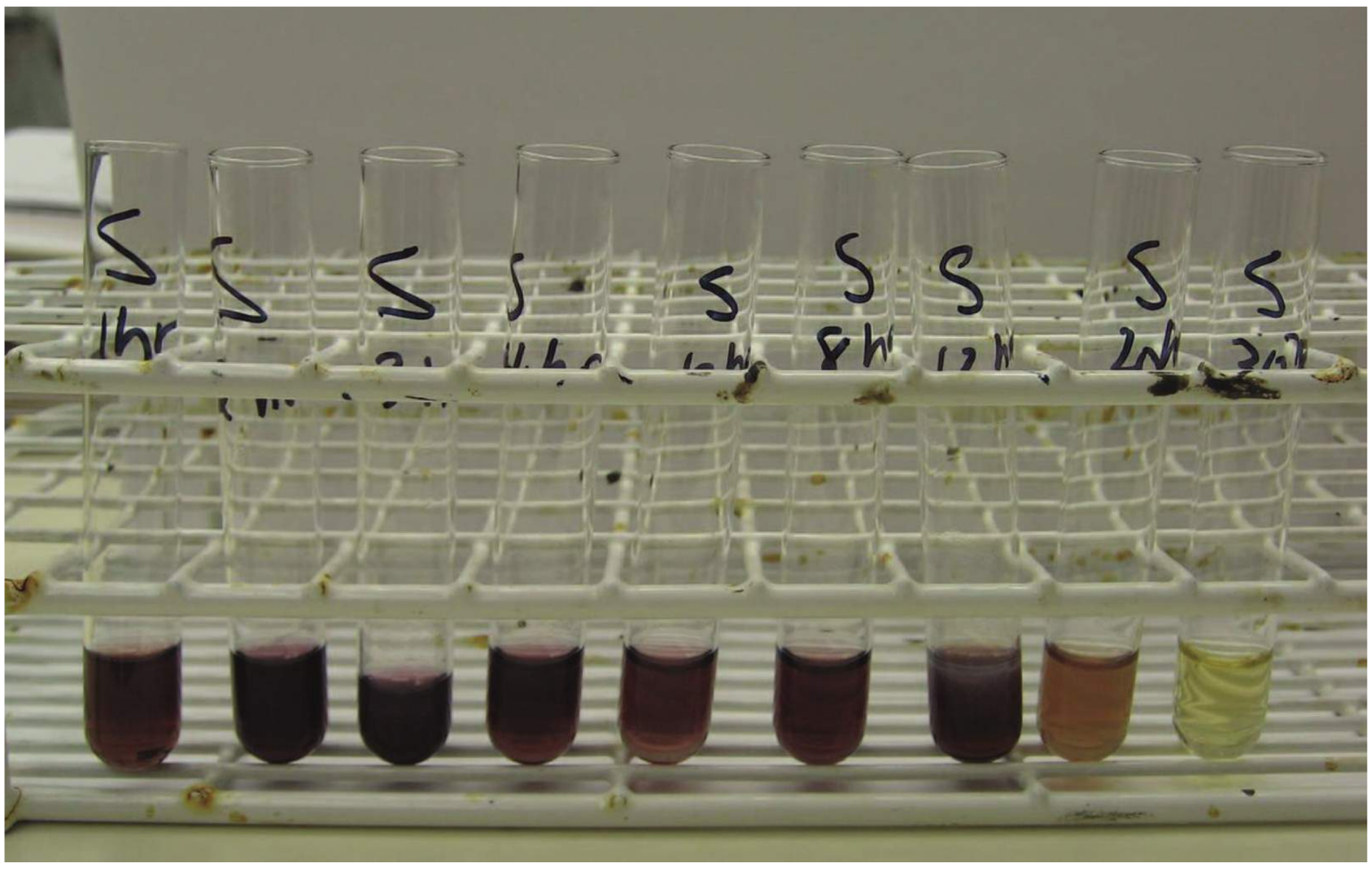

FIGURE 17.32 ■ **Trinder Reagent.** In the presence of salicylates, the addition of Trinder reagent to urine specimen will yield a purple color. This picture demonstrates the reaction to Trinder reagent from urine samples collected serially 1 hour to 30 hours after ingestion of 650 mg aspirin. (Photo contributor: Sheila Dawling, PhD.)

TOXIC ALCOHOL INGESTION

Clinical Summary

The commonly available toxic alcohols include ethylene glycol, methanol, and isopropanol. Ethylene glycol is a sweet-tasting liquid commonly found in antifreeze, as well as in brake fluid. Methanol is used in lock deicers, windshield wiper fluid, and industrial solvents. Isopropanol is commonly marketed as "rubbing" alcohol, although it is also found in nonstreaking glass and window cleaners, soaps, cosmetics, and antifreezes.

The parent toxic alcohols have the potential to intoxicate, but are not otherwise toxic to end organs. Sequential metabolism via alcohol dehydrogenase and aldehyde dehydrogenase produces the organic acids responsible for end-organ toxicity and metabolic acidosis. Ethylene glycol is metabolized to glycolic and oxalic acids; the former is responsible for the acidosis, while the latter is responsible for calcium oxalate deposition in the renal tubules and delayed acute renal failure (24-72 hours postingestion). Hypocalcemia may occur with severe intoxication. Cranial nerve palsies may also occur 5 to 20 days after ingestion. Although less intoxicating than ethanol, methanol is metabolized to formic acid, which is responsible for both acidosis and direct retinal toxicity. Patients often report blurred or dim vision ("snowstorm") prior to development of objective signs, including optic disc hyperemia, pupillary dilation, and poor accommodation. Pancreatitis and delayed basal ganglia lesions may occur. Isopropanol metabolism is limited to ketone formation and does not result in significant acidosis.

Management and Disposition

Decontamination options are limited, as activated charcoal does not bind alcohol and GI absorption is rapid. Emergency management is directed toward supportive care, diagnosis of the agent, and prevention of further metabolism. Methanol, ethylene glycol, and isopropanol levels may not be readily available. However, care should be taken in interpreting ancillary data, such as urinary fluorescence and the osmolar gap. Both ethanol and fomepizole competitively inhibit alcohol dehydrogenase. Both of these reduce metabolism of the parent compound, but do nothing for the toxic metabolites. Administration of folate (methanol) or pyridoxine and thiamine (ethylene glycol) may inhibit organic acid production or increase degradation by shunting metabolism to alternate pathways. Hemodialysis is indicated for signs of end-organ toxicity (eg, anion gap acidosis, renal failure, mental status changes) and should be considered for elevated toxic alcohol levels.

Pearls

1. Provided adequate metabolism has occurred, isopropanol ingestion will demonstrate the presence of large amounts of ketones on a urine dipstick assay.
2. Only a few sips of concentrated methanol or ethylene glycol are required to produce toxicity in a toddler;

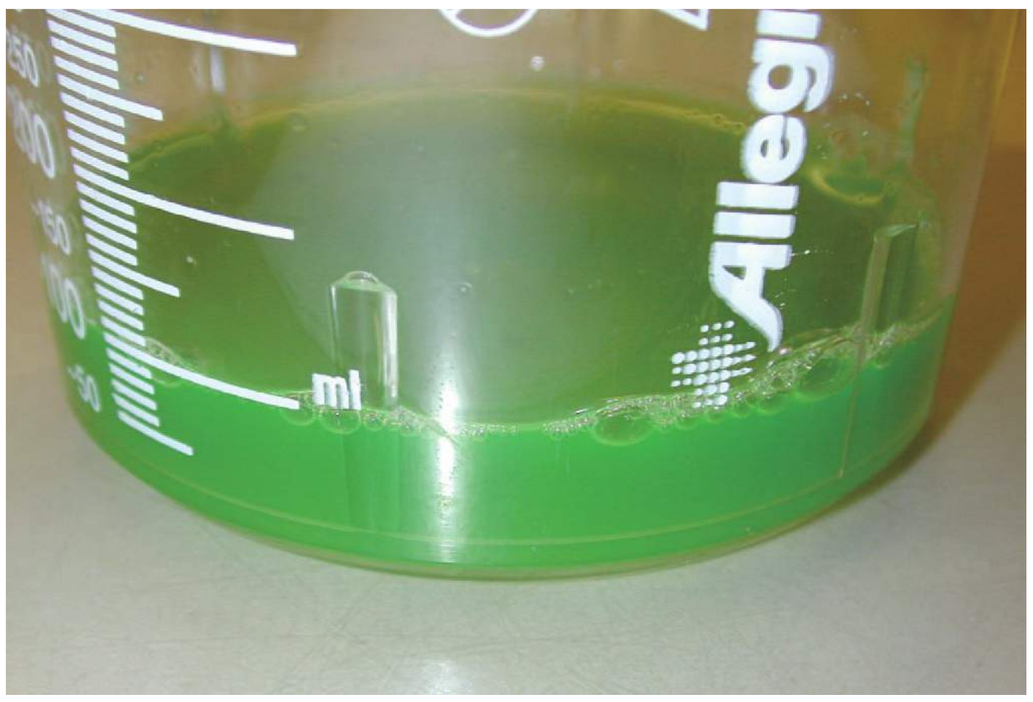

FIGURE 17.33 ■ **Antifreeze.** Addition of fluorescein to antifreeze gives colorless ethylene glycol its green appearance. (Photo contributor: Matthew D. Sztajnkrycer, MD, PhD.)

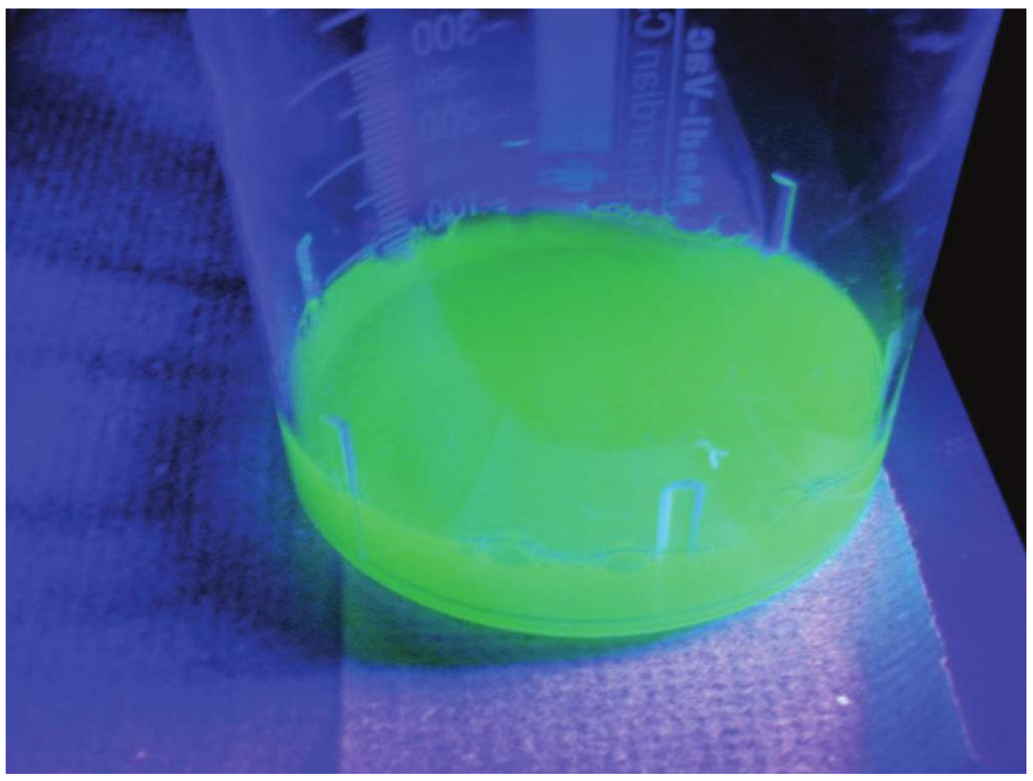

FIGURE 17.34 ■ **Antifreeze Fluorescence.** Application of a black light to antifreeze will demonstrate the fluorescence in body fluids, provided fluorescein has been added. This sample was obtained from the emesis of an overdose patient. (Photo contributor: Matthew D. Sztajnkrycer, MD, PhD.)

these ingestions should be viewed as a "one pill can kill" exposure.

3. Coingestion of ethanol may delay development of eventual toxicity due to preferential blockade of alcohol dehydrogenase.
4. Both ethanol and fomepizole inhibit metabolism of the parent compounds.
5. Due to the occurrence of hypocalcemia in ethylene glycol poisoning, careful monitoring of ionized calcium is critical when using sodium bicarbonate in these patients.

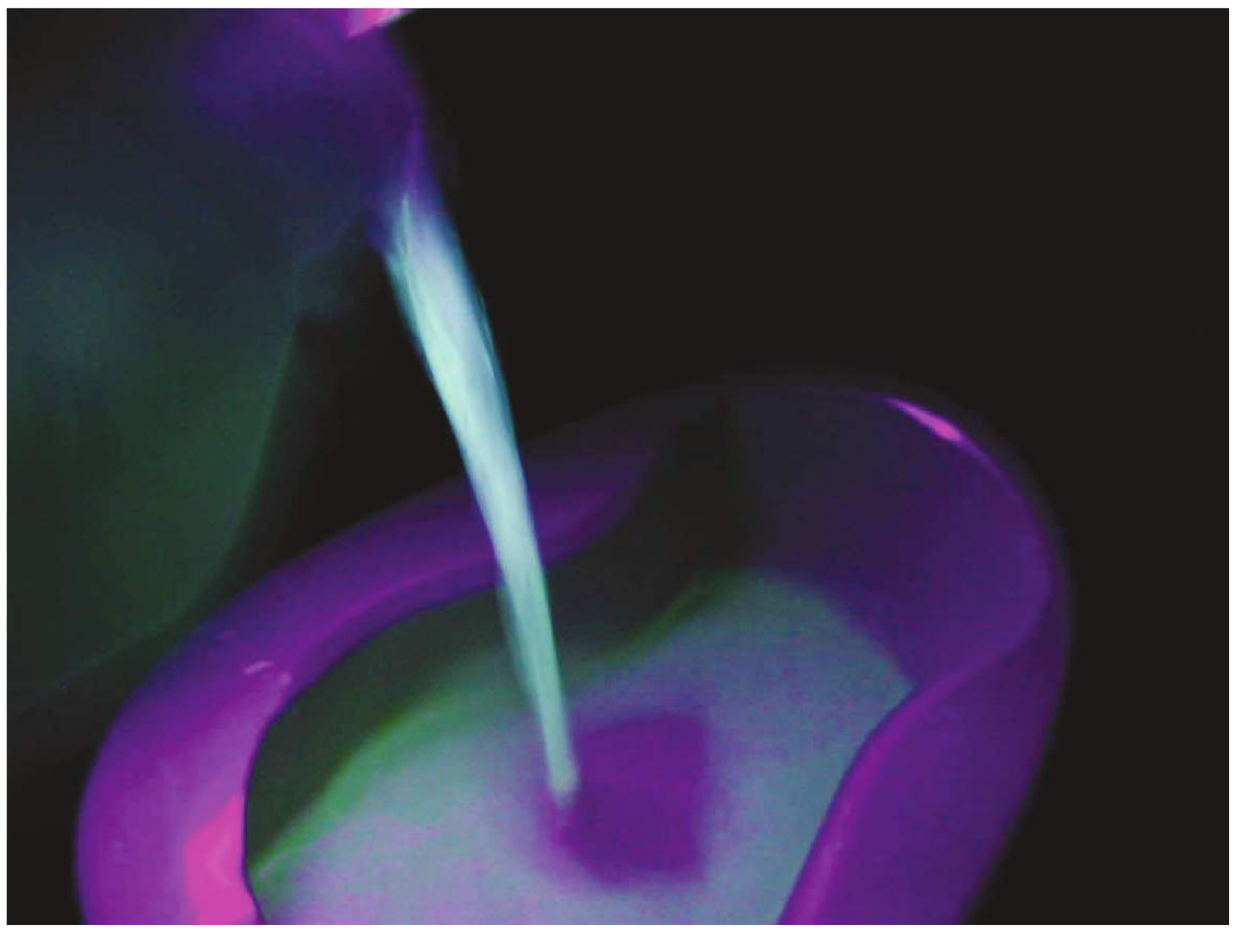

FIGURE 17.35 ■ **Urine Fluorescence.** Under black light, the urine of this ethylene glycol overdose patient shows a bright fluorescence. (Photo contributor: Matthew D. Sztajnkrycer, MD, PhD.)

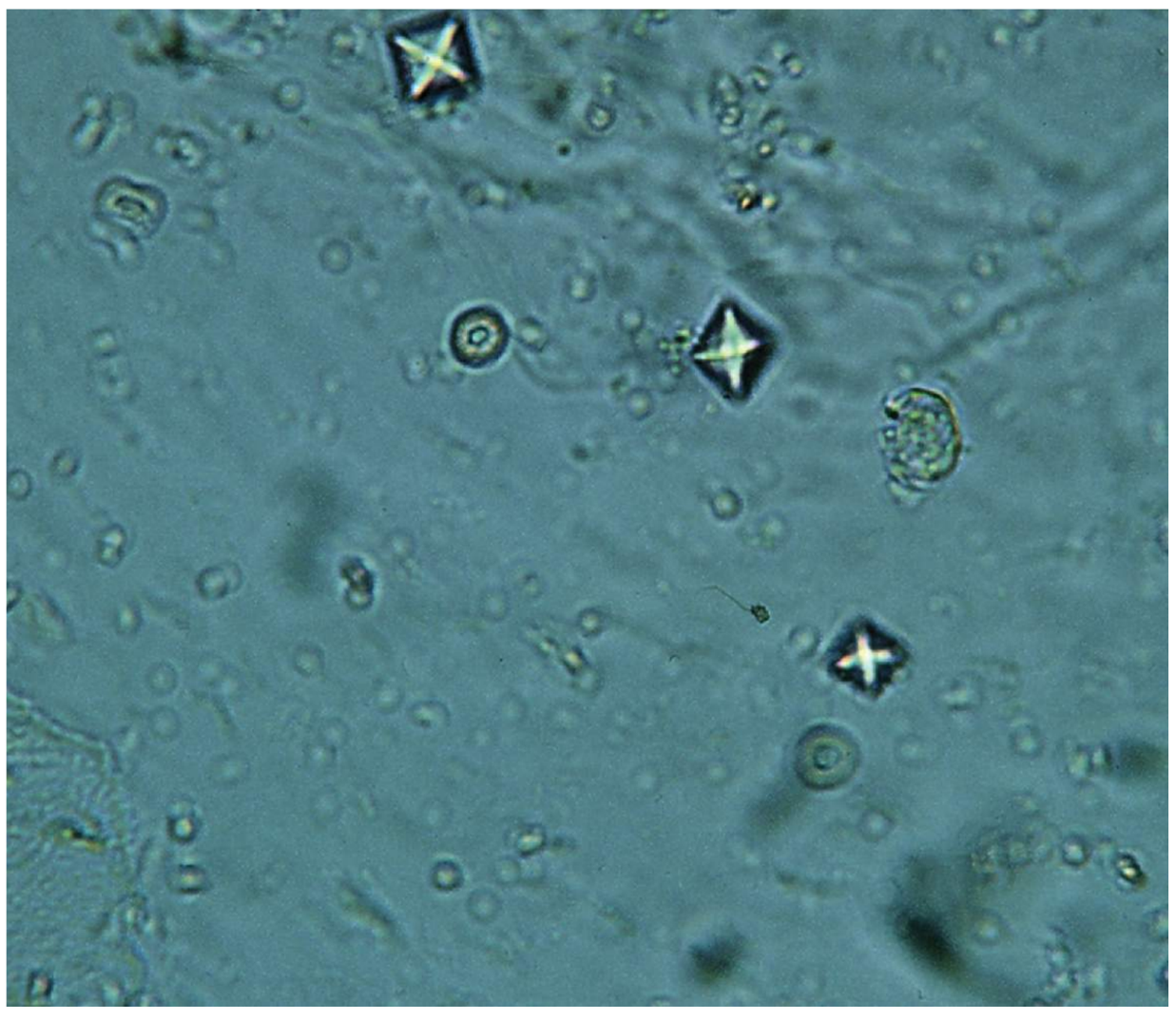

FIGURE 17.36 ■ **Calcium Oxalate Crystals.** Calcium oxalate crystals may be seen in the urine of the patient who ingested ethylene glycol and metabolized the parent compound to create oxalic acid. (Reproduced with permission from Strasinger SK, Di Lorenzo MS. Urinalysis and Body Fluids. 4th ed. Philadelphia, PA: F.A. Davis Company; 2001.)

TRICYCLIC ANTIDEPRESSANT POISONING

Clinical Summary

Despite the advent of the newer antidepressant agents (eg, serotonin-specific reuptake inhibitors), tricyclic antidepressant (TCA) toxicity remains a significant cause of poisoning morbidity and mortality in the United States. TCAs exert effects on multiple systems, including voltage-gated sodium channels, potassium channels, H_1-histamine receptors, D_2-dopamine receptors, M_1-muscarinic receptors, α_1-adrenergic receptors, and the GABA-A receptor complex.

TCA toxicity is related to pharmacological effects on the myocardium, CNS, and vasculature. M_1-muscarinic receptor blockade may result in an anticholinergic toxidrome. CNS toxicity may range from sedation to coma. Seizures, agitation, and delirium may occur. Inhibition of voltage-gated sodium channels results in characteristic widening of the QRS complex. A limb-lead QRS duration greater than 120 ms is associated with an increased incidence of seizures, while a limb-lead QRS duration greater than 160 ms is associated with an increased incidence of ventricular dysrhythmias. Similarly, in adults, a terminal R wave in lead aVR greater than or equal to 3 mm is associated with increased risk of seizure or dysrhythmias.

Management and Disposition

Signs and symptoms of significant overdose typically occur early. All patients presenting after TCA overdose should receive continuous cardiac monitoring and an ECG. Aggressive airway management may be indicated. No specific antidote exists for TCA poisoning. Benzodiazepines are the agent of choice for seizures. Management of QRS widening involves intravenous administration of sodium bicarbonate; controversy exists regarding optimal method of administration (intermittent dosing versus continuous infusion). Symptomatic patients should be admitted to the intensive care unit (ICU) due to the potential for rapid deterioration.

Pearls

1. In one study, half of all patients presenting to emergency department with trivial signs of poisoning had catastrophic deterioration within 1 hour.
2. Flumazenil and physostigmine are both contraindicated in the management of patients with ECG evidence of TCA poisoning.
3. Other xenobiotics that may cross-react with the TCA immunoassay on the urine drug screen include diphenhydramine, carbamazepine, cyclobenzaprine, and quetiapine.

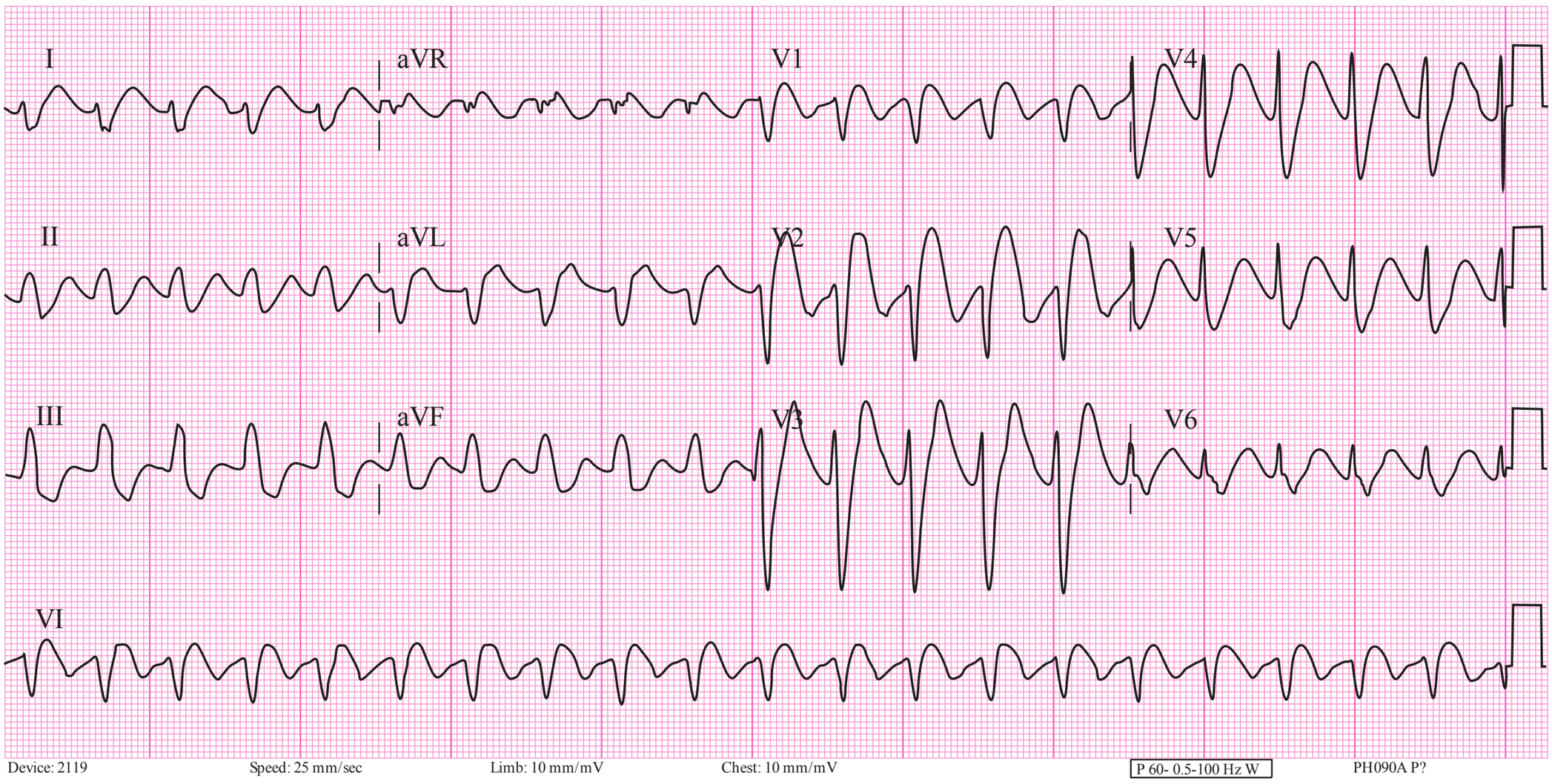

FIGURE 17.37 ■ **TCA Cardiotoxicity.** A 12-lead EKG of a patient who ingested a massive quantity of amitriptyline, demonstrating QRS widening. The patient presented awake and alert, but rapidly became obtunded. (Photo contributor: Thomas Babcock, MD and Clay Smith, MD.)

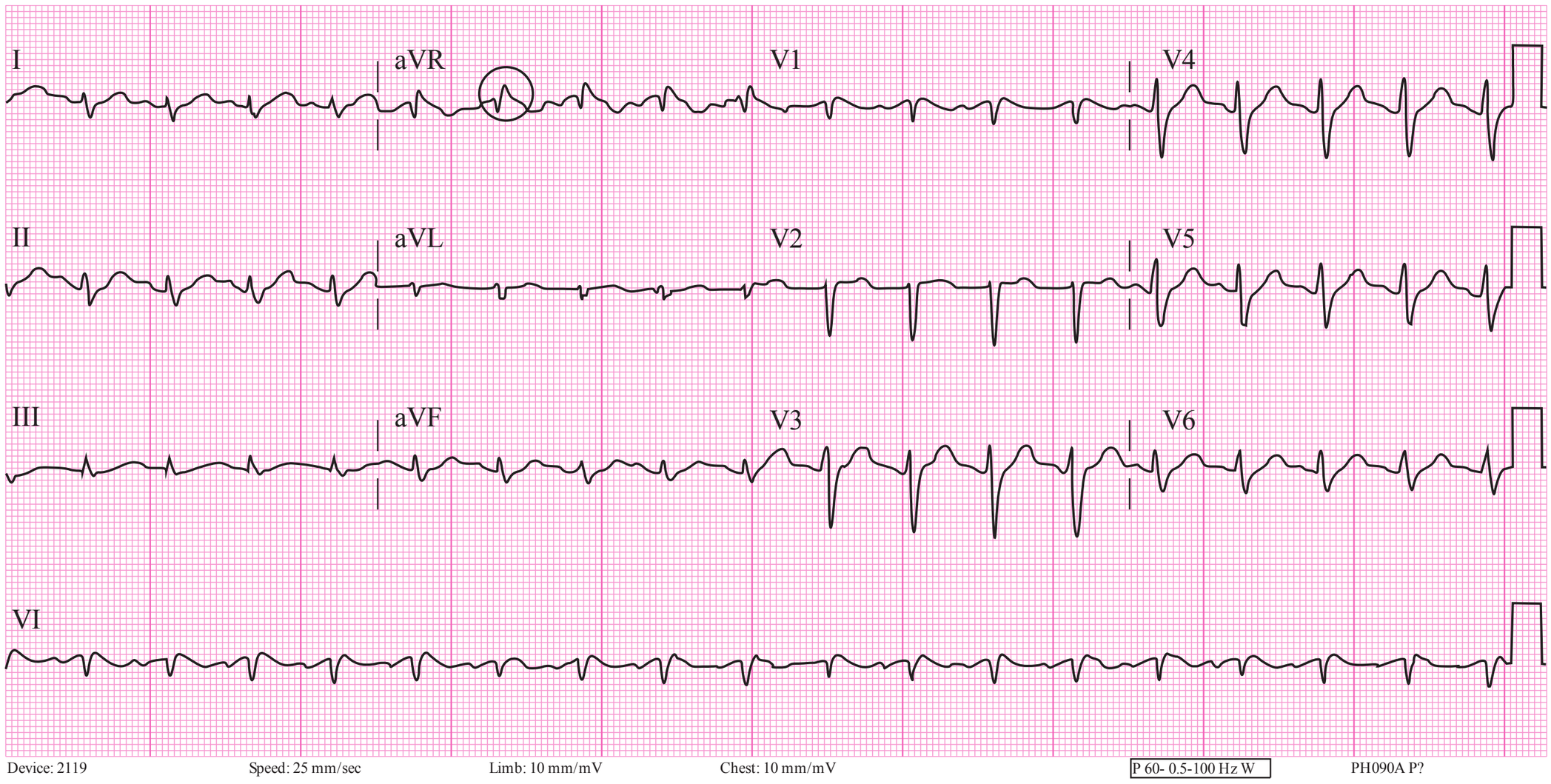

FIGURE 17.38 ■ **TCA Cardiotoxicity—Treated.** Repeat 12-lead EKG of the patient from Fig. 17.37 approximately 2 hours and 45 minutes after the first EKG. A total of 12 amperes of sodium bicarbonate had been administered intravenously. This EKG demonstrates the terminal R wave changes in aVR associated with sodium channel–blocking effects (circle). (Photo contributors: Thomas Babcock, MD, and Clay Smith, MD.)

POISONING BY β-BLOCKER AND CALCIUM CHANNEL BLOCKER AGENTS

Clinical Summary

β-Blockers and calcium channel blockers have various clinical indications, including the management of hypertension, myocardial infarction, and cardiac dysrhythmias, as well as the treatment of noncardiovascular conditions (eg, glaucoma, thyrotoxicosis, migraine headache prophylaxis). β-Blocking agents may be selective for B_1-adrenergic receptors, or nonselective. With therapeutic use, the commonly available calcium channel blockers are selective for the membrane-bound L-type calcium channel. Inhibition of this channel prevents influx of extracellular calcium.

Toxicity presents as an exaggeration of clinical effects, with significant toxicity manifesting predominantly as bradycardia and hypotension. β-Blocker toxicity may result in hypoglycemia, especially in children. Certain agents, such as propranolol, are associated with CNS toxicity (including seizures and CNS depression) and fast sodium channel blockade (analogous to TCA toxicity). Calcium channel blocker toxicity is associated with hyperglycemia, believed to be secondary to impaired insulin release (a calcium-dependent process) and impaired peripheral utilization.

Management and Disposition

The use of aggressive GI decontamination (eg, whole-bowel irrigation) has been advocated for sustained release preparations. In addition to standard Advanced Cardiac Life Support (ACLS) measures, glucagon has been used as a specific antidote for β-blocker toxicity. No treatment has been universally successful in the management of severe calcium channel blocker toxicity. Calcium, glucagon, high-dose insulin euglycemia, and intravenous lipid emulsion have all been tried with variable success. Management of these patients should involve early consultation with a poison control center or toxicologist.

Pearls

1. Topical β-adrenergic blocker administration (eg, for glaucoma) can result in significant systemic toxicity.
2. Development of toxicity may be appreciably delayed after ingestion of sustained-release formulations.
3. The presence of hyperglycemia versus hypoglycemia may help differentiate calcium channel blocker poisoning from β-blocker poisoning, respectively.
4. Due to the potential for significant local tissue toxicity, calcium chloride therapy should optimally be administered through a central venous catheter.

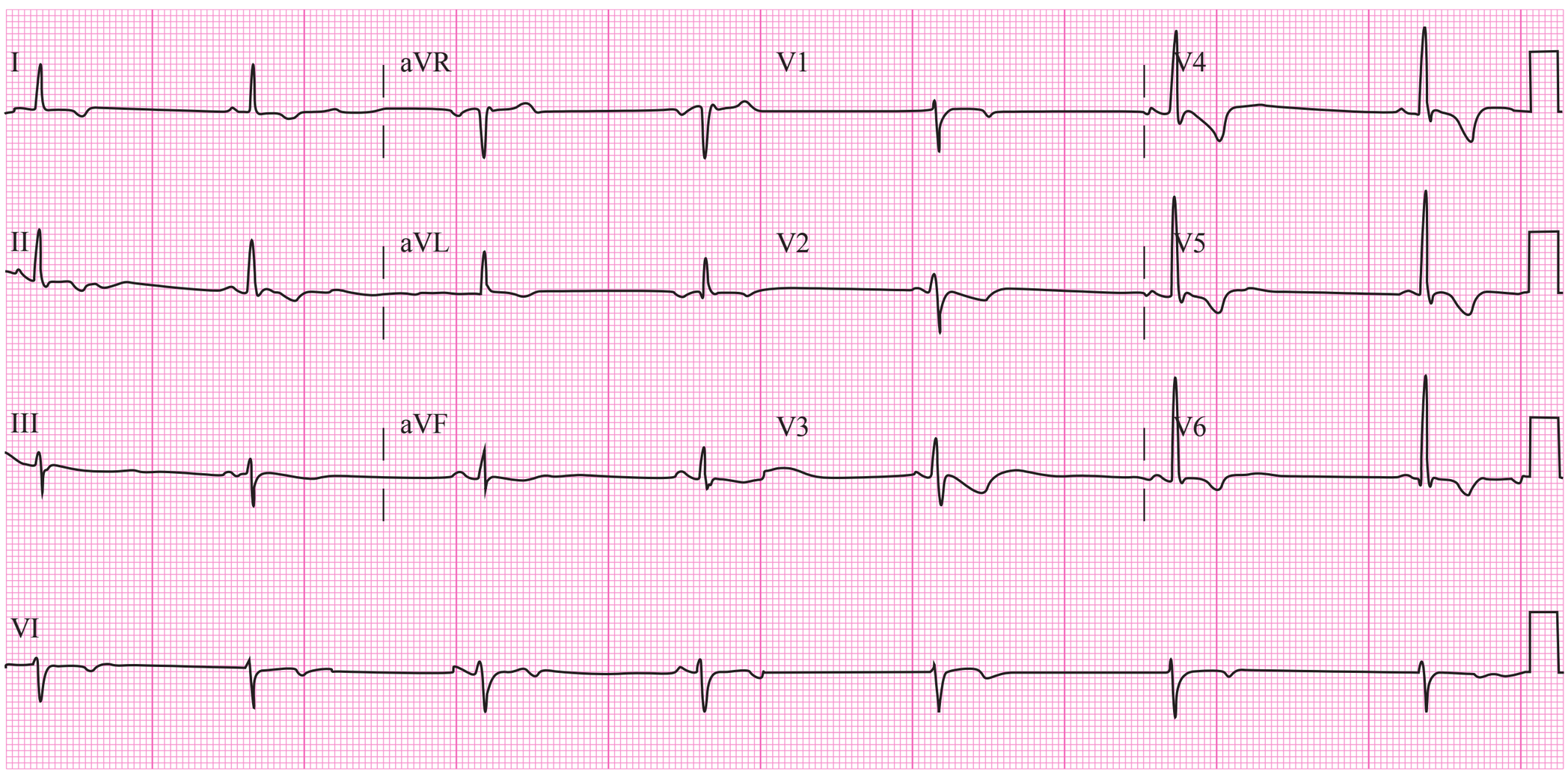

FIGURE 17.39 ■ **β-Blocker Overdose.** Atenolol poisoning resulting in severe bradycardia. (Photo contributor: Saralyn R. Williams, MD.)

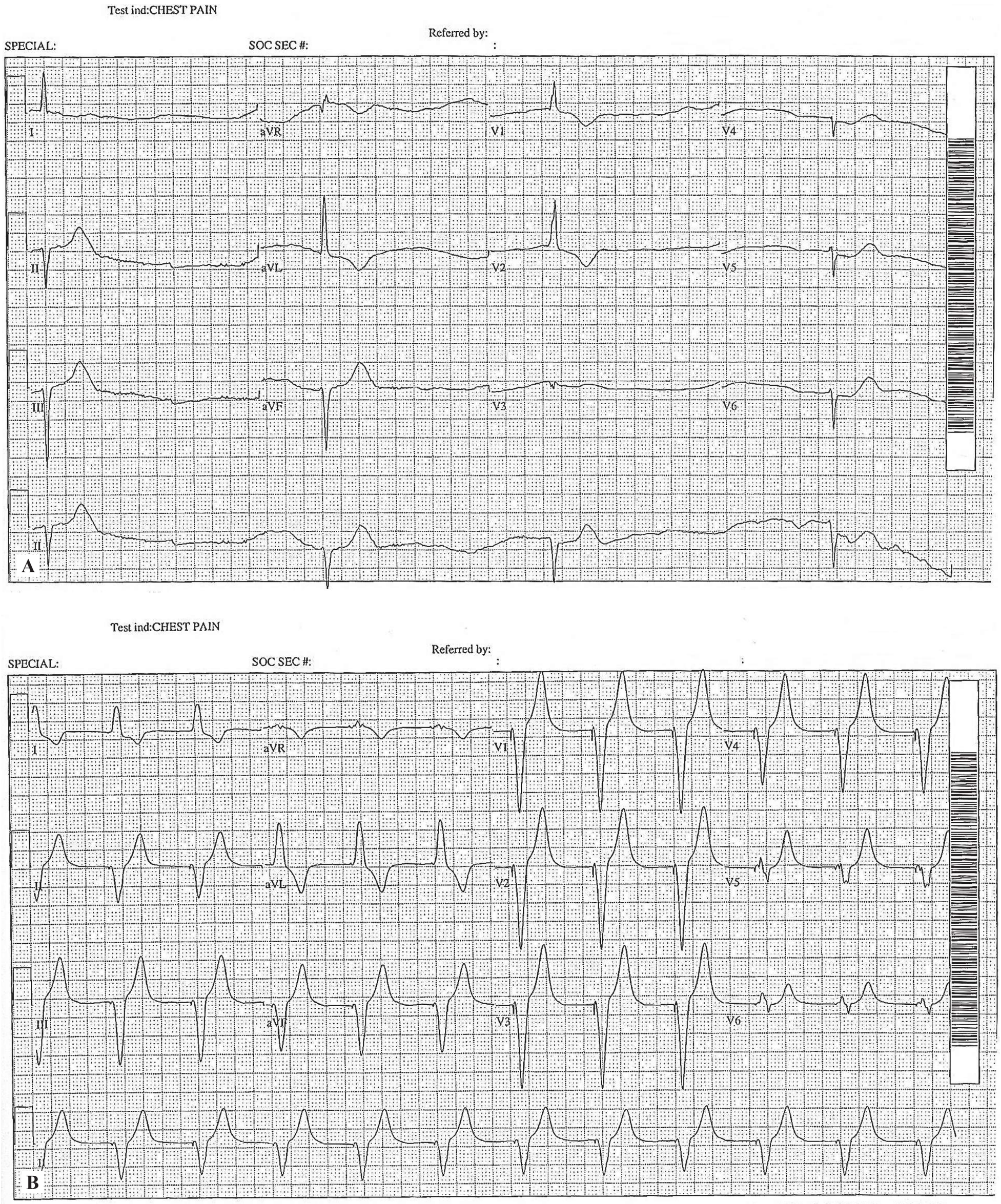

FIGURE 17.40 ■ **Calcium Channel Blocker Overdose.** (**A**) Verapamil poisoning causes profound negative inotropy and chronotropy. The 12-lead EKG demonstrates the bradycardia that may occur. (**B**) The same patient after transvenous pacing was initiated. (Photo contributor: Matthew D. Sztajnkrycer, MD, PhD.)

INHALANT ABUSE

Clinical Summary

Inhalant abuse, the intentional inhalation of vapors for the purpose of becoming "high," is more common among adolescents. Sniffing refers to the inhalation of the agent directly from a container, such as model airplane glue. Huffing involves placing solvent on some type of fabric and inhaling the vapors from the fabric. Bagging is the name given to the technique of spraying the solvent into a bag and then rebreathing from the bag. Occasionally the bag is placed over the head, potentially resulting in asphyxiant death. Inhalants are rapidly absorbed via the lungs and readily cross the blood-brain barrier. Initial effects include euphoria and occasional hallucinations. CNS depression may occur. Acute cardiotoxicity may also occur and is thought to be the cause of "sudden sniffing death." The cause of death is thought to be due to increased myocardial sensitization that promotes dysrhythmogenesis in the setting of a catecholamine surge. A defatting dermatitis may be evidence on the hands due to chronic exposure to solvents. Chronic effects from inhalant abuse include leukoencephalopathy, cardiomyopathy, cerebellar degeneration, and neuropathy.

Management and Disposition

Clues to the diagnosis of inhalant abuse are the presence of spray paint on the fingers or the face. Due to the increased solvent content in metallic-colored paints, gold and silver spray paint are particularly popular. Cardiac dysrhythmias are associated with a poor prognosis. Current recommendations suggest the use of β-blockers to treat ventricular dysrhythmias. Consider electrolyte abnormalities and acid-base status, particularly with toluene-based products. Benzodiazepines may be used for treatment of agitation.

Pearls

1. Chronic abuse of nitrous oxide (N_2O) may result in a megaloblastic anemia and distal axonal sensorimotor neuropathy that may be a result of irreversible oxidation of cobalamin (vitamin B_{12}). In addition to being used medicinally as "laughing gas," nitrous is abused from "whippets," which are the cartridges of compressed air used for whipping cream canisters.
2. Chronic abuse of toluene may result in potassium wasting renal tubular acidosis. Some of the carburetor cleaners that contain toluene also contain methanol.
3. Amyl, butyl, and isobutyl nitrites are strong oxidizers and may produce methemoglobinemia. These may be sold as "poppers."
4. Carbon monoxide poisoning may occur after methylene chloride inhalation.

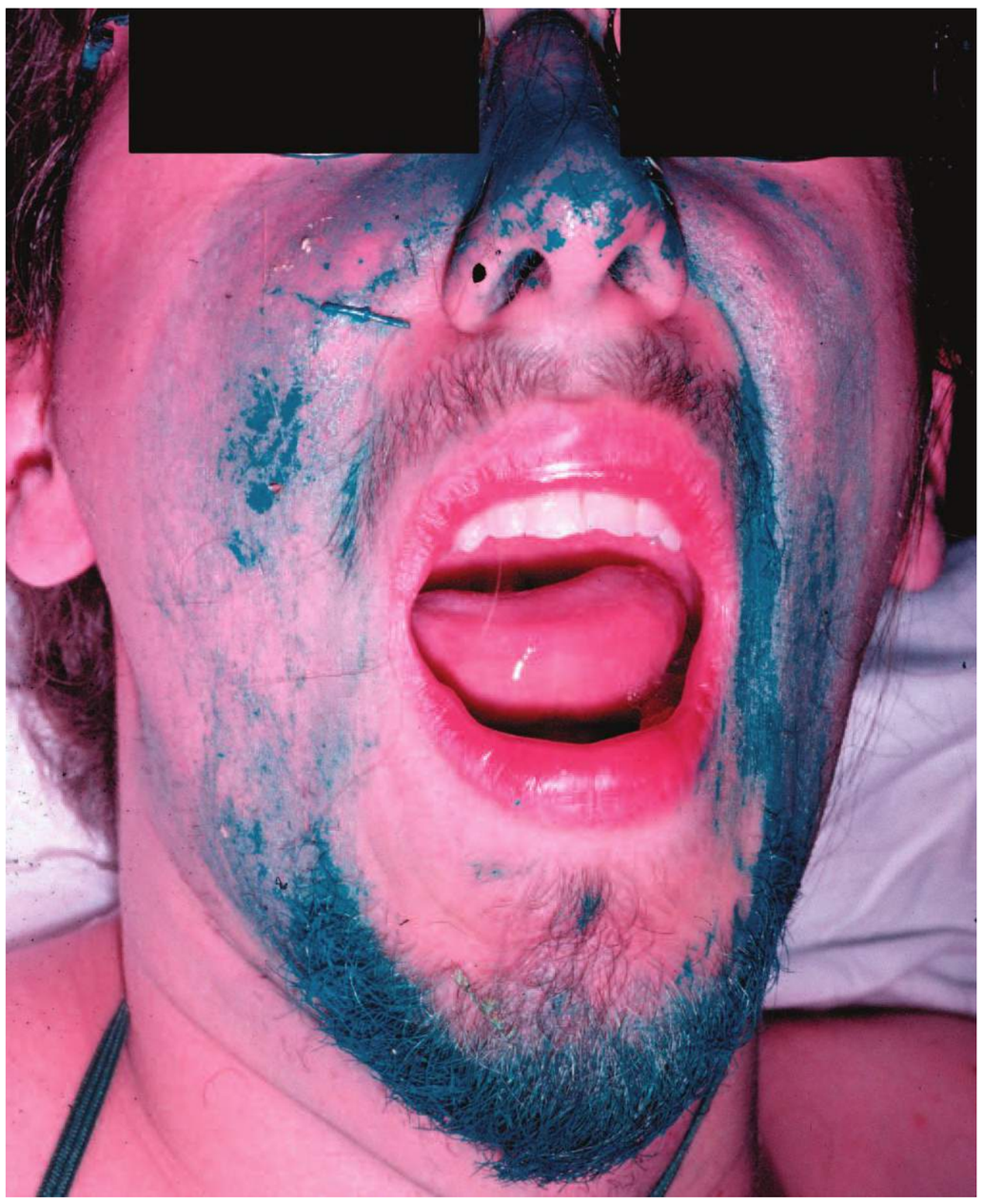

FIGURE 17.41 ■ **"Huffing."** Patients who huff spray paints may present with the paint on their face and hands. (Photo contributor: Alan B. Storrow, MD.)

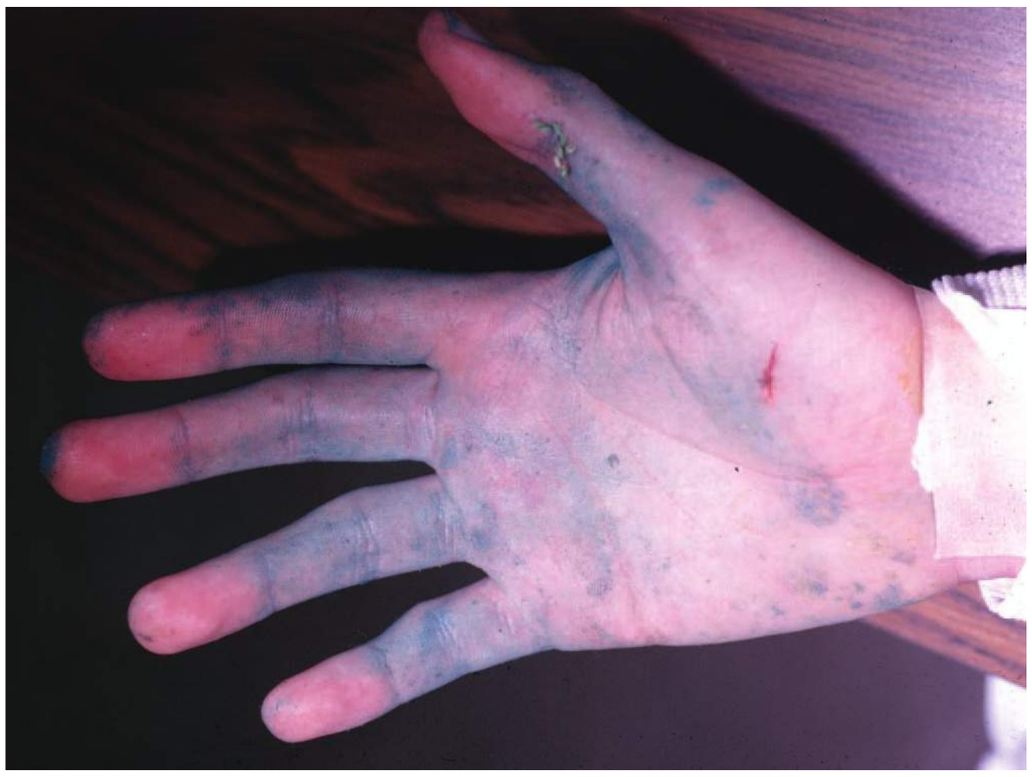

FIGURE 17.42 ■ **"Huffing."** The hand of the patient in Fig. 17.41. (Photo contributor: Alan B. Storrow, MD.)

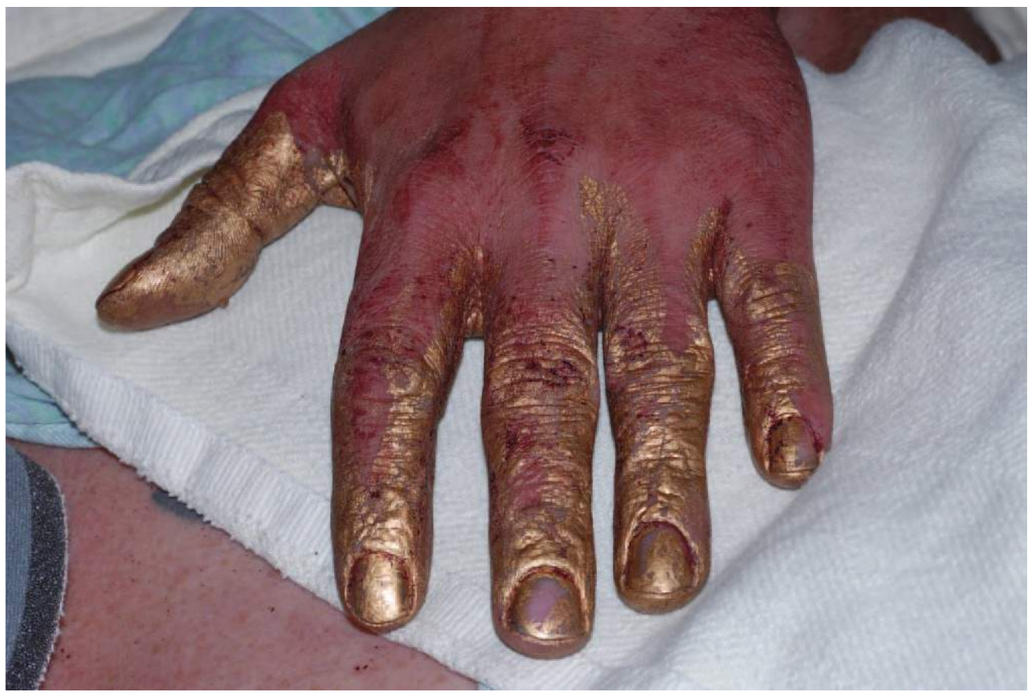

FIGURE 17.44 ■ **"Metallic Paint Abuse."** Gold and silver metallic paints are particularly popular for inhalant abuse due to the increased solvent content in the paint and a greater "high." (Photo contributor: R. Jason Thurman, MD.)

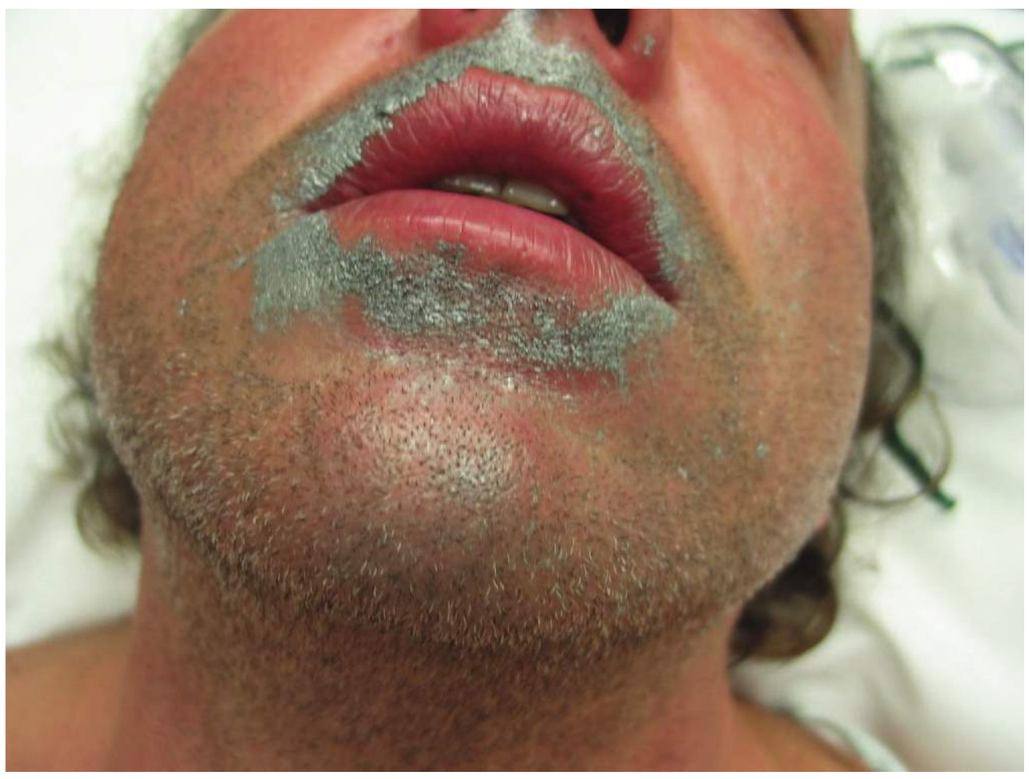

FIGURE 17.43 ■ **"Bagging."** Silver paint lining the perioral area in a patient abusing the paint by "bagging." (Photo contributor: R. Jason Thurman, MD.)

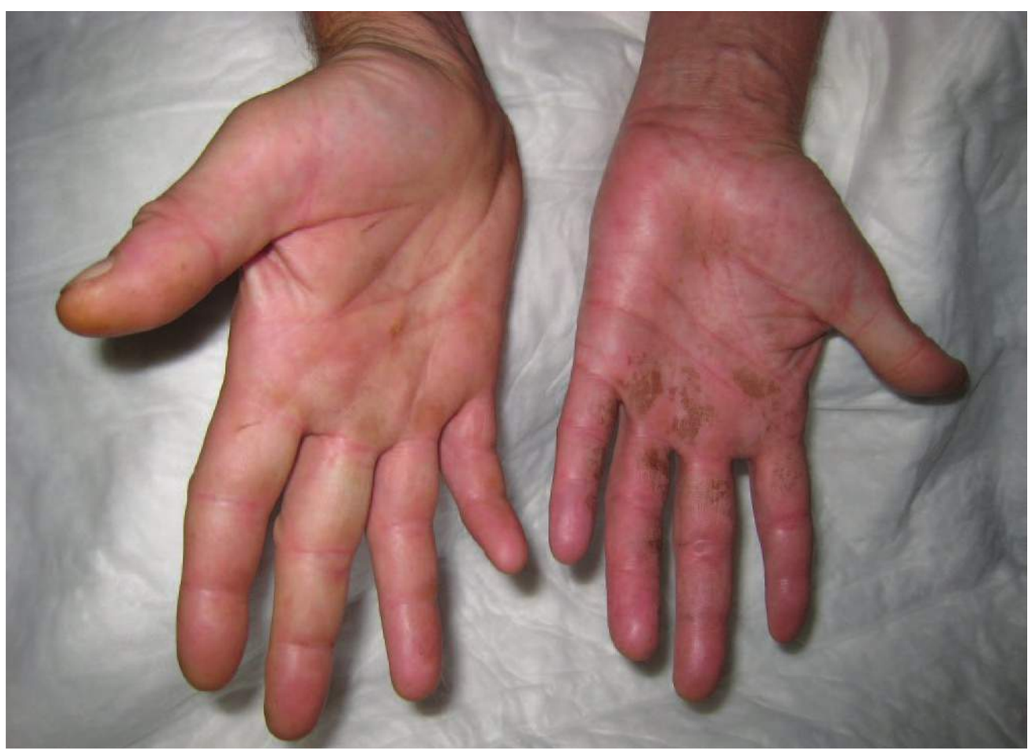

FIGURE 17.45 ■ **Motor Neuropathy of the Hand.** The hands of a chronic huffer demonstrate the muscle wasting in the left hand in addition to a mild defatting dermatitis on the palm of the hand. (Photo contributor: Saralyn R. Williams, MD.)

METHEMOGLOBINEMIA

Clinical Summary

Methemoglobin occurs when the iron atom in deoxyhemoglobin loses an electron, resulting in a ferric (Fe^{3+}) ion instead of the usual ferrous (Fe^{2+}) state. Ferric iron can no longer bind to oxygen, thereby reducing the oxygen-carrying capacity of hemoglobin. The presence of methemoglobin also shifts the oxygen hemoglobin dissociation curve to the left resulting in decreased release of oxygen to tissues. Infants are more susceptible to the development of methemoglobinemia due to reduced enzyme activity. Illnesses in infants such as diarrhea, dehydration, and acidosis may induce methemoglobin due to oxidant stress.

The most common causes of methemoglobin are acquired rather than congenital. Common pharmaceutical agents that cause methemoglobin include sulfonamides, dapsone, phenazopyridine, chloroquine, benzocaine, prilocaine, and more rarely lidocaine. Nitrites, which are used in the older cyanide antidote kit, induce methemoglobin.

Clues to the diagnosis include the patient who appears cyanotic and does not improve with the administration of oxygen. The pulse oximeter reading will drop to the mid 80% range but does not correlate with the percent of methemoglobin. The blood may appear chocolate in color and does not become red with exposure to oxygen. The arterial blood gas will demonstrate a normal partial pressure of oxygen with a resulting normal calculated arterial saturation. Methemoglobin may be measured via a co-oximeter using either arterial or venous heparinized blood.

Management and Disposition

Any patient who appears cyanotic should initially be treated with administration of supplemental oxygen and advanced airway management as appropriate. In general, any patient who is symptomatic from methemoglobinemia or has a level exceeding 25% to 30% should be treated with methylene blue. Methylene blue is available in a 1% solution and is administered as a 1 to 2 mg/kg dose intravenously over 5 minutes. This may be repeated if there is no initial response in 20 to 30 minutes. Patients who have methemoglobinemia from dapsone or aniline dyes may have recurrence and require additional dosing of methylene blue.

Pearls

1. High doses of methylene blue (5-7 mg/kg) may cause paradoxical methemoglobinemia and hemolysis.
2. The intravenous administration of methylene blue may interfere with the reading of the pulse oximeter and cause the reading to decrease transiently.
3. Methylene blue accelerates the ability of nicotinamide adenine dinucleotide phosphate (NADPH) methemoglobin reductase to reduce the ferric iron of methemoglobin back to a ferrous iron.
4. Methylene blue may not reverse methemoglobin in a patient with G6PD deficiency due to the absence of NADPH and may increase the risk of hemolysis.
5. Methylene blue has monoamine oxidase inhibitor activity; thus, use in patients who are on serotonin reuptake inhibitors may result in a serotonin syndrome.

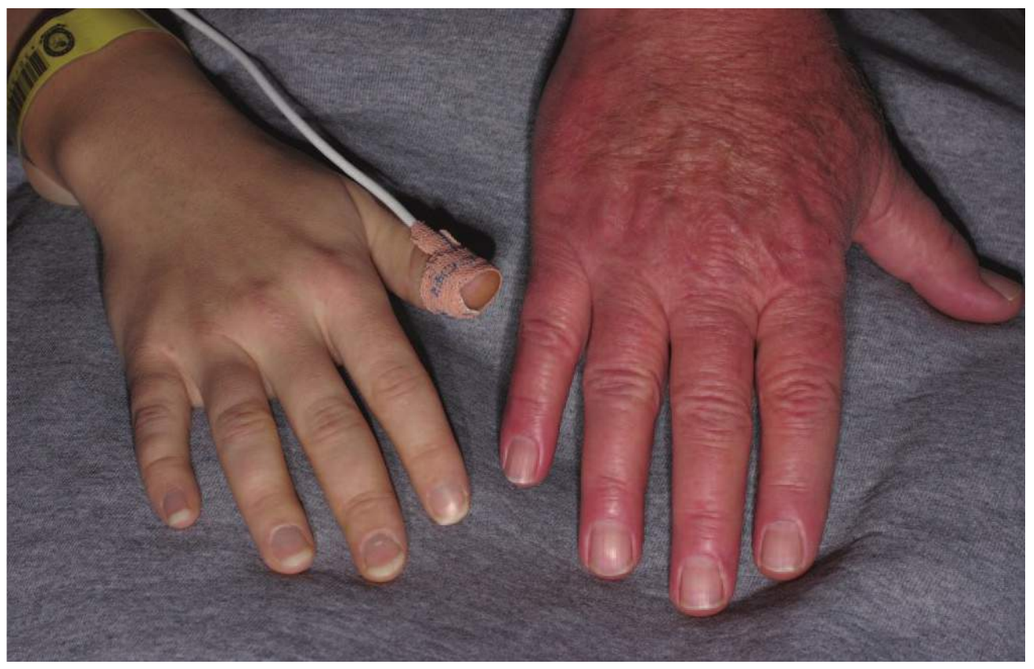

FIGURE 17.46 ■ **Methemoglobinemia—Cyanosis.** Methemoglobinemia resulted in the cyanotic appearance of this pediatric patient as noted on the hand on the left side of the image compared with the normal adult control on the right. (Photo contributor: Kevin J. Knoop, MD, MS.)

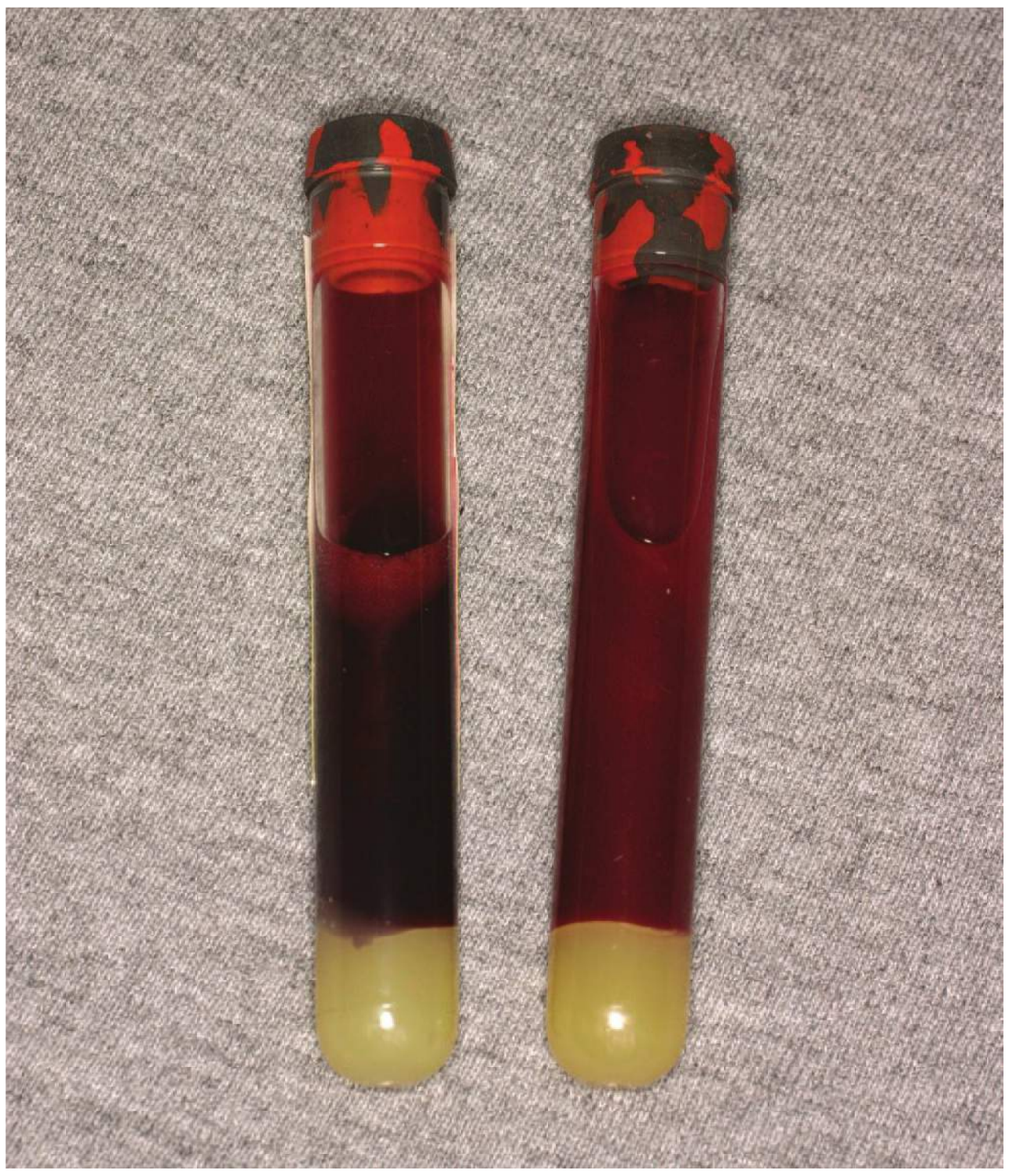

FIGURE 17.47 ■ **Methemoglobinemia—"Chocolate Blood."** "Chocolate blood" from an arterial sample of a patient with methemoglobinemia (left) compared to the normal bright red arterial blood (right). (Photo contributor: Kevin J. Knoop, MD, MS.)

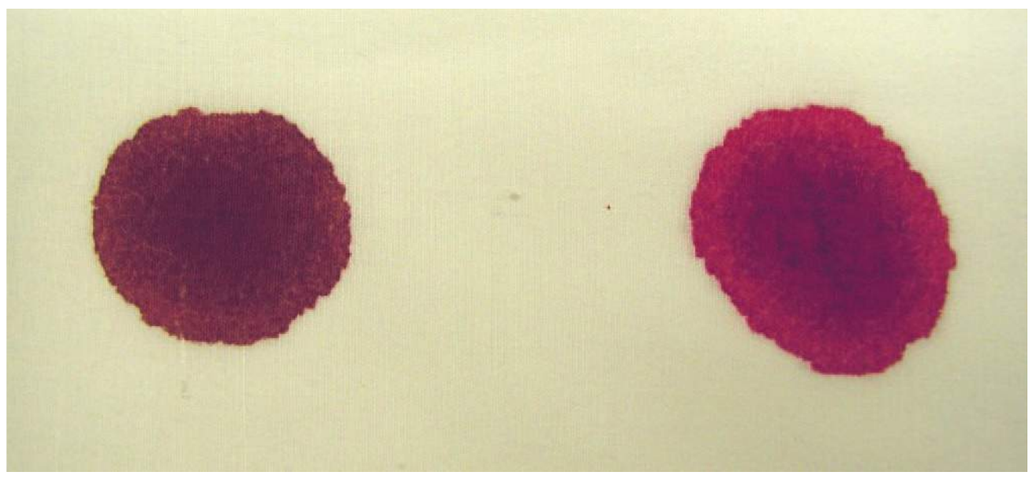

FIGURE 17.48 ■ **Methemoglobinemia—Exposure to Air.** The blood from a patient with methemoglobinemia on the left does not turn bright red upon exposure to air and will remain a "chocolate color" compared to the normal blood sample on the right. (Photo contributor: Louise Kao, MD.)

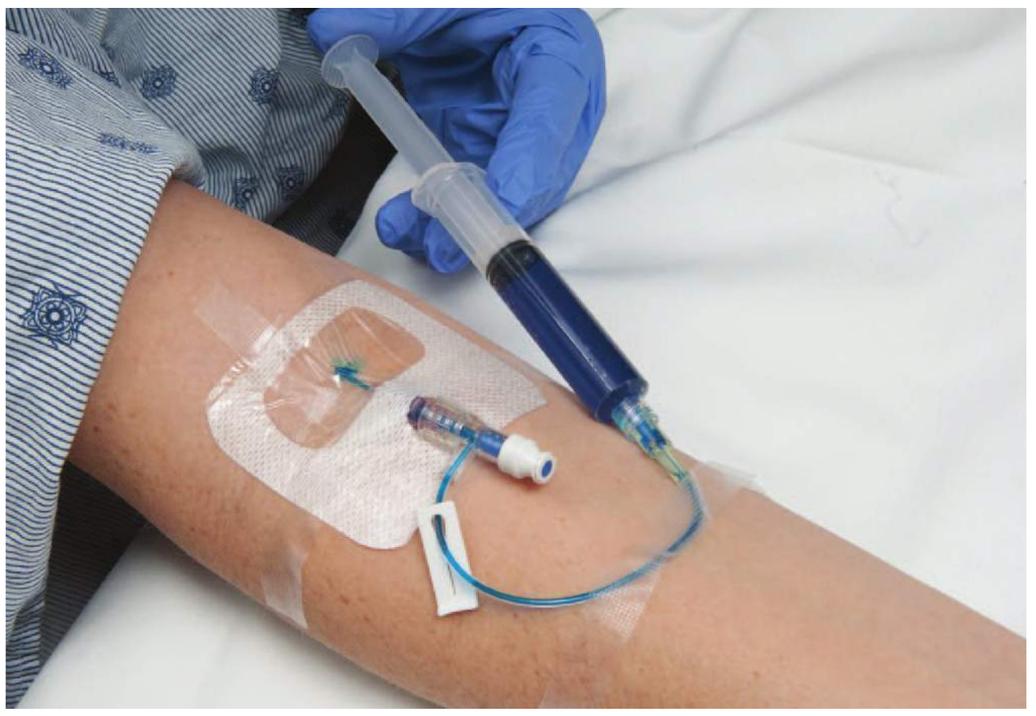

FIGURE 17.49 ■ **Administration of Methylene Blue.** The intravenous administration of methylene blue may be disconcerting to the patient who may not understand how a "blue dye" will help them. (Photo contributor: Lawrence B. Stack, MD.)

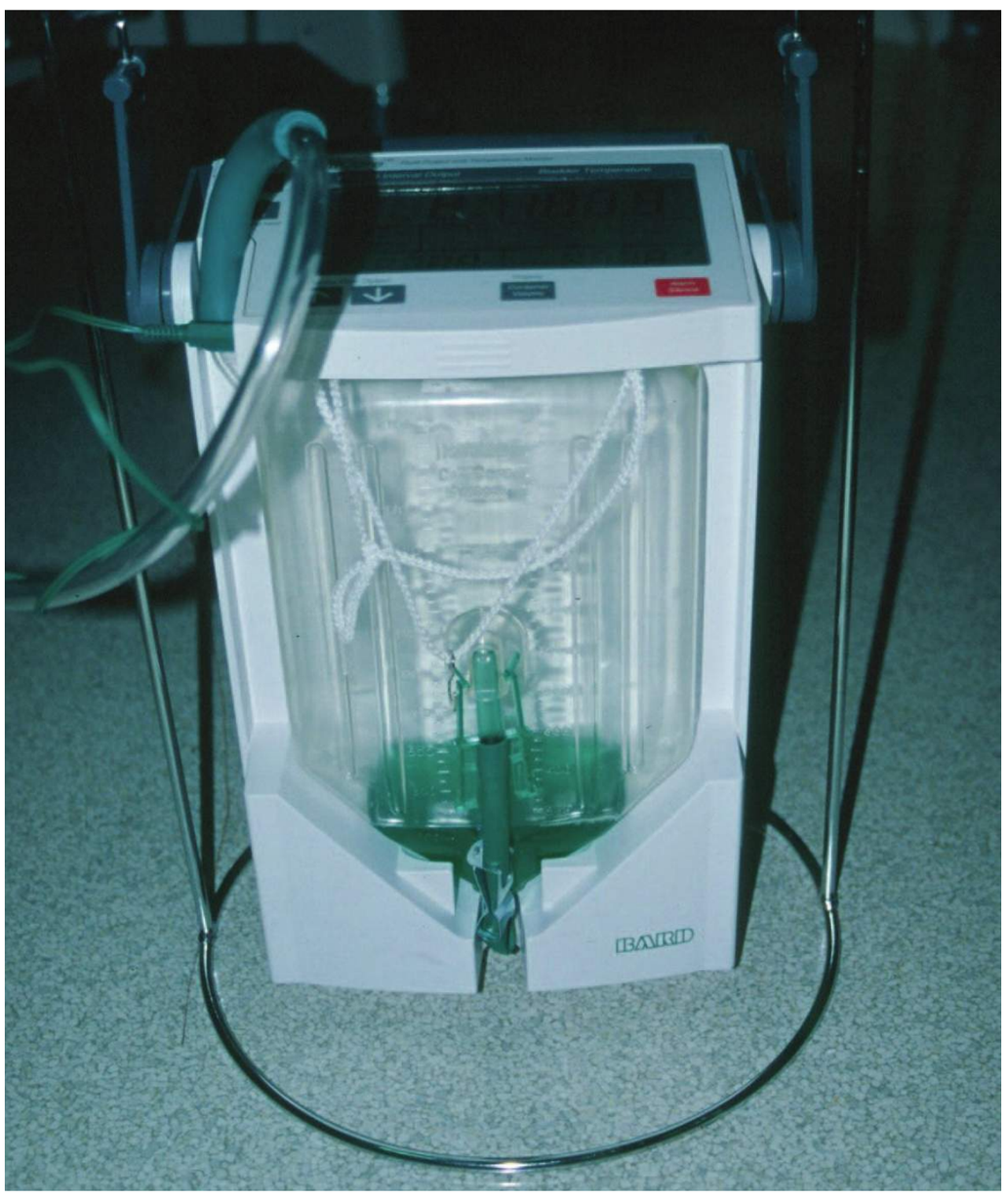

FIGURE 17.50 ■ **Methylene Blue Urine.** Methylene blue is excreted renally and gives a blue-green color to the urine. (Photo contributor: Division of Medical Toxicology, University of California, San Diego.)

CELLULAR ASPHYXIANTS

Clinical Summary

The cellular asphyxiants are a diverse group of substances including carbon monoxide (CO), cyanide, sodium azide, nitrites and other methemoglobin-producing oxidizing agents, and hydrogen sulfide, all of which interfere with the cellular utilization of oxygen. Depending on the substance, the interference may occur at the level of hemoglobin, the electron transport chain, or both. In contrast with the simple asphyxiants, ambient oxygen concentrations are not affected.

CO is a colorless and odorless gas generated from the incomplete combustion of carbonaceous compounds. The affinity of CO for hemoglobin is 250 times greater than that of oxygen. Binding of CO to hemoglobin shifts the oxyhemoglobin dissociation curve to the left, further impairing tissue oxygen delivery. Symptoms of acute poisoning may range from headache to ischemic chest pain, seizures, and CNS depression. Up to 40% of poisoned patients develop delayed neurologic sequelae (DNS); most cases of DNS are associated with an initial loss of consciousness.

Although a nonspecific enzyme inhibitor, cyanide interferes with oxidative phosphorylation. Sources of cyanide include industrial and household chemicals, plants, and structure fires. Clinical manifestations reflect dysfunction of oxygen-sensitive organs, including the CNS and cardiovascular systems. A cyanide toxidrome has been described, consisting of altered mental status, mydriasis, respiratory depression, hypotension, tachycardia, and metabolic (lactic) acidosis.

Management and Disposition

Immediate management focuses upon airway stabilization and antidotal therapy. Carboxyhemoglobin levels should be obtained in patients with suspected carbon monoxide poisoning. Pregnancy status should be determined in females presenting with suspected carbon monoxide poisoning. Blood cyanide levels are not typically available in the immediate care setting. While 100% oxygen is the accepted antidote for acute CO poisoning, controversy persists regarding the mode of administration (normobaric oxygen versus hyperbaric oxygen). Potential indications for hyperbaric oxygen include syncope, altered mental status (especially with evidence of cerebellar dysfunction), acidosis, and pregnancy. Therapy for cyanide poisoning includes intravenous administration of hydroxocobalamin. Hydroxocobalamin has the advantage of raising blood pressure, but also causes intense red skin discoloration and chromaturia.

Pearls

1. The decision to treat acute carbon monoxide poisoning is based upon history and physical examination, and not solely upon carbon monoxide level.
2. Maternal carboxyhemoglobin levels fail to accurately reflect fetal carboxyhemoglobin levels.

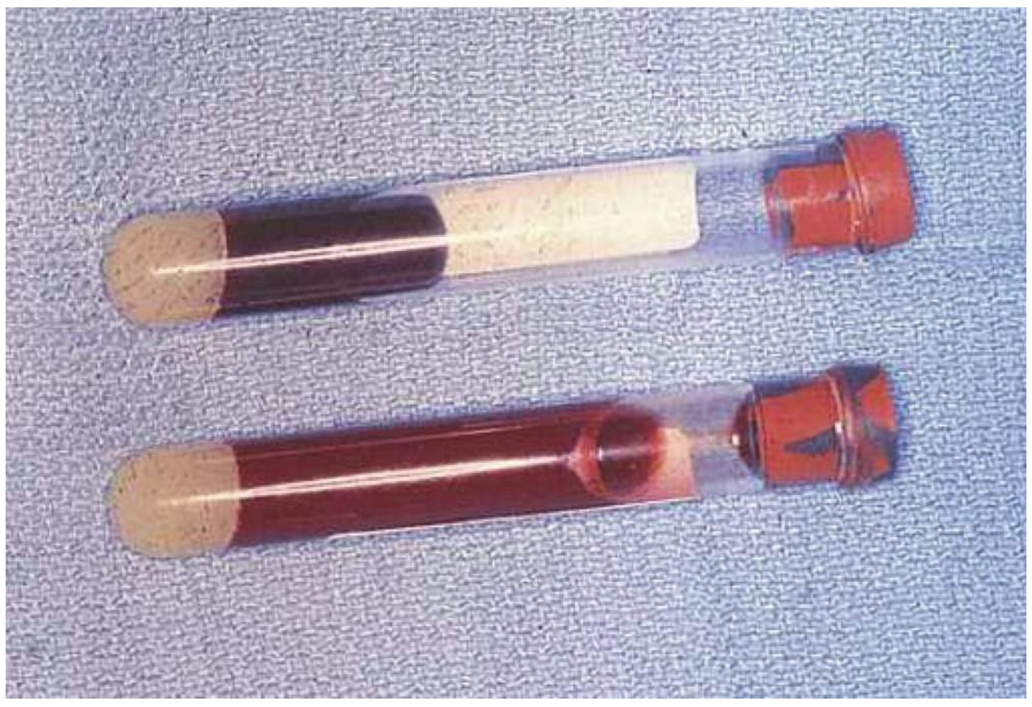

FIGURE 17.51 ■ **Carbon Monoxide Poisoning.** Venous blood samples with the bright red one (bottom sample) taken from a patient with acute carbon monoxide poisoning. The dark red venous blood (top sample) is a control sample from a patient with no carboxyhemoglobin. (Photo contributor: Daniel L. Savitt, MD.)

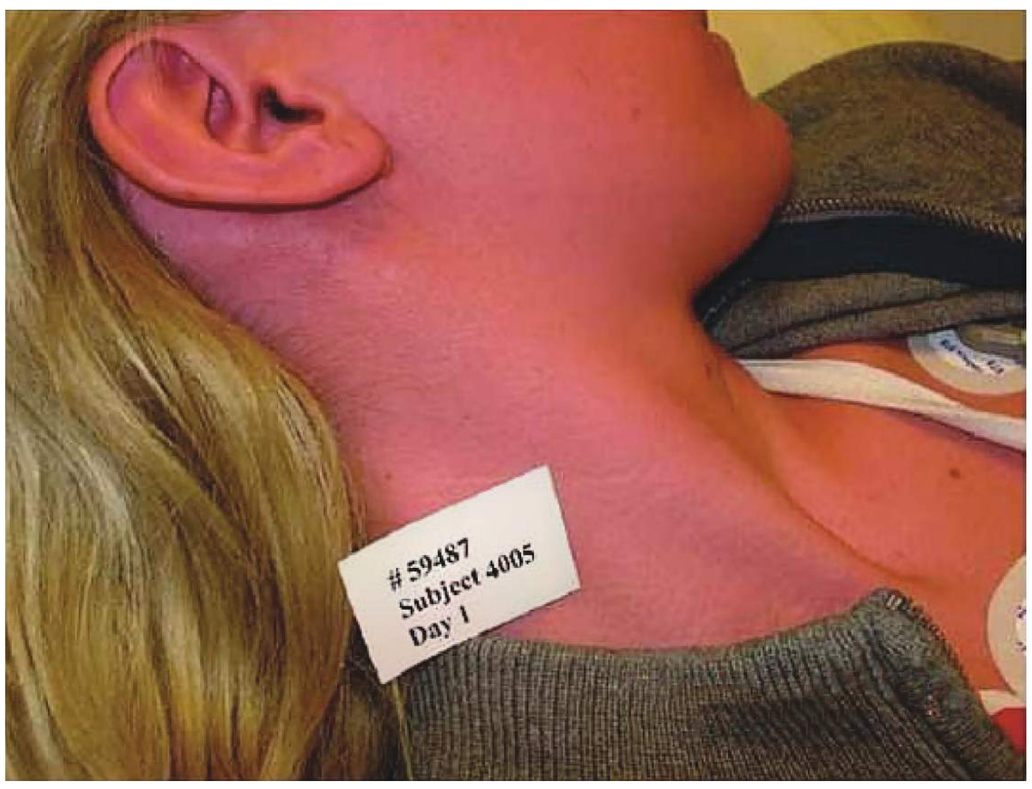

FIGURE 17.52 ■ **Skin Changes after Hydroxocobalamin.** After administration of therapeutic dosing of hydroxocobalamin, the skin of the patient may exhibit a bright red color and have chromaturia. (Reproduced with permission from Uhl W, Nolting A, Golor G, Rost KL, Kovar A. Safety of hydroxocobalamin in healthy volunteers in a randomized, placebo-controlled study. Clin Toxicol. 2006;44:17-28. Copyright © Informa Healthcare.)

3. Methylene chloride and nickel carbonyl are metabolized to carbon monoxide, resulting in on-going exposure and potential for toxicity.
4. In victims of structure fires who present without severe burns, a plasma lactate greater than 10 mmol/L correlates with cyanide level greater than 40 mumol/L.
5. Empiric therapy with hydroxocobalamin may be considered for victims of structure fires in whom suspicion exists for cyanide poisoning.
6. CO poisoning, as well as cyanide toxicity, may cause selective bilateral injury to the globus pallidus.

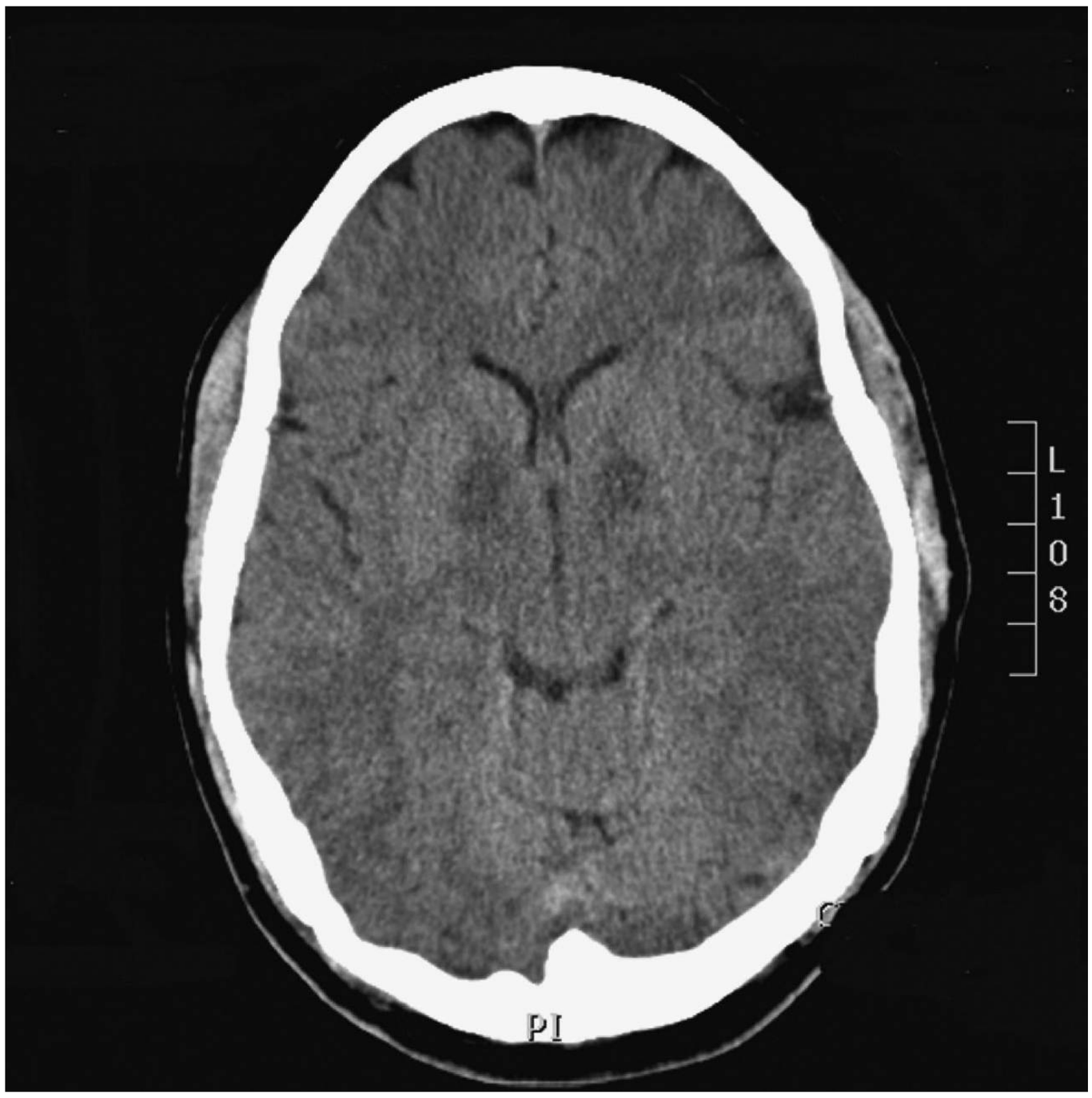

FIGURE 17.53 ■ **Bilateral Globus Pallidus Lesions.** Selective bilateral injury to the globus pallidus may be seen with cellular asphyxiants such as carbon monoxide or cyanide poisoning. (Photo contributor: Lawrence B. Stack, MD.)

VANCOMYCIN-INDUCED RED MAN SYNDROME

Clinical Summary

Vancomycin is a glycopeptide antibiotic that has activity against gram-positive bacteria. It has little to no activity against gram-negative bacteria or mycobacteria. It is poorly absorbed after oral administration, although it may be used orally for treatment of pseudomembranous colitis. Intravenous administration is the most common route. This is well tolerated with minimal burning at the site of the IV; however, rapid infusion may occasionally cause degranulation of mast cells and basophils. As a result, the patient experiences erythematous flushing, particularly of the face and neck, hence the name "red man syndrome." Tachycardia and hypotension may occasionally be seen.

Management and Disposition

Slowing the intravenous infusion usually resolves the flushing. Increasing the dilution of vancomycin in solution may also assist with preventing the flushing. Diphenhydramine has been used for treatment and may be used as a pretreatment.

Pearls

1. Other syndromes known to causing flushing include scombroid poisoning, disulfiram reactions, and hydroxocobalamin infusions.
2. Concomitant administration of aminoglycoside with vancomycin may increase the risk of nephrotoxicity.

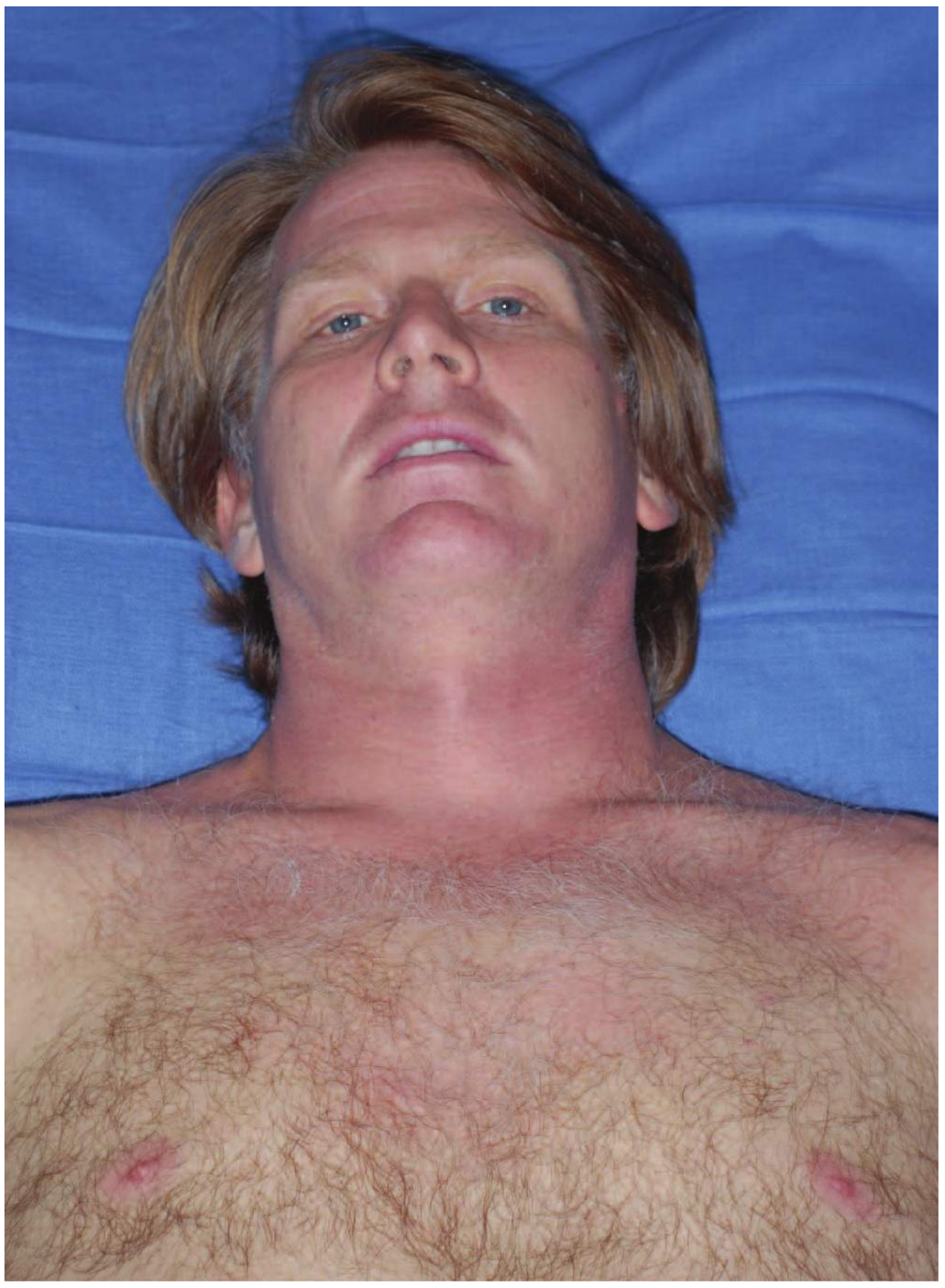

FIGURE 17.54 ■ **Red Man Syndrome.** Facial and neck flushing are manifestations that may be seen with red man syndrome from intravenous vancomycin infusion. (Photo contributor: R. Jason Thurman, MD.)

Clinical Summary

Botulinum is a potent neurotoxin that is derived primarily from Clostridium botulinum, although a few other clostridial species produce a homologous neurotoxin. Botulinum toxin blocks release of Ach, which results in decreased activation of muscarinic and nicotinic receptors. Initial effects may include nonspecific findings such as nausea and vomiting, constipation, and throat complaints. The classic neurologic findings are due to the lack of receptor activation of the nicotinic receptor at the neuromuscular junction. Dysarthria, dysphagia, diplopia, and mydriasis progress to a descending symmetric paralysis.

The common types of botulism include foodborne (ingestion of preformed toxin), infantile (in vivo production of toxin), and wound botulism (in vivo production of toxin). While foodborne has the features classically described, infantile botulism manifests as the constipated, floppy baby. Wound botulism is most commonly associated with "skin popping," a technique of subcutaneous injection of an illicit drug, usually black tar heroin. Diagnosis is initially a clinical one, with subsequent verification via a murine assay of the presence of botulinum toxin in a patient sample. This assay is performed through either the state department of health or the Centers for Disease Control and Prevention.

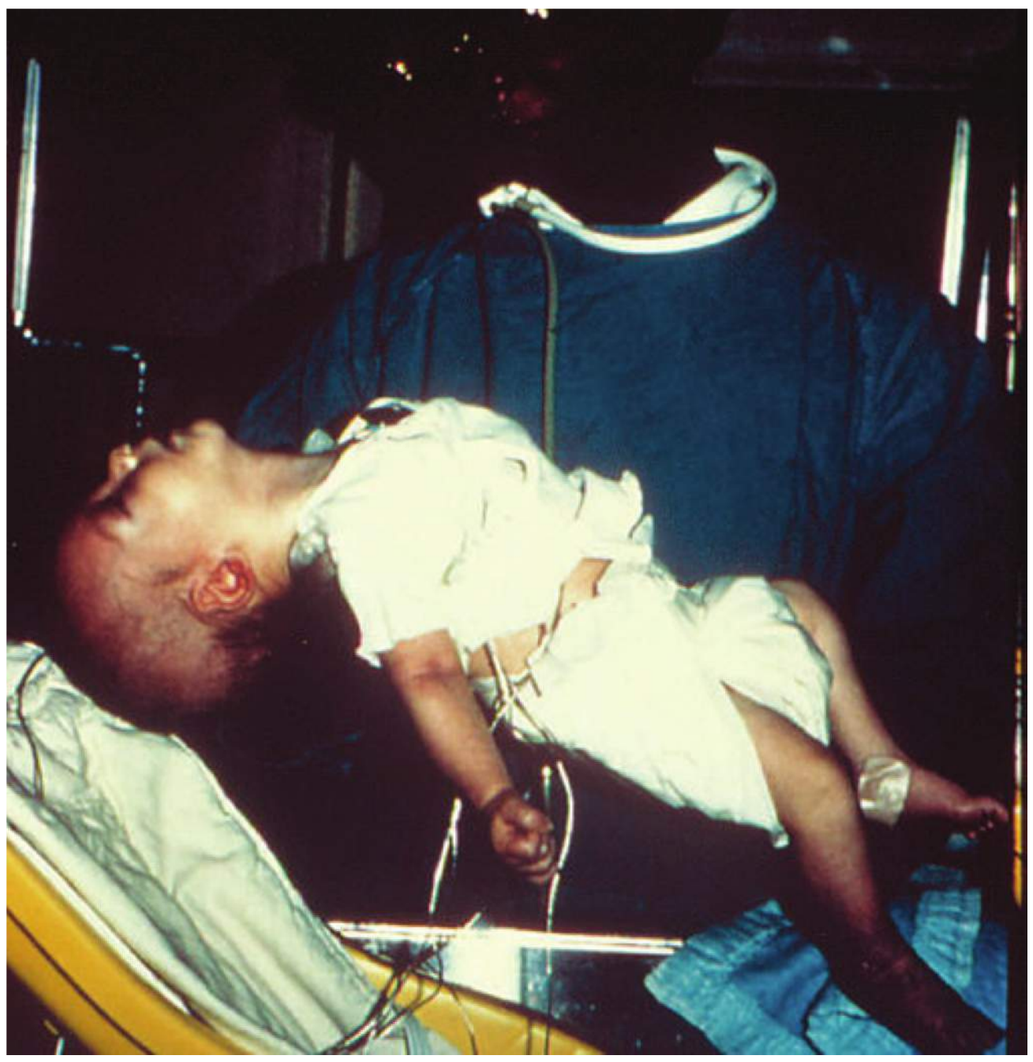

FIGURE 17.55 ■ **Infantile Botulism.** The floppy-constipated baby is a classic presentation of infantile botulism. (Photo contributor: Centers for Disease Control and Prevention.)

Management and Disposition

Any patient in whom botulism is suspected should be admitted to the hospital. Careful monitoring of the airway status is important to ensure that the patient has adequate ventilatory capacity. The local health department should be notified to assist with the procurement of botulinum antitoxin for foodborne and wound botulism patients. Human botulinum immune globulin is available through the California Department of Health for the treatment of infantile botulism.

Pearls

1. The initial chief complaint of a patient with wound botulism may be "sore throat" since the patient has dry mucus membranes and difficulty swallowing.
2. Since botulinum toxin does not cross the blood-brain barrier, the mental status should not be affected unless the patient has respiratory insufficiency.
3. Early signs of infantile botulism may be difficulty with feeding since feeding for an infant requires use of the cranial nerves.

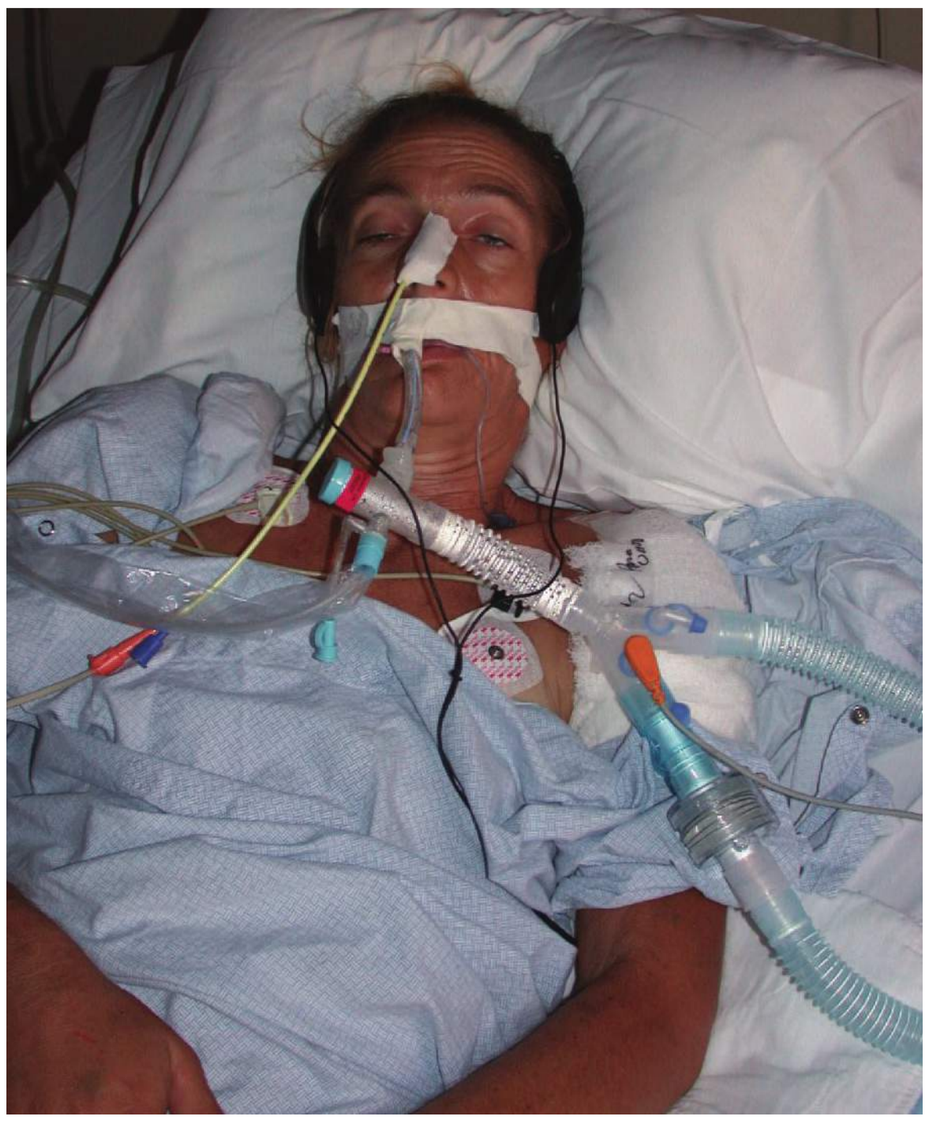

FIGURE 17.56 ■ **Wound Botulism.** Wound botulism occurs from the in vivo production of botulinum toxin. It manifests the same neurotoxicity with the ptosis, bulbar paralysis, and respiratory compromise as foodborne botulism. Note the profound ptosis in this patient. (Photo contributor: William H. Richardson, III, MD.)

Clinical Summary

Since the discovery of the cause of a hemorrhagic disorder in Wisconsin cattle in the early 20th century, warfarin and its analogues have been used as rodenticides and pharmacologic agents. Warfarin is actually named after the Wisconsin Alumni Research Foundation. Warfarin-like xenobiotics inhibit the activity of vitamin K 2,3 epoxide reductase, thus affecting the production of the vitamin K–dependent clotting factors II, VII, IX, and X. While the effect on the production of clotting factors occurs soon after absorption, the clinical effects are delayed until the available activated factors are depleted.

Long-acting anticoagulants, known as "Superwarfarins," were developed as rodenticides due to the development of warfarin resistant rodents. Their mechanism of action is the same as warfarin, but they are more potent and exhibit a much longer duration of effect. Poisoned patients may present with any sequelae of an anticoagulated state spanning the spectrum of easy bruising to severe life-threatening hemorrhage.

Management and Disposition

Patients who are over-anticoagulated may require reversal with the administration of vitamin K. Life-threatening hemorrhage may require immediate reversal with administration of fresh frozen plasma. Guidelines for correction of vitamin K antagonists are published by the American College of Chest Physicians. Patients with intentional poisonings

FIGURE 17.57 ■ **Rodenticide Package.** Brodifacoum is a common long-acting anticoagulant (a "superwarfarin") used as rodenticide for mice. Note that the percent of active ingredient is only 0.005%; thus, ingestion of a few pellets by a child is unlikely to cause clinically significant anticoagulation. The patient with this packet ingested a large amount and required long-term reversal. (Photo contributor: R. Jason Thurman, MD.)

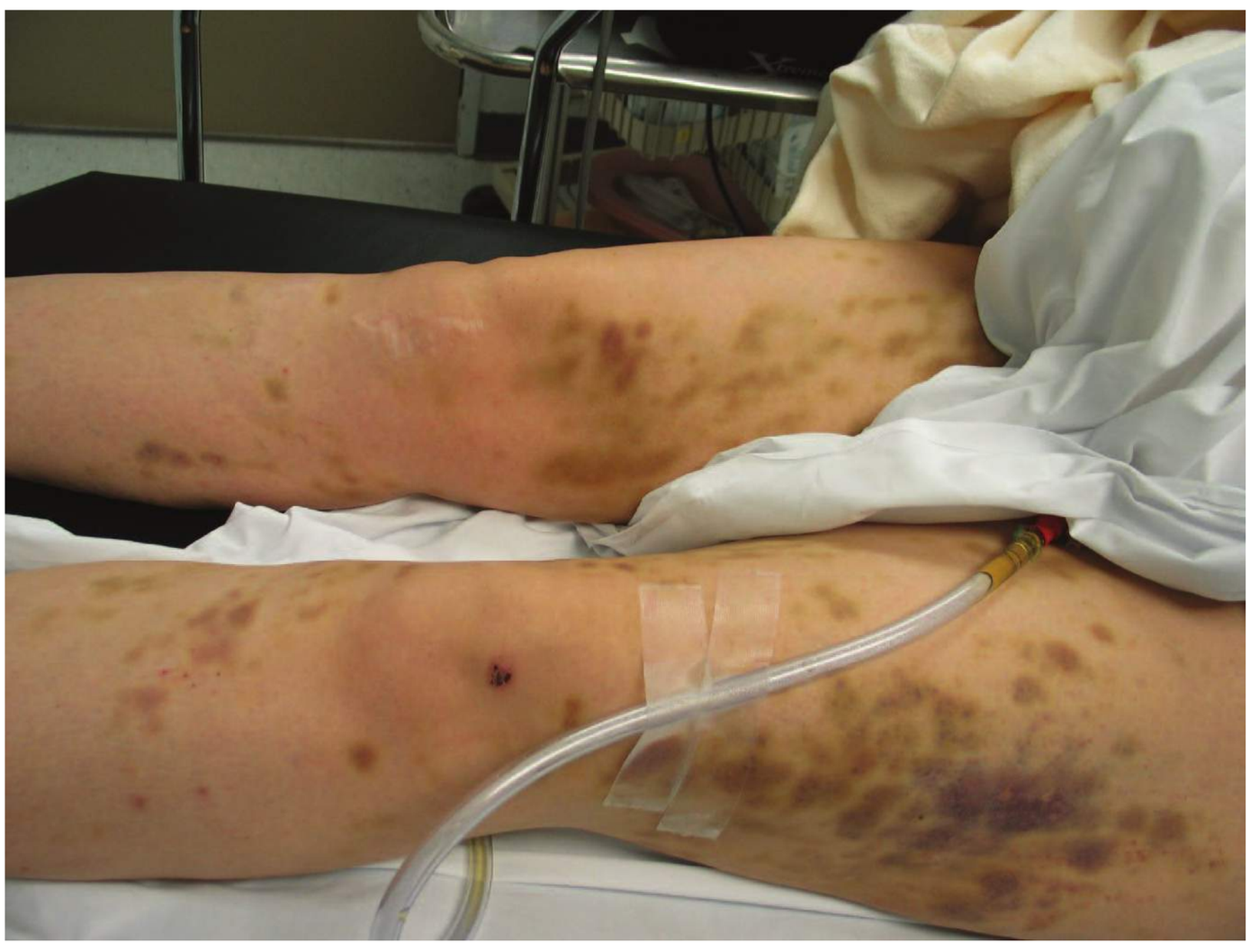

FIGURE 17.58 ■ **Warfarin Overdose.** Generalized bruising, as seen in this patient, is typical of a patient with a warfarin overdose. The INR of this patient was >10. (Photo contributor: R. Jason Thurman, MD.)

from the long-acting anticoagulants ("superwarfarins") may require high-dose vitamin K for several weeks to months due to the significantly prolonged effect of the drugs.

Pearls

1. Warfarin is actually a racemic mixture of R and S enantiomers which are metabolized by different CYP p450 pathways. The S enantiomer is more potent that the R enantiomer. Genetic polymorphisms influence the dose needed to achieve a therapeutic level.
2. Single unintentional ingestions of the "superwarfarins" by children under 6 years of age rarely result in clinically significant effects. Repetitive ingestions can result in coagulopathy. If a toddler has a vitamin K–dependent coagulopathy from a superwarfarin ingestion, the diagnosis of Munchausen by proxy should be entertained.
3. If a patient is on chronic warfarin therapy, be wary of the many xenobiotic interactions that can potentiate or antagonize the anticoagulant effect of the drug.

FIGURE 17.59 ■ **Rodenticide Pellets.** Typical appearance of the bluish-green brodifacoum pellets contained in the packaging. (Photo contributor: R. Jason Thurman, MD.)

CAUSTIC INGESTION

Clinical Summary

Caustics are a diverse group of household and industrial products and pharmaceutical agents that cause functional and histological tissue damage through direct contact. They represent the second most common toxic exposure for children 5 years of age or under. These agents are frequently described in terms of pH, with acids typically having a pH less than 3 and alkali (bases) typically having a pH greater than 11. Despite a near-physiologic pH, phenol may produce severe burns due to a high titratable acid reserve (TAR).

Alkali exposure results in a liquefactive necrosis, with deep and progressive tissue damage, predominantly to the esophagus. Endoscopic grading of esophageal burns is similar to thermal burns, ranging from mucosal hyperemia and edema (grade I) to full-thickness burns (grade III). Acid ingestion results in coagulative necrosis, which limits the depth of penetration. Damage is predominantly localized to the gastric mucosa, with pooling of the caustic agent in the antrum.

Management and Disposition

The primary goal of management is airway assessment and stabilization. Hypotension is a grave finding. A serum pH less than 7.20 may indicate the need for surgical exploration. Activated charcoal decontamination is relatively contraindicated. Endoscopy is recommended after large or deliberate caustic ingestion, presence of oral burns, or persistent refusal to take oral liquids. Steroids are occasionally used as an effort to prevention of esophageal strictures in selected patients, but the decision to administer is made based upon endoscopic grading in conjunction with the gastroenterologist.

Pearls

1. The absence of oropharyngeal burns is a poor predictor of distal esophageal injury. The presence of vomiting, drooling, or stridor is more predictive of significant esophageal injury on endoscopy.
2. Analogous to thermal burns after smoke inhalation, upper airway edema and airway obstruction may occur abruptly.
3. Ingestion of muriatic acid (HCl) results in an initial non-anion gap metabolic acidosis.

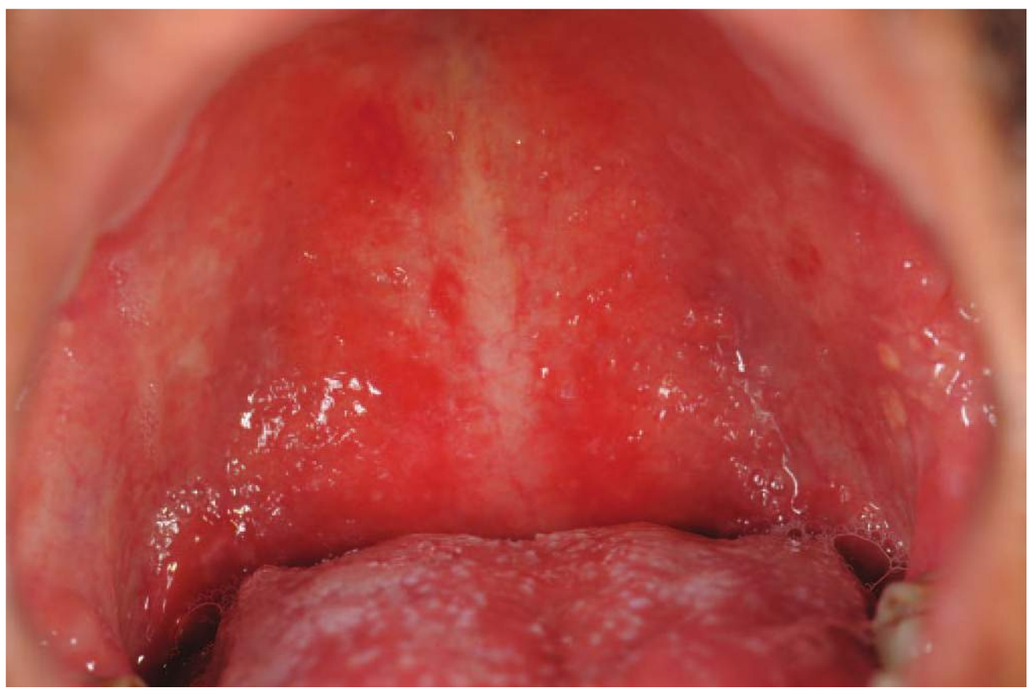

FIGURE 17.60 ■ **Caustic Oropharyngeal Burns.** This patient suffered caustic burns from the accidental drinking of a highly alkali solution that was stored in a soda can. (Photo contributor: Lawrence B. Stack, MD.)

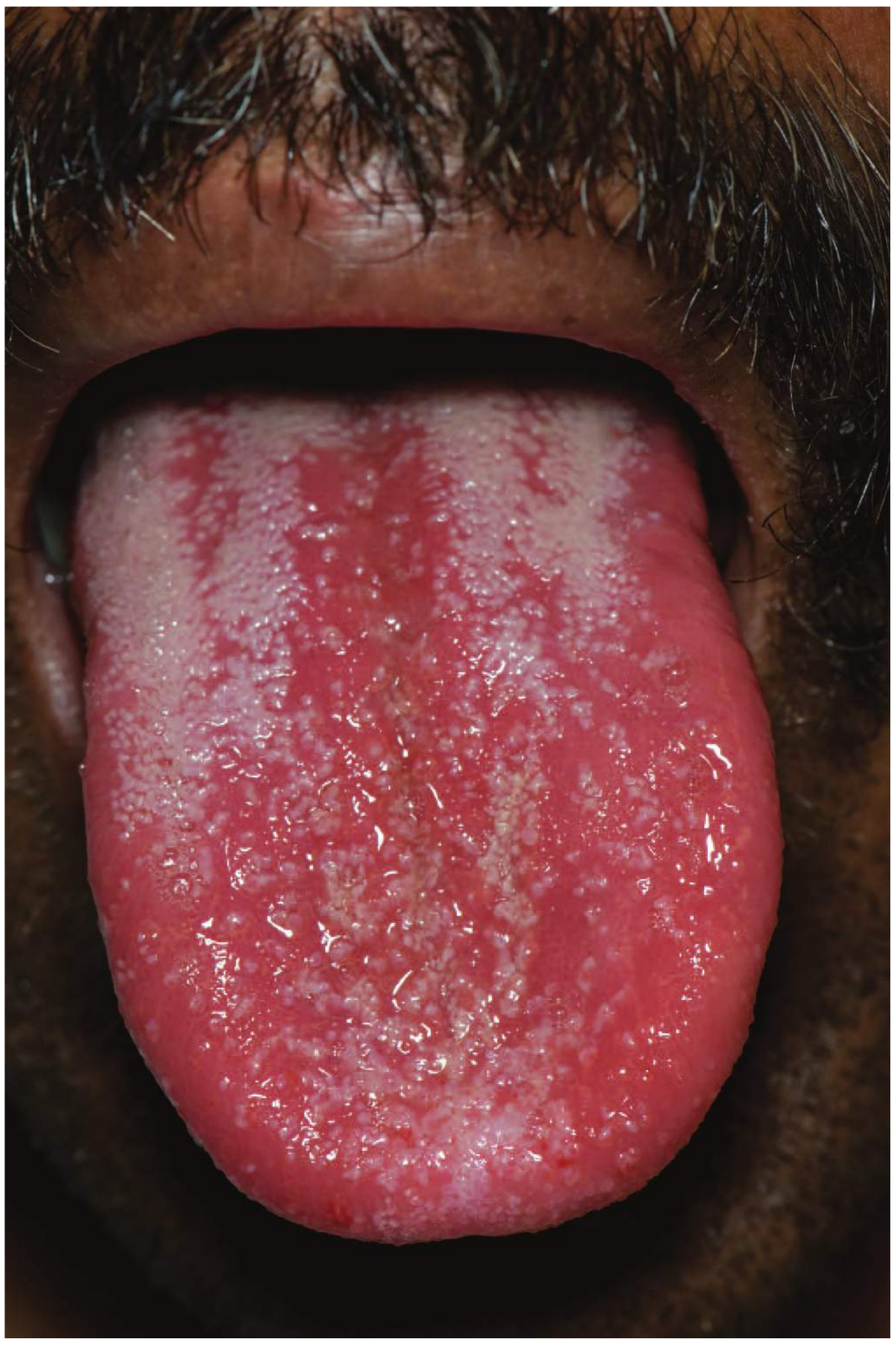

FIGURE 17.61 ■ **Caustic Oropharyngeal Burns.** Close-up image of the alkali burns on the tongue of the patient in Figure 17.60. (Photo contributor: Lawrence B. Stack, MD.)

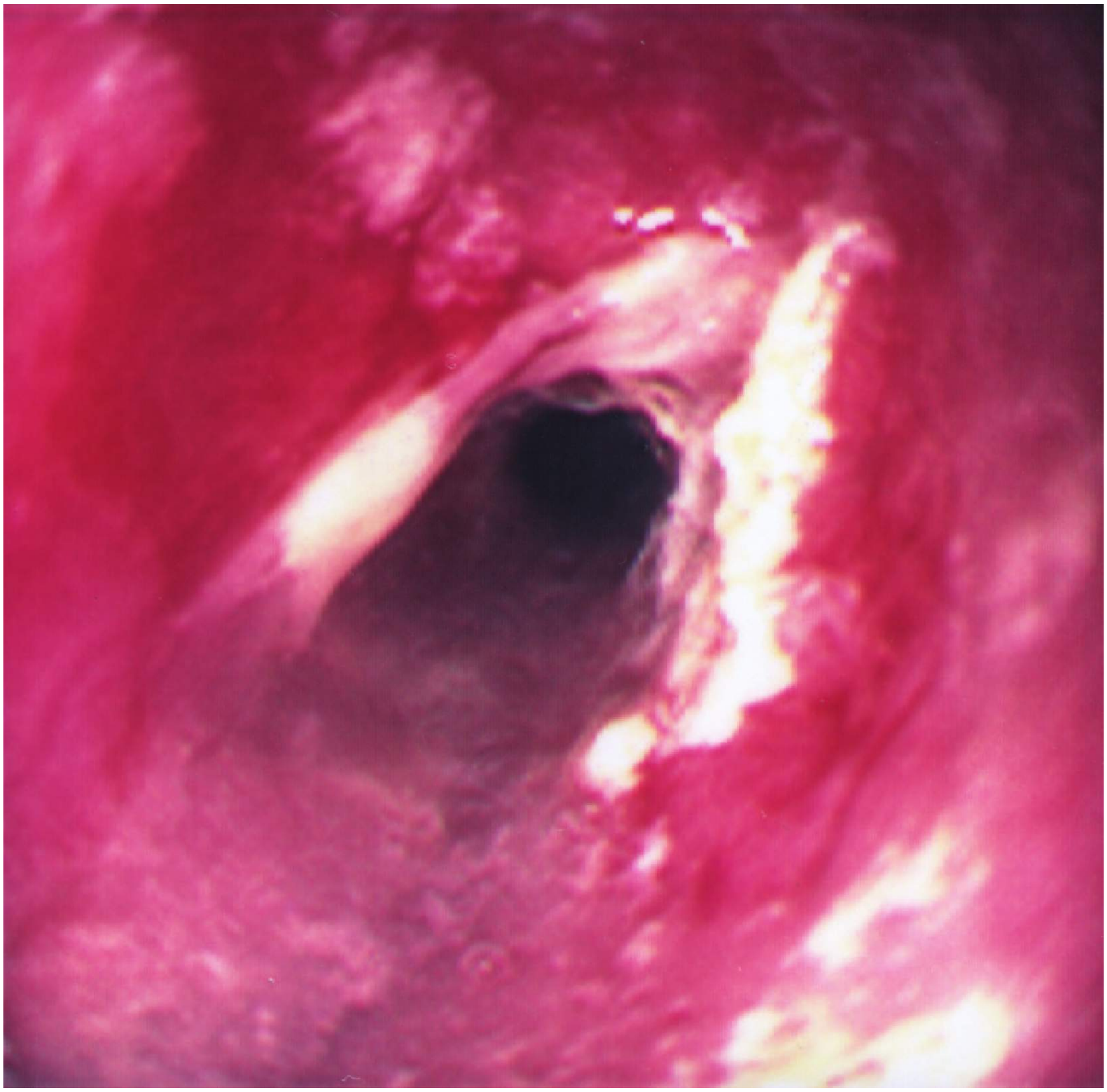

FIGURE 17.62 ■ **Caustic Esophageal Burns.** These esophageal burns were caused by an accidental ingestion of lye in a pediatric patient. (Photo contributor: Philip E. Stack, MD.)

HYDROFLUORIC ACID BURNS

Clinical Summary

Hydrofluoric acid (HF) is a colorless, corrosive liquid available in both commercial (>20%) and household (<20%, typically 6-12%) formulations. Commercially, HF is used in glass etching, electroplating, and semiconductor manufacturing. Consumer products are typically marketed as rust removers and chrome cleaners. Although toxic via the dermal, ocular, pulmonary, and GI routes, the majority of patients present after dermal exposure, typically to the hands and fingers. The severity of local injury depends upon the HF concentration and the extent of exposure.

Symptoms and tissue effects may be appreciably delayed, especially with household formulations. In the setting of hand exposure, pain is typically described as progressive severe unremitting deep burning sensation. Early local erythema is variable. Especially with higher HF concentrations, a pale blanched appearance may develop. In addition to the coagulative necrosis noted with other inorganic acids, HF causes toxicity by the binding and precipitation of calcium ions. In addition to local effects, significant and potentially life-threatening systemic effects may occur including hypocalcemia, hyperkalemia, and hypomagnesemia. Concentrations greater than 50% may cause rapid decompensation with even small dermal exposures (1% total body surface area[TBSA]).

Management and Disposition

Treatment varies depending upon the route of exposure, but is directed toward decontamination, neutralization of the fluoride ion, and pain control. In the setting of ingestion or significant dermal exposure (more than 5% TBSA of a household HF formulation), serum electrolytes, including calcium and magnesium, should be determined. In addition to pain control, management options for hand burns include commercially available calcium gluconate gel, subcutaneous calcium gluconate infiltration, and regional intravenous and intra-arterial calcium gluconate infusion.

Pearls

1. An expedient 2.5% calcium gluconate gel can be made by adding 3.5 g calcium gluconate powder to 5 oz (150 mL) of water-based lubricant. Alternatively, 10 crushed 1-g calcium carbonate antacid tablets may be added to 20 mL water-based lubricant. The resultant gel may be placed in a rubber glove and placed on the patient's hand for topical treatment.
2. With significant dermal exposure or ingestion, prolonged cardiac and serum electrolyte monitoring may be required; sudden, delayed cardiac arrest has occurred.
3. Replacement of calcium and magnesium may require substantially larger doses than typically required.

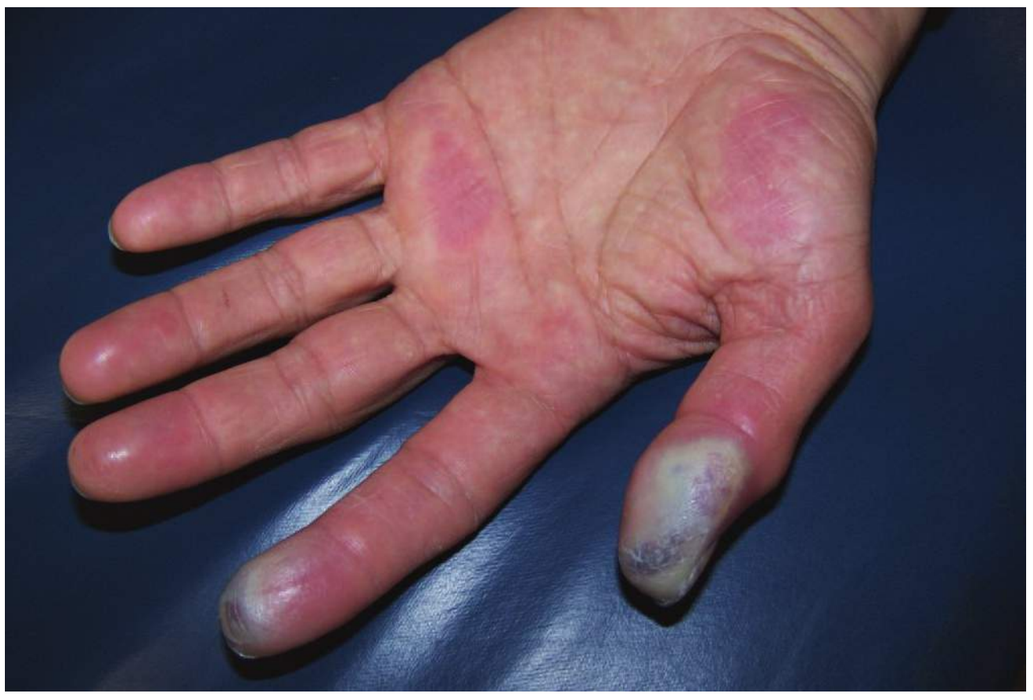

FIGURE 17.63 ■ **Hydrofluoric Acid Burns.** Hydrofluoric acid burn due to application of a rust remover agent. The patient presented hours later after initial use with severe, deep pain in the thumb and index finger. (Photo contributor: Karen Rogers, MD.)

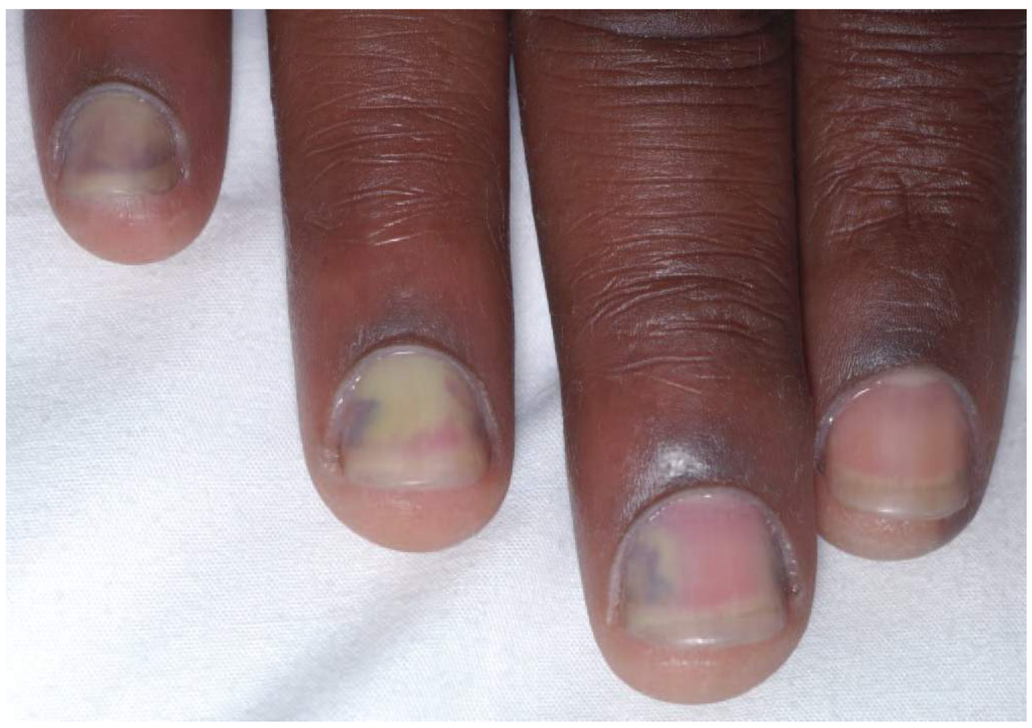

FIGURE 17.64 ■ **Hydrofluoric Acid Burn—Nail beds.** Hydrofluoric acid can seep underneath the nail beds, resulting in blanched discoloration. (Photo contributor: Lawrence B. Stack, MD.)

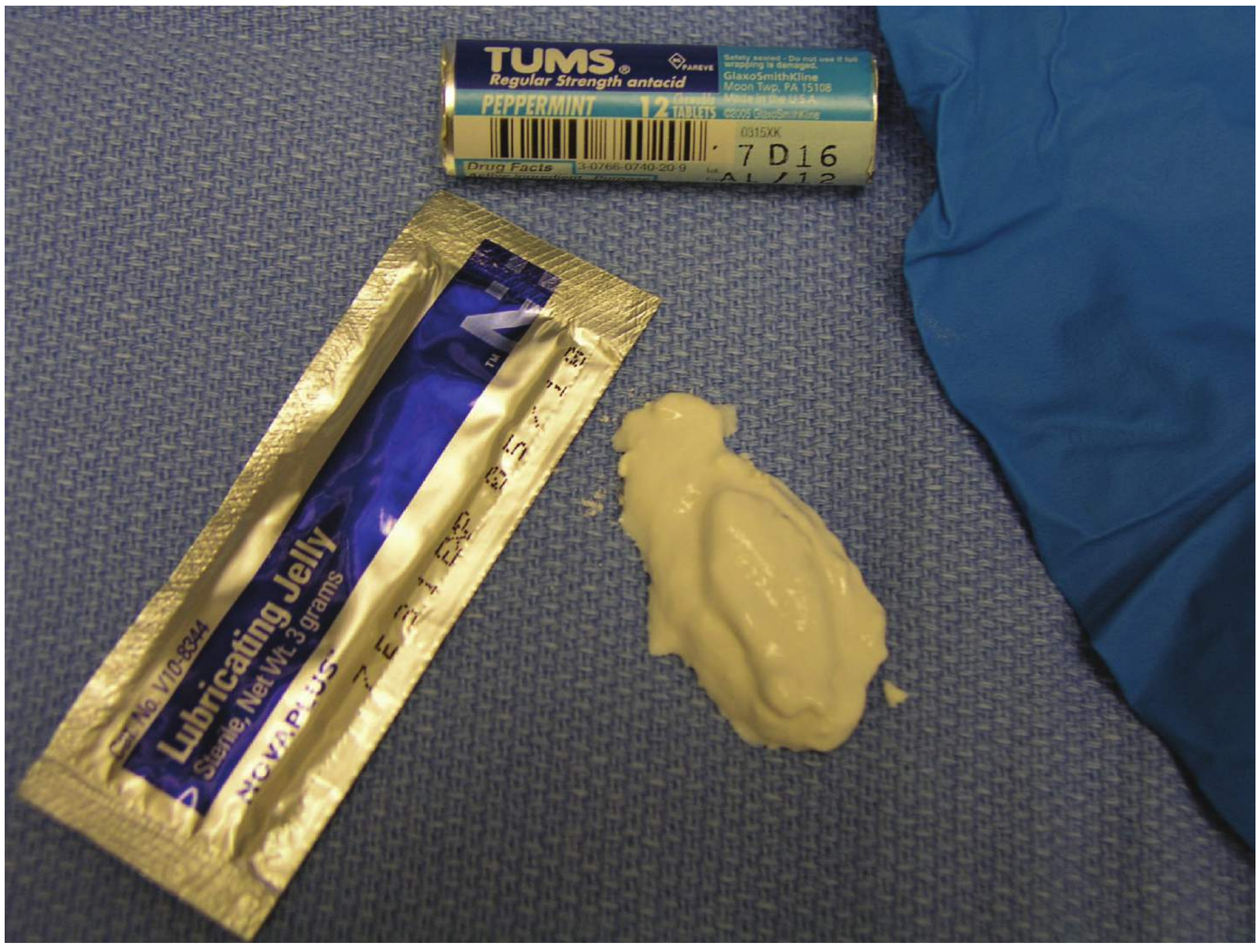

FIGURE 17.65 ■ **Hydrofluoric Acid Burn Treatment.** Expedient topical therapy for hydrofluoric acid burns can be made using crushed calcium containing antacids mixed with surgical jelly. The jelly may be placed in a rubber glove, then the glove on the patient's hand. (Photo contributor: Matthew D. Sztajnkrycer, MD, PhD.)

ARSENIC POISONING

Clinical Summary

Arsenic, a tasteless and odorless metalloid, is well absorbed by multiple routes of administration. Although arsenic exists in both inorganic and organic species, only the inorganic form is responsible for toxicity. Contaminated soil and water with inorganic arsenic are the primary sources of exposure to the general population. Chronic arsenic poisoning due to contaminated water continues to be a global health issue.

Arsenic inhibits multiple enzymes critical to the production of ATP. It inhibits pyruvate dehydrogenase complex, decreases the citric acid cycle, and decreases gluconeogenesis. Acute arsenic poisoning typically starts with acute onset of nausea, vomiting, abdominal pain, and "rice water" diarrhea. Acute encephalopathy, acute renal failure, lung injury, and death may occur. Later findings in survivors include alopecia, rash, Mees lines, and neuropathy. Chronic toxicity results in dermatologic changes such as hyperpigmentation or hypopigmentation. Hyperkeratosis may occur on the skin, particularly the palms and soles. Peripheral vascular disease (blackfoot disease) may occur. Arsenic is a known carcinogen and is associated with skin and lung cancers.

Management and Disposition

After an acute ingestion, an abdominal radiograph may demonstrate radiopaque material in the GI tract. Supportive care with maintenance of electrolytes is important. A 24-hour urine collection in a metal-free container is the optimal method for determining arsenic burden. However, the acutely ill patient will likely require chelation before urine results are available. Chelation is usually initiated with intramuscular dimercaprol (British anti-Lewisite, BAL). Succimer, an oral analogue of the BAL, may be useful in subacute poisoning. Patients with suspected acute arsenic poisoning should be admitted to an ICU.

Pearls

1. When a nonselective heavy metal urine test is performed for possible arsenic exposure, the measured arsenic typically reflects the presence of nontoxic organic species from dietary sources such as seafood, rather than toxic inorganic species. As such, urine should either be speciated, or the patient advised to refrain from seafood prior to urine collection.
2. Intravenous arsenic trioxide is approved by the Food and Drug Administration for treatment of acute promyelocytic leukemia unresponsive to other therapies.
3. Acute arsenic poisoning is one of the few heavy metals that is directly cardiotoxic as it blocks delayed rectifier channels. Torsades de pointes has been described in the setting of acute arsenic poisoning.

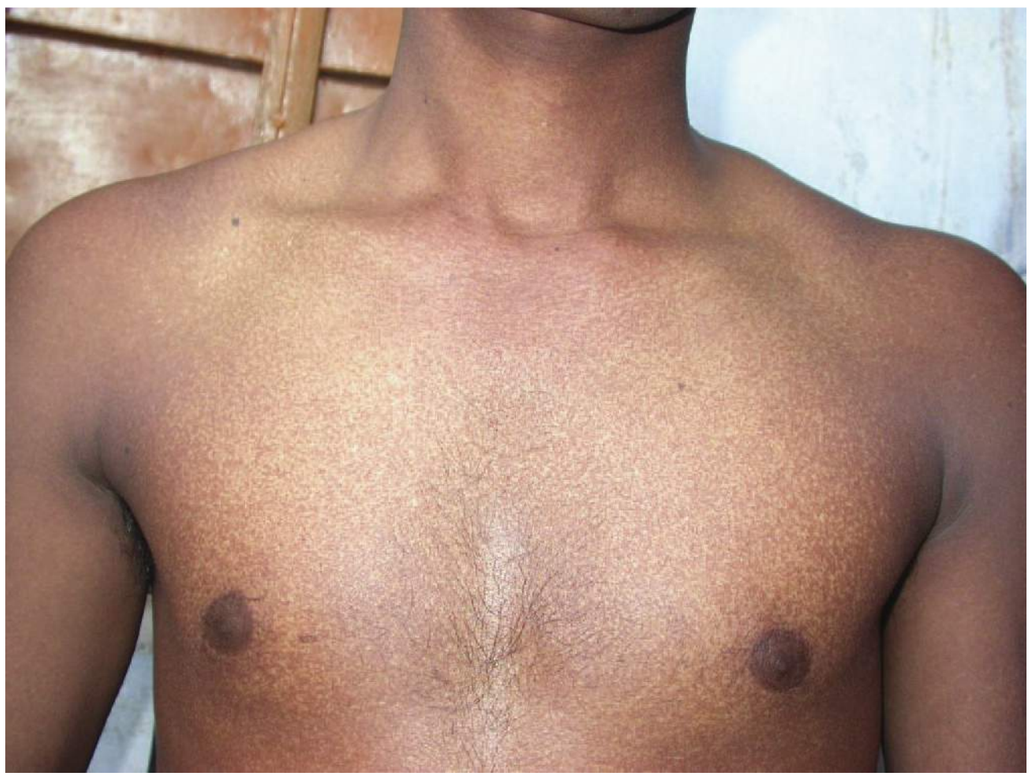

FIGURE 17.66 ■ **Chronic Arsenic Poisoning.** Hyperpigmentation of the skin is a clinical finding from chronic arsenic poisoning. (Photo contributor: Lawrence B. Stack, MD.)

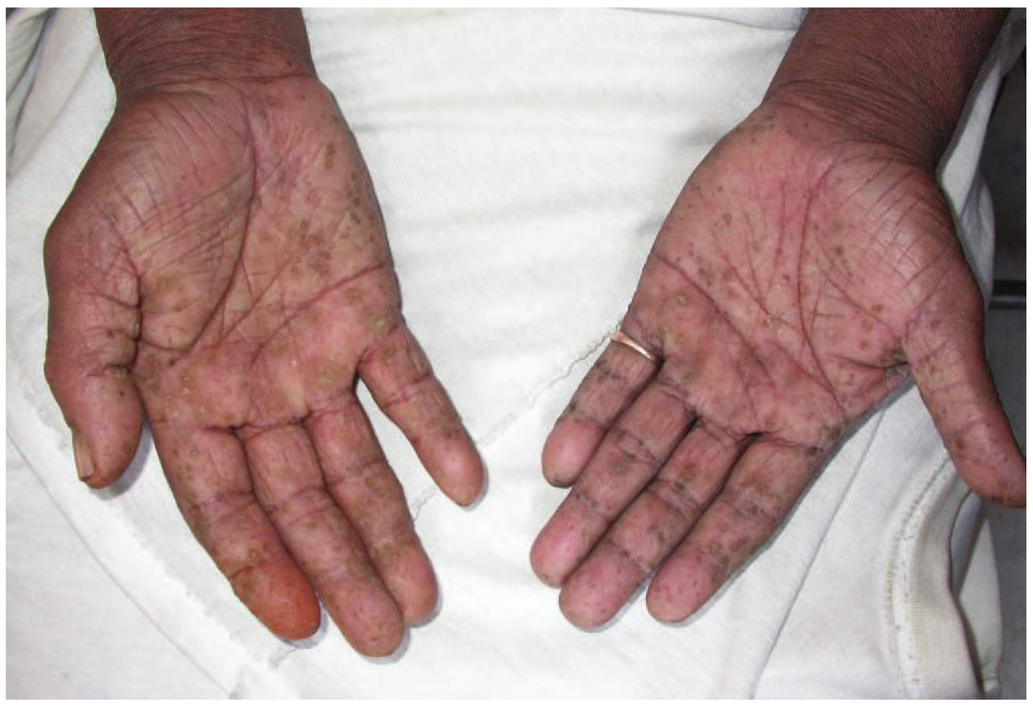

FIGURE 17.67 ■ **Chronic Arsenic Poisoning.** Hyperpigmentation and hypopigmentation along with hyperkeratosis are findings on the palms of patients with chronic arsenic poisoning. (Photo contributor: Lawrence B. Stack, MD.)

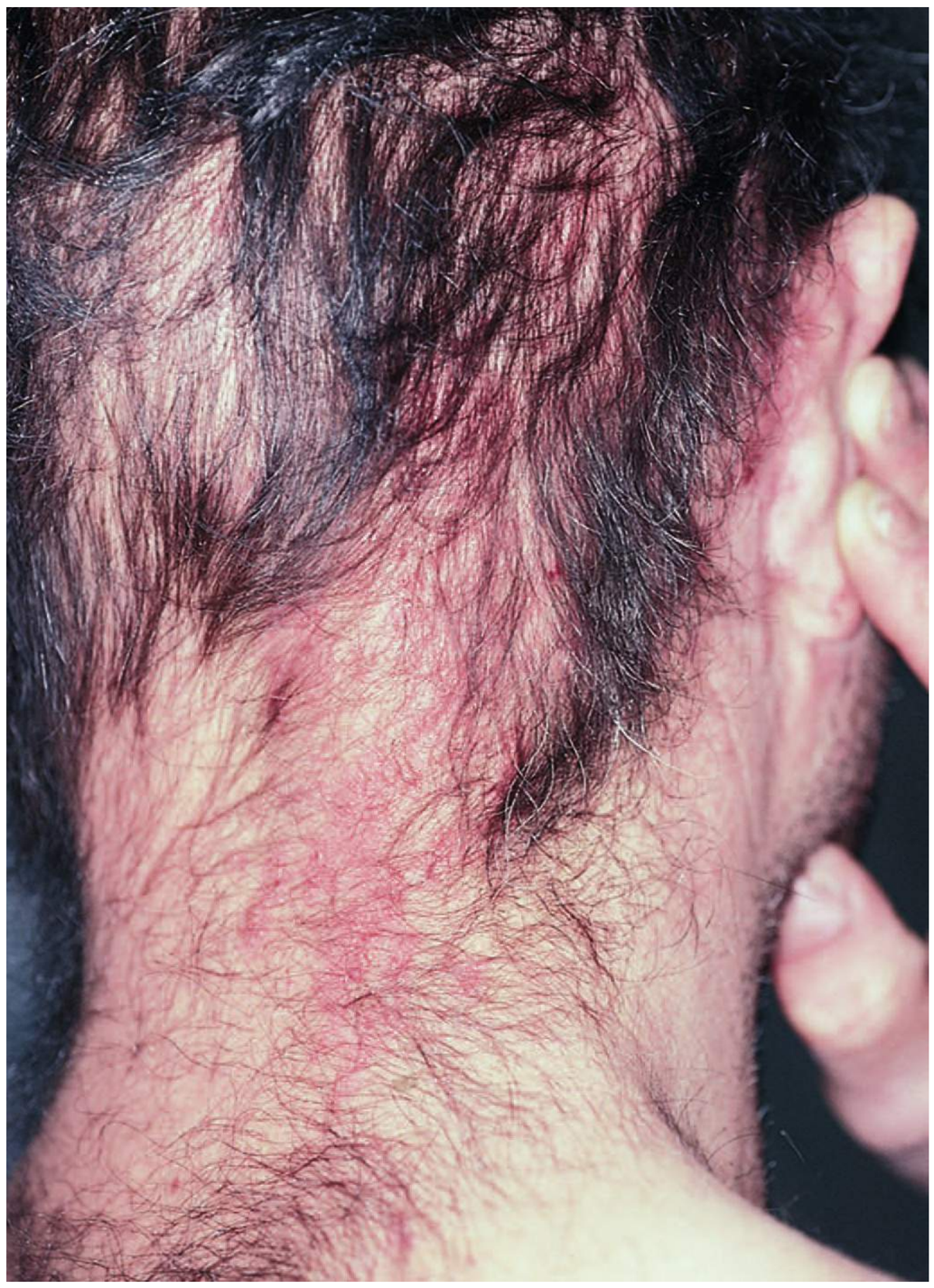

FIGURE 17.68 ■ **Chronic Arsenic Poisoning.** The patchy hair loss seen in this photograph is from chronic arsenic poisoning. (Photo contributor: Selim Suner, MD, MS.)

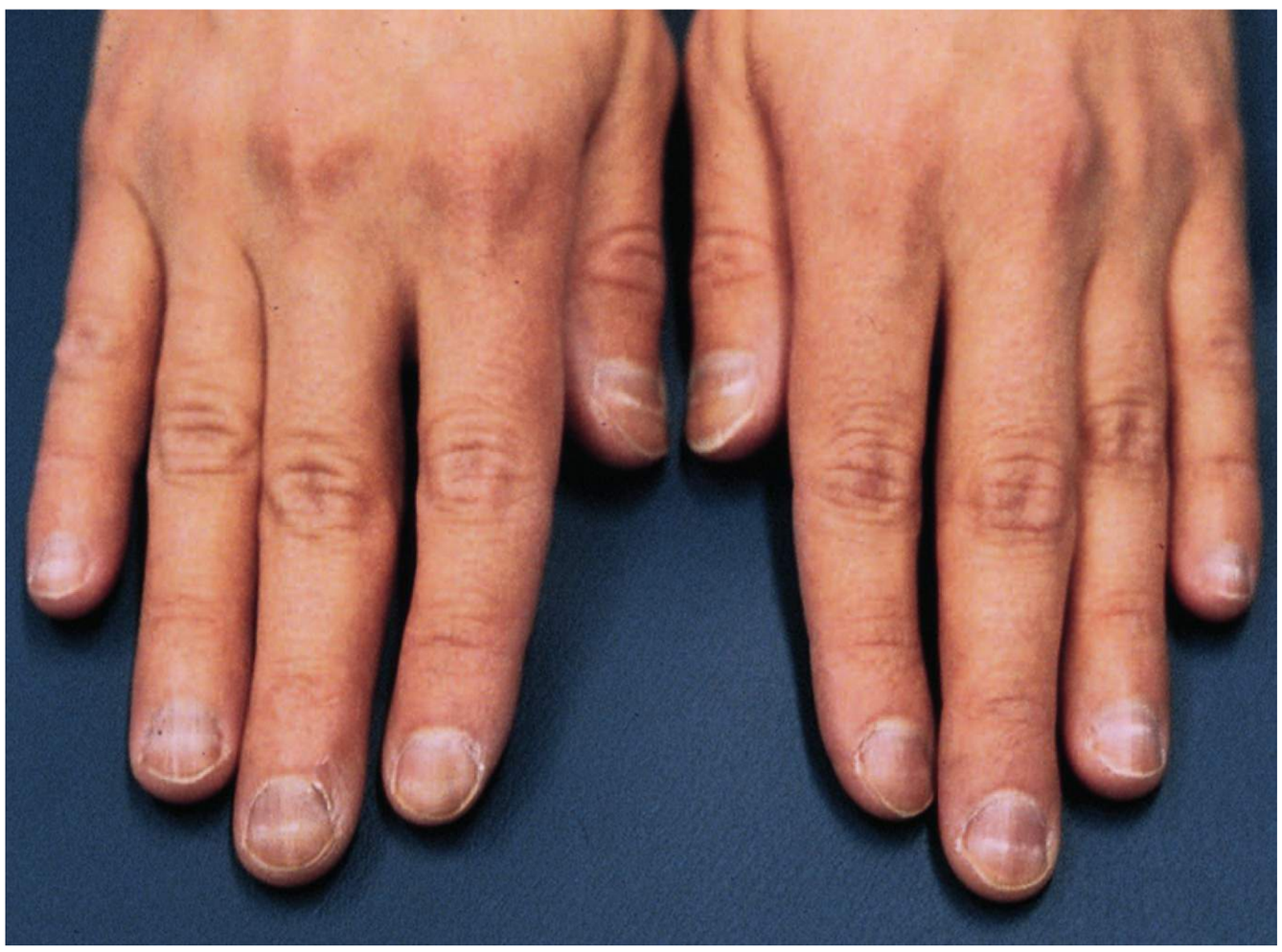

FIGURE 17.69 ■ **Mees Lines.** Characteristic Mees lines of chronic arsenic poisoning. Note the transverse white lines on all the nails of both hands. Mees lines are often seen in conjunction with polyneuropathy of arsenic poisoning. (Photo contributor: Robert S. Hoffman, MD.)

IRON POISONING

Clinical Summary

Iron is a commonly used pharmaceutical agent and supplement found in prenatal and multivitamins. Although the incidence has declined, acute iron poisoning remains a significant cause of pediatric morbidity and mortality. The toxic dose depends upon the quantity of elemental iron in the preparation, which in turn depends upon the iron formulation. While the minimum toxic dose remains controversial, ingestion of more than 40 mg/kg elemental iron may result in toxicity, while ingestion of more than 60 mg/kg elemental iron is associated with severe morbidity and possible mortality.

Iron toxicity is classically described as a four-stage process. Stage I develops within the first few hours of ingestion and reflects the direct caustic effects of iron on the GI tract. Signs and symptoms may include abdominal pain and GI bleeding. Stage II, variably present, is a redistributive or quiescent phase; although the initial GI symptoms resolve during this phase, acidosis and end-organ toxicity may still develop. With significant toxicity, individuals may progress directly from Stage I to Stage III. Stage III is the phase of overt shock, metabolic acidosis, and end-organ dysfunction (including delayed hepatic failure). Individuals who survive Stage III may rarely progress to Stage IV, gastric outlet obstruction secondary to the initial caustic insult of Stage I.

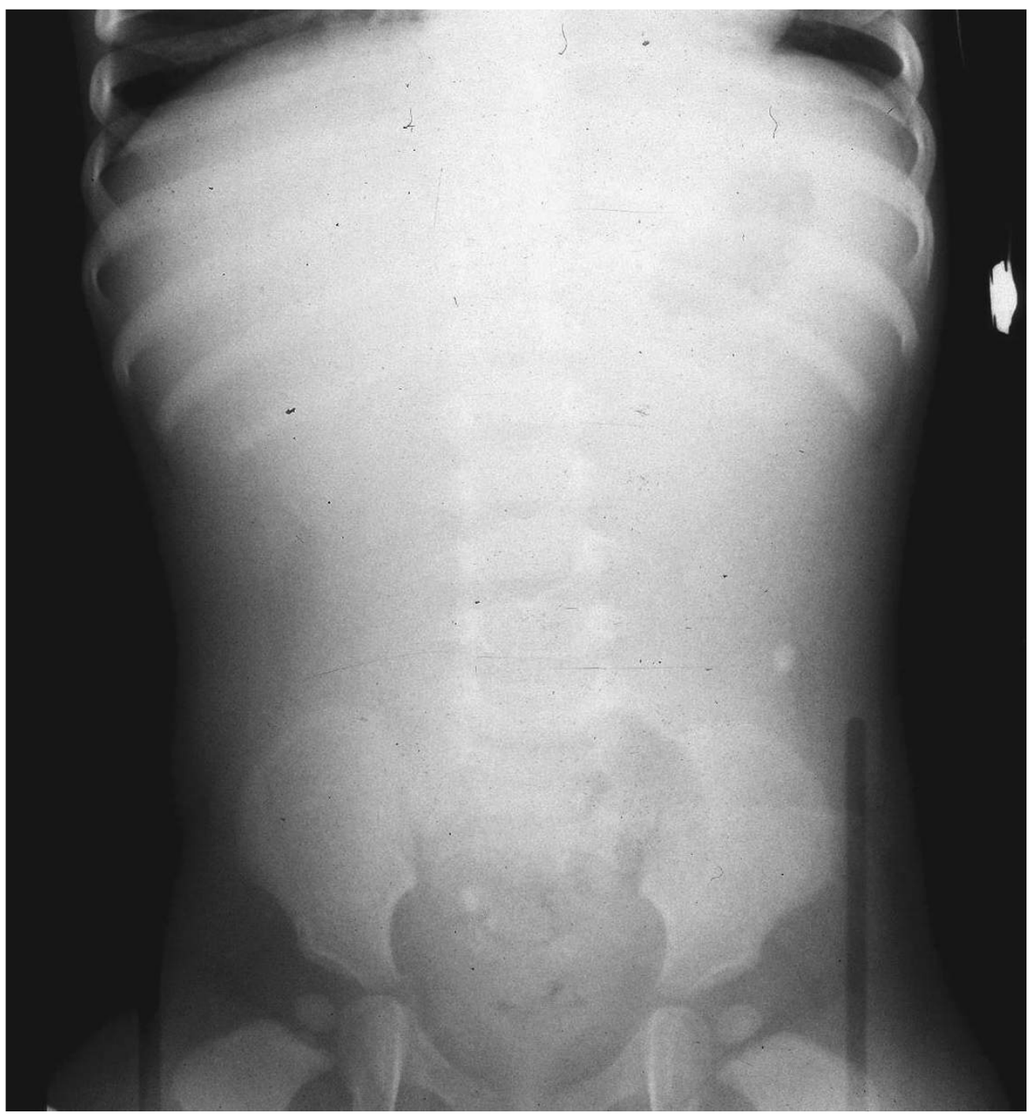

FIGURE 17.70 ■ **Radiopaque Iron.** KUB radiograph of a patient with an acute iron ingestion, demonstrating radiopaque foreign bodies as noted in the left mid-quadrant and right lower pelvis. (Photo contributor: Saralyn R. Williams, MD.)

Management and Disposition

Activated charcoal does not bind iron. Whole-bowel irrigation has been advocated for substantial ingestions and for patients with evidence of iron tablets on abdominal radiographs. Serum iron levels peak between 2 and 6 hours postingestion. Levels obtained more than 6 hours after ingestion are unreliable due to tissue redistribution. Patients with evidence of iron toxicity (eg, persistent vomiting, acidosis, altered mental status, and hypotension) or a 4- to 6-hour postingestion serum level more than 500 mcg/dL should receive chelation with deferoxamine.

Pearls

1. Acute iron ingestion and the risk for toxicity must be assessed based upon the quantity of elemental iron ingested, not the total amount ingested.
2. The absence of radiopaque materials on abdominal radiographs is not a reliable indicator to exclude potential iron toxicity; liquid and pediatric (chewable) formulations are not typically radiopaque.
3. Despite the potential for anaphylactoid reactions and hypotension, patients requiring chelation therapy should receive deferoxamine via the intravenous route.

FIGURE 17.71 ■ **Vin Rose Urine; Iron Poisoning.** A rare example of the progression of coloration of vin rose urine (from the excreted ferrioxamine complex) over 15 hours of chelation with deferoxamine is shown. Deferoxamine chelates free iron (but not iron present in the transferrin, hemoglobin, hemosiderin, or ferritin) (Reproduced with permission from Strange GR, Ahrens WR, Schafermeyer RW et al. Pediatric Emergency Medicine. 3rd ed. New York, NY: McGraw-Hill; 2009: Fig. 127-1.)

Clinical Summary

Although the prevalence of markedly elevated lead levels in the population has been declining, acute and chronic lead poisoning still occur. Lead is well absorbed by the lungs and less well via the GI tract. Lead paint in older homes is a continued source of lead exposure. Other possible exposures may occur from occupational exposures, retained lead bullets in synovial fluid, jewelry, lead-painted toys, fishing weights, ceramic glazes, and cosmetics. Severe lead poisoning in adults has also been associated with ingestion of contaminated moonshine.

Lead poisoning affects multiple organ systems. Neurotoxicity may range from subtle personality changes to encephalopathy and cerebral edema. At the societal level, even small lead burdens are associated with statistically significant decreases in intelligence quotient. Motor neuropathy such as foot drop and wrist drop may be seen in adult patients, especially after occupational exposure. Microcytic anemia may occur and basophilic stippling of the red cells may be seen. Hypertension and an acute nephropathy may occur. Abdominal pain may be described by patients but, unlike other heavy metal poisonings, constipation is more likely than diarrhea. Radiographic "lead lines," bands of increased density on long bones metaphyses, may be seen in young children. These densities are not due to deposition of lead but rather increased calcium deposition.

Management and Disposition

Whole-blood lead level is the primary measure of lead exposure, but is not usually available in real time. Radiographic studies may demonstrate radiopaque substances from ingested jewelry or paint chips in children. Lead encephalopathy must be aggressively managed. Dimercaprol (BAL) is administered intramuscularly and $CaNa_2EDTA$ is later given intravenously. Chelation with oral succimer is currently recommended in asymptomatic children with levels between 45 and 70 mcg/dL. Reducing the exposure in children is paramount to treatment and the source of the lead may be elusive.

Pearls

1. One source of lead exposure in children is through the occupation of the parent. Workers in a lead dust environment will bring home the lead dust on their clothes and shoes.
2. Imported eye cosmetics with lead have been a source of pediatric exposures in certain ethnic groups.
3. Azarcon and greta are lead-based remedies that are used to treat diarrheal illnesses.
4. Adults usually require much higher blood lead levels than children before encephalopathy occurs.

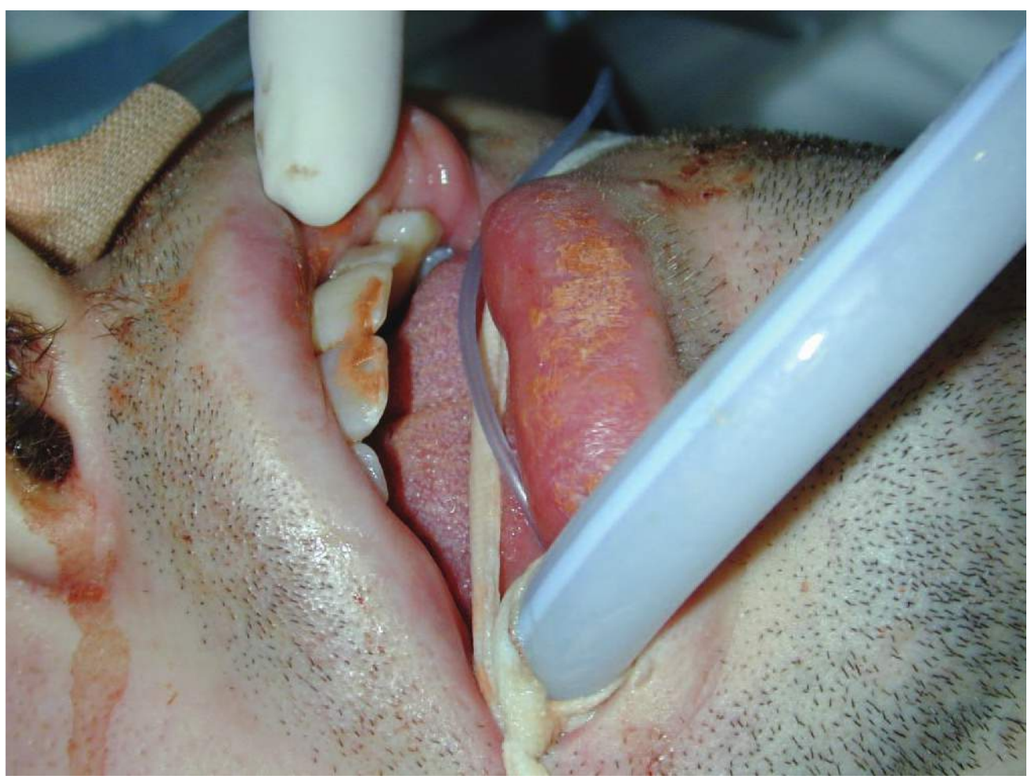

FIGURE 17.72 ■ **Acute Lead Poisoning.** This patient presented with acute encephalopathy after ingesting lead-based, tangerine-scented gloss glaze used for making pottery. The substance is present on his teeth, lips, and nose. (Photo contributor: Matthew D. Sztajnkrycer, MD, PhD.)

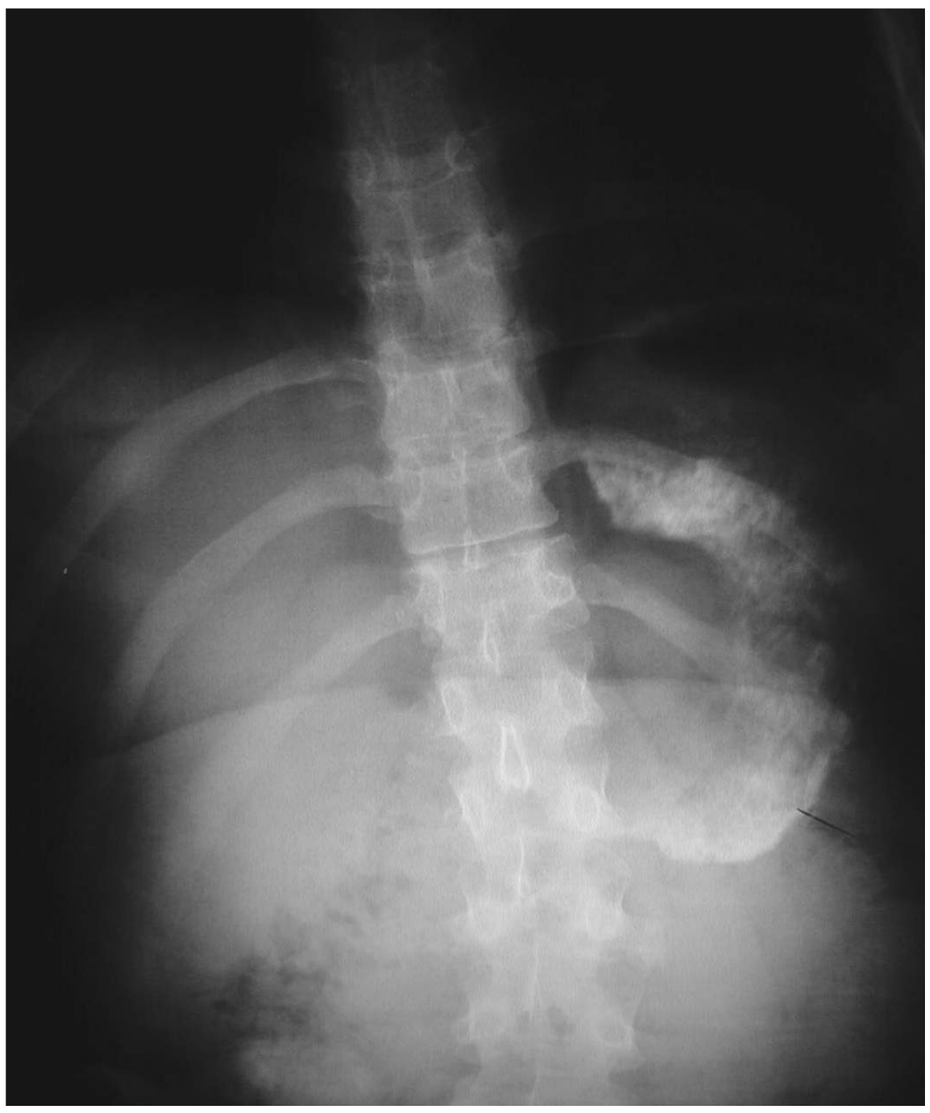

FIGURE 17.73 ■ **Radiopaque Lead.** The abdominal x-ray of the patient in Fig. 17.72. Lead is radiopaque when ingested. (Photo contributor: Matthew D. Sztajnkrycer, MD, PhD.)

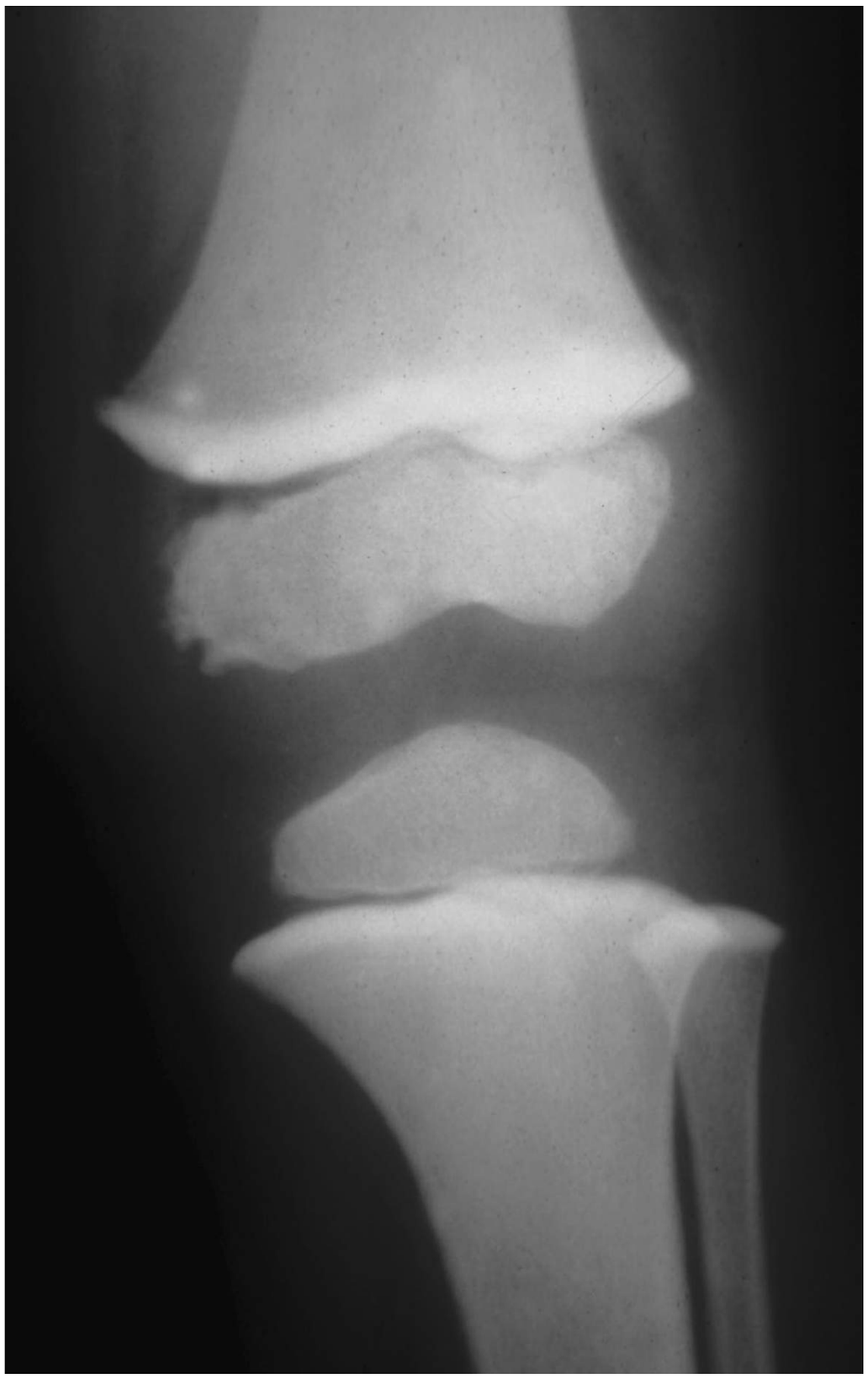

FIGURE 17.74 ■ **Lead Lines.** Lead lines seen in a pediatric patient with chronic lead poisoning. The increased radiographic densities on the metaphyseal growth plates demonstrate radiological growth retardation and increased calcium deposition. (Photo contributor: David Effron, MD.)

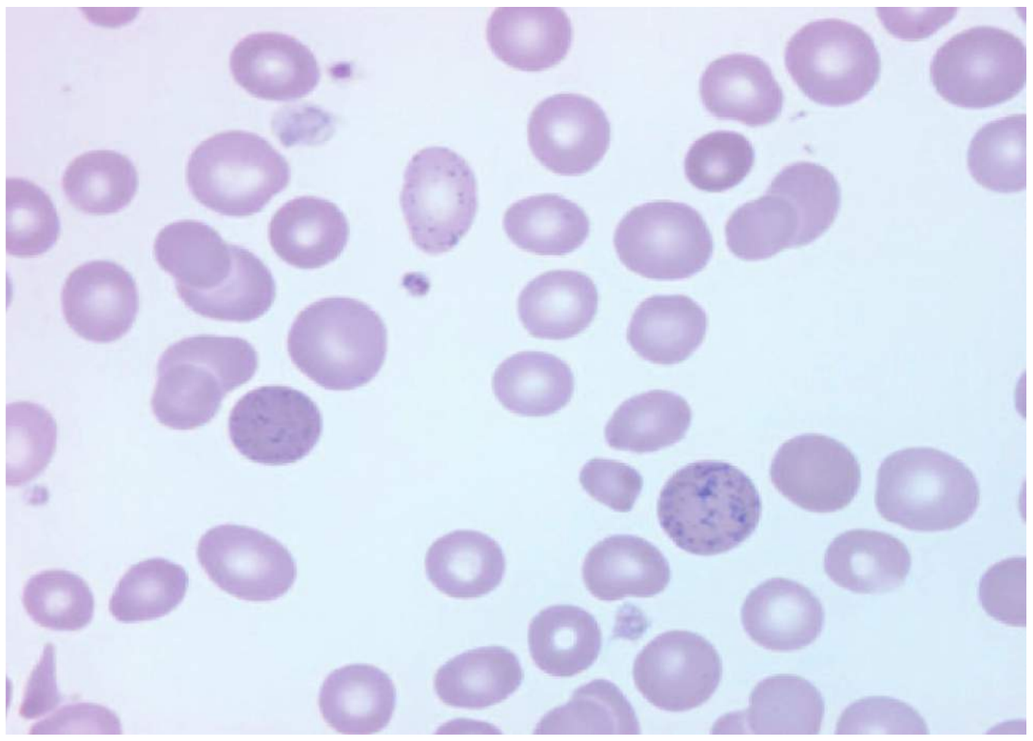

FIGURE 17.75 ■ **Basophilic Stippling.** Basophilic stippling along with a microcytic anemia may be seen in patients with chronic lead poisoning. (Photo contributor: Debbie Bennes, BS, MLT, ASCP.)

Clinical Summary

Mercury occurs in three different forms (elemental, inorganic, and organic), each with its own clinical pattern of poisoning. Elemental mercury ("quicksilver") is found in thermometers and sphygmomanometers. Elemental mercury poisoning is associated with inhalation of volatilized mercurial ions, which may occur after vacuuming or heating. Manifestations include cough, fevers, chills, and dyspnea. Acute interstitial pneumonitis may occur and may progress to severe lung injury and death. Inorganic mercury poisoning usually occurs from the ingestion of the mercurial salts. Initial presentation is acute caustic gastroenteritis that may be hemorrhagic. Renal failure is a prominent finding in these patients. Organic mercury poisoning occurs from ingestion of short-chain alkyl mercurial compounds. Methylmercury distributes into brain tissue and causes neurologic disease such as ataxia, paresthesias, visual difficulties, movement disorders, and speech difficulties. Methylmercury is also a known teratogen.

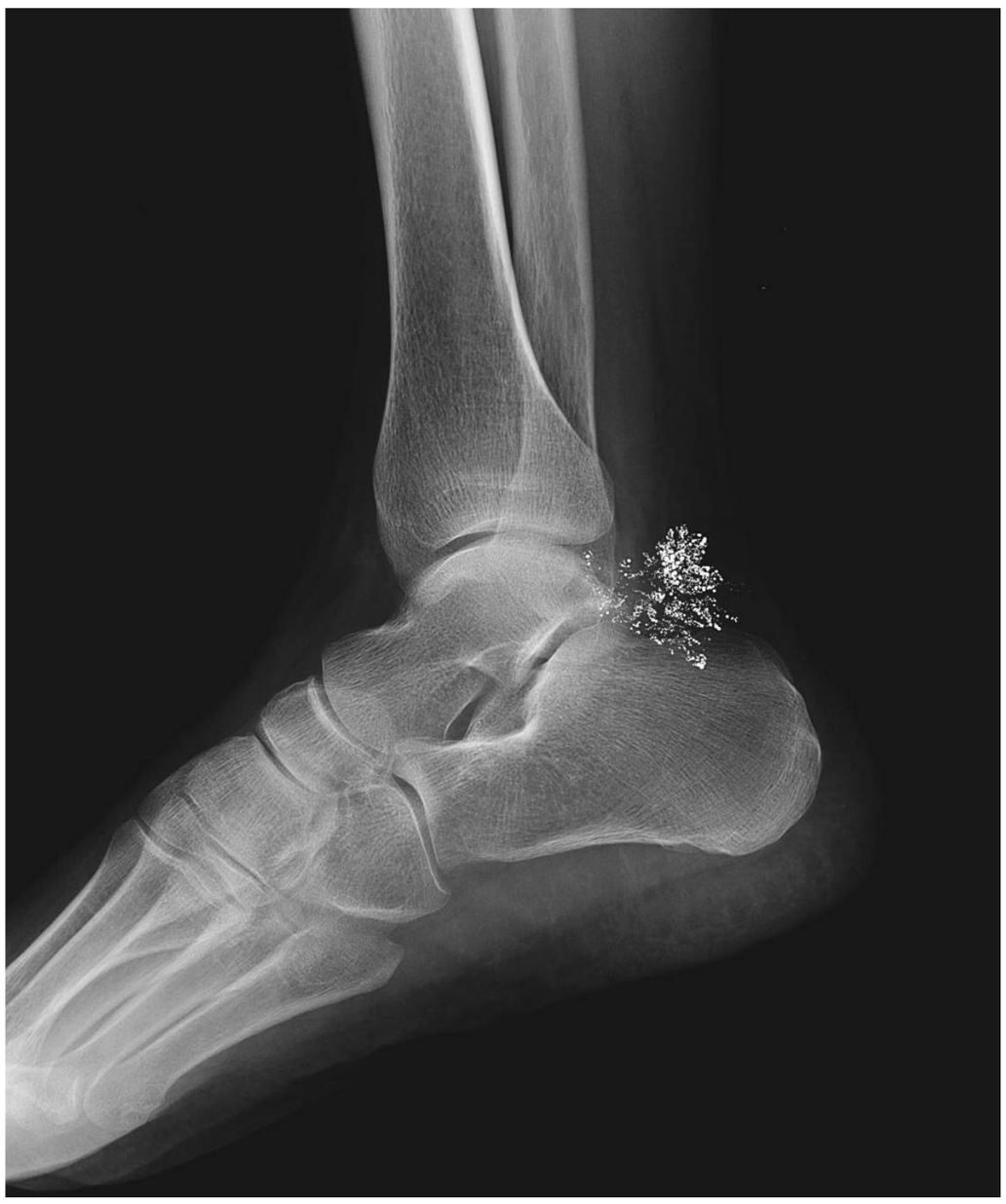

FIGURE 17.76 ■ **Subcutaneous Mercury.** Lateral radiograph of an ankle demonstrating elemental mercury in the tissues. The patient had a barometer break into his skin. (Photo contributor: Saralyn R. Williams, MD.)

Management and Disposition

After an ingestion of a mercurial substance, a radiograph may demonstrate radiopaque material in the GI tract. If elemental mercury was injected intravenously, mercurial emboli may be seen in the lungs. Local injection in the skin may demonstrate mercury deposition in the soft tissues. Ingestion of elemental mercury rarely results in significant absorption. For inhalational injury due to elemental mercury, respiratory support may be required. Ingestion of inorganic mercury may lead to early cardiovascular collapse as a result of the severe volume depletion. Fluid resuscitation and electrolyte management are critical. Chelation with dimercaprol (BAL) may be initiated early and when the patient is able to take oral medications, the chelator may be switched to succimer. For organic mercury poisoning, oral succimer may be the first-line agent.

Pearls

1. Elemental mercury toxicity has occurred when it is heated and used to extract gold from jewelry.
2. "Mad as a hatter" is a term used to describe the delirium for anticholinergic poisoning; however, the term is derived from the erethism and hatter's shakes from

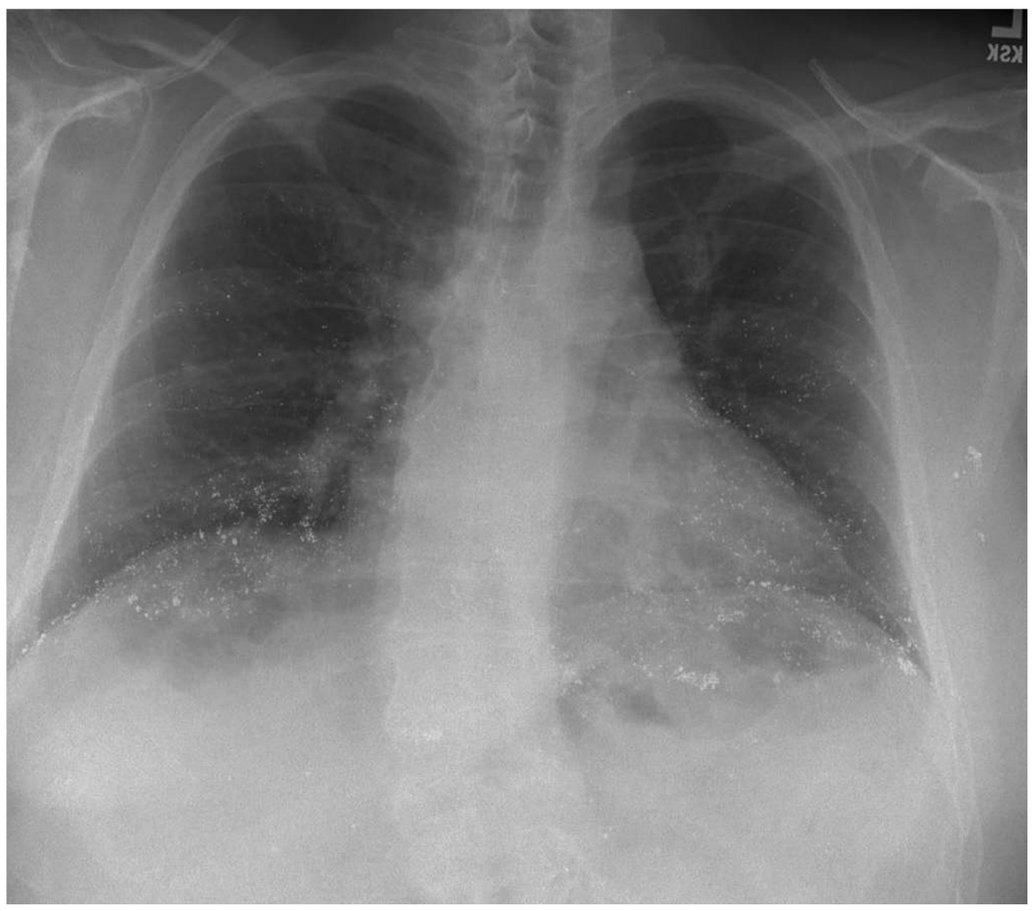

FIGURE 17.77 ■ **Mercurial Emboli.** Appearance of mercurial emboli in the pulmonary vascular tree on chest x-ray. Though this may be seen from intentional intravenous mercury injection, this patient absorbed the mercury intravenously following an accident involving multiple shattered thermometers. (Photo contributor: John Worrell, MD.)

mercury exposure during the felt-hat manufacturing process in the late 19th and early 20th century.

3. Organic mercury is eliminated via the fecal route, so urine samples for methylmercury will not be reflective of the body burden.
4. BAL is suspended in peanut oil, and so can only be administered as an intramuscular injection, and to nonpeanut-sensitive individuals.

FIGURE 17.78 ■ **Mercury Salts.** Mercury salts were used as topical antiseptics. Ingestion of inorganic mercury is caustic to the GI tract and causes rapid renal failure. (Photo contributor: Matthew D. Sztajnkrycer, MD, PhD.)

FIGURE 17.79 ■ **Mercury Tablets.** An example of the tablets from the bottle in Fig. 17.78. Although faded with age, the coffin-shaped tablets contain the word "poison" on one side and the "skull-and-crossbones" on the other. (Photo contributor: Matthew D. Sztajnkrycer, MD, PhD.)

Clinical Summary

Mushrooms are the fruiting bodies of certain fungi. While many species of mushrooms can cause toxicity when ingested, only a few contain amatoxins and account for most fatalities attributed to mushroom ingestion. Examples include Amanita phalloides (the "death cap") and Amanita ocreata (the "destroying angel") species. Amatoxin poisoning results in severe symptoms of gastroenteritis at least 6 to 24 hours after ingestion. Symptoms include nausea, vomiting, profuse watery diarrhea, and abdominal pain. GI symptoms may last 12 to 24 hours and are followed by a latent period of apparent improvement. This period is followed by a rise in liver enzymes and bilirubin. Fulminant hepatic failure and renal failure may become apparent.

The more common mushroom exposures include those with GI toxins. Ingestions result in an acute nausea, vomiting, and diarrhea that occurs within 2 hours of ingestion (eg, <6 hours of ingestion). Examples of mushrooms include the Chlorophyllum molybdites which looks like a toasted marshmallow in the grass. Other types of mushroom poisonings include gyromitrin-containing mushrooms that are misidentified for the popular morels. Gyromitrin mushrooms cause status epilepticus that is responsive to high-dose pyridoxine. Coprine-containing mushrooms only cause toxicity when ethanol is co-ingested as they cause a disulfiram reaction.

Management and Disposition

For the GI toxins containing mushrooms, management is supportive care. For the amatoxin containing mushroom, administration of activated charcoal may be recommended depending on the time since ingestion. Specific interventions that may be helpful but are yet unproved include charcoal hemoperfusion, high-dose cimetidine, high-dose penicillin, high-dose ascorbic acid, silibinum, and NAC. Consultation with the local poison center is recommended.

Pearls

1. A single "death cap" may contain enough amatoxin to kill an adult.
2. Cooking mushrooms does not substantially alter their toxicity.
3. Not all Amanita species of mushrooms cause hepatotoxicity when ingested. Some Amanita species are hallucinogens and one causes renal failure.
4. Be wary of using the "6-hour rule" with mushroom scavengers who may have ingested multiple species of mushrooms.

FIGURE 17.80 ■ Amanita phalloides. The "death cap" produces amatoxins and accounts for most of the fatalities due to mushroom ingestion. (Photo contributor: Edward J. Otten, MD.)

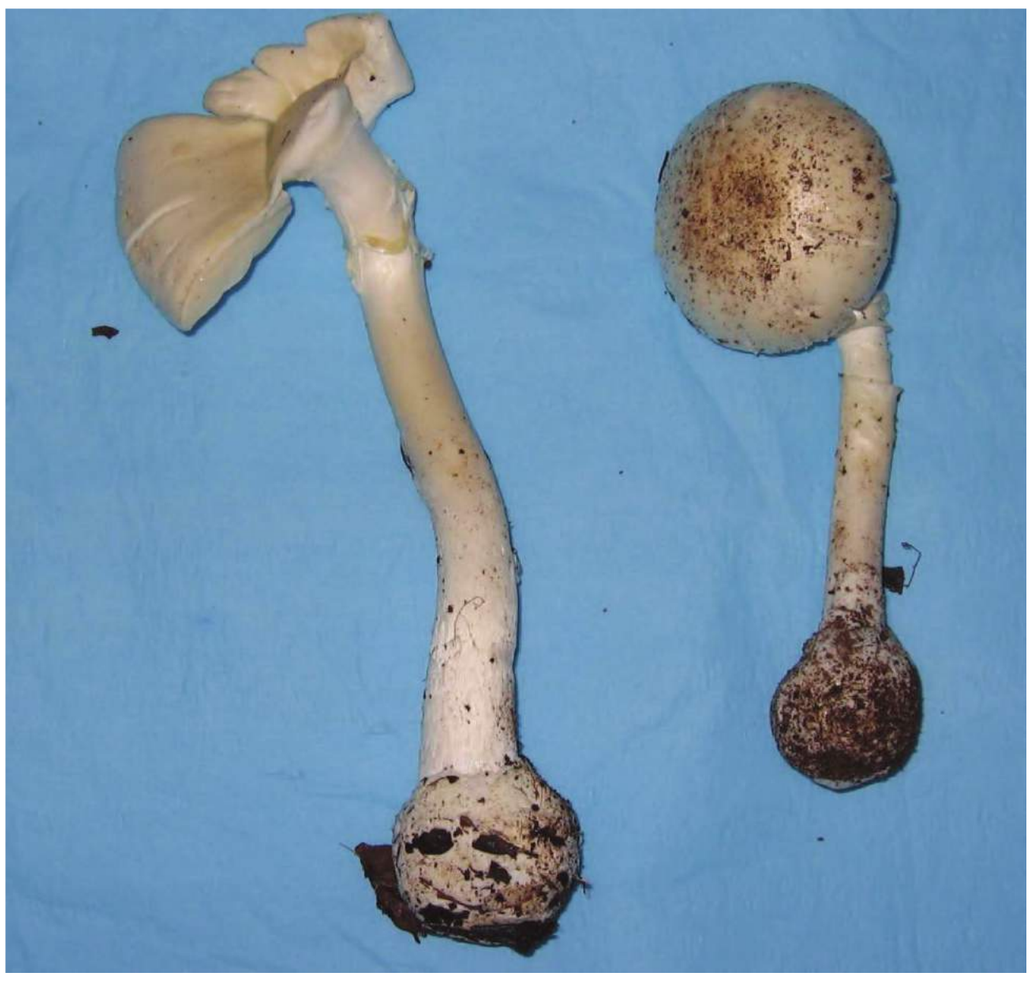

FIGURE 17.81 ■ Amanita ocreata. These mushrooms were samples of Amanita ocreata provided by a family who had ingested them and subsequently developed significant hepatotoxicity. (Photo contributor: Division of Medical Toxicology, University of California, San Diego.)

FIGURE 17.82 ■ **Morel Mushroom.** Morels are considered a delicacy; however, inexperienced mushroom hunters may collect a "false morel" which contains gyromitrin. Ingestion of gyromitrin results in status epilepticus that is responsive to intravenous pyridoxine. (Photo contributor: Saralyn R. Williams, MD.)

FIGURE 17.84 ■ **Coprinus Mushrooms.** Coprinus mushroom cause toxicity when ethanol is co-ingested, resulting in a disulfiram-like reaction. (Photo contributor: Matthew D. Sztajnkrycer, MD, PhD.)

FIGURE 17.83 ■ Chlorophyllum molybdites**.** This mushroom is ubiquitous and is a common culprit for mushroom toxicity. The patient typically presents with acute nausea vomiting less than 2 hours after ingestion. (Photo contributor: Saralyn R. Williams, MD.)

Clinical Summary

Cardiac glycosides (CGs) are found in the leaves, flowers, and seeds of Nerium oleander (common oleander), Thevetia peruviana (yellow oleander), Digitalis purpurea (foxglove), Strophanthus gratus (ouabain), Convallaria majalis (lily of the valley), Apocynum cannabinum (dogbane), Urginea maritima and Urginea indica (squill), and Cheiranthus cheiri (wallflower). If ingested, they produce clinical findings similar to digoxin toxicity. The drinking of foxglove and oleander tea may be a cause of CG toxicity. Therapeutic effects occur from inhibition of the cardiac cell membrane sodium-potassium ATP pump, resulting in increased automaticity, decreased conduction through the atrioventricular (AV) node, and improved inotropy.

Toxic effects are an exaggeration of therapeutic effects. Bradydysrhythmias may result from impaired pacemaker function. Tachydysrhythmias may occur from increased automaticity. Nausea, vomiting, abdominal pain, confusion, depression, and fatigue may be present. Headaches, paresthesias, weakness, scotomas, and visual color disturbances (yellow halos around lights) may also be seen.

Management and Disposition

Atropine may be initially given for bradydysrhythmias. Refractory bradydysrhythmias require pacing. Ventricular tachydysrhythmias have been treated with phenytoin or lidocaine when digoxin-specific Fab fragments are not available. Activated charcoal is the preferred method of decontamination. Cardioversion should be avoided in CG toxicity. Digoxin-specific Fab fragments are the treatment of choice for life-threatening dysrhythmias or CG-induced hyperkalemia.

Pearls

1. Treat CG overdose from plant exposure in the same way as an acute digoxin overdose. Higher doses of digoxin-specific Fab fragments may be required.
2. Calcium should be avoided in treating CG-associated hyperkalemia, as it may worsen ventricular arrhythmias.
3. Dysrhythmias characterized by increased automaticity coupled with the presence of conduction disturbances are highly suggestive of CG toxicity.

FIGURE 17.85 ■ Nerium oleander **(Common Oleander).** A common decorative plant in subtropical climates often seen lining roads and highways. Flowers may be white, yellow, red, or purple. Drinking a tea brewed from the leaves of oleander results in severe cardiac glycoside poisoning. (Photo contributor: Saralyn R. Williams, MD.)

FIGURE 17.86 ■ Digitalis purpurea **(Purple Foxglove).** The ornamental plant. (Photo contributor: Lawrence B. Stack, MD.)

FIGURE 17.87 ■ Convallaria majalis **(Lily of the Valley).** While both beautiful and fragrant, lily of the valley contains multiple types of toxic cardiac glycoside compounds. (Photo contributor: Saralyn R. Williams, MD.)

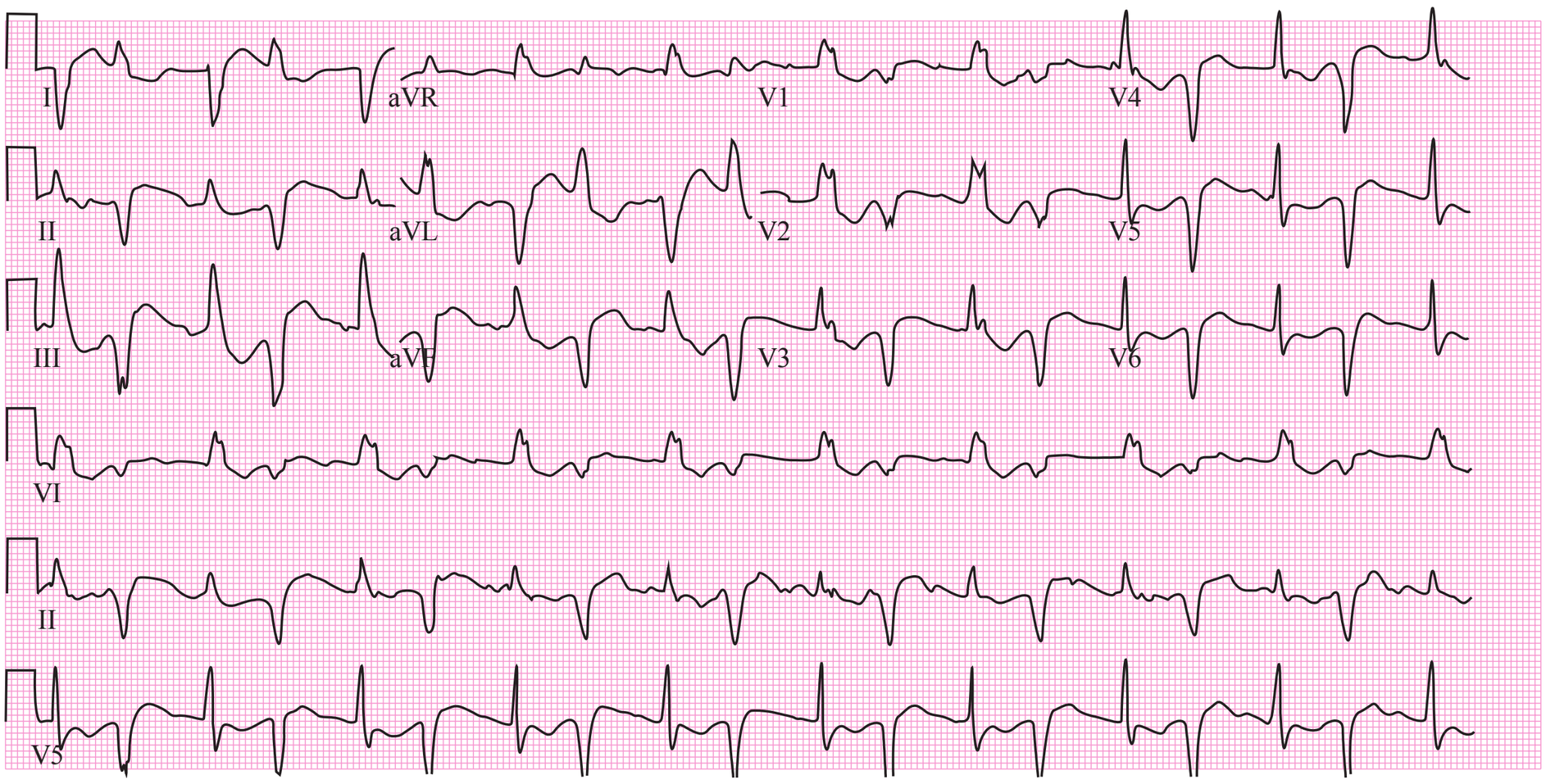

FIGURE 17.88 ■ **Bidirectional Ventricular Tachycardia.** An example of bidirectional ventricular tachycardia that occurred in a patient with digitalis toxicity. (Photo contributor: Binh Ly, MD.)

Clinical Summary

Many common houseplants such as dieffenbachia (dumbcane) and peace lily cause irritant effects when ingested owing to large amounts of insoluble oxalate crystals in its leaves. The oxalate crystals are highly irritating, and those who ingest the leaves experience painful burning of the lips, tongue, mouth, and esophagus. Marked swelling of the tongue, lips, and oropharynx can occur, and airway patency may become a major issue in managing these patients. Ocular exposures may occur as well, resulting in painful burning, erythema, and eyelid swelling. Fortunately, these calcium oxalate crystals are not absorbed and the hypocalcemia associated with soluble oxalates is not an issue.

Management and Disposition

Topical anesthetics are helpful in controlling severe pain from burning mucous membranes. Management is largely supportive, as the painful oral burns experienced with these exposures usually limit ingestion. As with any oropharyngeal burn, airway issues must be addressed. A period of observation is appropriate to make sure that airway compromise does not occur with continued swelling. If leaves are swallowed and the patients are symptomatic, GI consultation should be considered to assess the extent of esophageal injury. GI decontamination is usually not necessary.

Pearls

1. Performance of nasopharyngoscopy may be helpful in assessment of airway patency for more posterior burns.
2. Patient should be instructed not to swallow topical anesthetics, as toxicity may result with extensive use.

FIGURE 17.89 ■ Dieffenbachia. Dieffenbachia is a common houseplant because of its colorful appearance and ease of indoor growth. (Photo contributor: Kevin J. Knoop, MD, MS.)

FIGURE 17.90 ■ **Peace Lily.** The attractive foliage and blooms make this a popular house plant; however, it is not a true lily. (Photo contributor: Saralyn R. Williams, MD.)

JIMSONWEED INGESTION

Clinical Summary

Jimsonweed (Datura stramonium) is a toxic plant that contains tropane alkaloids consisting of atropine, scopolamine, and hyoscyamine compounds. Ingestion may occur through the drinking of tea made from the leaves or flowers of jimsonweed or from eating the plant's seeds or leaves. Poisoned victims demonstrate an anticholinergic toxidrome resulting from the antimuscarinic receptor effects of atropine and scopolamine. Patients may exhibit altered mental status, xerostomia, xeroderma, xerophthalmia, blurred vision, mydriasis, tachycardia, decreased bowel and bladder motility, and hyperthermia.

Management and Disposition

Treatment initially consists of assessing the ABCs (airway, breathing, circulation) and stabilization measures. Hypotension resulting from tropane alkaloid ingestion usually responds to fluid boluses. Vasopressor agents are rarely necessary. Activated charcoal may be recommended early after ingestion but may not change outcome as the toxins are absorbed rapidly. Whole-bowel irrigation is contraindicated with intestinal ileus and must be considered with great caution in jimsonweed ingestion due to decreased bowel motility. Physostigmine may be of benefit to treat severe anticholinergic toxicity, but may be better utilized as a diagnostic agent after consultation with the poison center. Severe agitation and psychosis may be treated with benzodiazepines and carefully administered properly dosed physostigmine.

Pearls

1. Examination of the axillae for xeroderma may be helpful to detect peripheral anticholinergic syndrome and distinguish between anticholinergic and sympathomimetic toxidromes.
2. Administering 1% pilocarpine eye drops does not reverse anticholinergic mydriasis.
3. Jimsonweed toxicity should be considered in the differential diagnosis of children and adolescents presenting with acute altered mental status, especially when accompanied by signs of anticholinergic toxicity.

FIGURE 17.91 ■ **Jimsonweed.** Jimsonweed seed pod with dried seeds. (Photo contributor: Matthew D. Sztajnkrycer, MD, PhD.)

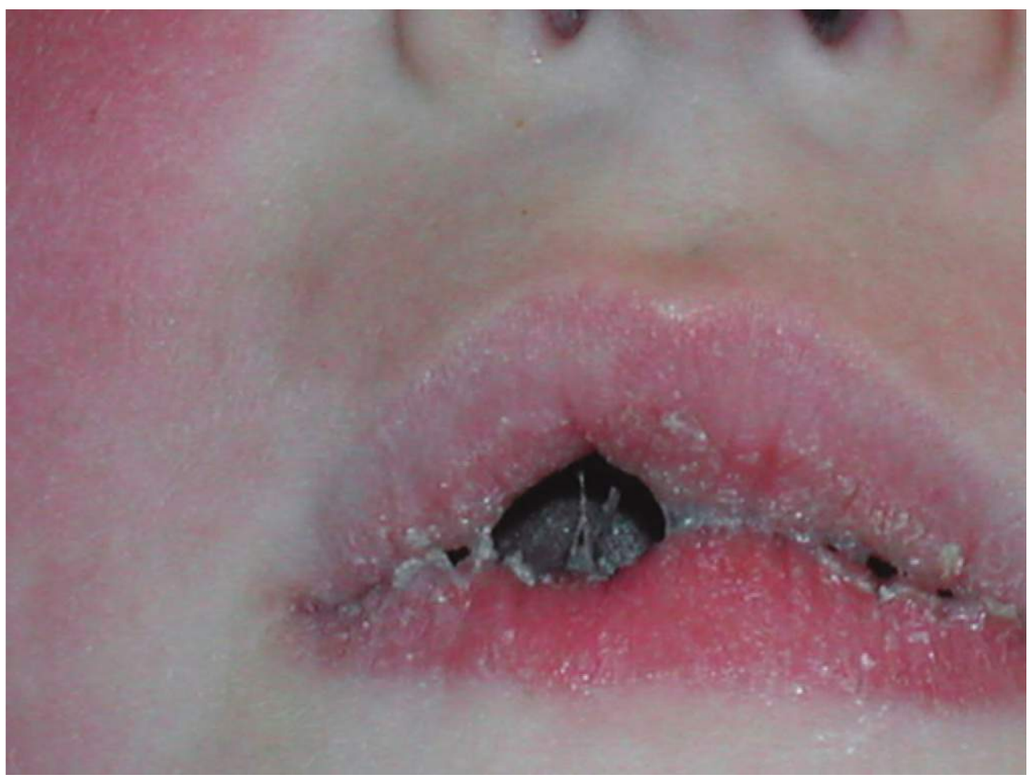

FIGURE 17.92 ■ **Jimsonweed-Induced Xerostomia.** A severe case of xerostomia from the antimuscarinic effects of jimsonweed ingestion. Note the associated flushing of the patient's cheek. (Photo contributor: R. Jason Thurman, MD.)

Clinical Summary

Peyote (Lophophora williamsii) is a cactus plant found primarily in the southwestern United States. The cactus contains a significant amount of mescaline, a potent hallucinogen with structural similarities to norepinephrine. Peyote buttons and seeds are frequently ingested for recreational use, but are also used in the religious ceremonies of some Native American groups. Toxicity of peyote is generally mild and self-limited, but hypotension and respiratory depression can occur. Mescaline induces some sympathomimetic effects due to its similarity to norepinephrine; marked visual hallucinations and a sense of depersonalization follow. These effects are often accompanied by unpleasant GI symptoms such as severe nausea and vomiting. Full recovery from these symptoms usually occurs within a few hours.

Management and Disposition

Treatment of peyote ingestion is largely supportive; severe toxic effects are uncommon. Marked agitation may be managed with benzodiazepines.

Pearls

1. An individual peyote button contains about 45 mg of mescaline; a mescaline dose of 5 mg/kg usually produces psychotropic effects.
2. Botulism poisoning has been reported from the ingestion of dried peyote buttons.

FIGURE 17.94 ■ **Peyote Cactus.** An individual crown of peyote. (Photo contributor: Martin Terry, PhD.)

FIGURE 17.93 ■ **Peyote Cactus Patch.** Patch of peyote crowns growing in the desert. (Photo contributor: Martin Terry, PhD.)

FIGURE 17.95 ■ **Peyote Button.** This desiccated button of peyote is the form that is ingested for recreational or religious purposes. (Photo contributor: Martin Terry, PhD.)

TOXALBUMIN INGESTION

Clinical Summary

The jequirity pea (Abrus precatorius) and castor bean (Ricinus communis) belong to a family of poisonous plants that contain toxalbumins. The chief toxin of the jequirity pea is abrin, which is structurally very similar to the toxin ricin of the castor bean. Ingestion of jequirity peas and castor beans rarely results in toxicity, as a majority of the plant toxin is concentrated within the hard shell of the seeds. However, when these seeds are chewed or the shell is digested, symptoms of severe gastroenteritis follow within 1 to 3 days. Nausea, vomiting, abdominal pain, and diarrhea are common but in severe cases may be accompanied by hemorrhagic gastritis and hematemesis, seizures, arrhythmias, marked dehydration, CNS depression, and even death. Unfortunately, because of the colorful attractive nature of jequirity peas and castor beans, most cases of ingestion occur in the pediatric age group. Because of the very high potency of these toxins, they are occasionally used for homicidal purposes and growing concern exists for their potential utilization as an agent of bioterrorism.

Management and Disposition

Treatment of jequirity pea and castor bean ingestions is largely supportive, as there is no specific antidote for abrin or ricin. Gastric decontamination may be considered and may include activated charcoal and whole-bowel irrigation. In asymptomatic patients, decontamination, careful observation, and close follow-up are adequate. With symptoms of toxicity, however, admission is recommended, as the potential for marked clinical worsening is present.

FIGURE 17.96 ■ **Castor Bean Plant.** The castor bean plant is large and leafy; it may reach a height of 10 to 12 ft. (Photo contributor: Alex Wilson.)

Pearls

1. Most jequirity pea and castor bean ingestions are benign, as the vast majority of toxin resides within the undigested shell of the plant.
2. The toxalbumins abrin and ricin are structurally similar to botulinum toxin, cholera toxin, diphtheria toxin, and insulin.
3. Severe allergic reactions with anaphylaxis have been reported with handling of the seeds of castor bean and are also seen among workers in factories where castor oil is produced.
4. Castor bean plant is commercially cultivated as a source of castor oil. Such oil has been used for centuries as a purgative and as a lubricant for machines.

FIGURE 17.97 ■ **Castor Bean.** Typical appearance of the castor bean. (Photo contributor: Alex Wilson.)

FIGURE 17.98 ■ **Jequirity Pea.** Jequirity peas are also known as rosary peas, Indian beans, Buddhist's beads, crab's eyes, and prayer beads. They are about 5 mm in diameter and have a colorful glossy shell, usually red with a black center, although black and white may also be seen. (Photo contributor: Kevin J. Knoop, MD, MS.)

Clinical Summary

Levamisole is a levo enantiomer of tetramisole and has immunomodulatory properties. It was first used as an anthelminthic for human and veterinary use. Initial human use in the 1970s for inflammatory conditions resulted in publications of levamisole-associated agranulocytosis and vasculitis. In 2003, the United States Drug Enforcement Agency identified levamisole as an adulterant in cocaine. In 2009, case reports of agranulocytosis and vasculitis associated with levamisole-contaminated cocaine were published. The dermatologic manifestations may include retiform purpura with possible skin necrosis and tend to appear on the ears and nose but can affect any area.

Complications have been reported from both cocaine hydrochloride and crack cocaine and all routes of use. The reason for adulterating the cocaine with levamisole is not clear. Theories include that the levamisole enhances the effects of cocaine via one of several potential mechanisms: enhancing noradrenergic neurotransmission, inhibiting monoamine oxidase, inhibiting acetylcholinesterase, and stimulating ganglionic nicotinic receptors.

Management and Disposition

Initial considerations for the differential diagnosis for agranulocytosis or the vasculopathy should be broad. The xenobiotic exposure history for the patient must also be carefully reviewed, inclusive of drugs of abuse. For both the agranulocytosis and the cutaneous vasculopathy, serologic testing assists with the differential diagnosis; however, no one classic pattern is diagnostic for levamisole as the etiologic agent.

In the setting of agranulocytosis, neutropenic fever may occur and should be managed accordingly with antibiotics. Deaths from infectious complications have occurred. Cessation of exposure to the levamisole is imperative—which means cessation of cocaine use.

Pearls

1. Case reports of levamisole-associated complications suggest that there is a high level of recurrence of complications upon reexposure to levamisole-contaminated cocaine.

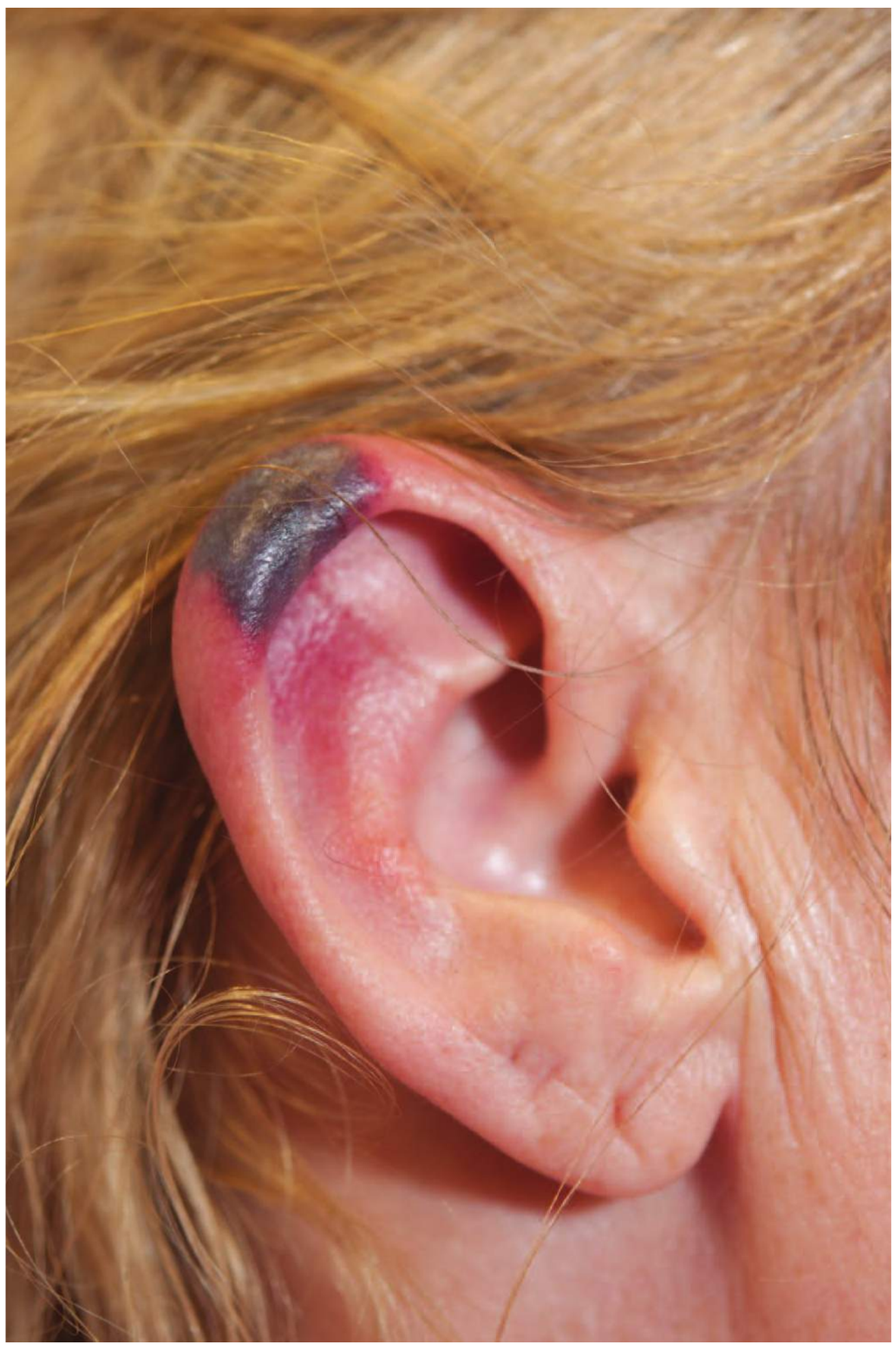

FIGURE 17.99 ■ **Levamisole-Induced Vasculitis (Ear).** The vasculitis associated with levamisole has a predilection for involving the ear. (Photo contributor: Lawrence B. Stack, MD.)

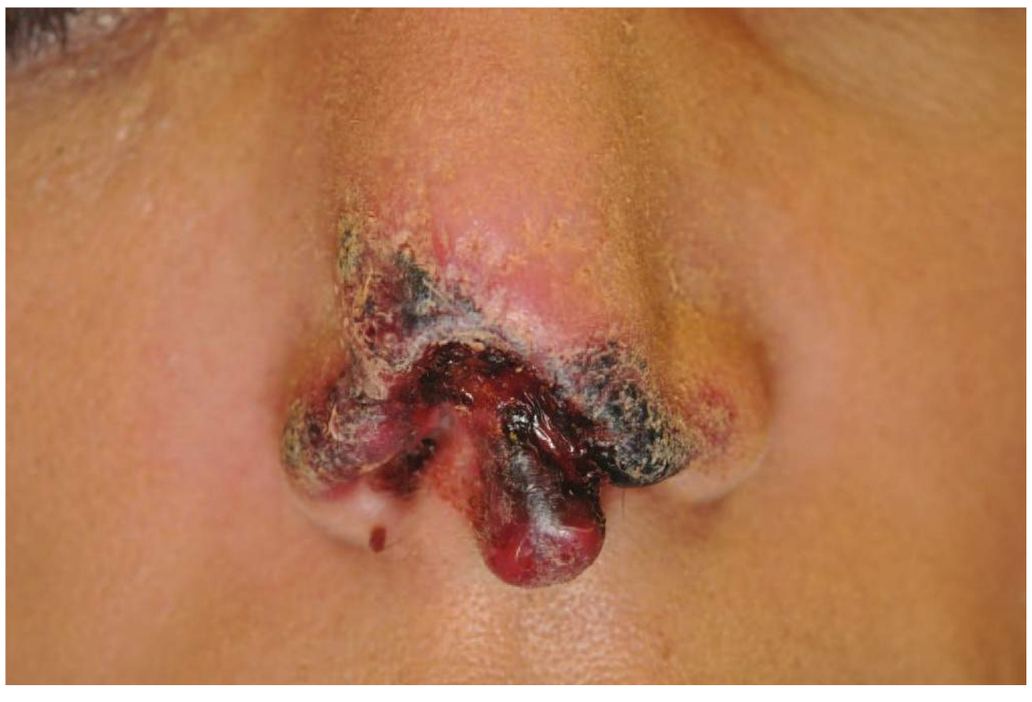

FIGURE 17.100 ■ **Levamisole-Induced Vasculitis (Nose).** Levamisole induced vasculitis can induce significant tissue necrosis requiring reconstructive grafts. (Photo contributor: R. Jason Thurman, MD.)

2. Based on case reports, the ears and nose tend to manifest the skin necrosis more often than other areas.
3. Urine drug screens usually check for the cocaine metabolite benzoylecgonine, which may be detectable in the urine for up to 3 days after cocaine exposure. Adulterants such as levamisole are not a part of the routine drug screens. Detection for levamisole requires additional techniques such as gas chromatography-mass spectrometry, liquid chromatography, or tandem mass spectrometry.

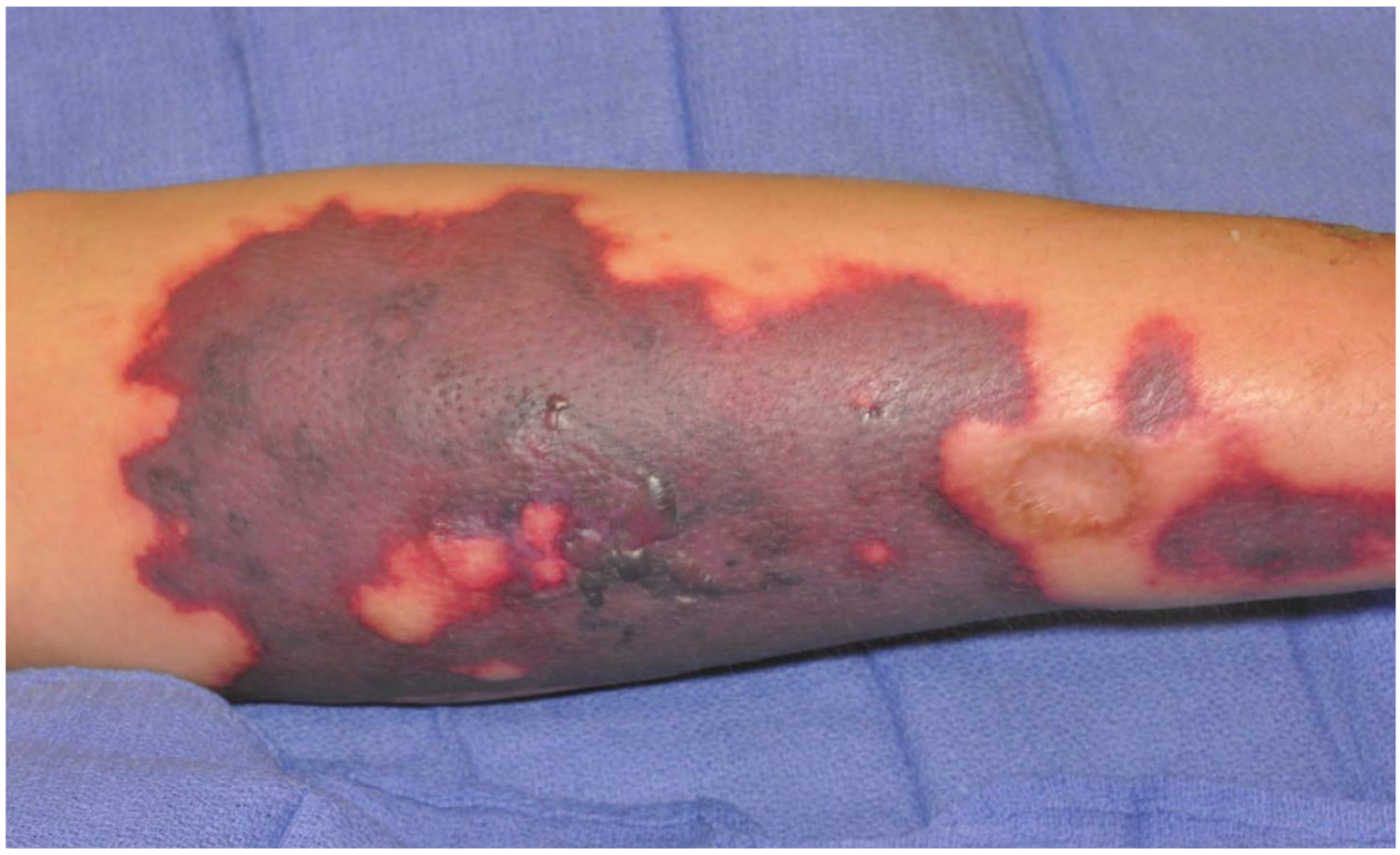

FIGURE 17.101 ■ **Levamisole-Induced Vasculitis.** Typical appearance of the purpuric lesions of levamisole-induced vasculitis. These lesions were acute and involved the leg of the patient in Fig. 17.100 who also had necrotic lesions from a previous case of levamisole-induced vasculitis. (Photo contributor: R. Jason Thurman, MD.)