# Chapter 46 Principles of toxicology

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## Introduction

Emergency personnel commonly encounter toxicological emergencies from accidental exposures (e.g. workplace incidents or drug interactions) or intentional exposures (e.g. drug abuse or suicide attempts). In 2011, over 2.3 million human toxin exposures were reported to the American Association of Poison Control Centers [1]. More than 93% of exposures were reported from residences, with routes of exposure by ingestion (83%), through the skin (7%), inhalation (6%), and through the eye (4%). Eighty percent of exposures were unintentional and 62% involved patients under the age of 20 years.

The outcome following a poisoning depends on numerous factors, including dose taken, time to first medical contact, and the patient’s preexisting health status. Poisonings recognized early and treated quickly often do well. The case fatality rate for self-poisonings in the modern health care setting is approximately 0.5%; however, in the developing world it is 10–20% [2]. Therefore, it is imperative that EMS personnel understand the basic management of the poisoned patient.

## Evaluation

When evaluating a patient with a potential toxicological emergency, it is important to maintain a broad differential diagnosis [3]. A comatose patient who smells of alcohol may be harboring an intracranial hemorrhage; an agitated patient who appears anticholinergic may actually be encephalopathic from an infectious etiology. Patients must be thoroughly assessed and appropriately stabilized. There is often no specific antidote or treatment for a poisoned patient and supportive care is the most important intervention.

### History

Emergency medical services personnel should gather as much information as possible about the type of toxin(s) to which the patient was exposed. Poisoned patients are commonly unreliable historians, particularly if suicidal or presenting with altered mental status [4]. If information cannot be obtained from the patient, it is beneficial to obtain information from others at the scene, such as family and friends. Bottles of possibly ingested substance or pills, even if not in the original containers, can assist hospital personnel and poison centers. Other helpful information includes the time of exposure (acute versus chronic), amount taken, route of exposure (e.g. ingestion, IV, inhalation, or dermal), reason for the exposure (e.g. accidental, suicide attempt, or abuse), other medicines routinely taken by the patient (including prescription, over the counter, vitamins, alternative medical preparations), and suicide note, if available. With any unknown exposure, a list of all medications in the home should be obtained, including those of current visitors to the home. This is especially important in an unknown pediatric exposure.

### Physical examination

In the emergency setting, patient stabilization takes precedence over a meticulous physical examination. However, a rapid directed examination can yield important diagnostic clues. Once the patient is stable, a more comprehensive physical examination can reveal additional signs suggesting a specific poison/exposure. Additionally, a dynamic change in clinical appearance over time may be a more important clue than findings on the initial examination. Taking note of odors emanating from the patient or the environment can provide valuable information. Some poisons produce odors characteristic enough to suggest the diagnosis upon first encounter ([Table 46.1](https://jigsaw.vitalsource.com/books/9781118990827/epub/OPS/c46.xhtml#c46-tbl-0001)). A complete set of vital signs can further assist the provider in narrowing the differential diagnosis [5]. The skin should be carefully examined by removing patient clothes and assessing for color, temperature, and the presence of dryness or diaphoresis. Absence of diaphoresis is an important clinical distinction between anticholinergic and sympathomimetic poisoning. The presence of bites or similar marks may suggest spider or snake envenomations. The presence of erythema or bullae over pressure points may suggest rhabdomyolysis in the comatose patient, while track marks suggest IV or subcutaneous drug abuse. Finally, a systematic neurological evaluation is important, particularly with patients exhibiting altered mental status. While the Glasgow Coma Scale (GCS) is useful for evaluating trauma victims, it has little role in predicting the prognosis of the poisoned patient [6].

[**Table 46.1**](https://jigsaw.vitalsource.com/books/9781118990827/epub/OPS/c46.xhtml#R_c46-tbl-0001) Odors that suggest a toxicological exposure

| **Odor** | **Possible source** |
| --- | --- |
| Bitter almonds | Cyanide |
| Fruity | Isopropanol, acetone |
| Garlic | Organophosphates |
| Gasoline | Petroleum distillates |
| Mothballs | Naphthalene, camphor |
| Pears | Chloral hydrate |
| Minty | Methylsalicylate |
| Rotten eggs | Hydrogen sulfide |
| Freshly mowed hay | Phosgene |

Seizures are a common presentation of an unknown overdose, and the list of toxins that can induce a convulsion is lengthy ([Table 46.2](https://jigsaw.vitalsource.com/books/9781118990827/epub/OPS/c46.xhtml#c46-tbl-0002)). Ocular findings helpful in narrowing the differential diagnosis include miosis and mydriasis ([Table 46.3](https://jigsaw.vitalsource.com/books/9781118990827/epub/OPS/c46.xhtml#c46-tbl-0003)). Other useful general neurological signs include fasciculations (from organophosphate poisoning), rigidity (tetanus and strychnine), tremors (lithium and theophylline), and dystonic posturing (neuroleptic agents).

[**Table 46.2**](https://jigsaw.vitalsource.com/books/9781118990827/epub/OPS/c46.xhtml#R_c46-tbl-0002) Examples of diverse classes of agents that can potentially cause seizures

| **Category** | **Examples of specific agents** |
| --- | --- |
| Analgesics | Meperidine, propoxyphene, tramadol |
| Antihistamines | Diphenhydramine |
| Antimicrobials | Isoniazid, penicillin |
| Botanicals | False morel mushrooms, tobacco, water hemlock |
| Drugs of abuse | Amphetamines, cocaine, phencyclidine |
| Inhalants | Carbon monoxide, chlorinated hydrocarbons |
| Methylxanthines | Caffeine, theophylline |
| Psychiatric medications | Bupropion, cyclic antidepressants, venlafaxine |
| Pesticides | Lindane, organophosphates |
| Withdrawal | Antiepileptic medications, ethanol, sedative hypnotics |

[**Table 46.3**](https://jigsaw.vitalsource.com/books/9781118990827/epub/OPS/c46.xhtml#R_c46-tbl-0003) Examples of potential toxins associated with miosis or mydriasis

| **Miosis** | **Mydriasis** |
| --- | --- |
| Antipsychotic agents | Anticholinergics |
| Carbamates | Sympathomimetics |
| Clonidine | Selective serotonin reuptake inhibitors |
| Opiates | Withdrawal syndromes |
| Organophosphates |  |
| Sedative-hypnotics |  |

### Toxidromes

A toxidrome is a toxic syndrome or constellation of signs and symptoms associated with a certain class of poisons. Rapid recognition of a toxidrome can determine the class or, in some cases, the specific poison responsible for a patient’s condition. [Table 46.4](https://jigsaw.vitalsource.com/books/9781118990827/epub/OPS/c46.xhtml#c46-tbl-0004) lists characteristics of selected toxidromes. It is important to note that patients may not present with every component of a toxidrome and that toxidromes are difficult to identify in mixed ingestions.

[**Table 46.4**](https://jigsaw.vitalsource.com/books/9781118990827/epub/OPS/c46.xhtml#R_c46-tbl-0004) Toxidromes

| **Toxidrome** | **Signs and symptoms** | **Potential agent example** |
| --- | --- | --- |
| Opioid | Sedation, miosis, decreased bowel sounds, decreased respirations | Codeine, fentanyl, heroin, hydrocodone, methadone, morphine, oxycodone |
| Anticholinergic | Mydriasis, dry skin, dry mucous membranes, decreased bowel sounds, sedation, altered mental status, hallucinations, urinary retention | Atropine, antihistamines, cyclic antidepressants, cyclobenzaprine, phenothiazines, scopolamine |
| Sedative hypnotic | Sedation, decreased respirations, normal pupils, normal vital signs | Benzodiazepines, barbiturates, zolpidem |
| Sympathomimetic | Agitation, mydriasis, tachycardia, hypertension, hyperthermia, diaphoresis | Amphetamines, cocaine, ephedrine, phencyclidine, pseudoephedrine |
| Cholinergic | Miosis, lacrimation, diaphoresis, bronchospasm, bronchorrhea, vomiting, diarrhea, bradycardia | Organophosphates, carbamates, nerve agents |
| Serotonin toxicity | Altered mental status, tachycardia, hypertension, hyperreflexia, clonus, hyperthermia | Overdose of serotonergic agents alone or in combination (i.e. selective serotonin reuptake inhibitors, dextromethorphan, meperidine) |

Certain aspects of a toxidrome can have great significance. For example, noting dry axilla may differentiate an anticholinergic patient from a sympathomimetic patient, and miosis may distinguish opioid toxicity from a benzodiazepine overdose. There are notable exceptions to the recognized toxidromes. For example, several opioid agents (meperidine, propoxyphene, and tramadol) are not always associated with miosis. In most cases, a toxidrome will not indicate a specific poison but rather a class of poisons. Several poisons have unique presentations that make their presence virtually diagnostic. For example, clonidine is associated with sedation, miosis, bradycardia, shallow respirations, and hypotension, yet the patient will become alert with stimulation and then drift rapidly back to sedation with no stimulation.

### Cardiac monitor and electrocardiogram

Electrocardiogram interpretation of in the poisoned patient can be challenging. Numerous drugs can cause ECG changes. The incidence of ECG changes in the poisoned patient is unclear, and the significance of various changes may be difficult to define [7]. Despite the fact that drugs have widely varying indications for therapeutic use, many unrelated drugs share common electrocardiographic effects if taken in overdose. Toxins can be placed into broad classes based on their cardiac effects. Agents that block the cardiac fast sodium channels and agents that block cardiac potassium efflux channels cause characteristic ECG changes, QRS prolongation, and QT prolongation, respectively. The recognition of specific ECG changes associated with other clinical data (toxidromes) can be potentially life saving [8].

The ability of drugs to induce cardiac sodium channel blockade prolonging the QRS complex has been well described in the literature [9]. Cardiac voltage-gated sodium channels reside in the cell membrane and open in conjunction with cell depolarization. Sodium channel blockers bind to the transmembrane sodium channels, decreasing the number available for depolarization. This creates a delay of sodium entry into the cardiac myocyte during phase 0 of depolarization. As a result, the upslope of depolarization is slowed and the QRS complex widens [10]. In some cases, the QRS complex may take the pattern of recognized bundle branch blocks [11,12]. With tricyclic antidepressant poisoning, rightward axis deviation of the terminal 40 msec of the QRS axis can be present, in addition to QRS widening [13,14]. In the most severe cases, QRS prolongation becomes so profound that it is difficult to distinguish between ventricular and supraventricular rhythms [15,16]. Continued QRS prolongation may result in a *sine wave* pattern and eventual asystole. It has been theorized that the sodium channel blockers cause slowed intraventricular conduction, unidirectional block, the development of a reentrant circuit, and a resulting ventricular tachycardia [17]. This can then degenerate into ventricular fibrillation. Differentiating a QRS prolongation due to sodium channel blockade in the poisoned patient versus other non-toxic etiologies can be difficult.

Drugs blocking myocardial sodium channels comprise a diverse group of pharmaceutical agents ([Box 46.1](https://jigsaw.vitalsource.com/books/9781118990827/epub/OPS/c46.xhtml#c46-fea-0001)). Patients poisoned with these agents have varied clinical presentations. For example, sodium channel-blocking medications such as diphenhydramine, propoxyphene, and cocaine may also develop anticholinergic, opioid, and sympathomimetic syndromes, respectively [18–20]. In addition, specific drugs may affect not only the myocardial sodium channels but also calcium influx and potassium efflux channels, resulting in ECG changes and rhythm disturbances not related entirely to the drug’s sodium channel-blocking activity [21,22]. All the agents listed in [Box 46.1](https://jigsaw.vitalsource.com/books/9781118990827/epub/OPS/c46.xhtml#c46-fea-0001) induce myocardial sodium channel blockade and may respond to therapy with sodium bicarbonate or hypertonic saline. Displacement of the sodium channel-blocking agents by hypertonic saline or sodium bicarbonate can improve inotropy and prevent arrhythmias.[9] It is therefore reasonable to treat poisoned patients with prolonged QRS intervals, particularly those with hemodynamic instability, empirically with 1–2 mEq/kg of sodium bicarbonate (the gold standard for treatment of sodium channel blockade). Shortening of the QRS can confirm the presence of a sodium channel-blocking agent.

## Box 46.1 Sodium channel-blocking drugs

|  |  |
| --- | --- |
| Amantadine | Diphenhydramine |
| Carbemazepine | Hydroxychloroquine |
| Chloroquine | Loxapine |
| Class IA antiarrhythmics | Orphenadrine |
| Disopyramide | Phenothiazines |
| Quinidine | Propranolol |
| Procainamide | Propoxyphene |
| Class IC antiarrhythmics | Quinine |
| Flecainide | Verapamil |
| Propafenone |  |
| Citalopram |  |
| Cocaine |  |
| Cyclic antidepressants |  |

Approximately 3% of all non-cardiac prescriptions are associated with the potential for QT prolongation [23]. Myocardial repolarization is driven predominantly by outward movement of potassium ions [24]. Blockade of the outward potassium currents prolongs the action potential [25]. This subsequently results in QT interval prolongation and the potential emergence of T- or U-wave abnormalities on the ECG [26]. The prolongation of repolarization causes the myocardial cell to have less charge difference across its membrane, which may result in the activation of the inward depolarization current (early after-depolarization) and promote triggered activity. These changes may lead to reentry and subsequent polymorphic ventricular tachycardia (VT), most often as the torsades de pointes variant of polymorphic VT [27]. QT prolongation is considered to occur when the QTc interval is greater than 440 msec in men and 460 msec in women, with arrhythmias most commonly associated with values greater than 500 msec. However, the potential for an arrhythmia for a given QT interval will vary from drug to drug and patient to patient [24]. Drugs associated with QT prolongation are listed in [Box 46.2](https://jigsaw.vitalsource.com/books/9781118990827/epub/OPS/c46.xhtml#c46-fea-0002) [28]. Management of QT prolongation includes infusion of magnesium and possibly calcium to prevent the development of polymorphic VT.

## Box 46.2 Drugs that block efflux from potassium channels

|  |  |
| --- | --- |
| Antihistamines | Class III antiarrhythmics |
| Diphenydramine | Amiodarone |
| Loratadine | Dofetilide |
| Antipsychotics | Ibutilide |
| Chlorpromazine | Sotalol |
| Droperidol | Cyclic antidepressants |
| Haloperidol | Erythromycin |
| Pimozide | Fluoroquinolones |
| Quetiapine | Hydroxychloroquine |
| Risperidone | Methadone |
| Thioridazine | Pentamidine |
| Ziprasidone | Quinine |
| Arsenic trioxide | Tacrolimus |
| Chloroquine | Venlafaxine |
| Cisapride |  |
| Citalopram |  |
| Clarithromycin |  |
| Class IA antiarrhythmics |  |
| Disopyramide |  |
| Quinidine |  |
| Procainamide |  |

There are many agents that can induce human cardiotoxicity, and the resultant ECG changes range from bradycardia (e.g. calcium channel blocker and beta-blocker toxicity) to tachycardia (e.g. sympathomimetics and anticholinergics). EMS personnel managing patients who have taken medication overdoses should be aware of the various ECG changes that can potentially occur.

## Treatment

All patients presenting with potential toxic exposures should be aggressively managed, as the majority of outcomes are good. Airway patency and adequate ventilation should be ensured. If necessary, endotracheal intubation should be performed. Too often, EMS personnel are lulled into a false sense of security by adequate oxygen saturations on high-flow oxygen. A poor gag reflex or inadequate ventilation may increase risk for subsequent aspiration or carbon dioxide retention with worsening acidosis. Intravenous access is generally recommended for poisoned patients, and hypotension should initially be treated with IV fluids. The patient’s pulmonary status should be closely monitored for the development of pulmonary edema as fluids are infused. Continuous cardiac monitoring, pulse oximetry, and frequent neurological checks should be documented, noting any changes over time. Glucose should be checked in all patients with altered mental status. EMS personnel must have a low threshold for suspecting carbon monoxide exposure in altered mental status patients. Carbon monoxide is a relatively common, potentially deadly, and easily missed poisoning. Carbon monoxide levels should be measured as early as feasible because these levels can diminish greatly during transport, especially when supplemental oxygen is administered.

Many toxins can also cause seizures. In general, toxin-induced seizures are treated similarly to epileptic seizures. EMS personnel should ensure a patent airway and measure blood glucose. Most toxin-induced seizures are self-limited. However, for seizures requiring treatment, the first-line agent should be parenteral benzodiazepines for all poisonings. The use of long-acting paralytic agents should be avoided in intubated poisoned patients because these agents may mask seizures.

After initial evaluation and stabilization, toxin-specific therapies should be initiated, and decontamination should be considered. Several poisons have specific antidotes which can be of great benefit if used in a timely and appropriate manner (see Volume 1, [Chapter 47](https://jigsaw.vitalsource.com/books/9781118990827/epub/OPS/c47.xhtml#c47)).

## Decontaminating the poisoned patient

External decontamination may be necessary for poisoning by dermal or ocular exposure. Additionally, 83% of poisonings occur by ingestion, which has prompted studies examining the use of gastrointestinal decontamination, which may be required, in the prehospital setting [1].

### Dermal decontamination

Patients with dermal contamination pose a potential risk of secondary exposure to health care personnel. Decontamination should occur before EMS transport. Personnel conducting dermal decontamination should don personal protective equipment (PPE) appropriate for the contaminating agent. Gas or vapor exposure does not require decontamination (the exception being a need for ocular decontamination in some cases); removal from the site should be sufficient. Potential off-gassing can be avoided by removing and sealing contaminated clothing in a plastic bag [29]. Exposure to liquids or solids requires dermal decontamination [29]. Proceeding from head to toe, brush all solids off the patient’s skin and clothing, irrigate the exposed skin and hair for 10–15 minutes with water or saline, and scrub with a soft surgical sponge, being careful not to abrade the skin. Patient privacy should be respected if possible, and warm water should be used to avoid hypothermia [29]. Irrigate all wounds for an additional 5–10 minutes. Stiff brushes and abrasives should be avoided because they enhance dermal absorption of the toxin and can produce skin lesions that may be mistaken for chemical injuries. Sponges and disposable towels are effective alternatives.

### Ocular decontamination

When required, ocular decontamination should be performed immediately by gentle irrigation of the affected eye(s) and contiguous skin [30]. Ocular irrigation with sterile normal saline or lactated Ringer’s solution should continue for at least 15–30 minutes [31]. Tap water is acceptable if that is the only solution available. However, due to its hypotonicity relative to the stroma, tap water may facilitate penetration of corrosive substances into the cornea and potentially worsen outcome [30,32]. Lactated Ringer’s solution may be a preferable irrigant due to its buffering capacity and neutral pH [30,32]. Irrigation should be directed away from the medial canthus to avoid forcing contaminants into the lacrimal duct. Longer irrigation times may be needed with specific substances and the endpoint of irrigation should be normalization of the eye’s pH. Because pH paper is not typically carried by EMS units (although it may be available on hazardous materials units), continuing irrigation during transport is frequently required.

### Gastrointestinal decontamination

Significant controversy exists concerning the need for routine gastric decontamination in the poisoned patient, and gastric lavage is no longer recommended. Gastric decontamination may be considered in select cases and specific scenarios, but in general, the prehospital care provider should focus on rapid transportation of the poisoned patient to the hospital. Before performing any gastrointestinal decontamination techniques, including the oral administration of activated charcoal, EMS personnel must clearly understand the hazards of these procedures. Personnel must carefully weigh the risks and benefits prior to making any decisions about the use of gastrointestinal decontamination. Contacting the local poison center (i.e. US poison centers at 1-800-222-1222) can guide decisions to pursue gastric decontamination.

Syrup of ipecac, previously a mainstay of poisoning management, is no longer recommended in the management of poisoning [33–35]. Emesis, either by mechanical stimulation (i.e. placing a finger down the throat) or by use of syrup of ipecac, should be avoided. The prehospital use of activated charcoal is currently controversial, and it is premature to recommend the administration of activated charcoal by EMS personnel without poison center guidance [34]. Activated charcoal is given orally to prevent gastrointestinal absorption of an ingested substance. The administration of charcoal is contraindicated in any person who demonstrates compromised airway protective reflexes unless he or she is intubated [36]. Intubation will reduce the risk of charcoal aspiration but will not totally eliminate its occurrence [37]. Charcoal is also contraindicated in persons who have ingested corrosive substances (acids or alkalis). Charcoal not only provides no benefit in corrosive ingestions, but its administration could precipitate vomiting, obscure endoscopic visualization, or lead to complications if a perforation develops and charcoal enters the mediastinum, peritoneum, or pleural space. Charcoal should be avoided in cases of pure aliphatic petroleum distillate ingestion. Hydrocarbons are not well adsorbed by activated charcoal, and its administration could lead to further aspiration risk. Other commonly encountered substances that do not readily bind to charcoal include lithium, solvents, most metals (iron, lead), potassium chloride, sodium chloride, fluoride, cyanide, and alcohols (to include ethylene glycol, methanol, diethylene glycol).

## Antidotes

The number of pharmacological antagonists or antidotes that EMS personnel may have access to in prehospital management is quite limited. There are few agents that will rapidly reverse toxic effects and restore a patient to a previously healthy baseline state. Administering some pharmacological antagonists actually may worsen patient outcome compared with simply optimizing basic supportive care. As a result, antidotes should be used cautiously and with clearly understood indications and contraindications. [Table 46.5](https://jigsaw.vitalsource.com/books/9781118990827/epub/OPS/c46.xhtml#c46-tbl-0005) gives a list of potential antidotes available to EMS providers. Many antidotes are covered in [Chapter 47](https://jigsaw.vitalsource.com/books/9781118990827/epub/OPS/c47.xhtml#c47) but two specific antidotes will be discussed here.

[**Table 46.5**](https://jigsaw.vitalsource.com/books/9781118990827/epub/OPS/c46.xhtml#R_c46-tbl-0005) Antidotes

| **Agent or clinical finding** | **Antidote** |
| --- | --- |
| Acetaminophen | N-acetylcysteine |
| Benzodiazepines | Flumazenil[\*](https://jigsaw.vitalsource.com/books/9781118990827/epub/OPS/c46.xhtml#c46-note-0001) |
| Beta-blockers | Glucagon |
| Cardiac glycosides | Digoxin immune Fab |
| Crotalid evenomation | Crotalidae polyvalent immune Fab |
| Cyanide | Sodium thiosulfate[\*](https://jigsaw.vitalsource.com/books/9781118990827/epub/OPS/c46.xhtml#c46-note-0001)Sodium nitriteHydroxycobalamin[\*](https://jigsaw.vitalsource.com/books/9781118990827/epub/OPS/c46.xhtml%22%20%5Cl%20%22c46-note-0001) |
| Ethylene glycol | Fomepizole |
| Iron | Deferoxamine |
| Isoniazid | Pyridoxine |
| Methanol | Fomepizole |
| Methemoglobinemia | Methylene blue |
| Opioids | Naloxone[\*](https://jigsaw.vitalsource.com/books/9781118990827/epub/OPS/c46.xhtml#c46-note-0001) |
| Organophosphates | Atropine[\*](https://jigsaw.vitalsource.com/books/9781118990827/epub/OPS/c46.xhtml#c46-note-0001)Pralidoxime[\*](https://jigsaw.vitalsource.com/books/9781118990827/epub/OPS/c46.xhtml#c46-note-0001) |
| Sulfonylureas | Glucose[\*](https://jigsaw.vitalsource.com/books/9781118990827/epub/OPS/c46.xhtml#c46-note-0001)Octreotide |

[\*](https://jigsaw.vitalsource.com/books/9781118990827/epub/OPS/c46.xhtml#R_c46-note-0001) Antidotes that may be available to EMS personnel.

### Flumazenil

Benzodiazepines are involved in many intentional overdoses. Although these overdoses are rarely fatal when a benzodiazepine is the sole ingestant, they often complicate overdoses with other central nervous system depressants (e.g. ethanol, opioids, and other sedatives) due to their synergistic activity. Flumazenil should *not* be administered as a non-specific coma reversal drug and should be used with extreme caution after intentional benzodiazepine overdose because it has the potential to precipitate withdrawal in benzodiazepine-dependent individuals and/or induce seizures in those at risk [38,39]. The initial flumazenil dose is 0.2 mg administered intravenously over 30 seconds. If no response occurs after an additional 30 seconds, a second dose is recommended. Additional incremental doses of 0.5 mg may be administered at 1-minute intervals until the desired response is noted or until a total of 3 mg has been administered. At present, flumazenil is very rarely used in the out-of-hospital setting.

### Naloxone

Opioid poisoning from the abuse of morphine derivatives or synthetic narcotic agents may be reversed with the opioid antagonist naloxone [40]. Naloxone is commonly used in comatose patients as a therapeutic and diagnostic agent. The standard dosage regimen is to administer from 0.4 to 2 mg slowly, preferably intravenously. The IV dose should be readministered at 5-minute intervals until the desired endpoint is achieved – restoration of respiratory function, ability to protect airway, and an improved level of consciousness [41]. If the IV route of administration is not viable, alternative routes include intramuscular injection, intraosseous, intranasal, or via nebulization [41]. Intramuscular administration is an accepted alternative route but if the patient is hypotensive, naloxone may not be absorbed rapidly from the intramuscular injection site. Intransal and intramuscular naloxone have been distributed to bystanders for use in heroin and opioid overdose situations [42–44]. The onset of action is longer with the intranasal form than the IV form (8–12 minutes versus 6–8 minutes), but similar to that of intramuscular naloxone [45,46]. One study suggests intranasal naloxone may induce a gentler reversal with less agitation compared to IV naloxone [45]. Early reports suggest an increased need for redosing with intranasal delivery but it is not clear if this is truly needed or a provider response to the longer onset of action [46].There are no published data on the optimal dose of intranasal naloxone, but in studies investigating intranasal naloxone delivery a 2 mg dose is frequently used and 1 mg is delivered in each nostril [42,47,48]. The cost of the mucosal atomization device that allows for intranasal drug delivery is prohibitive in many areas of the US and worldwide [42,49]. There is ongoing research on both intramuscular and intranasal naloxone in the prehospital setting for both bystanders and EMS providers.

A patient may not respond to naloxone administration for a variety of reasons: insufficient dose of naloxone, the absence of an opioid exposure, a mixed overdose with other central nervous and respiratory system depressants, or medical or traumatic reasons. When it does reverse opioid intoxication, naloxone can precipitate profound withdrawal symptoms in opioid-dependent patients. Symptoms of withdrawal include agitation, vomiting, diarrhea, piloerection, diaphoresis, and yawning [41]. There are reports of patients developing non-cardiogenic pulmonary edema in response to naloxone and as an effect of opioid intoxication itself without a clear understanding of the mechanisms behind this. Providers should use care in administering this agent, and only give the amount that is necessary to restore adequate respiration and airway protection.

## Special considerations: caustic exposures

Acids and bases are routinely grouped into a more general category called caustics. In most cases, the concentration of the product, duration of exposure/contact time, and route of exposure (ingestion, inhalation, dermal, ocular) determine the extent of injury suffered by an exposed patient.

Traditionally, acids and bases have been associated with different injury patterns. *Liquefactive necrosis* is a term often used to describe the type of tissue damage encountered with caustics that are characterized as “bases” [50,51]. Bases can deeply penetrate the tissue, causing fat saponification, protein dissolution, and emulsification of cell membranes. *Coagulation necrosis* is the type of injury associated with caustics characterized as “acids.” With coagulation necrosis, tissues become erythematous and ulcerated, mucous membranes slough, and eschars can form which theoretically prevent deeper penetration of the acid [50,51]. While these injury patterns apply to most caustics classified as acids or bases, there are exceptions to the rule.

One of these frequently encountered exceptions is hydrofluoric acid. Found in wheel cleaners and glass etching creams, hydrofluoric acid is considered an acid but rarely causes visible tissue damage. Instead, it penetrates the tissues and binds to intracellular calcium and magnesium, leaching them out of the cells, depleting the cells of these ions, and causing significant pain [52,53]. Patients exposed to this compound develop hyperkalemia, hypocalcemia, and hypomagnesemia, which can result in cardiac dysrhythmias and death. Thorough decontamination of the skin and eyes is necessary for any possible exposures. Antacids containing calcium and magnesium can be given orally in an effort to bind the fluoride molecule of the ingested hydrofluoric acid early, but this should not be done without poison center involvement, especially if multiple agents are ingested [54]. Additionally, treatment consists of aggressive IV electrolyte repletion and cardiac monitoring.

Once the patient has been removed from any caustic exposure source, stabilization of the airway, breathing, and circulation remains the initial priority. Stridor or drooling may indicate airway involvement/impending airway compromise, and EMS providers should pay close attention to these patients. The presence or absence of oral lesions does not provide an accurate indication of whether or not significant ingestion has occurred [55]. Decontamination at the scene is preferred if possible to prevent continued injury. The type of decontamination will depend on the route of exposure. The same principles of decontamination previously discussed can be used – for example, if the patient has been exposed to sodium hydroxide crystals, brushing the solid crystals off prior to removing clothing and washing the skin is necessary. For exposures involving inhalation and vapor exposure, removing the patient from the source and flushing the eyes is important. There are a few instances where dilutional therapy with milk or water may be recommended by the poison center [56–60]. This may be recommended prior to EMS arrival and has better results when performed within minutes of ingestion, but should not be attempted without poison center recommendation. Basic wound care dressings can be applied to injured skin after the wound has been decontaminated with water or normal saline.

## Protocols

The development of specific protocols for treating each individual type of poisoning is unrealistic due to the vast number of potential toxins. It is also impractical to have one protocol that could easily pertain to all cases of poisoning. It may be necessary to construct protocols for the different problems that require different treatments in the field (e.g. suspected opioid intoxication, carbon monoxide toxicity, and chemical dermal contamination). Integral to these protocols is an outline of the relevant history and physical findings that guide the provider to appropriate generalized management of the intoxicated patient. In addition, each protocol should contain the toll-free national poison center number (1-800-222-1222) where the EMS provider can obtain guidance 24/7 from experts in the field of medical toxicology.

## Conclusion

Emergency medical services providers are often required to care for poisoned patients. Many of these patients do well with standard medical management and never develop significant toxicity. However, for patients who present with serious toxic effects or after potentially fatal exposures, prompt action must be taken. As many poisons have no true antidote and the poison involved may initially be unknown, the first step is good supportive care. Attention to supportive care, vital signs, and prevention of complications are the most important steps. Taking care of these issues will often be all that is necessary to ensure recovery.

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