# Initial Management of Poisoned Patient

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## INTRODUCTION

The principles of critical care medicine and medical toxicology are intertwined like a Rod of Asclepius. This evidence maybe traced to medieval times: Treatise on Poison and their Antidotes by Moses Maimonides in late 12th century.[1] Intensive care physicians who treat poisoned patients should have a systematic approach to evaluation and management. Accidental or intentional poisoning from both licit and illicit substances can produce a wide range of symptoms and clinical findings. Hence, history and physical examination are of great importance in recognizing the poisoned patient. Initial management should be focused on acute stabilization and supportive care till the correct substance is identified. The plan of management is to provide supportive care, prevention of poison absorption, use of antidote wherever is indicated, and enhancement of elimination techniques.

## INITIAL ASSESSMENT

### Our First Priorities

As with any unstable or critically ill patient, the resuscitation (airway, breathing, circulation (ABC)) with basic life support takes priority. In addition to resuscitation, the intensivists must consider two crucial issues that may arise with severely poisoned patients: preserving the operational capacity and ensuring the safety of the healthcare workers. In the poisoned patient, diagnostic evaluation and therapeutic interventions often are initiated simultaneously.

### Risk Assessment

Following initial resuscitation and stabilization, a risk assessment is performed to predict the course of clinical toxicity, interventions required, and patient disposition. It is formulated using history, examination, and ancillary test results. The risk of a poisoned patient can be assessed by gathering the data either substance-based or system-based. The substances belonging to a particular class of toxin produce characteristic combinations of symptoms and signs, which is called toxic syndrome (toxidromes). The toxidrome-oriented physical examination may provide valuable insight into the class of toxin involved. The major toxidromes and their associated findings are summarized in Table 1.[2]

### Diagnostic Testing

Though toxidromes are created to assist diagnosis, a particular patient may not have all the symptoms associated with a given toxidrome; always some discrepancies are noted after the examination of a poisoned patient. History may be inaccurate and hence the following laboratory tests should usually be obtained:

- Complete blood count
- Basic serum electrolytes, blood urea nitrogen (BUN), and creatinine

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- Liver function test
- Serum lactate
- Arterial blood gas
- Electrocardiogram
- Urine pregnancy test in all women of childbearing age

Measurement of drug or toxin concentrations in body fluids is not required in most poisonings, but in some exposures, it does influence management. The list of drug concentrations that may assist patient assessment and management is shown in Table 2.

Toxicology screening assays are available commercially.[3] However, the results seldom directly influence patient management and they have their own limitations. Most of the tests use enzyme immunoassays that only detect typical drugs within a class. The time frame at which these screening assays are performed is a major concern. Drugs consumed by the patient may take days to weeks to be detected after exposure. A positive test may not account for current clinical findings. High possibilities of cross-reactivity among different groups of drugs occur. A negative drug screen does not exclude an exposure and sampling error is also a major limitation. On medicolegal grounds, performing a toxicology screening may serve the purpose. In contrast to the rapid immunoassay screens, comprehensive qualitative toxic screening of urine, blood, or other body fluids is done by liquid and gas chromatography and mass spectrometry.

## SUPPORTIVE CARE

### Airway Management

The loss of airway-protective reflexes and concern for aspiration or the presence of respiratory failure dictates the need to secure the airway. Unless the patient is moribund, rapid sequence intubation (RSI) with preoxygenation and neuromuscular blockade is the best approach to securing the airway.[4] It should be accomplished by tracheal intubation.[5] However, either due to an inability to adequately preoxygenate the patient or concerns that the patient may be difficult to intubate, strategies aside from RSI should be considered. Delayed sequence intubation (DSI) can be used as an alternate method to RSI. It comprises of administration of sedatives

**Table 1:** Common toxidromes

| Toxidromes | Mental status | Pupils | Vitals | Other manifestations | Examples of toxic agents |
|---|---|---|---|---|---|
| Sympathomimetic | Hyper alert, agitation, hallucination, paranoia | Mydriasis | Hyperthermia, tachycardia, hypertension, widened pulse pressure | Diaphoresis, tremors, hyperreflexia, seizures | Cocaine, amphetamines, ephedrine, theophylline, caffeine |
| Anticholinergic | Agitation, hallucinations, delirium, coma | Mydriasis | Hyperthermia, tachycardia, hypertension, tachypnea | Dry flush skin, dry mucous membranes, decreased bowel sounds, urinary retention, myoclonus | Antihistamines, TCA, antiparkinsonism agents, atropine, antispasmodics |
| Hallucinogenic | Hallucinations, perceptual distortions, depersonalization, agitation | Mydriasis (usually) | Hyperthermia, tachycardia, hypertension, tachypnea | Nystagmus | Phencyclidine, MDMA, MDEA |
| Opioid | CNS depression, coma | Miosis | Bradypnea, apnea | Hyporeflexia, pulmonary edema, needle marks | Heroin, morphine, methadone, diphenoxylate |
| Sedative-hypnotic | CNS depression, confusion, stupor, coma | Variable | Often normal; hypothermia, bradycardia, hypotension, bradypnea, apnea | Hyporeflexia | Benzodiazepines, barbiturates, alcohols, zolpidem |
| Cholinergic | Confusion, coma | Miosis | Bradycardia, hypertension, tachypnea, hypotension, bradypnea | Salivation, urinary and fecal incontinence, diarrhea, emesis, diaphoresis, lacrimation, GI cramps, bronchoconstriction, muscle fasciculations and weakness, seizures | Organophosphate and carbamate insecticides, nerve agents, nicotine, physostigmine, edrophonium |
| Serotonin syndrome | Confusion, agitation, coma | Mydriasis | Hyperthermia, tachycardia, hypertension, tachypnea | Tremors, myoclonus, hyperreflexia, clonus, diaphoresis, flushing, trismus, rigidity, diarrhea | MAOIs, SSRIs, meperidine, dextromethorphan, TCA |

TCA, tricyclic antidepressant; MDMA, 3,4-methylenedioxymethamphetamine; MDEA, methylenedioxymethamphetamine; CNS, central nervous system; GI, gastrointestinal; MAOI, monoamine oxidase inhibitor; SSRI, selective serotonin reuptake inhibitor

**Table 2:** Commonly measured drug concentrations

| | |
|---|---|
| Acetaminophen | Methanol |
| Carbamazepine | Methotrexate |
| Carbon monoxide | Organophosphorus |
| Digoxin | Paraquat |
| Ethanol | Phenobarbital |
| Ethylene glycol | Phenytoin |
| Iron | Salicylate |
| Lithium | Theophylline |
| Methemoglobin | Valproic acid |

that do not blunt the airway reflexes, followed by a brief period of preoxygenation before administering paralytics.[6,7] Orotracheal intubation, if possible, is preferred over nasotracheal intubation for many reasons. Nasotracheal intubation increases the incidence of sinusitis,[8] purulent and serous otitis,[9] ventilator-associated pneumonia,[10] and is technically more difficult compared with orotracheal intubation. An alternate strategy for securing the airway, and the means to establish a surgical airway if necessary (cricothyrotomy), must be immediately available.

## Respiratory Support

Several toxins interfere with oxygenation and ventilation. Hence, adequacy of respiration must be assessed immediately after the airway is secured.[11]

When determining the ventilator settings, a lung protective strategy should be employed.[12,13] Lung protective strategies prevent the development of ARDS from barotrauma and oxygen toxicity. While these strategies are commonly used in the ICU, they have not been studied in the poisoned patient.[14]

## Circulation and Hemodynamics

After establishing an airway and supporting respiratory function, the next priority is assessment of the circulatory status. In the poisoned patient, cardiovascular abnormalities commonly seen are hypertension, hypotension, cardiac arrhythmias, or conduction disturbances.

Elevated blood pressure in the poisoned patient may or may not be the result of exposure to any one of many substances. Of which, most common causes of elevated blood pressure are withdrawal (benzodiazepine or ethanol withdrawal), discontinuation of a therapeutically prescribed medication, such as clonidine or minoxidil, causing rebound hypertension and inadequately treated or untreated underlying hypertension.[15] The treatment of hypertension is determined by its underlying cause. When hypertension is caused by overdoses of drugs with direct adrenergic activity, such as amphetamines, ephedrine, or pseudoephedrine, direct vasodilators such as phentolamine or nitroprusside should be considered.[16] When hypertension is caused by drugs with indirect adrenergic activity or by drug-of-abuse withdrawal, sedation with benzodiazepines should be considered.[17]

Abnormal hemoglobins (i.e., methemoglobin, sulfhemoglobin, or carboxyhemoglobin) and toxins that disrupt the mitochondrial electron transport chain (e.g., cyanide, hydrogen sulfide, or sodium azide) prevent the use of oxygen at the molecular level[18–20] resulting in histotoxic hypoxia and shock. Elevated plasma lactate concentration accompanying a metabolic acidosis is often a marker of these toxicities.[21]

Myocardial depression, dysrhythmias, and conduction abnormalities may cause shock from impaired cardiac contractility. An electrocardiogram should be obtained in all the poisoned patients to assess for any cardiac abnormalities (Table 3), which may give clues as to the poison, the severity of the poisoning, and the treatment.[14]

Fluid resuscitation of the poisoned patient must be individualized. Initial resuscitation includes the administration of intravenous crystalloid fluid, whenever indicated; vasopressor infusion should be started as early as possible in the course of the resuscitation. In a distributive shock or cardiogenic shock, administration of vasopressors or inotropes (noradrenaline) is more appropriate than simply administering fluids.[14] Bedside sonography is a useful tool to determine volume responsiveness and to estimate cardiac contractility to further guide resuscitation.[22,23] There are very little data regarding the optimal vasopressor agents in poisoned patients.[24] Hence, the choice of vasopressor must be made on patient profile and clinical grounds.

Nonadrenergic vasoactive drugs are an effective therapy for shock caused by β-adrenergic blocking agents and calcium channel antagonists. Glucagon, the peptide hormone that is produced by alpha cells of the pancreas, stimulates adenyl cyclase, which in turn increases intracellular cyclic adenosine monophosphate (cAMP) through a nonadrenergic mechanism. This increase in cAMP causes an increase in intracellular calcium, which leads to positive chronotropic and inotropic actions.[14] Numerous case reports and laboratory investigations describe glucagon's effectiveness in reversing hypotension caused by overdoses of β-adrenergic blocking agents and calcium channel antagonists.[25,26] A glucagon dose of 5–10 mg administered intravenously over 10 minutes should be followed by a glucagon infusion (3–15 mg/hour). An antiemetic should be provided with glucagon as it decreases lower esophageal tone, which causes emesis.[14] More recently, high-dose insulin euglycemia (HIE) therapy is used to treat β-adrenergic blocking agents and calcium channel antagonists toxicity. The pathophysiology of calcium channel antagonist toxicity is decrease in insulin release from pancreatic β-cells causing insulin resistance in the myocardium and changes in myocyte metabolism from fatty acids to carbohydrates.[27] High-dose insulin euglycemia therapy improves myocyte use of carbohydrates as an energy source and therefore increases cardiac contractility and improves perfusion.[28]

The lipid emulsion therapy (LET) is one of the most recent advances in the care of the critically ill poisoned patient. It was used as a treatment for patients with local anesthetic toxicity. It has also been used in the management of toxicity from other poisoning. There are multiple reports of LET reversing the toxicity of calcium channel antagonists, tricyclic antidepressants, benzodiazepines, anticonvulsants, and β-adrenergic blocking agents.[29]

Extracorporeal membrane oxygenation (ECMO) is indicated in poisoned patients in refractory shock who fail conventional treatment.[30] In poisoned patients, ECMO serves as a bridge until the toxins are metabolized or eliminated,[31] at which time the patient should regain normal cardiovascular function. Although higher cost and adverse effects are associated with ECMO, recent advances in technology have made this a more practical alternative in the refractory shock patient.

## DECONTAMINATION

### Gastrointestinal Decontamination

Gastrointestinal (GI) decontamination, once a mainstay in the management of the poisoning, is no longer recommended. It is generally considered in patients who present very early (less than an hour after their ingestion) or for those patients who have taken a very large or dangerous overdose, where an antidote does not exist.[14] Ideally GI decontamination should decrease absorption of many ingested toxins but its use is not associated with improved outcomes (e.g., mortality, length of stay).[32] If GI decontamination is attempted, it should be done as early as possible in the emergency department. The patient is very unlikely to benefit from decontamination if it is started in the ICU.

### Activated Charcoal

Activated charcoal is a commonly used decontaminant. It is manufactured in a two-step process, starting with pyrolysis of various carbonaceous materials then by treating at high temperatures with oxidizing agents such as steam or carbon dioxide that "activate" it and increase its adsorptive capacity. Toxins within the GI lumen are adsorbed onto the activated charcoal and carried through the GI tract, limiting its absorption.[33] It doesn't effectively adsorb metals, corrosives, and alcohols. The decision to give

**Table 3:** Toxins causing dysrhythmias

| Heart rate | Narrow QRS | Wide QRS |
|---|---|---|
| Tachycardia | Amphetamines | Antihistamines |
| | Anticholinergic agents | Cocaine |
| | Theophylline | Propoxyphene |
| | | Sodium channel blockers |
| | | Tricyclic antidepressants |
| Bradycardia | α-Adrenergic lytic agents | β-Adrenergic blocking agents |
| | β-Adrenergic blocking agents | Calcium channel antagonists |
| | Calcium channel antagonists | |
| | Cardiac glycosides | |
| | Class Ia antiarrhythmics | |
| | Sodium channel blockers | |

activated charcoal requires individual patient risk assessment and is not considered as a routine management.[34]

## Whole Bowel Irrigation

Whole bowel irrigation (WBI) is another technique of decontamination, which works by enhancing the flow of toxin through the gut. It can be done by placing a nasogastric or orogastric tube and administering large amounts (1–2 L/hour) of osmotically balanced polyethylene glycol solution (PEG) until the patient has at least two clear, liquid stools. Unlike other forms of GI decontamination, WBI may be started or continued in the ICU. Body packers are traditionally treated with WBI. Body packers are individual who ingest large amounts of packets of illicit drugs for illegal transportation. If there is any accidental packet leakage, lethal amounts of the drug can get absorbed into the body packers' system, which can be life-threatening. So, WBI should be initiated in order to remove the packets as soon as possible, given the life-threatening risk associated with even a single packet leaking. Contraindications include patients with an ileus or obstruction or an injury to the GI tract.[14]

## ELIMINATION

### Multidose Activated Charcoal

Multidose activated charcoal (MDAC) is used to enhance the elimination of various ingested toxins. Multidose activated charcoal may benefit patients at risk from delayed absorption due to ingestion of delayed-release products. Patients who ingest toxins that undergo enteroenteric or enterohepatic circulation may also benefit from MDAC. In enterohepatic circulation, absorbed substances are secreted into the bile and then into the small intestine before being reabsorbed. In enteroenteric circulation, absorbed substances are secreted into the intestine before being reabsorbed. By administering MDAC, charcoal can adsorb toxins

that are secreted into the intestine before being reabsorbed, thereby enhancing elimination.[35] Multidose activated charcoal is generally administered at a dose of 0.5 g/kg following the initial standard dose of charcoal.[14]

## Urine Alkalinization

Alkaline urine favors ionization of acidotic drugs within renal tubules, preventing resorption of the ionized drug back across the renal tubular epithelium and enhancing elimination through the urine.[36] Urine alkalinization is most effective for weak acids like salicylate, phenobarbital toxicities. Preexisting fluid overload, renal impairment, and hypokalemia are contraindications to urine alkalinization. It can be instituted as follows:[34]

- Correct any existing hypokalemia.
- Administer 1–2 mEq/kg IV sodium bicarbonate bolus.
- Infuse 100 mEq of sodium bicarbonate mixed with 1 L of D5W at 250 mL/hour.
- A total of 20 mEq of potassium chloride may be added to maintain normokalemia.
- Check urine pH (every 15–30 minutes), aiming for a pH of 7.5–8.5.
- A further IV bolus of sodium bicarbonate may be warranted if sufficient alkalinization of the urine is not reached.

## Extracorporeal Removal

Extracorporeal removal techniques, including hemodialysis, hemofiltration, and continuous renal replacement therapies, have limited indications in poisoned patients. A toxin must possess a number of properties to be effectively removed by an extracorporeal technique: it should have low volume of distribution (VD < 1 L/kg), low molecular weight, low protein-binding capacity, and a low endogenous clearance.[37] The decision on use of the extracorporeal technique is shown in Flowchart 1.[38]

Flowchart 1: Decision tree for usage of extracorporeal removal of toxins
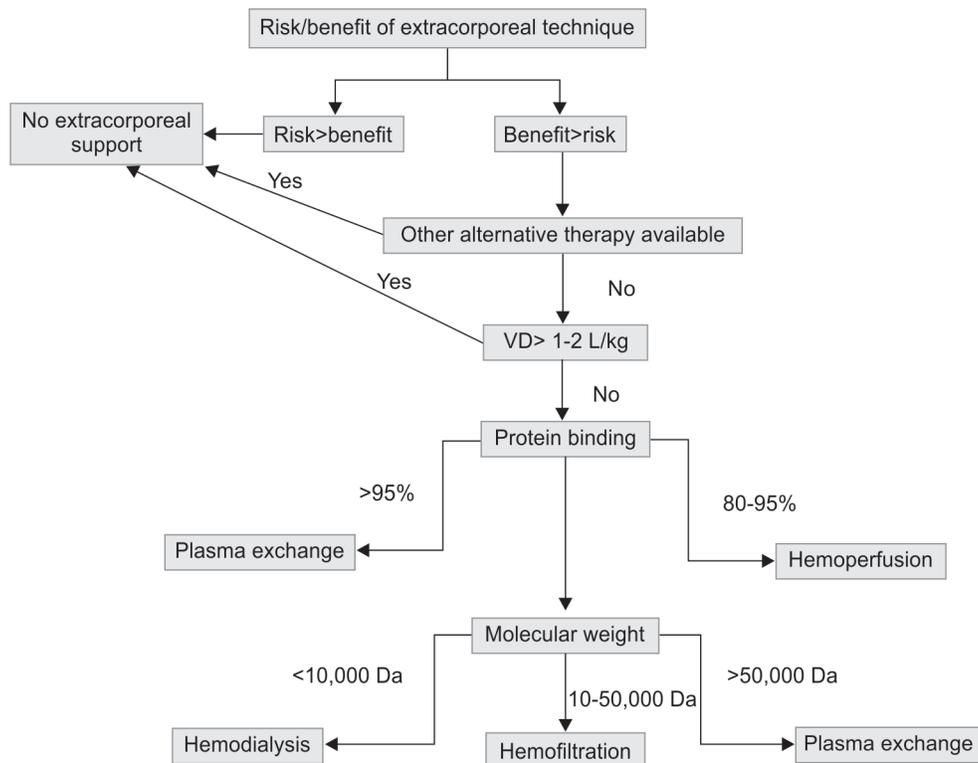
## ANTIDOTES

Most poisoned patients can be treated with standard supportive care. But in few circumstances, specific therapy or antidotes are required.[14] The list of antidotes of common poisonings given in the National Poisons Information Centre (NPIC), which is an integral part of National Poison Control Programme, is shown in Table 4.[39]

## ANCILLARY SUPPORT

Critically ill poisoned patients are at increased risk of GI bleeding. In the ICU, 75% of the poisoned patients have endoscopic evidence of gastric mucosal injury by 18 hours after admission, with 5% of patients developing overt bleeding.[40] Gastrointestinal bleeding prophylaxis should be started on admission to the ICU and can be

**Table 4:** Antidotes for some poisons

| Group | Poisons | Antidote |
|---|---|---|
| Agricultural pesticides | Organophosphates | |
| | Malathion | |
| | Acephate | |
| | Dichlorvos | |
| | Dimethoate | |
| | Fenitrothion | Atropine sulfate |
| | Monocrotophos | |
| | Phorate | |
| | Quinalphos | Pralidoxime |
| | Carbamates | |
| | Propoxur | |
| | Aldicarb | |
| | Carbaryl | |
| | Carbofuran | |
| | Methomyl | |
| | Organochlorines | |
| | Endosulfan | |
| | Gamma benzene hexachloride | Cholestyramine |
| | Heptachlor | |
| | Chlordane | |
| | Rodenticides | |
| | Cholestyramine bromadiolone | Vitamin K |
| Industrial chemicals | Lead | Dimercaprol |
| | | D-Penicillamine |
| | | Calcium disodium edetate |
| | Mercury | Dimercaprol |
| | | Dimercaptosuccinic acid |
| | | D-Penicillamine |
| | Arsenic | Dimercaprol |
| | | D-Penicillamine |
| | Methyl alcohol | Ethanol |
| | | Folic acid/folinic acid |
| | Ethylene glycol | Ethanol |
| | | Pyridoxine hydrochloride |
| | | Folic acid |
| | | Thiamine |
| | Cyanide | Amyl nitrite, sodium nitrite |
| | | Sodium thiosulfate(cyanide antidote kit) |
| | | Hydroxocobalamin |
| | | Dicobalt edetate |
| | Methemoglobinemia producing agents (nitrites, nitrates, dapsone, copper, aniline, chlorates, naphthalene) | Methylene blue |
| Drugs | Acetaminophen | *N*-Acetylcysteine |

*Contd…*

*Contd…*

| Group | Poisons | Antidote |
|---|---|---|
| | Iron | Deferoxamine |
| | Benzodiazepines | Flumazenil |
| | Opioids | Naloxone |
| | Isoniazid | Pyridoxine |
| | Digoxin | Digoxin-specific antibodies |
| Environmental toxins | Datura | Physostigmine |
| | Snake bites | Anti-snake venom |
| | Dog bite | Anti-rabies vaccine |
| | Botulism | Botulinum antitoxin |

achieved best through the use of histamine 2-receptor antagonists or proton-pump inhibitors.

Poisoned ICU patients are at risk for venous thromboembolic disease if they have a prolonged course requiring them to remain in bed. Approximately 33% of all ICU patients develop ultrasonographically detectable deep venous thrombosis (DVT) despite receiving prophylaxis. Meta-analyses show that the use of heparin or pneumatic compression stockings decreases the incidence of DVT by at least 50%.[41] Deep venous thrombosis prophylaxis should be initiated with unfractionated heparin, low-molecular-weight heparin, or compression devices as soon as the patient is admitted to the ICU if a prolonged stay is anticipated.

The goal of nutritional support is to meet the patient's nutritional needs without overfeeding. Overfeeding should be avoided because excess carbohydrates can lead to increased carbon dioxide production. Enteral feedings, which help maintain integrity of the gut's mucosal barrier, are preferred over the parenteral route.[14]

## Conclusion

Being critical care physicians, we often care for poisoned patients. Most of these patients will need only observation and they seldom develop toxicity. However, for patients who present with serious toxic effects, prompt action is required. The first step is to stabilize airway, breathing, and circulation as with any critically ill patient. Identifying the poison, either through history, toxidrome, or laboratory tests may direct the physicians in the right track. Antidotes can be used in instances where the exact poison agent is known.

Our government is having a National Poison Information Centre (NPIC) that is an integral part of Poison Control Programme and provides invaluable information 24 × 7 to physicians through a telephonic call. After providing the details of the substance consumed by the patient, the NPIC will give the possible diagnosis, how to proceed for emergency management, the antidote, and the source of the antidote if possible.

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