

Concepts of Toxidromes

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Abstract

Emergency physicians often encounter poisoned patients exposed to agents, intentionally or unintentionally, with known or unknown nature. The exposure may be iatrogenic (drugs interaction) or non-iatrogenic. The scenarios range from industrial disaster, occupational exposure, recreational mishap, natural catastrophe, chemical warfare, and acts of terrorism. We review papers of toxidromes regarding to clinical presentation, physical examination findings, and laboratory finding to aid emergency physicians differentiating commonly encountered poisons. Nevertheless, evidence-based approaches and clinical trials are limited. Current management is mostly based on expert-consensus from previous tragic experiences. In this review article, current accepted management for common poisonings also are introduced. (*Ann Disaster Med. 2005;4 Suppl 1:S1-S7*)

Key words: Toxidrome; Toxicology; Consensus

Introduction

In recent 10 years, several terroric attacks took place, such as the bombings of the World Trade Center(1993); bombing of Alfred P. Murrah Federal Building in Oklahoma City(1995) and the famous sarin attacks in Tokyo and Matsumoto(1995). Recently, terrorists declare extensive attacks involving biochemical weapons. These are large-scale activities. Many other similar but smaller attacks are not uncovered. For example, in Taiwan, cyanide poisons just took place not long ago. Why are there so many terroric attacks than before? It may be related to the easier access to such materials or methods either from network or books. These agents not only threaten our life but also cause fear, panic and even societal

disruption. As medical care-providers, to solve the civil fear is beyond our ability. We should realize the characters and toxidromes of the agents that would be encountered. Otherwise, an appropriate emergency department and hospital preparedness should be established. This reviewed article will introduce the management at the scene, characters of toxidromes, and the responses in the hospital.

General Principles

Emergency personnel at the scene of unknown chemicals should establish hot zone, decontamination zone and support zone. Treatment begins with ending the exposure. Well-trained emergency personnel with appropriate protective equipment enter the contamination zone and

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extricate the affected persons. In the decontamination zone, contaminated clothing are took off and enclosed in a plastic bag with a hazard mark. It can eliminate 85 or 90 percent of trapped chemical substances. The affected persons should be showered with water and then washed with soap and water. Though it is simple, it is effective for most situations. Except the aids of the emergency personnel, persons nearby the scene had some self-protective methods. If they are outdoors, they should leave away from the contamination to the upwind place with a shelter. If they are indoors, they should close all the exits that communicate with outsides. They can also decontaminate themselves as mentioned above.

Mass casualties may occur and most of victims are minimally exposed and ambulatory. Hospitals and triage centers should prepare advanced shower facilities for these persons. Mental support should also be provided because most victims are affected in the spirit aspects than the physical ones.

Toxidromes and Management

We will introduce four kinds of substances that may cause affairs attracting people's attention. They can lead to misery in gaseous form via respiratory tract or skin contact and in liquid form for skin or gastrointestinal exposure.

The toxidromes and management are discussed in the followings.

Initial Supportive Measures

Initial in-hospital management after decontamination is to resuscitate and stabilize patients. Simultaneously, history including type of toxins, quantity, time of exposure, any available information about the toxins and detail physical ex-

amination with neurologic examination should be carried out. Laboratory evaluation can also be complete thereafter. Except the initial decontamination of external exposure at the scene or the triage stations, there are some measures to decontaminate and eliminate toxins in the body. As follows:

Gastrointestinal decontamination

Nasogastric tube insertion can enhance elimination of slowly absorbed substance, usually within one to two hours after ingestion, if there is no contraindication. Activated charcoal could be given through the nasogastric tube to adsorb toxins except iron, lithium, sustained-release or enteric-coated substances and illicit drug packet. The dose suggested is 1 g/kg followed by 0.5-1 g/kg every 4 hours or infusion ≥ 12.5 g/hr. The airway should be protected to prevent aspiration. No evidence-base studies supporting the activated charcoal use. Whole bowel irrigation is another choice to decrease absorption. Large volumes of a polyethylene glycol electrolyte solution could be administered at 1-2 L/hr. The effect may be achieved when clear rectal effluent is observed. The contraindications include ileus, gastrointestinal obstruction or perforation, intractable vomiting or hemodynamic instability.

Enhanced elimination

Hemodialysis and hemoperfusion are usually reserved for elimination of specific life-threatening toxins. Hemodialysis is suitable for water soluble, low volume of distribution, low molecular weight and plasma protein binding materials. Instead, hemoperfusion serves as technique removing high plasma protein binding toxins. Both of hemodialysis and hemoperfusion

are not performed in hemodynamic unstable patients.

Asphyxiants

Asphyxiants can cause tissue hypoxia, lead to vital organ dysfunction, and present symptoms from mild to severe depending on the amount and character of the exposed toxins. They are classified as simple or chemical by their mechanism of toxicity. Simple asphyxiants such as methane, propane, nitrogen, carbon dioxide displace oxygen in inspired air, decreased F_iO_2 , which result in hypoxemia. Chemical asphyxiants such as carbon monoxide, cyanide, hydrogen sulfide, interfere with oxygen utility in cell levels and thereby cause tissue hypoxia leading to lactic acidosis. Mild symptoms of asphyxia include headache, fatigue, dizziness, and nausea. More severe symptoms range from dyspnea, altered mental status, cardiac ischemia, and syncope to coma and seizure. Respiratory failure generally results from depression of the central nervous system.

Simple asphyxiants are usually non-odor except for mercaptan added. Most of them have no irritant properties. According to the acting mechanism, arterial blood gas and pulse oximetry are of value to detect decreased oxygen saturation. Thereby, therapy for exposure is supplement of one hundred percent oxygen. Chemical asphyxiants described respectively as follows:

Carbon monoxide poisoning is most common of asphyxiant poisoning. Its incidence is greater in the winter season from the faulty heating systems. Other sources come from exhaust of motor vehicle and combustion appliance, smoke inhalation and metabolism of methylene chloride. It is non-odorous and not irritant. Car-

bon monoxide binds with hemoglobin to form carboxyhemoglobin which decreases oxygen carrying capability of hemoglobin. It also binds to myoglobin and cytochrome oxidase leading to decreased oxygen utility of cell. The acceptable carboxyhemoglobin level in plasma is 3 percent in nonsmoker and 10 percent in smoker. Half-life is about 4-6 hours in room air and 1-1.5 hours with 100 percent O_2 . If patients had altered sensorium, focal neurologic signs, seizure, pregnancy, higher carbonic monoxide level, hypercarbic oxygen therapy should be considered. Hypercarbic oxygen can decrease the half life to 15-30 minutes.

Cyanide comes from industrial or laboratory environments, smoke inhalation, electroplating, metabolism of acrylonitril and other nitrils (iatrogenic). It is also produced in a fire accident. In a sudden collapsed industrial or laboratory worker, cyanide poisoning should be taken into account. Fire accident survivors should be examined for blood cyanide level especially if there is much plastic product at the scene. Cyanide has bitter almonds odor and it is irritant to skin and eyes. The hallmarks of cyanide toxicity are persistent hypotension and acidemia despite adequate arterial oxygenation. Cyanide dose not interfere oxygen-carrying capability of hemoglobin and thereby the arterial blood gas or pulse oximetry would show normal saturation. Due to blocking the oxygen used by cells, the oxygen gradient between artery and vein is low. Treatment begins with providing 100 percent oxygen. Cyanide kit is used if cyanide poisoning is highly suspected. Cyanide kits include sodium nitrite and thiosulfate. Nitrite induces the formation of methemoglobin, which is bound by cyanide, yielding cyanomethemoglobin. Methemoglobin level

must be monitored for its decreasing the oxygen-carrying capacity of the blood. Thiosulfate acts to accelerate the detoxification of cyanide to thiocyanate. For cyanide poisoning due to smoke inhalation, use of thiosulfate, oxygen, and supportive measures is recommended and reserving nitrites for patients who are hypotensive, acidemic, or comatose.

Hydrogen sulfide comes from decaying fish, sewage, production of petroleum, paper mills. It has rotten egg like odor with strong irritant to skin, eyes and respiratory tract. Its poisoning mechanism is similar to cyanide. It is less toxic than cyanide due to its more rapid reversible effect on cell hypoxia. The patients should be provided with 100 percent oxygen. Thiosulfate is of no use, but nitril maybe tried.

Cholinesterase Inhibitor

This content introduces organophosphate, carbonate, and nerve agents. All act on inhibiting acetylcholinesterase resulting in cholinergic symptoms, with both muscarinic and nicotinic. Carbamates do not enter the central nervous system, and enzyme inhibition is reversible in minutes to hours resulting in limited toxicity. Organophosphates permanently inactivate acetylcholinesterase and penetrate the central nervous system, leading to greater toxicity and need for antidote administration. Nerve agents such as sarin, soman, tabun, VX, act as organophosphate. Mnemonics for anticholinergic symptoms is SLUDGE and Killer Bees which represents salivation, lacrimation, urination, diarrhea, gastrointestinal upset, emesis and bradycardia, bronchorrhea, bronchospasm respectively. Miosis, dim vision, headache and eye pain may also be observed. Its central nervous system effects include irritability, cogni-

tive impairment, convulsion and coma. Treatment should not wait for serum cholinesterase activity and begins with 100 percent oxygen, suction and mechanical ventilation as needed. There are three antidotes available – atropine, pralidoxime, and diazepam. Atropine acts to antagonize muscarinic effect. It is administered 2-4 mg intravenously every 5 to 10 minutes for respiratory symptoms control including dyspnea, airway secretion. Pralidoxime can reactivate cholinesterases if it is given before irreversible binding of toxin occurs (usually <24–48 hrs depending on the specific agent). The dosage WHO recommended is ≥ 30 mg/kg intravenous bolus and ≥ 8 mg/kg/hour infusion. Experimentally 1-2 g administered intravenously over a period of 20-30 minutes. As for seizure, benzodiazepines are the only effective anticonvulsant.

Respiratory Tract Irritants

Most commonly confronted are irritants to respiratory tract from industrial accidents. Less frequency are those seen in riots such as choking gases and tear gases. The physical effects depend on dose, water solubility and direct tissue reactivity. According to physic principle, more water soluble agent seldom enters lower respiratory tract. The effects are mainly restricted to upper airway with early warning symptoms. Less soluble irritants go deeper into lower airway and cause acute lung injury with delayed onset. Its irritant effects are more prominent on respiratory tract than skin or eyes. These irritants include chlorine, ammonia, phosgene. At high concentration exposure, both would cause upper and lower respiratory tract injury.

Phosgene has new-mown hay, moldy hay or green corn odor. It is low water soluble. After

exposing to phosgene, there may be no symptoms initially but delayed lung injury was ever reported as late as 15-48 hours. Poor prognosis is expected if dyspnea or chest x-ray film finding of lung edema occur within 4 hours after exposure. If remaining no symptoms and clear chest x-ray film after 8 hours after exposure, acute lung injury is less likely.

Treatment begins with supportive care, administration of oxygen and decontamination. If patients represent hoarseness, stridor, wheezing, altered consciousness, endotracheal intubation may be required to prevent airway obstruction secondary to edema or aspiration. Bronchodilator and steroid, used to decrease edema and inflammation, may be of some benefit. Mechanical ventilation with PEEP may be necessary for pulmonary edema to maintain adequate oxygenation. Prophylactic antibiotics are controversial.

Vesicants and Skin Caustics

Vesicants, blister causing agents, are irritant to airways, skin and eyes. The most famous is mustard, usually used in chemical warfare. It enters body circulation within minutes if absorbed, but a latency of 4-12 hours exists before symptoms. Therefore, decontamination soon after exposure is indicated.

Symptoms first recognized are effects on skin and eyes. These may result in conjunctivitis, corneal damage, even temporary or permanent blindness. Skin presentations may be erythema, vesicles, or bullae in intertriginous areas. Airway involvement may not be emerged as soon as in skin or eyes. It usually occurs after 24 hours, leading to epistaxis, pharyngitis, laryngitis, cough, dyspnea, hemorrhagic edema or airway obstruction. Mortality usually comes from pul-

monary complications. A late effect is hematopoietic suppression. Poor prognosis arise from pulmonary effect within 6 hours after exposure, greater than 25 percent burn injury of body surface and absolute white count $< 200/\text{mm}^3$.

Treatments are mainly supportive, including lung care as to irritant, ophthalmic treatments including topical anticholinergics, antibiotics, petroleum, skin burn injury care which no great amount fluid is lost and adequate hydration. No antidote is available. Nonsteroid anti-inflammatory drugs, thiosulfate, nonabsorbable antibiotics, granulocyte colony-stimulating factor may be tried.

Summary

Emergency doctors and even other clinical doctors may have to face patients exposed to unknown toxins. Sometimes doctors may become the first line personnel to involve in the management of a chemical disaster. Nevertheless, every one should have the concepts about the management at the scene, in the transportation, or in the hospital stage. Self-protective hardwares should be equipped before approaching patients. A detail history about events, including environment, possible substances, accessible facilities is required. Toxidromes identification and complete physical examination help to deal with patients. Do what you can do according to your level. If it is beyond your capability, transfer patients to higher-grade centers.

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