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Rapid Toxicologic Collapse

A man and a woman both die shortly after exposure to the same liquid toxin; he ingests it and she is injected intragluteally. In reporting this unfortunate case, the authors consider the limited range of agents capable of causing such swift hemodynamic collapse. The toxin ultimately identified as responsible is one that is easily obtained, and since the antidotes for this lethal agent must be given early, the authors recommend that they be stocked in the ED or possibly available to EMS.

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Case

Following a domestic dispute, a 41-year-old man injects his girlfriend, a 35-year-old woman, in her right buttock with a syringe containing a clear liquid. He then drinks some of the same liquid and collapses within 10 minutes. The woman's brother, who is nearby, responds to the woman's scream and is told the story, following which he calls 911. EMS finds the alleged assailant in asystole. They also find a bottle of household bleach and a bottle of ammonium on the table next to the partially filled syringe and an empty cup. Both patients are taken to the nearby hospital, where the man is immediately pronounced dead. The woman is in extremis.

In the ED, the woman is obtunded with the following vital signs: blood pressure, 80/40 mm Hg; heart rate, 40 beats/min; and respiratory rate, shallow. Her Spo_2 is 88% on 15 L oxygen. She is intubated and has persistent hypotension despite adequate volume resuscitation and rapid escalation of therapy to three vasopressors. Both EMS and the physician are under the impression that the patient was injected with a combination of ammonium and sodium hypochlorite (bleach), which were found on the kitchen table.

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Which agents can lead to such rapid hemodynamic collapse?

The combination of aqueous ammonium and sodium hypochlorite, both common household cleaning agents, can lead to formation of chloramine, a gas under standard conditions. When inhaled, this gas may produce irritant pulmonary injury. If an aqueous solution is ingested or injected, tissue irritation and/or necrosis are likely sequelae, but rapid collapse would be unexpected (though chloramine injection appears to be unreported in the medical literature).

The differential diagnosis for rapid cardiovascular collapse after exposure to a toxin is rather narrow. Most common culprits are mitochondrial toxins that interfere with oxidative phosphorylation and cellular energy production. Following exposure to the toxin, cells cease aerobic respiration and shift to anaerobic glycolysis for energy production, which is much less efficient. Potent mitochondrial toxins that cause rapid demise in small doses include the following: carbon monoxide, hydrogen sulfide, sodium azide, phosphine, and cyanide. All of these toxins inhibit cytochrome complex IV in the electron transport chain.[1]

Other etiologies to consider include paralytic agents, potent opioids like fentanyl, or GABA-ergic sedatives. However, these agents typically produce cardiovascular collapse secondary to respiratory arrest, so despite the outward appearance of coma or collapse, the patient's

hemodynamics are likely initially near normal. Convulsants, such as tetramine, or hypoglycemic agents, such as insulin, may similarly be associated with rapid collapse, but hemodynamic failure is a delayed consequence.

Delayed-onset toxins administered parenterally with harmful intent include methotrexate, ricin, and chemotherapeutic agents.

How can the differential diagnosis be narrowed?

The implicated toxin in this case is in a liquid form. Liquids are generally either chemicals that exist in this form under standard conditions or aqueous (water-based) or nonaqueous solutions. Almost any toxin that has the capacity to dissolve in a liquid (whether water or another liquid) could be considered as an etiology in this case. Of the agents mentioned above, only cyanide and sodium azide are typically found in liquid form.

Although carbon monoxide poisoning could readily explain the clinical findings in this patient, carbon monoxide is an odorless and colorless gas. Sources of exposure include coal burners, engines, hibachi grills, and, most importantly, fires.[2] The context of the story excludes carbon monoxide as a cause.

Hydrogen sulfide is a colorless gas with a characteristic odor similar to that of rotten eggs. It is produced by bacterial decomposition of proteins or decay of sulfur-containing products such as sewage, fish, and manure. With exposure to higher hydrogen sulfide concentrations, olfactory nerve paralysis ensues, decreasing the ability to detect the rotten-egg odor, thereby increasing the risk of poisoning. The dramatic collapse and demise following exposure is described as the "slaughterhouse sledgehammer effect." Of note, there has been a recent trend, primarily in Japan, to commit suicide using hydrogen sulfide generated in situ by combining chemicals within the confines of a motor vehicle or other enclosed space.[3,4]

Sodium azide is an inorganic salt, formerly widely used in automotive airbag systems and commonly found as a preservative in laboratory solutions. It is soluble in water, in which it forms hydrazoic acid, which itself is volatile and may be inhaled.

FAST TRACK

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Phosphine is a gas that forms upon contact of a phosphide salt (such as zinc or aluminum phosphide) with water. The gas can also be stored in compressed cylinders for industrial use. The phosphides are used in grain storage processes and during methamphetamine synthesis, and phosphine poisoning is associated with both situations.

Cyanide may also exist in the gaseous or aqueous forms. It can be found in the precursor form (eg, cyanogenic glycosides) in plants such as cassava (linamarin) and *Prunus* species (amygdalin) and in commercial liquids (eg, nitriles). Poisoning by a precursor form of cyanide has delayed onset (hours), while rapid demise occurs when cyanide is either inhaled (hydrogen cyanide), ingested, or injected as an aqueous salt solution (eg, sodium cyanide).

Ancillary information can be a valuable tool in clinical practice. In addition to medical history, current medication regimens, use of illicit drugs, and family history, the patient's occupational information can be revealing and may help the clinical team to home in on a diagnosis. It was discovered much later in the management of this case that the male patient was a jeweler. A simple investigation into compounds commonly used by jewelers could rapidly implicate cyanide salts, which are used for electroplating and metal cleaning.

What are the clinical implications of various routes of cyanide administration?

The most important clinical implication is the difference in onset of toxicity and time to death. Faster onset decreases the chance for timely antidote administration and therefore increases the likelihood of death.[5]

Cyanide gas, commonly in the form of hydrogen cyanide, is quickly absorbed and swiftly (within a min-

ute or two) affects all the organs. Death occurs within minutes of exposure. This form of cyanide poisoning is the most rapid.

Ingestion of cyanide-containing liquid leads to rapid absorption and distribution to target organs. Additionally, aqueous solutions of cyanide salts are caustic and may lead to direct mucosal injury of the gastrointestinal tract. Clinical effects begin with a few minutes of ingestion, and death ensues several minutes thereafter without therapy.

Intramuscular injection of cyanide is poorly described in the literature, though its kinetics are likely similar to those resulting from ingestion. Absorption is the rate-limiting step. Therefore, onset of toxicity may take longer than onset following inhalation or ingestion. The female patient, who received an intragluteal injection, was able to relate her story to her brother after the boyfriend succumbed to the effects of cyanide.

What are the potentially lifesaving prehospital measures in cases of sudden collapse from a presumed toxin?

There are limited therapies available to prehospital providers for the management of victims of exposure who have had rapid clinical decompensation/demise. EMS should consider contacting the local poison control centers from the scene or while en route to the hospital. The administration of a cyanide antidote is critical in the early course of toxicity.[6-8] Once cyanide distributes to target organs, which happens rapidly, the antidotes may not be as effective.

Case Conclusion

The female patient's venous blood gas analysis showed a profound metabolic acidosis (pH, 6.96) with a serum lactate concentration greater than 20 mmol/L. Based on her history of injection followed by rapid clinical decompensation, treatment for cyanide toxicity was recommended by the poison control center. The ED, however, did not have either hydroxocobalamin or the original three-part cyanide antidote kit, and antidote administration was delayed by 2.5 hours while a courier was dispatched to another hospital. The patient eventually received two doses of 5 g of hydroxocobalamin but died within 24 hours of hospital arrival. Initial blood cyanide concentration was 0.76 mg/L. Investigation confirmed that cyanide was present in both the drinking cup and the syringe.

The man's postmortem blood cyanide concentration was 335 mg/L, and the stomach contained 597 mg of cyanide. Autopsy demonstrated pharyngeal mucosal injury and gastric hemorrhage, which were likely a result of caustic injury induced by the ingested cyanide salt. He had red skin discoloration of the back.

The woman's postmortem blood cyanide concentration was 0.4 mg/L. Her autopsy demonstrated red-purple skin discoloration and organ decomposition. The site of injection in the buttock contained subcutaneous hemorrhage. Although red skin discoloration has been described postmortem in victims of cyanide poisoning, hydroxocobalamin is a red dye and may lead to red discoloration of the skin, as well.[9,10]

There are few toxins that result in rapid clinical deterioration and demise shortly after exposure. Cyanide is easily obtained, and effective antidotes are available. Thus, cyanide poisoning should be considered when clinical history is suggestive of such. The availability of cyanide antidotes to emergency medicine may facilitate early lifesaving treatment, and EMS or medical control should attempt contact with the poison control center as early as possible when cyanide poisoning is suspected. **EM**

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