Clinical Toxicology (2007) **45**, 420–423

ISSN: 1556-3650 print / 1556-9519 online
DOI: 10.1080/15563650601118010

informa
healthcare

CASE REPORT

Acute hydrogen sulfide poisoning in a dairy farmer

GREGG GERASIMON, M.D.[1], STEVEN BENNETT, M.D., FCCP[2], JEFFREY MUSSER, DO[3], and JOHN RINARD, DO[4]

[1]*Major, Medical Corps, U.S. Army, Internal Medicine, Womack Army Medical Center, Fort Bragg, North Carolina, USA*
[2]*Major, Medical Corps, U.S. Army, Pulmonary and Critical Care Medicine, Madigan Army Medical Center, Tacoma, Washington, USA*
[3]*Major, Medical Corps, U.S. Army, Critical Care Medicine, Madigan Army Medical Center, Tacoma, Washington, USA*
[4]*Captain, Medical Corps, U.S. Army, Internal Medicine, Madigan Army Medical Center, Tacoma, Washington, USA*

Introduction. Hydrogen sulfide is a lipid-soluble gas produced in occupational settings and from decaying organic matter. We present a 36-year-old man who developed acute respiratory arrest from hydrogen sulfide poisoning while performing work as a dairy farmer. Case *report.* The subject entered a poorly ventilated tank containing degrading eggs and, within seconds, collapsed. Coworkers were able to extract him within minutes but he was apneic. He was intubated by emergency medical services and subsequently managed with supportive care in the intensive care unit. Upon admission, a powerful rotten egg scent was noted and a hydrogen sulfide poisoning was suspected. Serum analysis for the presence of thiosulfate confirmed the diagnosis. Nitrite therapy was not administered as the subject arrived outside of the therapeutic window of effectiveness and showed evidence of excellent oxygenation. His examinations following arrival were consistent with an anoxic brain injury which slowly improved several months after the incident with intensive neuro-rehabilitation. *Discussion.* Hydrogen sulfide is a mitochondrial toxin and inhibits cytochrome-aa_3 and prevents cellular aerobic metabolism. Therapies for toxic exposures include removal from the contaminated environment, ventilation with 100% oxygen, and nitrite therapy if administered immediately after exposure. Hyperbaric oxygen (HBO) therapy has anecdotal support and remains controversial. *Conclusion*. Hydrogen sulfide is a significant occupational health hazard. Education, personal protective equipment, and early treatment are important in improving outcomes.

Keywords Hydrogen sulfide; Cytochrome-aa_3; Nitrite; Hyperbaric oxygen (HBO)

Introduction

Hydrogen sulfide (H_2S) is a toxic, colorless gas produced by decaying organic matter in the environment. Specifically, it occurs with the decay of sulfur-containing proteins and is a by-product of human and animal waste. It occurs naturally in crude petroleum, natural gas, volcanic gases, and in wetlands. Additionally, the compound is produced in a variety of occupational settings such as leather tanning, rubber vulcanization, synthetic fabric and paper production, and asphalt roofing to name a few (1). Despite the prevalence of the substance in industrial settings, human poisoning from H_2S exposures is uncommon.

When H_2S gas is inhaled it is rapidly absorbed through the alveolar-capillary membrane. It initially distributes to brain, liver, kidney, gut, and pancreas (2). Its toxicities occur through a mechanism similar to that of cyanide poisoning in that it competitively inhibits the cytochrome-aa_3 enzyme, thereby interrupting oxidative phosphorylation and cellular aerobic metabolism. The onset of action is rapid and causes the patient to experience acute oxygen deprivation or asphyxia described as histotoxic hypoxia (3). In addition, hydrogen sulfide gas is an irritant to the skin and mucosal membranes.

Therapy for acute hydrogen sulfide poisoning has traditionally been mechanical ventilation with 100 percent oxygen and supportive care. Nitrite therapy is helpful if given early but has little utility if delayed more than ten minutes after exposure. Hyperbaric oxygen therapy has a strong theoretical benefit in reversing the cellular anoxia caused by hydrogen sulfide poisoning. However, the documented benefit of hyperbaric oxygen treatment remains largely anecdotal at this time and it has not become the standard of care.

Given the prevalence of H_2S in industrial activities, it presents a significant public health hazard. According to the American Association of Poison Control Centers' annual report, there were 1,980 reported exposures in 2004. Of these cases, 375 were treated in a health care facility; nine had major morbidity from the exposure, and two died (4).

Received 30 September 2005; accepted 13 January 2006.

The views expressed in this article are those of the authors and do not reflect the official policy or position of the U.S. Army, the U.S. Department of Defense, or the U.S. Government.

Address correspondence to MAJ Gregg Gerasimon, M.D., Department of Internal Medicine, Womack Army Medical Center, Fort Bragg, NC 28310, USA. E-mail: gregg.gerasimon@us.army.mil

Case report

A 36-year-old man was working the late shift at a rural, corporate dairy farm in western Washington state. He had no significant past medical history and was on no medications at the time. He also was a non-smoker and had no history of alcohol or drug abuse. His job that evening was to partially clean a 50,000-gallon tank containing eggs that were not suitable for commercial use, and he had not done this job before. For unclear reasons, the tank did not have adequate ventilation at the time and personal protective equipment (PPE) was not used. Roughly thirty seconds after entering the tank through a small passageway at its base, he collapsed unconscious. Coworkers were nearby and managed to extract him after about five minutes. Three additional coworkers had brief inpatient hospital care due to exposure to hydrogen sulfide gas with no reported adverse effects.

He had no spontaneous respirations and CPR was performed following extraction. He was intubated emergently when paramedics arrived (roughly 10 to 20 minutes after exposure). He was directly admitted to the ICU on arrival to the hospital, about 45 to 60 minutes following exposure.

On arrival, he had a notable scent of "rotten eggs." He was placed on mechanical ventilation with 100 percent oxygen. Initial physical exam showed a temperature of 99.3 F, blood pressure 160/101, heart rate in sinus tachycardia at 141 bpm, and ventilated at 14 breaths per minute. He was not overbreathing the ventilator. He had a gag reflex with suctioning through the endotracheal tube. He had no spontaneous eye opening and withdrew his extremities to pain. Neurologic exam also showed spontaneous decerebrate posturing and upgoing toes bilaterally. He had minimal ocular involvement limited to local irritation.

Patient laboratory and radiological data were obtained after initial resuscitation. The patient had a mild lactic acidosis of 2.3 mmol/L (upper limit of normal is 2.2 mmol/L). This lactic acidosis trended downward and normalized over the next day. His arterial blood gas on 100 percent oxygen was pH 7.39, $PaCO_2$ 42, PO_2 273, bicarbonate 24.4, base deficit of 0.6, and SaO_2 100%. A methemoglobin level and carboxyhemoglobin level were checked, and both were negative. A blood thiosulfate level (to document sulfide exposure) was drawn on arrival (approximately 3 hours after exposure), with results not available until one week later; the thiosulfate level was elevated at 3.1 μg/mL (upper limit of normal is 2.0 μg/mL). Results of routine complete blood count and chemistry panels were unremarkable. A chest radiograph obtained upon arrival to the ICU revealed mild pulmonary edema, which was managed with positive pressure ventilation and careful volume management, and rapidly resolved over the initial 24 hours. He had no late or long term sequale from his acute lung injury. A brain MRI with diffusion-weighted imaging obtained on hospital day 2 showed areas of restricted diffusion in the left superior cerebral hemisphere and in the left basal ganglia and thalamus, consistent with acute CNS toxicity from high level exposure to hydrogen sulfide (3).

Since the patient had adequate evidence of tissue oxygenation and only a minimal lactic acidosis, nitrite therapy was not initiated for treatment of the hydrogen sulfide poisoning. The local hyperbaric oxygen center was contacted and, for similar reasons, HBO therapy was not pursued. He was managed with supportive care in the intensive care unit. His neurological exam showed gradual improvement, with progression from decerebrate to decorticate posturing and evidence of spontaneous eye opening over the next several days. The patient's family wished to proceed with full care, and a tracheostomy and PEG tube were placed. On hospital day 10, he was transferred to a neurological rehabilitation unit for continued treatment of the anoxic brain injury.

Discussion

The chemistry of hydrogen sulfide has been studied for several hundred years. In the 1800s, the Dutch pharmacist Petrus Johannes Kipp developed the "Kipp Generator" which facilitated the generation of hydrogen sulfide for scientific study (5). Hydrogen sulfide has a chemical structure similar to that of water. However, the compound is not nearly as polar as water due to electronegativity differences between the sulfur and oxygen atoms. As such, the melting and boiling points of hydrogen sulfide, as well as its chemical properties, are much different than those of water.

The toxicity of hydrogen sulfide on the body occurs as a result of inhibiting oxidative phosphorylation. It is a known inhibitor of cytochrome-aa_3 and is a more potent inhibitor than cyanide (3, 6). Because of the inhibition of cellular oxygen metabolism, it causes anaerobic respiration with a resultant metabolic acidosis and cytotoxic anoxia. Additionally, being an irritant gas, it can cause direct irritation to the skin and mucosal surfaces.

The effects of hydrogen sulfide exposure on the body vary with the concentration and duration of exposure. Concentration of the gas is far more important in determining toxicity than is the duration of exposure. This has been well studied, and the dose-response curve is quite steep (7). At levels of 0.003 ppm, olfactory perception of ambient hydrogen sulfide is possible, and the characteristic "rotten egg" scent is perceptible at 3 to 30 ppm (8). The detection of hydrogen sulfide by scent is only possible at very low concentrations; however; at concentrations above 100 ppm, the gas causes immediate olfactory paralysis after which odor perception is no longer possible (9). Thus, at levels above 100 ppm, toxicity can continue without the patient being aware.

Also at lower concentrations, a keratoconjunctivitis or "gas eye" can occur, which is a superficial inflammation of the cornea and conjunctiva. Keratoconjunctivitis has frequently been seen in industrial workers at sour gas plants who are routinely exposed to low concentrations of hydrogen sulfide (10). The keratoconjunctivitis is often associated with color distortion and visual changes. These changes are reversible after removal from the exposure.

At levels up to 250 ppm, pulmonary symptoms including bronchospasm and acute lung injury, as well as nausea and vomiting can occur. At a concentration of 500 ppm, the patient can have systemic symptoms such as hypotension or confusion, as well as alveolar hemorrhage and acute alveolitis (11). At ambient concentrations above 750 ppm, apnea, asphyxial seizures, and death can occur after only one breath (12). Given the rapid onset of respiratory arrest in our patient, we believe that the concentration he was exposed to was in excess of 750 ppm.

Hydrogen sulfide has a propensity to affect the lungs and brain as primary targets in the body. During the acute phase of exposure, acute lung injury is commonly seen on chest radiography. The venous PO_2 may transiently increase as well, due to the inhibition of cytochrome-aa_3 and impaired cellular utilization of oxygen (13). Other common pulmonary sequelae include cough, chest tightness, and hemoptysis. Our patient manifested evidence of mild pulmonary toxicity based on adequacy of oxygenation and rapid improvement of his pulmonary edema on serial chest radiographs. Neurologic symptoms may include dizziness, confusion, headache, pupil dilatation, and somnolence, along with direct cytotoxic injuries to the brain (14). Our patient's brain MRI findings did support the presence of direct injury to the CNS secondary to high level toxic exposure to hydrogen sulfide gas (3).

There is evidence to support that, at very high concentrations, hydrogen sulfide is selectively taken up in the lipophilic white matter centers of the brainstem (15). This selective uptake would concentrate the toxic effects of hydrogen sulfide on the brainstem respiratory centers, thereby explaining the acute apnea seen with inhalation at levels above 750 ppm.

Detoxification and elimination of hydrogen sulfide from the blood is clearly important in limiting patient injury. The elimination of sulfide occurs through its oxidation to sulfates, incluiding thiosulfate, and other sulfur compounds. Oxyhemoglobin, and to a certain extent methemoglobin, catalyzes this oxidation reaction (16). Pulmonary excretion of toxic hydrogen sulfide or metabolic by-products has not been described (17). The excretion of the nontoxic sulfate and sulfur compounds is primarily through the kidneys (18).

It has been proposed that therapy should be directed at three targets to minimize the toxic effects of hydrogen sulfide: promoting permanent detoxification of sulfide in the body, competitively inhibiting the sulfide-cytochrome-aa_3 interaction, and minimizing post-insult tissue damage (19). The theory behind nitrite therapy for hydrogen sulfide exposure rests on the fact that the methemoglobinemia induced by nitrites binds hydrogen sulfide and limits its toxic effect on tissues. Nitrites cause the formation of methemoglobin, which has been shown to have a higher affinity for the hydrogen sulfide molecule than cytochrome-aa_3, thereby binding it more avidly and freeing the cytochrome-aa_3 enzyme to resume aerobic cellular metabolism (20). In this manner, the methemoglobin competitively inhibits the sulfide-cytochome-aa_3 chemical interaction.

Additionally, the methemoglobin-hydrogen sulfide complex is long lived in the body and acts to sequester the hydrogen sulfide molecule while it is awaiting oxidative detoxification (21). Some have also shown that the methemoglobin acts as a better oxidation catalyst in detoxifying sulfide than normal oxyhemoglobin (22).

Inhalational nitrite therapy utilizing inhaled amyl nitrite is available for immediate intervention in the absence of intravenous access. If intravenous access is available, infusion of 0.33 mL/kg of 3% sodium nitrite (with a maximum of 10 mL), is given over 4–5 minutes (23). It is not necessary to give both inhalational and intravenous nitrites. Side effects of nitrite administration include nausea and vomiting, headache, and hypotension, but these effects can be minimized by slowing the rate of infusion to be given over 15 to 20 minutes (24).

Nitrites must be given soon after exposure due to the short lifespan of sulfide in oxygenated blood. It is recommended that nitrite therapy be given within the first few minutes after exposure (25, 26). This narrow window limits the utility of nitrite therapy to settings where hydrogen sulfide exposure is a known possibility, as in various occupational settings mentioned above, or in cases where rapid medical attention is possible. Additionally, the benefit of the nitrite-induced methemoglobinemia in sulfide-exposed patients must be weighed against the adverse effect methemoglobin has in adding to the body's anoxic burden. Since methemoglobin prevents normal hemoglobin from releasing oxygen to the tissues, a methemoglobinemia may worsen the degree of anoxia to oxygen-starved tissues.

Hyperbaric oxygen (HBO) therapy has shown promise in treating sulfide-exposed patients as well, though at this time its utility is largely anecdotal. The theory behind HBO use rests on competitively inhibiting the sulfide-cytochrome-aa_3 interaction. Oxygen competes with hydrogen sulfide for binding sites on cytochrome-aa_3. HBO therapy saturates tissues with oxygen and favors the cytochrome-aa_3-oxygen interaction over the cytochrome-aa_3-sulfide interaction. Furthermore, in patients who have a significant acidosis secondary to anaerobic metabolism that occurs following a hydrogen sulfide exposure, HBO therapy improves oxygenation to these tissues and, theoretically, limits damage (27).

HBO therapy is also theoretically beneficial when used in conjunction with nitrite therapy since it can limit tissue anoxic damage that is caused by a nitrite-induced methemoglobinemia. However, laboratory studies that have analyzed nitrite and HBO therapy as treatment of hydrogen sulfide poisoning have done so in controlled laboratory settings and have no practical corollaries to patient clinical scenarios. For example, in one study, sodium nitrite and HBO therapy were given within two minutes of the sulfide exposure (28). In most clinical settings, nitrite therapy is delayed until EMS arrives or until transport to the nearest medical facility, and HBO therapy can be delayed many hours beyond that simply due to resource availability.

For our patient, neither nitrite nor HBO therapy was given. The patient arrived to our hospital an estimated 45 to 60 minutes after exposure, well outside of the window recommended for administration of nitrites. He had a minimal lactic acidosis that resolved over the first night of admission. He did not have evidence of hypoxic damage to organs other than the brain (i.e., no cardiac dysrhythmias), and all parameters suggested that his tissue oxygenation was excellent. After extensive discussion with the local HBO center, it was not clear what benefit there would have been in instituting HBO therapy. The decision made to withhold HBO therapy was based on the subtle improvement in the patient's neurologic examination and a concern for the risk of air evacuation transport possibly causing a worsening in his oxygenation status by either loss of his controlled airway or exposure to altitude during transport.

Two months following exposure, we received an encouraging letter from the patient's wife documenting his progress. She stated that "he has learned to walk, but still has problems with balance…his speech is getting better every day…he can also read, but not at the level he used to…he's learned to eat though his feeding tube is still in…[he] will be coming home in three to four weeks."

Conclusions

Hydrogen sulfide is a significant industrial health hazard as it is produced extensively in nature as well as in many common occupational settings. It has a characteristic odor that is only perceptible at very low concentrations. Its effects on the body have a steep dose-response curve, with respiratory arrest and death occurring quickly when inhaled at high concentrations. While supportive care is a cornerstone of therapy, nitrite and HBO are also available if administered rapidly following hydrogen sulfide exposure. Further research is needed to help clarify the role HBO therapy plays in treating hydrogen sulfide poisoning. Education for workers, the use of personal protective equipment, physician awareness, accurate diagnosis, and early treatment are all crucial in improving the outcome in cases of high level toxic exposures.

Disclosures

The authors have no financial or proprietary interests to disclose.

References

1. Mari Poison Center. (Accessed January 2006, at http://www.maripoisoncenter.com/professionals/CTR%20PDFs/CTR%2025.12.pdf).
2. Voight G, Mueller P. The histochemical effect of hydrogen sulfide poisoning. Acta Histochem 1955; 1:223–239.
3. Byungkuk N, Hyokyung K, Younghee C. Neurologic Sequale of Hydrogen Sulfide Poisoning. Industrial Health 2004; 42:83–87.
4. Watson WA, Litovitz TL, Rodgers GC. 2004 annual report of the American Association of Poison Control Centers Toxic Exposure Surveillance System. Am J Emerg Med 2005; 23(5):589–666.
5. Aynsley E, Campbell W. The laboratory preparation of hydrogen sulfide: a historical survey. J Chem Educ 1958; 35:347–349.
6. Beck J. A mode of action for Hydrogen Sulfide is proposed. Toxicol 1983; 26:37–45.
7. Prior M, Sharma A, Yong S. Concentration-item interactions in hydrogen sulfide toxicity in rats. Can J Vet Res 1988; 52:375–379.
8. Milby T. Hydrogen sulfide intoxication: Review of the literature and report of unusual accident resulting in the two cases of nonfatal poisoning. J Occup Med 1962; 4:431–437.
9. Hydrogen Sulfide, Poisindex® Managements, vol. 121, September 2004.
10. Guidotti T. Hydrogen sulphide. Occup Med 1996; 46:367–371.
11. Richardson D. Respiratory effects of chronic hydrogen sulfide exposure. Am J Ind Med 1995; 28:99–108.
12. Beauchamp R, Bus J, Popp J. A critical review of the literature on hydrogen sulfide toxicity. CRC Crit Rev Toxicol 1984; 13:25–49.
13. Snyder J, Safir E, Summerville G. Occupational fatality and persistent neurologic sequelae after mass exposure to hydrogen sulfide. Am J Emerg Med 1995; 13:199–203.
14. Burnett W, King E, Grace M. Hydrogen sulfide poisoning: Review of 5 years experience. Can Med Assoc J 1977; 117:1277–1280.
15. Warenycia M, Goodwin L, Benishin C. Acute hydrogen sulfide poisoning. Demonstration of selective uptake of sulfide by the brainstem by measurement of brain sulfide levels. Biochem Pharmacol 1989; 38:973–981.
16. Beck J, Bradbury C, Connors A. Nitrite as an antidote for acute hydrogen sulfide intoxication? Am Indus Hyg J 1981; 42:805–809.
17. Susman J, Hornig J, Thomae S. Pulmonary excretion of hydrogen sulfide, methane-thiol, dimethylsulfide, and dimethyldisulfide in mice. Drug Chem Toxicol 1978; 1:327–388.
18. Marcus S. Hydrogen sulfide. Clin Toxicol Rev 1983; 5:1–2.
19. Smilkstein M, Bronstein A, Pickett H. Hyperbaric oxygen therapy for severe hydrogen sulfide poisoning. J Emerg Med 1985; 3:27–30.
20. Smith R, Gosselin R. On the mechanism of sulfide inactivation by methemoglobin. Toxicol Appl Pharmacol 1966; 8:159–172.
21. Beck J, Bradbury C, Connors A. Nitrite as an antidote for acute hydrogen sulfide intoxication? Am Ind Hyg Assoc J 1981; 42:805–809.
22. *Ibid.*
23. Guidotti T. Hydrogen sulphide. Occup Med 1996; 46:367–371.
24. Gunn B, Wong W. Noxious gas exposure in the outback: Two cases of hydrogen sulfide toxicity. Emerg Med 2001; 13:240–246.
25. Guidotti T. Hydrogen sulphide. Occup Med 1996; 46:367–371.
26. Agency for Toxic Substance and Disease Registry. Medical management guidelines for hydrogen sulfide. (Accessed January 2006, at http://www.atsdr.cdc.gov/MHMI/mmg114.html).
27. Smilkstein M, Bronstein A, Pickett H. Hyperbaric oxygen therapy for severe hydrogen sulfide poisoning. J Emerg Med 1985; 3:27–30.
28. Bitterman N, Talmi Y, Lerman A. The effect of hyperbaric oxygen on acute experimental sulfide poisoning in the rat. Toxicol Appl Pharmacol 1986; 84:325–328.