HYDROGEN SULFIDE

Hydrogen sulfide gas (H₂S) is heavier than air, colorless, and smells of rotten eggs. It is commonly found where organic material is decomposing or petrochemical operations occur. Common locations where people may be exposed to hydrogen sulfide include farms, septic tanks, sewers, natural gas operations, and in the holds of fishing vessels. The AAPCC reported a total of 1,418 exposures in 2002, 28% (398) of which were treated in a health care facility. Of those cases, 28% (113) suffered a moderate outcome, 6% (25) resulted in a major outcome and 2% (six) were fatal. All but six of the total exposures were unintentional and 75% (1,064) occurred in adults over the age of nineteen.¹

DOSSING

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<thead>
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<th>H₂S Concentration, ppm</th>
<th>Effect</th>
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<tr>
<td>0.15</td>
<td>Detectable odor</td>
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<tr>
<td>150</td>
<td>Ofactory nerve paralysis; mucous membrane irritation</td>
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<tr>
<td>500</td>
<td>Headache, pulmonary edema</td>
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<tr>
<td>700</td>
<td>Loss of consciousness</td>
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<tr>
<td>1000</td>
<td>Convulsions, coma, respiratory paralysis, death</td>
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The above table shows some common effects of hydrogen sulfide and the associated levels at which they may become apparent. The Occupational Safety and Health Administration (OSHA) and American Conference of Governmental Industrial Hygienists (ACGIH) have set short-term exposure limits of 10 to 20 PPM.

TOXICOLOGY

Upon exposure, hydrogen sulfide reacts with saline in the mucosa to produce sodium sulfate (Na₂SO₄), which causes local irritation, pharyngitis, cough and keratoconjunctivitis ("gas eye"). Its toxic effects impair respiration at both the pulmonary and cellular levels. On a gross scale, hydrogen sulfide interferes with alveolar macrophages and cilia. At the microscopic level, hydrogen sulfide temporarily binds with mitochondrial

PHARMACOLOGY AND KINETICS

Toxicity occurs on exposure to, or inhalation of, the gas. It is rapidly absorbed and distributed to body tissues, most significantly in the brain, liver and kidneys. Its half-life in the body is short, and it dissociates rapidly from the proteins to which it binds. It is metabolized through three pathways: oxidation to sulfate, methylation, and reaction with metalloproteins.² The resultant metabolites are subsequently excreted in the urine.

H₂S

cyt c⁺⁺⁺

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<th>H₂S</th>
<th>cyt a⁺⁺⁺</th>
<th>cyt a⁻⁻⁻</th>
<th>cyt a⁻⁻⁻</th>
<th>2H₂O</th>
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Hydrogen sulfide's inhibition of cytochrome a₃

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cytochrome a₃, which delays mitochondrial phosphorylation, before rapidly dissociating.

At low concentrations, hydrogen sulfide is notable by its characteristic sulfur smell; however, individuals exposed to higher concentrations of the gas may lose the ability to detect the odor due to olfactory nerve paralysis. Exposure to hydrogen sulfide has the potential to cause mental status changes, convulsions, and rapid loss of consciousness. These neurological effects may be caused by potassium channel mediated hyperpolarization, which inhibits neural conduction.²

The most toxic effects of hydrogen sulfide exposure occur when the compound binds to, and inhibits, cytochrome oxidase of the electron transport train. The resultant tissue hypoxia causes the cardiovascular collapse and non-cardiogenic pulmonary edema seen in the most severe cases.

LABORATORY ANALYSIS
Poisoning with H₂S causes a decrease in oxygen consumption by poisoning cytochrome oxidase. Theoretically, comparison of venous and arterial oxygen levels would show a decrease in the pO₂ gradient. The specificity and sensitivity of this test have not been determined. Measurement of hydrogen sulfide level in the blood is not commonly done. Pathologists use urine thiosulfate or plasma sulfide anion levels to help establish the cause of death, but results of these tests are not available in time to help with acute clinical management. Interestingly, due to the oxidative properties of hydrogen sulfide, coins in the pocket of an exposed victim may turn a blackish color. The brain, at autopsy, has also been described as having a greenish-black tinge.⁴

TREATMENT
Removal from the environment and supportive care, with particular attention to oxygenation and ventilation, are the most important initial actions. Convulsions are treated with benzodiazepines, barbiturates, or other agents in the standard manner. Similarly, non-cardiogenic pulmonary edema is treated the same way as in other cases of NCPE.

Although no conclusive benefit exists to suggest that the clinical picture is improved by treatment with hyperbaric oxygen, it has been used in some cases with mixed results. Although not the standard of care, it might be reserved for use where other measures have failed and the patient remains critically ill.⁵,⁶,⁷,⁸

Use of the nitrile portion of the cyanide antidote kit has shown a benefit in some animal studies. The proposed mechanism is that the sulfide ions leave the cytochromes for the ferric heme due to its greater affinity. The animals in the experiments were given massive amounts of sodium nitrite, generating methemoglobin levels on the order of 80%. The dose was administered only two minutes after the exposure to hydrogen sulfide. However, some case reports of human poisoning suggest there is a benefit.⁹,¹⁰,¹¹ At this point, two other proposed antidotes, pyruvate and dithiothreitol, cannot be recommended for treatment.

CONCLUSION
Hydrogen sulfide gas, a byproduct of organic decomposition, exists in a number of settings which may bring people in contact with it. The effects are related to concentration and time of exposure. Its most lethal effects stem from its inhibition of cytochrome a₃, and the resultant respiratory and cardiovascular compromise. An arterial-venous oxygen gap can be measured as a marker of toxicity. Although some case reports suggest hyperbaric oxygen may be useful, the treatment remains supportive. Understanding the sources and toxicity of hydrogen sulfide will help the physician diagnose and manage this poisoning.

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REFERENCES