Hydrogen sulphide

T. L. Guidotti

Occupational Health Program, University of Alberta, Faculty of Medicine, 13-103 Clinical Sciences Building, Edmonton, Alberta, T6G 2G3, Canada

Hydrogen sulphide (H_2S) is the primary chemical hazard in natural gas production in 'sour' gas fields. It is also a hazard in sewage treatment and manure-containment operations, construction in wetlands, pelt processing, certain types of pulp and paper production, and any situation in which organic material decays or inorganic sulphides exist under reducing conditions. H_2S dissociates into free sulphide in the circulation. Sulphide binds to many macromolecules, among them cytochrome oxidase. Although this is undoubtedly an important mechanism of toxicity due to H_2S, there may be others. H_2S provides little opportunity for escape at high concentrations because of the olfactory paralysis it causes, the steep exposure–response relationships, and the characteristically sudden loss of consciousness it can cause which is colloquially termed 'knockdown.' Other effects may include mucosal irritation, which is associated at lower concentrations with a keratoconjunctivitis called 'gas eye' and at higher concentrations with risk of pulmonary oedema. Chronic central nervous system sequelae may possibly follow repeated knockdowns: this is controversial and the primary effects of H_2S may be confounded by anoxia or head trauma. Treatment is currently empirical, with a combination of nitrite and hyperbaric oxygen preferred. The treatment regimen is not ideal and carries some risk.

Key words: Hydrogen sulphide; keratoconjunctivitis; pulmonary oedema; sour gas.

INTRODUCTION

Hydrogen sulphide (H_2S) is the primary chemical hazard of natural gas production. It is also encountered in municipal sewers and sewage treatment plants, swine containment and manure-handling operations, pulp and paper operations (in Kraft and especially sulphite mill technologies), construction in wetlands, asphalt roofing, pelt processing and in any contained spaces in which organic material, such as fish or offal, has decayed or in which inorganic sulphides exist under reducing conditions.[1–6] It is in oil and gas production, however, that hydrogen sulphide appears most frequently as an industrial hazard. It is most often a hazard in well-drilling and servicing, pumping and gas refining in Texas, Oklahoma and the Gulf Coast of the United States, Alberta, the North Sea and the Middle East.

Occupational exposure to hydrogen sulphide is primarily a problem in the sour gas segment of the natural gas industry, which refers to natural gas with a high concentration of natural sulphur. Although widely dispersed, sour gas is limited to relatively few natural gas fields worldwide. Sulphur is reduced to hydrogen sulphide during the prolonged degradation process of organic material underground that forms natural gas and petroleum. Hydrogen sulphide is a variable constituent of sour gas, ranging from low concentrations to 35% and more. The problem is uniquely severe in the Canadian province of Alberta, because of the heavy concentration of high-sulphur content oil and gas fields in the province.[4,7–9]

The H_2S in sour gas and pulp mills is accompanied by variable concentrations of methyl mercaptans (CH_3SH, $[CH_3]_2S$, and $[CH_3]_2S_2$) and carbonyl sulphide (COS), which are usually regarded to be of low toxicity. During gas processing some of these compounds are converted to H_2S. Mercaptans have a characteristic pungent odour. Mercaptans are also added to natural gas before distribution as a safety measure to ensure detection of leaks.[2,10]

TOXICOLOGY

The toxicology of H_2S has been extensively reviewed in recent years by Turner and Fairhurst,[11] Beauchamp

Correspondence and reprint requests to: T. L. Guidotti, Occupational Health Program, University of Alberta, Faculty of Medicine, 13-103 Clinical Sciences Building, Edmonton, Alberta, T6G 2G3, Canada.

et al.,[12] Reiffenstein *et al.,*[13] Guidotti[14] and by Glass.[15] These reviews and the older summary literature[16-18] provide most of the following discussion.

H_2S is inhaled and enters the circulation directly across the alveolar-capillary barrier, where it dissociates in part into sulphide ion, HS. Some remains as free H_2S in blood and this fraction appears to interact with metalloproteins, disulphide-containing proteins, and thio-S-methyl-transferase, forming methyl sulphides. The sulphide ion binds to haeme compounds and is itself metabolized by oxidation to sulphate. Infusion of the sulphide ion alone into the circulation mimics the systemic effects of H_2S inhalation but does not result in pulmonary oedema.

Sulphide interacts with a number of enzymes and other macromolecules, including haemoglobin and myoglobin. Although sulphaemoglobin may form after exposure, it does not appear to occur in sufficient quantities to contribute to the acute toxicity of H_2S. Most macromolecules are held together by disulphide bonds, which are easily disrupted by aqueous sulphide. The critical target enzyme of sulphide is generally thought to be cytochrome oxidase, a family of related enzymes constituting the electron transport system in oxidative phosphorylation, the principal energy-generating system of the cell. Oxygen is the final substrate of this system and is necessary to its function. The effect of sulphide in disrupting cytochrome oxidase activity is the same as oxygen deprivation or asphyxiation except that it may act more quickly. However, recent evidence suggests that other mechanisms besides cytochrome oxidase inhibition are responsible for the characteristic apnea of acute H_2S toxicity.[19]

The exposure–response curve for lethality is extremely steep for hydrogen sulphide. The primary determinant of toxicity is the concentration rather than the duration of exposure. Thus, H_2S does not follow 'Haber's Law,' that is the product of the concentration and the duration of exposure needed to achieve a given effect is not constant. Higher concentrations of H_2S gives little margin of safety. Olfactory paralysis at higher exposure levels quickly ends perception of the characteristic small of rotten eggs. Therefore, there is inadequate warning of the presence of H_2S despite the low odour threshold. The exposure–response curve, as noted, is very steep.[20] The loss of consciousness often associated with overwhelming exposure reduces chances of flight. For these three reasons, H_2S is an exceptionally difficult gas from which to escape.

Table 1 briefly summarizes the principal effects of H_2S and the approximate thresholds for these responses. Acute central neurotoxicity, pulmonary oedema and

Figure 1. Exposure–response curves for hydrogen sulphide by species, adapted from an unpublished report by Dr Robert Rogers for the Alberta Energy Resources Conservation Board, 1990.
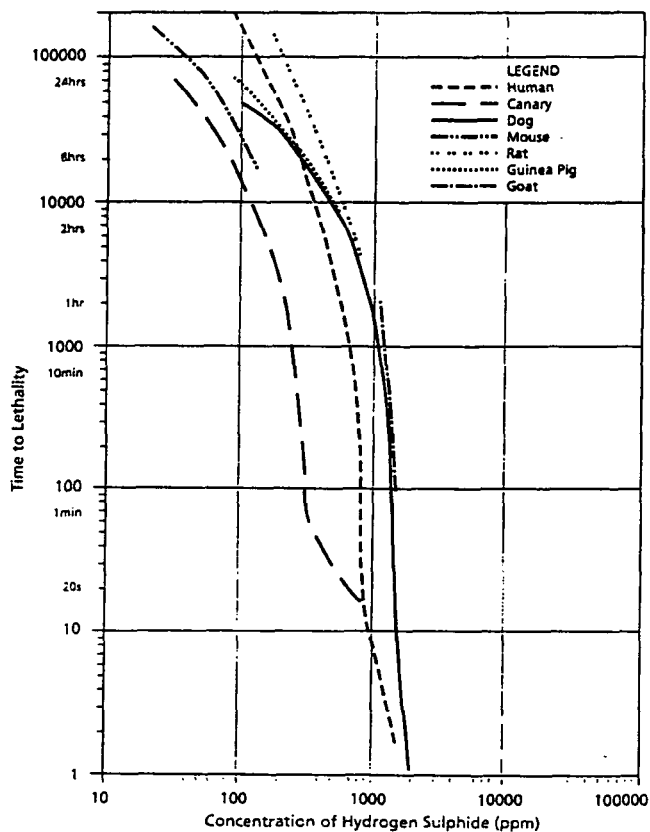
Table 1. Health effects of hydrogen sulphide at various exposure levels

Concentration (ppm)	Effects
0.01–0.3	Odour threshold (highly variable)
1–5	Moderate offensive odour, may be associated with nausea, tearing of eyes, headaches or loss of sleep with prolonged exposure; healthy young male subjects experience no decline in maximal physical work capacity
10	8 hour occupational exposure limit in Alberta
15	15 min occupational exposure limit in Alberta
20	Ceiling occupational exposure limit evacuation level in Alberta, odour very strong
20–50	Keratoconjunctivitis (eye irritation) and lung irritation. Possible eye damage after several days of exposure; may cause digestive upset and loss of appetite
100	Eye and lung irritation; olfactory paralysis, odour disappears
150–200	Sense of smell paralyzed; severe eye and lung irritation
250–500	Pulmonary oedema may occur, especially if exposure is prolonged
500	Serious damage to eyes within 30 min; severe lung irritation; unconsciousness and death within 4–8 hours; amnesia for period of exposure; 'knockdown'
1,000	Breathing may stop within one or two breaths; immediate collapse

the mucosal effects are well documented in association with H_2S. Odour followed by olfactory paralysis and keratoconjunctivitis are characteristic effects of H_2S at lower concentrations. The acute toxicity of hydrogen sulphide is extensively documented.[4,6,8,16,21–23]

H_2S-induced acute central toxicity leading to reversible unconsciousness is called a 'knockdown'. It is highly controversial whether repeated or prolonged knockdowns are associated with chronic neurological sequelae but the evidence is strongly suggestive. Knockdowns can be fatal as a consequence of respiratory paralysis and cellular anoxia. Respiratory paralysis may occur if exposure is prolonged, presumably as a direct consequence of sulphide toxicity inhibiting brainstem respiratory nuclei. Very high concentrations (500–1,000 ppm) may be associated with a knockdown. A knockdown may be fatal if exposure is prolonged. If exposure is transient, as usually happens in the oil patch, recovery may be equally rapid and apparently complete.[4,17]

H_2S paralyzes the olfactory nerve, preventing perception of the otherwise strong smell. After experiencing a strong odour of rotten eggs, the odour disappears because of olfactory nerve paralysis. This removes a vital warning to, for example, oilfield workers caught in a cloud or entering a depression in which the gas has collected.[11,16,18]

H_2S has a strong irritant effect on mucous membranes. The respiratory tract is particularly vulnerable because of its unprotected contact with the gas in air. H_2S penetrates deeply into the respiratory tract because its solubility is relatively low, rendering it capable of causing alveolar injury leading to acute pulmonary oedema. The irritant effect is also seen in the upper airway; experimental studies suggest that the olfactory mucosa do not recover as fast as the bronchial epithelium.

'Gas eye', or keratoconjunctivitis, is a superficial inflammation of the cornea and conjunctiva that is often recurrent in workers in sour gas plants that are exposed for prolonged periods to relatively low concentrations. A peculiar feature of this effect is that it can be associated with reversible chromatic distortion and visual changes. This effect is sometimes accompanied by blepharospasm, tearing and photophobia.

Pulmonary oedema is also a well-recognized acute effect of H_2S toxicity, especially when exposure is prolonged. The ultimate prognosis for recovery is generally good if the patient can be supported through the acute episode.[4,16,24]

Chronic central nervous system effects may be cumulative over several knockdowns, or if they represent the sequelae of minor brain damage resulting from anoxia or trauma. Investigators have found evidence for cognitive function abnormalities, labile affect and personality changes and anosmia, with a suggestion of increasing severity associated with length of time unconscious.[5,14,25–29]

Other possible effects of H_2S include respiratory, cardiac, eye, and host defense disorders but the evidence that H_2S exposure leads to clinical disorders of these organ system remains inconclusive.[14]

TREATMENT

The mainstay of immediate treatment is to remove the subject from the exposure, taking care to ensure that rescuers are properly protected and to resuscitate as required. Oxygen should be given at 100% by mask or by artificial ventilation and consideration should be given to hyperbaric oxygen in severe cases. Metabolic acidosis should be treated and the patient should be observed carefully for pulmonary oedema over the next 24 hours.[30]

Many specific antidotes to H_2S intoxication have been proposed but few are in regular use.[30–32] Sodium nitrite has been proposed and there are anecdotal reports of survival following heavy exposure to H_2S after treatment with nitrite. H_2S resembles cyanide in that both bind reversibly to cytochromes, although there appear to be differences at the biochemical level. For this reason, treatment with nitrites has been advocated as a therapeutic approach to H_2S toxicity, based upon the theory that the methaemoglobins so generated will displace the sulphide as they do with cyanide, and regenerate the active cytochrome oxidase.[31] However, investigators studying the kinetics of nitrite as an antidote have concluded that it can only be effective within the first few minutes following exposure and may actually slow sulphide removal thereafter. In laboratory studies, nitrite appears to work best as a pre-treatment rather than an effective treatment after exposure. However, it is attractive as a therapy because nitrite is readily available in emergency services. A practical problem is that methaemoglobinaemia may add to the anoxic burden that may already exist from the cytochrome poisoning, respiratory paralysis due to central toxicity, and ventilation-perfusion mismatch associated with pulmonary oedema. It may also induce hypotension (and reflex tachycardia) and further complicate the anoxia with hypoperfusion.[32–35]

Administration of nitrites is usually begun with inhalation of amyl nitrite (for 30 seconds out of every minute) followed by sodium nitrite intravenously, in the same dosages as for cyanide poisoning. Infusion of 300 mg of fluid containing 10 ml of 3% $NaNO_2$, over 4 min, has been suggested, titrating the infusion rate against the drop in blood pressure to maintain systolic pressure above 80 torr (10.6 kPa).[32–35]

In general, the accumulated experience with nitrite treatment suggests that alone it may be of benefit and in exceptional cases may even be lifesaving. If administered too aggressively, nitrite toxicity may complicate management and if administered too late it will be of no benefit. Such cases are too infrequent for centres to acquire such experience alone and the clinical literature is therefore inevitably anecdotal. With few documented cases on which to rely, the clinician in such circumstances is forced to use judgement in the

absence of experience. Nitrite treatment may be more effective in combination with hyperbaric oxygen but there are no published data.[3,23,26,29,32-37]

Sodium thiosulphate has also been proposed as a treatment on the grounds that methaemoglobin so produced would likewise compete with haeme from sulphide and that sulfoxidation may also promote clearance of sulphide. The concept is supported by limited laboratory studies suggesting that pre-treatment with thiosulphate reduces sulphide toxicity in animals. However, mammals generally clear sulphide rapidly anyway and thiosulphate is a metabolite of sulphide, not a substrate for enzymatic oxidation.[31] Treatment with thiosulphate does not appear to make sense biochemically. The sparse anecdotal data on human treatment does not support a recommendation of this approach to treatment.[22,30]

There is evidence that the respiratory paralysis observed in some fatal knockdowns is associated with monoamine oxidase inhibition.[38] This inhibition is reversed by dithiothreitol (DTT), which also displaces sulphide from brain tissue *in vitro* following exposure in animals.[39] DTT has also been found to be protective if given to animals as a pre-treatment prior to exposure. At present, this approach must be considered tentative and not ready for clinical application.

One report suggests administration of ascorbic acid (vitamin C) intravenously to reverse methaemoglogi-nemia. Although probably benign, the effectiveness of this treatment is not documented and methaemoglo-binaemia is not the primary problem. The approach cannot be recommended in the absence of evidence for utility.[40]

Treatment with oxygen and supportive care alone had been recommended in order to avoid further complicating the toxic effects with iatrogenic anoxia and nitrite toxicity. However, confirmation that oxygen therapy works alone is limited to anecdotal reports and experimental studies with H_2S-exposed mice which did not show increased survival with oxygen alone. Unlike cyanide intoxication, there is no evidence that H_2S intoxication would confer a risk on the rescuer during mouth-to-mouth resuscitation.[22]

Hyperbaric oxygen therapy is an attractive and logical option for treating H_2S intoxication. Laboratory studies and anecdotal evidence of selected cases suggests that it may be effective.[41,42] Given the low morbidity of hyperbaric oxygen treatment in skilled hands, it is a prudent intervention if facilities are available. Long-term use of hyperbaric oxygen, of course, is associated with the risk of oxygen toxicity but the duration of treatment in this instance is relatively short.[43] In the absence of a standard protocol, it would be reasonable to treat as for carbon monoxide. Although a reasonable approach to treatment, and perhaps lifesaving, hyperbaric oxygen therapy has failed to prevent neurological sequelae of H_2S intoxication.[26]

The sour gas industry and the gas industry generally present the opportunity for a variety of other occupational exposures, some of them related to the

processing and desulfuration of gas.[1,9,44] These exposures may be significant in special situations but few come close to the peril of hydrogen sulphide. Recently, the Canadian oil and gas industry has developed a code of practice for handling hydrogen sulphide and other chemical hazards associated with the industry.[45]

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