

# BLUE RIDGE ENVIRONMENTAL DEFENSE LEAGUE

---

www.BREDL.org ~ PO Box 88 Glendale Springs, North Carolina 28629 ~ Phone (336) 982-2691 ~ Fax (336) 982-2954 ~ BREDI@skybest.com

December 15, 2003

Tommy Jenkins, Hearing Officer  
Environmental Management Commission  
1641 Mail Service Center  
Raleigh, NC 27699-1641

**Re: Limits for Hydrogen Sulfide, H<sub>2</sub>S, 15A NCAC 2D .1104, 2Q .0702, 2Q .0706, 2Q .0711**

Dear Mr. Jenkins:

On behalf of the Blue Ridge Environmental Defense League, I write to provide additional information regarding the Division of Air Quality rulemakings which were subject to public hearing on November 5<sup>th</sup>. Please consider these remarks in addition to the oral testimony and written comments which I provided to you in Enka. We recommend that the Environmental Management Commission:

1. Adopt the lowest exposure level recommended by the independent NC Science Advisory Board, Option 1 under 2D .1104, which is 33 micrograms per cubic meter (g/m<sup>3</sup>) for the 24-hour acceptable ambient level, or AAL;
2. Reject the less stringent AALs proposed under Options 2, 3, 4, and 5 for 2D .1104;
3. Reject the exemptions for wastewater treatment systems at pulp and paper mills proposed under Options A and B of 2Q .0702;
4. Reject the exemption from toxic air pollutant procedures for facility modifications resulting in air pollution increases from so-called insignificant activities of 2Q .0706;
5. Adopt the lowest toxic permit emission rate (TPER) of 0.46 pounds/day and 0.013 pounds/hour, Option 2 under 2Q .0711;
6. Reject both proposed new procedures, Option A and Option B, which would apply only to exempted wastewater treatment at pulp and paper mills under 2Q .0714.

In addition to the above steps, we recommend that the Environmental Management Commission:

7. Take the SAB recommendation one step further and adopt the hydrogen sulfide 33 micrograms per cubic meter (g/m<sup>3</sup>) standard as a 1-hour AAL under 2D .1104;
8. Eliminate the exemption for hydrogen sulfide and all toxic air pollutant limits for all industrial and municipal waste water treatment facilities;
9. Eliminate the exemptions for hydrogen sulfide and all toxic air pollutant limits for intensive livestock operation waste lagoons.

According to documents provided to the EMC by the Manufacturers & Chemical Industry Council on February 12, 2003, much hydrogen sulfide is emitted by animal husbandry operations in North Carolina. Although we disagree with the MCIC representative regarding the relative

impact of pulp and paper industry emissions, we think that the EMC should take action to reduce hydrogen sulfide emissions from intensive livestock operations. As a matter of equity, no exemption or loophole for any industry group from these health measures should be permitted. Hydrogen sulfide from paper mills, municipal sewage, or livestock operations has been shown to be a potent neurotoxin in the human body with devastating health consequences. The negative impact of this pollutant on our most vulnerable citizens, especially for children, requires the EMC to adopt the strictest standards achievable with conventional pollution control measures for all sources of hydrogen sulfide. Attached to this letter please find a series of medical papers and other documents which detail the devastating effects of hydrogen sulfide on physiology and psychology. Hydrogen sulfide's critical role in the human body's neurological functioning must be accounted for in the EMC's deliberations. **The fact that hydrogen sulfide is naturally present in the human body is precisely the reason why it is such a pernicious and dangerous pollutant in the air.**

Commissioner Jenkins, although the publicity about the current rulemaking and paper industry exemption has presented the issue as solely about hydrogen sulfide, **the actual rule under discussion would exempt paper mill lagoons from limits on all 105 air toxins** regulated by the NC Toxic Air Pollutant program. At stake are North Carolina pollution limits on all 105 air poisons including benzene, arsenic, cadmium, dioxin, formaldehyde, and hydrogen sulfide. The proposed exemptions for the pulp and paper industry, if approved, will open the door for other industries wanting special treatment. Please do all you can to protect public health and maintain fairness by applying air toxic limits to all sources; no loopholes.

Respectfully submitted,

Louis Zeller  
Clean Air Campaign Coordinator  
Blue Ridge Environmental Defense League  
PO Box 88  
Glendale Springs, NC 28629  
(336) 982-2691  
BREDL@skybest.com

Cc: Thom Allen  
Jennie Odette

References attached

[1]

Arch Environ Health. 2001 Mar-Apr;56(2):123-31.

## **Health effects from chronic low-level exposure to hydrogen sulfide.**

**Legator MS, Singleton CR, Morris DL, Philips DL.**

University of Texas Medical Branch at Galveston, Department of Preventive Medicine and Community Health, 77555-1110, USA.

The acute toxic effects of hydrogen sulfide have been known for decades. However, studies investigating the adverse health effects from chronic, low-level exposure to this chemical are limited. In this study, the authors compared symptoms of adverse health effects, reported by residents of two communities exposed mainly to chronic, low-levels of industrial sources of hydrogen sulfide, to health effects reported by residents in three reference communities in which there were no known industrial sources of hydrogen sulfide. Trained interviewers used a specially created, menu-driven computer questionnaire to conduct a multi-symptom health survey. The data-collection process and questions were essentially the same in the reference and exposed communities. The two exposed communities responded very similarly to questions about the major categories. When the authors compared responses of the exposed communities with those of the reference communities, 9 of the 12 symptom categories had iterated odds ratios greater than 3.0. The symptoms related to the central nervous system had the highest iterated odds ratio (i.e., 12.7; 95% confidence interval = 7.59, 22.09), followed by the respiratory category (odds ratio = 11.92; 95% confidence interval = 6.03, 25.72), and the blood category (odds ratio = 8.07; 95% confidence interval = 3.64, 21.18). Within the broader health categories, individual symptoms were also elevated significantly. This study, like all community-based studies, had several inherent limitations. Limitations, and the procedures the authors used to minimize their effects on the study outcomes, are discussed. The results of this study emphasize the need for further studies on the adverse health effects related to long-term, chronic exposure to hydrogen sulfide.

PMID: 11339675

[2]

**Dear Dr. Weisler,**

**in response to your email, I would like to provide the following comments to assist the North Carolina Environmental Management Commission in their review of health standards for hydrogen sulfide. As you know, I am the author of the psychiatric textbook, "Environmental and Chemical Toxins and Psychiatric Illness" published by American Psychiatric Publishing, Inc. in 2002. Chapter 15 addresses the psychiatric effects of hydrogen sulfide exposure. The medical literature reports that the following signs and symptoms have been associated with hydrogen sulfide exposures: nervousness, depression, anxiety, irritability, mania, violence, personality changes, dementia, poor concentration, poor memory, amnesia, hallucinations, delusions, insomnia, nightmares, somnolence,**

**fatigue and decreased libido. These signs and symptoms have mostly been associated with high levels of hydrogen sulfide, but I am aware of emerging literature that suggests that low-levels of exposure might also be associated with many of these signs and symptoms. I would be especially concerned about the potential effects of low-level yet long-term or chronic exposure to hydrogen sulfide. I hope that I have been of some assistance in providing this information. James S. Brown, Jr., M.D.,MPH written 12/14/03**

[3]

Environmental and Chemical Toxins and Psychiatric Illness

ISBN 0-88048-954-5

Author: James S. Brown, Jr., M.D.

Publisher: American Psychiatric Publishing, Inc. <http://www.appi.org/index.cfm>

**James S. Brown Jr., M.D.**

Assistant Professor of Psychiatry at the Medical College of Virginia in Richmond

Director of the Mental Health Clinic at McGuire Veterans Affairs Medical Center

[4]

Hydrogen Sulfide: Human Health Aspects

Concise International Chemical Assessment Document 53, C.H. Selene J. Chou (ATSDR),

World Health Organization, Geneva, 2003, [http://www.who.int/pcs/cicad/full\\_text/cicad53.pdf](http://www.who.int/pcs/cicad/full_text/cicad53.pdf)

[5]

Neurosci Lett. 1989 May 8;99(3):323-7.

**Hydrogen sulfide exposure alters the amino acid content in developing rat CNS.**

**Hannah RS, Hayden LJ, Roth SH.**

Department of Anatomy, University of Calgary, Alta., Canada.

Hydrogen sulfide is a widespread environmental pollutant that may produce severe effects on the developing nervous system. Putative amino acid neurotransmitter levels in the rat cerebrum and cerebellum were determined to evaluate the effects of exposure to hydrogen sulfide during perinatal development. The levels of aspartate, GABA, glutamate, glycine and taurine were quantitated using high-performance liquid chromatography. With the exception of glycine, all of the amino acids examined were affected by the treatment. On day 21 postnatal, which was the last day of the exposure, aspartate, glutamate and GABA in the cerebrum and aspartate and GABA in the cerebellum were significantly depressed. The observed alterations in the amino acid levels during this critical phase of development may have chronically affected the activity of the neurotransmitters, their receptor sensitivity or their individual target areas. The consequence of one or a combination of such alterations may lead to behavioral

and structural abnormalities.

PMID: 2566964

[6]

Can J Physiol Pharmacol. 1992 Nov;70(11):1515-8.

### **Low concentrations of hydrogen sulphide alter monoamine levels in the developing rat central nervous system.**

**Skrajny B, Hannah RS, Roth SH.**

Department of Pharmacology and Therapeutics, Faculty of Medicine, University of Calgary, Alta., Canada.

The central nervous system is one of the primary target organs for hydrogen sulphide (H<sub>2</sub>S) toxicity; however, there are limited data on the neurotoxic effects of low-dose chronic exposure on the developing nervous system. Levels of serotonin and norepinephrine in the developing rat cerebellum and frontal cortex were determined following chronic exposure to 20 and 75 ppm H<sub>2</sub>S during perinatal development. Both monoamines were altered in rats exposed to 75 ppm H<sub>2</sub>S compared with controls; serotonin levels were significantly increased at days 14 and 21 postnatal in both brain regions, and norepinephrine levels were significantly increased at days 7, 14, and 21 postnatal in cerebellum and at day 21 in the frontal cortex. Exposure to 20 ppm H<sub>2</sub>S significantly increased the levels of serotonin in the frontal cortex at day 21, whereas levels of norepinephrine were significantly reduced in the frontal cortex at days 14 and 21, and at day 14 in the cerebellum.

PMID: 1296865

[7]

Clin Exp Pharmacol Physiol. 1995 May;22(5):379-80.

### **Alteration of the morphology and neurochemistry of the developing mammalian nervous system by hydrogen sulphide.**

**Roth SH, Skrajny B, Reiffenstein RJ.**

Department of Pharmacology and Therapeutics, Faculty of Medicine, University of Calgary, Alberta, Canada.

1. Hydrogen sulphide (H<sub>2</sub>S) is a broad spectrum toxicant that occurs widely in nature and is also released by a variety of industrial activities and processes. 2. The central nervous system (CNS) appears to be the major target organ. 3. There is great potential for insult or injury to the developing or immature CNS. 4. The risk of chronic or repeated exposures to low concentrations have not been well defined. 5. Exposure to low concentrations of H<sub>2</sub>S to time-pregnant rats from day 5 postcoitus until day 21

postnatal results in architectural modification of cerebellar Purkinje cells, alteration of putative amino acid neurotransmitters and changes in monoamine levels in the developing rat brain up to day 21 postnatal. 6. H<sub>2</sub>S-induced alterations in monoamine tissue levels observed in the developing rat brain return to control values if exposure is discontinued during development, that is, at day 21 postnatal.

PMID: 7554437

[8]

Toxicol Lett. 1996 Jan;84(1):43-53.

### **Effects of repeated exposures of hydrogen sulphide on rat hippocampal EEG.**

**Skrajny B, Reiffenstein RJ, Sainsbury RS, Roth SH.**

University of Calgary, Department of Pharmacology and Therapeutics, Calgary, Alberta, Canada.

Exposure to high levels of hydrogen sulphide (H<sub>2</sub>S) in humans has been associated with a number of respiratory and neurological symptoms. Acute toxicity following exposure to high concentrations is well-documented, however, there is little scientific information concerning the effects of exposure to low concentrations. The effects of low levels of H<sub>2</sub>S on electroencephalographic (EEG) activity in the hippocampus and neocortex were investigated on the freely moving rat (Sprague-Dawley). Hippocampal electrodes were implanted in the dentate gyrus (DG) and CA1 region. Activity was recorded for 10 min just prior to H<sub>2</sub>S exposure in the presence of air (pre-exposure). Rats were exposed to H<sub>2</sub>S (25, 50, 75, or 100 ppm) for 3 h/day; data was collected during the final 10 min of each exposure. The total power of hippocampal theta activity increased in a concentration-dependent manner in both DG and CA1; repeated exposures for 5 consecutive days resulted in a cumulative effect that required 2 weeks for complete recovery. The effects were found to be highly significant at all concentrations within subjects. Neocortical EEG and LIA (Large Amplitude Irregular Activity) were unaffected. The results demonstrate that repeated exposure to low levels of H<sub>2</sub>S can produce cumulative changes in hippocampal function and suggest selectivity of action of this toxicant.

PMID: 8597177

[9]

Int J Epidemiol. 1998 Feb;27(1):10-4.

### **Cancer incidence, morbidity and geothermal air pollution in Rotorua, New Zealand.**

**Bates MN, Garrett N, Graham B, Read D.**

Institute of Environmental Science and Research, Porirua, New Zealand.

**BACKGROUND:** The New Zealand city of Rotorua sits on a geothermal field. However, little is known about the possible health impacts of the geothermal emissions. This was an ecological study that examined cancer incidence and morbidity data for Rotorua.

**METHODS:** Cancer registry and hospital discharge (morbidity) data were obtained for the decade 1981-1990. Standardized incidence ratios (SIR) were calculated comparing Rotorua residents with those living in the rest of New Zealand. Diagnostic categories examined were based on known target organ systems of hydrogen sulphide toxicity.

**RESULTS:** Of the cancer sites, there was an elevated rate for nasal cancers. However, this was based on only four cases. The SIR for cancers of the trachea, bronchus and lung in Maori women was 1.48 (95% CI: 1.03-2.06). This was not explained by higher smoking rates. In the hospital discharge data, a number of diseases showed elevated SIR, notably diseases of the nervous system and the eye. To some extent, these effects were characteristic of effects induced by hydrogen sulphide and also mercury compounds. However, there were few data with which to assess whether significant mercury exposures had occurred, and other explanations were possible.

**CONCLUSIONS:** There are inadequate exposure data for Rotorua to permit conclusions on likely causal associations. However, some of the elevated disease rates were at least consistent with what one might expect to find if sufficient exposures to hydrogen sulphide and/or mercury were occurring.

PMID: 9563687

[10]

J Neuroendocrinol. 2000 Mar;12(3):225-33.

Erratum in:

J Neuroendocrinol 2000 Oct;12(10):1043.

**Evidence that hydrogen sulphide can modulate hypothalamo-pituitary-adrenal axis function: in vitro and in vivo studies in the rat.**

**Dello Russo C, Tringali G, Ragazzoni E, Maggiano N, Menini E, Vairano M, Preziosi P, Navarra P.**

Institute of Pharmacology, Catholic University Medical School, Rome, Italy.

The gas hydrogen sulphide (H<sub>2</sub>S) is normally produced in large amounts in the central nervous system during the metabolism of sulphur-containing aminoacids. H<sub>2</sub>S was recently shown to influence long-term potentiation in the rat hippocampus; this finding suggested that the gas may act as a neuromodulator in the brain. We therefore tested the effect of the gas on the release of corticotropin-releasing hormone (CRH) from rat hypothalamic explants. CRH immunoreactivity in the incubation media was taken as a marker of peptide release. We found that the addition of NaHS to incubation media was consistently associated with a concentration-dependent decrease in KCl-stimulated CRH release, whereas basal secretion was unaffected. Increased endogenous H<sub>2</sub>S

production may be also obtained using an indirect precursor of H<sub>2</sub>S formation, S-adenosyl-L-methionine (SAMe). The latter mimicked the effects of NaHS, since it reduced potassium-stimulated CRH release. In vivo, SAMe showed no effect on hypothalamo-pituitary-adrenal (HPA) function under resting conditions, but inhibited stress-related glucocorticoid increase.

PMID: 10718918

[11]

Gig Sanit. 2001 May-Jun;(3):34-7.

### **[Hygienic environmental characteristics and population health in areas of production of heavy oils and natural bitumen]**

[Article in Russian]

**Ivanov AV, Korolev AA, Tafeeva EA.**

The paper deals with the impact of production of heavy oil and natural bitumens on the environment and human health. It provides a sanitary characteristics of the degree of ambient air pollution, the quality of reservoir and drinking water and soil in the areas of production of heavy oil and natural bitumens. Human health was studied in all age groups by medical and demographic indices and diseases. Hydrocarbons, hydrogen sulfide, carbon oxide were found to be the leading pollutants in these areas. Production of heavy oil and natural bitumens pollutes surface and underground water-bearing horizons, which is a cause of worse conditions for the population to use water due to a 1.8-fold increase in water hardness and a 1.2-fold increase in the content of sulfates, chlorides, and nitrates, as compared to 1987-1991. The production of heavy oil and natural bitumens is a large source of soil pollution. The greatest soil pollution was observed in the areas of bitumen production by intraseam burning and vapour-heat exposure. There was a relationship of respiratory disorders to sulphur dioxide ( $r = 0.5-0.73$ ) and hydrogen sulfide ( $r = 0.6-0.82$ ), of blood and blood-forming organ diseases to nitrogen oxide ( $r = 0.58-0.79$ ), and of nervous and sensory diseases to sulphur dioxide ( $r = 0.73-0.82$ ). The study provided sanitary recommendations for environmental sanitation and health promotion in the areas of production of heavy oil and natural bitumens.

PMID: 11519457

[12]

Am J Ind Med. 1996 Feb;29(2):111-22.

### **Health effects of working in pulp and paper mills: exposure, obstructive airways diseases, hypersensitivity reactions, and cardiovascular diseases.**

**Toren K, Hagberg S, Westberg H.**



Department of Occupational Medicine, Sahlgrenska University Hospital, Goteborg, Sweden.

Workers in the pulp and paper industry are exposed to different substances, such as hydrogen sulfide and other reduced sulfur compounds, chlorine, chlorine dioxide, sulfur dioxide, terpenes, and paper dust. The exposure level depends on the process, i.e., sulfite, sulfate, groundwood, bleachery, or paper production. Hitherto, exposures have been poorly described and more studies are certainly needed. Workers with repeated exposure peaks to chlorine, e.g., bleachery workers, seem to have an impaired lung function and an increased prevalence of respiratory symptoms. Exposure to high levels of paper dust, ( $> 5 \text{ mg/m}^3$ ) causes impaired lung function. Therefore, exposure to respiratory irritants is an important, and probably overlooked, occupational risk among certain groups of pulp and paper workers. Some studies indicate that sulfate workers with high exposure to reduced sulfur compounds have an increased mortality due to ischemic heart disease. However, before any definite conclusions can be drawn, the impact of important confounders, such as shift-work and smoking habits have to be further evaluated.

PMID: 8821354

# BLUE RIDGE ENVIRONMENTAL DEFENSE LEAGUE

---

www.BREDL.org ~ PO Box 88 Glendale Springs, North Carolina 28629 ~ Phone (336) 982-2691 ~ Fax (336) 982-2954 ~ BREDI@skybest.com

December 15, 2003

Tommy Jenkins, Hearing Officer  
Environmental Management Commission  
1641 Mail Service Center  
Raleigh, NC 27699-1641

**Re: Limits for Hydrogen Sulfide, H<sub>2</sub>S, 15A NCAC 2D .1104, 2Q .0702, 2Q .0706, 2Q .0711**

Dear Mr. Jenkins:

I have attached to this cover letter an additional series of medical journal articles to be added to the public record along with my comments of November 5 and December 15, 2003. Thank you for your consideration of this additional information.

Sincerely,

Louis Zeller

Attachments

Cc: Thom Allen

Jennie Odette

[13]

Novel Neurotransmitters and their Neuropsychiatric Relevance, S. H. Snyder and C. D. Ferris, Am Jnl Psychiatry 157:11, November 2000

[14]

Arch Environ Health. 1996 Jul-Aug;51(4):315-20.

**The South Karelia Air Pollution Study: effects of low-level exposure to malodorous sulfur compounds on symptoms.**

**Partti-Pellinen K, Marttila O, Vilkka V, Jaakkola JJ, Jappinen P, Haahtela T.**

South Karelia Allergy and Environmental Institute, Tiuruniemi, Finland.

Exposure to very low levels of ambient-air malodorous sulfur compounds and their effect on eye irritation, respiratory-tract symptoms, and central nervous system symptoms in adults were assessed. A cross-sectional self-administered questionnaire (response rate = 77%) was distributed during March and April 1992 to adults (n = 336) who lived in a neighborhood that contained a pulp mill and in a nonpolluted reference community (n = 380). In the exposed community, the measured annual mean concentrations of total reduced sulfur compounds and sulfur dioxide measured in two stations were 2 to 3 micrograms/m<sup>3</sup> and 1 micrograms/m<sup>3</sup>, respectively. In the reference community, the annual mean concentration of sulfur dioxide was 1 micrograms/m<sup>3</sup>. The residents of the community near the pulp mill reported an excess of cough, respiratory infections, and headache during the previous 4 wk, as well as during the preceding 12 mo. The relative risk for headache was increased significantly in the exposed community, compared with the reference area: the adjusted odds ratio (aOR) was 1.83 (95% confidence interval [95% CI] = 1.06-3.15) during the previous 4 wk and 1.70 (95% CI = 1.05-2.73) during the preceding 12 mo. The relative risk for cough was also increased during the preceding 12 mo (aOR = 1.64, 95% CI = 1.01-2.64). These results indicated that adverse health effects of malodorous sulfur compounds occur at lower concentrations than reported previously.

PMID: 8757412

[15]

Beijing Da Xue Xue Bao. 2003 Feb 18;35(1):102.

**[Endogenous H<sub>2</sub>S is involved in the development of spontaneous hypertension]**

[Article in Chinese]

**Du J, Yan H, Tang C.**

Department of Pediatrics, Peking University First Hospital, Beijing 100034, China.

junbaodu@ht.rol.cn.net

Hydrogen sulfide (H<sub>2</sub>S) is recently found to be a new gaseous messenger playing an important role in many physiological and pathophysiological processes. The aim of this study was to explore the changes in endogenous H<sub>2</sub>S pathway and examine the effects of H<sub>2</sub>S on the development of spontaneous hypertensive rats (SHR). A controlled study on SHR and WKY rats at the age of 4 weeks showed that after 5 weeks of experiment, the blood pressure of SHR was markedly increased as compared with WKY rats (183.57 +/- 11.80 mm Hg vs 107.5 +/- 22.68 mm Hg, P < 0.05) and the ratio of left heart weight to whole heart weight of SHR was also increased as compared with WKY rats (0.85 +/- 0.02 vs 0.83 +/- 0.02, P < 0.05). While, the aortic H<sub>2</sub>S producing rate and H<sub>2</sub>S plasma level were decreased in SHR compared with WKY rats (15.63 +/- 2.89 nmol.min<sup>-1</sup>.g<sup>-1</sup> vs 25.31 +/- 5.99 nmol.min<sup>-1</sup>.g<sup>-1</sup>, 20.35 +/- 9.20 μmol.L<sup>-1</sup> vs 48.40 +/- 13.36 μmol.L<sup>-1</sup>, P < 0.05). NaHS, however, attenuated the high blood pressure and the ratio of left heart weight to whole heart weight of SHR (158.13 +/- 12.52 mm Hg vs 183.57 +/- 11.80 mm Hg and 0.83 +/- 0.03 vs 0.85 +/- 0.02), respectively. The above findings suggested that the reduced production of endogenous H<sub>2</sub>S was important in the development of spontaneous hypertension. The authors also observed that 5 weeks after the experiment the relaxing rate of aortic rings in response to acetylcholine in SHR was higher than that of WKY rats and NaHS enhanced the relaxing-response of aortic rings to acetylcholine in SHR significantly (P < 0.05). The aortic relaxing activities in both SHR and WKY rats displayed a dose-dependent response to different doses of NaHS. In conclusion, the reduced production of endogenous H<sub>2</sub>S in aorta is involved in the pathogenesis of spontaneous hypertension and is of great biological importance in modulating vasorelaxation.

PMID: 12920821

[16]

Toxicol Ind Health. 1995 Mar-Apr;11(2):185-97

### **Hydrogen sulfide and reduced-sulfur gases adversely affect neurophysiological functions.**

**Kilburn KH, Warshaw RH.**

University of Southern California School of Medicine, Environmental Sciences Laboratory, Los Angeles, USA.

Hydrogen sulfide (H<sub>2</sub>S) above 50 parts per million (ppm) causes unconsciousness and death. Lower doses of H<sub>2</sub>S and related gases have been regarded as innocuous, but the effects of prolonged exposure have not been studied. This study was designed to determine whether people exposed to sulfide gases as a result of working at or living downwind from the processing of "sour" crude oil demonstrate persistent neurobehavioral dysfunction. Thirteen former workers and 22 neighbors of a refinery complained of headaches, nausea, vomiting, depression, personality changes, nosebleeds, and breathing difficulties. Their neurobehavioral functions and a profile of mood states (POMS) were compared to 32 controls, matched for age and educational level. The exposed subjects' mean values were statistically significantly abnormal compared to controls for two-choice reaction time, balance (as speed of sway), color discrimination, digit

symbol, trail-making A and B, and immediate recall of a story. Their POMS scores were much higher than those of controls. Visual recall was significantly impaired in neighbors, but not in exworkers. It was concluded that neurophysiological abnormalities were associated with exposure to reduced sulfur gases, including H<sub>2</sub>S from crude oil desulfurization.

PMID: 7491634

[17]

South Med J. 2003 Jul;96(7):639-46.

### **Effects of hydrogen sulfide on neurobehavioral function.**

**Kilburn KH.**

Environmental Sciences Laboratory, Keck School of Medicine, University of Southern California, Los Angeles, CA 90033, USA. kilburn@usc.edu

**BACKGROUND:** Nineteen hydrogen sulfide (H<sub>2</sub>S)-exposed patients were compared with 202 unexposed subjects. This 1997-to-2001 case-referent series was compared with 16 previous (1991-1996) case-referent patients. **METHODS:** New patients were bystanders of H<sub>2</sub>S exposure and none had been unconscious. In contrast, 13 members of the prior group were exposed at work and 7 had been unconscious. The three groups were compared on the basis of 8 physiologic and 12 psychological measurements. Observed measurements were compared with predicted ones after adjusting for age, sex, educational attainment (years), and other significant factors (observed/predicted x 100). **RESULTS:** The new group performed poorly compared with unexposed controls and were similar to the first group on balance, reaction time, color discrimination, visual performance, hearing, Culture Fair, digit symbol, vocabulary, verbal recall, peg placement, trail making A and B, and information. **CONCLUSION:** H<sub>2</sub>S impairments associated with H<sub>2</sub>S were similar in 19 workers (44% had been unconscious) and in 16 bystanders who had not been unconscious.

PMID: 12940311

[18]

Arch Environ Health. 2001 Mar-Apr;56(2):132-7

### **Function testing for chemical brain damage: a review.**

**Kilburn KH.**

Environmental Sciences Laboratory, University of Southern California, Keck School of Medicine, Los Angeles 90033, USA.

Testing of neurobehavioral functions for evaluation of the effects of chemicals on the human brain from community (i.e., environmental) exposures is logical and may be a preferred initial step. Sensitivity is improved (1) by adjusting individual tests for influential factors, found by

regression modeling and by retaining significant coefficients; and (2) by the calculation of predicted values for each test for each subject. This two-part approach allows for adjustments in age, sex, educational level, and other factors before comparisons are made. Visual fields, color discrimination, reaction time, balance, and digit symbol are the most sensitive tests, followed by 6 sensitive psychological tests and less-discriminating physiological measurements. Hydrogen sulfide, polychlorinated biphenyls, and arsenic are the most toxic chemicals, followed by chlorine, chlorpyrifos, formaldehyde, nickel carbonyl, and ammonia. The least toxic chemicals, which are hydrochloric acid and chlorine, were determined 7 wk following a community spill. The least toxic chemical among those identified herein is methyl ter butyl ether.  
PMID: 11339676

**[19]**

J Neurosci. 2002 May 1;22(9):3386-91.

**Hydrogen sulfide is produced in response to neuronal excitation.**

**Eto K, Ogasawara M, Umemura K, Nagai Y, Kimura H.**

National Institute of Neuroscience, National Center of Neurology and Psychiatry, Kodaira, Tokyo 187-8551, Japan.

Although hydrogen sulfide (H<sub>2</sub>S) is generally thought of in terms of a poisonous gas, it is endogenously produced in the brain. Physiological concentrations of H<sub>2</sub>S selectively enhance NMDA receptor-mediated responses and alter the induction of hippocampal long-term potentiation (LTP). Here we use cystathionine beta-synthase (CBS) knock-out mice to clearly show that CBS produces endogenous H<sub>2</sub>S in the brain and that H<sub>2</sub>S production is greatly enhanced by the excitatory neurotransmitter l-glutamate, as well as by electrical stimulation. This increased CBS activity is regulated by a pathway involving Ca<sup>2+</sup>/calmodulin. In addition, LTP is altered in CBS knock-out mice. These observations suggest that H<sub>2</sub>S is produced by CBS in response to neuronal excitation and that it may regulate some aspects of synaptic activity.  
PMID: 11978815

**[20]**

Biochem Biophys Res Commun. 2002 May 24;293(5):1485-8.

**Brain hydrogen sulfide is severely decreased in Alzheimer's disease.**

**Eto K, Asada T, Arima K, Makifuchi T, Kimura H.**

National Institute of Neuroscience, National Center of Neurology and Psychiatry, 4-1-1 Ogawahigashi, Kodaira, Tokyo 187-8551, Japan.

Although hydrogen sulfide (H<sub>2</sub>S) is generally thought of in terms of a poisonous gas, it is endogenously produced in the brain from cysteine by cystathionine beta-synthase (CBS). H<sub>2</sub>S

functions as a neuromodulator as well as a smooth muscle relaxant. Here we show that the levels of H<sub>2</sub>S are severely decreased in the brains of Alzheimer's disease (AD) patients compared with the brains of the age matched normal individuals. In addition to H<sub>2</sub>S production CBS also catalyzes another metabolic pathway in which cystathionine is produced from the substrate homocysteine. Previous findings, which showed that S-adenosyl-l-methionine (SAM), a CBS activator, is much reduced in AD brain and that homocysteine accumulates in the serum of AD patients, were confirmed. These observations suggest that CBS activity is reduced in AD brains and the decrease in H<sub>2</sub>S may be involved in some aspects of the cognitive decline in AD.

PMID: 12054683

## [21]

[Ultrastructure of the cerebral cortex after exposure to gas containing **hydrogen sulfide**  
[Ul'trastruktura kory bol'shogo mozga pri vozdeistvii serovodorodsoderzhashchego gaza.]  
**Morfologiya** 2002;122(6):11-3 (ISSN: 1026-3543)

Solnyshkova TG; Shakhlamov VA; Volodina EP

Laboratory of Experimental Pathology of the Cell, Scientific Research Institute of Human Morphology, Moscow.

In experimental animals exposed to **hydrogen sulfide**-containing gas, electron microscopic study of cerebral cortex indicated the variability in the reaction of layer V neurons: along with neurons demonstrating irreversible damage, some cells with single signs of alteration were found. The reaction of different types of glial cells was also non-uniform. During initial 12 h following single exposure, oligodendrocytes showed the signs of intensified endocytosis. Following repeated exposures, severe destructive changes were found in myelinated nerve fibers and in single neurons, in which the karyolysis and cytoplasmic swelling were observed.

7783-06-4 (**Hydrogen Sulfide**)

Language: Russian

MEDLINE Indexing Date: 200307

PreMedline Identifier: 0012630085

Unique NLM Identifier: 22517747

Journal Code: IM

## [22]

Ultrastructural and morphometric characteristics of nerve cells and myelinated fibers in the cerebral cortex after chronic exposure to natural gas containing **hydrogen sulfide** in low concentrations [In Process Citation]

**Bull Exp Biol Med** 2002 Oct;134(4):411-3 (ISSN: 0007-4888)

Solnyshkova TG; Shakhlamov VA

Laboratory of Experimental Cell Pathology, Institute of Human Morphology, Russian Academy of Medical Sciences, Moscow.

We studied ultrastructural and morphometric characteristics of nerve cells and myelinated fibers

in the cerebral cortex after chronic exposure to natural gas containing **hydrogen sulfide** in low concentrations. Radioisotope assay revealed activation of protein synthesis in nerve cells after chronic exposure to natural **hydrogen sulfide**-containing gas in low concentrations (10 mg/m<sup>3</sup>) by H<sub>2</sub>S) for 2 weeks. After 1 month the ultrastructure of myelinated fibers was characterized by sectorial loosening and demyelination.

Language: English

MEDLINE Indexing Date: 200301

Publication Type: Owner: NLM; Status: In-Process

Publication Type: Journal Article

PreMedline Identifier: 0012533774

Unique NLM Identifier: 22421173

Journal Code: IM

## [23]

Community-based exposure estimate for **hydrogen sulfide**.

**J Expo Anal Environ Epidemiol 2002 Mar;12(2):124-9** (ISSN: 1053-4245)

Inserra S; Phifer B; Pierson R; Campagna D

Agency for Toxic Substances and Disease Registry, Health Investigations Branch, 1600 Clifton Road, NE, MS E-31, Atlanta, Georgia 30333, USA. [sai0@cdc.gov](mailto:sai0@cdc.gov).

Indoor and outdoor air pollution monitoring may indicate potential human exposure to air contaminants. Individual and population exposures to air contaminants depend upon many factors including time spent outdoors and indoors, permeability of housing structures, and mobility within a community. In this report, we illustrate an approach for using long-term air monitoring to establish patterns or changes of environmental exposures, improve validity and representativeness of data, and prevent exposure misclassification. Long-term air monitoring for **hydrogen sulfide** (H<sub>2</sub>S) at 14 Dakota City, Nebraska, residences identified differences in area-wide concentration levels, geographic locations, and **seasonal** exposures. Air data for 1999 indicated that Dakota City residents were repeatedly exposed, both indoors and outdoors, to moderate levels ( $\geq 90$  parts per billion [ppb]) of H<sub>2</sub>S. Using GIS modeling and kriging, we produced a geographic gradient of exposure estimate or map for ambient H<sub>2</sub>S. These findings formed the basis for designing two health investigations for this community.

7783-06-4 (**Hydrogen Sulfide**)

Language: English

MEDLINE Indexing Date: 200205

Publication Type: Owner: NLM; Status: Completed

Publication Type: Journal Article; Validation Studies

PreMedline Identifier: 0011965529

Unique NLM Identifier: 21962063

Journal Code: IM

## [24]



Investigation of health effects of **hydrogen sulfide** from a geothermal source.

**Arch Environ Health 2002 Sep-Oct;57(5):405-11** (ISSN: 0003-9896)

Bates MN; Garrett N; Shoemack P

Institute of Environmental Science and Research Ltd. (ESR), Porirua, New Zealand.

[m\\_bates@uclink.berkeley.edu](mailto:m_bates@uclink.berkeley.edu).

Little is known about health effects from chronic exposure to **hydrogen sulfide** (H<sub>2</sub>S). The city of Rotorua, New Zealand, is exposed to H<sub>2</sub>S by virtue of its location over a geothermal field. In this study, the authors classified areas within Rotorua as high-, medium, or low-H<sub>2</sub>S exposure areas. Using 1993-1996 morbidity data, standardized incidence ratios were calculated for neurological, respiratory, and cardiovascular effects. Poisson regression analysis was used to confirm results. Results showed exposure-response trends, particularly for nervous system diseases, but also for respiratory and cardiovascular diseases. Data on confounders were limited to age, ethnicity, and gender. The H<sub>2</sub>S exposure assessment had limitations. Assumptions were that recent exposure represented long-term exposure and that an individual's entire exposure was received at home. The results of this study strengthen the suggestion that there are chronic health effects from H<sub>2</sub>S exposure. Further investigation is warranted.

7783-06-4 (**Hydrogen Sulfide**)

Indexing Check Tags: Female; Human; Male; Support, Non-U.S. Gov't

Language: English

MEDLINE Indexing Date: 200303

Publication Type: Owner: NLM; Status: Completed

Publication Type: Journal Article

PreMedline Identifier: 0012641180

Unique NLM Identifier: 22527726

Journal Code: AIM; IM

[25]

Ann N Y Acad Sci. 2000;917:638-46.

**Gaseous neuromodulators in the control of neuroendocrine stress axis.**

**Navarra P, Dello Russo C, Mancuso C, Preziosi P, Grossman A.**

Institute of Pharmacology, Catholic University Medical School, Largo Francesco Vito 1, 00168 Rome, Italy. [pnavarra@rm.unicatt.it](mailto:pnavarra@rm.unicatt.it)

The gaseous neuromodulator carbon monoxide has been shown to reduce the stimulated release of stress neuropeptides, such as vasopressin and oxytocin, from the rat hypothalamus in vitro, while evidence concerning corticotropin-releasing hormone is controversial. In vivo studies have been conducted in the rat, inhibiting heme oxygenase activity--and hence carbon monoxide biosynthesis--in the central nervous system by means of specific heme oxygenase blockers; these studies showed that basal heme oxygenase activity tends to oppose exaggerated increases in vasopressin secretion following immune-inflammatory challenges, whereas it favors the normal

rise in circulating ACTH which follows footshock. Another gas normally produced in mammalian brains under basal conditions, hydrogen sulfide, also appears to play a role in the control of the hypothalamo-pituitary-adrenal axis. Indeed, increases in hydrogen sulfide levels within the hypothalamus, either obtained with hydrogen sulfide-enriched media or by the addition of the hydrogen sulfide precursor S-adenosyl-methionine, are associated with the inhibition of the stimulated release of corticotropin-releasing hormone from rat hypothalamic explants. Parellel in vivo experiments in the rat under resting conditions and after stress-induced adrenocortical activation show that S-adenosyl-methionine significantly reduces the rise in serum corticosterone levels caused by 1-h exposure to cold. These results demonstrate the pathophysiological importance of both carbon monoxide and hydrogen sulfide in the regulation of neuroendocrine function.

[26]

Mol Neurobiol. 2002 Aug;26(1):13-9.

### **Hydrogen sulfide as a neuromodulator.**

**Kimura H.**

National Institute of Neuroscience, Kodaira, Tokyo, Japan. kimura@ncnp.go.jp

Hydrogen sulfide (H<sub>2</sub>S) is a well-known toxic gas with the smell of rotten eggs. Since the first description of the toxicity of H<sub>2</sub>S in 1713, most studies about H<sub>2</sub>S have been devoted to its toxic effects. Recently, H<sub>2</sub>S has been proposed as a physiologically active messenger. Three groups discovered that the brain contains relatively high concentrations of endogenous H<sub>2</sub>S. This discovery accelerated the identification of an H<sub>2</sub>S-producing enzyme, cystathionine beta-synthase (CBS) in the brain. In addition to the well-known regulators for CBS, S-adenosyl-L-methionine (SAM) and pyridoxal-5'-phosphate, it was recently found that Ca<sup>2+</sup>/calmodulin-mediated pathways are involved in the regulation of CBS activity. H<sub>2</sub>S is produced in response to neuronal excitation, and alters hippocampal long-term potentiation (LTP), a synaptic model for memory. can also regulate the release of corticotropin-releasing hormone (CRH) from hypothalamus. Another H<sub>2</sub>S producing enzyme, cystathionine gamma-lyase (CSE), has been identified in smooth muscle, and H<sub>2</sub>S relaxes smooth muscle in synergy with nitric oxide (NO). Recent progress in the study of H<sub>2</sub>S as a novel neuromodulator/transmitter in the brain is briefly reviewed.

PMID: 12392053

[27]

J Neurosci. 2002 May 1;22(9):3386-91.

### **Hydrogen sulfide is produced in response to neuronal excitation.**

**Eto K, Ogasawara M, Umemura K, Nagai Y, Kimura H.**

National Institute of Neuroscience, National Center of Neurology and Psychiatry, Kodaira, Tokyo 187-8551, Japan.

Although hydrogen sulfide (H<sub>2</sub>S) is generally thought of in terms of a poisonous gas, it is endogenously produced in the brain. Physiological concentrations of H<sub>2</sub>S selectively enhance NMDA receptor-mediated responses and alter the induction of hippocampal long-term potentiation (LTP). Here we use cystathionine beta-synthase (CBS) knock-out mice to clearly show that CBS produces endogenous H<sub>2</sub>S in the brain and that H<sub>2</sub>S production is greatly enhanced by the excitatory neurotransmitter l-glutamate, as well as by electrical stimulation. This increased CBS activity is regulated by a pathway involving Ca<sup>2+</sup>/calmodulin. In addition, LTP is altered in CBS knock-out mice. These observations suggest that H<sub>2</sub>S is produced by CBS in response to neuronal excitation and that it may regulate some aspects of synaptic activity.

PMID: 11978815

---