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Evaluation of Exposure Limits to Toxic Gases for Nuclear Reactor Control Room Operators

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ABSTRACT

We have evaluated ammonia, chlorine, Halon (actually a generic name for several halogenated hydrocarbons), and sulfur dioxide for their possible effects during an acute two-minute exposure in order to derive recommendations for maximum exposure levels. To perform this evaluation, we conducted a search to find the most pertinent literature regarding toxicity in humans and in experimental animals. Much of the literature is at least a decade old, not an unexpected finding since acute exposures are less often performed now than they were a few years ago. In most cases, the studies did not specifically examine the effects of two-minute exposures; thus, extrapolations had to be made from studies of longer-exposure periods. Whenever possible, we gave the greatest weight to human data, with experimental animal data serving to strengthen the conclusion arrived at from consideration of the human data. Although certain individuals show hypersensitivity to materials like sulfur dioxide, we have not attempted to factor this information into the recommendations.

After our evaluation of the data in the literature, we held a small workshop. Major participants in this workshop were three consultants, all of whom were Diplomates of the American Board of Toxicology, and staff from the Nuclear Regulatory Commission. Our preliminary recommendations for two-minute exposure limits and the rationale for them were discussed and consensus reached on final recommendations. These recommendations are: 1) ammonia-300 ppm; 2) chlorine-30 ppm; 3) Halon 1301-5%; Halon 1211-2%; and 4) sulfur dioxide-100 ppm. Control room operators should be able to tolerate two-minute exposures to these levels, don fresh-air masks, and continue to operate the reactor if the toxic material is eliminated, or safely shut down the reactor if the toxic gas remains.

EXECUTIVE SUMMARY

In order to insure safe operation of the commercial nuclear power plants, control room operators personnel must be protected from dangers arising from possible exposure to hazardous chemicals. One scenario is that control room operators in a nuclear plant could be exposed to high levels of certain gases. Under such circumstances, it is imperative that exposure of nuclear control room operators to such materials be less than those that would prevent them from safely operating the plant. It is expected that trained operators could don protective apparel within two minutes. Thus, protective emergency limits should be based on levels that will allow operators to function during a two-minute period while fresh-air mask and protective clothing are put on, and for up to 8 hours afterward if the toxic material is eliminated.

Five gases have been considered for their possible effects during an acute two-minute exposure. These are ammonia, chlorine, Halon 1211, Halon 1301, and sulfur dioxide. We have conducted a literature search to find the most pertinent data regarding toxicity in humans and in experimental animals.

Most of the pertinent literature is at least a decade old, not an unexpected finding, since high level, acute exposure studies are less often performed now than they were several years ago. In all cases, studies did not specifically examine the response to two-minute exposures. We have, therefore, used professional judgments to arrive at our recommendations for setting two-minute protective exposure limits. Whenever possible, we have given the greatest weight to human data, with experimental animal data serving to strengthen the conclusion arrived at from consideration of the human data.

Our recommendations for two-minute exposure limits are: (1) ammonia - 300 ppm; (2) chlorine - 30 ppm; (3) Halon 1301 - 5%; Halon 1211 - 2%; and (4) sulfur dioxide - 100 ppm. Control room operators should be able to tolerate two-minute exposures to these levels, don fresh-air masks, and continue to operate the reactor if the toxic material is eliminated, or safely shut down the reactor if the toxic gas remains.

Certain factors should be noted. There are a few persons who are allergic to SO_2 and show skin reactions to a few ppm. Asthmatics as a group are extremely sensitive to SO_2 and show decreased pulmonary competence after exposures to 0.5-1.0 ppm. Consequently, the above recommendations for sulfur dioxide (SO_2) are not considered appropriate for these individuals who may be extremely sensitive to SO_2. Although the same may be true for exposures to the other gases, we found no documentation to that effect.

Another factor that could affect the safety of control room personnel exposed to halon is the relative humidity. Although both Halon 1301 and 1211 are colorless gases, the rapid cooling caused by the sudden release of Halon into a room can cause formation of fog if the humidity is high. Lack of visibility could become a safety hazard in that situation. Our assumption is that relative humidity in the control room will be low enough to prevent such an occurrence.

Finally, it is assumed that control room personnel are trained to not leave the premises on detection of the gases by odor or irritating effects. Although there is a possibility that operator's performance could be reduced as a result of exposure to toxic gases in the control room, it was assumed that exposure at the recommended levels would not prevent the operators from accomplishing their job for two minutes, albeit with some decrement in performance.

The recommended values and the accompanying support information were evaluated and reviewed by a panel of experts, (USNRC, 1990) and recommended changes were incorporated into this document.

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GLOSSARY

PEL	Permissible Exposure Limit. The PEL is the OSHA standard found in 29 CFR 1910.1000 and is often referred to as the Federal Standard. Values are usually expressed as work-shift time-weighted average (TWA) levels.
TLV-TWA	Threshold Limit Value - Time Weighted Average. The TLV-TWA is issued by the American Conference of Governmental Industrial Hygienists (ACGIH) and is defined as the time-weighted average concentration for a normal 8-hour work day and a 40-hour work week, to which nearly all workers may be repeatedly exposed without adverse effect.
TLV-STEL	Threshold Limit Value - Short-Term Exposure Limit. The TLV-STEL, issued by ACGIH, is the concentration to which workers can be exposed for short periods of time without suffering from irritation, chronic or irreversible tissue damage, or narcosis of sufficient degree to increase the likelihood of accidental injury, impair self-rescue or materially reduce work efficiency, and provided that the daily TLV-TWA is not exceeded.
IDLH	Immediately Dangerous to Life and Health. The concentration represents a maximum level from which a worker could escape within 30 minutes without any impairing symptoms or any irreversible health effects.
ERPG-3	Emergency Response Planning Guideline. An ERPG-3, issued by The American Industrial Hygiene Association (AIHA), is the maximum airborne concentration below which it is believed that nearly all individuals could be exposed for up to one hour without experiencing or developing life-threatening health effects.
ERPG-2	An ERPG-2, issued by AIHA, is the maximum airborne concentration below which it is believed that nearly all individuals could be exposed for up to one hour without experiencing or developing irreversible or other serious health effects or symptoms which could impair an individual's ability to take protective action.
ERPG-1	The ERPG-1, issued by the AIHA, is the maximum airborne concentration below which it is believed that nearly all individuals could be exposed for up to one hour without experiencing other than mild, transient adverse health effects or without perceiving a clearly defined objectionable odor.
EEGL	Emergency Exposure Guidance Level (formerly EEL) is defined as a concentration of a substance in air (as a gas, vapor or aerosol) that will permit continued performance of specific tasks during rare emergency conditions lasting for periods of 1-24 hours. EEGL's have been developed by the Committee on Toxicology of the

National Research Council (NRC) for military or space operations but are not standards or judgment of acceptable risk.

SPEGL — Short-term Public Exposure Guidance Level (formerly SPEL) is defined as a suitable air concentration for unpredicted, single, short-term, emergency exposure of the general public. SPEGL's, developed by NRC, consider a wide range of susceptibility of the general public such as sensitive populations.

TDLo (TCLo) — Toxic Dose or (Concentration) Low: The lowest dose (concentration) of a substance by any route* over any given period of time reported to produce any toxic effect in human or to be carcinogenic, neoplastigenic, or teratogenic in animals or humans. (*TCLo is used exclusively for inhalation exposures).

LDLo (LCLo) — Lethal Dose or (Concentration) Low: The lowest dose (concentration) of a substance by any route* over any given period of time in one or more divided portions and reported to have caused death in humans or animals. (*TCLo is used exclusively for inhalation exposures).

LD_{50} (LC_{50}) — Lethal Dose (Concentration) Fifty: A calculated dose (concentration) of a substance which is expected to cause the death of 50% of an entire defined experimental population within a given time period, e.g. 1-hour LC_{50}. (LD_{50} is defined for any route of exposure except inhalation; LC_{50} is defined for inhalation exposures).

INTRODUCTION

Criterion 4 of Appendix A entitled "General Design Criteria for Nuclear Power Plants" to 10 CFR Part 50 entitled "Licensing of Production and Utilization Facilities" requires that "structures, systems and components important to safety be designed to accommodate the effects of and to be compatible with the environmental conditions associated with operation, maintenance, testing and postulated accidents." Criteria 19 entitled "Control Room" requires that a control room be provided from which actions can be taken to operate the nuclear power unit safely under normal conditions and to either maintain or shut down the reactor safely under accident conditions.

Ammonia, chlorine, Halon 1211, Halon 1301, and sulfur dioxide are gases that may be utilized in and around nuclear power reactors. The release of these gases could potentially result in control room operators becoming incapacitated; thus, the control room design must have features and procedures that will protect the operators against accidental releases. For ammonia, chlorine and sulfur dioxide two accident scenarios can be postulated. One scenario would be that the gas would involve low leakage rates over a long term. The second scenario would involve a rapid short-term release, sometimes referred to as a "puff" release. It is the latter to which this document addresses itself. In particular, it addresses the maximum limits that can be accepted for two minute exposures. This document does not deal with modeling the spread or dispersion of such a release within the control room, but only deals with the toxicity of the gas.

Inherent in the concept of establishing permissible exposure limits for 2-minute exposures is the assumption that operators can function during the two minutes and can begin to use breathing apparatus and procedures within that time frame. It also assumes that the function of the operators during periods subsequent to a 2-minute exposure will not be altered in such a detrimental way that the control room cannot be operated safely. It should be noted that these exposure limits are considered to be emergency limits and useful for maintaining proper function of the control room. In general, these limits do not deal with the potential for long term health effects resulting from such exposures.

For many industries there is an assumption that a worker can limit his/her exposure by leaving an area at the onset of danger or when a certain exposure limit has been reached. This is not possible to do in a nuclear facility, and personnel may be required to don protective equipment and continue to work until either the danger has been ameliorated or until the facility can be safely shut down. The permissible exposure levels that are recommended must take this into account because safety of the facility operation becomes the overriding criterion to be considered.

Regulatory Guide 1.78 (USAEC, 1974) was issued in 1974 to identify those chemicals which, if present in sufficient quantities, could result in the control room becoming uninhabitable. Two-minute exposure limits were given in this guide for these gases as follows: ammonia, 100 ppm; chlorine, 15 ppm; and sulfur dioxide, 5 ppm. The toxicity limits in the guide were adopted from

data of Sax (1968), but the basis, in terms of toxicity, for each value is unclear. The purpose of this evaluation is to provide recommendations for 2-minute exposure limits based on current toxicity data and newer insights regarding emergency exposures that may be pertinent to support the licensing reviews of the Nuclear Regulatory Commission.

APPROACH USED IN THIS STUDY

The approach used here was to perform initially an extensive literature search for information on the toxicology of ammonia, chlorine, Halon 1211, Halon 1301, and sulfur dioxide. We then obtained copies of as much of this literature as was possible including papers on both animal and human data. In many cases the available literature was limited to studies approximately a decade or more of age. Moreover, much of the data did not deal with extremely high acute exposures, and often involved exposures that were 15 minutes or longer. We have therefore, used professional judgment in establishing permissible exposure limits from data which were obtained from experiments in which the exposure periods were not the same as desired to be used here. Of the data that were available to us, we examined all aspects relative to use for establishing 2-minute exposure limits. This included outright toxicity as measured by mortality; it also included physiological alterations such as impaired pulmonary function. Factors not normally considered appropriate, such as visibility problems are also considered. An aspect that is more difficult to evaluate but which must be given consideration is that of a normal response to obnoxious materials. For example, it is well known that in refrigeration plants the detection of ammonia by odor usually results in people fleeing the premises, a response that is obviously not appropriate for nuclear reactor control room operators. We have taken the position that control room personnel through appropriate training will not desert their post on detection of material by odor or other means.

Another aspect that must be considered is that of sensitive populations. For example, it has been well demonstrated that asthmatics are highly susceptible to the effects of sulfur dioxide. We have based our recommendations for non-sensitive persons. These recommendations are not appropriate for severely affected asthmatics and other uniquely sensitive persons.

It is tempting using common toxicological thinking to set exposure limits on the basis of levels which first produce a visible reaction in human subjects. While this may be acceptable procedure for situations that are ordinarily encountered in the work place, such an approach is unsuitable for setting 2-minute exposure limits. Thus, although ammonia, chlorine and sulfur dioxide are irritants for the respiratory tract and can first be detected by people because of these properties, the lowest detectable levels are not necessarily the maximum that people could tolerate and still perform their necessary duties. For example, the current 2-minute exposure limit set for chlorine does not appear to be based on maintenance of function. It is likely that higher levels can be tolerated if we are concerned about the ability of the individual to function appropriately during the exposure. Thus, although we considered setting limits on the basis of preventing either temporary short-term or delayed long-term health effects, our recommendations reflect levels that we believe can be tolerated and still permit the operator to function.

Several exposure guideline standards are used in industrial hygiene to evaluate the hazards of chemical exposure. For the purpose of this appraisal,

the TLV-STEL, IDLH, ERPG and EEGL were the most relevant limit values. Table 1 contains a comparative summary of current guidelines for four of the gases of interest. Each were compared and considered, when available, in the process of establishing recommendations for "two-minute protective actions limits".

AMMONIA

Identification

Chemical Name: Ammonia
Synonyms: Ammonia gas, anhydrous ammonia
CAS Number: 007664417
Molecular formula: NH_3

Chemical and Physical Properties of Ammonia

Physical State and Appearance: Colorless gas
Odor Description: Sharp, irritating, pungent
Molecular Weight: 17
Conversion Factors: 1 mg/m^3 = 1.44 ppm
1 ppm = 0.70 mg/m^3
Boiling Point: -33.5°C at 769 mm Hg
Vapor Density: 0.59 relative to air
Stability and Reactivity: Forms ammonium hydroxide on contact with water
Solubility in Water: Extremely soluble
Toxicity: Inhalation-rat LCLo = 2000 ppm/4 hr
rat LC_{50} = 40,300 ppm/10 min Appleman et al.
mouse LC_{50} = 10,000 ppm/10 min Silver and MacGrath

Current Exposure Guidelines

PEL	=	50 ppm
TLV-TWA	=	25 ppm
TLV-STEL	=	35 ppm
TLV-(5 min ceiling)	=	50 ppm
IDLH	=	500 ppm
ERPG-3	=	1000 ppm
ERPG-2	=	200 ppm
ERPG-1	=	25 ppm
EEGL-1 hr	=	100 ppm
24 hr	=	100 ppm
NRC-2 min	=	100 ppm

Recommended Two-Minute Exposure limit

300 ppm

General Biological Properties

Ammonia vapor has a sharp, irritating, pungent odor that can act as a warning of exposure. The odor threshold concentration for ammonia has been reported as low as 0.7 ppm in very sensitive people, and as high as 50 ppm in others. A reasonable average value for odor threshold concentration is probably about 5 ppm.

Acute exposure to ammonia can result in mild irritation, hoarseness, excess salivation, sneezing, cough, productive cough, hemoptysis, rales and, in severe cases, symptoms of laryngeal edema with asphyxia, pulmonary edema and bronchial pneumonia. Of great concern is the laryngeal spasm and reflex bronchial constriction that high concentrations of ammonia can produce. Laryngeal edema may develop several hours after acute exposure and such exposure often results in an initial impression of less severe damage. (National Academy of Sciences, National Research Council, Washington, D.C., Committee on Medical and Biological Effects of Environmental Pollutants. Ammonia 1977.)

Human Studies

As has been pointed out by Griffiths and Megson (1984) there are many sources of uncertainty relative to the toxicity of ammonia for humans. For example, the National Academy of Sciences report summarizes several studies of humans including one performed in 1886. In that study, the author exposed himself to ammonia concentrations at 330 ppm for 30 minutes and concluded that concentrations of 300 - 500 ppm could be tolerated for protracted periods. In another study, six volunteers exposed for 10 minutes to 30 or 50 ppm reported little irritation and a highly penetrating odor at the lower concentration and moderate irritation at the higher concentration. Ten subjects exposed for five minutes to ammonia at 32, 50, 72 and 134 ppm reported minimal symptoms at the two lower concentrations, some irritation at 72 ppm, and lacrimation and significant eye, nose and throat irritation at 134 ppm.

A significant amount of human data comes from accident cases in which small numbers of people have been exposed acutely to high concentrations of ammonia gas. The weakness in these studies is that in most cases the actual concentration to which people were exposed is unknown and indeed was not estimated by most authors. Nonetheless, these studies offer a perspective of what can happen. For example, in 1938 Slot (NIOSH, 1974a) reported six cases of acute ammonia gas exposure following rupture of a pipe containing ammonia. Varying degrees of symptoms of acute inflammation of the respiratory tract and chemical skin burns were observed. In two of the six cases, residual chronic bronchitis was evident. One worker died one month after the accident, and the autopsy revealed acute laryngitis, tracheitis, bronchial pneumonia and pulmonary edema. In addition, the kidneys showed congestion and early hemorrhagic nephritis.

In another study, Caplin in 1943 (quoted in NIOSH, 1974a) published a case report of 47 persons involved in a mass exposure of ammonia in a London air raid shelter when a connecting pipe of a ammonia condenser was ruptured. He divided the people into three groups depending on the extent of the respiratory involvement. The signs and symptoms ranged from mild upper respiratory irritation to inflammatory processes of the entire respiratory tract with complications of pulmonary edema and bronchial pneumonia. Nine "mild" cases exhibited only slight eye and upper respiratory irritation with hoarseness and tightness in the throat. These people recovered quickly and were discharged from the hospital in a few hours. There were 27 "moderately" affected individuals who showed more pronounced upper respiratory irritation and who had a productive cough with tenacious sometimes blood-stained sputum.

They also had moist rales in the lungs suggesting an extension of the inflammatory process into the lower respiratory tract. Three of these patients developed pulmonary edema within six hours and died. In addition, another nine patients developed bronchial pneumonia on the second and third days and three of these nine died. The remaining fifteen in this moderately affected group made an uneventful recovery in one week. The third group was classified by Caplin as "severely" affected patients. These people had signs and symptoms of pulmonary edema with cyanoses, persistent cough with frothy sputum and intense dyspnea. Seven out of the eleven patients in this group died.

A few cases of exposure to ammonia have been examined for possible changes in pulmonary function. In one of these studies, a single worker who had incurred an acute ammonia exposure of undefined concentration or duration was followed for more than a year. During this time the maximum breathing capacity decreased from 97 to 52 liters per minute, the vital capacity from 3.09 to 2.05 liters, and the ratio of residual volume to total lung capacity increased from 49 to 58%. Diffusion capacity as measured by the carbon monoxide method diminished from 9.4 to 6 mls per minute. All of these results were suggestive that there was moderate progressive airway obstruction and a diminishing diffusion capacity. In another case a 28 year old man was struck by a jet of liquid ammonia from refrigeration equipment. This individual developed pneumonitis in the base of the right lung, but no residual damage to lung or eyes occurred. Pulmonary function tests three years later were normal (NIOSH, 1974a).

In still another case, White (1971) reported that a twenty-year old worker was found unconscious in a compression room approximately five minutes after he had been overcome by an ammonia release from defective safety valve. No estimates of air concentrations were made. Rales were heard in both lungs suggesting fluid in the lower respiratory tract. Five hours later the patient was still unresponsive and respiration was irregular. He had marked conjunctivitis and pupils were constricted. Lungs revealed generalized rales in bronchi with expiratory wheezing which improved over the next two weeks. After six months the patient had no pulmonary symptoms except for a mild bronchitis.

In 1972 Walton (NIOSH, 1974a) reported on four ammonia incidences involving seven men. There was one fatal case in which autopsy showed a marked laryngeal edema, acute congestion, and edema of the lung and a loss of bronchial epithelia. The remaining six were examined at yearly intervals for five years. All six were classified as moderate smokers (15-20 cigarettes per day). Although exposures were not described in any detail, one man with a light ammonia exposure exhibited only mild symptoms of bronchial spasm and recovered quickly. Forced vital capacity (FDC) and forced expiratory volume in one second (FEV 1) were better than predicted values based on sex, age and height. However, the gas transfer factor (GTF) a measure of diffusion capacity, was low throughout the follow-up period. This last finding was explained by the author as probably associated with the cigarette smoking. The other five men with "heavy exposure" showed acute symptoms and signs of chemical burns to the nose, mouth and throat, moderate eye irritation, marked dyspnea with cyanosis, cough with blood stained sputum and pulmonary

congestion. However, there was little evidence of any radiological abnormalities in the chest. Almost all of the pulmonary function tests, which were abnormal immediately after the accident, showed a gradual improvement during the first two years. In one case, FDC, FED1 and GTF were all above predicted values during the entire five-year followup period. In another the FDC, and the FED1 remained considerably below normal values throughout the followup period while the GTF recovered to nearly normal. In a third case the FDC returned to normal although the FED1 and the GTF remained well below normal. The fourth case showed progressive improvement in ventilation but a consistent depression of the transfer factor. The fifth case showed gradual improvement to normal for the two ventilatory measurements, however, the GTF stayed at low normal values. The author attributed the residual abnormal pulmonary function tests in two cases to the ammonia exposure, whereas in two other cases the pulmonary function abnormalities were attributed to the patients continued smoking habit. In general, the types of symptoms seen in individuals with high acute exposures and those seen with lower longer term exposures seem to be similar. These last several cases have been summarized in a 1974 NIOSH Criteria Document.

In general, it is believed that ammonia absorption takes place in the upper respiratory tract so that with moderate exposures, very little of the ammonia reaches the deep lung. Silverman et al. (1949b) [NIOSH, 1974a] observed that with 500 ppm delivered for 30 minutes by a nasal-oro mask ammonia retention decreased progressively until an equilibrium of 24% retention was reached at the 19th minute. Ammonia in expired breath was not detected beyond the 18th minute after exposure. These same authors also analyzed blood for blood urea nitrogen (BUN), nonprotein nitrogen (NPN), urinary urea and urinary ammonia. They also examined the carbon monoxide combining power. All of these measures remained normal. These data seem to confirm the idea that the absorption of ammonia was largely in the upper respiratory tract. A study by Landahl and Herrmann in 1950 (NIOSH, 1974b) examined the short-term retention of ammonia in the nose of four human subjects. Their results indicated that an average of 83% of the dose of ammonia was retained in the nose. In contrast to the results of Silverman et al. (1949b), Schmidt and Vallencourt (1948 in NIOSH, 1974a) found that human exposure for four hours to an ammonia concentration of 530-560 ppm produced a number of changes. They found that blood urea nitrogen and serum creatinine remained unchanged throughout the exposure as did the carbon dioxide combining power of the blood plasma. They did, however, find that repeated blood pressure readings during the experiment showed a linear drop from 127 millimeters to 102 millimeters. They also found that the serum NPN increased from 27 milligrams to 57 milligrams per 100 grams of blood and the blood ammonia rose from non-detectable levels to values of 36.4 milligrams per 100 grams of blood. This last finding has been criticized as being unrealistic from both a theoretical basis and from an experimental animal basis.

A few studies of workplace environments have been made. In 1955, Vigliani and Zurlo (NIOSH, 1974a) reported that in a plant that they classified as "ammonia works" concentrations of 100 ppm could not be continuously inhaled for lengthy periods without irritation of the upper respiratory tract and eyes. They also reported that workers that were accustomed to 20 ppm of ammonia did not complain but did show slight redness

of the conjunctiva. Those not accustomed to ammonia exposures also had eye and respiratory discomfort and irritation. These data suggest that the threshold for response to ammonia may be changed as exposures continue. Mangold has been quoted in the Criteria Document concerning his investigation of complaints of eye irritation in a blueprint shop. He found that during a one week period when eye complaints occurred that air sampling showed concentrations of ammonia ranging from 4 to 29 ppm. No reference was made to the type or level of any respiratory complaints in this blueprint shop. Previous evaluation in the same shop had reported air levels below 5 ppm of ammonia associated by the workers and/or the industrial hygienist with barely noticeable eye irritation. It was concluded that intermittent peak exposures in the range of 20 ppm of ammonia caused moderate eye irritation.

The NIOSH criteria document also quotes Pagnotto who reviewed the files of surveys performed by the division of occupational hygiene of the Commonwealth of Massachusetts from 1940-1972. Several plant surveys mention irritating effects. A survey of refrigeration equipment in an ice cream plant disclosed that ammonia concentrations in air ranged from 9-37 ppm. At these concentrations, odor fatigue was reported by the industrial hygienist who stated that the odor of ammonia was noticeable but that the sense of smell was quickly deadened to the presence of the gas. In an insole cementing operation, ammonia concentrations were 15-28 ppm in the work area and very slight eye irritation was reported. In a blueprint machine room a concentration of 45 ppm was found and the industrial hygienist had commented that there was some eye irritation, but that one quickly becomes accustomed to it. Samples ranging from 3-29 ppm were collected near a printing machine with a comment from the industrial hygienist that the odor of ammonia was quite marked, but not disagreeable. All of these studies were more or less anecdotal studies that did not use rigidly defined protocols.

Animal Studies

Because controlled highly toxic experiments cannot be done ethically with human beings, it is necessary to consider data obtained from carefully controlled animal studies. The question, of course, is how to extrapolate these data to the human situation. We will first consider the kinds of symptoms that have been observed in these animal experiments as have been compared to human exposures. In 1933 the Underwriters Laboratory exposed 8 guinea pigs to ammonia concentrations of 5-6 thousand parts per million. Two animals were removed from the test chamber at the end of 5, 30, 60 or 120 minutes and all were observed for ten days. Within 30 seconds all eight of these guinea pigs were lacrimating profusely, discharging from their nose and exhibiting labored breathing. At the end of 5 minutes, eyes and noses were intensely inflamed, respiration was irregular and frequent retching movements were noted. Violent coughing occurred after 30 minutes, breathing was shallow at 60 minutes and barely perceptible at 120. However, all animals survived, although they showed increasing severity of respiratory irritation depending on exposure time. In this study, a second group of four guinea pigs was exposed to ammonia concentrations of 20,000 to 25,000 ppm. Two animals were removed after 5 minutes. They were blind and showed signs of respiratory irritation. Both recovered fully within one week, except for permanent blindness in one of the two. One of the remaining animals died after nine

minutes of exposure, apparently as a result of reflex stoppage of respiration since autopsy results were minimal. The fourth guinea pig was exposed for 30 minutes and displayed marked respiratory difficulties. However, it recovered except for permanent blindness.

Silver and MacGrath in 1948 (NIOSH, 1974a) exposed nine groups of 20 mice to ammonia for 10 minutes, with each group receiving different concentrations. Exposures ranged from approximately 8800 to 13,000 parts per million. All test animals showed great excitement and severe eye and upper respiratory tract irritation. They closed their eyes immediately and within one minute were gasping, pawing and scratching their noses. Death with convulsions occurred after about 5 minutes in 100 of the 180 animals that died before the 10-minute exposure was completed. The 80 surviving animals recovered rapidly after removal from the chamber demonstrating normal behavior in many of cases within 10 minutes. Between the 6th and 10th post-exposure days 7 of the 80 died compared with no deaths in controls. The lethal concentration for 50% or 10-minute LC_{50} was estimated to be about 10,000 ppm.

Appelman, ten Berge, and Reuzel (1982) also examined the toxicity of ammonia in rats relative to the length of exposure. They found that the correlation between exposure concentration (c), exposure period (t), and mortality expressed in probits was expressed by the equation:

$$\text{Probit} = 2.3 \ln[c^{2.02} \times t] - 47.8$$

From this equation, another equation can be derived that describes the correlation between LC_{50} and exposure time:

$$LC_{50}^{2.02} \times t = 9.87 \times 10^{9} \ [(mg/m^3)^{2.02} \times min]$$

Values for LC_{50} in their study ranged from 40,300 ppm for 10-minute exposures to 16,600 ppm for 60-minute exposures.

Coon et al. (1970) studied the effects of exposure to ammonia in rats, guinea pigs, rabbits, monkeys and dogs. At 221 ppm, there were no signs of exposure in any of the animals even after 30 exposures for 8 hr/day, 5 days/week. Only mild to moderate symptoms of lacrimation and dyspnea were noted during the first week of exposure to 1000 ppm. Continuous exposures to 375 ppm for 90 days did not produce any mortality and few symptoms; whereas, continuous exposure to 650 ppm resulted in deaths of 32 out of 51 rats by day 25 of the exposure and 50 by day 65. No deaths were seen for the other species. However, continuous exposure at 677 ppm caused deaths in 13 of 15 rats and in 4 of 15 guinea pigs.

An interesting study has been reported by Dodd and Gross (1980) in which they examined the effects of 1000 ppm of ammonia in healthy cats. They performed this study because in an accident where a domestic cat was exposed to high levels of ammonia along with human beings, the cat demonstrated a clinical syndrome very similar to that described in human victims. The syndrome included chronic bronchial pneumonia, chronic bulbus emphysema,

bronchial ectasis and interstial fibrosis. Their experimental study looked at both pulmonary function and microscopic pathology. They anesthetized 20 cats with a combination with acepromazine maleate and ketamine hydrochloride. All animals were exposed to 1000 ppm ammonia gas for 10 minutes. Twenty-four hours later five of the cats were reanesthetized and pulmonary function tests that had been performed prior to ammonia exposure were repeated. Following the completion of the pulmonary function test the cats were euthenized by an overdose of pentobarbital. Lungs were removed in total and pressure instilled with buffered formalin. Other cats were anesthetized and tested on day 7, 21 and 35 days post exposure, respectively. After each pulmonary function evaluation the cats were sacrificed and the lungs removed. Six different measures of pulmonary function were performed including airways resistance, pulmonary resistance, inspiratory and expiratory tissue resistance, functional residual capacity, anatomical dead space and dynamic compliance. Twenty-four hours after exposure all cats were in poor condition with severe dyspnea, anorexia and dehydration. Auscultation revealed bronchial breath sounds, sonorous and sibilant rhonchi and coarse rales. At necropsy lungs showed varying degrees of congestion, hemorrhage, edema, interstitial emphysema and collapse. None of these lesions were more apparent or specific to a particular exposure day. However, bronchial pneumonia was seen as a common lesion after day 7. On microscopic examination, the basic lesion found in cats sacrificed 24 hours postexposure was necrotizing bronchitis which was most prominent in the large conducting air ways. The main stream bronchi showed necrosis and sloughing of the epithelium with attended acute inflammatory reaction. Damage was minimum at the bronchiolar level. By seven days post-exposure, mucosal lesions were resolved in all cats necropsied. There was some clumping of macrophages in the bronchioles which may or may not have been related to the initial insult.

Pulmonary function tests showed no change in anatomical dead space at any time of examination. Functional residual capacity was almost doubled in value on day 21 but not at other times. The work of breathing for both inspiration and expiration was increased significantly on day one after which they returned to the original baseline levels until day 21 at which time it was again significantly increased. Dynamic compliance for all times of measurements were significantly decreased. Pulmonary resistance during both inspiration and expiration increased significantly and remained significantly higher than the baseline levels throughout the study. Tissue resistance was significantly greater than baseline values on day 1, 7 and 21 but not significantly changed as a result of the initial insult on day one.

Another interesting study was performed by Stombaugh et al. in 1969 (NIOSH, 1974a) to evaluate the effects of ammonia on pigs. One pig exposed to 280 ppm showed immediate irritation of the nose and mouth and abnormal respiratory patterns and by the 36th hour of exposure had convulsions and extremely shallow and irregular breathing. Convulsions continued for three hours after exposure ended, but the animal appeared normal several hours later.

In each of two trials four exposure groups of nine pigs each were continuously exposed to ammonia for 5 weeks. Concentrations of ammonia were measured daily and the average exposure to the groups were 12, 61, 103, and

145 ppm. It was found that both feed consumption and average daily weight gain were adversely affected by increasing ammonia concentrations. The pigs exposed to the three higher concentrations had excessive nasal, lacrimal and oral secretions, but these symptoms were less pronounced in those exposed to 61 ppm. Pigs exposed to the 61 ppm appeared to adjust within 3-4 days so that their secretory rate was only slightly higher than that of animals exposed to 12 ppm. Pigs exposed to the two higher concentrations coughed approximately 3 times as much as those exposed to the lower concentrations and coughing at 61 ppm was slightly more frequent than at 12. When animals from each exposure group were autopsied and examined grossly or microscopically, all findings were normal.

In another study with pigs, Doig and Willoughby (1971 NIOSH, 1974a) found no adverse effects on food intake, weight gain or frequency of coughing when weanling pigs were exposed to ammonia up to 6 weeks at an average concentration of 106 ppm. Slight eye irritation with evidence of photophobia and excess lacrimation were noticed during the first week of exposure but thereafter the pigs appeared to be acclimatized. Hematologic and blood chemistry measurements were unchanged. Although effects on bronchi, bronchioles and alveoli were not observed there was some thickening in the tracheal epithelium and a decrease in the number of goblet cells in the trachea.

Summary and Conclusions

In general, the animal experiments indicate that the main toxic effect of ammonia is on the respiratory tract and on the eyes, a finding consistent with observations of humans (Table 2 and 3). It appeared that the exposure of experimental animals up to concentrations of 5-6 thousand ppm for up to 2 hours markedly irritated the respiratory tract. LC_{50} values that were obtained for animals exposed for 10-60 minutes appeared to be in the range of 10,000 ppm. This value is of interest since Mulder and Van der Zalm in 1967 (NIOSH, 1974a) described an acute exposure case in which a worker was exposed to a very high concentration of ammonia, which was estimated to be about 10,000 ppm. The person immediately experienced cough and vomiting and had difficulty in breathing. The length of exposure was not stated, but the person performed small jobs for the remaining 3 hours of work before he was seen at a clinic. By this time his face was red and swollen. He had conjunctivitis, his mouth and throat were red and raw, his voice was disappearing, and he had labored breathing. The heart appeared to be normal, but while x-rays were being taken, the heart stopped. He was revived by massage and artificial respiration and transferred to a hospital. Six hours after the accident his heart stopped again and he died. Autopsy showed marked inflammation of the respiratory tract although surprisingly no pulmonary edema was present, however the tracheal epithelium was almost completely denuded. It thus appears that the lethal level for humans is probably in the 5,000 to 10,000 ppm range, although there is a substantial amount of uncertainty in these estimates.

Examination of the data from these studies suggests that humans can tolerate levels of ammonia in excess of 100 ppm rather well, especially for short periods. Observational findings suggest that persons exposed up to 700

ppm or 490 mg/m^3 would probably have no serious long lasting effects even after one-half to one hour of exposure. At higher levels, there is concern that there might be a triggering of respiratory spasms that might be of potentially serious consequence to the individual. Experimental animal data appear to substantiate this conclusion, since the cat which appears to be one of the more susceptible species recovered from exposures of 1000 ppm for ten minutes. If we evaluate these data in terms of levels that could be tolerated for two minutes and still allow the individual to operate the plant safely, probably 400-500 ppm could tolerated. If, on the other hand, one is concerned that not only should a person be able to don appropriate protective apparel but also not be subject to longer-lasting effects, an appropriate exposure limit is probably more in terms of about 300 ppm. Lacrimation would probably occur at this exposure, but would clear upon removing the source or upon donning respiratory equipment. Performance would most likely be impaired at exposures to concentrations greater than 300-400 ppm for two minutes.

CHLORINE

Identification

Chemical Name: Chlorine
CAS Number: 007782505
Molecular Formula: Cl_2

Chemical and Physical Properties of Chlorine

Physical State and Appearance: Greenish-yellow gas
Odor Description: Pungent and irritating/bleach
Molecular Weight: 70.9
Conversion Factors: 1 mg/m^3 = 0.3 ppm
1 ppm = 3.0 mg/m^3
Boiling Point: -34.6°C
Vapor Density: 2.5 relative to air
Stability and Reactivity: Highly oxidizing; not found free in nature
Solubility in Water: 5.7 g/L at 30°C
Toxicity: Inhalation-rats LC_{50} - (1 hr) = 293 ppm

Current Exposure Guidelines

PEL	= 1 ppm
TLV-TWA	= 0.5 ppm
TLV-STEL	= 1 ppm
IDLH	= 25 ppm
ERPG-3	= 20 ppm
ERPG-2	= 3 ppm
ERPG-1	= 1 ppm
EEGL-1 hr	= 3 ppm
-24 hr	= 0.5 ppm
NRC-2 min	= 15 ppm

Recommended Two-Minute Exposure Limit

30 ppm

General Biological Properties

Chlorine gas has been shown to be a severe irritant of the eyes, mucous membranes and skin (Sittig, 1985). Nasal irritation and coughing are frequent consequences of chlorine exposure. The odor threshold for chlorine has been reported at various concentrations and appears to be between 0.2 and 0.4 ppm. The nasal irritation and coughing appear to occur at about 0.5 ppm. As with ammonia, there appears to be some olfactory fatigue when persons are exposed to concentrations of approximately 1 ppm (Stokinger, 1981). A special caution from these data is that odor detection is not a good warning device for chlorine hardened workers.

According to the review by Withers and Lees (1985a), the symptoms of chlorine poisoning are irritation of the nose, throat and eyes with cough and tears at concentrations of about 15 ppm. Restriction of breathing and chest pain occur at about 30 ppm while development of pulmonary edema occurs about 50 ppm. As has been stated by Haggard (1924 in NIOSH, 1976), ammonia produced intense congestion of the upper respiratory passages and immediate death from laryngeal spasm or edema. Chlorine appears to act on both upper and lower respiratory tract. Nonetheless, McPherson et al. in Diseases of the War, (1923) as quoted in Withers and Lees (1985a), expresses the following, "The points where the gases classified as acute lung irritants exercise their most pronounced effect are the alveoli of the lungs and the smaller bronchial tubes and the great danger to be feared which is common to them all is the onset of acute pulmonary edema. It is in the main edema which in the acute stage of poisoning threatens the life of the subject for if abundant it causes death by asphyxiation. The patient being in fact drowned by his own exudation."

An additional quote from the "Diseases of the War" as given in Withers and Lees's review says the following: "all the men gave a similar description of what they felt as the greenish-yellow fumes* enveloped them. Immediate choking, coughing, gasping for breath, an inability to speak proved the irritation and spasm of the respiratory tract. In many, the eyes smarted and ran with water. Retching was at once experienced by some, but many did not vomit until an hour or two later. It was severe behind the sternum and soon radiated outward on each side of the chest and added greater suffering to the distressed breathing. The throat burned and the dry mouth produced an intense sensation of thirst. Very soon the developing pulmonary edema led to the phenomena of oxygen shortage with headache, a sense of weakness in the legs and such lassitude that the men dropped prone upon the ground. Milder cases in areas where the concentration of chlorine in the air was relatively low, suffered chiefly from lassitude and great fatigue ...."

Human Studies

Much of the information on chlorine poisoning came as a result of casualties of World War I. Persons exposed were followed by a number of investigators. Most of the next segment of information will come from the NIOSH criteria document of May 1976. For example, Meakins (1919 in NIOSH, 1976) reviewed the after-effects of chlorine war gas poisoning by following 700 cases in the admission and discharge books of the Canadian Field Ambulances serving in Ypres, France for several weeks in the spring of 1915. Of these, 222 (31.7%) had no further details of clinical conditions ascribed to gas poisoning in their records. Four hundred and seventy-eight were evacuated to the base. Of the 478, 146 or 20.8% were treated at the hospital. Six of the hospital patients died and the remainder returned to duty. Of the others, 332 or 47.4% were evacuated to the United Kingdom for further treatment. Of these 332, 80 returned to France and resumed duty. Forty had irritable heart, 10 bronchitis and 4 gastric symptoms while in the hospital. Of 204 sent to Canada, 118 had symptoms of irritable heart, 30 symptoms of bronchitis and pneumonia, and 4 of symptoms with hemoptysis, 22 with asthma

*Chlorine gas becomes visible at high concentrations of 2-3% (about 20,000 ppm or 60 g/m^3); NIOSH, 1976.

and 20 with symptoms of neurosis. The remainder (30) were grouped in an "indefinite symptoms" category. The average duration of hospitalization before personnel were invalided to Canada was 17 weeks. Four years after exposure to chlorine, 188 of the men invalided to Canada were studied, seventy-eight of the men had irritable heart, 18 had neurosis, 8 had asthma, 18 had bronchitis and 14 could not be traced. Fifty-four were reported to have no appreciable disease.

In another study, Berghoff (1919 in NIOSH, 1976) observed a total of 520 soldiers who 3-4 months earlier had been exposed to chlorine during warfare. Clinical examinations revealed instances of bronchitis and emphysema but the author did not distinguish between physical findings unique to those soldiers exposed to chlorine and those findings resulting from exposure to other war gases.

According to Gilchrist and Matz in 1933 (NIOSH, 1976) U.S. War Department statistics showed that 1843 casualties out of a total of 70,742 casualties caused by gas poisoning were the result of exposure to chlorine. A study of 838 of these casualties were made for the purpose of ascertaining the sequelae. Of these 838, 28 had died. Four of the deaths were attributed to later effects of chlorine gassing, including bronchial pneumonia, lobar pneumonia, purulent pleurisy, and tubercular meningitis. Nine of the 838 were discharged because of disabilities attributable to gassing. These disabilities included pulmonary tuberculosis, bronchitis, pleurisy, neurocirculatory asthenia, tachycardia, dyspnea and nephritis. Another 39 were disabled at the time of discharge in conditions attributed to chlorine gassing which included bronchitis, pleurisy, laryngitis, valvular heart disease, keratitis, and conjunctivitis. Of the 838, 96 were reexamined clinically and by x-ray at the time of the study. The authors concluded of these 96, nine showed definite asystematic or systematic residual effects which could be attributed to chlorine gassing. Relationship of disabilities to chlorine gassing is questionable in seven instances. In 80 patients, disabilities found at the time of the study were concluded to be in no way related to chlorine gassing incurred during the service. Of those nine showing definite residual effects five had pulmonary tuberculosis with co-existing emphysema in three. Three of the nine had evidence of chronic bronchitis of which one had a co-existing emphysema. One had chronic conjunctivitis and one was free of co-existing conditions. One of the nine men had chronic adhesive pleurisy. In analyzing the five cases of pulmonary tuberculosis, the authors conclude that it was probable that gassing led to reactivation of previously quiescent tuberculous lesions.

Several studies have reported the effects of chlorine following exposure to release from accidents. For example, Romcke and Evensen in 1940 (NIOSH, 1976) reported an accident in Norway that released 7-8 tons of chlorine. The number of those exposed was not given, but 85 were hospitalized and 3 died. The authors comment that some victims had latent periods as long as several hours before they developed symptoms of pulmonary congestion disturbing enough to seek medical attention. The authors also commented that the most severe symptoms of pulmonary edema developed most rapidly in those subjected to physical exertions. In the milder cases, the pulmonary symptoms disappeared in 2-3 days. Fifty-four of the hospitalized patients were discharged in 3

days. In other hospitalized patients the bronchitic sounds lasted 8-10 days. Signs of pulmonary edema occurred in 6 patients. When two of the three victims were autopsied, intense tracheal bronchitis, hyperplasia of the brain and intensely edematous lungs were found.

Chasis et al. (1947 in NIOSH, 1976) reported a study of 418 persons who were exposed to chlorine that had leaked into a subway. The chlorine created a visible cloud but no other estimates of actual concentrations or duration of exposure were made. Of the 418 persons exposed and examined, 208 were hospitalized (133 were in one hospital under the care of the authors). Of these, 33 exhibited moderate to severe chlorine intoxication and remained in the hospital from one to two weeks. Thirty-five others had milder symptoms and the rest left to seek care elsewhere. The records of the 140 admitted to other hospitals (75 directly and 65 by transfer from the first hospital) were reviewed and where possible the attending physicians were interviewed. When first exposed, most persons were overcome by choking, nausea, vomiting, anxiety and syncope. The 33 who remained in the first hospital appeared acutely ill on admission and were in moderate to marked respiratory distress. Twenty-eight of the 33 had a slight fever, approximately half were cyanotic. Pulmonary sounds were present in all with 28 exhibiting dry rales. Subsequent moist rales developed in all but two patients. Pulmonary edema was seen in 23 of 30 patients. Respiratory distress subsided for the great majority within 24 hours; however, in five patients it ceased in 6 days and one patient had prolonged dyspnea, a symptom to which preexisting heart disease was presumed to have contributed. Substernal pain generally subsided in the first 3 days leaving a soreness attributed to tracheobronchitis. A dry cough was present initially in every patient but promptly became quiescent with administration of oxygen and codeine only to return in most patients in 2-5 days with the production of tenacious mucopurulent sputum, blood-tinged when first produced. Dry rales cleared by the tenth day, moist rales were still present in 20 patients during the second week. The febrile period lasted 2-13 days. Chest x-rays showed mottling, patches of irregular densities, and differences in the degree amount of aeration in both lung fields. X-ray changes in most patients were not remarkable and it was felt that readings of single x-rays could easily have been judged to be normal. Serial ECG tracings on 12 patients showed either no abnormality or preexisting heart disease. For eight patients, vital capacity determined 48 hours after exposure gave values ranging from 16-57% of the predicted normal. A special follow-up clinic was established and attended by 29 of the 33 patients, for about 16 months after exposure. Eleven of these had no abnormal symptoms or signs. One patient had cough and sputum for six months with moist rales at the base of the left lung for three months. This patient died 10 months after exposure and a post mortem examination showed a pulmonary embolus but otherwise normal lungs and bronchi.

Sixteen patients had what were considered anxiety reactions with phobia, hysterical phenomena, and psychosomatic dysfunctions for 1 to 16 months, including anorexia, nausea, vomiting, weakness, nervousness, dizziness, palpitation, a sense of suffocation and the odor and taste of chlorine. In addition, two intrauterine pregnancies were reported to be unaffected by the exposure but no details were given. There was no correlation between severity

of symptoms during hospital stay and the continuance of symptoms thereafter. No pulmonary function studies were reported from the special followup.

In another industrial accident, there was a release of large amounts of chlorine from a mill. Although only 190 of the 900 workers of the mill were at work, the wind carried the cloud of gas into the town. Supposedly, 240 people were taken to clinics. Four workers died and another 42 people were in very serious condition. The signs and symptoms present in 46 patients examined by the author were as follows: fever, moist rales in some pulmonary fields, dyspnea, blood in sputum, tachycardia, vomiting or nausea, reduced arterial pressure, cyanosis, blood in urine, coated tongue, headache, severe diarrhea, sticky sweat, fainting, infrasternal pains, constipation, pains below the costal ridge, heart pains, bradycardia, and arrhythmia. Three autopsies were performed and aside from the pulmonary edema, emphysema, and the presence of bronchial pneumonic condensation in the lungs, the most striking findings were small hemorrhages in the white matter at the cortex, corpus, callosum, internal capsule and cerebellum (NIOSH, 1976).

In 1962, there was a spill of 36 tons of liquid chlorine in Louisiana. Three hours later concentrations of 10 ppm were found at the fringes of the contaminated area. By 7 hours after the spill, levels of 400 ppm were recorded 75 yards from the spill. Approximately 100 people were treated for exposure to chlorine at various degrees. Of the 65 casualties handled in one hospital, 15 were admitted; 3 children and 1 adult were unconscious on admission. An eleven month old infant died. Ten of the hospitalized patients developed frank and unmistakable pulmonary edema. All heavily exposed victims experienced severe dyspnea, coughing, vomiting, and retching. Most of the patients complained of burning of eyes and had acute conjunctival irritation with profuse tearing and photophobia. Seven years later Weil reviewed the case histories of 12 of those who had been exposed to the 1962 spill. In general, these 12 patients had been the ones most severely exposed. Three of the 12 had been studied three years after exposure. Observed values for total lung capacity, vital capacity, residual volume, and forced expiratory volume at one second were all within two standard deviations of predicted value. The subjects were essentially asymptomatic from a respiratory standpoint. Chest x-rays were also normal in all cases (NIOSH, 1976).

Kowitz et al. in 1967 (NIOSH, 1976) presented details on an accidental chlorine exposure of approximately 156 workmen during cargo unloading. No estimates of chlorine concentrations or durations of exposure were reported, but most men experienced acute symptoms. All were taken rapidly to 3 local hospitals and 37 of 156 were admitted. Several of the men returned to the hospital within 48 hours and were admitted at that time. There were no recorded deaths. Of the 17 subjects admitted to the first hospital 11 were studied serially. All 11 had shown respiratory distress on admission, it was judged to be severe in 7 of the 11. One developed bacterial pneumonia. Other clinical findings included hemoptysis, rales, wheezes or rhonchi or both and edema of the lungs. Within one to three weeks all findings had disappeared except for symptoms of exertional dyspnea, easy fatigability and cough. Two months after exposure, all 11 appeared clinically recovered, however, there were findings of reduced lung volumes, reduced arterial oxygen, partial pressures at rest, which were significantly lowered upon mild exercise and

hyperventilation at rest and upon exercise. Six months later mean total lung capacity was still reduced, mean vital capacity was further reduced, and mean airway resistance was significantly increased. There was arterial hypoxemia at rest and after exercise and a decrease in degree of hyperventilation. Lung volumes were still low for up to three years after the accident while airway resistance remained elevated. Carbon dioxide partial pressures and blood pH returned to normal levels, although hyperventilation was still apparent 14 months after the study.

All of the people in the accident were asked to participate in a respiratory disease study approximately 18-20 months after the accident. Seventy-three of the 156 were evaluated. Of the 73, twelve were excluded because of conditions other than chlorine exposure which might have altered pulmonary function. In the studies, two were incomplete leaving 59 for analysis. These 59 included the original 17 admitted to the first hospital. All but two of the 59 subjects were black with an average age of 51.3 years. At the time of followup examination the authors judged 16 of the 59 to have moderate to severe dyspnea on the basis of subjective complaints. Other signs and symptoms in order of decrease in frequency were cough, non-specific chest pain, oral pharyngeal membrane irritation, decreased stamina and muscular weakness. Abnormal findings included diminution of chest expansion, decreased breath sounds, and prolongation of the expiratory phase. Leube and Krieter (1971 in NIOSH, 1976) examined 90 persons acutely poisoned by chlorine gas blown across a factory site. These people were treated at a local hospital, 72 as inpatients and 18 as outpatients. No estimate of degree of exposure was made. The following signs and symptoms were reported in 88 of the 90; coughing in 97%, dyspnea 75%, headaches in 66%, retrosternal pain in 47%, nausea in 44%, vertigo in 33% and vomiting in 11%. All inpatients had chest x-ray examinations between 5 and 8 hours after exposure. Ten showed pulmonary edema. In 48 that had ECG examinations, there were several instances of significant sinus tachycardia, isolated ventricular extrasystole and a disturbance in repolarization of the left ventricle. Blood sedimentation rates were normal in the 30 patients that were checked. Two hours after exposure, leukocytosis was marked in 60 of the 68 inpatients so tested. The number of white cells was about 10,000 per cubic mm. Within 7 hours, 36 patients still had values of over 10,000, but on the following day, only 6 persons still showed white cell values that high.

There is another factor to be considered after exposure to high levels of chlorine that may not have significance for persons exposed to relatively high levels of ammonia. That aspect is that physical exertion following exposure may be dangerous even when the person appears originally unaffected. Withers and Lees quote Veddar as giving the following explanation for sudden death following exertion. "Sudden death following exercise or struggling has often been observed in soldiers in the field and in experimental animals. The cause of these sudden deaths is readily demonstrated. In a normal animal when the corpuscles are saturated with oxygen the oxygen in the arterial blood fluctuates between 94 and 98%. The oxygen percentage in the venus blood is generally half that of the arterial blood. Barcroft found after gassing a goat with a moderate concentration of chlorine that the oxygen percentage in the arterial blood dropped to about 80%. This may cause headache, impaired vision, and inability to work, but is by no means dangerous to life. However,

when the same goat struggled, the arterial oxygen dropped abruptly to 44%. This is caused by the greatly increased consumption of oxygen by the tissues during exercise. Such a high degree of anoxemia affects at once both the cardiac and respiratory centers of the brain."

It should be noted that later evaluations of the statements of the "Disease of War" suggest that some of the conclusions were not totally correct. In fact, some of the observations may deal with cases in which the soldiers had been exposed to mixtures of chlorine and phosgene. This is especially true when it comes to the prevalence of pulmonary edema among people gassed by chlorine in industrial accidents. For example, Jones stated that in the period 1932-1948 he and his colleagues dealt with 820 such cases in which 9 were severe, but that even in these severe cases neither pulmonary edema nor pneumonia ensued. Although he indicated awareness of pneumonia in other cases, Haggard (1924 in NIOSH, 1976) further spoke to the industrial gassing situation by stating "even an exposure insufficient to induce the acute symptoms of lung irritation may lead to the development of pneumonia and under industrial conditions the infections thus produced constitute a greater cause of death than primary pulmonary edema." On the other hand, the accounts of Black et al., (1915 in NIOSH, 1976) who treated 685 cases of chlorine poisoning between May 2-7, 1915, before phosgene had been used, showed clearly that acute deaths involved pulmonary edema. Confirmation was obtained by 10 post mortem examinations that were carried out. Various authors have dealt with the possibilities of delayed death due to chlorine poisoning. Black et al. (1915 in NIOSH, 1976) stated that the acute stage passed in about 36 hours, followed by a quiet stage of 12 hours and that bronchial infection was then likely to develop. Underhill (1920) found that dogs which survived gassing were likely to die of pneumonia and set 3 days after gassing as the dividing line between acute and delayed deaths. The cause of delayed death has been described variously as bronchitis, bronchial pneumonia or pneumonia.

However, it appears that persons who have been exposed to chlorine and which showed pulmonary edema but survived had very little long-term damage when examined at 3 and 7 years after the event. A summary of symptoms found on humans exposed to various concentrations of chlorine is listed in Table 4.

Animal Studies

Acute mortality to chlorine at various exposure periods has been studied in several animal species and a summary of some of these results are presented in Table 5. Effects observed in animals from inhalation exposure include blinking eyes, sneezing, lacrimation, coughing, inflammation of the conjunctiva, and labored breathing. As the concentrations are increased respiratory tissue becomes injured with the development of delayed pulmonary edema, bronchial spasms occur, and immediate or delayed death results.

When mice were exposed to chlorine for 10 minutes by inhalation and evaluated during a 10-day period, an 10-minute LC_{50} of 618 ppm was estimated (Silver et al., 1942). More recent studies in mice have reported somewhat lower values of 302 and 209 ppm for 10 and 11 minute exposure, respectively (Alarie, 1980; Bitron and Aharonson, 1978). The LC_{50} of mice exposed for 30 minutes was 127 ppm (Schlagbauer and Henschler, 1967), whereas an LC_{50} for one

hour exposures was estimated to be 137 ppm (Back et al., 1972, cited in Merck Index, 1989). On the other hand, Bitron and Aharonson (1978) reported an LC_{50} of 170 ppm in mice exposed for 55 minutes. The LC_{50} in the rat following one-hour exposures was estimated to be 293 ppm (Back et al., 1972).

Early studies estimated the time-to-death after rats and mice were exposed to various concentrations of chlorine. Exposures to 1000 ppm resulted in 50% mortality in 53 and 28 minutes for rats and mice, respectively. At 250 ppm the 50% mortality occurred at 440 minutes for both species and at 63 ppm mortality was less than 50% after 16 hours exposure. Underhill exposed dogs to different concentrations of chlorine for 30 minutes and reported 11, 29, and 40% mortality at concentrations of 164, 491 and 600 ppm, respectively; they estimated the 30-minute LC_{50} to be 650 ppm.

Results of studies in mice exposed for 10 minutes to concentrations of chlorine varying from 0.7 to 38.4 ppm, suggested that the respiratory rate was decreased by 50% at 9.3 ppm and by 10% at 1.1. ppm (Barrow et al., 1979). Jiang et al. (1983) studied the acute effects of chlorine gas at concentrations of approximately 9-11 ppm (the concentration expected to reduce the respiratory rate by 50%) in rats exposed for 6 hours/day for 1, 3, or 5 days. Degenerative changes occurred in the olfactory and respiratory epithelia of the nasal passages with loss of respiratory and olfactory cilia.

Barrow et al. (1979) exposed rats to 1, 3, or 9 ppm chlorine gas for 6 hours/day, 5 days/week for 6 weeks (30 days) and reported decreased body weights in both sexes at 3 and 9 ppm and in females at 1 ppm. Pulmonary, renal, hepatic and gastrointestinal lesions were observed in both sexes at 9 ppm. The severity of the pulmonary lesions were similar at 1 and 3 ppm and other changes were less extensive. Three of 20 rats died at 9 ppm. Females exposed at 1 or 3 ppm had histological evidence of focal inflammation of the nasal turbinates and peribronchiolar lymphoid infiltration. A slight to moderate inflammation of the respiratory bronchioles and alveolar ducts was observed in males exposed to 1 or 3 ppm. Rhesus monkeys were exposed to concentrations of 0.1, 0.5 or 2.3 ppm of chlorine gas, 6 hours/day, 5 days/week for one year (Klonne et al., 1987). The monkeys exposed to 2.3 ppm exhibited signs of ocular irritation during exposure and superficial conjunctival irritation at the end of the study. Minor lesions in the respiratory epithelium of the nasal passage of animals exposed to 2.3 ppm was the most significant change. They concluded that chlorine was an upper respiratory irritant in monkeys at the highest exposure studied and that the monkey appeared less sensitive than the rat to chlorine when inhaled.

Female rats were exposed to chlorine (HOCL) in the drinking water for 2.5 months prior to mating at concentrations of 1, 10, or 100 mg/L and throughout gestation (Abdel-Rahman et al., 1982). Chlorine was slightly embryotoxic but not teratogenic at the highest concentration. A study to evaluate the induction of chromosomal aberrations and micronuclei in bone marrow of CD-1 mice after oral administration of chlorine (hypochlorite and hypochlorous acid) for 5 days were negative (Meier et al., 1985). However, oral administration of chlorine to mice (pH 8.5 where hypochlorite predominates) at doses of approximately 4 or 8 mg/kg/day for 5 days induced significant increases in spermhead abnormalities.

Summary and Conclusions

Certainly from the various studies that have been made of people that have been exposed to chlorine other than low concentrations, it seems that persons consistently show pulmonary edema, dyspnea, coughing, and rales (Table 4). In addition, it appears that some of the measures of pulmonary function were adversely affected and were maintained for some period of time (many months). Also, from the data of Leube and Kreiter (1971 in NIOSH, 1976), there appeared to be cardiac changes which were important.

It should also be noted at this time that the American Conference of Governmental and Industrial Hygienists (ACGIH, 1980) have set a TLV for chlorine of 1 ppm and a short time exposure limit of 3 ppm. Examination of the data in Griffiths and Megson (1984) suggest that 30 ppm is the minimum value to cause coughing and that 40 to 60 ppm may be dangerous after 40 to 60 minutes of exposure. Zielhuis (1970) on the other hand, feels that any concentration above 30 ppm is dangerous and possibly lethal after 30 minutes. Withers and Lees (1985a; 1985b) have presented perhaps the most complete analysis of the effects of chlorine exposure. They have attempted to take into account vulnerable populations as well as differences in inhalation rates depending upon activities. They have assumed that normal physical activity would lead to an inhalation rate of 12 liters per minute compared to 6 liters per minute at the base level of activity and that the level of oxygen consumption is also going to be greater. This level of activity basically increases the toxicity of chlorine by a factor of two. For example, they estimated that exposure to a concentration of 250 ppm for 30 minutes would cause 10% mortality. For more active populations they estimated 125 ppm. In the first case, this calculates to a $CT^{0.5}$ (concentration X $time^{0.5}$) of approximately 1370 ppm minutes, and in the latter case 685 ppm minutes. If the time is shortened to 10 minutes of exposure for a level of physical activity that would correspond to the second group above, the concentration expected to give 10% mortality was estimated to be 270 ppm with a $CT^{0.5}$ of 685. It would require a concentration of 395 ppm to produce the same value for a two-minute exposure. Intuitively this is too high for even emergency use since it is based on presumed mortality. However, it does seem that a value between 25 and 30 ppm could be tolerated with minimal effects for a 2-minute exposure based on the human and animal data suggesting that exposures greater than this may cause pulmonary edema. We are therefore recommending 2-minute limit of 30 ppm for healthy workers with good pulmonary function.

Although some tearing may occur at concentration lower than 30 ppm, it would clear rather quickly after exposure without causing temporary blinding or permanent scarring. The potential development of pulmonary edema, which would be expected to occur at concentrations greater than 30 ppm, is the limiting criteria for recommending a limit of 30 ppm.

Identification

Chemical Name: Trifluoromonobromomethane (Halon 1301); diflurobromochloromethane (Halon 1211)
CAS Number: Halon 1301-75-63-8; Halon 1211--353-59-3
Molecular Formula: Halon 1301 $Br F_3 C$
Halon 1211--$Br F_2 Cl C$

Chemical and Physical Properties of Halon

Physical Appearance: Colorless gases
Odor Description: Halon 1301--odorless
Halon 1211--faintly sweet

Conversion Factors: 1 mg/m^3 = 0.164 ppm Halon 1301
1 mg/m^3 = 0.148 ppm Halon 1211
1 ppm = 6.10 mg/m^3 for Halon 1301
1 ppm = 6.76 mg/m^3 for Halon 1211
Boiling Point: Halon 1301 = -57.75°C
Halon 1211 = -4°C
Vapor Density: Halon 1301 - 5.0 relative to air
Halon 1211 - 5.7 relative to air

Stability and Reactivity: Stable except at high temperatures; both halons undergo decomposition above 482°C (900°F)
Solubility in Water: 300 ppm at 77°F (Halon 1301)
Toxicity: Halon 1301 - inhalation/rat LC_{50} = 2300 ppm/1 hr
Halon 1211 - inhalation/rat LC_{50} = 200,000 ppm/15 min
- inhalation/rat LC_{50} = 31,258 ppm/4 hr

Current Exposure Guidelines

Halon 1301

PEL	1,000 ppm
TLV-TWA (8 hr)	1,000 ppm
TLV-STEL (15 min)	1,200 ppm
IDLH	50,000 ppm
EEGL	25,000 ppm

Recommended Two-Minute Exposure Limit

Halon 1301 - 5%
Halon 1211 - 2%

General

Halon is an abbreviation for halogenated hydrocarbons which are hydrocarbons with hydrogen atoms replaced with atoms from the halogen series, fluorine, chlorine, bromine or iodine. The U.S. Army Corps of Engineers has established a logical series of numbers (1211, 1301 etc.) for quick and convenient identification of the halon series. The first digit represents the number of carbon atoms in the molecule, the second the number of fluorine atoms, the third the number of chlorine atoms, the fourth of bromine atoms and the fifth the number of iodine atoms (van Stee, 1974). Although a number of halon agents have been used as fire extinguishing materials, the most commonly used are Halon 1211 and Halon 1301, bromochlorodifluoromethane and bromotrifluoromethane, respectively. There has also been interest in some other halons such as Halon 1011, but in general these have not been as widely used as Halon 1301 and Halon 1211.

Both halons can undergo decomposition upon exposure to a flame or to a hot surface above approximately 900°F (482°C). In the presence of available hydrogen such as from water vapor or the combustion itself, the main decomposition products are the halogen acids (HF, HBr) and free halogens (BR_2, F_2, Cl_2) with small amounts of carbonile halites (COF_2, $COBr_2$). The decomposition products of Halon 1301 and Halon 1211 have characteristic sharp acrid odors, even in concentrations of only a few parts per million. The characteristic odor provides a built-in warning system for the agent, but at the same time creates a noxious irritating atmosphere for those who must enter the hazard during or following the fire.

The amount of halon that can be expected to decompose in extinguishing a fire depends on a large extent on the size of the fire, the concentration of halon vapor, and the length of time the agent is in contact with flame or heated surfaces above 900°F. For example, extinguishing a 25 sq ft heptane fire in a 10,000 cubic-foot enclosure within 0.5 of a second produced only 12 ppm of HF. A similar test having an extinguishment time of 10 seconds produced an average HF level over 250 ppm of a 9 minute period. In a similar type of experiment, two heptane fires were burned in a 2.5 square foot tray in a 25,000 cubic-foot room. The first fire was extinguished by Halon 1211 in 10 seconds. When the air was analyzed, it was found to contain 50 ppm of HCl plus HBr, 10 ppm of HF, 2.5 ppm of Cl_2 plus Br_2. F_2 was not detected meaning that it was present in less than 0.25 ppm (National Fire Protection Association, 1987). It needs to be recognized that these decomposition products are toxic in their own right and may contribute to the refinement of limits of exposure based only on the halon themselves.

General Biological Effects

The major effects of the halons appear to be mediated through the nervous system. Light headedness, paresthesia, and feelings of impending unconsciousness have been reported by human volunteers. Loss of equilibrium and consciousness as well as increased cardiac excitability has been noted in experimental animals. The pitch of voices is also lowered because of the high density of the halons. For summaries of studies on halon, the reader is

referred to van Stee (1974), Reinhardt and Reinke (1972), and the toxicity review package prepared by Graham at DuPont's Haskell Laboratory (1981).

Human Studies

In his review of the toxicology of halons, van Stee (1974) refers to the study of Hine et al.(1968), those of the Haskell Laboratory, and of Call (1973) all of whom have conducted human exposures. Hine et al. (1968) reported that exposure to 10 - 15% Halon 1301 decreased human performance in 5 of 6 psychomotor tasks. The volunteers in this study also reported subjective changes in sensory perception. Call (1973), using volunteer male military personnel 20-35 years of age, exposed the subjects to either 4 or 7% Halon 1301 for 3 minutes in a hypobaric chamber maintained at the equivalent at sea level, 5,000 feet or 18,000 feet altitude. Electrocardiograms were obtained during and after exposures. Physical examinations and pulmonary function measurements were also taken. Call found that both 4 and 7% halon in the atmosphere were tolerated fairly well although 6 of 8 subjects exposed to the 7% level had subjective symptoms of dizziness, faintness or drowsiness. Three of the subjects reported the symptoms during each exposure of the 7% levels at all three simulated altitudes. ECG's obtained during or after the exposure to halon showed no effect directly attributed to the exposure or to the assimilated altitude used. However, there was an increase in reaction time of the subjects when they were performing a complex reaction time test. This increase was similar whether the subjects were breathing 4% or 7% Halon 1301. In another task, the Mays tracking task, several measures were taken. One was the time required to perform the task; two, the number of errors committed, three, the time spent in error; and four, average time per error. None of these measures were affected by the exposure to the halon. Interestingly enough however, the numbers of errors on the Mays tracking task was found to be significantly increased by exposure to simulated altitudes.

Another study by Smith and Harris (1973) also exposed volunteer subjects to 4 or 7% Halon 1301. Their tests were conducted at cabin pressure altitudes from sea level to 30,000 ft. The exposures were for 3 minutes and continuous ECG monitoring was carried out for 5 minutes after the discharge. No adverse biomedical signs were noted upon examination of subjects following the exposures and there was no indication on the ECG's of cardiac arrhythmias or any other adverse effects.

In the Haskell laboratory study, exposures up to 10% of Halon 1301 were conducted. Light headedness, paresthesia, and diminished performance during exposure were reported. Similarly, Clark (1972) exposed human volunteers to 4 or 5% of Halon 1211; he also reported a feeling of light headedness and paresthesia at both levels of exposure. There were also signs of CNS depression in persons exposed to the 5% level.

There have not been controlled exposures of human volunteers to Halon 1011. However Rutstein (1962) published 3 case reports which involved accidental human exposures to Halon 1011. The absorbed doses could not be estimated in these studies. However, the subjects initially lost equilibrium and then consciousness. Svirbely et al. (1947) have reported a similar loss of consciousness with Halon 1011 using mice; the LD_{50} was 2.9%.

Hine et al. (1968) have also reported feelings of impending unconsciousness during exposure of human volunteers to 15% Halon 1301. There has been much attention directed toward the potential problem of cardiac arrhythmias caused by exposure to halons. In particular, there seems to be a sensitization of the heart in the presence of epinephrine, thus several studies have been performed in which experimental animals have been exposed to the halon of interest and then been given large doses of epinephrine. Under these circumstances a large increase in the incidence of cardiac arrhythmias occurs. However, it is not clear that the situation in man is modeled very closely by this approach. Hine et al. used a slightly different approach by exposing dogs to Halon 1301 and then increasing endogenous epinephrine and other stressor materials by frightening the dogs with stroboscopic lights and noise. No dog in that study developed ventricular fibrillation. van Stee and Back (1969), however, did report the death from ventricular fibrillation of one dog exposed to 40% Halon 1301 and not given any additional drugs. Marked excitement was shown by the experimental animal. Hine et al. (1968) looked at ECG activity during exposure of human volunteers to concentrations of 5, 10 or 15% Halon 1301. A-V dissociation and premature ventricular contractions were recorded to exposure to the highest concentrations (maximum 16.9%).

Exposure to fluoroalkanes often caused a reversible concentration-dependent fall in mean arterial blood pressure. Rhesus monkeys exposed to either 80% Halon 1301 or 12% Halon 1211 showed a decreased blood pressure, although they developed a markedly elevated diastolic pressure.

Other studies by van Stee and colleagues have shown that coronary sinus blood oxygen content is increased during exposure to Halon 1211 and Halon 1011 but not by exposure to Halon 1301. The significance was not explained but did suggest that individuals who had a coronary reserve limited by atherosclerosis or other disease and who might be suffering from intermittent amounts of angina pectoris could be adversely affected by exposure to relatively high levels of Halon 1211 or Halon 1011. Fortunately, exposure to Halon 1301 did not seem to affect the coronary venus blood oxygen levels.

The solubility of Halon 1301 in fat is not very high and thus its residence half-time in the body is relatively short. Halon 1211 and Halon 1011 are more lipid soluble, and residual effects can be seen after cessation of exposure to these materials. For example, venous partial pressure of oxygen remained elevated for at least 30 minutes after the end of exposures to Halon 1211 and Halon 1011, a finding not observed following exposure to Halon 1301. van Stee and colleagues have estimated that elimination half-time for Halon 1301 was approximately 1-2 minutes. The paper by Griffin, Byard and Coulston (1972) in which they looked at the levels of Halon 1301 in rat blood following a single 50 minute exposure, seems to generally substantiate that conclusion. For example, their data show that blood levels of 5.6 micrograms per gram immediately following exposures fell to 0.62 micrograms per gram by 15 minutes post exposure and 0.35 micrograms per gram by 60 minutes post exposure. It further fell to approximately 0.05 micrograms per gram by 2-4 hours. van Stee did not measure the elimination half-times for Halon 1211 or Halon 1011 but estimated that they would be much higher than for Halon 1301, a suggestion in keeping with their finding that the Halon 1211 and Halon 1011

were much more soluble in an *in vitro* olive oil test than was Halon 1301 (van Stee, 1974).

van Stee used data from a number of studies to calculate exposure criteria for Halons 1301, 1211 and 1011. He arrived at the conclusion that Halon 1011 was approximately 30 times more toxic than Halon 1301 and Halon 1211 was approximately 5 times more toxic. He calculated that 3-5 minute exposure to 7% Halon 1301, 1.2% Halon 1211 or 0.23% Halon 1011 would have little or no effect. If the exposure were lengthened to 20 minutes, values of 5, 0.8 and 0.17%, for Halons 1301, 1211 and 1011 respecitvely, could be expected to produce little or no effect. A 20-minute exposure to 10, 1.7 and 0.33% for the three halons would be expected to produce a moderate effect. A moderate effect would be defined as a definite feeling of light headedness that might be perceived by some individuals as symptom of impending unconsciousness. Tingling sensations or paresthesia would be expected to be experienced by some. Heart rate would be expected to accelerate moderately, but few individuals would be expected to develop serious electrocardiographic abnormalities.

The following reports may have some bearing on setting limits for halon. A report by Sass-Kortsak, Holness and Stopps (1985) reported that the accidental discharge of a Halon 1301 total flooding fire extinguishing system resulted in dense fog filling a room. This fog hindered visibility to an extensive degree and made it difficult for people to exit the room. This observation was rather unexpected on the basis of the physical characteristics of Halon 1301 and may reflect an unusually high relative humidity as well as the presence of some material in the ducts through which the halon passed. There were also some subjective complaints of abnormal feeling by workers that were exposed to the Halon 1301. These included a higher frequency of light headedness, headache, nasal complaints and disorientation. These workers also noticed the pitch of their voices was lower in the initial period of exposure to the halon. The light headedness is probably to be expected since the halon is a central nervous system depressant even though the concentrations to which these workers were exposed was probably below about 5%. Certainly the change in the pitch of the voice is well recognized and is due to the high density of the halon gas relative to air.

Probably some of the feelings that accompany exposure of workers to the halon in the foregoing study could be avoided by training or educating the workers prior to a discharge occurring. They should be aware that there could be a loud noise and turbulence that is associated with the discharge of such a system. These alone may produce anxiety and disorientation for those unaware to what is happening.

Animal Studies

Beck, Clark and Tinston (1973) performed studies with Halon 1211 using rats, mice, guinea pigs, dogs and a monkey. They used exposure concentrations from 5 to 30% in their studies with rats, mice, and guinea pigs. Animals were exposed to 6% Halon 1211 in a small chamber. After 12 minutes rats and mice exhibited slight tremors while various slight tremors developed in the guinea pigs after 21 minutes. When rats were exposed to 30% Halon 1211, marked

tremors of the head and limbs occurred within 2 minutes and convulsions within 5 minutes. However, on removal of animals from the atmosphere recovery was rapid, usually within 1 or 2 minutes. Even after exposure to 30% Halon 1211, the rats were apparently normal within 5 minutes. When death occurred, it did so following a period of profound depression of the central nervous system. A monkey was exposed to a nominal concentration of 8.8%; however, this concentration was not attained until 15 minutes after beginning exposure due to the size of the chamber and flow rate. Slight tremors and loss of balance occurred after 10 minutes of exposure when the measured concentration was 8.5%. Severe tremors occurred at 15 minutes of exposure. The monkey required about 15 minutes to return to normal after exposure. However, this may have been due in part to the characteristics of the chamber which did not permit an immediate replacement of the atmosphere by fresh air. Exposure of dogs to 1% Halon 1211 for 5 minutes was without effect. Exposure of 2% Halon 1211 caused an increase of heart rate of approximately 20% and a slight depression of the T-wave of the ECG. Again the changes were rapidly reversed on exposure to fresh air. Six dogs were exposed to 5% 1211 for 30 minutes with their ECG's monitored continuously by radiotelemetry. Trembling of all limbs occurred within 3 minutes of the start of the exposure. This became progressively more marked until after 15 minutes there were marked tremors with head shaking and loss of balance. The dogs staggered and often fell when they turned around in the chamber. However, there was variability in the response. One dog only trembled slightly during the 30 minute exposure whereas one dog had such severe convulsions that exposure was stopped after 7 minutes. One dog started convulsing 26 minutes after start of exposure. During the convulsions, several ventricular atopic beats were noted on these ECG. A few seconds later ventricular fibrillation developed and the dog died. The heart rate always rose during the 30 minute exposure but with exception of the dog that developed ventricular fibrillation, there were no marked ECG changes. Dogs also rapidly recovered from the effects of the exposure and within one minute of cessation of exposure had stopped trembling and were able to walk normally. Three dogs were exposed to 7% Halon 1211 in a larger exposure chamber and they started trembling within 2 minutes, with the tremors becoming progressively more severe as the exposure continued. One dog did not progress beyond the stage of marked tremors even though the exposure continued for 30 minutes. But the other two dogs had convulsions after 15-20 minutes. There were no marked ECG changes during exposure to 7% Halon 1211, but the heart rate did rise markedly. Convulsions were always associated with a burst of tachycardia, the heart rate rising as high 350 beats per minute. Recovery from the exposure was rapid and uneventful. Within 2 minutes of the end of exposure the dogs were apparently normal and the heart rate had fallen to just over 100 beats per minutes. None of the 3 dogs died and none showed ill effects during the subsequent four weeks. This study also included taking blood samples for measurement of Halon 1211. The data showed that the blood values rose rapidly during the first minute of exposure and more slowly thereafter. But when exposure was terminated, there was fairly rapid initial fall in blood levels followed by a more prolonged decline. Examination of the curve of blood concentrations suggest that the initial phase involved an elimination half-time of approximately 2-3 minutes.

These same authors (Beck et al., 1973) exposed rats to 10,000 ppm Halon 1211, 6 hours per day, 5 days per week for 3 weeks. Animals were weighed

daily and observed for toxic signs and abnormal behavior. Food and water consumption was measured before and during the experimental period. Immediately after the last exposure, the animals were placed in metabolism cages and their pooled urine was collected in cool containers for 18 hours. Blood was taken from the tail vein for hematologic examination and the rats were killed and subjected to detailed post-mortem and histopathologic exam. Exposure to the 10,000 ppm resulted in a reduced response to noise and slight lethargy within 3 hours of the start of the first exposure. The rats recovered rapidly when they were exposed to fresh air in their cages, however. Similar patterns were followed during each exposure but the severity did not increase as the experiment progressed. Body weight gains were normal in males but lower than controls in females. Hematologic exam of the rats at the end of the experimental period showed no change in hemoglobin content or packed cell volume. Biochemical analysis of the urine did not reveal any changes and blood urea was within control values. Gross and histopathologic examination of the lungs, liver, kidney, spleen, heart, thymus, intestines and gonads showed no remarkable effects.

Other animals were exposed to 3300 ppm of Halon 1211. This concentration did not result in any toxic signs. Rats ate and drank and gained weight normally. No changes were found in hematology or upon histopathologic examination of the above organs.

These authors also examined the effect of exposure to Halon 1211 on cardiac sensitization. Although the animal numbers were small, in general, brief exposures at the higher concentrations of 8 to 10% and longer exposures at levels below that were required to sensitize the animals. They were also able to show that exposure to Halon 1211 did not induce a lasting changes in the heart relative to sensitivity to epinephrine-induced arrhythmias.

Mullin, Reinhardt and Hemingway (1979) reported on a study of the effects of Halon 1301 on cardiac sensitization to epinephrine. Dogs were exposed by inhalation to concentrations from 5 to 20% and after 5 minutes of exposure were given epinephrine by interveneous injection. ECG's were recorded. Serious cardiac arrhythmias were produced with concentrations of 7.5% or greater. These authors also examined the blood concentrations of Halon 1301 during exposure. They found that the mean blood concentrations at equilibrium were directly proportional to the airborne concentrations. At a concentration of 5% in air arterial blood was 19.2 micrograms per milliliter while venous was 13.6 micrograms per milliliter. At 7.5% of Halon 1301, arterial values rose to 30.6 micrograms per ml with venous values being 28.4 micrograms per ml. At 10% the arterial value was 40.2 micrograms per ml and the venous concentration was 32.1. The data also showed that the blood values fell very rapidly upon cessation of exposure.

Summary and Conclusions

Both humans and experimental animals appear to tolerate relatively high concentrations of Halon 1301 (Table 6 and 7), lesser amounts of Halon 1211 and relatively low amounts of Halon 1011. For example, the data of Engibous and Torkelson (1960) as presented by van Stee (1974) indicate that rats and guinea pigs can tolerate atmospheres containing 60% Halon 1301, 20% Halon 1211, and

2% of Halon 1011 for up to one hour. Work by van Stee and his colleagues at the Aerospace Medical Research Laboratory at Wright-Patterson found that rats and guinea pigs can tolerate 80, 15 and 1% concentrations, respectively.

The National Fire Protection Association in their national fire codes for 1987 have essentially derived the following exposure limits for Halon 1301 and Halon 1211. Their statement is "It is considered good practice to avoid all unnecessary exposure to Halon 1301 and to limit exposure to the following times, 7% and below, 15 minutes; 7-10%, one minute; 10-15%, 30 seconds; and above 15%, prevent exposure. Furthermore, anyone suffering from the toxic effects of Halon 1301 vapor should immediately move or be moved to fresh air. Moreover, the use of epinephrine or similar drugs should be avoided because they could produce cardiac arrhythmias including ventricular fibrillation."

After examination of the above data it would appear that a 2-minute exposure to approximately 5% Halon 1301 could be tolerated and still permit workers to don safety apparel. Furthermore, it would appear that exposure limits for Halon 1211 should be set at approximately from 2 - 3 fold lower than those for Halon 1301. Thus, an exposure level for 2 minute exposure should be no more than approximately 2%. The potential for cardiac arrhythmia and the risk of decreased ability to escape because of dizziness or disorientation at greater concentrations of halons were the criteria for these limits.

SULFUR DIOXIDE

Identification

Chemical Name: Sulfur dioxide
CAS Number: 007446095
Synonyms: Sulfurous anhydride, sulfurous oxide

Chemical and Physical Properties

Physical State and Appearance: Colorless gas
Odor Description: Characteristic, pungent, irritating
Molecular Weight: 64.06
Conversion Factors: 1 mg/m^3 = 0.38 ppm
1 ppm = 2.62 mg/m^3
Boiling Point: -10°C
Vapor Density: 2.26 relative to air
Stability and Reactivity: Fairly reactive
Solubility in Water: 22.8 g/100 ml at 0°C
Toxicity: Inhalation/hamster - TCLo = 4 ppm; inhalation/rat - LCLo = 1000 ppm

Current Exposure Guidelines

PEL	=	5 ppm
TLV-TWA (8 hrs)	=	2 ppm
TLV-STEL (15 min)	=	5 ppm
IDLH	=	100 ppm
EEL (10 min)	=	30 ppm
(30 min)	=	20 ppm
(60 min)	=	10 ppm
(24 hr)	=	5 ppm
NRC-2 min	=	5 ppm

Recommended Two-Minute Exposure Limit

100 ppm

General

Sulfur dioxide is widely used industrially in the manufacture of sodium sulfite and as an intermediate in the manufacture of sulfuric acid. It is also used in refrigeration, bleaching, fumigating and preserving operations as well and as an antioxidant in the melting, pouring and heat treatment of magnesium (Patty, 1963).

General Biological Properties

Sulfur dioxide, due to its high solubility in water, is largely absorbed from nasal passageways. Thus, nose-only exposures produce less coughing and irritation of the throat and chest than does mouth breathing. However, at sufficiently high concentrations, SO_2 will irritate the nose and throat and

produce rhinorrhea, choking, sneezing and coughing. Eye discomfort and lacrimation may occur. As with other irritant gases, continued exposure to low levels can result in acclimation of the subject responses (NIOSH, 1974b).

Human Studies

Report of possible harmful effects from sulfur dioxide exposure date back to complaints of workers in the textile industry in France in 1821. They complained that sulfur dioxide in the bleaching of textiles caused an irritant effect on them. This was followed by a report from Germany in which workers were exposed to SO_2 in the process of drying sugar beets (Lehmann, 1893, NIOSH, 1974b). In this case, SO_2 was reported to cause pneumonia, gastritis, enteritis and even vaginitis. Finally, in 1893 the first measurements of occupational and environmental concentrations of SO_2 were reported from Germany. In this case, certain operations in the bisulfite paper-making industry contained from 6-30 ppm SO_2. The workers, alleged to have the appearance of good health, ignored any effect. However, the author of the report, Dr. Lehmann and his two assistants, unaccustomed to SO_2 reportedly experienced nasal irritation after 10 minutes exposures to 6.5 and 11.5 ppm. They definitely found 30-57 ppm disagreeable. This as well as evidence obtained later indicates that acclimatization to subjective effects sulfur dioxide can occur (Kehoe, 1932; Anderson, 1950).

In 1930 Rostoski (NIOSH, 1974b) reported on the acute effects of exposure to SO_2 following the explosion of a digester vessel. There were 18 workers involved in the accident. One died in 10 months and another 15 months later from intercurrent pulmonary infection. Three years later 8 others were still incapacitated by radiologically confirmed chronic bronchitis and emphysema. Those that returned to work complained of dyspnea and bronchial catarrh. There is some question, however, if all of these effects were due to SO_2 or whether they were due to wood and its products which were in the digester.

Charan et al. (1979) reported on the results of an accident that occurred in a paper mill in which five previously healthy individuals were acutely exposed to very high, but unknown, concentrations of SO_2. Two of these individuals died almost immediately and the 3 survivors were extensively examined over a period of 116 days for changes in respiratory function. The two persons with the highest exposures to SO_2 that died immediately after exposure were noted to have pink frothy secretions at the mouth. They were 56 and 59 years of age and were nonsmokers with no prior medical problems. At post mortem examination, the predominant abnormalities were confined to the upper and lower respiratory tract. Lungs of both subjects were heavy, weighing in excess of 3000 grams and the airways were filled with pink fluid. Histologic exam was similar for both subjects. The mucosal surface of the large airways showed extensive sloughing with complete denudation at several places. Mucous cells were normal. There was no disruption of the alveolar walls and alveolar spaces were filled with protein rich edema fluid and in some cases areas of hemorrhage. The acute symptoms in the three survivors were identical including irritation and soreness of the eyes, nose, mouth and throat, tightness in the chest and intense dyspnea. Their eyes revealed

severe conjunctivitis and superficial corneal burns. The pharyngeal mucosa was hyperemic but no ulcerations were seen. Examination of the chest revealed markedly decreased breath sounds, diffuse rales and rhonchi. X-rays of the chest were essentially normal. Mild hypoxia was seen in all three subjects. Two of the patients developed airway obstruction with small changes in pulmonary function.

Most concern about exposure to extremely high levels of SO_2 is that asphyxia will most probably result. However, if death does not result from asphyxia, a chemical bronchial pneumonia with bronchiolitis obliterans may develop which may be fatal after an interval of several days. A report by Galea in 1964 (NIOSH, 1974b) described an incident in a paper pulp plant where a worker was exposed to a high but undetermined concentration of SO_2 for 15 to 20 minutes. This worker died 17 days later.

There are also data in the literature that suggest that high exposure to SO_2 may cause a person's lungs to be more susceptible to bacterial infections. These bacteria may establish a suppurative bronchitis secondary to the inflammatory effects of the sulfur dioxide.

In general, chronic exposures to SO_2 are of more concern than acute exposures. As noted previously however, exposures in industrial situations often occur with exposures to other substances such as sulfuric acid aerosols, metallic oxides, other gasses or particulate material. However, there have been reports of chronic exposure to pure sulfur dioxide gas which at one time was used as a refrigerant. Kehoe et al. in 1932 (NIOSH, 1974b) reported a study of 100 men having a mean employment exposure of 3.8 years (47 employees had from 4-12 years employment exposure) to atmospheric concentrations averaging 20-30 ppm, with a range from 5-70 ppm. These levels prevailed at the time of the study, but prior to 1927 the SO_2 levels had been much higher averaging 80-100 ppm. Kehoe questioned these men plus 100 control subjects relative to the length, and the nature of exposure to SO_2. He also obtained urinalysis and chest x-rays.

Initial symptoms of SO_2 exposure were confined to the respiratory tract and consisted of irritation of the upper respiratory tract, coughing, epistaxis, constriction in the chest and hemoptyses. Other symptoms included morning cough, prolongation of common colds and expectoration. A statistically significant higher incidence of nasopharyngitis, alteration in the senses of smell and taste and increased sensitivity to other irritants was noted. There was a significantly higher incidence of increased fatigue, dyspnea on exertion and longer duration of colds (although the frequency was no greater). Increased acidity of the urine was common in the exposed group. However there were no significant differences in the incidence of chest abnormalities as noted on x-rays.

Acclimatization occurred in 80% of the exposed group. The mean time necessary for acclimatization was calculated to be 2.84 months with a large standard deviation. Acclimatization was considered to be an acquired ability to withstand the customary basic exposure without experiencing a notable intensity of initial symptoms. In general, there seems to be a high degree of

adaptability among people to regular moderate exposures to SO_2. It also appears that there were no serious permanent types of damage occurring.

Anderson (1950 in NIOSH, 1974b) reported on the effects of sulfur dioxide exposure in Iranian oil refinery workers. Usual exposures in this industry ranged from 0-25 ppm. However, levels between 60 and 100 ppm had been recorded during times when plant maintenance was relatively low. No significant differences were reported between exposed and nonexposed controls in weight, systolic blood pressure or chest x-ray findings. However, no mention was made of pulmonary irritation, coughing, nasal irritation etc. which are often associated with SO_2 concentrations at these levels.

Skalpe in 1964 (NIOSH, 1974b) reported on a study of workers in four different paper pulp mills in Norway, a study prompted by the worker complaints of chronic cough. Sulfur dioxide concentrations ranged from 2-36 ppm; certain of the workers had experienced concentrations of up to 100 ppm, although usually for relatively short periods of time. During these periods, pulmonary irritation was so intense that gas masks had to be used. Mean duration of employment exposure was 6.8 years for subjects under 50 years of age and 20.3 year for those over 50 years. It was found that there was a significantly higher frequency of cough, expectoration, and dyspnea on exertion than was found in the control group. The average maximal expiratory flow rate was also significantly lower in exposed groups than in the controls for men under 50 years of age. Beyond 50 years of age there was no significant difference between control and exposed. Vital capacity values also showed no differences and cigarette smoking did not appear to have a significant influence.

Although there are no studies that implicate SO_2 as a complete carcinogen in man, it has been postulated that SO_2 may act with other chemicals in the work environment to enhance their carcinogenic effects. Lee and Fraumeni (1969 in NIOSH, 1974b), studying smelter workers, found a higher incidence of lung cancer in workers exposed to both arsenic and SO_2 than in those exposed to either material alone. Laskin et al. (1970 in NIOSH, 1974b) obtained evidence for a promoting effect of SO_2 in rats treated with benzo[a]pyrene. Peacock and Spence (1967 in NIOSH, 1974b) also found that exposure to SO_2 accelerated tumor development in tumor-susceptible mice.

There have also been studies on respiratory function in humans. Sim and Pattel in 1957 (NIOSH, 1974b) exposed volunteers to 50 ppm for 10 minutes or 5 ppm for 60 minutes. Of these volunteers 50% of the subjects experienced an increase in airway resistance of more than 20% above normal. This was accompanied by rhinorrhea and lacrimation. High pitched rales were noted over the larger bronchi for the 10 minute exposures and moist rales occurred over the lung periphery at the 60 minute exposures. At exposures to 30 ppm for 10 minutes or 5 ppm for 60 minutes little change was noted clinically or in lung resistance to air flow.

Andersen et al. (1974) studied the responses of 15 young men during 6-hour exposures to 1, 5, or 25 ppm SO_2. They examined nasal mucus flow rates, airway resistance and subjective responses to the SO_2. They found a significant decrease in nasal mucus flow rate during 5 and 25 part per million

exposures. This decrease was greatest in the anterior nose and in subjects with initially slow mucus flow rates. An increased nasal airflow resistance, and a fall in forced expiratory volume in one second and forced expiratory flow during the middle half of expired volume was found at all exposure levels. There was, however, no change in closing volume. Discomfort was proportional to SO_2 concentrations but never excessive. Subjects with initially slow nasal mucus flow rates experienced the greatest discomfort.

There are groups of people that need special consideration in an evaluation of the effects of SO_2. One such group has been designated as "hyper-reactors" by Burton et al. (1969 in NIOSH, 1974b). These are persons who appear to react to concentrations of SO_2 that in other persons elicit a much milder response. Burton et al. (1969 in NIOSH, 1974b) have estimated this group constitutes 10-20% of the healthy young adult population. A second group of particular concern is that of asthmatics (Balmes, Fine, and Sheppard, 1987; Linn et al., 1983a, 1983b, 1984a, and 1984b; Hackney et al., 1984; Rondinelli, Koenig and Marshall, 1987; Roger et al., 1985) which have been shown to be extremely sensitive to low concentrations of SO_2 (< 1.0 ppm). Asthmatics often develop wheezing, chest tightness, and dyspnea after exposure to 0.5 ppm. Increased specific airway resistance and bronchial constriction are produced by 0.5 to 1.0 ppm. These effects are exacerbated by exercise. A third group, which apparently is small, is characterized by a high skin sensitivity to SO_2. These individuals show skin eruptions and swelling of the eyelids, a response similar to that observed after an allergic response. Treatment with antihistamines appear to counteract the symptoms.

There have been a number of studies of exposure of persons to concentrations of 10 ppm or less, these kinds of studies have little application to the question of short term exposure limits.

Animal Studies

It is worthwhile to consider studies in which animals have been exposed to high levels of SO_2. However, in general, man is considered to be more sensitive than other mammals to the effects of SO_2 with the possible exception of the cat. Interestingly enough, the effect of SO_2 on all mammals is qualitatively the same, respiratory and mucus irritation and reflex bronchial constriction with increased airway resistance.

Reid (1963 in NIOSH, 1974b) exposed young rats to 300-400 ppm SO_2 for 5 hours per day, 5 days per week for 6 weeks. There was increase in mucin containing cells in the large bronchi and the cells were observed in peripheral bronchioles where they are not normally found. There was evidence of increased mucus secretion but no signs of increased invasions by infective microorganisms. This excess of mucin containing cells persisted for at least 3 months after the termination of exposure.

In a study by Alarie et al. (1972) cynomolgus monkeys were exposed 24 hr per day to 0.1, 0.6, 1, or 5 ppm of SO_2. Evaluations were made on the mechanical properties of the lung, distribution of pulmonary ventilation, diffusing capacity of the lung, arterial blood tension, lung histology, hematologic and blood biochemical indices and organ histology. No deleterious

effects could be contributed to concentrations of 0.1 - 1.28 ppm SO_2 even after exposures up to 78 weeks. However, in the 5 ppm group, an accidental over-exposure occurred for 1 hour to concentrations between 200-1,000 ppm SO_2; this occurred after 30 weeks of exposure to the 5 ppm concentration. Therefter this group was maintained on pure air for the remainder of the experimental period. The accidentally exposed group showed deterioration in pulmonary function, which persisted during the remaining 48 weeks of observation. Microscopic examination of the pulmonary tissues of this one group showed scattered foci of alveolar proteinosis and numerous alveolar macrophages. The alveolar walls were moderately thickened and infiltrated with histocytes along with moderate hyperplasia of the bronchial epithelia. Eight of the nine animals involved had moderate bronchiectasis. The major value of this study for purposes here is to indicate that permanent damage can occur to the respiratory tract upon exposure to high levels of SO_2.

A note should be added about the study by Bitron and Aharonson (1978) in which they looked at the effect of SO_2 at levels of 900, 1400, and 1900 ppm on the mortality of mice. They found at the higher levels that a number of deaths occurred at 5 to 10 days after exposure. They also found that at exposures of 900 ppm no deaths occurred in animals that were exposed for 42 minutes to these levels. In fact only a very low percentage died after exposure for 105 minutes to the 900 ppm. However after exposure to 1400 ppm for 23 minutes, approximately 20% of the animals died.

Summary and Conclusions

The present threshold limit value for SO_2 is 2 ppm or approximately 5 mg per cubic meter. The short term exposure limit is 5 ppm or approximately 15 mg per cubic meter. These standards are meant to prevent any damage to persons experiencing longer exposures to SO_2. However, it is obvious that there have been many workers exposed to levels of 10 to 30 ppm, and in many cases, short term exposures up to 100 ppm have been experienced. According to the NIOSH criteria document, SO_2 concentrations above 20 ppm have a marked irritant, choking, and sneezing effect. Acute exposures to concentrations of about 50 ppm will promptly cause irritation of the nose and throat, rhinorrhea and cough. Their conclusions are that these symptoms are sufficiently disagreeable that most persons would not tolerate them for more than 15 minutes. Certainly high exposures will cause reflex bronchial constriction and some increase in bronchial mucous secretion accompanied by increased pulmonary resistance to air flow.

Patty (1963) indicates that 50 - 100 ppm is considered the maximum permissible exposure limit for 30 - 60 minutes of exposure. He considered 400 to 500 ppm as immediately dangerous to life.

After consideration of the available data, part of which is summarized in Tables 8 and 9, we conclude that healthy individuals should be able to tolerate 100 ppm for two minutes and therefore recommend that level. It should be noted that our recommendation does not apply in the case of asthmatics and "hyperreactors".

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Table 1. Summary of Current Guidelines for Ammonia, Chlorine, Halon 1301 and Sulfur Dioxide (ppm)

	PEL	TLV	STEL	IDLH	ERPG-1	ERPG-2	ERPG-3	EEGL	NRC*
Issuing Organization	OSHA	ACGIH	ACGIH	NIOSH	AIHA	AIHA	AIHA	NAS	NRC
Exposure Period	8 hr	8 hr	15 min	30 min	1 hr	1 hr	1 hr	1 hr	2 min
Guideline									
Chlorine	1	0.5	1	25	1	3	20	3	15
Ammonia	50	25	35	500	25	200	1000	100	100
Halon 1301	1000	1000	1200	50000	--	--	--	25000	--
Sulfur Dioxide	5	2	5	100	--	--	--	10	5

*USAEC Regulatory Guide 1.78.

Table 2. Summary of Human Symptoms after Short-term Exposure to Ammonia

Exposure (ppm)	Exposure Time (min)	Observations
30 ppm	30 min	Tolerated by subject
32 or 50 ppm	5 min	Minimal response
30-50 ppm	10 min	Highly penetrating odor; little to moderate irritation
72 ppm	5 min	Some irritation
134 ppm	5 min	Lacrimation; nose, throat and eye irritation

Table 3. Summary of Animal Data for Ammonia

Exposure (ppm)	Exposure Time	Species	Effect
5,000-6,000	5-120 min	Guinea Pig	Profuse lacrimation; labored breathing
20,000-25,000	5-30 min	Guinea Pig	Respiratory irritation; blindness; death
8,800-13,000	10 min	Mouse	Respiratory irritation; death (100/80); survivors recovered; LC_{50} estimated to be 10,000 ppm
221	8 hr/d, 5 d/ 2k, 30 exp.	Rat Guinea Pig Rabbit Monkey Dog	No symptoms
375	90 d	Rat	Few symptoms
650	25 d, 65 d	Rat	Death in 32 of 51; death in 50 of 51; no deaths in other species
1000	8 hr/d, 5 d/ wk, 5 exp		Mild lacrimation and dyspnea
280	36 hrs	Pig	Respiratory distress and convulsions
61-145	5 wks	Pig	Nasal, lacrimal and oral secretions; coughing

Table 4. Summary of Human Symptoms after Exposure to Chlorine

Exposure (ppm)	Symptoms and Comments
0.2-0.4, 3.5	Odor threshold
1-3	Slight irritation
5	Severe irritation
15	Irritation of nose, throat, and eyes; coughing and tears
30	Restriction of breathing; chest pain
50	Pulmonary edema

Table 5. Estimates of LC_{50} in Animals Exposed to Chlorine for Short Time Periods

Length of Exposure (min)	Species	LC_{50} (ppm)	Author
10	Mouse	618	Silver
10	Mouse	302	Alarie
30	Mouse	127	Schlagbauer
55	Mouse	170	Bitron
60	Rat	293	Back

Table 6. Summary of Symptoms Observed in Humans Exposed to Halon Compounds

Concentration (percent)	Duration of Exposure	Effect
Halon 1301		
15	1 min	Severe dizziness and marked paresthesia. Increased heart rate and T-wave depression (EKG). Recovery was rapid and complete within 5 minutes.
10-15	--	Decreased performance; changes in sensory perception
12	1 min	Severe dizziness and mild paresthesia in 1/2 subjects. T-wave depression and increased heart rate.
10	1 min	No effect for the first 30 seconds followed by slight dizziness and paresthesia (1/2). Heart rate increased and T-wave was depressed in 1/2 subjects.
10	3-3.5 min	Light headedness increasing to near unconsciousness. Slight disturbance tests (balance and reaction time).
10	20 min	Euphoria (2/6), light-headedness (3/6), paresthesia (1/6), tinnitus (1/6), slight to moderate eye/nose irritation (2/6), pulmonary discomfort (2/6).
9	2 min	After 1 min of exposure dizziness was felt which increased in intensity. Increased heart rate.
7	3 min	Exposure during flight, no adverse effects.
7	3 min	Dizziness, faintness and drowsiness (6/8). Different altitudes had no effect on subjective symptoms.
7	3-3.5 min	Light-headedness.
6	3 min	Slight paresthesia, dizziness.
5	3-3.5 min	No effects observed.

Table 6. Continued

Concentration (percent)	Duration of Exposure	Effect
Halon 1301		
5	20 min	Euphoria (2/4), light headedness (2/4), pressure in the ears (1/4), or in the head (1/4), slight eye and nose irritation (1/4), slight pulmonary discomfort (1/4).
4	3 min	Dizziness, faintness and drowsiness (3/8).
3	3-3.5 min	No effects observed.
1	3-3.5 min	No effects observed.
Halon 1211		
4-5%		Light-headedness, CNS depression
Halon 1101		
Acute		Lost equilibrium and consciousness

Table 7. Effects of Halon Exposure in Animals

Exposure Level	Time	Species	Effect
Halon 1301			
5-20%	5 min	Dog	Cardiac arrhythmia (77.5%)
Halon 1211			
6%		Rat Mouse	Slight tremors
30%	2 min	Rat Mouse	Marked tremors, convulsions, death
8.8%	15 min	Monkey	Severe tremors, loss of balance
1%	5 min	Dog	No effect
2%	5 min	Dog	Increased heart rate
5-7%	30 min	Dog	Trembling (2-3 min), staggering, convulsions, ventricular fibrillation, death
10,000 ppm	6 hr/d	Rat	Lethargy (3 hrs), no hemoglobin or histopathological changes

Table 8. Summary of Symptoms Associated with Sulfur Dioxide Exposure to Humans

Exposure	Number Studied	Symptoms
Acute	18	Death, chronic bronchitis, emphysema
Acute	5	Death
Acute 15-20 min	1	Death
Chronic	100	Irritation of respiratory tract, coughing, epistaxis, chest constriction, nasopherynigitis
Chronic - 2-36 ppm - 100 ppm		Chronic cough Intense pulmonary irritation
50 ppm (10 min)		Increase in airway resistance
9 ppm (60 min)		Rhinorrhea, lacrimation
30 ppm (10 min)		No effect
5 ppm (60 min)		No effect
1,5,25 ppm (6 hrs)	15	Decrease in nasal mucus flow, increase in airflow resistance

Table 9. Effects of Exposure to Sulfur Dioxide in Animals

Exposure Level	Exposure Time	Species	Effect
300-400 ppm	5 hr/d 5d/wk 6 wks	Rat	Persistent increased mucus secretions
0.1, 0.6, 1	24 hr/d 78 wks	Monkey	No effects
5 ppm (+200-1000 ppm)	30 wks (1 hr)	Monkey	Decreased pulmonary function for 48 wks, hyperplasia, bronchiectasis
900 ppm	42 min	Mouse	No deaths
900 ppm	105 min	Mouse	Death
1400 ppm	23 min	Mouse	20% mortality

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10. SUPPLEMENTARY NOTES

11. ABSTRACT *(200 words or less)*

We have evaluated ammonia, chlorine, Halon (actually a generic name for several halogenated hydro-carbons), and sulfur dioxide for their possible effects during an acute two-minute exposure in order to derive recommendations for maximum exposure levels. To perform this evaluation, we conducted a search to find the most pertinent literature regarding toxicity in humans and in experimental animals. Much of the literature is at least a decade old, not an unexpected finding since acute exposures are less often performed now than they were a few years ago. In most cases, the studies did not specifically examine the effects of two-minute exposures; thus, extrapolations had to be made from studies of longer-exposure periods. Whenever possible, we gave the greatest weight to human data, with experimental animal data serving to strengthen the conclusion arrived at from consideration of the human data. Although certain individuals show hypersensitivity to materials like sulfur dioxide, we have not attempted to factor this information into the recommendations. After our evaluation of the data in the literature, we held a small workshop. Major participants in this workshop were three consultants, all of whom were Diplomates of the American Board of Toxicology, and staff from the Nuclear Regulatory Commission. Our preliminary recommendations for two-minute exposure limits and the rationale for them were discussed and consensus reached on final recommendations. These recommendations are: 1) ammonia-300 to 400-ppm; 2) chlorine-30 ppm; 3) Halon 1301-5%; Halon 1211-2%; and 4) sulfur dioxide-100 ppm. Control room operators should be able to tolerate two-minute exposures to these levels, don fresh-air masks, and continue to operate the reactor if the toxic material is eliminated, or safely shut down the reactor if the toxic gas remains.

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