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CONTENTS

ARSINE

AsH_3

TLV, 0.05 ppm (≈ 0.2 mg/m³)

Arsine is a colorless gas with a disagreeable garlic odor. It has a molecular weight of 77.93, specific gravity of 2.695, melting point of −113.5° C, boiling point of −55° C, a vapor pressure of ≥ 1 atmosphere and decomposes at 230° C. It is soluble in water, slightly soluble in alcohol and alkalies.

It is used in organic synthesis; as a military poison gas; doping agent for solid state electronic compounds.

Most cases of arsine poisoning do not result from the manufacture or use of the gas itself; rather they come from formation of arsine as a byproduct of a chemical reaction involving, in most instances, a base metal, an arsenic impurity, and an acid, or, rarely, a strong alkali.

The extreme acute toxicity of arsine is well known; 250 ppm for 30 minutes is fatal, and 3 to 10 ppm can cause poisoning symptoms in a few hours.[1] Nau[2] found that animals exposed three hours a day to concentrations between 0.5 and 2 ppm developed blood changes in a few weeks.

Published reports of occupational and other poisoning from arsine describe some 310 cases, 74 of them fatal, through 1959.[3] Several reports since 1960 record 28 cases, with two deaths, in this country[4-7] and abroad.[8-10] Typical cases resulted in hemoglobinuria, jaundice and hemolytic anemia.

While data on the actual concentrations causing acute intoxication are lacking, post event concentrations of 70 to 300 ppm (Morse and Setterlind, fatal cases,[11] 5 ppm Kipling and Fothergill[8] and 0.5 ppm Elkins[3] were reported. When urine samples were analyzed at early stages concentrations of arsenic ranging from 0.5 to 2 mg/L were the rule, but occasionally much higher values were found.

Bulmer *et al*[12] reported a number of cases of chronic poisoning, with severe anemia. Urinary arsenic levels averaged 2.3 mg/L, dropping to 0.66 mg/L three days later. Greig *et al*[13] recorded three relatively mild chronic cases with arsenic in urine levels of 0.5 mg/L.

In an extensive clinical study of 14 simultaneous cases of arsine poisoning,[14] tissue arsenic levels, determined by neutron activation analysis, indicated a total body content of arsenic one-third to one-half the lethal dose (300 mg), if one "assumes" that the poisoning action of the hydride follows to some extent that of the trioxide, none of the cases were fatal, but ranged from mild to very severe. Hemolysis and renal damage typified the toxic responses. The most severely poisoned had oliguria for 40 days and required hemodialysis 10 times, but hemolysis disappeared in a few days in all others. In four cases, renal function was impaired for a long time, but was finally restored.

Since arsenic appears to be excreted rather freely in the urine,[15] the levels found in the urine of intoxicated workers could have resulted from inhalations of concentrations below 1 mg/m³ or 0.25 ppm. The recommended TLV of 0.05 ppm (0.2 mg/m³) is the same as that of other inorganic arsenic compounds, which are considered substantially less toxic.

Other recommendations: Cook (1945) 1 ppm; Smyth (1956) and Elkins (1959) 0.05 ppm; USSR (1966) 0.1 ppm; Czechoslovakia (1969) 0.06 ppm.

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ASBESTOS

TLV, Appendix A1a— Recognized Carcinogen

0.5 fiber > 5 μm/cc — Amosite
2.0 fibers > 5 μm/cc — Chrysotile
0.2 fiber > 5 μm/cc — Crocidolite
2.0 fibers > 5 μm/cc — Other forms

According to recent authoritative mineralogical definitions,[1] asbestos is "1) A collective mineralogical term encompassing the asbestiform varieties of various minerals; 2) An industrial product obtained by mining and processing primarily asbestiform minerals."

For the purpose of considering a recommendation for a threshold value of asbestos dust in the workplace, only the second definition above is applicable. Although there are four types of natural mineral fibers that have been in industrial use, only three have been used in the United States: chrysotile, amosite, and crocidolite. The fourth, anthophyllite, is mined and used in Finland. Of the three types of asbestos that have been used in North America, Canadian chrysotile has formed 95% of all natural mineral fibers used, with amosite and crocidolite (both imported from South Africa) constituting the other 5%. It should be noted that chrysotile is classified as a serpentine mineral, whereas the other three types of asbestos are amphiboles.

It is now generally recognized that excessive inhalation of asbestos dust causes chronic inflammations of lung tis-

sue and pleural membranes as well as cancers. Whereas identification of asbestos dust as a cause of fibrosing inflammation of lung tissue occurred as early as 1907,[2] it was not until 1930 that a more definitive study by Merewether and Price[3] resulted in the regulations which greatly improved hygienic conditions in asbestos factories in the United Kingdom. The development of lung cancer in asbestos workers, first reported by Wood and Gloyne[4] in the U.K. in 1934 and by Lynch and Smith[5] in the U.S. in 1935, was not firmly established until 1955 by the publication of Doll[6] of a study of workers in an English asbestos textile factory, and in the United States by the paper of Selikoff *et al*[7] in 1964 concerned with cancers in insulation workers. In 1960 the relationship between the inhalation of asbestos dust and mesothelioma was demonstrated by Wagner *et al*.[8]

Asbestosis is a diffuse but nonuniform fibrosis of the lungs that is generally most severe in the basilar portions. As a result of the fibrosis some of the airspaces (alveoli) are not perfused with blood and alveoli that are perfused with blood may not be adequately ventilated because of stiff, thickened alveolar walls. The fibrosis makes the lungs less compliant, thereby increasing the energy requirement of breathing. There is increasing impairment in diffusion of gases leading to increasing breathlessness.

It is not uncommon to find thickening of the visceral pleura, sometimes very severe, by extension of the parenchymal inflammation. This causes an additional increase in the effort of breathing.

The parietal pleura may show patches of severe thickening, particularly over the diaphragm and the lower portions of the chest wall — resulting in the so-called pleural hyaline plaques. These may become visible in X-ray films of the chest — particularly, if they become impregnated with calcium salts. Such pleural plaques may develop from asbestos exposure in the absence of asbestosis. They cause no symptoms.

A study of the members of an asbestos insulators union revealed that deaths from lung cancer in this population was much greater than expected.[7] A later investigation by Hammond and Selikoff of a much larger number of these workers (17,800) showed that nearly all cancers occurred in cigarette smokers.[9] The conclusion of these authors was as follows:

> *"It seems clear, then, that lung cancer is uncommon among asbestos insulation workers who have no history of cigarette smoking, and that if the risk is increased such an increase is not great."*

The total lung cancer rate in this cohort of workers was 4.8 times the expected. The asbestos insulators who had a history of cigarette smoking had a lung cancer rate 5.4 times the expected rate; but compared to the lung cancer rate of the nonsmoking workers, the smoking insulators' lung cancer rate was 14 times greater.

All types of asbestos are known to cause the inflammatory changes in the lungs and pleurae described above and lung cancer. However, there is experimental and epidemiologic evidence that there may be differences in the potential of the different asbestos types to produce disease. Thus, it has been suggested that crocidolite has the greatest potential to produce disease; chrysotile, the smallest; with amosite occupying an intermediate position.[10] In a study of 1348 retirees from the asbestos industry by Enterline and Henderson,[11] the respiratory cancer rate of men exposed only to chrysotile was 2.4 times the expected, whereas this rate was 5.3 times the expected for men who had been exposed to a combination of chrysotile and crocidolite. In the asbestos cement industry a similar difference was observed. Workers exposed only to chrysotile and cement (shingles and sheets) had a respiratory cancer rate of 1.4 times the expected, whereas workers exposed to both, chrysotile and crocidolite and cement (asbestos cement pipes), had a respiratory cancer rate 6.1 times the expected.

Mesotheliomas are rare, usually rapidly fatal cancers that originate from the surface lining the chest or abdominal cavity. From 1960 through 1975, 4539 mesotheliomas have been reported worldwide.[12] The vast majority of these cancers were in people exposed to crocidolite alone or in combination with other types of asbestos. McDonald and McDonald[12] tabulated those reports of mesothelioma where the type of asbestos exposure was known. Although the number of such cases is small, where the exposure was to crocidolite alone or in combination with other types of asbestos, death from mesothelioma constituted 6.1% of the deaths from all causes, with a range of 2.42% to 16.07%. In contrast, deaths from mesothelioma in workers exposed only to chrysotile constituted only 0.3% of the deaths from all causes, with a range of 0.24% to 0.87%. An even greater contrast is found in the Finnish statistics of workers exposed to anthophyllite. Meurman *et al*[13] investigated 216 deaths that occurred among approximately 900 miners and millers of anthophyllite during the 32-year period 1936-1967 and found not one case of mesothelioma.

Not all mesotheliomas result from asbestos exposure. There is a background of "naturally" occurring mesotheliomas that has been estimated to be about ten for males and four for females per million persons aged 45 years and older.[12] Furthermore, it is not uncommon in the various epidemiologic studies reported that 15% or more of the mesothelioma cases have no history of ever having been exposed to asbestos. Perhaps the most important indication that mesotheliomas may result from causes other than asbestos exposures; in this instance, also environmental, comes from a report by Baris *et al*[14] who described a mesothelioma incidence of 2.3% in 1974 in the village of Karain in Turkey (population, 604). This population has been exposed for many generations to dust from the soil that contains kaolin, mica, and vulcanic glass particles, but no asbestos.

A small excess of deaths from gastro-intenstinal cancers have been noted in several epidemiologic studies of asbestos workers.[9,15] An association of laryngeal cancer with asbestos exposure has been claimed. Pancreatic cancers and lymphomas have also been mentioned in this connection. However, conversion of the association to a causal relationship rests, as yet, on an insecure basis.

Whether or not there is a dose-effect relationship associated with asbestos dust has been answered affirmatively by a number of epidemiological surveys.[15-19] Whereas this relationship is clear-cut with regard to asbestosis and lung cancer, it is less well-marked with regard to mesothelioma; but it is, nevertheless positive. McDonald[20] points to a case-control analysis based on seven cases of mesothelioma at Thetford Mines that includes no case with less than

30 mppcf-years exposure and which suggests that the risk increases with exposure. McDonald further points out that, although fiber-equivalents for the dust concentrations in mppcf are difficult to estimate, there is evidence for believing that the conversion factor cannot be less than two. The data of Newhouse and Berry[21] demonstrates a doubling of the incidence of mesothelioma for males who had severe exposures as compared to that of the workers who had light or moderate exposures. This was equally true for those employed less than two years. In all of the other investigations of mesothelioma incidence, the degree of dust exposure was not indicated, thereby preventing the determination of any dose-effect relationship.

The only reliable exposure data from the asbestos industry on which a recommendation for a threshold limit of asbestos exposure can be based, stem from England.[19,22] Using the presence of persistent high-pitched rales in the basal portions of the lungs as criterion for the diagnosis of asbestosis, it was determined from a population of asbestos textile workers that less than 100 fiber-years of exposure (2 fibers/cc over a 50 year working period or 4 fibers/cc over a 25 year period) would cause the development of asbestosis in no more than 1% of the workers.[22] This departure from the previous dust standard of 5 mppcf was in recognition of the variability of the asbestos fiber content of factory dust and that the disease was related to the number of asbestos fibers inhaled and not to the amount of nonfibrous dust particles. Also, it was specified that the counted fibers were to be longer than 5 μm.

The size limit placed on the counted fibers (longer than 5 μm) was because it was not practical to count shorter fibers with an optical microscope (400 to 450 x magnification under phase-contrast illumination, with a 4MM objective). It is recognized that for every asbestos fiber longer than 5 μm, there may be as many as 100 or more fibers shorter and thinner that are not visible under the optical microscope. However, there is considerable experimental evidence to indicate that asbestos fibers shorter than 5 μm are not pathogenic.[23]

A recent publication by Gillam *et al*[24] indicated that the present limit of 2 asbestos fibers/cc longer than 5 μm set by OSHA is inadequate to protect workers against nonmalignant as well as malignant respiratory disease. This conclusion was based on a study of 440 hard rock gold miners who had been exposed to an asbestiform mineral (cummingtonite-grunerite). These investigators found 10 respiratory cancer deaths (including a carcinoma of the maxillary sinus and a mediastinal carcinoma) when only 2.74 such deaths had been expected. Five deaths from nonmalignant respiratory diseases other than influenza and pneumonia when 1.85 death from these causes had been expected. These deaths included those from silicosis (the respirable dust contained 13% free silica!).

It is of interest that although the diagnosis of asbestosis was not mentioned in the paper, Gillam *et al*[24] emphasized the finding taht the ambient air in the gold mine contained an average of 4.82 fibers/cc, 80 to 80% of which were fibrous amphiboles, *"and 60 to 70% of the latter were fibrous grunerite (amosite)."* Fibers longer than 5 μm, averaged 0.36 fibers/cc; and approximately 94% of the airborne fibers were less than 5 μm long, averaging 0.13 in diameter and 1.1 μm in length.

McDonald *et al*[25] investigated the records of the same gold mine as Gillam *et al*, but their cohort consisted of 1321 men who had completed 21 years service with the mining company (in contrast to the cohort of 440 men studied by Gillam *et al*).[24] The following is a summary of their findings:

> *"All but 10 of the men were traced to the end of 1973 when 651 were still living; cause of death was ascertained for 657 of the 660 who had died. The numbers of deaths observed in various diagnositc categories, with 'expected' figures in parenthesis, were as follows: — respiratory cancer — 17 (16.5); abdominal cancer — 39 (35.1); other malignant diseases — 37 (39.0); pneumoconioses — 39 (0); respiratory tuberculosis or silico-tuberculosis — 39 (3.6); heat disease — 264 (232.5). Silicosis was given as the cause in 37 of the 39 pneumoconiotic deaths and mentioned on the certificate in 28 of the 264 coded to heart disease. The occurrence of deaths ascribed to pneumoconiosis, tuberculosis and heart disease was in each case related directly to dust-exposure category, whereas deaths coded to respiratory, abdominal and other cancers showed no such relationship. The pattern of mortality of men with long employment in this industry indicates a serious pneumoconiotic hazard characteristic of hard rock miners but not of cancer."* (See Table 1.)

It would appear from the McDonald *et al* study[25] that there is no basis for the claim made by Gillam *et al*[24] that the OSHA standard of two fibers longer than 5 μm/cc is inadequate to protect the health of workers, or that asbestos fibers shorter than 5 μm produce deleterious health effects.

In an 8 year follow-up of the same population of asbestos workers from which the 100 fiber-years exposure was derived as a reasonably safe level, it was found that mortality was increased for lung cancer.[19] There were 31 deaths from this cause whereas only 19.3 had been expected. From non malignant respiratory disease, there were 35 deaths, where 25.0 had been expected. In addition, there were five deaths from pleural mesothelioma.

It was determined that the mean dust level of the workers had been below 5 fibers/cc only in the last decade. In 1951 the mean dust level was 10.8 fibers/cc and 89% of the men had been exposed to mean levels above 5 fibers/cc. In 1972, the mean dust level was 2.9 fibers/cc and only 3% of the men were exposed to a mean level greater than 5 fibers/cc, 65% were exposed to a mean level between 2 and 5 fibers/cc and 32% to a mean level below 2 fibers/cc.

Because there is a delay of 15 or more years between first exposure and any resulting cancer, the authors consider that the increased mortality demonstrated does not reflect the effects of working conditions over the last 15 or 20 years. They therefore propose to continue the follow-up on workers entering scheduled areas since 1951. In terms of the 100 fiber-year or 2 fibers/cc standard suggested by the British Occupational Hygiene Society (B.O.H.S.), it is apparent that the excess mortality reported above can be attributed to asbestos exposures considerably above this level.

The workers in the asbestos textile factory, from which the B.O.H.S. standard of 2 fibers/cc was derived, have been

studied by highly qualified investigators whose reports were published in 1955,[6] 1965,[16] 1968,[26] and 1977.[19] These workers represent the only cohort of asbestos workers in the world in which health effects have been correlated with definitive exposure data defined as fibers per cc. It would be premature and ill advised to change the present OSHA standard of 2 fibers longer than 5 μm/cc for chrysotile without indications from this study population of the advisability for such change. The same TLV is assigned to other forms of asbestos not specifically named herein.

The exposure level of crocidolite and amosite, particularly of the former, must be sharply lower than that of chrysotile because of their greater potential for disease production. In view of the lack of accurate information of the dose-effect relationship pertaining to these two types of asbestos, the arbitrary assignment of 0.5 fiber/cc longer than 5 μm appears reasonable and prudent for amosite. Since crocidolite may be more pathogenic than amosite, a TLV of 0.2 fiber/cc longer than 5 μm is recommended, as well as the A1a, proven carcinogen, designation for all types of asbestos.

Tabulation of Significant Findings in Two Epidemiologic Investigations of Workers in the Same Hard Rock Gold Mine

		McDonald et al[25]		Gillam et al[24]	
Size of Cohort		1321		440	
Number of Deaths		Observed	Expected	Observed	Expected
Respiratory Cancer		17	16.5	10	2.74
Nonmalignant Respiratory	Pneumoconiosis	39*	0	5	1.85
	Respiratory TBC Silico-TBC	39	3.6		
	Other Nonmalignant Respiratory Disease	?	?		

*37 of the 39 deaths were ascribed to silicosis.

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