# INDUSTRIAL HYGIENE AND TOXICOLOGY

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*Lead arsenite*, approximately $Pb(AsO_2)_2$, with 49.2 per cent lead and 35.6 per cent arsenic, is likewise a dense, white powder. Its specific gravity is 5.85.

It is probable that the arsenic exposure from lead arsenate and lead arsenite need not be seriously considered because of the relatively greater hazard of the lead content of these insecticides.

### 3. *Determination in the Atmosphere*

Arsenic dusts and mists may be collected by impingement into dilute alkali or other media, or by the electrostatic precipitator. Fumes are more reliably collected by the precipitator. Estimation can then be made by the Gutzeit[1] or other methods.[2,3]

### 4. *Physiological Response*

*Acute effects.* Acute or subacute industrial poisoning from ingestion, skin contact, or inhalation of arsenical dusts is not common. Symptoms include gastrointestinal disturbances, irritation of the nose and conjunctiva, skin eruptions, and inflammation. Laryngitis, bronchitis, and huskiness of the voice can result from relatively brief, massive doses of arsenicals by inhalation. Systemically, arsenic relaxes the capillaries[4] and increases their permeability, simulating inflammation, and this dilation introduces changes in the circulation that cause disturbances in organic function.

*Chronic effects.* After chronic exposure to arsenic compounds perforation of the nasal septum is a common occurrence, as well as irritation, and occasionally ulceration, of the skin. Pigmentation also may be produced. Peripheral neuritis[5] is said to occur in less than 5 per cent of the cases, tremors in 10 per cent, gastric symptoms in one third, and rashes in the majority of cases of chronic poisoning. Loss of nails and hair may result. Carcinoma of the lung is said to have been produced experimentally in animals with arsenic compounds, but no evidence has been presented to indicate such occurrence among human beings from industrial exposures.

Small amounts of arsenic are thought to have a beneficial effect in treating leukemias, anemias, and skin diseases. Arsenic in organic forms is used in the treatment of syphilis: for example, Mapharsen or the arsphenamines. Arsenic was formerly used extensively, even indiscriminately,[4] as an alterative and tonic in all kinds of blood disturbances. Small amounts of arsenic have been found to have a beneficial effect upon animals, especially animals on a diet containing selenium.[6]

[1] M. B. Jacobs, *Analytical Chemistry of Industrial Poisons, Hazards, and Solvents*. Interscience, New York, 1941.
[2] D. M. Hubbard, *Ind. Eng. Chem., Anal. Ed., 13*, 915 (1941).
[3] K. Bambach, *Ind. Eng. Chem., Anal. Ed., 14*, 265 (1942).
[4] T. Sollmann, *A Manual of Pharmacology*. 6th ed., Saunders, Philadelphia, 1944.
[5] T. Legge, *Industrial Maladies*. Oxford Univ. Press, London, 1934.
[6] A. L. Moxon, C. R. Paynter, and A. W. Halverson, *J. Pharmacol., 84*, 115 (1945).

### 5. *Absorption, Retention, and Excretion*

Arsenic may be absorbed industrially by inhalation, ingestion, and through the skin. It is largely eliminated in the urine, some in the feces, hair, epithelium, nails, and possibly small amounts in the exhaled breath. Excretion is slow, requiring up to ten days after an acute absorption; sometimes more than a year after prolonged absorption. After subcutaneous injection of potassium arsenite, human beings, and all animals except rats, showed very small amounts of arsenic in the blood[7] and no evidence of accumulation in rapidly growing tissues. Arsenic is retained and stored in all the tissues, the bones, and especially the hair. It is said that the arsenic content of long hair, in relation to that of close-cropped hair, can be used to give an indication of the time and extent of absorption. Arsenic content of the hair several years after death has been presented as evidence of nonindustrial arsenic poisoning.

### 6. *Tests Indicating Exposure*

The arsenic content of the urine of exposed persons is significant in evaluating their exposure. The normal excretion of arsenic has been found to be about 0.015 mg. As per liter,[8] with occasional values up to 0.06 mg. per liter. The average urinary arsenic excretion among orchardists during periods of relatively high exposures averaged 0.22 to 0.24 mg. per liter, with many values above 0.5 and one value as high as 2.0 mg., although no signs of adverse effects from the arsenic were exhibited. Values as high as 3 mg. arsenic per liter of urine have been reported elsewhere without detectable signs of intoxication. Just where on this scale a mark can be chosen to indicate excessive exposure will require further study. Kunkele[9] considers amounts above 0.1 mg. arsenic per liter of urine, and 3 micrograms arsenic per gram of head hair, to indicate poisonings, but reports results as high as 1.5 mg. per liter of urine and 120 micrograms per gram of hair. Young and Rice[10] were unable to distinguish between internally and externally deposited arsenic in the hair and question the value of tests for arsenic in the hair.

In isolated instances, men exposed to up to 0.6 mg. per cubic meter arsenicals (computed as arsenic trioxide) in the atmosphere, during the manufacture of arsphenamine and related compounds over an extended period, excreted from 1 to 5 mg. arsenic (computed as the trioxide) per liter of urine, and exhibited minor symptoms of arsenic poisoning.[11]

[7] F. T. Hunter, A. F. Kip, and J. W. Irvine, Jr., *J. Pharmacol.*, *76*, 207 (1942).
[8] P. A. Neal, W. C. Dreessen, T. I. Edwards, W. H. Reinhart, S. H. Webster, H. T. Castberg, and L. T. Fairhall, *U.S. Pub. Health Service Bull.* No. 267 (1941).
[9] E. F. Kunkele, *Chem. Ztg.*, *64*, 29 (1940).
[10] E. G. Young and F. A. H. Rice, *J. Lab. Clin. Med.*, *29*, 439 (1944).
[11] R. M. Watrous and M. B. McCaughley, *Ind. Med.*, *14*, 639 (1945).

### 7. *Maximum Permissible Concentrations*

Maximum permissible concentrations that vary from 0.15 to 5.0 mg. per cubic meter of air have been proposed. The higher limit may permit excessive amounts, but the lower limit appears unnecessarily severe and too low to be of practical value from an engineering standpoint. A value on the order of 1 to 2 mg. per cubic meter appears more logical, but the problem requires further study.

## ARSINE

Arsine, $AsH_3$, is a gas that results whenever nascent hydrogen is formed in an acid, alkaline, or neutral solution containing arsenic.

### 1. *Industrial Exposures*

Exposure to arsine gas may result from the action of acids on metals containing arsenic, from the use of impure sulfuric acid made from pyrites containing arsenic, or from the use of hydrochloric acid made from impure sulfuric acid that contained arsenic. Arsine poisoning has resulted from slushing out steel tanks that had previously contained a commercial grade of sulfuric acid, the diluted acid acting upon the metal tank to generate hydrogen, which combined with arsenic impurities in the acid. Arsine may arise from the pickling of any metal containing arsenic; it has been formed from the action of water on metallic arsenides or hot dross containing arsenic and aluminum. Arsine may occur as an impurity in acetylene and present an exposure either in its manufacture or use. It may occur in soldering, etching, lead plating, electrolysis of arsenious solutions, by the action of moisture on ferrosilicon or from the use of impure or inhibited acids[12] for scale removal. It has not been a hazard associated with the manufacture, maintenance, or use of lead storage batteries in the United States, where arsenic-free lead and sulfuric acid are used.

### 2. *Physical and Chemical Properties*

Arsine, $AsH_3$, is a colorless gas with a slightly obnoxious odor somewhat resembling garlic. It is 2.7 times as heavy as air. It boils at −55° C. and decomposes at 230°. It is soluble in water to the extent of about 20 volumes in 100 volumes at 20° C. It is inflammable.

1 mg./l. ≏ 313 p.p.m. and 1 p.p.m. ≏ 3.19 mg./cu.m. $AsH_3$ (or ≏ 3.07 mg. As, or ≏ 4.05 mg. $As_2O_3$) at 25° C., 760 mm.

### 3. *Determination in the Atmosphere*

Arsine can be collected by scrubbing the atmosphere through normal nitric acid and estimated by the Gutzeit method[1] or other means. If 1 p.p.m. arsine is considered the maximum permissible concentration, 2 to 4 liters of air makes a conveniently sized sample, but it is desirable to collect an excess and use an aliquot. Qualitative and semiquantitative tests[1] with either silver nitrate or

[12] G. F. Hawlick and E. B. Ley, *Occupational Med.*, *1*, 383 (1946).

mercuric chloride[13] test papers are of some use. The reaction is obscured by hydrogen sulfide, phosphine, and stibine. Hydrogen sulfide can be readily filtered out with lead acetate paper, while stibine and phosphine have a comparable order of toxicity to arsine so that for control purposes this simple test may give useful information, especially if the colors are compared with freshly prepared standards obtained with gas–air mixtures of known compositions.

#### 4. *Physiological Response*

*Acute effects.* It is thought that arsine first combines with the hemoglobin in the blood corpuscles[14] in some manner, and soon thereafter hemolysis of the cells occurs, resulting in the destruction of the cells and solution of the hemoglobin in the serum. More arsenic has been demonstrated in the corpuscles than in the serum. During the ensuing anemia the blood count falls rapidly and hemoglobin is excreted in the urine. Within a few days destruction of the red cells may progress to the point where death occurs from anoxemia, and may be considered a form of chemical asphyxia. It is said that death frequently occurs from pulmonary edema[15] resulting either from primary irritation or secondary to failure of the circulation. Symptoms are similar to those observed in other forms of anoxemia: headache, weakness, vertigo, and nausea. Pain in the kidneys and liver develops,[4] and the kidneys may be blocked. Jaundice, both from disintegration of red blood cells and from disorder of the liver, appears and blends its yellow with the cyanotic pallor to create a peculiar bronze tint of the skin. The symptoms of arsenic poisoning (as opposed to those of arsine) may be present in addition to the ones described. Death may occur 2 to 9 days following exposure or, if due to nephritis from arsenic, may be delayed. Recovery, even from severe poisoning, is possible in the majority of instances where the cause is recognized early[16] and prompt measures taken.

TABLE 1

*Physiological Response to Various Concentrations of Arsine*[13]

| Response | Concentration, p.p.m. |
|---|---|
| Maximum concentration allowable for prolonged exposure | 1 |
| Slight symptoms after exposure of several hours | 3–10 |
| Maximum concentration that can be inhaled 1 hr. without serious consequences | 6–30 |
| Dangerous after exposure of 30 to 60 min | 16–60 |
| Fatal after exposure of 30 min | 250 |

*Chronic effects.* In prolonged exposure to low concentrations of arsine the symptoms bear more relation to effects produced by dusts and fumes of arsenic

[13] *Dept. Sci. Ind. Research (London), Leaflet* No. *9* (1939).
[14] F. Flury and F. Zernik, *Schädliche Gase.* Springer, Berlin, 1931.
[15] Y. Henderson and H. W. Haggard, *Noxious Gases.* 2nd ed., Reinhold, New York, 1943.
[16] C. A. Nau, W. Anderson, and R. E. Cone, *Ind. Med., 13,* 308 (1944).

compounds, and albumen may appear along with hemoglobin in the urine. Prolonged exposure of animals to low concentrations of arsine[17] produced a compensated destruction of red blood cells, which gradually deteriorated to a stationary level of anemia. There was little injury to other organs. Chronic arsine poisoning[18] occurred in a group of nine men exposed several months to undetermined amounts of arsine in the cyanide extraction of gold. These men complained of headache, weakness, nausea, and vomiting, the attacks increasing in frequency and severity. Puffiness of face and eyelids, tingling sensation in the toes, lumbar and epigastric pains, garlic-like odor of the breath, and change of complexion were also common symptoms. The red blood cells were markedly reduced, eight of nine cases having lows of 0.4 to 2.4 million per cubic millimeter. The arsenic content of the urine ranged from 0.3 to 3.3 mg. per liter (0.37 to 4.3 mg. $As_2O_3$). The maximum arsenic excretions in the urine of seven of the nine men ranged from 1.0 to 3.3 mg. As per liter, with an average of 2 mg. per liter. Three months later one man was excreting slightly above 1 mg. per liter, one 0.4 mg. per liter, and the others were approaching normal levels. All of the men recovered.

*5. Absorption and Excretion*

Arsine is absorbed through the lungs, and the arsenic is largely excreted through the kidneys. The arsenic content of the urine is indicative of the extent of exposure when other possible sources of As have been considered.

*6. Maximum Permissible Concentration and Warning Properties*

The maximum permissible concentration of arsine in the atmosphere has frequently been placed at 1 p.p.m. This is equivalent to 3.2 mg. arsenic per cubic meter of air. A figure of $^1/_2$ p.p.m. (1.6 mg./per cubic meter) would appear to be a more logical limit. The odor of this concentration of arsine is easily noticeable, but does not constitute a satisfactory warning. The inflammable properties of the gas present no hazard of interest to industrial hygienists because concentrations in the inflammable range do not occur in industry.

## ARSENIC TRICHLORIDE

Arsenic trichloride, $AsCl_3$, is an oily liquid boiling at 130.2° C. It is said to have been tried experimentally in mosquito-control work, and has been considered for use as an irritant war gas. It fumes when exposed to the air, and decomposes in an excess of water. Industrial exposures, except in its manufacture, are improbable. Its property of decomposition in moist, warm air makes it more effective in the lungs than on the upper respiratory tract. In addition to its strong, irritant action are, of course, the effects of arsenic.

[17] M. Kiese, *Arch. exptl. Path. Pharmakol., 186*, 337 (1937).
[18] F. M. R. Bulmer, H. E. Rothwell, S. S. Pollack, and D. W. Stewart, *J. Ind. Hyg. Toxicol., 22*, 111 (1940).

deaths may result from daily doses on the order of 0.8 mg. per kilogram when injected subcutaneously. There are no published data on maximum permissible limits for man, but from experience with animals it appears advisable to limit exposures to about 1 mg. per cubic meter of air where the length of exposure is 6 or 8 hours per day for prolonged periods. The odor of such a concentration of phosphorus vapor, though it can be smelled upon entering, does not give adequate warning.

## PHOSPHINE

Phosphine, $PH_3$, molecular weight 34.04, is a gas that results whenever nascent hydrogen is formed in a solution containing phosphorus. It may occur during the manufacture of phosphorus, from the action of water on metallic phosphides, from the action of moisture on ferrosilicon containing phosphorus, and in fact may frequently accompany arsine because arsenic and phosphorus often occur together as impurities of metals. Phosphine also occurs as an impurity of acetylene.

### 1. *Physical and Chemical Properties*

Phosphine is a colorless gas with a foul odor slightly resembling decayed fish. It is 1.17 times as heavy as air. Its melting point is —133.5° C. and its boiling point is —87.4°. Twenty-six volumes of the gas are soluble in 100 volumes of water at 17° C. Phosphine ignites spontaneously in the air.

### 2. *Determination in the Atmosphere*

Phosphine can be determined in the same manner as arsine, and the two gases occurring together may be absorbed by scrubbing through bromine water, and the combined arsenic and phosphorus determined in an aliquot after expelling the bromine. The Denigès[23] (molybdenum blue) method is satisfactory. Phosphine also can be estimated by exposing mercuric chloride test paper to a measured volume of phosphine–air mixture and comparing the resultant color with similarly prepared standards. Also see method given under determination of phosphorus.

1 mg./l. $\simeq$ 719 p.p.m. and 1 p.p.m. $\simeq$ 1.39 mg./cu.m. at 25° C., 760 mm.

### 3. *Physiological Response*

*Acute effects.* Phosphine differs in its action from that of arsine in that it does not hemolyze the red blood cells. Early symptoms of poisoning are a feeling of coldness and a pain in the region of the diaphragm. Dyspnea, weakness, vertigo, bronchitis, edema, convulsions, and death may result from exposure to phosphine.

[23] M. B. Jacobs, *Analytical Chemistry of Industrial Poisons, Hazards, and Solvents.* Interscience, New York, 1941.