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2. **Ingvar Lundberg:** Medicinsk undersökning av färgindustriarbetare långvarigt exponerade för en blandning av organiska lösningsmedel.
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ARBETE OCH HÄLSA
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ARBETE OCH HÄLSA 1981:21

SCIENTIFIC BASIS FOR SWEDISH OCCUPATIONAL STANDARDS

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ISBN 91-7464-111-5
ISSN 0346-7821

PREFACE

The Swedish Criteria Group for Occupational Standards was created in 1978 within the Department of Occupational Health of the National Board of Occupational Safety and Health (NBOSH).

The Criteria Group has the task of gathering and evaluating relevant scientific information on substances which may present an occupational health risk, and preparing reports to be used as background material for the Board's proposals on occupational standards (exposure limit).

Searches of the literature and collection of material were handled partly by the members of the Criteria Group and partly by external experts who were specialists in the various areas. The resultant reports - criteria documents - have been published separately in Arbete och Hälsa, a scientific periodical from NBOSH.

For many substances, the Criteria Group has drawn information primarily from the evaluations made by the Nordic Expert Group for the Documentation of Occupational Exposure Limits, which have also been published in Arbete och Hälsa.

Both the criteria documents and the opinions were discussed within the Criteria Group before they were approved. This is the first published version. These concensus reports were reviewed and approved by the Criteria Group up to June 1980.

The Criteria Group has the following membership (as of November 1980).

Nils Lundgren	chairman	Dept. Occup. Health, NBOSH
Ulf Ulfvarsson	v. chairman	Dept. Occup. Health, NBOSH, Technical Hygiene Unit
Olav Axelson		Dept. Occup. Medicine, Univ. Hospital, Linköping
Birgitta Baltzar	observer	Dept. Supervision, NBOSH, Medical and Social Unit
Harald Frostling	deputy	Swedish Employers' Confederation
Francesco Gamberale		Dept. Occup. Health, NBOSH, Work Psychology Unit
Gideon Gehardsson		Swedish Employers' Confederation
Lennart Holm	observer	Dept. Supervision, NBOSH, Chemistry Division
Bo Holmberg		Dept. Occup. Health, NBOSH, Occupational Toxicology Unit
Stig Holmquist		Swedish Confederation of Professional Associations
Bengt Knave		Dept. Occup. Health, NBOSH, Medical Unit
Gösta Lindstedt		Dept. Occup. Health, NBOSH, Chemistry Unit
Per Lundberg	secretary	Dept. Occup. Health, NBOSH
Egon Magnusson	deputy	Swedish Trade Union Confederation
Marcello Malentacchi		Swedish Metal Workers' Union
Nils Masreliez	deputy	Swedish Employers' Confederation
Gunnar Nerell		Central Organisation of Employees in Sweden
Staffan Skerfving		Dept. Occup. Medicine, Univ. Hospital, Lund
Jan Wahlberg		Dept. Occup. Health, NBOSH, Medical Unit
Ullrik Wallström		Swedish Painters' Union
Arne Wennberg		Dept. Occup. Health, NBOSH, Medical Unit
Olof Vesterberg		Dept. Occup. Health, NBOSH, Chemistry Unit
Peter Westerholm		Swedish Trade Union Confederation
Sven Yllner		The Swedish Philips Concern Swedish Employers' Confederation

CONTENTS

CONSENSUS REPORT FOR DBCP

(1979-05-30)

1,2-dibrom-3-chlorpropane (DBCP) is absorbed via the skin, lungs and digestive tract. Biotransformation has not fylly been researched.

DBCP is mutagenic for Salmonella typhimurium and Escherichia coli. Metabolic activation increases the mutagenic effect.

Oral administration of DBCP to rats results in cancer of the stomach squamous epithelium and causes carcinoma of the mammary glands in females. Oral administration to mice also results in cancer of the stomach epithelium. DBCP reduces the fertility of rats.

There are no published case studies or epidemiological investigations of tumors associated with occupational exposure. Sterility and reduced sperm count has been found in occupationally exposed men.

DBCP is regarded as oncogenic for experimental animals. There is no information on cancer with human exposure.

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CONSENSUS REPORT FOR METHYL IODIDE

(1979-05-30)

Methyl iodide can be absorbed via the skin, digestive tract and lungs. Retention of inhaled methyl iodide by human subjects has been measured at 72 percent. In rats, methyl iodide is biotransformed and excreted as various methyl conjugates.

Methyl iodide vapor is an alkylating agent and mutagenic for Salmonella typhimurium. Intraperitoneal injection of methyl iodide yields a dose--related increase in the frequency of lung tumors in mice. Subcutaneous injection of rats yields local tumors with metastases in the lungs.

There are apparently no case studies or epidemiological surveys of cancer in persons occupationally exposed to methyl iodide.

Methyl iodide is regarded as oncogenic for laboratory animals. There is no information on cancer with human exposure.

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CONSENSUS REPORT FOR FORMALDEHYDE

(1979-11-20)

At room temperature, formaldehyde is a colorless, irritating gas, easily soluble in water. Formalin is a 37 percent saturated, aquaeous solution of formaldehyde, usually stabilized with methanol (up to 15 percent).

In the working environment, the most important path of uptake is via the lungs. With direct contact, mucous membranes and skin can also be effected.

Formaldehyde is highly reactive and reacts with proteins, which are denatured with high formaldehyde concentrations.

Half of the people in a test group reported noticing the smell of formaldehyde at air concentration of 0.06 mg/m^3 (0.05 ppm).

Slight irritation of the eyes and nose is noticed by many people when they are exposed to air concentrations of 0.4-1.2 mg/m^3 (0.3-1.0 ppm). The irritation becomes more obvious when the concentration reaches 2.4 mg/m^3 (2 ppm); 7 percent of a test group reported extreme irritation of the eyes, and 10 percent moderate irritation.

At concentrations of 1.1-1.9 mg/m^3 a number of people experience dryness and burning in the throat; at 4.8 mg/m^3 this becomes severe irritation. It disappears quickly when exposure is terminated. Irritation increases along with the degree of exposure, and becomes intolerable for most people when air concentrations reach 12-18 mg/m^3 (10-15 ppm), at which they begin to experience coughing fits and shortness of breath.

A concentration of 60 mg/^{3} (50 ppm) produces severe irritation in the bronchial tubes, and 240 mg/m^3 (200 ppm) can cause serious damage to the mucous membranes in the bronchial tubes.

Formaldehyde is allergenic. Allergic reactions most often affect the skin, but can also affect the bronchial passages.

There have only been a few studies of possible hereditary damage or carcinogenic effects, and the evidence is inconclusive.

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CONSENSUS REPORT FOR CHROMIUM

The use of chromium and chrome compounds has been summarized in a promemoria (1) at the request of the criteria group. In Sweden, chromite ore (trivalent chromium) is widely used in the production of chromates and steel (eg stainless steel). Trivalent chromium is used as a pigment (chrome green) and in chrome tanning. Hexavalent chromium compounds are used in lithography, but their main use is as chromic acid in metallization and chromating. Water-soluble hexavalent chromium compounds are also found in welding gases when plated electrodes are used in welding stainless and high-alloy steels. Chromium also occurs with other kinds of welding in sparingly soluble form, the valence of which has not yet been established. Exposure to chromium also occurs with polishing, cutting and welding of steel and of surfaces coated with rustproofing or paint containing chrome, as well as with spray painting with such paints. These pigments are sparingly soluble.

Occupational exposure to hexavalent chromium compounds, particularly chromic acid (CrO_3), can result in hypersensitivity (skin allergy), irritation of the mucous membranes, and perforation of the nasal septum, as well as cancer in the respiratory passages (2,3). These cancers can proobably be initiated at exposure levels lower than those necessary to cause perforations of the nasal septum. Skin allergies are a result of direct contact and therefore can not be used as a basis for exposure limits applying to air concentrations.

Oncogenic effects have been observed with occupational exposure to some hexavalent chrome compounds (2-6). It has not yet been possible to completely explain the underlying mechanism with experimental studies. Hexavalent chromium is reduced in the organism to trivalent chromium, which shows strong bonding to macromolecules such as proteins and nucleic acids (2, 3). It seems as though the different solubilities of the various chrome compounds can imply different grades of risk for mucous membrane damage and tumors (2, 3). Reports published so far seem to indicate that the risk for cancer is greatest with the manufacture of certain chromate

pigments (sparingly soluble compounds), and is less with chromating (water-soluble compounds) (2, 3, 6). On the basis of present knowledge, it would be unwise to exempt any of the hexavalent chrome compounds from the suspicion of having carcinogenic qualities. There is so far no basis for assuming a cancer risk with the manufacture of ferrochromium or with welding.

Trivalent chromium can not penetrate the cells to any notable extent. Exposure to trivalent chrome compounds probably does not constitute an increased cancer risk for man. Available data indicate that metallic chromium and trivalent chrome compounds have low toxicity (2, 3).

With chromating, air concentrations in excess of 0.1 mg of chromic acid (probably CrO_3) per cubic meter of air have caused damage to the mucous membranes of the nose (4). In the manufacture of sparingly soluble chromates (zinc chromate), concentrations of 0.5 mg/m^3 or more have been associated with a significant increase in the frequency of lung cancer (5). Information on cancer frequency at lower exposure levels is extremely scarce. The detection limits for measurement of chromium as an air pollutant are somewhere below 1 microgram per cubic meter of air (7). It is possible to distinguish hexavalent chromium compounds from trivalent compounds by chemical analysis, if the compounds are water-soluble.

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CONSENSUS REPORT FOR TRICHLOROETHYLENE

(1979-12-14)

Synonyms: trichloroethylene, TRI, ethen, trichloro-

Boiling point: 87°C at 760 mm Hg

1 ppm = 5.35 mg/m^3; 1 mg/m^3 = 0.19 ppm

The summary given below is based primarily on a newly published survey (1).

TRI is used in large quantities as a cleaning and degreasing agent for metal parts, etc, often in special degreasing halls. Exposure with this use is as a rule not more than 160 mg/m^3. With open use, as with vulcanizing and gluing of rubber and plastic products and in industral laboratory work, exposures can exceed 500 mg/m^3. In recent years, use of TRI has decreased considerably due to its replacement by other agents such as 1,1,1-trichlorethane. When heated to 300-600°C, TRI can yield phosgene gas, which is a powerful lung irritant. Industrial qualities of TRI generally contain stabilizers, which can sometimes explain mutagenic effects, etc (2).

Fifty to 70 percent of the amount inhaled is absorbed. With higher air concentrations or heavier work, the relative uptake is reduced. Some of the amount taken up is retained in adipose tissue, but within a few days 35-70 percent of the absorbed amount is biotransformed and the transformation products excreted, primarily in urine. The rest is exhaled. Biotransformation can be accelerated (induction) by some substances, and retarded by others (such as alchohols).

The table shows the effects of different levels of TRI.

It should be mentioned that there have been no reports of reduced reaction time (3) or of demonstrated allergy.

Mutagenic effects have been demonstrated in short-term tests using micro-organisms (1). TRI also shows effects in cell transformation tests. In a long-term study in which mice and rats were exposed orally to trichloroethylene, the mice, but not the rats, showed a dose-related increase in the frequency of spontaneous hepatocellular carcinomas (4). However, these studies do not provide adequate basis for assuming the existence of a cancer risk for man. In an epidemiological study of degreasers with several years of exposure to levels of 160 mg/m^3 or higher, no increased frequency of cancer was observed (5).

Table 1. Effects on human subjects of exposure to different levels of TRI.

16000 mg/m^3 (3000 ppm):	loss of consciousness; respiratory and/or cardiac arrest
2700 mg/m^3 (500 ppm):	damage to the brain, peripheral nervous system, liver and kidneys
500 mg/m^3 (100 ppm):	minor neurovegetative symptoms with short-term exposure. Minor psychomotor symptoms/disturbances. Reversible EEG changes.
400-1100 mg/m^3 (75-206 ppm)	chromosome changes in blood cells after several years of exposure.
250-500 mg/m^3 (50-100 ppm):	minor irritation of the mucous membranes. Neurovegetative symptoms with prolonged exposure.
100-500 mg/m^3 (20-100 ppm):	detectable by smell.

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CONSENSUS REPORT FOR CADMIUM

(1980-01-18)

A pro memoria has recently been drawn up at the request of the Criteria Group (1).

Cadmium and cadmium compounds are used as pigments; as stabilizers in plastics; in alloys (eg cadmium silver solder); and in alkaline accumulators. Ten to 40 percent of the amount inhaled is absorbed; the higher figures apply to small particles (<5 um) such as those in smoke.

Cadmium can enter the body through occupational exposure and also via some foods contaminated by artificial fertilizers, etc. Average daily intake in Sweden is about 40 ug/day, only about 5 percent of which is resorbed. Snuff and cigarettes make some contribution to this amount - it is estimated that smoking 20 cigarettes adds about 1 um of cadmium to the body. Heavy smokers in particular can show a 30 percent increase in body burden.

Cadmium is excreted from the body very slowly, usually about 1 ug/day (circa 0.01 percent of body burden), mainly via urine. With kidney damage, this excretion can increase to considerable amounts. The normal biological half-life is quite long - about 15-30 years. Most of the absorbed amount is stored in the liver and kidneys. The critical level, at which there are observable dysfunctions of the kidneys, is about 200 ug/g of kidney cortex (2). This corresponds to a total body burden of 100-200 mg. If this level is exceeded, urine concentrations of low-molecular proteins such as β_2-microglobulin increase (3). There are detailed theoretical calculations (1) of the exposure level which would produce this critical concentration in the kidney cortex. Based on a biological half-life of 19 years and a 25 percent absorption with inhalation, air concentrations would have to be 13 ug/m^3. This assumes an exposure of 8 hours per day, 225 days per year, over 25 years.

One study has reported increased protein excretion in over half of a group of workers exposed for several (20-40) years to respirable cadmium in concentrations of about 20 ug/m^3. The long-term significance of a slightly increased protein excretion of this type as far as health is concerned is still not clear.

A 10-50 percent prevalence of proteinurea has been reported in subjects exposed for many years to respirable cadmium at concentrations of 50-100 ug/m^3. It must be pointed out that in studies where increased protein excretion has been found, there is great uncertainty regarding the cadmium concentrations each individual has been exposed to, and often considerable uncertainty regarding the concentrations of respirable dust. The latter is extremely important, since absorption is highest for this fraction.

With major kidney damage calcium metabolism is also affected, and increased frequency of kidney stones has earlier been observed with exposure levels considerably higher than that presently allowed in Sweden.

Short-term exposure to a high concentration of small (< 5 um) particles of cadmium in inhaled air (>0.25 mg Cd/m^3) can cause changes in lung tissue (pneumonitis). Poisoning, sometimes fatal, can occur after eight hours of inhalation of 1-5 mg/m^3. With prolonged exposure to lower air concentrations (<0.1 mg/m^3) the kidneys are the critical organs.

There are some epidemiological surveys which indicate some connection between prolonged exposure to high concentrations of cadmium and increased frequency of prostate cancer. An expert group assembled by WHO, however, has recently declared this data inconclusive. There is no sure data on exposure levels, but they were certainly several times as high as those presently allowed.

The cadmium concentrations which have been measured in human embryos are extremely low, and risk for damage to the embryo is therefore considerd to be negigible.

Cadmium uptake via inhalation is highly dependent on particle size, but in addition it can be difficult to estimate the proportion taken up via foods and tobacco contaminated in the workplace.

Uptake of cadmium can be estimated by a "biological exposure control" which measures cadmium concentrations in blood and urine. Measurements of total and β_2-microglobulin in urine provide information on possible changes in kidney tissue. Directives regarding this type of monitoring, as well as for air analyses, are given in the National (Swedish) Board of Occupational Safety and Health Directive "Cadmium", No. 123 (1978).

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CONSENSUS REPORT FOR p-AMINOAZOBENZENE

(1980-02-29)

p-aminoazobenzene (aniline yellow, AAB, 4-(phenyl-azo) benzenamine) (Color Index No. 11000; CAS No. 60-09-3) consists of golden brown needles with a bluish luster. It has a melting point of 124-126^{0}C. AAB is soluble in organic solvents and somewhat soluble in water. It can be used as a pigment in lacquers, waxes and styrene resins, and can occur as an intermediate reactant in the production of some coloring agents (eg diazo dyes). In Sweden, AAB is used in some plastics industries (9).

With injection into the peritoneal cavities of rats, the substance has caused formation of methemoglobin, with a consequent reduced capicity for oxygen transport, in red blood cells (6). Like other aromatic amines, AAB is transformed within the organism to N-hydroxylated products before excretion (8). The substance has been tested for mutagenic and carcinogenic activity. It has been possible to demonstrate mutagenic activity on bacteria after metabolic activation (1, 2, 7, 11), but not on fruit flies (Demerc et al, 1949, cited in Reference 4). Increased frequency of liver tumors (carcinoma 2/16, hepatoma 5/16) has been observed in rats after administration of 2000-10000 ppm in food for up to 104 weeks (5). Skin tumors (100%) have been noted in rats whose skin was painted twice a week during their entire life span (3). In frogs, an overfrequency of kidney tumors (adenocarcinomas) was noted after injection of 0.3-0.5 mg AAB into the kidneys (10). Other animal experiments can not be evaluated because of shortcomings in methodology (4). On the basis of the available information, AAB must be regarded as a carcinogenic substance.

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CONSENSUS REPORT FOR 1,2-DICHLORETHANE

(1980-02-29)

1,2-dichlorethane (ethylene chloride, CAS No. 107-06-2) is used as an intermediate reactant in the synthesis of vinyl chloride, and is also used in the production of methyl chloroform, trichlorethylene, perchlorethylene, vinylidene chloride and ethylene amines (1). It can sometimes be found as an additive in leaded gasoline. Further uses are as extractant, degreaser and foaming agent.

1,2-dichloretahne can irritate mucous membranes and air passages, and damage the liver and nervous system (2). It easily penetrates the skin.

The substance is mutagenic for barley and for Salmonella, both with and without microsomal activation (3). It also causes mutations in fruit flies. 1,2-dichlorethane is biotransformed to chloracetaldehyde, which is mutagenic for Salmonella.

Given orally to mice and rats (3, 4) 1,2-dichlorethane induces dose-related tumor formation. Inbred mice were given time-weighted average doses of 195 mg/kg/day for males and 290 mg/kg/day for females in the highest dose groups, and 97 mg/kg/day for males and 149 mg/kg/day for females in the lowest dose groups. The substance was administered 5 times per week for 78 weeks, and dosage had to be adjusted a couple of times during the study. Increased incidence of tumors was observed in the mammary glands, forestomach, spleen (hemangiosarcomas), liver (hepatocellular carcinomas) etc.

Rats were given time-weighted average doses of 95 mg/kg/day for both males and females, per os 5 days per week for 78 weeks. Increased tumor incidence was observed for the forestomach and mammary glands of both sexes, and the males showed hemangiosarcomas in various organs.

There are no epidemiological studies of human exposure in relation to cancer occurrence.

1,2-dichlorethane is regarded as a carcinogen. For both mice and rats, the substance seems to be more potently carcinogenic with oral administration than other hydrocarbons - eg chloroform, carbon tetrachloride, perchloretylene, trichlorethylene - studied by NCI.

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CONSENSUS REPORT FOR METHYLENE CHLORIDE (DICHLORMETHANE)

(1980-02-29)

CAS No. 75092. 1 ppm = 3.48 mg/m^3

Odor threshold is given at about 730 mg/m^3 (210 ppm)

Note: If methylene chloride comes into contact with open flame or high heat, it can form phosgene gas.

This summary is based on a criteria document published by the Nordic Expert Group for Documentation of Occupational Exposure Limits (1), with certain additions.

Uptake

With occupational exposure to methylene chloride, most uptake is via the respiratory organs. Uptake of methylene chloride vapor is about 50-55 percent of the inhaled amount while resting, about 40 percent with light work, and about 25 percent with heavy physical labor. Like many other solvents, methylene chloride is resorbed remarkably well through the skin (2). For methylene chloride in liquid form, skin uptake can under some circumstances be large enough to contribute significantly to the appearance of toxic effects.

Transformation

Methylene chloride is transformed within the body to carbon monoxide (3), and the resulting CO concentrations in the organism are the critical factor on which to base discussion of exposure limits. It should, however, be remembered that inhaled carbon monoxide and that formed from methylene chloride may have different effects at the cellular level. The summation effects of methylene chloride and carbon monoxide may also have some significance, but there is no data on this.

Some idea of the significance of carbon monoxide formation can be obtained indirectly - with the above-mentioned reservations - by comparisons with the effects of inhaled carbon monoxide. In the low-dose range relevant in this context, carbon monoxide inhalation affects the cardiovascular system and has toxic effects on behavior. In an assessment of carbon monoxide made by NIOSH (4), it was concluded that to avoid these effects exposrues should be held below the level which results in a 5 percent carbon monoxide saturation of blood hemoglobin (5% COHb).

This degree of saturation corresponds to a state of equilibrium with CO concentrations of about 35 ppm in inhaled air, for non-smokers. Heavy smoking can contribute up to 10% COHb, and more moderate smoking about 5%. This degree of saturation is added to that due to the CO in the surrounding air and/or biotransformation of methylene chloride.

Among the individual factors which increase sensitivity to CO should be mentioned reduced hemoglobin concentrations in the blood, ie anemia of various sorts. Environmental factors with a similar effect include reduced oxygen concentrations in inhaled air, as at high altitudes.

Acute and chronic effects

Exposure to 350 mg/m^3 of methylene chloride for 7½ horus per day on five consecutive days has been shown to produce a maximum 5.7% COHb in non-smokers. The same length of exposure to 175 mg/m^3 yields a maximum COHb value of 2.9%. The half-life of COHb is much longer for carbon monoxide originating from methylene chloride than for inhaled CO. This is largely due to the fact that methylene chloride is accumulated in fatty tissue, from which it is gradually redistributed. The half-life of methylene chloride in subcutaneous fat is about 8 hours (5). There is probably no day-to-day accumulation of methylene chloride in fatty tissues if the exposure level at work does not exceed 250 mg/m^3.

As with other solvents, when the effects of air concentrations of methylene chloride are assessed it is necessary to consider the possible effects of physical excretion. Exposure to a particular air concentration results in an addition of about 0.5 g COHb per 100 ml blood both at rest and during work, corresponding to 3.2% COHb with a normal hemoglobin concentrations of 15.4 g/100 ml of blood (6). COHb content rises both during and after exposure, and rises more rapidly during rest than during physical labor. The reason for this is probably that the CO is exhaled more rapidly during work than during rest. These results imply that in discussing the COHb concentrations corresponding to a given methylene chloride concentration in inhaled air it is not necessary to consider the increased production of CO resulting from the greater absolute uptake of methylene chloride during physical exertion. On the other hand, the nervous system is affected earlier if subjects are exercising during exposure. These effects, however, do not occur unless concentrations in inhaled air are considerably higher than those associated with a COHb concentration of 5%.

In addition to this indirect evidence of methylene chloride's toxicity, there are some direct observations of effects which may be connected to carbon monoxide formation. There are case descriptions of myocardial infarct and EKG changes associated with high exposure to methylene chloride. Prolonged exposure to low concentrations (ca 100-420 mg/m^3) has not been found to result in increased mortality from heart disease (7).

With air concentrations of 300 mg/m^3 or higher there have been observations of various acute and possibly chronic effects on the nervous system.

Special chronic effects

Methylene chloride has been shown to be mutagenic in the Ames' test, and has also been found to cause malign cell transformations in another biological model system.

As to carcinogenicity, the above-mentioned cohort study (7) of workers exposed to air concentrations of around 100 to 420 mg/m^3 gave no evidence of increased mortality in any form of cancer.

With regard ro prenatal damage, there are some observations of disturbance in calcification of the sternum in rats and mice whose mothers had been exposed to a relatively high dose of methylene chloride during pregnancy.

There are no descriptions of allergic reactions to methylene chloride.

The effects of methylene chloride can be summarized as follows (1):

Ca 3500 mg/m^3 (1000 ppm)

Dogs and monkeys exposed continuously for four weeks showed some effect on the liver. Continuous exposure for 14 weeks produced kidney changes in rats. Headache was reported by 2 of 3 experimental subjects after one hour.

Ca 1000 mg/m^3 (300 ppm)

The lowest concentration at wich effects are observed in psychophysiological tests. All subjects tested after two to four hours exposure showed impaired performance in the Critical Flicker Fusion test. With exposure over four hours, performance in a vigilance test was also affected.

Ca 350 mg/m^3 (100 ppm)

Exposure for 7.5 hours per day for five consecutive days can cause COHb values to exceed 5%. Values return to normal after a weekend without exposure.

Ca 175 mg/m^3 (50 ppm)

Exposure for 7.5 hours per day for five consecutive days yielded no COHb values over 3%. Values return to normal overnight.

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CONSENSUS REPORT FOR STYRENE

(1980-02-29)

CAS No. 100426 1 ppm = 4.25 mg/m^3

This summary is based on a criteria document published by the Nordic Expert Group for Documentation of Occupational Exposure Limits (1), with some additions.

Uptake

Most body uptake of styrene vapor occurs via inhalation. About 65 percent of the amount of styrene inhaled is absorbed, regardless of whether exposure occurs during labor or rest or during the first or second half of the work shift. The health risk associated with skin uptake of styrene vapor is negligible, but under some circumstances styrene in liquid form can be taken up by the skin in appreciable amounts (2).

Acute effects

Acute subjective symptoms such as abnormal fatigue or feelings of intoxication have been reported by workers exposed to levels of 85-420 mg/m^3 (20-100 ppm). Further, impaired performance has been demonstrated in tests of perception, coordination, vigilance and reaction time (3, 4). An increased frequency of abnormal EEG readings has been reported for workers exposed for long periods to levels of 210-420 mg/m^3 (3, 5). With short-term exposure (30 minutes), impaired performance is not noted until concentrations exceed 420 mg/m^3 (100 ppm) (6). It is not clear whether or not these effects remain after exposure is terminated. Investigations of people employed in the manufacture of plastic boats (7) have shown that reaction time is affected by concentrations around the occupational exposure limit. The effect could also be observed 16 hours after exposure was terminated. Some recovery could be noted after longer exposure-free periods (8).

It is important to consider the fact that styrene uptake increases with physical effort; effects can thus be excepted with lower air concentrations. With acute exposure during rest, a significant increase of reaction time was demonstrated with a total styrene uptake of 600 mg (9) - a level reached after about two hours of exposure to 200 ppm in inhaled air. With a degree of physical exertion not uncommon in industry (lung ventilation ca 20 liters/minute) the same level is reached after about 4 hours of exposure to a concentration of only 0.21 mg/l (50 ppm) (9).

Chronic effects

Styrene exposure has been associated with increased frequency of chromosome aberrations, in animal experiments as well as in occupational groups exposed to styrene. In the latter case, an increase was noted with exposure to air concentrations of 20-40 ppm. Since the publication of the Nordic Expert Group's report (1), new informations on styrene's carcinogenicity has become available. In a newly published study (10) in which mice and rats were given the maximum tolerable dose (MTD) orally five times per week for 78 weeeks, no overfrequency of tumors was observed in any organ. An epidemiological study of reinforced plastics workers exposed to styrene (11) did not find evidence of increased morbidity due to tumor diseases. This study allowed no definite conclusions regarding the carcinogenicity of styrene, since both exposure times and observation times were quite short.

The risk of allergic reactions to styrene seems to be minimal.

The effects of exposures to concentrations up to 500 ppm can be summarized as follows (19:

420-2100 mg/m^3 (100-500 ppm)

With 918 mg styrene/m^3 of air (216 ppm), irritation of the eyes, nose and respiratory passages is apparent within 20 minutes; impaired performance in tests of reaction time, coordination, etc; function of peripheral nervous system affected (exposure level not clarly defined).

210-420 mg/m^3 (50-100 ppm)

Performance is affected in tests measuring visual perception, psychomotor functions and vigilance; increased frequency of abnormal EEG readings.

85-294 mg/m^3 (20 ppm)

Increased frequency of chromosome aberrations in the lymphocytes of occupationally exposed workers; impaired performance in tests of visual perception, coordination and vigilance; abnormal fatigue and symptoms of intoxication were reported by exposed workers more often than by a control group.

Below 85 mg/m^3 (20 ppm)

Exposure of pregnat rats to 1.5-5 mg of styrene/m^3 of air produced effects on the embryos.

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CONSENSUS REPORT FOR TETRACHLORETHYLENE

(1980-02-29)

Synonyms: Ethylene tetrachlorethylene per, perc, perchloroethylene, tetrachlorethene.

1 ppm = 6.89 mg/m^3 1 mg/m^3 = 0.145 ppm

The following survey is based primarily on a report recently published by the Nordic Expert Group for Documentation of Occupational Exposure Limits (1).

Tetrachlorethylene at room temperature is a colorless, transparent, non-flammable liquid which is used primarily as a dry cleaning fluid, and to a lesser extent as an industrial degreasing agent. It can also be used in the extraction of oil-soluble substances and as an intermediate reactor in the production of fluoridated hydrocarbons.

Resorption can occur via the lungs, the digestive tract and the skin. According to Reference 1 (page 9), during eight hours of exposure to 100 ppm retention drops from an initial 91 percent to 36 percent, and averages 48 percent - ie, with prolonged exposure, retention gradually decreases.

Biotransformation is negligible. Only a small percentage of the tetrachlorethylene absorbed is metabolized; some of it becomes trichloroacetic acid, which can be demonstrated in urine.

Elimination proceeds slowly, primarily because tetrachlorethylene, like other lipid-soluble organic solvents, is deposited in adipose tissue, and after exposure is terminated is released gradually over several days. Elimination is a two-phase process, proceeding rapidly for the brief initial phase (a few hours), and slowly for the second phase, which lasts for several days. Most tetrachlorethylene is eliminated via the lungs. Only a small portion is excreted by the kidneys, som of it in the form of trichloroacetic acid.

Acute effects are described for the skin, eyes, respiratory system and central nervous system (see Table 1).

Effects of long-term exposure are of considerable interest, especially with regard to low concentrations (ie levels near the occupational exposure limits). There are unfortunately very few systematic (epidemiological) studies which are relevant here. There is one American study (2) of workers in dry-cleaning establishments, in whom occurrence of psychological problems and signs of functional disturbance in the peripheral nervous system were investigated. Exposure levels were relatively low (time-weighted average value in the most exposed group was 37 ppm, with peak values averaging 215 ppm). This study found no significant differences between the exposed group and the control which could be ascribed to the exposure to tetrachlorethylene, but unfortunately the study methods used make it impossible to say whether there was any damage to the nervous system.

It is well known (3) that psychological symptoms of the type included in the "neurasthenic syndrom" (tiredness, lack of initiative, loss of memory, headache, irritability) are an early sign of chronic, or at least sub-chronic, effects of solvents on the central nervous system.

It is mentioned in Reference 1 (page 17) with support from three previous reports, that such symptoms have been observed in persons working with tetrachlorethylene, but there are no details on the conditions of exposure.

The first of these papers (4) is from 1953, and reports a study of exposed workers only. Exposure levels were high - 232 to 385 ppm. Acute effects on the central nervous system were reported, but the authors mentioned no chronic or sub-chronic effects. It can be supposed that this was not their primary interest.

The other work (5) is from Germany. This is an extremely thorough epidemiological study of 112 workers in a railway factory and 101 controls. The study was intended to clarify effects on the liver and kidneys, and the psychological problems are mentioned only briefly. Exposure levels were moderate: in 75 percent of the measurements the concentration was below 50 ppm, and in only 3 percent did it exceed 150 ppm. With regard to psychological problems, the authors say nothing about whether the observed difference between the two groups was statistically significant, but judging from the diagram in the report such was probably not the case. For acute effects, on the other hand, the differences are larger and probably statistically significant. For example, 45 percent of the exposed group reported dizziness while at work, against only three percent of the control.

The third work is the American study described earlier (2), and as already mentioned, it provides little useable material on the question of neurasthenic syndrome.

There is reason to suppose that tetrachlorethylene, like other organic solvents, can cause chronic or sub-chronic neurasthenic syndrome, but there are unfortunately no studies which could help to identify the exposure level at which this can occur. Continued study of the matter is necessary for the establishment of reasonable exposure limits.

Peroral administration of tetrachlorethylene has been found to yield a dose-related increase of hepatocellular carcinomas in mice of both sexes (6). Exposure to tetrachlorethylene has also been associated with increased risk for malign diseases in man, primarily liver cancer and leukemia (7). High doses are probably necessary, but this report gives no detailed information on exposures. The report mentions in closing that a cohort study is being conducted to more closely investigate the cancer risk.

Rats show no increassed frequency of liver tumors (6). Liver and kidney damage has been noted in animal experiments and in people occupationally exposed to tetrachlorethylene, but exposure levels have usually been higher than those associated with acute effects on the nervous system.

Interaction. One study (8) demonstrated that with low exposure (25 ppm), alcohol intake (blood alcohol concentration of 0.3 to 1.0 mg %) so affected the uptake of tetrachlorethylene that its concentration in blood increased by 75 percent. This effect was not noted at higher exposure (100 ppm).

Exposure levels current in Swedish dry-cleaning establishments are usually around 10 ppm or less. However, there are probably a significant number of shops where exposure may be as high as 40 ppm, but levels higher than this occur only exceptionally (eg with a defective ventilation system) (E. Lindberg, NBOSH. pers. Communication).

Table 1. Acute effects of exposure to tetrachlorethylene

Concentration (ppm)	Effect
5	Odor can be noticed
100	Temporary irritation of the mucous membranes of the nose and throat. Slight drowsiness with prolonged (7 hours) exposure. Slight headache and/or dizziness.
200	Irritation of the eyes, headache, drowsiness, dizziness.
300	Smarting of the eyes, feelings of intoxication and reduced inhibition, difficulty in coordination. Temporary nausea.

Table 1 (cont'd)

Concentration (ppm)	Effect
500	Increased salivation, with a sweetish, metallic taste in the mouth. Nausea.
600	Dizziness, difficulties in coordination. Stiffness and numbness of lips.
900	Weakness, extreme drowziness. Burning eyes. Lowered blood pressure, numbness in lips and nose.

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CONSENSUS REPORT FOR TOLUENE

(1980-02-29)

CAS No. 108883. 1 ppm = 3.75 mg/m^3 at 20^{0}C and 760 mm Hg.

Explosive concentrations are given as 1.2-7.1 percent by volume.

Limits of detection by odor have been established at 1-10 mg per m^3 of air.

This summary is based on a criteria document published by the Nordic Expert Group for Documentation of Occupational Exposure Limits (1), with certain additions.

Uptake and distribution

With occupational exposure to toluene vapor, most body uptake is by inhalation. There is rapid and high retention during the first half hour, followed by gradual reduction to an uptake of about 50 percent of the inhaled amount. This proportion is maintained during the entire work pass, reflecting a state of equilibrium between uptake and elimination. Under certain circumstances, toluene in liquid form can be taken up through the skin (2). Toluene is highly soluble in oil, and accumulation of toluene in fatty tissues should therefore be noted in discussions of toxicity. The biological half-life of toluene in such tissues has been calculated to be about 3 days. This, however, does not exclude the possibility of some day-to-day accumulation of toluene in body fat, at least in the begining of the exposure period.

Acute effects

Discussions of exposure limits for toluene are based primarily on its effects on the central nervous system. Experimental exposure of human subjects have demonstrated acute depressive effects on psychomotor functions. Seven hours of exposure to 750 mg/m^3 (200 ppm) resulted in prolonged reaction time (3). With short-term exposure, a clear dose-effect connection was observed in several psycho-physical tests (4). Tests of reaction time were most sensitive, showing a significant increase with 300 ppm, while no increase in reaction time was observed with 100 ppm, the next-lower concentration studied. Concentrations of 500 ppm or more also affected perception ability. Since the toluene concentration in the organism surely did not reach a maximum during this brief exposure (20 minutes), it is probable that there are effects of this sort with considerably longer exposure times.

When evaluating the results from studies of the sort mentioned above, in which physically inactive persons are exposed to toluene, it must be remembered that with the same concentrations in actual work situations the organism can take up two or three times as much as at rest. The following calculation is based on this fact: in short-term experiments during rest a significant increase of reaction time was demonstrated with a total toluene uptake of 170 mg (5), a concentration reached after about 1½ hours of exposure to 100 ppm. With a degree of physical labor normal in industrial contexts (lung ventilation 20 liters per minute), the same total toluene uptake is reached after 1½ hours of exposure to concentrations of only about 50 ppm. Even though published documentation contains no direct proof of an effect at such low exposure levels, the above reasoning indicates the need for a safety margin to compensate for increased uptake during physical exertion.

Effects of long-term exposure

Other effects on the central nervous system which have been described for the low-dose area are headache, fatigue and dizziness, and symptom complexes of the type called "psycho-organic syndrome" in occupationally exposed persons. Of particular interest here are results from print shops, where toluene is a major exposure factor for ceratin occupational groups even though there is also some exposure to other solvents. "Psycho-organic syndrome" was diagnosed in 21 percent of a group of typographers exposed to an average 300 ppm for 33 yeras, and in 40 percent of a group of print-shop workers exposed to an average 430 ppm over 17 years (6). During recent years, there has been increasing indication that effects of this type can appear in occupational groups which have been exposed for long periods to low concentrations of solvent mixtures including toluene, sometimes in high proportion (7, 8).

The above studies obviously provide no clear proof of the toxicity of toluene by itself, but on the other hand they do provide a strong incentive for continued research, particularly on the effects of prolonged exposure to concentrations of 50-100 ppm or less. To what extent the above-mentioned exposures to solvent mixtures, besides having acute and sub-acute effects, also involve chronic effects (ie lasting damage), can not yet be established.

In addition to effects on the nervous system, certain other factors should be considered in the context of exposure limits, but the matter of interpretation is more uncertain. For example, menstrual dysfunction has been reported. There are also reports of effects on some blood cells and their enzymes and on liver cells and liver enzymes in blood serum. The clinical implications of these discoveries are unclear.

Special chronic effects

There is no clear evidence that toluene has embryotoxic, carcinogenic or allergenic effects. We have found no reports of toluene passing the placenta. There are indications that exposure to toluene may cause chromosome changes, but the evidence here is contradictory. With regard to possible immunological effects, it can be mentioned that glomerulonephritis has been correlated to solvent exposure, though not specifically to toluene; an autoimmune reaction was hypothesized.

Research results on acute or chronic effects of toluene at exposure levels below 375 mg/m^3 (100 ppm) are scarce and difficult to interpret. This applies particularly to field studies, where dose data is uncertain at best and where exposure to other substances is either definitely or most likely part of the picture. No dose-response relationships have been demonstrated for 8-hour exposures to concentrations below 100 ppm.

The following table summarizes research results for exposure to different concentrations of toluene (1):

1875-2625 mg/m^3 (500-700 ppm), short-term exposure

Symptoms of extreme CNS depression. Prolonged reaction time and choice reaction time. Reduced perception speed.

1125 mg/m^3 (300 ppm), short-term exposure

Prolonged reaction time in 8 of 12 subjects exposed.

1125 mg/m^3 (300 ppm), long-term exposure

Incipient reduction in superior CNS functions. This effect may be seen at even lower exposure levels.

750 mg/m^3 (200 ppm), 6-8 hours

Clear symptoms of incipient CNS depression and possibly intoxication. Prolonged reaction time.

375-750 mg/m^3 (100-200 ppm), long-term exposure

Some research results indicate possible chromosome changes. Effects on liver enzymes, but still within normal limits.

375 mg/m^3 (100 ppm), long-term exposure

Morphology of leucocytes affected. Menstruation disturbed. Probable symptoms of incipient CNS depression in some subjects.

161-375 mg/m^3 (43-100 ppm), long-term exposure

Effects on lymphocyte morphology and on leucocyte and lymphocyte enzymes.

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CONSENSUS REPORT FOR XYLENE

(1980-02-29)

Xylene (dimethyl benzene) occurs as three isomers: ortho-, meta-, and paraxylene. Technical grade (industrial) xylene is a mixture of these with a specific amount of ethyl benzene, usually 6-10 percent. There can also be traces of other substances such as benzene, but benzene concentrations are now usually less than 0.001 percent. When uesd as a solvent, xylene is often mixed with other solvents such as toluene. This, as well as the addition of ethyl benzene, makes it largely impossible to obtain epidemiological information on the effects of xylene alone. Pure xylene isomers are used mainly as a raw material in the production of chemicals. About 70 percent of the xylene manufactured is probably used for this purpose. The exposure problems arising with this use, however, are smaller than those occurring with the use of xylene as a solvent.

CAS No. for	orthoxylene	95476
	metaxylene	108383
	paraxylene	106423

1 ppm = 4.33 mg/m^3

Odor threshold: Established at 0.14 and 20 ppm in two different experiments (remarkably large difference!). In both cases the values were lower than those for toluene.

This summary is based on a criteria document published by the Nordic Expert Group for Documentation of Occupational Exposure Limits (1), with certain additions.

The Nordic document deals with xylene isomers in mixtures with ethyl benzene, and the toxicity of ethyl benzene is therefore not discussed separately. Some information about it, obtained from animal experiments,

is referenced in the NIOSH criteria document on xylene from 1975 (2). These experiments indicate that the toxicity of ethyl benzene may be somewhat greater than that of xylene isomers. It can be mentioned here that ACGIH (3), in its TLV list, proposed somewhat lower STEL values (15 minutes short-term exposure limits) for ethyl benzene than for xylene; however, there seems to be no official documentation for this.

There is no adequate basis for differentiating between the three xylene monomers with regard to toxicity. Under the circumstances, it would probably be best to adopt the opinion of the Nordic expert group: that the toxic qualities of the three substances are probably very similar.

Uptake, distribution and transformation

With occupational exposure, xylene usually enters the body via the lungs. Of the amount entering the lungs, about 65 percent is absorbed during rest; 60-65 percent during light exertion; and 50 percent during heavy physical labor. With massive exposure to xylene in liquid form, considerable amounts can be absorbed through the skin. Skin absorption of xylene in vapor form is probably of negligible importance. It should be remembered, however, that xylene - and other solvents as well - are more easily absorbed by skin which is damaged by skin disease or injury.

Xylene is easily soluble in blood and fatty tissues. About 95 percent of the amount taken up is metabolized. The primary end product, methyl hippuric acid, can be identified in urine and provides an index of the amount of xylene absorbed. Xylene is metabolized rapidly in the liver. It has been calculated that metabolizing capacity is fully exploited when inhaled concentrations are around 770 ppm and physical activity results in lung ventilation rates of about ten liters/minute.

Acute effects

In discussing exposure limits for xylene, it is the acute effects on the nervous system and the minor irritations which can be held to with most certainty. There is scarcely any information which can be used for estimates of possible long-term effects in the low dosage area.

The most unequivocal information about acute effects comes from experiments with human subjects, which demonstrated significant effects on reaction time, etc with short-term exposure to air concentrations of 1300 mg/m^3 (300 ppm) (4). The total body uptake of xylene should not be allowed to exceed 600-1000 mg if acute effects are to be avoided. Irritation and other negative effects have been shown for concentrations of 300-400 ppm or more.

With xylene, as with other solvents, it is necessary to consider the differences between uptake during physical exertion and that during rest. With exposures to 870 mg/m^3 (200 ppm) during two hours of alternating exercise and rest, the amount of xylene absorbed amounted to about 1.4 g - about 60 percent of the total amount (5). As indicated earlier, at this level there is probably some depressive effect on the central nervous system.

Xylene's high solubility in lipids implies that its storage in fatty tissues should be considered in assessments of toxicity. The half-life of m-xylene in subcutaneous fat varies from one to about 6 days (6). Because of xylene's relatively long elimination time from subcutaneous adipose tissue, a certain accumulation will occur during the first weeks of normal occupational exposure (five-day work weeks). Since xylene is metabolized rapidly and blood circulation in subcutaneous fat is relatively low, the stored amount will be relatively small - at most, ten percent of the xylene entering the body.

Long-term effects

Even though there are no clear data on the effects of long exposure to xylene, it must be noted that there have been observations of changes in the central nervous system which can be interpreted as chronic or long-lasting in workers exposed to solvent mixtures including xylene. The possibility that long-term exposure to xylene may have neurotoxic effects can therefore not be dismissed.

Among other observations not adequate as a basis for defining exposure limits are observed correlations between glomerulonephritis and exposure to solvents. Some animal experiments indicate that xylene can cause kidney damage. Some biochemical indication of xylene toxicity in the lungs can also be mentioned in this context.

Vacuoles of a temporary nature have been reported in the corneas of a group of spray laquerers who were probably exposed to very high concentrations of nearly pure xylene.

Special chronic effects

Very little is known about the possible mutagenic and teratogenic effects of xylene. A few animal experiments give reason to suspect that relatively low air concentrations of xylene might affect development of the embryo. There seem to be no published works on the mutagenic characteristics of xylene. There is also very little data on carcinogenicity.

A single case of suspected allergy is described. This was a case of contact urticaria, where a patch test with xylene gave a positive result. Whether an allergy mechanism lay behind the reaction is unclear.

The effects of xylene can be summarized as follows (1):

3000-3500 mg/m^3 (ca 700-800 ppm)	Animal experiments: Rats and dogs exposed for 65 days showed no effects. Rats, guinea pigs and dogs exposed for 30 days showed no effects on growth or hematology, and no pathological changes were observed in examined organs. Rats and rabbits exposed for 130 days acquired subacute (chronic) glomerulonephritis.
3000 mg/m^3 (ca 700 ppm)	Slight irritation of eyes, nose and throat. Feelings of intoxication and minor disturbance of balance.
1300 mg/m^3 (300 ppm)	Slight deterioration of higher nervous functions in persons doing light work. Prolonged reaction time with short-term exposure.
1000 mg/m^3 (230 ppm)	Minor embryotoxic effects on rat embryos.
870 mg/m^3 (200 ppm)	Disturbed sense of balance with day-long exposure having peaks up to 400 ppm. Prolonged reaction time in one of five persons exposed for an entire work day.

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CONSENSUS REPORT FOR INORGANIC LEAD

Introduction

A number of surveys of the risks of exposure to inorganic lead in the general environment and in the working environment have been published in recent years (8, 12, 14, 21, 24, 27). This summary is an evaluation and amplification of the information in those studies.

Exposure

Exposure to inorganic lead occurs via food, water and air. In Sweden, this background exposure is low. Occupational exposure to lead occurs in Sweden primarily in the following contexts: with smelting, refining, casting and polishing of lead-containing alloys; in lead accumulator factories; in the manufacture of lead crystal, lead-glazed ceramics, and certain plastics with additives of lead-containing pigments or stabilizers (eg PVC); in spray painting with paints containing lead pigment; and with scrapping/-torching of lead-coated materials.

Metabolism

Exposure to inorganic lead in the working environment occurs primarily via inhalation of lead-containing aerosols. The amount of lead uptake via the lungs depends on the lead content of the air, the nature of the work (as it affects lung ventilation), the size of the particles in the aerosol and the solubility of the lead compound in question. When lead-containing aerosols with a particle size below 5 um are inhaled, about 20-40 percent (by weight) is absorbed. About 5-10 percent of lead which is swallowed is absorbed in the digestive tract. Substantial exposure to lead through food or tabacco (snuff) contaminated at the workplace is now rare.

Inorganic lead is accumulated throughout the body. The largest lead depot (ca 95 percent) is in the skeleton. More than 95 percent of the lead in blood is bound to the blood cells. Swedes not occupationally exposed to lead have a blood lead content (B-Pb) of about 0.5 umol/liter.

Lead is excreted from the body via urine (ca 80 percent) and feces. The excretion process is complicated. After exposure is terminated, B-Pb declines with a speed which in the beginning probably reflects changes of lead concentrations in soft tissues. The half-life of lead in this reservoir is about a month (17). Lead deposited in the skeleton decreases much more slowly; it has a half-life of several years. The lead content of the blood reflects current exposure as well as the size of the depot in the skeleton, and thus also earlier exposurers.

Effects

Inorganic lead can affect the body in a number of ways. In studies, these effects have for the most part been correlated to B-Pb. There is very little data relating effects to lead concentrations in air. In estimating the health risks of different lead concentrations in air, it is therefore first necessary to correlate effects to B-Pb, and then to establish the relationship between B-Pb and air concentrations. Particularly the latter is afflicted with considerable uncertainty.

Effects (except those on genetic material and reproduction) of inorganic lead on adult individuals with different lead concentrations in the blood are summarized in Figure 1.

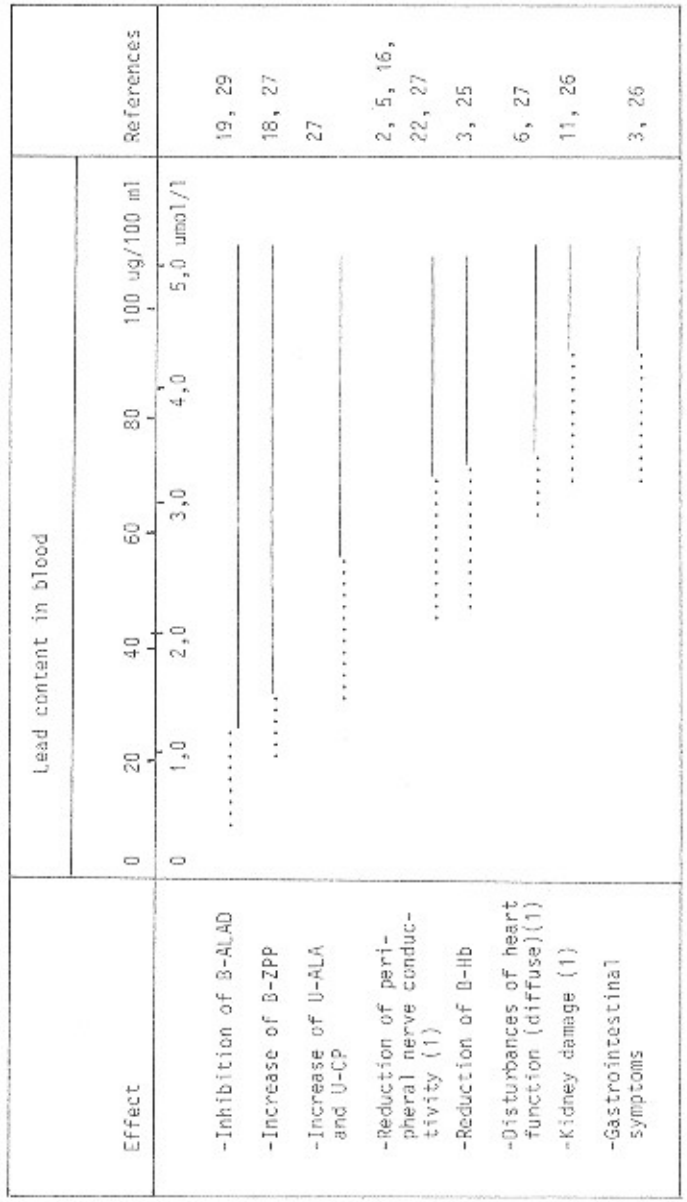

Figure 1. Lead content in the blood related to its effects on adults. Minor changes in a small proportion of those exposed = ... Definite changes in 50 percent or more = _____.

(1) After several years of exposure

Heme synthesis

The most well-known effect of inorganic lead is its disturbing influence on several steps in the chain of reactions leading to the formation of heme, a constituent of hemoglobin, and of a number of enzymes in the body. Even a very small increase of lead in the blood produces a measureable inhibition in activity of the enzyme δ-aminolevulinic acid dehydrase in blood cells (B-ALAD). Greater exposure to lead brings an increase in concentrations of protoporphyrin (particularly zink protoporphyrin, ZPP) in the blood cells, and increased excretion of δ-aminolevulinic acid (U-ALA) and coproporphyrin (U-CP) in urine. These changes have not in themeselves been shown to be detrimental to health, but they can be used as a biological index of lead exposure. A slight increase in U-ALA and U-CP is usually not associated with any measurable effect in the form of reduced hemoglobin concentrations in the blood. With greater degrees of exposure (B-Pb ca 3-4 umol/liter), disturbance of heme synthesis together with shortened life span of the blood cells can contribute to a reduction in blood hemoglobin (B-Hb), resulting in anemia. Heme synthesis is also disturbed in organs other than the blood-forming bone marrow, and lead thus affects other enzymes in the body. The exposure level precipitating harmful effects of this type is not known.

The nervous system

Exposure to inorganic lead can damage the nervous system. Several studies have shown that chronic exposure decreases the speed of conductivity in perpheral nerves. Discrete effects of this nature probably occur with B-Pb concentrations as low as 2.5 umol/l (22, 27), even though in some studies (15, 23) concentrations as high or higher have not been associated with functional disturbances. The discrepancy may be due to differences in exposure patterns and/or methodology. The significance of such disturbances is not clear; the effect may be reversible (1). With higher exposure levels, there can be serious changes in nervous tissue.

Inorganic lead also affects the brain. These effects are difficult to measure. In psychometric tests, it has been possible to demonstrate minor effects in groups with B-Pb levels of 3.0 umol/l or higher. An increased frequency of subjective symptoms (fatigue, anxiety, loss of memory, etc) has also been reported (7, 27).

Kidneys and digestive tract

Higher body burdens of lead (B-Pb ca 3.5 umol/l) can lead to kidney damage. Gastrointestinal symptoms are common with blood lead levels higher than about 3.5 umol/l. For both kidney damage and gastrointestinal symptoms, the background material on which to base estimates of exposure/response curves is limited.

Reproduction

Experimental exposure of male animals to high peroral doses of inorganic lead has resulted in decreased fertility, and their offspring have shown increased perinatal mortality (17). Sperm damage has been reported in workers exposed to lead (B-Pb of 2-4 umol/l), as has an increased frequency of abortions in their female partners (10). This survey can however be criticized on methodological grounds.

Lead passes through the placenta to the embryo. The lead concentration in blood in the umbilical cord is about the same as that in the bloodstream of the mother. Lead is secreted in milk. Animal experiments exposing pregnat rodents to high doses of inorganic lead resulted in resorbtion of the embryo, and offspring showed reduced weight, birth defects, increased perinatal mortality and developmental disturbances (17). Indications of abortion-inducing effects and prenatal damage in human subjects can be found in older studies, but the information is incomplete.

Even though the data is not conclusive, inorganic lead must be regarded as potentially toxic with prenatal exposure in humans. There is no information which can be used to estimate the relationship between dose and effect/response. It is nevertheless reasonable to assume that the nervous system of an unborn child is at least as sensitive as that of an adult. Exposure time, however, is relatively short.

If exposure to lead is terminated as soon as pregnancy is diagnosed, the lead content in soft tissues (and probably also in the embryo) can usually be expected to drop by 50 percent within a month or two. This implies that the embryo can be exposed to high concentrations of lead during most of the period that embryotoxic effects would be expected. Toward the end of pregnancy - when toxic effects would hit primarily the nervous system of the fetus - concentrations will be much lower than before exposure was terminated.

Mutagenicity and carcinogenicity

Genotoxic effects in the form of chromosome changes in lymphocytes from peripheral blood have been noted in some studies of people exposed to lead (13, 27). The significance of this as far as health is concerned is unclear. Even though some animal experiments provide indications that inorganic lead can be carcinogenic, epidemiological studies of workers exposed to lead do not support the existence of such an effect in man (27).

Airborne lead/B-Pb

It seems reasonable to assume some sort of connection between lead concentrations in air and B-Pb. A number of studies have been made in attempt to clarify this relationship (4, 9, 28). The results, however, have shown poor correlations or none at all. This may be due to several factors, eg particle size and solubility of the lead in the aerosol; the physical effort involved in the work; and/or exposure by pathways other than air. Estimates of lead uptake based on lead concentrations in air can thus be misleading. This is a strong argument in favor of biological monitoring of exposed workers.

WHO, in spite of all the possible arguments against it, has made an extremely rough estimate of the correlation between lead concentrations in air and B-Pb (27). With lead concentrations up to about 50 ug/m^3 of air, every increase of 10 ug/m^3 in long-term exposure (particle size etc unspecified) yields an average increase of about 0.25 umol/l in B-Pb. In populations like that of Sweden, with a basal B-Pb of about 0.5 umol/l, an exposure of 50 ug/m^3 would correspond to an average B-Pb of about 1.75 umol/l.

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Summary

Scientific Basis for Occupational Standards. Arbete och Hälsa 1981:21 pp 1-62.

Critical evaluations of those scientific data which are relevant as a background for discussion of Swedish occupational standards. These are the consensus reports given by the Criteria Group at the Swedish National Board of Occupational Safety and Health between May, 1979 and June, 1980.

Key words: 1,2-dibrom-3-chlorpropane, Methyl iodide, Formaldehyde, Chromium, Trichlorethylene, Cadmium, p-Aminoazobenzene, 1,2-Dichlorethane, Methylene chloride, Styrene, Tetrachlorethylene, Toluene, Xylene, Inorganic lead.

Sammanfattning

Underlag för hygieniska gränsvärden. Arbete och Hälsa 1981:21, s 1-62.

En sammanställning baserad på en kritisk genomgång och värdering av de vetenskapliga fakta, vilka är relevanta som underlag för fastställande av hygieniskt gränsvärde. Sammanställningen omfattar de utlåtanden som Kriteriegruppen för hygieniska gränsvärden avgivit under perioden maj 1979 - juni 1980. (På engelska).

Nyckelord: 1,2-dibrom-3-klorpropan (DBCP), Metyljodid, Formaldehyd, Krom, Trikloretylen, Kadmium, p-Aminoazobensen, 1,2-Dikloretan, Metylenklorid, Styren, Trikloretylen, Toluen, Xylen, Oorganisk bly.