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SCIENTIFIC BASIS
FOR
SWEDISH OCCUPATIONAL STANDARDS
V

Criteria Group for Occupational Standards
National Board of Occupational Safety and Health
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PREFACE

The Swedish Criteria Group for Occupational Standards was created in 1978 within the Research Department 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 limits).

Searches of the literature and collection of material are handled partly by the members of the Criteria Group and partly by external experts who are 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 consensus reports are discussed within the Criteria Group before they are approved. The now presented reports were reviewed and approved by the Criteria Group during the period July, 1983 to June, 1984. This is the fifth collection of consensus reports published by the Criteria Group; the four previous collections were published in Arbete och Hälsa 1981:21, 1982:9, 1982:24, and 1983:36 respectively.

The consensus reports were translated from Swedish by Ms Frances van Sant, who also prepared the final manuscripts on a word processor.

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CONTENTS

CONSENSUS REPORT FOR POLYAROMATIC HYDROCARBONS
February 15, 1984

This report is based primarily on a criteria document (17) written for the Criteria Group. The reader is referred to Appendix 2 in this document for chemical-physical data on individual polyaromatic hydrocarbons (PAH) and for synonyms, structural formulas and CAS numbers in table form.

The present report does not take up substituted PAH such as nitroarenes.

Occurrence in the working environment

PAH in the working environment is practically always in the form of mixtures, which vary in composition from workplace to workplace. There are relatively few detailed monitoring studies; most studies cover only benzo(a)pyrene (BaP). A survey of BaP concentrations in various Swedish working environments, measured primarily with stationary instruments, has recently been published (16). The highest concentrations (10 µg BaP/m^3 or higher) were found at gas works and coking plants, within the aluminum industry, and in association with the production of tar and asphalt.

In more detailed analyses, up to 30 different PAH substances were measured, and data from these analyses were used to construct a "PAH profile" in which the relative amounts of the different PAH substances, in percent of total PAH, were plotted against each polyaromatic in order of volatility. Different working environments showed different PAH profiles (2). It was found that PAH emissions from a particular source keep a fairly constant profile. This profile can change, however, if process conditions are altered.

Occupational exposure to PAH can also occur in iron and steel works and metal foundries; and while cleaning chimneys or working around internal combustion engines. It should be emphasized that at present no analysis of PAH in the working environment is anywhere near as thorough as the available analyses of automobile exhausts, for example with regard to the composition of the gas phase, particle-bound substituted PAH, etc. Such research is urgently needed.

Uptake, biotransformation and excretion

PAH is taken up in the body primarily via inhalation, either in gaseous form or, more usually, bound to airborne particles. When rats were forced to inhale a BaP aerosol, after one hour the highest tissue concentrations (per gram wet weight) were found in the intestine, lungs, trachea, lymphatic glands and nasal epithelium (20). After 24 hours the tissue concentration had dropped to 1% of the post-exposure maximum. Particles enhance the uptake of BaP and thus the accumulation of a high local dose in the lungs. PAH and its biotransformation products are excreted primarily via gall and urine. Urine contains mainly the water-soluble conjugated products (22).

BaP is the most thoroughly studied of the PAH substances and its biotransformation can be considered to provide a model for the biotransformation of the others. A fairly detailed summary of the biotransformation of BaP has recently been published (5). Biotransformation occurs via several enzymatic reactions, which create several different products. The proportional amounts of the different products produced are dependent on the amounts and activity of the enzymes involved. From a toxicological (carcinogenic) point of view, the most important transformation product of BaP is a diolepoxide which can bind to DNA. In animal experiments (13), a binding between BaP-diolepoxide and DNA was noted in all the soft organs observed.

PAH can itself induce the enzymes which participate in its biotransformation. There seems to be no correlation between the induction ability of a particular PAH and its carcinogenic effect. Enzyme activity after induction varies with the type of tissue and the species, as well as with the type of inducer used (17).

It is impossible to use experimental data on exposure to a single PAH as a basis for estimating risks for a human population exposed to PAH mixtures or to PAH and other substances simultaneously.

Toxic effects

The primary risk associated with exposure to PAH is that for cancer, particularly of the lungs, bladder and skin. Other diseases suspected to increase in frequency with exposure to PAH are chronic respiratory diseases and heart diseases.

Epidemiological studies

The pattern of causes of death was studied for 11,500 English gas workers (3). They were divided into three groups: a) massively exposed in coking plants; b) intermittently exposed; and c) not exposed. Industrial hygiene monitoring studies made in gas work retort houses at the same time as this survey (15) showed an average BaP concentration of 3 $\mu g/m^3$. The highest values (average concentration 200 μg BaP/m^3) were measured above the horizontal ovens. In group a) there were 3.4 deaths from lung cancer/1000 person-years; in group c), there were 1.6/1000. The average for England and Wales was reported to be 2.6/1000. Smoking habits in the different groups were apparently about the same. Deaths from bladder cancers were significantly higher in group a) than in group c), but the increase was considered to be caused by beta-naphthylamine (3). The

study also provides some support for assuming a dose-related increase of risk for death due to ischemic heart disease. There is also a German study of gas works employees (19), in which aromatic amines (beta-naphthylamine) are regarded as causing cancer.

In an American study (15, 23) of nearly 60,000 steelworkers, 3,500 of whom worked in a coking plant, it was noted that for those working around the coke ovens the risk of lung cancer was 2.5 times higher than that for the group as a whole. For persons who worked over the ovens, the risk was ten times as high. No increased mortality due to bladder cancer was noted, but there was an increased frequency of kidney cancers. Though these cases did not occur among the most highly exposed workers, they seemed related to work around the coke ovens.

Two cases of lung cancer were recorded in a mortality study of personnel at a Swedish coking plant (1), but an increased morbidity was not definitely established (2 cases against 0.6 expected).

In a Finnish mortality study (14) of about 3,900 foundry workers, it was shown that mortality from lung cancer was higher in iron foundries, primarily among moulders and core makers, than in other metal industries.

A study (25) of 4,000 workers retired from iron and steel works, coke ovens and municipal gas works in Japan reported the following relationships between found and expected cases of lung cancer: 2.37 for iron and steel mill workers, 1.28 for coke oven workers, and 0.82 for workers in municipal gas works.

An American mortality study of 22,000 men working in the aluminum industry (4) yielded a SMR (Standard Mortality Ratio) of 87 for the entire cohort, compared with the national average. Increased mortality due to lung cancer was reported for

workers in the electrolysis hall (SMR 121); the increase was more pronounced for workers around the horizontal Söderberg electrodes (SMR 162). In one study (6) from Canadian aluminum reduction plants, the number of "tar years" were calculated for nearly 6,000 persons. In the group with more than 20 "tar years", the risk for lung cancer was nearly tripled.

Nearly 6,000 asphalt and tar workers, primarily roofers, were studied in the USA (7). For those who had been working 20 to 29 years, mortality due to lung cancer, expressed in SMR, was 152; for those employed 30 to 39 years 150; and for those employed more than 40 years 245. For the group as a whole, there was increased risk of bladder cancer (SMR 169). In addition, there were three deaths from skin cancer (besides melanomas), against an expected 0.75, among those who had joined the union more than 20 years previously. Leukemia was also reported in overfrequency among workers who had been union members for a long time (13 cases against 7.8 expected).

In a Swedish study (8, 9) of over 2,000 chimney sweeps, the reported incidence of lung cancer was nearly tripled (32 observed cases against 12.1 expected). Smoking habits were reported to be no different from national averages. A doubled risk for leukemia was also noted, as was some increased incidence of cancers of the esophagus and liver, and of ischemic heart disease.

Experimental studies, carcinogenicity

A survey of the carcinogenicity of individual polyaromatic hydrocarbons has been made by IARC (11). A summary is presented in Table 1. The scant toxicological information on interactions among different PAH substances indicates that interaction effects of PAH mixtures must be established empirically and can not be predicted from data on the individual substances involved.

Table 1. PAH shown experimentally to be carcinogenic (17).

Benz(a)anthracene*	Mice, rats
Benz(e)acephenantrylene*	Mice (skin painting, injection)
Benzo(j)fluoranthene	Mice (skin painting)
Benzo(a)pyrene*	Several species
Benzo(e)pyrene	Mice (skin painting)
Chrysene*	Mice (skin painting, injection)
Dibenz(ah)anthracene*	Several species
Dibenzo(h,rst)pentafene	Mice (injection)
Naphtho(rst)pentafene	Mice (skin painting, injection)
Dibenzo(bdef)chrysene	Mice, rats (skin painting, injection)
Benzo(rst)pentafene	Mice, hamsters (skin painting, injection)
Indeno(1,2,3-cd)pyrene*	Mice (skin painting, injection)

* Substances shown to be complete carcinogens (both promotors and initiators). This property has not been studied for the other substances.

Dose-response/dose-effect relationships

It is not possible to use the epidemiological studies as a basis for establishing a dose-response relationship, since the data on the working environment is too scanty, the BaP determinations uncertain, and the BaP concentrations given for the same occupations vary too much from study to study and place to place.

There are dose-response data from several experimental cancer studies with animals, and these seems to indicate a linear dose-response relationship (10, 12). The shape of the dose-response curve seems to depend more on the length of exposure than on the total dose (21); that is, several small doses produce more tumors than a single dose, even though the total amounts are the same. The dose-response curve for a mixture of several carcinogenic PAHs was less steep than that of BaP alone, although the mixture was more potent; at higher doses the substances seem to work against each other to inhibit effects. The binding of BaP to DNA is a function of the dose. The curve is linear up to about 1 mg BaP/kg body weight, and at higher concentrations it develops a sigmoidal shape corresponding to the doses of BaP which are followed by enzyme induction within 24 hours (18).

BaP as a risk indicator

BaP has often been used as an indicator of the PAH content of air pollution due to combustion gases. However, BaP concentrations from different combustion processes vary quite a bit, and BaP represents only a small portion of the mutagenic and carcinogenic potential of such pollutants (10). For example, smoking is associated with low BaP concentrations but presents a higher cancer risk than occupational exposure to considerably higher BaP concentrations. BaP (as well as other individual polyaromatic hydrocarbons) can thus be regarded as an inadequate risk indicator for the carcinogenic effects of air pollutants. For dose-response relationships (and exposure limits) it would be preferable to express the dose as concentration of BaP, total PAH, or in some other way, for each type of process or each working environment, rather than to have a generally applied single value for BaP, as this can give a misleading idea of the cancer risk. At present there is no scientific data on which to base a dose-response relationship.

Conclusions

A large number of individual PAH substances are carcinogenic, as are PAH mixtures. There is an increased risk of cancer, primarily of the lungs, bladder and skin, with exposure to combustion products from the burning of fossil fuels. There is no substance which can serve adequately as a general risk indicator. Nor is there any basis for discussion of a dose-response relationship for any occurrence of occupational exposure.

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APPENDIX

Analysis methods for polyaromatic hydrocarbons

Polyaromatic hydrocarbons in the working environment never occur singly, but always in mixtures containing several dozen closely related hydrocarbons in addition to other substances with similar structures, such as nitrogenous derivatives.

It is therefore necessary, when choosing a method to analyze polyaromatics, to consider just what result is desired: either a picture of the hydrocarbon mixture which is as complete as possible, or a determination of a component or group of components. Occupational exposure limits in many different countries have been set in accordance with the analysis technique used.

A. Determination of the greatest possible number of components in a PAH mixture

Samples of higher polyaromatic hydrocarbons in air are usually taken on a filter. The lower PAH (2 to 4 rings) have a relatively high vapor pressure, and therefore occur in the air primarily as vapors. The filter must therefore be connected in series with a wash bottle containing some solvent (e.g. ethanol) which will trap the more volatile components. Andersson et al (1) have described a lightweight personal sampler in which a fiberglass filter is combined with a solid adsorbent (Amberlite XAD-2) which binds PAH in vapor form. The PAH is eluated from the filter or adsorbent with some solvent, usually benzene, cyclohexane or ether. Long-term extraction in a Soxhlet, which was common earlier, has largely been replaced by short-term treatment with ultra-sound at room temperature.

The only methods which can separate the complicated PAH mixtures from different working environments (usually derived from coal tar) are gas chromatography using a capillary column and high-pressure liquid chromatography (HPLC). Bjørseth (3) has described gas chromatographic determination of a large number of PAH components from several different working environments. About 1 ng of each component can be shown by using a flame ionization detector and a capillary column.

NIOSH (6) describes separation of PAH components by liquid chromatography. Detection is by UV absorption. Recovery was 90--100% for some 30 PAH substances and a number of derivatives; the detectability limit was about 3 ng/m^3 for 1.5 m^3 air volume. Considerably higher sensitivity can be achieved with a fluorescense detector, since all PAH substances are strongly fluorescent.

Analyses such as those above are extremely time-consuming, particularly since identification of the various components is usually the main problem. The mass spectrometer as a "detector" after the gas chromatograph can provide a sensitive determination, and usually certain identification, but certain PAH isomers can not be separated by their mass spectra. The analysis of course becomes easier if only ten or so of the main components are to be identified. Such analyses have been described by Andersson et al (1) and some others.

B. Determination of only one PAH component, usually BaP

Most analyses of BaP material are concerned only with benzo(a)-pyrene (BaP). This substance can of course be determined with any of the chromatographic methods mentioned under A above, but the analysis can be made much simpler if only BaP is to be determined. Thin-film chromatography can be used for the separation method. Several methods to separate BaP from other components have been described (9).

The best method for quantification of BaP is fluorimetry. Measurements can be made directly from the thin-film plate with a suitable scanning instrument, or can be made from solution after scraping and eluation. The former method is both faster and more sensitive. The fluorescence maximum for BaP in cyclohexane, as well as on thin film, is about 410 nm. A Hg lamp (365 nm) is usually used for excitation.

The standard method used by the Swedish Board of Occupational Safety and Health (2) involves sampling on a fiberglass filter from which the PAH is liberated by sublimation in a vacuum. PAH is then eluated from the sublimate, and the BaP is isolated on thin film. Fluorescence is measured directly on the plate. It is linear within the interval of 1 to 200 ng BaP on each thin film.

If it proves impossible to separate BaP completely from the other components, a fluorimetric method described by Sawicki (8) is more suitable for quantification of BaP. BaP in concentrated sulfuric acid yields a characteristic fluorescence at about 540 nm. About 20 other PAHs showed little or no fluorescences under the same conditions.

C. Non-specific analysis methods

A specific determination of individual PAHs is complicated and time-consuming, and it is still not possible to draw any conclusions about the carcinogenic effects of the mixture even when the composition is known. In several places, therefore, there have been attempts to develop simple methods for estimating the total amount of PAH in an air sample.

The simple (in principle) method of weighing the benzene extracted from the filter has been widely used. This method provides the basis for the occupational exposure limits set for PAHs in the USA and several other countries. According to

NIOSH (7), the particles are collected on a filter which is subsequently extracted with benzene and ultra-sound. The extract is condensed in a vacuum into a plastic beaker, and the increase in the weight of the beaker is determined. With a 300-liter air sample, the detection limit is reported to be 0.067 mg/m^3; i.e. a third of the exposure limit set by ACGIH. The weighing must be done very carefully, since occupational exposure limits correspond to a weight difference of only 12 µg. This apparently simple analysis can thus be rather difficult in practice. The method is suitable only for working environments in which tar or pitch is the PAH source. It is definitely not suitable for estimating PAH in engine exhausts, etc., since in such cases the benzene extract would consist primarly of uncombusted aliphatic hydrocarbons.

Fjeldstad and Halgard (4) have used the absorbance of ethanol extract at 250 nm as a measure of PAH concentration, and found a relatively good correlation with the sum of PAH components which could be determined by chromatographic methods. The same authors (5) further developed this method to include separation in a thin-film system which collects all PAH components on a single spot. This is then scraped off and extracted with ethanol, and absorbence is measured at 254 nm. The method must be calibrated against a gas chromatographic analysis of a sample from the same source. The "total PAH" thus determined corresponds on average to 20% of the weight of the benzene fraction. A large part of this fraction thus consists of undefined substances whose only shared characteristic is their solubility in benzene.

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REVISED CONSENSUS REPORT FOR CADMIUM
February 15, 1984

This is a revision of the Criteria Group's consensus report of Jan. 18, 1980 (22). Occupational exposure to cadmium can cause kidney damage as well as lung damage (5, 17). The possible cancer risk has also been discussed during the past few years (2).

Kidney damage

The early stage of kidney damage caused by cadmium is characterized by proteinurea, specifically an increased excretion in urine of low-molecular proteins such as beta-2-microglobulin, which is a sign of damage to the renal tubules. In more advanced cases the proteinurea is more general, with increased excretion of several different types of proteins and in some cases also sugar, amino acids and calcium. In serious cases, cadmium-caused kidney damage can lead to reduced glomerular filtration, and in severe cases to uremia (urine poisoning).

Disturbances of calcium metabolism can occur as a secondary effect of cadmium-caused kidney damage; symptoms may be in the form of kidney stones, or in rare cases (not described in Sweden) brittleness of the bones. Kidney damage caused by exposure to cadmium does not appear immediately; as a rule several years of exposure are necessary. Using data from studies of cadmium-exposed battery workers in Sweden (15), it was calculated that workers exposed for 10 years to cadmium dust at an average air concentration of 200 µg Cd/m^3 run a 50% risk of acquiring cadmium-caused kidney damage in the form of increased excretion of low-molecular proteins. With lower exposure the risk is reduced, and has been estimated to be about 10% with 25 years of exposure to 16 µg Cd/m^3 (14).

At an early stage, kidney damage caused by cadmium is clinically benign and very seldom leads to serious complications if exposure to cadmium is stopped. The damage to the renal tubules is usually irreversible, however (18), and should be regarded as an undesirable effect and as the first symptom of a more serious condition.

Lung damage

Inhalation of air with high concentrations of cadmium, above 1 to 5 mg/m^3, can be directly lethal. Edema can develop in the lungs within a few hours, or up to a week after exposure. Long-term exposure to lower concentrations of cadmium, around 100 µg Cd/m^3 or more, can also cause emphysemous changes in lung tissue (5, 17). English workers exposed for long periods to high concentrations of cadmium during the 30's, 40's and 50's have shown a greatly increased mortality due to chronic obstructive lung disease (respiratory problems) (2, 3).

Cancer

Cadmium can give cancer to rats when given by intramuscular injection (6, 7); and also with inhalation of relatively low concentrations of cadmium chloride (12.5 to 50 µg/m^3) for long periods (18 months) (21).

A number of epidemiological studies regarding cause of death and occurrence of cancer among cadmium-exposed workers have been published (1-3, 9, 10, 13, 16, 19, 20). Several of the studies indicate a somewhat increased mortality due to certain types of cancers, primarily of the lung or prostate (1, 2, 13, 16, 20). Both smelter workers exposed to cadmium (9, 10, 16) and battery workers exposed to cadmium and nickel (1, 13, 19, 20) were examined, and the results were similar. It should be

pointed out here that occupational exposure to certain nickel compounds has been shown to cause respiratory cancers (23).

In Sweden, Andersson et al (1) have studied cause of death among workers exposed to nickel and cadmium in a battery factory. The 525 men who were exposed to cadmium for at least 1 year showed a lower total mortality than expected, 105 deaths before the age of 80, compared to 122 as calculated from the national average. Of the workers, 273 had been employed for at least five years prior to 1962 and thus had been exposed to air concentrations of cadmium exceeding 300 µg/m^3. Six of these highly-exposed workers had died of lung cancer and 4 of prostate cancer, compared to a predicted 3.8 and 2.4, respectively. The 185 workers who had been exposed to cadmium and nickel for at least 15 years also showed a somewhat lower total mortality than predicted. In this group of workers with long-term exposure, there had been a total of 3 deaths due to prostate cancer, against an expected 1.6. Two cases of bladder cancer had occurred, compared to an expected 0.4. Three of the workers had died from lung cancer, against an expected 2.5.

In both the Swedish survey (1) and surveys made in other countries (2, 3, 9, 10, 13, 16, 19, 20), the increased risks for death due to lung or prostate cancer have been small and seldom statistically significant. The possible connection between cancer and occupational exposure to cadmium is therefore not yet clear (11). It should be emphasized that in the industries showing an increased cancer mortality exposure to cadmium was so high that many of the workers had suffered lung damage and/or damage to the renal tubules.

Biological monitoring

Uptake of cadmium can be estimated by "biological exposure control", measurement of cadmium in blood and urine. Cadmium in

blood reflects primarily current exposure, whereas cadmium in urine is as a rule primarily related to body burden (5, 8, 17). Cadmium in whole blood can therefore be used to monitor current exposure to cadmium -- a low value means that current exposure can not be high. A high blood cadmium content, on the other hand, can reflect a high current exposure, a high body burden resulting from earlier high exposure, or a combination of both. Smokers generally have much higher cadmium levels in both blood and urine than non-smokers (4, 8, 12), and with measurement and interpretation of cadmium levels in biological samples smoking habits should always be taken into consideration.

Measurement in urine of low-molecular proteins such as beta-2-microglobulin can provide information on possible changes in renal function. Reduced tubular function greatly increases excretion of low-molecular proteins.

Critical effects

Judging from present knowledge, the damage to the renal tubules should be considered the critical effect of long-term exposure to cadmium. This means that the kidneys are the organs first damaged by long-term exposure to cadmium. If occupational exposure to cadmium is kept to a level too low to cause kidney damage in the form of low-molecular proteinurea, the risk for more serious kidney or lung damage, and for cancer, should be minimal.

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APPENDIX

Analysis of cadmium

Sampling of cadmium and cadmium compounds in air is best done with a membrane filter. If the respirable fraction is to be analyzed, a pre-filter is used. The analysis is usually performed with atomic absorption spectrophotometry. Since the sensitivity for cadmium is high, the ordinary flame technique is quite adequate. NIOSH (2) recommends dissolving the filter in nitric acid and analysis by atomic absorption at 228.8 nm. The method has been proven for concentrations ranging from 4 to 84 $\mu g/m^3$ and 240 liters air volume, and the detectability limit in this air volume is reported to be below 0.1 $\mu g/m^3$.

As an alternative, NIOSH suggests emission spectrography with induced coupled plasma (ICP) (3). The detectability limit is on about the same order of magnitude as that for atomic absorption, but with the more advanced instruments several elements can be determined at the same time.

The X-ray fluorescence technique can be used to determine cadmium and several other elements directly on the filter.

Determination of cadmium in blood is prescribed for control of exposure (1). It is usually done with flameless atomic absorption (carbon rod technique) (4), but ashing in a Delves cup (a nickel crucible) followed by flame atomization is also effective (5). These methods can be used for concentrations down to 4 or 5 nmol/liter, normal values for persons not occupationally exposed.

The carbon rod technique is the best analysis method for cadmium in urine (6). A concentration of 10 nmol/liter can be determined with a sample volume of 5 µl.

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REVISED CONSENSUS REPORT FOR INORGANIC ARSENIC (EXCLUDING ARSENIC HYDRIDE)
February 15, 1984

This statement is based on a criteria document compiled earlier at the request of the Criteria Group (75). It has been supplemented with subsequently published data of relevance for risk assessment.

Occurrence and exposure

Arsenic is semi-metallic and occurs naturally in both inorganic and organic compounds. The most common valences are +III and +V. Inorganic arsenic occurs in several sulfides, often together with copper, lead, gold or silver. High arsenic concentrations are also found in some kinds of coal; this can lead to considerable air emissions from coal-fired power plants.

The arsenic concentration in the air is generally very low (<0.01 $\mu g/m^3$), but levels can be higher in metropolitan areas and around arsenic-emitting industries. Concentrations exceeding 1 $\mu g/m^3$ have sometimes been measured in the vicinity of smelters (43, 67). Elevated air concentrations in the working environment occur in smelters and in connection with the manufacture of some products containing arsenic, such as pesticides, insecticides or fungicides. Airborne arsenic in smelters occurs primarily in inorganic form, usually as arsenic trioxide, while fungicides can contain both inorganic and organic arsenic compounds. Exposure to inorganic arsenic compounds can also occur during wood impregnation, where chrome-copper-arsenate salts have come into widespread use.

Data on arsenic concentrations in drinking water in Sweden are limited; however, elevated As concentrations have been measured in well water in the vicinity of the Rönnskär smelter. The over 200 workshops at which wood is impregnated are a potential problem, since arsenic salts are used and there is often considerable contamination of the ground and consequent risk for leakage to groundwater.

The arsenic content in most foods is below 0.25 mg/kg (85). Some saltwater fish and crustaceans, however, can contain over 10 mg As/kg body weight (10). Most of this arsenic occurs in organic form, primarily as arsenobetaine (11, 50). The total daily intake of arsenic for persons not occupationally exposed is usually below 200 µg, 10 to 50 µg of which is inorganic arsenic (86).

Arsenic concentration in urine can be used as an indicator of exposure to inorganic arsenic, provided that the analysis method makes it possible to differentiate between metabolites of inorganic arsenic and those organic arsenic compounds occurring in fish and shellfish (49).

Metabolism

Most of the arsenic taken up orally is absorbed in the digestive tract, unless it is in compounds that are particularly difficult to dissolve. Absorption of particle-bound arsenic trioxide, which is often inhaled, is probably also quite high --- either directly via the lungs, or from the digestive tract after clearance from the respiratory passages. Retention and distribution of arsenic from occupational exposure is dependent mostly on its chemical form at intake and its subsequent biotransformation (76). Inorganic arsenic, both trivalent and pentavalent, is methylated in the body to mono- and dimethyl arsenates (MMA an DMA), which are excreted fairly quickly in

urine (7, 78). Since arsenic is alsq a substrate for certain redox reactions, As(V) can be reduced to the more toxic As(III) --- or, with exposure to As(III), there can be some oxidation to As(V) (77).

It is primarily the inorganic, non-methylated arsenic that binds to body tissues (78). Trivalent inorganic arsenic, possibly after reduction to As(I) (27), binds primarily to SH groups, and the longest retention times are in keratin-rich tissues such as hair, skin and nails, as well as in the lining of the digestive tract (32). Occupationally exposed persons can have high arsenic concentrations in the lungs for several years after termination of exposure (5). It has been shown in animal experiments that lung retention varies with the type of arsenic compound (56). Calcium arsenate remains in the lungs much longer than arsenic trisulfide or arsenic trioxide.

Arsenic is excreted primarily via the kidneys. This process is slower in man than in most animals, probably because of a smaller degree of methylation. Persons given low oral doses of As(V) in solution excreted about 40% in urine within 2 days and about 60% within 5 days (30% as DMA, 12% as MMA and 16% as inorganic arsenic) (70). Persons exposed to As(III) in solution excreted about 33% within 2 days and 45% within 3 days (24% as DMA, 10% as MMA and 11% as inorganic arsenic) (7).

Health effects

Non-carcinogenic effects

There are good descriptions of both acute and sub-acute effects from several occurrences of mass poisoning by inorganic arsenic. A daily intake of about 3 mg over a few weeks can cause death to infants and symptoms of poisoning in adults (17, 38, 40). The lethal dose for an adult has been reported to be

70 to 100 mg with intake of arsenic trioxide (79). Gastrointestinal symptoms are common, as are reversible ECG changes and bone marrow depression. Peripheral neurological symptoms can occur a few weeks after exposure, as can light-colored transverse bands on the nails ("Mees lines").

Chronic effects can occur in several organ systems, usually the same ones affected by acute poisoning. Damage to the peripheral nervous system and the bone marrow has been noted after occupational exposure and after intake of drinking water containing high concentrations of As (13, 20, 28, 72). The bone marrow damage is typically marked by disturbed erythropoesis, and sometimes also by granulocytopenia. (Erethropoesis = formation of red blood cells; granulocytopenia = shortage of granulocytes, a type of white blood cell.)

Wart-like changes on the palms of the hands or soles of the feet, "palmoplantar hyperkeratosis", is a characteristic effect of long-term intake of inorganic arsenic via drinking water, medicine, etc. (15, 74). As a rule, skin changes do not occur until after about two years of exposure, indicating that a total arsenic dose of about 0.5 to 1 g is required.

Intake of inorganic arsenic via drinking water can also cause peripheral vascular damage, sometimes leading to gangrene (Blackfoot disease). These effects have been observed in some parts of Chile and Taiwan, where As concentrations in the water are on the order of 0.5 to 1 mg/liter (4, 74). It also seems that some minor disturbances in peripheral circulation can develop in smelter workers exposed to arsenic (29). In two studies (3, 30), this group also showed increased mortality from cardiovascular disease.

There are a number of case histories in which treatment with inorganic trivalent arsenic for several years was connected to portal hypertension without liver cirrhosis (9, 22, 26, 39, 42, 69). Liver cirrhosis has also been reported after medical treatment with arsenic, but these data are not conclusive. It is nevertheless worth noting that increased mortality due to liver cirrhosis has been reported in several occupational groups exposed to inorganic arsenic compounds (3, 30, 65).

Occupational exposure to irritating arsenic compounds such as arsenic trioxide can cause inflammatory damage to the respiratory passages, primarly the upper portions (34, 37, 59). Earlier, when air concentrations of arsenic were often extremely high, perforation of the nasal septum was not uncommon in exposed workers.

Genotoxicity and effects on reproduction

Inorganic arsenic is teratogenic in animal experimental systems (14, 21). However, there are very little data which can be used for a detailed analysis of the effects of arsenic on human reproduction. Nordström et al (47, 48) have reported lower birth weight and an increased frequency of malformations in children of women who worked at the Rönnskär smelter during their pregnancy. Miscarriages were also reported to be more frequent among these women. Since there was no detailed analysis of the source of information or of the relative importance of the various exposure factors, the role of arsenic in these findings can not be determined (68).

Inorganic arsenic does not seem to be mutagenic in bacterial tests (35, 64). Arsenic can disturb DNA repair in both bacterial and human cells (25, 63), which may well indicate a co-carcinogenic effect. An increased frequency of chromosomal aberrations has been noted in workers exposed to arsenic and in patients treated for long periods with medicine containing arsenic (44, 45, 58). With regard to sister chromatid exchange, results are equivocal (8, 45, 84). In experimental

systems inorganic arsenic, particularly the trivalent form, induces both chromosome aberrations and sister chromatid exchange (1, 41, 46, 51, 54, 58, 82, 87).

Carcinogenic effects

Increased mortality from lung cancer has been noted among workers who made pesticides containing inorganic arsenic compounds (19, 36, 53). Both trivalent and pentavalent compounds, e.g. calcium arsenate, lead arsenate and sodium arsenate, were used in the manufacturing processes. There are some case histories in which use of these substances in spraying crops is also related to lung cancer (16, 66).

Workers exposed to arsenic in copper smelters run an increased risk of acquiring lung cancer (3, 30, 61, 73). The three most thoroughly studied smelters are in Montana (Anaconda) and Washington (Asarco) in the USA, and in Västerbotten (Rönnskärsverken) in Sweden. During recent years there have been several, partly overlapping, epidemiological studies of workers in these smelters (12, 18, 31, 33, 55, 62, 81, 83). In general, there has been a positive correlation between the estimated exposure to arsenic and the increase in risk for lung cancer. In those studies intended to determine the effects of other exposure factors such as sulfur dioxide or smoking, no other factors could explain the difference. Regarding the interaction between smoking and exposure to arsenic, results are not clear, but at least one study (55) implies that smoking multiplies the risk for lung cancer.

In spite of the strong epidemiological evidence that inorganic arsenic has a carcinogenic effect, animal experiments have usually had negative results (23). Recently, however, intratracheal instillations of arsenic trioxide, the most common compound in many occupational exposure situations, have caused malignant lung tumors in hamsters (57). This study also

indicated that benz(a)pyrene tends to have a promotive effect with arsenic in the occurrence of a certain kind of lung tumor.

Occupational exposure to arsenic has also been correlated to tumor development in organs other than respiratory organs. An increased incidence of cancer in the digestive tract has been noted in smelter workers exposed to arsenic (31, 80); angiosarcomas in the liver of vinyard workers (65); and tumors of the blood-forming organs in smelter workers (3) and workers producing fungicides (53). A cause-effect relationship for these tumor forms can not yet be regarded as established. Although exposure to inorganic arsenic via drinking water or medicine is known to cause skin tumors, such tumors have seldom been reported among occupationally exposed persons. This may be because the epidemiological studies are usually concerned with mortality, and the arsenic-induced skin tumors are often not very malign.

Risk evaluation

Lung cancer is the critical effect of chronic inhalation of arsenic. The risk at low doses is often calculated using a linear dose-response curve and the assumption that there is no threshold value (24, 71). This is the model accepted and used in the evaluation of arsenic made recently by the World Health Organization (86). It is emphasized, however, that use of this kind of model, particularly with extrapolation to extremely low doses, can only give a rough approximation of the cancer risk.

Calculation of a dose-response relationship between lung cancer and occupational exposure to arsenic is coupled with considerable uncertainty. Exposure data is inadequate, particularly for exposures occurring a long time ago. It is also uncertain which model best describes the relationship between lung cancer and arsenic exposure. Risk estimates are often made using a

"relative risk model": the risk in a particular exposure group is regarded as proportional to the background risk, e.g. the risk of lung cancer in a population not exposed to arsenic.

A couple of the above-mentioned studies of smelter workers in the USA allow some quantitative estimate of the lung cancer risk at different exposure levels (12, 31). Of particular interest for the establishment of occupational exposure limits are the risks demonstrated in those groups which had the lowest exposure. In one of the studies (12), there was a statistically proven increase of 128% (SMR:228) in the risk for lung cancer in a group with a calculated average arsenic concentration of 163 µg/l in urine. This corresponds to an air concentration of about 50 $\mu g/m^3$ (60). The average exposure time for this group was estimated to be about 15 years. Assuming that the risk for lung cancer is related to the cumulative dose of arsenic (concentration x time) the elevated risk could be calculated at about 5% per µg As/m^3 after 30 years of exposure.

In the other study (31) a similar statistically significant increase of lung cancer risk was noted in the lowest exposure group. Here the risk increase was 131% (SMR:231). The average air concentration of arsenic for the group was calculated to be 290 $\mu g/m^3$ (33). There was no data on the average exposure time. A calculation was made using that portion of the group which had been employed for 25 years or more; here the risk was 227% or 180%, depending on date of initial employment. This corresponds to a risk increase of 0.8% and 0.6% per µg As/m^3 (>25 years of exposure).

When the relative-risk model is used the two studies thus give quite different risk estimates. The reason for this is unclear, but the uncertainties in the calculations should be borne in mind --- particularly those regarding the exposure estimates. It is also possible that models other than the relative-risk model would provide a better estimate of the

connection between lung cancer and exposure to arsenic (6). The risk estimate made by WHO (86), which was used in the previous criteria document (2), lies about midway between the higher and the two lower risk estimates, while the estimate made by OSHA lies closer to the lower values (52).

No certain conclusions can be drawn about possible differences in the carcinogenic activity of different arsenic compounds. Experimental studies, however, seem to indicate that the solubility of the arsenic compound affects its retention in the lungs, which can in turn affect the cancer-causing ability of the substance. Until further knowledge is obtained , however, discussions of occupational exposure limits must treat inorganic arsenic as such, without reference to its chemical form.

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APPENDIX

Analysis methods for arsenic

In the method given by NIOSH (1), arsenic compounds in both particle and vapor form are sampled on a filter of cellulose acetate impregnated with a sodium carbonate solution. The filter is then dissolved with nitric acid and hydrogen peroxide, and the arsenic in the solution is determined by atomic absorption (carbon rod technique). The method is proven in the interval from 0.7 to 32 µg As/m^3 with a 400-liter air sample. The detectability limit is given at 0.15 µg/m^3 with the same air volume.

An alternative method is emission spectrography with induced coupled plasma (ICP). NIOSH reports that the detectability limit with this method is marginally worse than that for atomic absorption (2). This method, however, allows simultaneous analysis of several elements, as does analysis by X-ray fluorescence.

Biological exposure control of arsenic is complicated. Determination of total arsenic in urine is of little value, since concentrations are strongly affected by intake of such foods as fish or shellfish. According to Norin and Vahter (3), inorganic arsenic and its metabolites in urine can be determined with the "hydride method". The urine is treated directly with hydrochloric acid and sodium borohydride, forming arsenic hydride. This gas is led via a stream of hydrogen gas into a heated cuvette in the atomic absorption instrument, where the arsenic hydride is split and the free arsenic can be determined. With this technique it is possible to determine 0.05 µmol/liter of inorganic arsenic+ metabolites (methylated arsenic compounds) in the presence of a large amount of "fish arsenic".

"Fish arsenic" can be determined by calculating the difference between total arsenic and arsenic given by the hydride method. If necessary, inorganic arsenic in urine can be separated from metabolites by the ion exchange technique.

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CONSENSUS REPORT FOR BERYLLIUM

April 25, 1984

This report is based primarily on a criteria document written at the request of the Swedish Criteria Group (13).

Occurrence and use

Beryllium is a metallic element occurring in several minerals in the earth's crust and as a "contaminant" in e.g. coal and oil. In the nuclear power industry, the electronics industry and the aviation industry, the metal occurs in various types of alloys -- primarily with copper, cobalt and nickel. Beryllium oxide is used in the chemical industry and in nuclear reactors.

Occupational exposure to beryllium in the form of dust or aerosols (soluble compounds) can occur during mining or processing of beryllium ore; in the production or processing of alloys containing beryllium; and in the production and use of beryllium compounds, primarily oxides.

Uptake, biotransformation, excretion

When rats were given doses of 0.6 to 6.6 µg Be/day in the form of $BeSO_4$ in their drinking water, an estimated 20% of Be was absorbed in the digestive tract (19).

Clearance of inhaled beryllium particles is a two-phase process: a rapid phase which can be ascribed to mucociliary transport, and a slower phase attributed to the activity of macrophages in the lungs (3). The uptake of beryllium by the macrophages depends on the solubility of the compound; sparingly soluble beryllium compounds are taken up quite rapidly.

Uptake is proportional to the number of particles, up to a plateau at about 2.5 µg/ml (11).

The uptake of beryllium ions from the lungs is a slow process. The combination of lung clearance and slow uptake makes the kinetics of beryllium absorption in the lungs quite complicated. When rats inhaled $BeSO_4$, the level of Be in the lungs gradually increased for 36 weeks; but then it reached a plateau, where it remained for the next 40 weeks of inhalation (21). In one study (14), 18% of a dose of $BeCl_2$ given by intratracheal injection was accumulated in bone tissue, and in another similar study (2) 36% of the dose had accumulated in bone tissue after only 15 minutes.

The distribution of beryllium to different organs depends on both the kind of exposure and the nature of the beryllium compound. After intratracheal injections of $BeCl_2$ most of the beryllium is found in the lungs; whereas after intravenous, intramuscular or intraperitoneal injection about half the dose is found in bone tissue and smaller amounts in the liver and spleen, but there are no detectable amounts in the lungs (2). With long-term exposure to low doses of beryllium, most of it seems to accumulate in bone tissue (20).

Absorbed beryllium is excreted primarily via urine (5, 6), probably after an active tubular secretion. Excretion via the gall bladder seems to depend on the ability of the components of the bile to bind beryllium (5).

Toxic effects

Effects on the skin

Contact with soluble beryllium salts can sensitize the skin and cause allergic contact eczema, a delayed allergic reaction.

Beryllium fluoride has a stronger effect than ammonium beryllium fluoride, beryllium sulfate or beryllium chloride (10). Beryllium compounds can also cause granulomas --- both foreign-body granulomas and granulomas regarded as immunogenic. Beryllium oxide thus has the tendency to induce a granulomatous allergic reaction (9).

Effects on respiratory organs

Acute effects in the form of lung inflammation (pneumonitis) have been reported as an occupational illness among beryllium workers exposed to high concentrations of fluoride. There is a dose-effect correlation between the size of the dose, the length of time before appearance of symptoms, and the duration of the illness (28). The risk of pneumonitis is dependent on the solubility of the beryllium compound. Oxide produced at 1500°C has not caused pneumonitis. It is less soluble and has a larger particle size than oxide produced at 500°C, which has had acute effects at air concentrations of about 1 mg Be/m^3. Beryllium sulfate has acute effects at concentrations as low as 0.1 mg Be/m^3 (8, 25).

Inhalation of beryllium can also produce chronic effects in the form of berylliosis (beryllium dust lung), which has symptoms similar to those of asbestosis (22). There seems to be no dose-effect or dose-response relationship. In a couple of case studies, berylliosis was reported after exposure to Be in concentrations lower than 1 $\mu g/m^3$ (4, 15); pathological studies indicate, however, that these effects could be manifestations of an allergic nature.

Carcinogenic effects

In a mortality study made of two beryllium industries (17), there were 20 cases of cancer of the respiratory tract. There was no control group included in the study. In a follow-up

study of the same industries (18), a cohort of 3,685 beryllium workers was compared with a cohort of 5,929 workers in a rayon industry. Mortality due to lung cancer (age-standardized) was 50% higher among the beryllium workers for whom exposure had begun at least 15 years previously.

A further analysis (29) from one of the two industries, covering employees exposed for less than 15 years, revealed that most of the workers had been exposed for less than five years and that the group with more than 5 years of exposure was too small to provide a statistical basis for establishing a dose-response relationship. Neither smoking habits nor occupational exposure to other substances could explain the increased incidence of lung cancer among workers for whom it had been more than 15 years since the beginning of exposure (29). A microscopic examination of the lung tumors showed that 32% (8 of 25) were adenocarcinomas, compared to a normal frequency of about 15% in the USA (24).

Rats have developed lung cancer after inhalation of beryllium ore, beryllium sulfate, beryllium fluoride and beryllium oxide (12). The lowest air concentration shown to cause lung cancer in experimental animals after several months of exposure was 30 to 40 µg Be/m^3. Intravenous injections of beryllium compounds have caused osteosarcoma (bone cancer) in rabbits (20).

Other toxic effects

Beryllium chloride has caused chromosome aberrations in vitro (26) and an increased misincorporation of DNA by inhibition of polymerase activity (16). Beryllium sulfate has induced morphological transformation in hamster embryonic cells in vitro (7).

Soluble beryllium compounds which have been injected are more toxic to the liver than beryllium sulfate in particle form

(27), and cause necrosis (cell death) of parenchymous cells. The necrosis does not seem to be connected with binding of beryllium in the cell nucleus (23).

Beryllium has been shown to inhibit the activity of several enzymes (13, 20).

Conclusions

Exposure to beryllium can cause contact eczema, granuloma and berylliosis. It is not completely clear whether the last-named effect is of an allergic nature.

Beryllium and beryllium compounds are carcinogenic. They have caused lung cancer and osteosarcomas in experimental animals, and epidemiological studies indicate an increased frequency of lung cancer among beryllium workers. It seems that the lung cancer appears in the workers after high exposures (over 1 mg/m^3) (13). Most studies lack data on exposure levels, and therefore a dose-response, dose-effect relationship can not be calculated. Air concentrations of 0.1 mg Be/m^3 (sulfate) and 1 mg/m^3 (oxide) are regarded to have acute effects on the lungs, while chronic effects (berylliosis) can be assumed to occur at concentrations 100 to 1000 times lower.

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APPENDIX

Analysis of beryllium

Samples of beryllium in air should be taken on a filter of either the millipore or the membrane type. The filter and the dust sample are then dissolved in a mixture of acids such as nitric acid and sulfuric acid. The solution is then evaporated and the remaining substance is dry-ashed at 400°C and dissolved in dilute sulfuric acid containing sodium sulfate.

Determination of beryllium is usually made by atomic absorption. Since it is necessary to determine extremely low concentrations, the graphite oven technique is the best. NIOSH (2) gives an absolute detection limit of 5 pg per sample, corresponding to 0.5 µg Be/m^3 for a 90-liter air sample.. Absorption is measured at 234.9 nm.

An alternative method given by NIOSH (3) is emission spectrography with induced coupled plasma (ICP). At a wavelength of 313 nm, the detection limit for the solution is 1.5 ng/ml, equivalent to about 0.2 µg/m^3 for a 100-liter air sample.

X-ray spectrographic methods can not be used for beryllium because of its low atomic number. The characteristic radiation has such a long wavelength that it can not be measured with standard instruments.

There is also a sensitive fluorimetric method for beryllium. Beryllium in an alkaline solution with morin produces a fluorescence with a maximum at 550 nm. Concentrations down to about 2 µg/m^3 can be determined in a 10-liter air sample, making this method as sensitive as the spectrographic method described above (1). It is probable, however, that the fluorimetric method is more sensitive to disturbances from other substances.

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CONSENSUS REPORT FOR INORGANIC MERCURY

April 25, 1984

Background

Mercury (Hg) occurs in nature as metallic Hg (Hg^0), as monovalent (Hg^+) and divalent (Hg^{2+}) inorganic salts, and also in organic Hg compounds. The most important of these in terms of effects on the outdoor environment are alkyl mercury compounds of the methylmercury type (CH_3Hg^+).

A large number of surveys of the toxicology of mercury have been published in recent years (4, 5, 11, 23, 24, 29, 33, 34). There is an enormous amount of literature on mercury. The following discussion takes up only those matters of central relevance for setting exposure limits for inorganic mercury in the working environment.

Occupational exposure to vapors of metallic mercury is most common during the mercury refining process; in the chlor-alkali industry, where metallic mercury is used as a cathode in the electrolysis of sodium chloride to chlorine gas and caustic soda; and in dentistry. In addition to this, occupational exposure to metallic mercury occurs in metal refineries, in the manufacture of batteries and fluorescent lamps, and in the manufacture and maintenance of electrical rectifiers and instruments containing metallic Hg.

In the chlor-alkali industry there is also some exposure to divalent Hg salts. Such exposure can also occur in the chemical industry -- where divalent Hg salts are sometimes used as catalysts -- and in some other working environments. Occupational exposure to divalent Hg is less common than exposure to metallic Hg.

Occupational exposure to monovalent salts of mercury is rather rare.

The following discussion centers primarily on the risks of exposure to metallic mercury and secondarily on risks of exposure to divalent Hg salts.

Metabolism

Metallic mercury is easily absorbed when it is inhaled in vapor form. There is probably also some absorption via the skin. Uptake via the digestive tract is limited. Hg is accumulated in the central nervous system (CNS), kidneys, etc. Metallic mercury is oxidized in the body to divalent Hg. It is excreted via urine and feces.

Salts of divalent Hg in aerosol form can be absorbed in the lungs, but just how readily is unclear. Absorption via the skin and digestive tract is limited. Divalent mercury is accumulated primarily in the kidneys, and only slightly in the CNS.

Measurement of exposure

The degree of exposure to vapors of metallic Hg can be measured by air analyses. Concentrations in the breathing zone have a much higher information value than area measurements.

Additionally, Hg contents in blood (B-Hg) and urine (U-Hg) can be used as exposure indices. Neither one, however, is optimal for the purpose. Analysis problems are common, and there is also considerable individual variation in both B-Hg and U-Hg at a given air concentration of Hg. This means that individual readings must be interpreted with caution. Group averages or

repeated readings from an individual, however, are useable. U-Hg seems to reflect the degree of exposure for several weeks or months prior to sampling, whereas B-Hg probably reflects a somewhat shorter time span. Neither measurement seems to indicate the degree of accumulation in the organs of interest here (see below).

B-Hg is more affected than is U-Hg by exposure to methylmercury, which is found in persons who eat fish -- particularly fish from Hg-contaminated waters. U-Hg thus seems to have some advantage over B-Hg as a measure of occupational exposure. U-Hg should be determined in morning urine and readings should be corrected for dilution of the urine.

"Normal" U-Hg for persons without occupational exposure or substantial intake of methylmercury via fish is below 20 µg/l. "Normal" B-Hg is about 5 µg/l.

Effects

Vapors of metallic mercury affect the central nervous system; symptoms are at least partially reversible if exposure is terminated. The peripheral nervous system (PNS) can also be affected. Effects here seem to be less clearly expressed, however, and there is no evidence that they appear at lower exposures than do the CNS symptoms. Metallic mercury can also cause kidney damage, primarily glomerular, but also tubular. It is not clear whether the CNS or the kidneys are the critical organs, i.e. which of them is negatively affected at a lower exposure. Either CNS symptoms or kidney symptoms can appear first, apparently depending on the individual. Exposure-response correlations for the CNS and kidneys are therefore presented together below. Salts of divalent Hg can damage kidneys, but do not affect the CNS.

Mercury from exposure to vapors of metallic (but not divalent) Hg passes through the placenta. There is thus a potential for damage to the embryo, particularly to its CNS. This potential risk has not been verified either experimentally or clinically, and can therefore not be quantified.

Inorganic Hg can cause immunological reactions. Exposure carries with it some risk for allergic contact eczema. There may also be immunological mechanisms behind the glomerular kidney damage. Inorganic Hg can bring on a general reaction, acrodynia, particularly in children. This probably has an immunological basis as well.

Inorganic Hg seems to have very little negative effect on the genetic material itself. However, it can damage the spindle pole and thus cause maldistribution of chromosomes during cell division. There is no clear evidence for such effects in man, possibly because studies have so far not been optimally designed to show them. The clinical importance of such damage to nuclear material is unclear. It seems most likely that it would have some bearing on the appearance of embryo damage due to chromosomal aberrations in either the gametes or the embryo. There is no data on this, however.

There has been almost no research into the possible carcinogenic qualities of inorganic Hg. The studies of mutagenicity do not seem to indicate carcinogenicity.

Exposure-response correlation

The following discussion covers the relationship between exposure to metallic Hg in vapor form and the response of the CNS and kidneys. The conclusions are based primarily on studies of exposed persons.

There are several problems involved in interpretation of available data on the relationship between exposure and effect/response. Information on exposures is usually inadequate; reports often include air measurements from only one occasion, leaving earlier concentrations unknown. Since Hg has a definite tendency to be retained for a long time in the CNS and probably also in the kidneys, this can be a major source of uncertainty. For instance, it is often not clear whether an effect is due to recent exposure or to long-term exposure. Moreover, many measurements were not made with personal samplers, adding a further source of error in estimating actual exposure levels.

Reports frequently contain information on U-Hg, and sometimes also on B-Hg. But here too, samples may have been taken on just one occasion and the data thus reflect only exposure during the period immediately prior to sampling. And further, most of these reports contain no information on the reliability of the analysis method.

Nor are the data unambiguous with regard to effect. Available studies are of the cross-sectional type, and selection can thus not be ruled out. Furthermore, it is the subtle effects, not the clearly manifest damage, which are of primary interest. With regard to the CNS, the problem is that most of the interesting symptoms are both subjective and non-specific. Several groups of scientists have therefore measured objective parameters which are considered to reflect slight effects on the CNS. One of the problems with this is that is not always clear whether the effects demonstrated are relevant to the individual's health. The same applies to minor effects on the kidneys. Another problem is that the studied parameters also show considerable inter-individual variation in an unexposed population.

In general, the necessary basis for construction of well-defined dose-response curves for the effects of Hg does not exist. This is hardly surprising, considering the inadequacy of the exposure information and the nature of the effects in question. There is considerable variation in the exposure/effect data, in the few cases where comparable parameters can be found in the publications. The data usually give only a rough picture, from which it is difficult to determine exactly at what exposure a given effect becomes apparent. It is also problematical that, in a number of studies, effects are described at U-Hg and B-Hg levels very near "normal".

With regard to the CNS, it can be stated that subjective symptoms which can indicate slight poisoning ("micromercurialism") are reported more frequently by workers exposed to air concentrations of 10 to 100µg Hg/m^3. Reported symptoms include "nervousness", "uncertainty", insomnia, loss of appetite and weight reduction. Objective observations include data indicating that cognitive functions and short-term memory are affected at U-Hg levels of 60--110 µg/l (7, 10, 12, 18, 21, 25, 26, 30, 31, 35). Some evidence may indicate that psychomotor functions are affected at about the same U-Hg levels (7, 10, 12, 14, 17-19, 22, 35). Pronounced tremor is an important symptom of poisoning, and is preceded by change in the frequency of the spontaneous tremor. Such changes are observed at U-Hg levels of 50--100 µg/l (14, 17, 22); in one case this effect was observed at a U-Hg of only 20 µg/l (8). The clinical importance of these changes in tremor is unclear, although they can indicate a slight effect on the CNS. Sub-clinical effects on the PNS have been reported at U-Hg levels of 90--120 µg/l or higher (2, 3, 16, 21, 30--32).

With regard to the kidneys, discrete increases in secretion of protein, indicating effects on the glomerules, have been found in groups of persons with U-Hg levels of 100--200 µg/l or higher (6, 9, 13, 15, 20--22); in one case, however, at about 35 µg/l (27). The clinical importance of this proteinurea is unclear. It must, however, be regarded as a potential health risk, since clinically significant glomerular damage is found in highly exposed Hg-workers. Typical tubular proteinurea with excretion of low-molecular proteins (e.g. beta-2-microglobulin) seems not to occur this early. However, several groups of authors have discovered increased excretion of a number of lysosomal enzymes, which can indicate a slight effect on the tubular epithelium. Such enzyme leakage has been noted at U-Hg of 50 -100 µg/l or higher (1, 6, 13, 20, 28). In one case (13) there were some indications of effects at about 35 µg/l. The clinical significance of this kind of observation is, however, unclear.

Summary

A number of studies have shown that discrete but clear effects on the CNS and kidneys, the critical organs, occur at exposure to vapors of metallic Hg corresponding to a U-Hg of about 50 µg/l or g creatinine (about 250 nmol/liter or 30 umol/mol creatinine) or higher. In some studies, effects were noted at U-Hg concentrations as low as 20--35 µg/l. Interpretation of these latter data is, however, difficult. U-Hg of 50 µg/l generally corresponds to an air concentration of about 30 µg/m^3 and a B-Hg of about 20 µg/l (100 nmol/l).

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APPENDIX

Analysis methods for mercury and mercury compounds

There are several methods for direct measurement of metallic-mercury vapor in air. Analysis ampules are the simplest; they provide a reading after a few minutes of collection time. The detectability limit is relatively high, however -- about 0.05 mg/m^3, or 0.02 mg/m^3 if the collected air is first dried. An average value for longer periods (up to 8 hours) can be obtained with a "diffusion dosimeter", which can be worn by the employee. The subsequent analysis must be made at a laboratory, usually with flameless atomic absorption (see below).

Instruments for direct readings of mercury vapor in air have been in use for a long time. Nearly all of them are based on the light absorption of mercury vapor at the resonance wavelength of 253.7 nm. These instruments in their simplest form are sensitive to all other substances which absorb light at the same wavelength: sulfur dioxide, ozone, aromatic hydrocarbons, etc. There are various ways to eliminate this source of error, such as dividing the airstream through the instrument into two branches. One branch flows through a filter that removes the mercury vapor; the resulting difference in light absorption then reflects only the Hg concentration in the air. Gold and other noble metals make suitable filters, since they bind Hg by amalgamation. Such a double-stream instrument can detect mercury vapor in air down to 1 µg/m^3.

If there are no direct instruments available, samples of Hg vapor in air can be taken in a wash bottle containing a solution of potassium permanganate and sulfuric acid. This oxidizes the metallic mercury to Hg^{2+} salt, which stays in the solution. For personal samplers, there is a more suitable chemisorbtion method using granular manganese dioxide as

adsorbent (2). In the laboratory this is completely dissolved in a mixture of nitric acid and hydrochloric acid.

In both these cases the analysis is made with a special variation of the flameless atomic absorption method. The solution (in the first case after reduction of the surplus permanganate) is mixed with a reducing agent such as stannous chloride, which liberates the mercury from the solution. The mercury vapor is then transported over to the measuring instrument via air or nitrogen blown through the solution. The measurement is based on light absorption at 253.7 nm, and can be made either with the instruments used for direct measurement of Hg vapor in air or with an atomic absorption instrument. These methods are described in the method collection of the National (Swedish) Board of Occupational Safety and Health (1). The detectability limit is given as 2.5 µg Hg/m^3 for both methods: with a 10-liter air sample for sampling in a gas wash bottle and with a 30-liter sample for the chemosorption method.

Samples of inorganic Hg compounds in particle form are best taken on a filter, such as one of inert fiberglass. The particles can then be dissolved in acid and analyzed in the same way as the sample solutions from Hg vapor. NIOSH (5) describes a sampling arrangement in which inorganic mercury compounds are collected on a filter and soluble organic mercury compounds thereafter collected on a molecular sieve (Carbosieve B), and finally the Hg vapor on an adsorbent containing silver. These three fractions are analyzed separately by thermal desorption and flameless atomic absorption. The sensitivity is extremely high: 0.001--0.01 µg Hg per sample can be detected, depending on the measuring instrument; the sensitivity is 0.1--1 $\mu g/m^3$ with an air volume as low as ten liters.

Biological monitoring of mercury exposure is usually done by analysis of blood or urine. Blood concentrations are affected fairly quickly by exposure to mercury in air, whereas urine values are more difficult to interpret and in general probably reflect the body burden.

For analysis of biological samples, the flameless atomic absorption method is used. Samples can be prepared by partial wet-ashing, e.g. with potassium permanganate-sulfuric acid for urine, or treatment with an acid mixture at 70° for blood (3, 6). After reduction with stannous chloride or sodium borhydride, the samples are analyzed with the same methods used for air samples. There are, however, methods described in which reduction is accomplished by alkaline solution without previous enrichment of the sample (4).

Analysis of mercury by flameless atomic absorption is easily automated, and several devices have been described in the literature. As a rule, a detectability limit of about 0.3 ng Hg/sample can be reached; with a sample volume of 0.2 ml (blood or urine) this corresponds to about 1.5 ng Hg/ml. The normal blood concentration for unexposed persons is 4 to 5 ng/ml.

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CONSENSUS REPORT FOR FURFURAL

April 25, 1984

Physical-chemical data, use

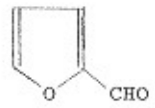
CAS No: 98-01-1

Systematic name: 2-furaldehyde

Synonyms: furfuraldehyde, furfurol

Molecular weight: 96.08

Formula: $C_5H_4O_2$



Boiling point: 161.7° C

Melting point: -36.5° C

1 mg/m^3 = 0.26 ppm; 1 ppm = 3.9 mg/m^3 (20° C, 101.3 kPa)

Furfural at room temperature is a colorless fluid which turns red-brown on exposure to light. It is easily soluble in alcohol, ether and benzene, but only sparingly soluble (about 8%) in water. The odor is rather like that of benzaldehyde (bitter almond).

Furfural is used as a solvent in oil refineries, in the plastics industry, etc., and is also used as a fungicide.

Uptake, biotransformation, excretion

In one study (6) in which test subjects inhaled between 7 and 30 mg/m^3 furfural, retention was calculated to be about 78%, while uptake via skin was estimated to be about 20%. This uptake increases with increasing air temperature and humidity (6). It was calculated that with direct contact 1 cm^2 of skin on the hand resorbs about 0.003 mg furfural per minute.

In man, the primary biotransformation products are furoylglycine (via conjugation with glycine) and 2-furanacryluric acid. The biological half time for furfural is a little over 2 hours. Biotransformation products are excreted primarily via the kidneys.

Toxic effects

In one older study (12) concentrations of 1.9 to 14 ppm furfural were reported to have caused headache and irritation of the eyes and throat. Similarly, it was noted in a NIOSH study (15) that furfural in concentrations of 5 to 16 ppm caused irritation of the eyes and respiratory passages. Although there are apparently no long-term studies regarding occupational exposure, it can be noted (1) that no illnesses caused by exposure to furfural have been reported.

In a Russian study (quoted in Reference 17) it was noted that occupational exposure to concentrations of 30 to 130 mg/m^3 have caused hepatitis (liver inflammation) and affected the nervous system. In experimental studies (18) furfural concentrations of 1.0 to 1.5 mg/m^3 affected the sense of smell, and a concentration of 0.31 mg/m^3 affected the eye's sensitivity to light.

In one study in which hamsters were exposed for 13 weeks (6 hours/day, 5 days/week) to 0, 20, 115 and 552 ppm furfural, animals in the two highest dose groups showed atrophy of the olfactory epithelium and hyperplasia of the lamina propria in the nasal cavity (5). At 552 ppm, there was also irritation of the eyes and nose.

Structural analogy suggests that substances with a structure similar to that of furfural can cause group allergies (7) but there are no studies in this area.

Several studies (2, 8--11, 16) have demonstrated effects of furfural on enzymes. A reduction of activity in the respiratory enzyme of the kidney mitochondria was noted in rats (9). (Mitochondria are the energy-producing organelles within the cell.) A simultaneous increase of enzymes in the endoplasmatic network and the lysosomes was also demonstrated (10).

After inhalation of 20 mg furfural/m^3 for 3 months (5 hours/day, 6 days/week), adult rats showed reduced activity of alkalic phosphatase in blood serum (16). Rats 6 to 7 weeks old given the same dose for four weeks also had less calcium in the skeleton than controls (16). After twelve weeks of inhalation (5 h/day, 6 days/week) of 200 mg furfural/m^3, rats showed neurochemical disturbances in the central nervous system as well as disturbances in the metabolism of steroid hormones (2). The disturbances were measured as reduced levels of adrenalin and noradrenalin and increased cholinesterase activity.

It is unclear whether these demonstrated enzymatic and histological changes indicate a definite health risk after occupational exposure to furfural in concentrations below present exposure limits (5 ppm; 20 mg/m^3).

Mutagenicity studies with Ames' test have given equivocal results. Some studies have reported furfural to be mutagenic and others have reported it to be non-mutagenic (13, 14, 19).

In one cancer study (3) in which hamsters were given furfural, benzo(a)pyrene or both by intratracheal instillation once a week for 36 weeks, it was noted that tracheobronchial cancer appeared earlier in the group exposed to both substances than in the group exposed to benzo(a)pyrene alone. This probably indicates that furfural has a cocarcinogenic effect. The study (3) contains no indications that furfural alone has any carcinogenic activity.

In a later study (4) in which hamsters inhaled 400 ppm furfural for 9 weeks followed by 330 ppm for 11 weeks and finally 250 ppm for 32 weeks (7 hours/day, 5 days/week), and simultaneously received weekly intratracheal instillations of benzo(a)pyrene, it was concluded that the carcinogenic effect of benzo(a)pyrene was not affected by the exposure to furfural. The furfural dose was reduced during the course of the experiment because of the obvious effects on the animals receiving furfural alone: reduced body weight, yellowing of the fur, irritation of nasal mucosa and atrophy of the olfactory epithelium.

Conclusions

The critical effects of exposure to furfural are irritation of the eyes and respiratory passages. There are no studies which can be used to estimate a dose-response/dose-effect relationship.

It should be noted that furfural in the gas phase can be absorbed by the skin.

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APPENDIX

Analysis methods for furfural

The method series published by the National Swedish Board of Occupational Safety and Health (1) recommends sampling of furfural in air by absorption on Amberlite XAD-2. After desorption with diethyl ether the analysis is performed by gas chromatography. Furfuryl alcohol can be determined simultaneously. A five-liter air sample is sufficient for detection of concentrations down to 1.5 mg furfural/m^3 air.

NIOSH (2) recommends sampling in a gas wash bottle containing Girard's T-reagent (carboxymethyl-trimethyl ammonium chloride hydrazide), dissolved in water containing a citrate-phosphate buffer. This reagent combines with furfural to form a hydrazide which can then be determined by liquid chromatographic analysis (HPLC). A UV-detector is used at 312 nm. The method has been tested in the interval of 10 to 40 mg/m^3, but the detection limit is estimated to be about 0.2 mg/m^3 with a 120-liter air sample.

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CONSENSUS REPORT FOR ALICYCLIC HYDROCARBONS, CYCLOALKANES
April 25, 1984

This document includes the alicyclic hydrocarbons containing from 5 to 15 carbon atoms in a ring system. For most of them, there is no data in the literature relevant to the establishment of occupational exposure limits.

Physical - Chemical data

Cyclopentane

CAS No.: 287-92-3
Formula: C_5H_{10}
Synonym: Pentamethylene
Molecular weight: 70.14
Boiling point: 49.3°C
Vapor pressure: 53.3 kPa (31°C)
1 ppm = 2.87 mg/m^3; 1 mg/m^3 = 0.35 ppm

Cyclohexane

CAS No.: 110-82-7
Formula: C_6H_{12}
Synonyms: Hexamethylene, Hexahydrobenzene
Molecular weight: 84.16
Boiling point: 80.7°C
Vapor pressure: 13.3 kPa (61°C)
1 ppm = 3.44 mg/m^3; 1 mg/m^3 = 0.29 ppm

Cycloheptane

CAS No.: 291-64-5
Formula: C_7H_{14}
Synonym: Heptamethylene
Molecular weight: 98.19
Boiling point: 118.5°C
1 ppm = 4.02 mg/m^3; 1 mg/m^3 = 0.25 ppm

Cyclooctane

CAS No.: 292-64-8
Formula: C_8H_{16}
Synonym: Octamethylene
Molecular weight: 112.21
Boiling point: 149°C (99.8 kPa)
1 ppm = 4.59 mg/m^3; 1 mg/m^3 = 0.22 ppm

Others

Formula: C_nH_{2n}
Molecular weight: increases by 14 units for every CH_2

Occurrence, etc.

Cycloalkanes are produced from crude oil and occur as components in various distillation products. They (primarily those of low molecular weight) are used as solvents and extractants in the paint industry and in the chemical and pharmaceutical industries.

At room temperature the low-molecular cycloalkanes are liquids, whereas those with higher molecular weights are solid. They are sparingly soluble in water but easily dissolved in alcohol.

Occupational exposure can occur either via direct skin contact or by inhalation of aerosols or vapors containing cycloalkanes (primarily the low-molecular ones).

Uptake, biotransformation, excretion

Occupational uptake of cyclohexane was studied in 22 shoe factory workers (8). Concentrations in factory air were 17 to 2,482 mg cyclohexane/m^3, and measured concentrations in alveolar air were about 75% of these. The cyclohexane content of the blood was noted to be about 30 to 350 µg/liter, which corresponds to an uptake of about 35% to 65% of the amount inhaled. In another study (7) the uptake via lungs was reported to be 23%. Less than 10% of the total uptake is excreted via exhalation after termination of the work shift.

The urine of persons occupationally exposed to cyclohexane was analyzed within 6 hours after exposure during a workshift. Analyses indicated that cyclohexanol and cyclohexanone were the primary biotransformation products (7, 9), but excretion of these substances accounted for no more than 0.1% to 1% of the absorbed cyclohexane (7, 8).

For the other cycloalkanes, no data have been found regarding either uptake, biotransformation or excretion in man.

In one study (11) in which rats inhaled 300, 1,000 or 2,000 ppm cyclohexane 6 hours/day, 5 days/week for two weeks, a dose-dependent concentration was observed in perirenal fat.

Toxic effects

Undiluted cyclopentane, cyclohexane, cycloheptane and cyclooctane, as well as 25% cyclododecane (in paraffin), applied to

the skin of guinea pigs, caused symptoms of irritation and thickening of the skin, and also affected arginase enzyme activity in the epidermis. The effect was more pronounced for hydrocarbons of higher molecular weight (1).

In one experiment 0.2 ml doses of various hydrocarbons were placed in the mouths of anesthetized rats, which were thus forced to inhale the entire dose. One of the three animals which received cyclopentane died within an hour or so, as did two of the three animals receiving cyclohexane, two of three receiving cycloheptane, and all three of the animals receiving cyclooctane. Cause of death was reported to be heart failure and asphyxiation (3).

In one inhalation study, microscopic reversible degenerative changes were noted in liver and kidneys of rabbits exposed to 2.65 mg cyclohexane/liter for fifty 6-hour periods. Exposure to 1.46 mg/liter caused no visible changes. Exposure to 11.23 mg/liter (or less) for a total of 300 hours caused no deaths or signs of poisoning (12).

In one LD_{50} study (4), in which undiluted cyclohexane was given orally to rats, it was observed that the substance is less toxic to full-grown young rats (LD_{50} = 39 ml/kg body weight) than to rats only 14 days old (LD_{50} = 8 ml/kg) or to older adults (LD_{50} = 16.5 ml/kg). It should be noted that there is a very small margin between narcosis and death for all cycloalkanes from cyclopentane onwards (10).

In one epidemiological study (6), in which persons occupationally exposed to a mixture of hydrocarbons for one to 25 years were compared with a control group, neurophysiological effects were noted in the exposed group. The main components in the mixture were n-hexane and cyclohexane. The authors suggest that cyclohexane may have a synergistic effect with n-hexane, which is a known neurotoxin.

There is one case study (2) of toxic neuropathy in an individual who worked painting automobile bodies. Monitoring measurements showed that cyclohexane (20 mg/m^3), acetone (4 mg/m^3), toluene (125 mg/m^3), xylene (29 mg/m^3) and isobutanol (119 mg/m^3) were present in the air in the workplace. (The values given above are 60-minute averages.) The authors believe that the polyneuropathy could be a result of the toxicity of cyclohexane.

Inhalation of cyclohexane (16.8 mg/m^3) by female mice for 0.5 to 3 days induced the liver's microsomal monooxygenase (enzyme) system in the same way as did phenobarbitol (5). This can have relevance for cases of simultaneous exposure to cyclohexane and substances which depend on the enzyme system for biotransformation and have toxic biotransformation products. In the same study (5) it was shown that cyclohexane reduced the sleeping time caused by hexobarbital.

Table 1. Effects on rabbits of inhalation of cyclohexane (data from Reference 12).

Dose (mg/m^3)	Time	Effect
1,460	50x6 h	No microscopic organ changes.
2,650	50x6 h	Microscopic changes in kidney and liver.
11,230	50x6 h	No signs of poisoning.
25,100	10x6 h	Slight narcosis, increased respiration, 1 of 4 animals died.
31,090	25x6 h	Tremor, loss of coordination, increased respiration, salivation; 3 of 4 animals died.
42,400	10x6 h	Convulsions, slight narcosis, increased respiration, salivation; 1 of 4 animals died.

Conclusions

For most cycloalkanes, there are no toxicological or medical data which can provide a basis for establishing occupational exposure limits.

For cyclohexane, no visible toxic effects were noted in rabbits exposed to 11,230 mg/m^3 for 300 hours. Exposure to 2,650 mg/m^3 for 300 hours caused microscopic changes in liver and kidney of rabbits, but no changes were noted with exposure to 1,460 mg/m^3.

There is no conclusive data regarding interaction effects between cyclohexane and other solvents.

It should be borne in mind that cyclohexane in liquid form can irritate the skin.

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APPENDIX

Analysis of cycloalkanes (C_5--C_{15})

Cycloalkanes can be determined by the graphite rod technique (1). It is also possible to take gaseous samples for later analysis, using for example a motor-driven syringe (5). Several individual methods are described by NIOSH (2) for cyclohexane and methylcyclohexane. A range of 100 to 3,000 mg/m^3 is given for cyclohexane, and for methylcyclohexane 200 to 6,000 mg/m^3. In both cases much lower concentrations should be detectable (2). Cycloalkanes occur in many hydrocarbon compounds. NIOSH (2) describes analysis by the graphite rod technique of products with boiling points from 120°C to 147°C, and from 154°C to 195°C, which can contain cycloalkanes from C_8 to C_{11}.

A Swedish standard (3) for determination of total hydrocarbon content in air in the workplace can also be mentioned as a possible method for cycloalkanes. The method is based on sampling with a graphite rod, extraction with carbon tetrachloride and IR analysis. The method description, which is experimental in nature, mentions no sensitivity limit.

Cycloalkanes C_{12}--C_{15} have a boiling point above 200°C. With increasing boiling point there is increasing probability of condensation. The special problems that this causes in sampling and analysis have been discussed in an earlier Consensus Report in connection with oil mists (4).

Continuous registration of cycloalkanes in air can be done with direct-measurement instruments using flame ionization, photoionization or an IR detector.

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CONSENSUS REPORT FOR HYDROGEN FLUORIDE

April 25, 1984

This report is based primarily on a criteria document from the Nordic Expert Group for Documentation of Occupational Exposure Limits (13).

Physical and chemical data, characteristics and occurrence

CAS No. 7664-39-3
Systematic name: hydrogen fluoride
Formula: HF
Molecular weight: 20.01
Boiling point: 19.5°C
Freezing point: -83°C
1 mg/m^3 = 1.2 ppm; 1 ppm = 0.8 mg/m^3 (20°C; 101.3 kPa)

Anhydrous hydrogen fluoride occurs mainly as $(HF)_6$, or at higher temperatures usually as monomeric (HF). Hydrogen fluoride is a colorless, sharp gas. It is easily dissolved in water, forming hydrofluoric acid. Anhydrous hydrogen fluoride reacts strongly with sodium hydroxide, sulfuric acid, etc., as well as with numerous organic compounds, but has almost no effect on glass or metals.

Industrial hydrofluoric acid usually contains from 35% to 100% HF, and contains in addition to dissolved HF also H_3O^+, F^- and water. It can etch glass and dissolve quartz and silicates.

HF is usually produced from fluorite by treatment with concentrated sulfuric acid. Anhydrous hydrogen fluoride is used as a catalyst in condensation reactions and as a raw material in the production of fluorides and fluorocarbon compounds. Hydro-

fluoric acid is used in oil refining, etching of glass and metals, and in removal of rust and enamel from metal objects. HF can occur as a contaminant in the working environment in aluminum plants and in the clay and ceramics industries.

Uptake, distribution, excretion

Hydrogen fluoride in aqueous solution diffuses through biological membranes primarily as the undissociated monomer, HF (23). Rats exposed to 32--185 mg HF/m^3 absorbed nearly 100% in the upper respiratory passages (19). There was a high correlation between fluoride concentration in the blood plasma and the level of inhaled HF. The relationship seems to be the same for man (22).

Experiments with rats indicate that HF in the gas phase is absorbed via skin, and effects on other organs are the same as they are after inhalation of HF (21). Two cases of serious poisoning were considered to result from skin uptake (1, 22).

Fluoride is distributed via the blood to all the organs of the body, where concentrations soon exceed those in the blood. About 75% of the fluoride in blood is in plasma and 25% in the red blood cells (2, 12). The biological half time in plasma has been reported to be between 4 and 9 hours (9). About 99% of the body's total fluoride content is in the skeleton, where it is reversibly bound in the form of fluoroapatite (15). There is considered to be some risk for accumulation with exposure to 3.3 mg fluoride/m^3 (gas phase) or 5 mg/m^3 (dust) (or higher) (3).

The most important path of excretion is via the kidneys (6). Studies of occupationally exposed persons have revealed a relatively high correlation between fluoride concentration in

urine after a work shift and that in air in the workplace. In one study (11) it was calculated that 8 mg F^-/liter in urine corresponded to 3 to 5 mg F^-/m^3, and in another study (14) that the same amount of fluoride in urine was related to exposure to 1.5 mg/m^3.

A considerable portion of absorbed fluoride is eliminated with perspiration (4); up to 75% of the amount excreted in urine.

Toxic effects

Effects on skin, eyes and mucous membranes

Both HF gas and hydrofluoric acid have a strong caustic effect on skin and cause intense pain. Symptoms are noted immediately with exposure to hydrofluoric acid in concentrations of over 70%; if concentrations are 30% or less, there can be a latency time of up to 24 hours. HF in concentrations lower than 1.7 mg/m^3 and hydrofluoric acid with less than about 5% HF have little or no effect on skin (13). Volunteers exposed for several days to HF in a concentration near 3 mg/m^3 developed symptoms in the form of a smarting sensation on the skin and in the eyes and nose. At higher concentrations there is reddening of the skin (16).

Examination of workers in aluminum electrolysis halls revealed a significant overfrequency of pharyngitis (throat inflammation) after exposure to an average 1 mg total fluoride/m^3. With certain operations air concentrations were as high as 34 mg F^-/m^3, but HF concentrations were considered to be minimal here.

Effects on the respiratory passages

Lung edema, often with fatal consequences, has been reported as a consequence of exposure to high concentrations of HF following accidental emissions (20). In one case (22) the edema seemed to be a result of HF absorption via skin. There are numerous reports of asthma-like complaints among workers in the aluminum industry (20). The reaction is described as a reversible, non-allergic, obstructive hyper-reactivity reaction. In addition to HF, workers were also exposed to SO_2, fluoride dust and other dust onto which HF could have been adsorbed.

Hyperreactivity reactions have not been observed in workers exposed to high concentrations of HF during the production of glass, enamelware or sulfuric acid. These observations indicate that adsorption of HF to particles may make it possible for the HF to penetrate more deeply into the respiratory passages and cause the hyperreactivity (13).

Studies at American aluminum works have reported an excess mortality due to emphysema (18). A reduction of lung capacity over a work shift was noted in one study of electrolysis workers in an aluminum smelter (14).

Occupational exposure to less than 10 mg HF/m^3 seems to cause lung damage (asthma-like symptoms) only if there is simultaneous exposure to pollutants in the form of airborne particles.

Effects on the skeleton

High uptake of fluoride over long periods leads to skeletal fluorosis, characterized by increased mineralization of the skeleton (osteosclerosis). Osteosclerosis is generally not associated with functional impairment. A simultaneous calcification of sinews can, however, cause some pain and difficulty

of motion. No changes in the skeleton have been found after ten to 46 years of exposure high enough to yield urine concentrations of about 8 mg F^-/liter (measured after a workshift). In one case, osteosclerotic changes were observed in a person who had worked with HF production for 16 years (24). The twenty-four hour urine concentration was 15 mg F^-/liter.

Other toxic effects

No association has been shown between fluoride exposure and cancer (8).

After one accident in which there was a high intake of HF, the patient died from heart failure (22). In another case, where intake of HF was lower, the patient died of heart failure after 12 days (10). The heart failure was considered to be a result of the fact that HF inhibits the cells's breakdown of carbohydrates.

Dose-response/dose-effect correlations

100 mg HF/m^3	The highest air concentration two men could endure for longer than 1 minute. The skin began to sting within a minute. Irritation of eyes and respiratory passages (17).
50 mg HF/m^3	Strong irritation of eyes and nose, stinging in the upper respiratory passages (17).
26 mg HF/m^3	The air could be tolerated for several minutes. Slight smarting of eyes and nose (17).

<10 mg HF/m^3	Exposure to pure HF seems to have no effect on lungs (13, 19).
3.38 mg F^-/m^3	Average exposure during an average employment time of 14.3 years in the phosphate industry. Somewhat elevated skeletal concentrations were noted in 17 of 74 persons. The magnitude of exposure to HF was not reported (5).
>2.9 mg HF/m^3	Six hours. Skin reddening. Stinging sensation and slight irritation of the nose. No demonstrable systemic effects (16).
1.3--4.2 mg HF/m^3	Average exposure for six hours resulted in slight burning of the face and eyes, and light irritation of the nose (16).
2.65 mg F^-/m^3	Average exposure during average employment time of 14.3 years in the phosphate industry. No skeletal changes were observed in 57 of 74 exposed (5).
0.02--1.0 mg F^-/m^3 in gas phase and 0.02--0.04 mg/m^3 fluoride particles	No demonstrable lung or skeletal changes in 85 examined aluminum smelter workers (25).
Urine fluoride concentration 10--15 mg/l	Exposure to HF for 10 to 17 years resulted in osteosclerosis but no subjective symptoms (24).
Urine fluoride concentration 8 mg/l (after workshift)	Ten to 43 years exposure in aluminum electrolysis halls seems to involve no risk of fluorosis (7).

Conclusions

The critical effect of exposure to HF is irritation of the skin and mucous membranes. It should be noted that HF is easily absorbed via skin. The risk of uptake via the lungs is increased if the HF is adsorbed onto respirable particles.

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APPENDIX

Analysis of hydrogen fluoride and fluorides

Hydrogen fluoride in air can be measured directly with analysis ampules, which are reported to function within the range 1.5 to 15 ppm and to be specific. High humidity can disturb the readings.

Hydrogen fluoride and solid fluorides in particle form often occur together in air in workplaces. Sampling of both together is easiest with the "double filter method". The collection apparatus consists of a holder for a cellulose-acetate filter backed by a support impregnated with sodium formate (1). When air is sucked through this arrangement, the particles stick to the filter and the hydrogen fluoride is bound to the impregnated support. After sampling, the filter holder must lie sealed in a drying cabinet at 60°, so that the hydrogen fluoride that collected on the filter can diffuse over to the support.

Analysis of fluoride is done with an ion-specific electrode. The support is leached with a buffer having a pH between 5.0 and 5.5. This also contains complex-formers to bind the disturbing metal ions and a certain amount of salt to maintain a constant ion strength. The fluoride concentration in the solution can be measured directly with the electrode.

Since the particles on the filter can contain large amounts of disturbing metals (Al, Fe, etc.), the hydrogen fluoride is separated from the particles by diffusion in a closed crucible after acidification with perchloric acid. The hydrogen fluoride is taken up by sodium hydroxide, and the analysis is done in the same way with the ion-specific electrode. The detectability limit for the electrode is about 0.2 mg F^-/liter. In

the recommended sample volume (30 liters of air) it is possible to determine as little as 0.15 mg F^-/m^3 of both hydrogen fluoride and solid fluorides.

Biological exposure control for fluorides is done by analysis of urine. After addition of a buffer solution, measurements can be made directly with an ion-specific electrode (2). It is possible to determine as little as 0.2 mg F^-/liter, corresponding approximately to the lowest concentration occurring in people not occupationally exposed. For these people, the fluoride concentration in urine is usually about the same as that in the local drinking water.

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CONSENSUS REPORT FOR 2-BUTANOL, ISOBUTANOL AND TERT-BUTANOL
June 6, 1984

Butanol is an alcohol which has four different isomers: 1-butanol, 2-butanol, isobutanol and tertiary butanol. 1-butanol is treated in a previous report (16), so only the other three isomers are taken up here. This document is based primarily on a previously published criteria document on butanol and butyl acetate (3) which was written at the request of the Swedish Criteria Group.

The butanols are chemically similar, but this doesn't necessarily mean that they have similar biological effects. Up to this time, however, studies of the effects of butanols other than 1-butanol are rare, and the information has here been collected in a single document.

2-butanol

CAS No.: 78-92-2
Synonym: secondary butanol
Boiling point: 99.5°C

Isobutanol

CAS No.: 78-83-1
Synonym: 2-methyl-1-propanol
Boiling point: 108.1°C

Tert-butanol

CAS No.: 75-65-0
Synonyms: tertiary butanol, 2-methyl-2-propanol
Boiling point: 82.2°C

For all of the above:
Formula: C_4H_9OH
1 ppm = 3.03 mg/m^3; 1 mg/m^3 = 0.330 ppm (25°C)

All these isomers are colorless liquids, easily soluble in most organic solvents, but they have different solubilities in water.

Uses

All the isomers are used as solvents in various kinds of lacquers. 2-butanol is also used as a solvent in enamels, vegetable oils and rubber. Both 2-butanol and isobutanol are used in the production of paint removers, detergents and hydraulic brake fluids. Other uses of 2-butanol include fruit flavorings and perfumes, in which tert-butanol is also used. Tert-butanol is used rather seldom in industry; some areas in which it occurs are water removal, extraction of drugs, recrystallization of chemicals, and in cellulose esters and plastics.

Exposure to butanol in vapor form, usually mixed with other solvents, may occur in the textile and dye industries. Reported concentrations refer to total exposure for isomers of butanol and are in the range 2 to 20 ppm (3).

Uptake, biotransformation, excretion

All the isomers of butanol can be taken up by the respiratory passages and in the digestive tract, and isobutanol can also be absorbed via skin (13). 2-butanol seems to be distributed to the blood and liver (5). For the other isomers, there is no data on distribution.

When rats were given an oral dose of 2-butanol corresponding to 1776 mg/kg body weight, measured blood concentration was 0.59 mg/ml after two hours and 0.05 mg/ml after 16 hours (5).

Isobutanol is transformed by oxidation to aldehyde or carboxyl acid; 2-butanol is oxidized to ketone. Tert-butanol has been regarded as impossible to oxidize, but some recent results indicate that some oxidative breakdown nevertheless does occur (1).

A small amount of 2-butanol is transformed to glucuronide, but most of it is oxidated to 2-butanone and the secondary products formed from this ketone. 2-butanone is excreted via the lungs, and untransformed 2-butanol via urine (5). There is no further data on excretion.

Toxic effects

Nervous system

At high doses, the isomers of butanol have had toxic effects on experimental animals, primarily on their central nervous systems. Similar brain damage has not been observed in human subjects, however. The effects shown by experimental animals are: narcotic effect from exposure to isobutanol (12); intoxication from all three isomers (17); and various kinds of behavioral changes from exposure to tert-butanol (8, 10, 11, 15). In the latter four experiments, animals (mice and rats) were exposed to tert-butanol in concentrations of 1,000--2,000 mg/kg either via food (8, 15) or by injection (10, 11). Two of the reports (8, 10) refer to mg/kg body weight, but the others (11, 15) refer to amounts in food or solution. The kinds of behavior affected by the exposures were mobility (10), avoidance of electrical shocks (15) and some reflexes (11).

In one experiment (14), dizziness was reported in 5 of 7 human subjects who had been exposed to isobutanol for periods of two months to two years. However, the report makes no mention of exposure levels.

Other effects

Other effects include fat accumulation in the liver, demonstrated in mice after inhalation of 2-butanol, isobutanol and tert-butanol (18). Accumulation of fats in the liver has also occurred in rats after oral administration of a single dose of tert-butanol (1,850 mg/kg) (2).

Some accumulation of fat has also been observed in kidneys after inhalation of the three butanol isomers discussed here (18), and in a few cases fat accumulation in the heart was noted after inhalation of isobutanol (18).

In one reported case, exposure to tert-butanol in suntan oil caused contact eczema in a human patient (6). Isobutanol may also be a skin irritant (13).

Irritation of the eyes and throat and blistering of the cornea were reported in workers exposed to high concentrations of isobutanol while lacquering cables (13). The report contains no information on exposure levels, however.

Some behavioral abnormalities have been noted in the young of mice exposed for 14 days during pregnancy to concentrations of 0.75% to 1.00% tert-butanol in liquid food (4). (A concentration of 0.50% gave no such effects, however.) This may mean that tert-butanol has some teratogenic effects.

An increased frequency of malignant tumors was noted in one study in which rats were exposed to isobutanol in drinking

water (7). However, the methods used in this study make it difficult to evaluate. In another study (9), an increased frequency of mutation was noted in a cell culture after addition of tert-butanol.

Dose-effect relationships

In animal experiments, various effects have been produced by different doses, primarily one-time doses, of the different isomers of butanol. A summary of the reported results is presented in table form below:

Table 1. Relationship between exposure and effect after oral intake or injection of the isomers of butanol.

Substance (butanol)	Amount (mg/kg)	Exposure (oral/inj)	Effect	Ref.
iso-	3,030	one dose (oral)	lethal (rabbits)	12
iso-	1,406	one dose (oral)	narcosis (rabbits)	12
tert-	2,690	30 days (oral)	behavioral disturbances (newborn rats)	8
tert-	1,850	one dose (oral)	fat accumulation in liver (rats)	2
tert-	1,080 (mg/kg in solution)	one dose (injection)	loss of reflexes (mice)	11

Conclusions

For human subjects, the reported effects of long-term exposure to isobutanol are primarily irritation of the eyes and mucous membranes, and also some dizziness. Reported cases include no information on exposure levels.

No effects on man have been reported for the other isomers, except for one case of contact eczema from tert-butanol.

Experimental animals have shown effects on the central nervous system after exposure to relatively high doses of tert-butanol or isobutanol. It is not known, however, whether similar effects can appear in man.

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APPENDIX

Analysis of butanols (excluding n-butanol)

Isobutanol (2-methyl-1-propanol), secondary butanol (2-butanol) and tertiary butanol (2-methyl-2-propanol) in air can all be determined by the carbon rod method (1). The individual procedures are described in the NIOSH Manual of Analytical Methods (2), which gives the following concentration ranges:

isobutanol	30 -- 900 mg/m^3
secondary butanol	45 -- 850 "
tertiary butanol	30 -- 750 "

It should be possible to detect considerably lower amounts with the same methods (2).

It is also possible to take samples in gaseous form for subsequent gas-chromatographic analysis, for example by using a motor-driven syringe (3).

Butanol in air can be continuously monitored with instruments giving direct readings. If an instrument with an IR detector is chosen, disturbance from other substances can often be reduced by choice of an appropriate wavelength.

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CONSENSUS REPORT FOR 1-BUTYL ACETATE
June 6, 1984

CAS No.: 123-86-4
Synonyms: n-butyl acetate, acetic acid butylester
Formula: $C_6H_{12}O_2$
Boiling point: 125°C
1 ppm = 4.75 mg/m^3; 1 mg/m^3 = 0.211 ppm (25°C)

1-butyl acetate is a colorless liquid with a fruity odor. Its solubility in water is relatively low.

1-butyl acetate is one of four isomers of butyl acetate; the others are: 2-butyl acetate, isbutyl acetate and tertiary butyl acetate. This document discusses only 1-butyl acetate, which is the most commonly occurring of these isomers. The literature has also been reviewed for the other isomers, but no information was found regarding their possible biological effects.

This report is based primarily on a previously published criteria document covering butanol and butyl acetate (2), which was written at the request of the Criteria Group.

Occurrence in the working environment

1-butyl acetate is used as a solvent in the manufacture of textiles, plastics, artificial leather and coated paper, and in the extraction of oils. Butyl acetate also occurs in the production of perfumes, vitamins, hormones and antibiotics, lacquers, synthetic resins and natural rubber. It is used as an extractant in the production of phenol, writing ink, paint removers and flavoring extracts.

Industrial workers are most often exposed to a mixture of butyl acetate and other solvents. The concentrations of 1-butyl acetate measured in industrial environments are around 3 to 9 ppm. These values were found in the paint and textile industries and in automobile painting halls, where exposure is to 1-butyl acetate in vapor form only (2).

Uptake, biotransformation, excretion

1-butyl acetate is taken up via the lungs and the digestive tract, and to some extent through the skin (5). It is broken down by hydrolysis in the blood plasma and the liver; the end products are 1-butanol and acetic acid.

1-butyl acetate is probably excreted partly in unchanged form via exhaled air and urine, and partly after transformation in the body. The literature contains very little detailed information on the metabolism of 1-butyl acetate.

Toxic effects

Skin and mucous membranes

Observed effects on skin are fissures and loss of fat (3). However, it has not been possible to demonstrate effects on skin in animal experiments using 1-butyl acetate (6).

One case of contact allergy has been reported after exposure to 1-butyl acetate (9).

Human subjects exposed to 1-butyl acetate for short periods have developed irritation in the throat at 200 ppm and irritation in the eyes and nose at 300 ppm (8). In animal experiments, similar effects have been noted in cats and guinea pigs at considerably higher doses (3, 1).

The central nervous system

The odor threshold for 1-butyl acetate has been reported to be 10 ppm (4).

The literature contains no information on the effects of 1-butyl acetate on the central nervous system of humans. In animal studies, however, long exposure (up to 13 hours) to 1-butyl acetate in high concentrations (7,000 to 12,000 ppm) has been demonstrated to have a narcotic effect on guinea pigs, mice and cats (5).

Other effects

The other organs reported to be affected by 1-butyl acetate are the respiratory passages (where irritation was demonstrated), liver, kidneys and blood (1, 4, 5). In all of these cases experiments were made with animals, usually using high doses of 1-butyl acetate.

In one study of chicken embryos, 1-butyl acetate injected in the yolk sac was shown to have several effects (7). The number of hatched eggs decreased, and with lower doses (9 to 27 mg 1-butyl acetate per egg) damage to the eyes and kidneys was observed. Possible embryotoxic effects to humans can not be commented on the basis of this study.

Other effects of 1-butyl acetate which have been noted in animal studies are weight reduction, weakness etc. In most cases it has been a matter of high doses (3,000 to 4,000 ppm) (5), but 65 days of exposure to 900 ppm caused weakness in guinea pigs and cats (5, 3).

Dose-effect relationship

Short-term exposure to high doses of 1-butyl acetate has caused narcosis in guinea pigs and cats. Exposure to low doses has irritation effects on human subjects. Table 1 shows the dose-effect relationships reported in various studies.

Table 1. Relationship between exposure to butyl acetate and effect.

Conc. (ppm)	Exposure (time)	Effect	Reference
14,000	4 h	narcosis, lethal (guinea pigs)	3, 1
7,000	13 h	deep narcosis (guinea pigs)	3, 1
6,100	6 h	light narcosis (cats)	3, 1
1,600	6 h	eye irritation (cats)	3, 1
3,300	13 h	severe irritation of eyes and nose (man)	3
300	3--5 min.	irritation of eyes and nose (man)	8
200	3--5 min.	throat irritation (man)	8
100		highest concentration considered by test subjects to be acceptable with 8-hour exposure (man)	8

Conclusions

1-butyl acetate has been shown to irritate the eyes, nose and throat of human subjects. This effect can be considered the critical one, since it occurs at the lowest concentrations: 200 to 300 ppm.

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APPENDIX

Analysis of butyl acetate

All the acetates of the four isomeric butanols can be determined by the carbon rod method (1). The individual procedures are described in the NIOSH Manual of Analytical Methods (2). NIOSH reports the following concentration ranges:

n-butyl acetate	71 -- 2130 mg/m^3
isobutylacetate	70 -- 2100 "
secondary butylacetate	95 -- 2850 "
tertiary butylacetate	95 -- 2850 "

It should be possible to detect considerably lower amounts with the same methods (2).

It is also possible to take samples in gaseous form for subsequent gas-chromatographic analysis, for example by using a motor-driven syringe (3).

Butyl acetate in air can be continuously monitored with instruments giving direct readings. If an instrument with an IR detector is chosen, disturbance from other substances can often be reduced by choice of an appropriate wavelength.

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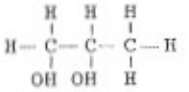
CONSENSUS REPORT FOR PROPYLENE GLYCOL
June 6, 1984

This report is based primarily on a criteria document from the Nordic Expert Group for Documentation of Occupational Exposure Limits (13).

Physical and chemical data. Uses

CAS No.: 57-55-6
Systematic name: 1,2-propanediol
Synonyms: Methyl glycol, 1,2-dihydroxy propane, methylethylene glycol
Formula: $C_3H_8O_2$

Structural formula:



Molecular weight: 76.1
Boiling point: 187.4°C (101.3 kPa)
Vapor pressure: 10.6 kPa (20°C)
1 mg/m^3 = 0.32 ppm; 1 ppm = 3.1 mg/m^3 (25°C, 101.3 kPa)

Propylene glycol is a clear, colorless, slightly viscous, odorless liquid with a weak, bitter-sweet taste. It is hygroscopic and soluble in water.

Propylene glycol is used as an antifreeze, in heat exchangers, as a brake and hydraulic fluid, as a solvent in the plastics and chemicals industries, and as a solvent and additive in the food and cosmetics industries. Propylene glycol is used to generate smoke in discotheques. Occupational exposure can be via both inhalation (gas, vapor or aerosol) and skin resorption.

Uptake, biotransformation, excretion

When propylene glycol was applied to the skin of human subjects, uptake could be measured (4). Uptake can increase if the skin is damaged.

No studies were found which described quantitative resorption in the lungs, but it is probable that propylene in the gas phase is resorbed via the lungs (13). The concentration of propylene glycol in blood has been shown to increase rapidly, with a maximum within 30 minutes after peroral intake (5, 14).

Propylene glycol is distributed rapidly by the blood to all tissues and organs (7). Within the cells it can oxidize to lactic acid and pyruvic acid, which are normal constituents of carbohydrate metabolism and yield carbon dioxide and water as end products (11). In animal diets, up to 5% of the carbohydrates in the food can be replaced by propylene glycol without affecting the animals' development (14).

Untransformed propylene glycol is excreted primarily via the kidneys. Human subjects who received 1 ml propylene glycol/kg body weight excreted about 20% unchanged in urine within 8 to 12 hours (5).

Toxic effects

Effects on skin, mucous membranes and respiratory organs

Direct application of propylene glycol to the mucous membranes of the mouth or the conjunctiva of the eyes results in a slight, temporary irritation (12). Propylene glycol can irritate the skin if it is applied under a tight bandage (occlusion), but not if it is applied only once to exposed skin. A few cases of allergic contact eczema have been report-

ed to result from exposure to propylene glycol in heavy-duty commercial cleaning preparations, etc., but there have been no reports of cases resulting from occupational exposure.

When propylene glycol comes into contact with connective tissue (in sores, etc.) it causes a strong local inflammatory reaction which heals slowly and leaves a scar (7).

Continuous exposure to propylene glycol in concentrations of up to 94 mg/m^3 (average 69 mg/m^3) for several weeks had no negative effects on the mucous membranes of the upper respiratory passages of children (6). There are no reports of damage to respiratory organs resulting from occupational exposure to propylene glycol (10).

Other toxic effects

Administration of large doses of propylene glycol has led to temporary albuminuria (albumin in urine). Intravenous injection can lead to intravasal hemolysis (disintegration of red blood cells), probably because of propylene glycol's hygroscopic properties (8, 14). Histopathological examination of monkeys and rats after 12 to 18 months of exposure to air saturated with propylene glycol revealed no abnormalities in lungs, kidneys, liver, spleen or bone marrow (9). Administration of 1 to 1.5 g/kg body weight in medicine has sometimes resulted in slight dizziness (4).

Propylene glycol has not been shown to be either mutagenic or carcinogenic (1--3, 14).

Conclusions

There have been no reports of negative effects resulting from occupational exposure to propylene glycol. Propylene glycol

can be considered to have low toxicity. There are no studies which can be used as a basis for discussion of occupational exposure limits.

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APPENDIX

Analysis of propylene glycol (1,2-propane diol)

No method for analysis of propylene glycol has been published, but there is a published method for analysis of ethylene glycol (4) which should be applicable to propylene glycol. Samples are taken on fiberglass filters mounted in series with a glass tube filled with silicon gel. The extractant is analyzed by gas chromatography.

Glycols yield trace effects on many gas-chromatographic columns; this is the case for the column recommended for the above method (4). A variant using another sort of column has been reported by DiCorica (2). An alternative sampling method uses an impinger bottle filled with water (1).

A method for determination of propylene glycol in blood serum has been published (3). It is based on distillation of diol derivatives with p-bromine phenylboric acid.

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SUMMARY

Scientific Basis for Swedish Occupational Standards. V. Arbete och Hälsa 1984:44, pp 1 - 118.

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 July, 1983 and June, 1984.

Key words: Polyaromatic Hydrocarbons, Cadmium, Arsenic, Beryllium, Mercury, Furfural. Cycloalkanes(C_5-C_{15}), Hydrogen Fluoride, Butanol, Butyl Acetate, Propylene Glycol.

Sammanfattning

Underlag för hygieniska gränsvärden. V. Arbete och Hälsa 1984: 44, s 1 - 118.

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 Kriterigruppen för hygieniska gränsvärden avgivit under perioden juli 1983 - juni 1984.(På engelska)

Nyckelord: Polyaromatiska kolväten, Kadmium, Arsenik, Beryllium, Kvicksilver, Furfural, Cykloalkaner(C_5-C_{15}), Fluorväte, Butanol, Butylacetat, Propylenglykol.

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