International Journal of Occupational Medicine and Environmental Health, Vol. 11, No 2, 129 – 143, 1998

REVIEW PAPERS

UPDATING OF HYGIENE STANDARDS FOR CARBON DISULFIDE BASED ON HEALTH RISK ASSESSMENT

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Key words: Carbon disulfide, Health effects, Hygiene standards, Review

Abstract. In 1995 the hygiene occupational standard values of carbon disulfide (CS_2) were established in Poland: the maximum allowable concentration, eight-hour time weighted average (MAC-TWA) – 18 mg/m^3, and the short time exposure level (STEL) – 30 mg/m^3. For lack of reliable retrospective data on the CS_2 exposure levels in the work environment and the dose-response relationship, the following have been taken into account in establishing these values:

- the nervous and vascular systems are recognized as the main CS_2 exposure targets;
- long-term exposure to CS_2 in the work environment, exceeding 30 mg/m^3, induces the toxic effect in the nervous and cardiovascular systems;
- chronic exposure to CS_2 at concentration below 20 mg/m^3 does not produce adverse effects in the peripheral nervous and vascular systems; coronary heart disease does not occur more frequently in workers exposed to CS_2.

Aiming at updating the 1995 MAC value for CS_2 the authors carried out an analysis of the recent literature data on the relation between exposure levels and health risk. The results of clinical and epidemiological studies published in 1995 – 1997 did not provide evidence that adverse health effects in the cardiovascular and neurological systems in persons occupationally exposed to CS_2 at concentration below 48 mg/m^3 is likely to occur. The studies of the harmful effects of low CS_2 concentration on the reproductive system have not proved that CS_2 affects the embryo and fetus. Moreover, in Poland the employment of women under conditions of CS_2 exposure (regardless of concentrations) during pregnancy and breast feeding is banned. Because the latest reliable studies have not indicated that chronic CS_2 exposure at the level of 20 – 48 mg/m^3 exerts toxic effect on humans, CS_2 concentration of 18 mg/m^3 as MAC-TWA and 30 mg/m^3 as STEL, adopted in 1995, need not to be updated.

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INTRODUCTION

Carbon disulfide (CS_2) is mainly used in the viscose rayon industry for manufacturing artificial fibres and cellofane. In different branches of industry it is also utilised as a solvent. In addition, it is involved in the production of herbicides and floatation agents, as well as in processes of rubber and neoprene material production (10,61,91).

CS_2 is an industrial substance generating manifold adverse effects. At present, there are virtually no cases of acute CS_2 poisoning. They may happen only as a result of an accidental massive short-term exposure to concentrations of 10 0000 mg/m^3 or more, causing coma or eventual death. Poisoning to 3000 – 5000 mg/m^3 are associated with psychiatric and neurological symptoms like extreme irritability, uncontrolled anger, hallucinations, paranoic and suicidal tendencies as well as manic-depressive psychosis. Acute circulatory failure can be observed as well (91). Due to the modernization of viscose rayon fibres production, acute CS_2 poisoning has been completely eliminated (12). Long-term exposure over many years may produce the syndrome of chronic poisoning, demonstrated by a variety of signs and symptoms.

In the United States the value of 60 mg/m^3 was adopted in 1946 – 1947 as maximum allowable concentration (MAC-TWA) for CS_2 (2). The majority of experimental and clinical studies of CS_2 toxicity have been carried out since that time. Together with the improvement of working conditions, more rigorous compliance with the hygiene standards and increased workers awarness, the profile of chronic CS_2 poisoning has entirely changed.

HEALTH EFFECTS OF OCCUPATIONAL CS_2 EXPOSURE: RECAPITULATION OF THE EPIDEMIOLOGICAL AND CLINICAL DATA PUBLISHED BY 1994, THE BASIS FOR MAC VALUES ADOPTED TO DATE IN POLAND

The most common health effects resulting from CS_2 exposure used to date as the basis for setting hygiene standards are as follows:

Disorders of the central nervous system. Encephalopathy with an organic syndrome manifested by clinical neurological symptoms, EEG abnormalities, and somato-psychic disorders predominate at high CS_2 concentrations (60 – 125 mg/m^3) (17,44,66,68,72,73). Aaserud et al. (3,4) applying more sophisticated diagnostic methods (CT, Doppler USG) reported CNS functional disorders with concurrent organic pathologies (atrophy in different cerebral areas, circulatory impairments, etc.) in workers chronically exposed for tens of years to CS_2 concentrations ranging from 10 to 50 mg/m^3 (peak concentration > 90 mg/m^3). Olejnik and Shilova (54), as well as Hirata et al. (40), measuring hearing evoked potentials, found CNS disorders in workers exposed for more than 30 years to CS_2 concentrations about 35 mg/m^3. Since pathological changes come out only if exposure duration exceeds 20 years, it may be assumed that the changes were not only due to the exposure duration but also due to higher CS_2 concentrations to which workers under study were exposed in the past.

Exposure to CS_2 concentrations higher than 30 mg/m^3 (30 – 60 mg/m^3), and ranging from 10 to 35 years may be responsible for psycho-motor disorders, distraction, anxiety, lower intelligence quotient, dysmnesia, and difficulties in memorizing (13,14,32,47,48).

Disorders of the peripheral nervous system. Disorders manifested by polyneuropathy have been diagnosed on the basis of clinical examinations and measurements of sensory (SCV) and motor (MCV) conduction velocity in peripheral nerves of workers exposed to CS_2 concentrations above 95 mg/m^3 (43), 30–125 mg/m^3 (65,81), and 60 mg/m^3 (31). The reduction in MCV and SCV was observed in persons exposed to CS_2 concentrations ranging between 10 and 50 mg/m^3 (3). However, the dose-effect relationship should be assessed with great concern as the concentrations to which workers were exposed differed and accounted for 3–50 mg/m^3 (62,63); 10–50 mg/m^3 (3); > 30 mg/m^3 (14); and 3–21 mg/m^3 (39), therefore, it is rather difficult to attribute the observed effects to a given concentration.

Disorders of the cardiovascular system. A number of studies which focused on the populations exposed to CS_2 concentrations of 30–180 mg/m^3 (35–37,83); 40–120 mg/m^3 (51); 60–120 mg/m^3 (82); ~60 mg/m^3 (80); > 50 and < 50 mg/m^3 (8,9); and 30–95 mg/m^3 (6), revealed an increased incidence of coronary heart disease (CHD) and first fatal myocardial infarctions, as well as enhanced mortality from coronary heart disease. CS_2 concentrations of 30 mg/m^3 and below do not increase CHD risk, and the rate of mortality from myocardial infarction is the same as in the general population (18,30,53). According to Sweetnam (75), an increased mortality from CHD results from cumulative exposure (past and current exposure). Moreover, CHD death risk was higher in persons exposed in the past. More frequent abnormalities in the values of CHD risk factors, such as higher systolic blood pressure, enhanced total cholesterol and LDL-cholesterol, and lowered HDL-cholesterol were observed in persons exposed to CS_2 at concentrations of 30–90 mg/m^3 (26,30,51,64,82–84,89,90).

Disorders of the reproductive system. An increased incidence of ovarian failure leading to disturbed menstrual cycle was reported in women working under exposure to CS_2 concentrations of 1.7–14.8 mg/m^3 (93) and 35–50 mg/m^3 (11). The relationship between CS_2 exposure and increased incidence of spontaneous abortion has not as yet been evidenced explicitly. Petrov (56) revealed more advanced changes, imminent abortions and preterm births in women, aged 20–29 years, working under exposure to CS_2 concentration of 27 mg/m^3, including the period of pregnancy. However, numerous researchers (7,27,29,36,49,67,93) have not reported any gestation abnormalities in women exposed to CS_2 concentration of 10 mg/m^3 both before conception and during pregnancy. Bearing in mind the aforesaid data it can be assumed that exposure to CS_2 concentration about 30 mg/m^3 may only affect the ovarian function (disturbed menstrual cycle).

MAXIMUM PERMISSIBLE CS_2 CONCENTRATIONS IN VARIOUS COUNTRIES

Following the analysis of the above mentioned studies facilitating the establishment of the dose-effect relationship, it was proposed to accept the following values of maximum allowable concentration (MAC) as obligatory in Poland (24):

1. The value of 18 mg/m^3 as MAC, eight-hour time weighted average (MAC-TWA), under condition that the preventive measures are taken to identify CHD risk in persons entering the employment or in those already employed under CS_2 exposure;

2. The value of 30 mg/m^3 as a short time exposure level (STEL).

The proposed values were based on the following indications:

– the exposure to CS_2 at concentrations above 30 mg/m^3 is harmful to the peripheral nervous and vascular systems;

– the exposure to CS_2 at concentrations below 20 mg/m^3 neither increases the incidence of coronary heart disease, especially if persons with enhanced CHD risk are not allowed to work under exposure, nor generates other adverse health effects;

– the literature data on the attempts aimed at finding out whether the concentration/biological relationship does really exist, do not provide reliable evidence that CS_2 exposure at the concentration of 30 mg/m^3 is harmful to health, thus, the value of 30 mg/m^3 was adopted as a threshold value for setting hygiene standards.

In the United States the hygiene standards for carbon disulfide have been changed twice over a period of the last twenty years. The National Institute of Occupational Safety and Health (NIOSH) recognized that chronic exposure to CS_2 concentrations above 30 mg/m^3 is responsible for diseases of the circulatory and neurological systems; concentration of 30 mg/m^3 may lead to changes in the reproductive system; and acute exposure to CS_2 concentrations above 60 mg/m^3 may induce psychological and behavioural disorders. A safety margine was adopted in order to prevent adverse health effects, and the following values were proposed: 10h TWA – 10 mg/m^3 (male) and 3 mg/m^3 (female of fertility age), and 15 min STEL – 30 mg/m^3 (50).

In 1989, the Occupational Safety and Health Administration (OSHA) recognized that the compliance with the following hygiene standards for CS_2: the permissible exposure limit – PEL – 12 mg/m^3, and STEL – 36 mg/m^3 would contribute greatly to diminishing the risk of cardiovascular and neurological diseases and it would prevent against adverse effects on reproductive functions (28). Nevertheless, experts and people involved raised a protest against these standards, so that the US Court of Appeals vacated these hygiene standards, and at present values adopted previously (PEL-TWA – 60 mg/m^3, and ceiling – 90 mg/m^3) are obligatory (1,5).

In 1991, the American Conference on Governmental Industrial Hygienists (ACGIH) recognized that the exposure to carbon disulfide at eight-hour time weighted average concentration of 31 mg/m^3, would be safe enough, and as such would pose no risk of acute health effects like headaches and deaths from cardiovascular diseases; TWA-TLV of 31 mg/m^3 (10 ppm) was adopted (1,2,5).

In Federal Republic of Germany, the value of maximum concentration in the workplace (MAK) – 10 mg/m^3 and STEL – 30 mg/m^3 were established as hygiene standards. According to the currently available information that exposure of pregnant women to CS_2 pose a risk to embryo or fetus, carbon disulfide was classsified to group B of toxicity (Table 1).

Maximum permissible concentration of CS_2 in various countries established on the basis of the results of clinical examinations and epidemiological studies are presented in Table 1. The differences presented in the table may result from:

1. Different definitions of hygiene standards in individual countries;

Table 1. Maximum allowable concentrations of carbon disulfide in different countries (1,19,24,41,50)

Country	TLV-TWA	STEL	Comments
Australia	30	–	S
Belgium	31	–	S
Czech Republic	10	20	
Denmark	15	–	S
Finland	30	60	S
France	30	75	S
FRG	10	30	S, B
Great Britain	10	30	S
Hungary	5	10	S
Japan	31	–	S
Poland	18	30	S
Sweden	16	25	S
Switzerland	30	60	S
USA			
ACGIH	31	–	S
OSHA	60	90(*)	S
NIOSH	3	30(**)	S
WHO	10(M) 3(F)	60(**)	

(*) – Ceiling
(**) – STEL (15 min)
S – Substance absorption by skin
B – Substance impairs the embryo and fetus
M – males; F – females

2. Dissimilar sensibility to CS_2 effect in investigated populations of different countries. According to ACGIH (2) the same level of occupational CS_2 exposure affected more seriously European than American workers. These differences may depend on the demographic character of the population, the way of performing individual jobs, the amount of CS_2 absorbed by the skin, the nutritional status, genetic predispositions, and inadequate exposure assessment (methods of collecting air samples in the working environment);

3. The lack of reliable data on harmful effects of exposure to CS_2 low concentrations (under 20 mg/m^3). Health effects were frequently attributed to low CS_2 concentrations, however, it is well known that it was not feasible to maintain such low CS_2 concentrations, as the technological processes used in the past for obtaining fibres with appropriate diameter did now allow to diminish the amount of CS_2 to such an extent to retain CS_2 concentrations at work posts within the limits between 10 and 20 mg/m^3 (the authors' own information gathered during the 1994 visits to viscose rayon plants in Poland);

4. The health effects are due to 'cumulative' exposure to concentrations changing in the work environment over a period of several to several dozen mg-years. Neither identification of real concentrations of CS_2 vapours in the ambient air at working posts, to which the working population is exposed, nor attribution of certain health effects to given CS_2 concentrations is feasible. Everyone who tries to attribute health disorders that has been developing for years of occupational CS_2 exposure to CS_2 concentrations occurring currently commits a mistake.

5. Values that characterise the exposure magnitude, derived from the measurements of CS_2 vapours at work posts, and not from individual exposure assessment are not accurate, and they do not illustrate the real exposure level, particularly if we consider the fact that during several years, persons under study have been employed at different work posts.

UPDADTING OF TWA-PEL FOR CS_2: CURRENT DATA ON HEALTH RISK WITH PARTICULAR REFERENCE TO LOW LEVEL EXPOSURES (THE 1994–1997 EPIDEMIOLOGICAL DATA)

The analysis of the literature published during the last three years reveals that harmful effects attributed to CS_2 exposure at the concentration lower than 30 mg/m^3 result rather from past exposure to concentrations considerably exceeding current values, which has been taken as the basis for the establishment of the relationship between concentration and biological effect. A few authors have considered this fact in their studies. New data obtained from epidemiological studies, performed properly and based on the verified estimation of CS_2 concentration level, apply mainly to changes in the cardiovascular, central and peripheral nervous systems.

The cardiovascular system. Swaen et al. (74) carried out an in-depth analysis of death causes in the cohort of 1,438 persons exposed to CS_2 during the years 1947–1980, and followed-up through 1988, and in 1,880 unexposed persons. In 1984–1990, average CS_2 concentration, determined by means of individual dosimeters, ranged from 9 to 107 mg/m^3. In the preceding years the values had been higher, reaching 148 mg/m^3. Of the total cohort observed, 762 persons died. In the group exposed, a slight but statistically significant excess mortality from cardiovascular diseases (SMR = 115.7, 95% CI: 100.5–132.7) was observed. The risk of death from cardiovascular and coronary heart diseases was not related to the exposure level (expressed in the form of cumulative exposure index). The highest risk of death from CHD was observed after 20–30 years of exposure (SMR = 175, $p < 0.05$). After the exposure cessation (changed job, pension etc.) the risk of death from cardiac disease diminished (SMR = 127).

In the early 1990s, Stanosz et al. (69,70) evaluated the health status of women employed at the Wiskord Plant of Chemical Fibres, Szczecin. The authors reported that carbon disulfide concentrations ranging between 9 and 23 mg/m^3 were responsible for disorders of the circulatory system:

A. raised total serum cholesterol and LDL-cholesterol, and decreased serum HDL- cholesterol (69);

B. increased number of thrombocytes in blood and increased serum serotonin concentration (which was correlated with hypertension) (70).

However, their data on exposure levels are insufficient, since the health effects are due to cumulative exposure to both current and past CS_2 concentrations in the work environment. The controls and CS_2 exposed groups have to be matched by age, shift work, time of employment.

Liss and Finkelstein (46) analysed causes of death among persons who used to work for two viscose plants in Ontario, Canada, one producing viscose fibres and the other paper and paper-pulp. In the former, CS_2 concentrations, estimated retrospectively, ranged from 10 to 120 mg/m^3, in certain periods of time, the

concentration reached even 760 mg/m^3 and it was higher than in the the paper plant. At both plants there were fewer deaths from CHD then expected. The proportional mortality ratios (PMRs) were 83 at viscose fibres plant, and 95 in paper-pulp plant, but more deaths then expected from cerebrovascular disease (PMRs were 115 and 149, respectively) were found at these two plants.

The majority of persons died at the age above 65 years. The mean life-span of workers exposed to higher CS_2 concentrations accounted for 71.3 years, and of those exposed to lower concentrations 67.4 years. CHD proportionate mortality ratio (PMR) among persons aged above 65 years, exposed to higher CS_2 concentrations for a period longer than five years was lower than expected (PMR = 82), whereas the number of deaths from strokes was greater then expected (PMR = 207, $p < 0.05$). In the group of persons (of both plants) who died older than 65 years of age, a significant excess mortality from cerebral stroke was found. PMR for cerebral stroke among the former workers of the viscose fibre and paper plants was higher than expected and it equalled 228 and 152, respectively. The risk of stroke was associated with the employment duration in high-carbon-disulfide areas (OR/years = 1.03, 95% CI: 0.96 – 1.10).

In a series of reports, Drexler et al. (22,23) presented the results of cross sectional studies covering 247 workers, employed in the viscose industry for a period between 4 and 220 weeks (median = 66 weeks). The measurement of CS_2 concentrations in the air, ranging from 0.6 to 205 mg/m^3, cumulative exposure index, estimated by means of individual dosimetres, and the urinary level of metabolites for each person under study, served as the basis for the assessment of CS_2 exposure size (20,21). The control group consisted of 222 unexposed persons matched by age, body mass, kind of work performed, employment duration, education etc. Neither multifactorial analysis of variance, including the level of individual CS_2 exposure for each person under study, nor the comparison with the control, revealed CS_2 exposure-related enhanced arterial blood pressure, hyperlipoproteinaemia, changes in HDL-cholesterol level, apolipoprotein A-I, total cholesterol, blood clotting index, fasting glucose concentration. Only negative correlation between the level of these indicators and CS_2 concentrations was found. The multifaceted heart examination (ECG, echocardiography, USG) disclosed a negative, inotropic effect of CS_2 on myocardium but without clinical significance (23). Based on the results obtained, the authors drew a conclusion that occupational exposure to carbon disulfide at modest concentrations, below 30 mg/m^3, did not contribute to increased arterial hypertension, disorders of blood lipoprotein and glucose concentrations, changes in blood clotting indices or direct cardiotoxic effects (21,22). This conclusion proved that the study was performed properly: the size of CS_2 exposure was estimated precisely for each study participant; all parametres necessary to evaluate the cardiovascular system, including CHD markers, were analysed taking into account individual CS_2 exposure.

The nervous system. Neurotoxic properties of carbon disulfide on the central and peripheral nervous systems have been well known for many years. Encephalopaties and peripheral neuropathies have frequently occurred as a carbon disulfide syndrome induced by chronic exposure to CS_2 concentrations ranging from 60 to 120 mg/m^3. However, more recently a number of publications have focused on the evaluation of the nervous system in workers exposed to CS_2 at the concentration of 30 mg/m^3.

Hirata et al. (38) performed electrophysiological examinations of the peripheral nervous system in 46 workers of the viscose rayon industry exposed to CS_2 and in 26 unexposed persons matched by age and employment duration. The time-weighted average of exposure to CS_2 among spining workers ranged from 7 to 53 mg/m^3 (median = 15 mg/m^3) for the period of 4 – 19 years (median = 11.4 years). The spot sampling data revealed 0.6 to 750 mg/m^3. Of the 46 exposed workers in the viscose rayon plant, 22 persons were removed from CS_2 exposure for 1 – 19.2 years (median = 6.2 years), the remaining, currently employed workers were exposed for the period of 4 – 19 years. A significant reduction in conduction velocity in motor peroneal and sensory sural nerves of workers currently exposed to CS_2 was found in comparison with the control group. In persons removed from CS_2 exposure, conduction velovity in both nerves did not differ significantly from that in controls. The authors consider that CS_2-induced functional disorders are at least partially reversible after exposure cessation. As the quantitative evaluation of the exposure level to which individual workers were exposed was not feasible, the relationships between CS_2 concentrations, duration of employment and intensity of CS_2-induced peripheral neuropathy were not analysed.

Reinhardt et al. (60) presented the results of the peripheral and vegetative nervous system evaluation in 222 workers, employed in the viscose rayon industry, exposed to CS_2 at concentration ranging from 0.6 to 205 mg/m^3 (median = 12 mg/m^3) for a period between 1 and 18 years (median = 6 years). Cumulative CS_2 exposure was estimated for each worker, based on the level of excreted CS_2 metabolites (4-thiotiasalidine-4-carbonic acid), and measurements using individual dosimetres (20,21). It was revealed that the mean CS_2 concentrations to which workers under study were exposed were below MAK value binding in Germany (MAK = 30 mg/m^3). The control group consisted of 191 unexposed workers. After performing biochemical tests (indicating carbohydrate-deficiency transferrin) chronic alcoholics were excluded from the study. Together with routine blood and urinary tests, motor and sensory nerve conduction velocity, somatosensory evoked potentials, thermotesting and investigation of forced respiration sinus arrythmia were performed. When compared with controls, insignificant, and within normal limits, reduction in the peripheral nerve motor conduction velocity (by 0.76 m/s median = 48 m/s) was observed in CS_2 exposed workers. No relationships between CS_2 exposure level, the peripheral nerve sensory conduction velocity, latency of somatosensory evoked potentials, changes in cutaneous sensibility of high and low temperature and effort-related variability of heart action, were found. In the authors' opinion, the indication of reduced motor conduction velocity in CS_2 exposed workers without highlighting its significant association with the exposure level, does not prove that the reduction indicated results from a toxic effect of carbon disulfide. Thus, it may be concluded that carbon disulfide concentrations below 30 mg/m^3 do not generate harmful effects in the peripheral nervous system of occupationally exposed persons.

The reproductive system. Information regarding the reproductive system vs carbon disulfide exposure dates from 1969 – 1991. However, bearing in mind the significance of this issue, the literatue data have been reevaluated.

In females occupationally exposed to CS_2 concentrations about 30 mg/m^3, hormonal changes indicating ovarian failure leading to disturbed menstrual cycle (11,56,87,93) or premature menopause (58,71) have been only reported. In women

exposed during pregnancy to CS_2 concentrations about 30 mg/m^3 or lower, neither significant pregnancy complications, spontaneous abortions or preterm births (56), nor disorders of the reproductive cycle (lowered fertility, increased frequency of spontaneous abortions, preterm births, developmental malformations in still births or infant mortality) were revealed. There were neither pathological changes in semen in males exposed to CS_2 in the working or communal environment (11,29,36,49,67,93). Bao et al. (7) have not found pregnancy complications in women exposed to CS_2 concentrations of 10 mg/m^3 prior or during pregnancy. Based on the data cited, it may be assumed that the exposure to CS_2 concentrations about 30 mg/m^3 may only affect the function of ovaries (disturbed menstrual cycle).

The effect of carbon disulfide on the development of progeny has not as yet been fully elucidated. Developmental malformations in the progeny born to women (Chinese) occupationally exposed to CS_2 concentrations of 10 mg/m^3 have been reported only by Bao et al. (7). However, bearing in mind that the authors did not discuss the relationship between the exposure level and the incidence of congenital malformations, and that a detailed characteristics of the population of exposed women was lacking, these data do not allow to draw final conclusions. Neither the studies provided decisive data on the effect of carbon disulfide on the development of progeny in experimental studies on laboratory animals (inhalatory exposure). The results of the studies carried out by Tabacova et al. (76–79) demonstrating the occurrence of congenital malformations in the offsprings born to rats exposed to CS_2 concentrations ranging from 0.03 to 200 mg/m^3 were not corraborated in any other animal studies (45,92). Similarly, Choundhury and Manson (16), as well as Hardin et al. (33) did not demonstrate developmental defects in the offsprings born to female rats exposed to high CS_2 concentrations (60, 120, 900 and 1,800 mg/m^3). The following also counts for the lack or limited significance of the results obtained by Tabacova, the incidence of hydrocephalus in rats, reported by Tabacova, was very high accounting for 10.5%. If we assume that sensibility to teratogenic CS_2 effect in rats is close or similar to that in humans, and that maximum allowable concentration in the ambient air is 0.03 mg/m^3, then the incidence rate of this malformation in humans should be 1.050 per each 10 thousand births. Whereas, in the years 1980–1988, the hydrocephalus incidence rate in the European population of infants was 2.2–5.3 per 10 thousand births (Congenital Malformations Worldwide. A report from the International Clearinghouse for Birth Defects Monitoring Systems. Elsevier Science Publishers, Amsterdam, 1991).

Carcinogenic effect of carbon disulfide. According to data published to date, carcinogenic effect of occupational CS_2 exposure has not been proved.

Nurminen and Hernberg (52) evidenced the lack of relationship between CS_2 exposure and the development of any kind of neoplasm. Some data (15,88) may support the hypothesis that the relationship between CS_2 exposure and the incidence of lymphatic leukaemia does exist. However, these results should be interpreted very carefully as the cohort of workers employed in the rubber industry was exposed not only to carbon disulfide but also to other 24 solvents, including carbon tetrachloride and benzene.

In the cohort of 2,291 persons with diagnosed occupational disease manifested by chronic CS_2 poisoning, Pepłońska et al. (57) demonstrated a significant excess mortality from malignant neoplasm of large intestine (SMR = 233; 95% IC: 107–442). Although, the total number of observed neoplasms was lower than

expected (SMR = 91). This observations, however, requires more advanced analysis. It should be also emphasised that chronic CS_2 poisoning in the cohort under study resulted from occupationl exposure to very high CS_2 concentrations, exceeding 50–150 mg/m^3, that occurred in the 1940s and 1950s.

THE RELATIONSHIP BETWEEN CS_2 EXPOSURE LEVEL AND ADVERSE EFFECTS IN THE CARDIOVASCULAR AND NEUROLOGICAL SYSTEMS

Price at al. (59) reassessed the results of the studies performed by Egeland et al. (26) and Johnson et al. (42) among workers employed in the viscose rayon industry. They also supplemented these results with data obtained from the NIOSH data base, and considered at the same time a number of potential counfounders.

Johnson et al. (42) investigated the effects of CS_2 exposure in 157 males and in 233 persons from control groups, employed in two artificial fibre plants. The mean duration of CS_2 exposure was 12 years (6–18 years), and the mean CS_2 concentration accounted for 23 mg/m^3 (ranging from 1.9 to 50 mg/m^3). The persons were stratified in three subgroups exposed to mean CS_2 concentrations, 3.1, 13.0 and 22 mg/m^3. The control group consisted of persons exposed to CS_2 concentrations below 0.6 mg/m^3. In persons exposed, minor, however, statistically significant slowing of sensory conduction velocity in fibres of the sural nerve and motor conduction velocity in fibres of the peroneal nerve was noted. The increase in disorders of conduction velocity was proportional to cumulative exposure effect. Other results of electrophysiological tests (distal and residual latencies, and amplitude of potentials) did not differ from those obtained in the control group.

Egeland et al. (26) performed cross-sectional studies in the group of 410 males. Of this number, 165 males were exposed to CS_2 low (0.6–6 mg/m^3), moderate (10–15 mg/m^3) and high (19–37 mg/m^3) concentrations. The control group consisted of 245 unexposed persons. The mean employment duration was similar in both groups, among those exposed to CS_2 and controls. In the studies such confounders as mass body index, smoking habits and alcohol intake were also taken into consideration. The blood lead level was determined as well. In persons exposed to low, moderate and high CS_2 concentrations, the blood lead levels accounted for 0.65, 0.70 and 0.82 μmol/l, respectively. Taking into account confounding factors, and comparing with the control group, significantly increased level of blood LDL-cholesterol ($p = 0.02$) and diastolic blood pressure enhanced by 3.16 mmHg ($p = 0.09$) were found in the group of persons exposed to high CS_2 concentrations. The relationships between exposure and the amount of triglycerides and blood HDL-cholesterol, the increase rate of fasting glucose concentration and changes in systolic blood pressure were not revealed. The authors emphasised that the increased LDL-cholesterol resulted most likely from exposure to CS_2 concentrations ranging from 19 to 37 mg/m^3. But the enhanced systolic blood pressure in those exposed to CS_2 was related to the logarithm of blood lead concentrations (regression coefficient = 3.06; $p = 0.04$).

The reassessment of data presented by Egeland et al. (26) and Johnson et al. (42), performed by Price et al. (59), aimed at defining the so called 'benchmark concentration' for the relationship between CS_2 concentration and biological

response. In this study the benchmark concentration means such a CS_2 concentration that causes a 10% increase in additional risk of abnormal responses in CS_2 exposed persons accounting for the occurrence of abnormal responses in unexposed persons (controls) and counfounders like age, body mass index, height, smoking habits, alcohol intake.

In order to assess CHD risk, the levels of total cholesterol, LDL-cholesterol, HDL-cholesterol, and blood triglycerides, fasting glucose concentration and systolic and diastolic blood pressure were analysed. Age, height and mass body index were the most significant confounders. Other factors such as smoking habits and alcohol intake did not influence significantly the parameters involved. Taking into acount the confounders, the relationship between CHD risk and the level of CS_2 exposure within the range of $0.6-37$ mg/m^3, was not revealed.

Electrophysiological tests of peripheral nerves (ulnar, sural and peroneal) was performed in persons exposed to CS_2 concentrations ranging from 1.9 to about 50 mg/m^3. After considering significant confounders (age, height) in the regression analysis, no changes in sensory conduction velocity in the sural nerve and motor conduction velocity in the ulnar nerve, associated with the level of CS_2 exposure were found. Based on the regression analysis, and considering age and height as significant confounders, it was indicated that a 10% reduction, above the value of standard deviation, in peroneal nerve motor conduction velocity might occur at CS_2 concentration of 50.5 mg/m^3. This value is the CS_2 benchmark concentration for significant reduction in peroneal nerve MCV. The CS_2 benchmark concentration defined for the amplitude ratio of peroneal nerve, taking into account age as a confounder, accounted for 57.7 mg/m^3. In the conclusion, the authors stressed that they had failed to demonstrate significant relationship between additional increase in CHD risk, PNS disorders, and the exposure to CS_2 concentration below 48 mg/m^3.

CONCLUSIONS

1. Considering new data on the effects of occupational CS_2 exposure, based on the exposure assessment properly performed (active and passive individual dosimeters, urinary metabolite levels), and the epidemiological analysis excluding various confounders, it can be assumed that adverse health effects in the cardiovascular and neurological systems in persons occupationally exposed to CS_2 concentrations under 48 mg/m^3 is not likely to occur (59).

2. Data regarding harmful effects of low CS_2 concentrations on the reproductive system do not provide enough evidence to prove that they affect the fetus and the course of pregnancy. In Poland, the Directive of the Council of Ministers, issued on 19 September 1996 banned the employment of women under conditions of CS_2 exposure (regardless of concentrations) during pregnancy and breast feeding (25).

3. New data show that CS_2 concentrations of 18 mg/m^3 (MAC value established in Poland in 1995) (24) should neither increase the risk of coronary heart disease nor generate impairments of the nervous system. In view of the above, it can be considered that MAC values – CS_2 concentrations of 18 mg/m^3 as eight hour time weighted average (TWA), and 30 mg/m^3 as the short time exposure level (STEL), adopted in 1995 need not to be updated.

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Received for publication: May 15, 1998
Approved for publication: May 30, 1998