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Assessment of coronary heart disease risk among viscose rayon workers exposed to carbon disulfide at concentrations of about 30 mg/m³

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FRANCO G, MALAMANI T, GERMANI L, CANDURA F. Assessment of coronary heart disease risk among viscose rayon workers exposed to carbon disulfide at concentrations of about 30 mg/m³. *Scand j work environ health* 8 (1982) 113—120. Total cholesterol, high-density lipoprotein cholesterol, triglycerides, blood pressure, and two coronary heart disease risk indices were assessed for a group of 70 male viscose rayon workers exposed to carbon disulfide (CS_2) and individually matched for age, height, and weight with 70 male referents. Environmental CS_2 levels were below 35 mg/m³ during 1972—1979. The study, undertaken to define some risk factors for coronary heart disease and to determine some parameters of lipid metabolism, found no differences between the group of CS_2-exposed workers and the referents. Apart from a possible toxic effect directly induced by CS_2 on the myocardium, the results suggest that CS_2 exposure up to about 30 mg/m³ does not promote coronary atherosclerosis and hence does not increase coronary heart disease by this mechanism.

Key terms: coronary risk factors, lipid metabolism, lipid profile.

Carbon disulfide (CS_2) causes atherosclerotic changes in experimentally poisoned animals and in occupationally exposed workers (3, 38). The biological mechanisms involved in the occurrence of these changes have not been clarified as yet. One of the mechanisms proposed in a recent report of an international group of experts consists of alterations of lipid metabolism (total lipids, cholesterol, lipoproteins, triglycerides) (38). Such disturbances have been found both in animals and in man.

Epidemiologic surveys have demonstrated increased mortality from coronary heart disease (CHD) among workers exposed to CS_2 in England, Norway, Finland, and the United States. In viscose rayon workers exposed to CS_2, when compared with nonexposed workers, there was evidence of a 2.5- to 3-fold excess mortality (27, 28). The excess mortality from CHD in CS_2-exposed workers was confirmed in a multistage investigation (17). The 5-a mortality from coronary heart disease was 4.7-fold as compared to that of a carefully matched reference group (17). In the continuation of the follow-up, the ratio of coronary death between exposed and nonexposed workers decreased to 2.6 for the 10-a period, being 1.9 only during the second 5-a period (19, 32). Finally a preliminary report to the US National Institute for Occupational Safety and Health has demonstrated that coronary mortality was increased also among CS_2-exposed American workers; the standard mortality ratio for CHD was the highest in the spinning and twisting departments (23).

Furthermore a higher incidence of angina (31), an increased prevalence of coronary electrocardiographic findings (2, 7, 13, 31), and impaired left ventricular

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contractility compatible with mild coronary dysfunction (9, 37) have also been found in some studies. However, a joint Finnish-Japanese survey did not reveal any increased prevalence of angina or electrocardiographic findings in Japanese viscose rayon workers, whereas among Finnish workers the CS_2 exposure was associated with an excess of angina and a slightly higher blood pressure (30). So far, all mortality studies have confirmed the capacity of CS_2 exposure to increase coronary mortality (18), while morbidity studies show some discrepancies. These discrepancies may be explained by different exposure intensities, difficulties to assess past exposure levels, and by misinterpretations of the results. However, because of the multifactorial etiology of CHD (eg, smoking, blood pressure, blood lipids, diabetes, weight excess, physical inactivity), the effect of CS_2, being only one of the risk factors, is complicated to determine. The purpose of this study is to evaluate the effect of CS_2 exposure upon some known risk factors of CHD in a group of viscose rayon workers by assessing a lipid profile and by calculating two risk criteria.

Materials and methods

We have studied 70 men (mean age 40.2 a, range 17—62 a) exposed to CS_2 in a viscose plant. They were individually matched for age (± 3 a), height (± 5 cm), and weight (± 4 kg) with 70 male referents (mean age 40.2 a, range 18—62 a) working in the textile section of the same plant and not exposed to CS_2.

The distribution of the subjects by years of exposure is shown in table 1.

Fig 1 shows the mean values and ranges of the CS_2 concentrations in the spinning room (center of the aisle and worksite) in 1963—1979. From 1963 through 1970, the environmental measurements of CS_2 were made occasionally, ie, some tens annually and only at the center of the aisle.

In 1970—1971 a first comprehensive environmental survey showed that the mean value of 97 measurements taken in the spinning department, at the worksites, was 83 mg/m³ (range 9—596 mg/m³). Thanks to these observations the plant was substantially improved technically. A repeated survey in 1972 showed a substantial improvement in environmental conditions. The mean value of 114 measurements made in the department was 24.9 mg/m³ (range 3.7—191 mg/m³) for the same worksite, while the mean value of 48 measurements made in the center of the aisle was 11.1 mg/m³ (range 2.2—25.3 mg/m³). Measurements made during a survey in 1974 confirmed those made in 1972.

In the period 1974—1979, some occa-

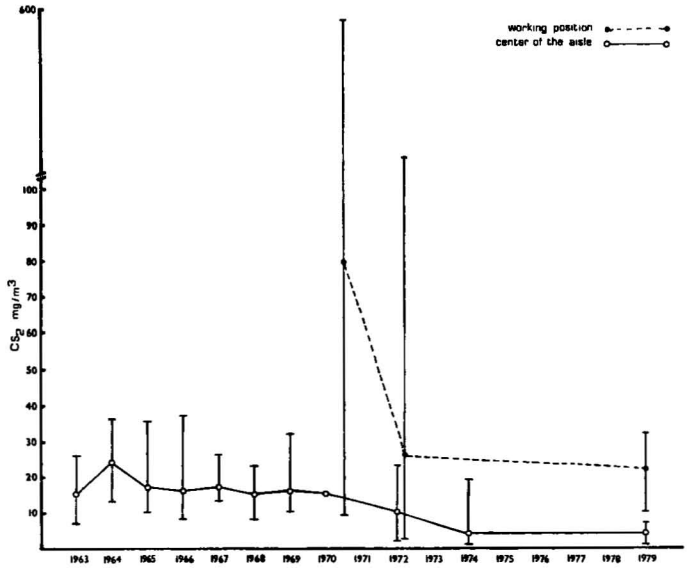

Fig 1. Mean and range concentrations of CS_2 measured in close proximity to the machines (work position) and in the area separating individual machines (center of the aisle).

sional measurements showed the same levels as found in 1972 and 1974.

The latest survey dates back to 1979, and it confirmed the previous results. In the center of the aisle the mean value of 10 measurements was 2.8 mg/m^3 (range 1.2—5.0 mg/m^3), whereas at the worksites the mean value of eight measurements was 23.6 mg/m^3 (range 13.7—31.4 mg/m^3). Since the plant had not been changed substantially during 1972—1979, one may assume that the CS_2 levels have been similar to the values obtained in 1972 through 1979.

Such an assumption has been confirmed by measurements taken twice a month during 1 a.

Fasting blood samples were collected by venipuncture for measurement of the following parameters: (i) total cholesterol by an enzymatic colorimetric method (Bio Rad kit no 1825001B), (ii) high-density lipoprotein cholesterol by the sodium phosphotungstate magnesium chloride precipitation procedure (Bio Rad kit no 1825001), (iii) triglycerides by an enzymatic colorimetric method (Bio Rad kit no 1923050D), (iv) the ratio of high-density lipoprotein cholesterol to total cholesterol.

Each subject was also given a simple standardized interview regarding cigarette and alcohol consumption (39); the questions were asked by a physician. The weight (kg), height (cm), and the systolic and diastolic blood pressures, according to the criteria of the American Heart Association (21), were measured by the same physician. The relative weight, ie, the ratio of the actual weight to the ideal weight, according to Metropolitan Life Insurance Company tables (8), was calculated. Table 2 reports the distribution of these parameters, and it shows that the groups are comparable in this respect.

Two different types of CHD risk were assessed, the first, defined as risk I, according to Castelli & Levitas (5) and the second, defined as risk II, according to Williams et al (39). According to Castelli & Levitas (5), the risk of development of CHD associated with the total cholesterol level can be determined from fig 2, derived from his original work (5). The average risk of development of CHD is defined as 1.00. The risk factor associated with any total cholesterol is multiplied by the risk factor associated with the high-density lipoprotein cholesterol. The product of the numbers represents the risk factor of the development of CHD in respect to the average. Risk II was calculated from the evaluation of relative weight, diastolic blood pressure, cigarette smoking, and serum cholesterol levels (39). Each parameter was considered to have the same weight, and was given a score of 0, 1, or 2, depending on whether it was normal or not, as indicated in table 3. The sum of the scores of the individual parameters constituted risk II.

Student's t-test and chi-square (binomial model) test were employed for testing statistical significance between the examined parameters.

Results

Table 4 shows the distribution of the systolic and diastolic blood pressure of the subjects. No differences were observed for these parameters between the CS_2-exposed subjects and the referents.

Table 1. Distribution of exposure years for the CS_2-exposed workers.

Exposure (a)	Number of subjects
< 5	14
5— 8	24
9—12	13
13—16	8
17—20	4
>21	7

Table 2. Distribution of the parameters alcohol consumption and smoking.

Parameter	CS_2-exposed workers (N = 70)	Referents (N = 70)
Alcohol consumption (l/d)		
0	10	8
1	55	55
> 1	5	5
Cigarette consumption		
0	30	30
1—20	35	37
> 20	5	3

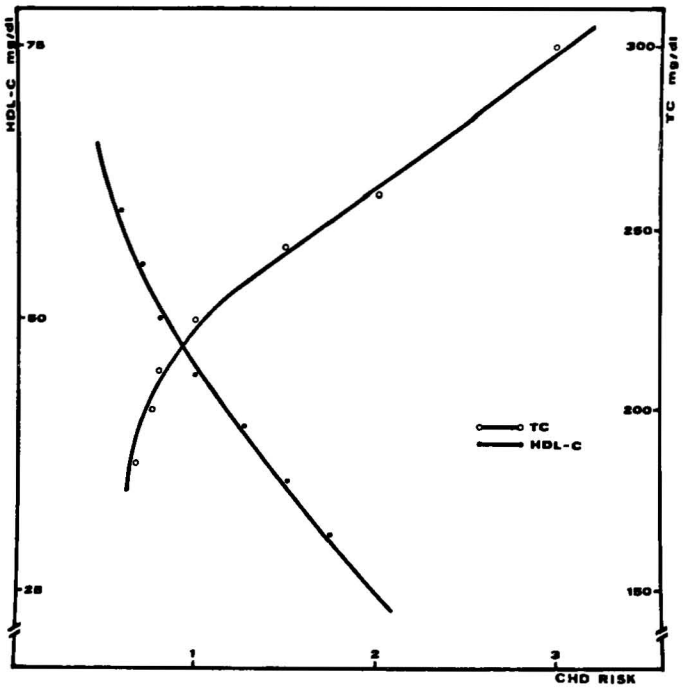

Fig 2. Risk of development of coronary heart disease (CHD) associated with the total cholesterol (TC) and high-density lipoprotein cholesterol (HDL-C). Data derived from Castelli & Levitas (5).

Table 3. Risk rating score sheet.

Parameter	Score
Relative weight (%)	
< 100	0
100—120	1
> 120	2
Diastolic blood pressure (mm Hg) [a]	
< 90	0
90—110	1
> 110	2
Cigarette smoking (n/d)	
0	0
0—20	1
> 20	2
Total cholesterol (mmol/l)	
<6.76	0
6.76—7.80	1
>7.80	2

[a] 1 mm Hg ≈ 133.322 Pa

Table 4. Distribution of the parameters systolic and diastolic blood pressure.

Parameter	CS_2-exposed workers	Referents
Systolic blood pressure (mm Hg) [a]		
< 130	42	35
130—145	23	25
> 145	5	10
Diastolic blood pressure (mm Hg) [a]		
< 90	55	50
90—110	15	19
> 110	0	1

[a] 1 mm Hg ≈ 133.322 Pa.

The results of blood lipid measurements are shown in table 5. The mean values for total cholesterol and triglycerides were slightly higher for the exposed group, but the differences were not significant. Neither did the values for high-density lipoprotein cholesterol or the high-density lipoprotein cholesterol to total cholesterol ratios show any significant difference. In the same table the risk factors, defined as risk I and risk II, are shown. The values were not significantly different between the groups. Furthermore, there were no significant differences between the prevalence of risk I (> 1.00) and risk II (≥ 5) in the two groups (table 6).

Discussion

Cardiovascular effects of CS_2 (blood pressure, angina pectoris, coronary electrocardiographic signs, nonfatal myocardial infarction, and death from myocardial in-

Table 5. Blood lipid profile, total cholesterol, triglycerides, high-density lipoprotein cholesterol, ratio of high-density lipoprotein cholesterol to total cholesterol, and coronary risk values for the 70 pair-matched CS_2-exposed and nonexposed workers.

Parameter	CS_2-exposed workers (N = 70)		Referents (N = 70)		t	p
	Mean	SD	Mean	SD		
Total cholesterol (mmol/l)	5.05	1.95	5.00	1.95	0.193	NS
Triglycerides (mmol/l)	1.16	0.56	1.14	0.54	0.143	NS
High-density lipoprotein cholesterol (mmol/l)	1.60	0.44	1.62	0.49	0.210	NS
High-density lipoprotein cholesterol:total cholesterol	0.32	0.22	0.32	0.25	1.077	NS
Risk I	0.87	0.21	0.89	0.24	0.326	NS
Risk II	2.97	1.75	2.66	1.60	1.38	NS

farction) have been examined in two reviews, in 1975 (29) and 1980 (18). The data strongly support the existence of an association between long-term exposure to CS_2 and an increased risk of developing CHD. Nevertheless the toxic effect may not always be clearly demonstrable, except when there are clinical signs of angina or myocardial infarction, or electrocardiographic changes.

Until recently the causal relationship between cardiovasculopathy and exposure to CS_2 was based on clinical observations. However at least four epidemiologic studies on the mortality of CS_2-exposed workers have confirmed the relationship between CS_2 exposure and coronary mortality. The results of morbidity studies do not agree completely. The differences may be caused by different levels of exposure, but one cannot rule out the influence of factors linked with the particular groups that have been examined, ie, ethnic differences, food habits, climate, etc.

The present study was mainly designed to evaluate blood lipid profiles. Several studies have associated low levels of high-density lipoprotein with an increased incidence of CHD (4, 12, 26, 34, 40). Furthermore it has been suggested that a high level of high-density lipoprotein facilitates the removal of cholesterol deposits from the arterial wall and may therefore protect against arterial disease (4). A recent report stresses that low concentrations of high-density lipoprotein are potent markers of an increased risk of CHD (14). The relationship between CHD and fasting lipid level suggests that a lipid profile based on high-density lipoprotein cholesterol and triglycerides is a preferable method for estimating the CHD risk associated with lipid characteristics (4, 20). However there is no reason for discarding total cholesterol as a predictor of CHD (20). Therefore the measurements of triglycerides, high-density lipoprotein cholesterol, and total cholesterol provides a better estimate of risk (20).

Table 6. Distribution of risk factors I and II.

	CS_2-exposed workers	Referents
Risk I		
< 0.20	9	8
0.21—0.40	33	34
0.41—0.60	17	16
0.61—0.80	6	4
0.81—1.00	1	3
> 1.01	4	5
Chi square = 1.19 (df) = 5 p = NS		
Risk II		
0	3	6
1	6	7
2	12	21
3	27	15
4	13	14
5	9	7
Chi square = 7.24 (df) = 5 p = NS		

The results obtained in the present study showed that there were no significant differences between CS_2-exposed subjects and referents. The smoking and

alcohol habits (known from interviews) of the two groups were practically identical. The same is true for the systolic and diastolic blood pressures. Neither did the exposed subjects show different blood lipids profiles as compared with those of the referents. The same was true for the values of coronary risk I and II.

The comparison of our results with those published by other authors shows some differences. In previous studies it was possible to demonstrate increased blood lipid levels (11, 25, 27, 33, 36). Significant increases in the cholesterol triglycerides and low-density lipoprotein cholesterol levels were recently found in a Belgian population of viscose rayon workers exposed to a CS_2 concentration of about 100 mg/m^3; no other factor could explain these differences (35). On the other hand, these results disagree with some others. For example, only a small and nonsignificant increase in blood cholesterol was found in Finnish viscose rayon workers (16), even though they had excess coronary morbidity (31).

Our observations did not reveal differences among some other risk factors of CHD in the two groups, in contrast with what has been previously published. For example, some studies have shown a significant increase in systolic-diastolic blood pressure for CS_2-exposed populations (22, 30, 31, 35). Of course the exposure levels in other studies have been higher than the ones we have studied.

In short, even with the limited purpose of defining some risk factors for CHD and determining some parameters of lipid metabolism, our study found no differences between the group of CS_2-exposed workers and the referents. In other words, no difference attributable to exposure to CS_2 below 35 mg/m^3 was observed. Despite the difficulties to evaluate negative findings (15), we may therefore suppose that concentrations of CS_2 in the range 30—35 mg/m^3 over a period of 5 a do not modify the parameters considered, ie, blood lipid profile, blood pressure, and the assessed CHD risk.

However, since a remarkable excess morbidity from CHD has been demonstrated even in the absence of metabolic alterations, a direct cardiotoxic effect cannot be excluded. In fact alterations of some systolic time intervals, in the absence of any clinical symptom of heart disease, have been observed in CS_2-exposed workers (9, 37). These alterations, comparable to mild CHD dysfunction, were interpreted as a consequence of an impaired left ventricular contractility. At least two mechanisms might be involved in the toxic action of CS_2 on the myocardial tissue: (i) interference with the energy metabolism by the inadequate availability of thiamine (1) and nicotine amide (6, 10), or a direct inhibition of cytochrome (6, 10) and (ii) interference with the cathecolamine metabolism and defective hormonal control of the energy utilization process (6, 24, 25).

Apart from a possible toxic effect directly induced by CS_2 on the myocardium, the results of this study do not indicate the existence of any difference in risk factors between the CS_2-exposed population and the referents. Therefore we would believe that CS_2 exposure to the levels examined do not promote coronary atherosclerosis and hence do not increase the CHD risk by this mechanism.

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