COHORT STUDY OF THE HYPERTENSIVE EFFECTS OF CARBON DISULFIDE IN VISCOSE RAYON WORKERS

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ABSTRACT

Records of blood pressure and body weight of CS₂ workers were analyzed in relation to the levels of CS₂ exposure at a Japanese rayon-producing factory. A cohort of 46 CS₂ workers who had later been transferred to non-CS₂ jobs showed first a statistically significant rise, which was then followed by two consecutive episodes of statistically significant falls in systolic blood pressure. These episodes corresponded precisely to the initial increase in CS₂ concentration at workplaces due to the increased output of thicker threads, the subsequent decrease in concentration due to the improvement of the working environment and finally to the transfer of most of the members of the cohort to non-CS₂ jobs. Body weight also revealed statistically significant changes corresponding to the changes in CS₂ levels. Time-weighted average CS₂ concentration of 329 air samples taken at the breathing zones of three spinners was 17.4 ppm in 1972. It is concluded that CS₂ causes mild and reversible hypertension and that the CS₂ concentrations of 15–20 ppm may not be completely safe when the exposure of workers is continuous throughout their workdays.

INTRODUCTION

Carbon disulfide (CS₂) occupies a peculiar position among the industrial chemicals in that it has posed a great variety of toxicological problems during the long history of its use in industry. Although the working environment was gradually improved, it was rarely good enough to protect the health of workers completely from CS₂ intoxication. It was such unsatisfactory improvement which gave rise to prolonged exposure of workers to hazardous levels of CS₂. As a result, several chronic types of intoxication, especially vasculopathies of the brain, heart, and kidney emerged as new and problematic...
aspects of CS₂ intoxication.

Fujii and Hirose (1934)³ were probably the first to note the vascular toxicity of carbon disulfide. They described clinical and pathological findings of a case of chronic CS₂ poisoning and attributed most of the systemic effects of CS₂ such as lesions of the heart, liver, kidney, spleen, lung, and central nervous system to circulatory disturbances. Lewey (1941)⁴ reported unusually high prevalence of hypertension and arteriosclerosis of peripheral blood vessels among viscose rayon workers in the United States. Since about 1950 a series of papers⁵⁻¹³ reported outbreaks of a new type of chronic CS₂ intoxication among European viscose rayon workers, which was characterized mainly by atherosclerosis of the blood vessels of the central nervous system. This type of CS₂ poisoning was named Encephalopathia diffusa sulfocarbonica.⁶ Kidney lesions similar to vascular nephropathy have also been described in several papers.²,¹⁰,¹⁴,¹⁵ Recent epidemiological studies suggest that chronic CS₂ exposure may precipitate coronary heart disease.¹⁶⁻¹⁸

Effects of CS₂ exposure on blood pressure, however, have not received due attention by epidemiologists in spite of the fact that blood pressure data are relatively easy to obtain. Although several recent papers¹⁷⁻¹⁹ give some evidence of increased blood pressure among CS₂ workers, there have been few reports of epidemiologically designed studies, especially in combination with the measurement of CS₂ concentrations in the working environment.

In the course of a follow-up study of a small group of former CS₂ workers, one of the present authors unexpectedly found that some of the workers experienced recovery of blood pressure from hypertensive to normal levels without medical treatment after they had been transferred to non-CS₂ jobs. This could be traced in most cases by the past records of blood pressure measured in periodic health examinations. Therefore, the authors aimed to obtain more concrete evidence of the induction of the hypertensive state by CS₂ and spontaneous recovery by the workers after removal from CS₂ exposure. Cohort analysis was applied to blood pressure data which were found to have been recorded for a sufficient number of former CS₂ workers. Another purpose of this study was to relate the hypertensive effect of CS₂, if any, with the quantitative level of exposure.

MATERIALS AND METHODS

Because the primary objective of the study was to prove the recovery of blood pressure after transfer to non-CS₂ jobs, records of blood pressure were collected for former CS₂ workers in a synthetic fiber factory in Japan. Data
were obtained for 110 male workers who comprised about two-thirds of all the individuals who had been transferred from CS₂ to non-CS₂ jobs within the period 1959 through 1971 at the factory. Since most of the remaining one-third had either retired from the company or transferred to factories located in other districts, their follow-up records were not available for analysis. All the 110 subjects were those who had worked at the spinning area of a viscose rayon factory and had later been transferred to a nylon factory located in the same yard. They were transferred because extensive mechanization of the rayon production line enabled considerable reduction in the number of CS₂ workers and the newly constructed nylon factory was a suitable workplace for them to be relocated. It should be emphasized that the selection of the individuals to be transferred was not based on their health condition. This fact eliminates the possibility that a significant sampling bias occurred at this stage.

Seven of the 110 subjects were found to have been under medical care for hypertension and they were excluded from the analysis. The records of blood pressure and body weight were obtained for the period 1959 through 1971. The number of workers comprising the cohort and the number of available data are listed in Table 1.

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Blood pressure of CS₂ workers has been measured routinely since 1963, but the records are poor for some years, as shown in the table. They were especially unsatisfactory in the period 1960–1964. Virtually no measurement was performed during 1960–1962. Fortunately, 85 of 93 persons were measured
in 1959 because the plant physician at this factory was apparently concerned about the cardiovascular effect of CS$_2$. However, probably because he could not find any evidence of elevated blood pressure at that time, he did not continue measuring blood pressure in the following three years. Since 1963, blood pressure levels were measured as a part of the periodic health examinations. The measurements were performed regularly in the same week in autumn by several trained nurses. No significant changes were introduced in the facilities or methods of measurement in the observation period. In order to analyze the sequential changes of blood pressure in relation to CS$_2$ exposure, it was necessary to select a smaller cohort consisting of individuals whose blood pressure data were available throughout the observation period. A cohort of 46 individuals was finally selected for the analysis whose blood pressures were recorded in 1959, and also in either of the two years, 1963 or 1964, i.e., those years excluding 1960, 1961, and 1962 when the available data were few in number. The available blood pressure data for this final cohort of 46 persons are listed in Table 2. Because the smallest number was 38 in 1965, the data are considered sufficiently representative of the cohort in each year of the observation period.

Body weight measurement data were more complete, as shown in Table 1. Therefore, the body weight data were perfect for the final cohort except for 1959 when only one out of 46 was lacking (Table 2).

Table 2

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The concentration of CS$_2$ in the ambient air of the same viscose rayon factory was determined in autumn of 1972. Air sampling was performed intermittently at the breathing zones of three randomly selected CS$_2$ workers throughout their working days. Actually the number of samples totalled 329 during the 18 hours worked by the three subjects. The sampling frequency turned out to be once every three minutes and 17 seconds on the average. CS$_2$
was trapped and determined by a slightly modified version of the method reported by McKee.\textsuperscript{20}

Output records of rayon fibers were obtained at the same factory for the period 1959 through 1971.

RESULTS

The mean age of the cohort of 46 former CS\textsubscript{2} workers was 41.7 years at the end of 1971 and the range was 32–51 years. The mean systolic and diastolic blood pressures were 123.1 and 72.9 mmHg respectively. The ranges were 102–146 mmHg (systolic) and 58–88 mmHg (diastolic). Therefore, no one in the cohort was considered hypertensive during the observation period. Means

\begin{table}
\centering
\caption{Systolic and diastolic blood pressures}
\begin{tabular}{lcccccccc}
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Systolic blood pressure & N. & 46 & 46 & 38 & 42 & 40 & 40 & 45 & 46 & 46 \\
Mean & 122.4 & 126.1 & 126.2 & 122.2 & 122.8 & 121.9 & 120.0 & 122.4 & 123.1 \\
S.E. & 2.20 & 1.44 & 2.03 & 1.98 & 1.80 & 1.74 & 1.65 & 1.64 & 1.53 \\
Diastolic blood pressure & N. & 46 & 46 & 38 & 42 & 40 & 40 & 45 & 46 & 46 \\
Mean & 69.7 & 38.8 & 73.3 & 71.4 & 72.9 & 73.9 & 72.2 & 69.2 & 72.9 \\
S.E. & 1.58 & 1.31 & 1.77 & 1.71 & 1.50 & 1.55 & 1.45 & 1.28 & 1.25 \\
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\end{tabular}
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![Fig. 1 Systolic blood pressure in CS\textsubscript{2} workers (Means)]
and standard errors of the systolic and diastolic blood pressures for each year are shown in Table 3. The mean systolic blood pressure rose from 122.4 (1959) to 126.1 (1963 and 1964), fell from 126.2 (1965) to 122.2 (1966), and fell again from 121.9 (1968) to 120.0 (1969). This is shown in Figure 1. The rise and subsequent falls are statistically significant at 2.5%, 0.5%, and 5% levels of significance respectively when tested with paired t-test for each pair of data for 1959 versus 1963 and 1964, 1965 versus 1966, and 1968 versus 1969. No consistent changes were observed in diastolic blood pressure. The mean body weight, on the other hand, gradually fell during the period 1959–1964, increased since 1965, and continued to rise throughout the rest of the observation period, as shown in Figure 2.

These rise and falls in systolic blood pressure and body weight of the workers of this cohort appear to be quite meaningful when observed in relation to the levels of CS₂ exposure. From information gathered at the factory, CS₂ concentration rose from 1959 to 1963 due to increased output of thicker threads. In order to produce thicker threads, larger amounts of CS₂ must be consumed per unit of time resulting in increased leakage of CS₂ into ambient air. The trend of the output of thicker threads is shown in Figure 3. Because this increase in production was achieved without being accompanied by appreciable improvement in hygienic conditions during 1959–1963, CS₂ concentration inevitably rose during this period. Although reliable data are
lacking, a rough estimate of CS₂ concentration during the period 1960–1964 may have been around 20–50 ppm but may not have been higher than 30 ppm on a time-weighted average basis. It is noted that the period of the initial rise in blood pressure corresponded to the period of deterioration of the working environment caused by the increased production of thicker threads.

In 1964 extensive improvement of the working environment was initiated accompanying the mechanization of production lines. This was completed in spring of 1966 as shown in Figures 1 and 2. It is noted that the first drop in the mean blood pressure in 1966 corresponded to this improvement. As a result, the CS₂ concentration of the general environment in the spinning room is estimated to have fallen to less than 5 ppm on the average. However, the spinners ("doffers") were usually required to take out cakes of thread from spinning pots by hand. This was one of the few manual operations left after
the improvement. Because it was necessary to remove the casings of spinning machines at this job, the spinners were exposed to higher concentrations of CS$_2$ at the breathing zones.

CS$_2$ concentrations of 329 air samples taken at the breathing zones of three randomly selected spinners in 1972 are shown in Figure 4. The range was 1.2–130 ppm, the arithmetic mean was 17.4 ppm, the geometric mean was 13.6 ppm and the geometric standard deviation was 2.08. Because there had not been any appreciable change in the working environment since 1966, the levels of the actual exposure of the workers of the cohort since 1966 may have been similar to the data obtained in 1972, that is, around 15–20 ppm. An important point is that the spinners performed this operation almost continuously during their entire work shift. As a result, they were exposed to unusually constant CS$_2$ concentrations of 15–20 ppm for some 6 to 8 hours a day.

The numbers of the workers transferred to non-CS$_2$ jobs each year are shown in Figure 5. It is remarked that most members of this cohort were transferred in 1968. Again, the mean blood pressure fell in this period between 1968 and 1969 with a statistically significant difference.

Although the determinations of blood pressure are usually subject to considerable variation, the observed changes were very consistent with the changes in the level of CS$_2$ exposure. Essentially, the same findings were also observed in the cohort of 103 persons.

**DISCUSSION**

From the above evidence, it is strongly suggested that CS$_2$ has a mild hypertensive effect which can be normalized by the decrease or the elimination of exposure. However, several other factors such as work load and tempera-
Hypertensive Effects of CS$_2$

ture may also have been causally related to the observed changes in blood pressure. The first rise of blood pressure in the period 1959–1964 was associated with a drop in body weight of about 2 kg on the average, as shown in Figure 2. Because the output of thicker threads increased during this period, both blood pressure and body weight may have been affected by the increase in work load. However, the increase in the output of total products was not as large as that of the thicker threads. For instance, while the output of the thicker threads of 150 denier or more increased sharply by 50% from 1961 to 1963, that of the total threads increased only by 7% in the same period. Therefore, even though the work load of CS$_2$ workers probably increased, it is unlikely to have been so much as to be causally related to the decrease in body weight and the rise in blood pressure. Similarly, the subsequently observed falls in blood pressure were apparently not associated with the decrease of work load. The work shift schedules were exactly the same for both the rayon and nylon factories.

On the other hand, it should be noted that earlier literature frequently described loss of appetite and emaciation in CS$_2$ workers. Miyazaki conducted a questionnaire survey of subjective complaints on 352 rayon spinners and 99 control workers in addition to a clinical observation on 66 rayon spinners, and concluded that weight loss was one of the most common symptoms in chronically exposed CS$_2$ workers. Taking into account these reports together with the results of this study, the loss of body weight is considered to have been caused by the increase in CS$_2$ exposure rather than by the increase in work load.

Temperature of the working environment was somewhat lower in the nylon factory than in the rayon factory, so the fall of blood pressure following the transfer to the nylon factory cannot be explained by the change in temperature.

From these considerations, it may be safely concluded that CS$_2$ can cause mild hypertension when workers are exposed to certain concentrations of the vapor of this substance over a given period of time. The type of hypertensive state found in this study was reversible probably because the duration of hazardous exposure was not long enough to induce irreversible vasculopathies such as have been previously reported.

The data obtained in this study suggest that even at a mean CS$_2$ concentration of 15–20 ppm, a level which has long been assumed to be safe, workers may not be completely free from adverse effects of CS$_2$ if they are continuously exposed to this level throughout their workdays.
ACKNOWLEDGEMENT

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REFERENCES


