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Mortality of Dutch workers exposed to carbon disulfide

Abstract Epidemiological studies carried out in Great Britain, Scandinavia and the United States indicate that workers exposed to carbon disulfide are at an increased risk for cardiovascular disease (CVD) mortality, and in particular for ischemic heart disease (IHD) mortality. In the epidemiological study reported here a retrospective cohort design was used. The total study population consisted of 3322 workers from a Dutch viscose textile plant who had all been employed for at least half a year between 1 January 1947 and 1 January 1980. Only production and maintenance workers were selected for the study. A group of 1434 workers who had been exposed to carbon disulfide was identified from the files available at the plant. The remaining 1888 workers who had not been exposed to carbon disulfide were used as a reference group. The total study population was followed for mortality until 1 January 1988. For the 762 workers who had died before that date, the causes of death were checked at the Central Bureau of Statistics. The results show a slightly but significantly increased risk for CVD mortality (CVD-specific SMR of 115), despite the observation of the so-called healthy worker effect and the statistical uncertainties inherent to this type of study. The results indicate that exposure to relatively low levels of carbon disulfide increases the risk of CVD mortality.

Key words Carbon disulfide · Occupational exposure Cardiovascular mortality · Epidemiology

Introduction
Carbon disulfide (CS₂) is an organic solvent with restricted applications. One of the industrial processes in which CS₂ is used is the production of viscose rayon yarn. In this process CS₂ is used to dissolve cellulose.

Viscose rayon is made from thoroughly prepared cellulose. The cellulose is made from wood chips that are cooked, ground, bleached, and pressed into sheets. These sheets are steeped in lye, milled into white flocks, and subsequently mixed with CS₂. The resulting xanthate is dissolved in lye and forms an orange-brown liquid called viscose. From this viscose solution yarn is spun. In the plant studied here, viscose textile is manufactured by both a spool-spinning procedure and a continuous-spinning procedure. Exposure to CS₂ occurs in particular during spinning and subsequent washing and bleaching.

A number of health effects related to exposure to CS₂ have been reported. Central nervous system effects range from psychosis in acutely intoxicated individuals to small but statistically significant aberrations detectable in psychological tests in groups of exposed workers compared to nonexposed workers (WGD 1990). These effects are no longer detectable at exposures below 30 mg/m³ (Cirla and Graziani 1981). Peripheral nervous system effects range from severe polyneuro- and myopathy in individuals with very high exposures to a small but statistically significant decrease in the conduction velocity of the slow motor nerve fibers at long-term exposures around 24 mg/m³ (WGD 1990; Ruitjen et al. 1988).

Animal experiments indicate that exposure to CS₂ can have an adverse effect on the cardiac muscle tissue and on the wall of the aorta. Chandra et al. (1972) observed increased myocardic necrosis in rats that had been exposed to CS₂.

The first indication of increased cardiovascular mortality among CS₂-exposed workers came from an exploratory study on British death certificates (Tiller et al. 1968). In an extended follow-up of the same population until 1982, Sweetnam et al. confirmed the previous results (1986). The workers from the spinnery department who had the highest CS₂ exposures (exceeding 60 mg/m³ in almost half of the air samples), experienced significant mortality mainly because of coronary heart disease.
In this group the mortality correlated well with exposure, especially in the last 2 years prior to retirement. After retirement at the age of 65, however, the mortality decreased in an inverse relation to previous exposure. In the authors’ opinion this is not supportive of an etiologic role of CS$_2$ in the development of atherosclerosis and in favor of a directly cardiotoxic or thrombotic effect of CS$_2$. In a retrospective mortality study over the period 1967–1972, the “coronary” mortality ratio among 343 exposed Finnish workers was found to be 4.8 times higher than in controls. The average exposure concentration was between 60 and 90 mg/m$^3$, with much higher exposures in the past (Tolonen et al. 1975). This study was later extended up till 1977. From 1972 onwards, preventive measures had lowered the exposure to below 30 mg/m$^3$. The overall relative risk of death by coronary attack was 2.2 for the exposed workers over the entire period. The rate ratio was more than 50% lower over the period 1972–1977 as compared to 1966–1972.

During the following period the relative risk for exposed workers was reduced to 1. This is of course partly due to the reduction of exposure to below 30 mg/m$^3$. However, a no-effect level could not be established. In addition to the technical measures to reduce exposure, all workers with risk factors for coronary heart disease were transferred to worksites without exposure. As a result, the relative risk for exposure plus previously exposed workers normalized at 1 (Hernberg and Tolonen 1981).

In a retrospective cohort study of 10418 American workers employed between 1957 and 1979 with follow-up until 1983, a small but significant excess of deaths (SMR = 124) from atherosclerotic heart disease was found in the subgroup of 4448 workers with the potentially highest exposure. The formation of exposure subgroups was based on job titles and estimation of exposure, but not on any actual exposure data (MacMahon and Monson 1988).

Several studies indicate that workers exposed to high concentrations of CS$_2$ (> 60 mg/m$^3$) are at an increased risk for cardiovascular morbidity. Increases in prevalence of high blood pressure, hypercholesteremia, ECG abnormalities, and clinical ischemic heart disease have been reported in varying degrees (WGD 1990). At lower levels of exposure no significant increases in risk factor for ischemic heart disease were observed (Cirila and Graziani 1981; VanHoorne and Verheyden 1987).

Triggered by the study results described above, an epidemiologic study was carried out among the workers and former workers of a Dutch plant where viscose rayon textile fibers are produced. The main aim of the study was to investigate whether these workers, exposed to CS$_2$ have experienced increased mortality from cardiovascular diseases and, if so, to establish a no-observed adverse effect level.

### Materials and methods

**Design of the study**

The epidemiologic study that was carried out had the design of a retrospective cohort study. All workers who had ever been employed at the particular plant between 1 January 1947 and 1 January 1988 were reviewed for eligibility for the study. Next, for all eligible workers data were collected on date of birth, last known place of residence, jobs held at the plant, and the workplaces where they held these jobs. Finally, all medical files were searched to identify workers who had been employed since 1 January 1947.

During this selection process a total number of 3322 eligible employees or former employees were identified. The following eligibility criteria were used:

1. Only workers who were employed by the company for at least half a year
2. Only workers who were employed between 1 January 1947 and 1 January 1980
3. Only production workers and maintenance personnel
4. Only workers with Dutch citizenship
5. Only male workers

During the data collection process it was noted that for many workers who had been employed for a period shorter than half a year no data were available about the jobs they had during that period. Therefore, it was decided to restrict the exposed cohort as well as the nonexposed cohort to workers who were employed for longer than half a year.

Workers who were not directly employed in the production process or maintenance were not incorporated in the exposed and nonexposed cohorts. Employees who held jobs in offices, security, general maintenance, warehouses, or the cafeteria remained outside the study population. The advantage of this approach is that the exposed and nonexposed cohort have a better comparability.

Dutch citizenship was taken as an eligibility criterion because no vital statistics are available for foreigners living in the Netherlands. The lack of such data renders it impossible to calculate expected numbers of deaths for foreign workers in the exposed group and the nonexposed group.

The final eligibility criterion was gender. The group of female workers in production and maintenance worked on day shifts only and was very small. Thus the mortality patterns in this group would have been quite sensitive to chance fluctuations. Therefore it was decided not to include female workers in the study population.

Information regarding workers to be included in the study was abstracted from annual lists of newly hired or discharged workers. Information about jobs held and workplaces were abstracted from the medical files.

**Exposure assessment**

The study population was subdivided into several exposure groups according to the work history of the individual workers. In several departments exposure to CS$_2$ occurred continuously, while in other departments exposure to CS$_2$ had a more intermittent character. This is not identical to a lower exposure. Emergency repairs, for instance, may have been associated with very high peak exposures. The exposure groups were as follows:

1. Continuous exposure ($n = 672$ workers): spool-spinning department, continuous-spinning department, and bleaching department
2. Intermittent exposure ($n = 762$ workers): sulfidizing department, sponge production, and diverse viscose rooms (production departments), and sampling and quality control, chemical laboratory, and several maintenance departments (nonproduction departments)