

Effects of exposure to vinyl chloride

An assessment of the evidence

by Sir Richard Doll, FRS¹

DOLL R. Effects of exposure to vinyl chloride: An assessment of the evidence. *Scand J Work Environ Health* 14 (1988) 61-78. This paper reviews the possible effects of vinyl chloride on the mortality of occupationally exposed men and the carcinogenic effects that might be observed in the general population as a result of environmental pollution with vinyl chloride. The results of four studies fulfilling the criteria of providing substantial numbers of observations more than 25 years after first exposure and covering a period long enough for more than 10 % of the workers to have been expected to die constitute the basis for the assessment of the occupational hazards. Other studies provide only supplementary information. The data permit two conclusions. First, men occupationally exposed to vinyl chloride have experienced a specific hazard of angiosarcoma of the liver. Second, any other occupational hazards that may have existed have been small. No positive evidence of a hazard of any nonmalignant disease or any type of cancer other than angiosarcoma of the liver has been found except possibly for a small hazard of lung cancer when exposure was heavy. More definite conclusions might be reached if those who have studied exposed employees could present their results in appropriate and comparable ways. A very small risk of angiosarcoma may have occurred as a result of vinyl chloride escaping into the environment around plants handling vinyl chloride in the past, but the evidence indicates that the current risk to the general public (if any) must be negligible.

Key terms: angiosarcoma of the liver, cancer, lung cancer, mortality, polyvinyl chloride, review, vinyl chloride monomer.

For many years the inhalation of large amounts of vinyl chloride has been recognized as potentially hazardous. Concentrations of the order of 10 000 ppm in the air induce unconsciousness and cardiac arrhythmia, while prolonged exposure to concentrations an order of magnitude lower have been liable to cause a specific pathological syndrome. This "vinyl chloride illness" has been characterized by four cardinal signs, namely, enlargement of the liver and spleen with a specific histological appearance, patchy infiltration of the skin resembling scleroderma, bony changes in the tips of the fingers described as acroosteolysis, and peripheral circulatory changes identical with the classical picture of Raynaud's disease. These pathological reactions may occur singly or together and may possibly be accompanied by other less characteristic effects. They can, however, be completely avoided if exposure never exceeds the level of a few hundred parts per million, ie, the level to which exposures were generally reduced in the mid-1960s.

One other serious effect has, however, been observed that may not be avoidable in the same relatively easy way, namely, the production of angiosarcoma of the liver. It must, indeed, be presumed that some risk of developing the disease will persist from exposure to

doses that are even lower than the current industrial levels of 5 ppm or less, as vinyl chloride has been shown to act as a mutagen (23), and it cannot be assumed that a threshold exists below which no carcinogenic risk persists. Moreover, the possibility has to be considered that vinyl chloride may cause some cancers other than angiosarcoma of the liver, partly because laboratory studies have shown that it causes other cancers in animal experiments and partly because the initial studies demonstrating the production of angiosarcoma of the liver in humans were inadequate in size to exclude a material increase in the risk of cancer in common sites, such as the lung and large bowel. Since no threshold dose can be postulated, it also follows that some cancers may have been produced in the general public by the small amounts that have escaped into the general environment.

Consideration also needs to be given to the possibility that exposure to vinyl chloride over a long period may have noxious effects on humans that cannot be seen easily in animal experiments (by, for example, producing chronic respiratory disease), and, as it is a mutagen, there is also a possibility that it may act as a teratogen and cause congenital malformations in offspring.

In this review I have not examined the possibility that vinyl chloride acts as a teratogen or that it causes mutations in germ cells, as there is too little serious evidence to justify inclusion. Reviews carried out for sections of the industry by Downs et al (unpublished report to the Society of Plastic Industries Inc in 1977)

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