

The development of angiosarcomas and other tumors in rats exposed to vinyl chloride was first described in 1971 and confirmed in 1973 in another experiment. Late in 1973 by virtue of some intensive investigation 3 workmen, all employed in one vinyl chloride manufacturing facility were discovered to have died of angiosarcoma of the liver. These men died at different times over a period of at least 6 years. The possible association to their work was completely overlooked until a specific investigation was made.

At the present time 3 animal experiments have shown an association between exposure to vinyl chloride and the development of angiosarcoma of the liver. At least (14) men employed in the manufacture of vinyl chloride have been shown to have developed angiosarcoma of the liver. Any quantitative estimate of the exposure to vinyl chloride of any of these 14 men can only be speculative. Vinyl chloride has, until very recently been looked upon as quite innocuous and of no real concern. As a result, there is little data available on workers exposed over the past 35 years.

*OR IN PVC Polymerization*

Men employed in vinyl chloride manufacture are exposed to the material by inhalation and percutaneous absorption. There is no reliable data available to indicate the relative importance of these two routes as a source of exposure. In the mid-sixties, the association of acroosteolysis (bone resorption of the terminal phalange) with cleaning of vinyl chloride reactors was first discovered. Angiosarcomas are tumors of the blood vessels in the liver. They

are not true liver tumors. Here then we have a newly described occupational disease in which the blood vessels seem to be the target organ and in which the route of absorption may be cutaneous, respiratory or both or for that matter, it may also be by mouth.

Thus far the men who developed angiosarcoma are all reported to have had high exposures to vinyl chloride. The anecdotal report is that each one had been carried unconscious off of a vinyl chloride reactor at least once. Despite 30 or more years of experience and more than 100,000 people exposed, there are relatively few cases so far discovered. Even if we assume that twice as many cases will eventually be discovered, this is still a small number of cases in relation to the number presumed to be at risk.

As we look at the present situation there are a number of questions that must be asked. These are:

1. Why are there so few cases?
2. Is there any antigenic difference among those developing angiosarcoma?
3. What is the metabolism of vinyl chloride?
4. Is there any alteration in the molecule in its passage through the skin?
5. What is the action of vinyl chloride on the vascular cell?
6. Is there a concentration which will not cause tumor development during the lifetime of the animal?
7. Are there any undiagnosed tumors attributable to vinyl chloride from use of vinyl chloride or from community exposure?

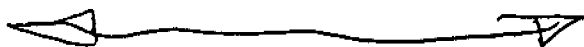
Further animal studies are necessary to help answer No. 6, but it is unlikely that any study using less than 10,000 animals per test level will be accepted as meaningful by the statisticians. The basic studies to answer Nos. 3, 4 and 5 should be initiated immediately. It is doubtful that Nos. 1 and 2 can be answered soon, and No. 7 will be answered as more epidemiological investigations are mounted.

The question of vinyl chloride use will continue to be raised. Is it safe? At present, based on available information it appears that only very high concentrations of vinyl chloride will result in the development of angiosarcomas in man and that skin exposure as well as respiratory exposure are likely to be involved. Thus, it is unlikely that fabrication or use of <sup>POLY</sup> vinyl chloride <sup>(PVC)</sup> poses a problem. A parallel situation may be the development of lung cancer among workers processing chrome ore but not among the people using chrome.

Each year in the United States a number of people are killed because of auto accidents caused by dogs running loose. Despite these deaths, it is very difficult to get a leash law passed in most communities. Psychologically and socially there should be no difference in the prevention of human death but in fact there are great differences in the public's reaction. Deaths from an occupational cause are not tolerable. Death from cancer has a particularly violent emotional reaction. Therefore, the vinyl chloride situation will not be glossed over or treated lightly. Ethyl's ~~exposure~~ is very great because of the vertical integration in vinyl ~~chloride~~ plastics. Unless some additional understanding of the mechanism of action of vinyl chloride

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is gained quickly, it will be difficult to plan prevention on a national basis other than by zero exposure. No one appears to be going after basic information about mechanism of action. I would, therefore, suggest that Ethyl, alone or in concert with others, appropriate \$250,000 and find investigators who would pursue the question of mechanism at the cellular level.



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