

Mr Chairman, Ladies and Gentlemen,

I would like to report on two epidemiological investigations, the first by my own company, the second by Tishman Cooper Associates on behalf of the Manufacturing Chemists Association in the USA.

When ICI decided to look at the mortality experience of employees who had worked on VCM and PVC plants, the only information concerning the potential carcinogenicity of VCM was the work of Viola & Helton on rats. Work on other species had not begun, and it was known that in the USA the annual reported incidence of angiosarcoma of the liver was about 20 per 100 million population. It did not seem likely that a threat to man would be discovered. It nevertheless seemed to us to be important that if such a threat did exist, it should be investigated.

Availability of records was, of course, an essential constraint on such a survey. At one of our VCM manufacturing plants in operation since the early 1920s, it was possible to trace all employees and ex-employees back to 1926. In a PVC producing plant on the same site, records for the past 12 years were available, and we used as a control population a factory chosen at hand, and again all records of men working in the factory for the previous 12 years were used.

The populations were divided into 4 groups, i.e., VCM workers, PVC autoclave workers, other PVC workers (e.g., drier operators and loggers) and the control group.

The numbers of men involved were:

VCM	232
PVC autoclave workers	334
Plastics, others	516
Control	657

The mortality of the populations were compared with a calculated expected mortality based on the experience of the general population. Age-specific death rates were obtained from published tables.

All records were then identified as belonging to employees still alive, ex-employees still alive and pensioners still alive, and causes and dates of death of all others were based on the records available in France or in London, where all death certificate copies are stored for the United Kingdom. Our record is complete up to the end of 1972.

Actual and expected total mortality together with actual and expected cancer deaths have been compared.

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Total mortality is less than expected in all three groups, which may be the result of medical or self-selection of individuals for the PVC process work.

Deaths due to all neoplasms and neoplasms of the haemolymphatic system are similar to the expected in all three groups, and although slightly higher in the VCM group the difference is statistically not significant.

There was, therefore, no evidence of an unfavourable mortality experience in men handling VCM or manufacturing PVC.

It was only after completion of this survey that the occurrence of angiosarcoma of the liver was discovered. He was a man who had a post-mortem in 1973. He was 71 years of age and had worked on PVC manufacture for 20 years.

Since the reports from the USA and other countries of angiosarcoma of the liver in men working with vinyl chloride, together with our own case, it has been decided in the UK that the Employment Medical Advisory Board will carry out a full epidemiological survey on all PVC companies engaged in PVC and PVC manufacture, as, of course, the survey that I have just described was severely limited in size of population and in the length of time that it covers.

In spite of the fact, however, that this survey did not show anything dramatic when it was commenced in late 1971, the BSA in the USA, in the knowledge that the size of their exposed population is large, also decided to commission an epidemiological study and this was done by Tabachow Co. & Associates.

Forty-three plants were identified in the USA belonging to 19 companies which either used or produced vinyl chloride for the PVC process. A brief questionnaire was sent to each plant to obtain an estimate of the exposed population and to find how far back in time personnel records could be obtained. To determine whether job histories were available for retired and terminated workers.

On the basis of the replies, 4 plants were dropped from the survey because they had begun operation after 1941. It was felt that exposure in such plants would be too recent and too brief to provide useful data. Only one other plant was deferred because it had stopped production of vinyl chloride 7 years ago, and appeared to present difficulties in identifying an exposed population.

In addition, 5 more plants were excluded from analysis. When data analysis began, it was found that information from these plants was defective in several respects (e.g., no exposure data, no job histories available for terminated employees etc.).

The study population finally had 5354 individuals (1971). Eighty-nine per cent have been traced.

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The major findings of this historical prospective mortality survey are:

1. The overall mortality of the study population was approximately 75% of what would be expected in a comparable population of Whites.
2. No cause of death showed a statistically significant excess over what would be expected in a comparable White population.
3. Six cases of angiosarcoma of the liver had been found by April 15, 1974.
4. Cancers of the liver (primarily angiosarcoma), respiratory system, brain, and cancers of unknown primary sites, as well as laryngeal cancer, occurred more often than expected in those members of the study population with the greatest exposure. Even though the excesses were not statistically significant, the findings warrant further study.
5. Other cancers occurred at lower levels than in the general White population with the exception of cancers of the buccal cavity and pharynx. There was an excess of these cancers which, however, was inversely related to exposure. The explanation for this finding is not apparent.

Mr Chairman, Thank you

R&S 025727

Mr Chairman, Ladies and Gentlemen,

June 1, 1974

W. H. R. R. R.

I have been asked to let you hear of the latest results obtained from Ind-Biotest, who are carrying out animal studies for the Manufacturing Chemists Ass. in the USA.

The study was designed to complement the work being done by Professor Maltby.

One hundred rats, hamesters and mice of each sex, 600 total per exposure group are being exposed to 0, 2500, 5000 or 10000 ppm of VCII in air per day, 5 days per week. Mice will be exposed for 9 months and kept for an additional 9 months. Rats and hamesters will be exposed for 12 months and kept for an additional 12 months.

The rats are Cobs Charles River, the mice are CDB Swiss Charles River and the hamesters are Golden Syrian from the same source. Food is removed during exposure, water is present and no bedding is used at any time.

Morbidity and dead animals, when possible, receive gross autopsies and are photographed. The major organs of all animals are fixed for histological examination.

Only the tissues from a few animals have been examined so far. The first results affect mice only and are as follows:

1. Alveotogliic adenomas of lung - zero in the control group, 2 in the 50 ppm group, 12 in the 200 ppm group and 28 in the 2500 ppm group.
2. Angiosarcoma of liver - zero in the control group, 2 in the 50 ppm group, 11 in the 200 ppm group and 28 in the 2500 ppm group.
3. Adenocarcinoma of mammary gland - zero in the control group, 2 in the 50 ppm group, 3 in the 200 ppm group and 6 in the 2500 ppm group.

These results follow about 8 months exposure. No direct numerical comparison can be made with the control group, as they have not been selected in the same way. Only mice with tumours have been examined in the exposure groups. No tumours have been observed grossly as yet in any of the control mice.

In addition to the tumours in mice, a few tumours have been observed in rats and hamesters, but because of autolysis, the diagnosis at this time must be regarded as tentative. It appears that angiosarcomas may have been observed in one male hamester and one male rat exposed to 2500 ppm and in one female rat exposed to 200 ppm. No tumours have been observed in rats or hamesters exposed to 50 ppm, but one male control was found to have a dental fibroma.

A draft of the paper presented on May 10, 1974 in New York has been submitted for publication.