

POLYVINYL CHLORIDE



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Address communications to:

Editor, ENVIRONMENTAL HEALTH PERSPECTIVES
National Institute of Environmental Health Sciences
Box 12233
Research Triangle Park, North Carolina 27709

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Print Schedule: Volume 42 will present the proceedings from the Symposium on Environmental Epidemiology

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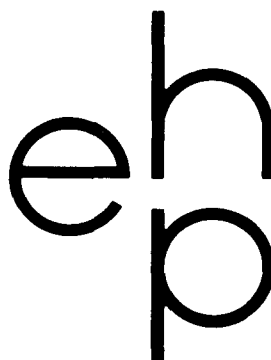
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**ENVIRONMENTAL
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**Conference to Reevaluate the Toxicity
of Vinyl Chloride Monomer, Poly(vinyl
Chloride) and Structural Analogs**

**National Institutes of Health, Bethesda, MD
March 20-21, 1980**

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Introduction

It has been over 30 years since the first suggestive evidence was published by Tribukh to indicate that vinyl chloride monomer (VCM) is acutely toxic in man. Chronic toxicity in animals was subsequently demonstrated by Torkelson in 1961, but it was an outbreak to VCM-induced acroosteolysis in the 1960's that focused attention for the first time on the occupational toxicity of this important industrial chemical. The carcinogenicity of VCM was recognized in 1974 following the nearly simultaneous reports of an association between exposure to VCM and angiosarcoma of the liver (ASL) in man (reported by Creech and Johnson) and in animals (reported by Maltoni). These reports precipitated a thorough international review of the toxicity of VCM at the New York Academy of Sciences. Since then, enormous research efforts have been undertaken to expand our knowledge of the toxicity of vinyl chloride. Many of the research efforts stimulated by the events of the 1970's have now come to fruition, and are appropriately brought together in these proceedings.

The proceedings begin with a presentation of the most extensive animal research on the carcinogenicity of VCM ever published. In these data, dose-response curves can be examined by site and type of tumor, by route and schedule of exposure, and by species and strain of animal. This study and other research on the carcinogenicity of VCM reported in this volume indicate the importance of cofactors such as age at exposure and simultaneous exposure to ethyl alcohol in VCM toxicity. Evidence that even a single exposure to VCM induces

experimental neoplasia is significant from the standpoint of both occupational and nonoccupational exposures.

The updated epidemiologic studies presented in this volume of mortality among workers exposed to vinyl chloride reinforce the laboratory findings of multisite carcinogenicity. Data demonstrating the mutagenic and transplacental effects of VCM are also updated and summarized. The lack of predictivity of one prospective liver screening program suggests the need for further work in identifying effective medical surveillance techniques for early recognition of liver abnormalities.

While thousands of workers are exposed to VCM vapor, many more are exposed to its polymer, poly(vinyl chloride) (PVC). The carcinogenicity of PVC dust is evaluated both experimentally and epidemiologically in these proceedings. The results are not definitive. Nonmalignant respiratory system effects from PVC dust are suggested by a number of papers at this conference.

Finally, the extension of the findings of carcinogenicity of VCM to its structural analogs, vinylidene chloride, trichloroethylene and tetrachloroethylene, and its brominated equivalent, vinyl bromide, serves as another lead in our effort to understand some fundamental concepts of chemical carcinogenesis.

RICHARD J. WAXWEILER
PHILIP J. LANDRIGAN
PETER INFANTE
RAYMOND SHAPIRO

Carcinogenicity Bioassays of Vinyl Chloride Monomer: A Model of Risk Assessment on an Experimental Basis

by Cesare Maltoni,* Giuseppe Lefemine,* Adriano Ciliberti,* Giuliano Cotti* and Donata Carretti*

Data are presented regarding the final results of the Bentivoglio (Bologna) project on long-term carcinogenicity bioassays of vinyl chloride (VC).

The experimental project studied the effects of the monomer, administered by different routes, concentrations and schedules of treatment, to animals (near 7000) of different species, strains, sex and age. To our knowledge this is the largest experimental carcinogenicity study performed on a single compound by a single institution.

The results indicate that VC is a multipotential carcinogen, affecting a variety of organs and tissues. In the experimental conditions studied, the neoplastic effects of the monomer were also detected at low doses. The experimental and biological factors greatly affect the neoplastic response to VC. Long-term carcinogenicity bioassays are, at present, a unique tool for the identification and quantification of environmental and occupational risks. Precise and highly standardized experimental procedures are needed to obtain data for risk assessment.

Introduction

The present report deals with the presentation of the final results of our project on the long-term carcinogenicity bioassays of vinyl chloride (VC) (BT project).

To our knowledge this project is the most extensive experimental carcinogenesis study ever performed on one industrial compound by a single institution.

Planning, Materials, Methods and Performance of the Experiment

Planning

The experiments of the project were planned (a) to test the carcinogenicity of the compound;

(b) to obtain information on the site and type of tumors; (c) to evaluate the possible effects of the routes of administration, with particular regard to the ones reproducing potential human exposure; (d) to assess, in quantitative terms, the level of risk. The planning of the experiments was aimed at achieving these goals.

The compound was tested on animals of different species, strain, sex and age (Table 1), since it is known that these factors may modify the neoplastic response qualitatively and quantitatively. The choice of the animals was made with the intention of having an integrated system of complementary biological models which could express a range, as wide as possible, of neoplastic responses.

VC was administered by different routes: intraperitoneal (IP) injection, subcutaneous (SC) injection, inhalation and ingestion (by stomach tube), the latter two being the major routes of potential human exposure.

The monomer was administered at different concentrations: 14 by inhalation levels and 6 ingestion levels for various periods of time, by continuous or intermittent treatment (Table 2).

*Institute of Oncology and Tumor Center, Bologna, Italy.