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Vinyl Chloride

MEETING REPORT
MCA Vinyl Chloride Committee
University of Louisville, Medical Department
June 14, 1978

Those Attending for MCA were:

Ted Torkelson	- Dow Chairman
Nick Wheeler	- Union Carbide
Tina Karey	- Shell
Bob Laundrie	-- General Tire
Dr. Creech	- Louisville plant doctor who first found angiosarcoma in vinyl chloride workers
Maurie Johnson	- Goodrich
Bill Becker	- Goodrich, Louisville Plant
Bill Bucey	- Pathological Consultant for Dow
Dr. McBirney	- Diamond
? Judge	- W. R. Grace
Walt Harris	- Uniroyal
Joe Seawell	- MCA

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The University of Louisville has been involved with the Goodrich PVC plant problem apparently since the 60's when acroosteolysis was first found. When Dr. Creech found angiosarcoma among the workers the University became involved. They saw VC as a unique opportunity to study carcinogenesis using VC as a simple chemical model. They have developed an interdisciplinary program of chemists, biochemists, pharmacologists, microbiologists, ~~immunologists~~, pathologists, epidemiologists, etc. Morale seems high. This is the type of program which is very important if we are to understand the cause of cancer and if we are ever to control it. They are in the unique position of having a large population of people who have been exposed to VC at varying concentrations for a long period. They have wisely chosen to work quietly with both the employees and the management. Cooperation of workers has been excellent. They have been able to get a high degree of cooperation when they have wanted blood samples and even liver biopsies. However, their program extends from basic research on chemical structure activity relationships to how to consult with patients and finally the family during final stages and after death.

Dr. Wong's group (chemistry) prepares the chemicals including tagged materials for the various researchers. They have an extensive program utilizing various in vitro bacterial tests. In addition to the Ames Salmonella and Subtitis tests they feel that the SOS repair test in combination to the other two types gives them a good picture of which chemicals are likely to be carcinogenic. Dr. Wong's group cooperate in study of metabolic pathways and synthesize the various suspected active metabolites such as the oxide of VC, styrene oxide etc. They are studying a wide range of vinyl monomers including VC, VF, VBr, Vinyl acetate, acrylonitrile (V cyanide), styrene, butadiene, ethyl vinyl ether, vinylidine chloride and bromide,

trichloroethylene and chloroprene. They have synthesized and tested the epoxide of VC and chloroacetaldehyde as well as sytrene oxide. While all three of these are active as mutagens they believe styrene oxide is not a carcinogen because of its behavior in the SOS (emergency) repair test.

In their epidemiolgoical studies everything poirts to VC as the carcinogen in the Louisville plant. Acrylonitrile is used in this plant but they feel it is not contributing to cancer among the workers. It was mentioned in passing that Dr. Creech has a gut feeling that VC effects people who were going to get cancer anyway i.e., have defective repair mechanisms at the cellular level. He thinks that if they haven't gotten cancer within about 30 years of first exposure they probably won't get it. They were inclined to think that the problem is almost over. I explained to Dr. Tamburro privately that they may get an erroneous picture from the Goodrich plant because they had acroosteolysis in the 60's and probably reduced exposure more in the late 60's than some of us. I also gave him a copy of my projections which he found most interesting and promised to study. I feel that what is learned about VC and AN will be of tremendous value in understanding carcinogens in general.

They explain that vinyl chloride itself is not a carcinogen. It is metabolized in the liver to the epoxide and chloroacetaldehyde, both of which have carcinogenic potential. The epoxide is extremely reactive so probably is bound to the cell nucleus materials in the liver. This may explain why it causes angiosarcoma (a cancer of the blood vessel) in the liver but not at distant sites. This would not rule out other cancers ~~at other cancers~~ at other sites due to the chloroacetaldehyde metabolite but its lower activity may result in such a low incidence (if any) that it will be buried in the normal cancer incidence.

One of the very interesting techniques they are doing is to expose (injection or inhalation) a mouse with a tagged chemical, quick freeze and cut it into whole body slices lengthwise with a microtome and transfer these sections to x-ray film. The developed film shows exactly where the chemical is located in the body. By exposing different animals for different time periods it is possible to see just how the chemical moves in the body. This serves as a guide to later work. Combined with urine, feces, breath and specific tissue analysis a great deal can be learned.

Another interesting technique they are using involves dissolving the connective tissue of a living organ by injecting specific enzymes and subsequently isolating a suspension of living cells than exposing the cells to the suspect chemicals. The cells are only good for a few hours.

I feel that this team has reached the stage that they will be able to learn a great deal at relatively low cost. Their work should be continued preferably by the Federal government but if not, then the chemical industry should supply the support.

A copy of the program is attached.

W. D. Harris