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TABLE OF CONTENTS FIRST PAGE

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Editorials

EXPERIMENTAL LUNG CANCER

GREAT caution must be exercised in assigning a causative relation between inhaled materials and lung cancer in human beings. In considering the cause of lung cancer and in experimental studies of lung cancer, one naturally examines critically those materials which get into the lungs and which may have a local effect on lung tissue. Thus, various industrial dusts and fumes, tobacco smoke, and exhaust gases from heavy automotive traffic have been suggested as possible factors in lung cancer. These materials have been tested chiefly on the skin of mice. However, the mere demonstration of materials in the air which are known to be carcinogenic to mouse skin is not proof that they can cause human lung cancer. Experimental carcinogenesis has taught that different species react differently to the same material (i. e., the mouse skin is very receptive to methylcholanthrene but the rat and guinea pig skins are very insensitive) and different tissues of the same species have widely varying sensitivity to the same material (i. e., the rat skin is unresponsive to carcinogens but the rat subcutaneous tissues are so reactive that they respond with sarcoma production even to glucose).

Human epidemiological data give the only really sound way of associating human cancer with an environmental exposure. In the collection of such data, a sufficiently large sample must be obtained to permit statistical analysis and valid conclusions. Even so, causal relationships must be further validated by continuing epidemiological methods, supplemented by animal experimentation. It is neither valid to conclude that animal experimentation provides definitive answers to the human cancer problem nor valid to conclude that it offers nothing to an understanding of the human cancer problem. Intelligent use of data obtained with animals should be coupled with intelligent application of the information learned from human epidemiological data, in order to understand the further research effort needed and the practical control methods indicated.

Skin carcinogenesis in the mouse has been used, and effectively, as a guide to the control of potential occupational skin carcinogens in man. The whole field of experimental skin carcinogenesis arose out of the epidemiological studies of occupational skin cancers in humans, begun some 35 to 50 years ago, and yet today a complete understanding of the mechanism of human skin carcinogenesis has by no means been realized. For instance, the relative importance of carcinogens and co-carcinogens in skin carcinogenesis is still being intensively investigated.

The mechanism of lung carcinogenesis in the mouse has not yet been worked out, let alone this mechanism in the human. We are today in about the same stage of understanding lung carcinogenesis as we were in skin carcinogenesis in 1900, prior

to the artificial production of skin tumors in experimental animals. A study of occupational lung cancers suggests that a completely different set of mechanisms may be at work. Thus, chromium and nickel under some conditions, asbestos, and an as yet unidentified factor in isopropyl alcohol manufacture are today most suspect as human pulmonary carcinogens. The only experimental lung cancers produced by inhalation have been in response to beryllium and radioactive metals.

It therefore seems highly dangerous to draw conclusions about human lung cancer from experimental evidence based on the presence of mouse skin carcinogens. Rather would it be wiser to display temperance in the interpretation of present day data until we have developed a much greater fund of knowledge concerning the mechanisms of lung carcinogenesis.

ROBERT E. ECKARDT
PHILIP DRINKER



(Courtesy of the *Saturday Review* and of the artist, Robert Kraus.)