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RECENT ADVANCES IN OCCUPATIONAL CANCER

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ABSTRACT

The contribution of occupational and environmental exposures to the etiology of cancer is a topic of considerable scientific and public interest. If an occupational environmental exposure is associated with cancer in man, then both the exposure and the disease are preventable by appropriate protection. In order to enhance the awareness and timeliness of new information concerning occupational cancer, the University of California, San Francisco, School of Medicine in conjunction with the Northern California Occupational Health Center and the National Institutes of Occupational Safety and Health, the American Cancer Society sponsored a two day meeting in San Francisco at the end of 1983. Five of the presentations are highlighted in this review. In addition, twenty special questions of clinical relevance concerning occupational and environmental cancers are reviewed with the consensus answers given.

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INTRODUCTION

The contribution of occupational exposures to the etiology of all cancer is a topic of considerable scientific and public debate. Those occupational exposures recognized as potential carcinogens pose important questions for health professionals. When potential carcinogen exposures occur in the workplace the resulting illnesses are indeed "man made". If an occupational exposure is associated with cancer in man, then both the exposure and the diseases are preventable, and appropriate protection is of critical importance.

Public pressure for regulatory preventive actions results in demands on scientists for conclusive statements regarding the carcinogenic potential of individual substances or combinations and of the industrial processes themselves. Recent news coverage of ethylene dibromide residues in food stuffs and polychlorinated biphenyls in transformer fluid leaks and fires are dramatic examples of the public and scientific pressure which can be generated in these situations.

In evaluating the extent to which a given cancer has an occupational etiology, physicians may be slow to appreciate the risk of previous exposure to cancer. Clinicians, researchers and those charged with developing regulatory strategies must be concerned about the timeliness and quality of available information and the scientific merits and limitations of current methods of interpreting the data.

In order to enhance the awareness and timeliness of new information in occupational cancer, the University of California, San Francisco, School of Medicine in conjunction with the Northern California Occupational Health Center, the National Institute of Occupational Safety and Health and the American Cancer Society sponsored a two day meeting in San Francisco at the end of 1983. The conference focused on assay systems for predicting carcinogenesis and mutagenesis, on clinical recognition techniques for environmental and work-related cancers and on practical guidelines to interpreting epidemiological studies. Special attention was also given to methods of making risk assessments in formulating cancer policies.

While differences of opinion did exist amongst the conference speakers and the audience regarding potential carcinogenesis of various substances or the utility of various assay systems, all speakers stress the need to improve current systems of data collection, analysis and dissemination. Specific research goals identified included larger and more inclusive tumor registries, establishment and followup of occupational cohorts, improvement in death certificate coding of diseases and continuing education in occupational medicine for clinicians in general medicine and other specialties.

Five of the conference speakers, Bruce Ames, Ph.D., Kim Hooper, Ph.D., Linda Rosenstock, M.D., David Wegman, M.D. and Philip Landrigan, M.D. have consented to summarize their

remarks from the conference. In addition, all of the faculty entered into a discussion of 20 specific questions which were posed and discussed. This format was a highly popular one and will be repeated again in San Francisco on December 7 and 8, 1984. The explosion of scientific information on the recognition, prevention and control of cancer necessitates a high index of suspicion that occupational and environmental factors contribute to cancer in our society.

QUESTION 1

What percentage of cancer is due to occupational and/or environmental factors?

This is a widely debated issue, and recent estimates of occupational cancer as a percentage of all cancers in the U.S. population have ranged from approximately 5% to as much as 38%. Epidemiologic issues such as the appropriate population base for denominator incidence data, the degree of certainty in associations between exposure to various agents and carcinogenesis, and the assumptions regarding historical exposures in the absence of good data make it unlikely that a single estimate will be agreed upon. If the more conservative figures of 5-15% of cancers caused by work are accepted, however, this still implies that a significant share of all malignancies in the U.S. are preventable. Environmental factors including diet and cigarette smoking give estimates of 70-90% of all cancers.

Both workplace and environmental exposures associated with cancer are preventable.

QUESTION 2

How does asbestos cause cancer? Can asbestos-induced malignancy be predicted by short term bioassay systems?

We do not know the cause of the accelerated risk of lung cancer associated with asbestos exposure nor the cause of mesothelioma. Asbestos and other mineral fibers are frequently negative in genotoxic assays and in some animal models; research over the past decade has primarily associated oncogenesis in animal models with the physical characteristics of fibers (dimensions, particularly length-to-diameter ratios). Asbestos fibers are found in the lungs of individuals who have no apparent cancer at autopsy, and no tests exists for the prediction of asbestos-induced malignancies.

QUESTION 3

Is lead a carcinogen?

The International Agency for Research on Cancer (IARC) has found sufficient evidence to consider lead a carcinogen in animal models; oral, parenteral and intraperitoneal administration of lead salts including lead acetate, subacetate and phosphate have variously produced renal tumors, gliomas, and lung adenomas in rats and mice. Tetra-alkyl lead has not been sufficiently studied. It should be noted that while these soluble lead

salts have been shown to be carcinogenic in rodents, humans are exposed primarily to metallic lead and lead oxide, which has not yet been adequately tested; futher epidemiological studies of cancer associated with lead exposure in humans are also necessary.

QUESTION 4

Can sperm morphology assays be used to predict the risk of occupational cancer?

Sperm morphology and other indications of spermatotoxicity may be useful in predicting some cancers, because the mechanism is presumed to be a mutagenic effect. Clinically, agents demonstrated to be spermatotoxic should be considered to be risk factors for carcinogenesis, and patients should be protected from such exposures. Sperm morphology as a test suffers from having at least a 50 percent false negative rate; the advantage of the test is that there are very few false positives. A negative test does not rule out the possibility of a carcinogenic effect.

QUESTION 5

Is sister chromatid exchange a useful way of monitoring workers exposed to carcinogens?

Sister chromatid exchange is a new test procedure which may be valuable in predicting somatic cell mutations. It is important

to emphasize that this is clearly not a routine test but is currently only useful in carefully controlled research protocols. The specificity and sensitivity of this method for "monitoring" workers has not been defined, nor has the predictive value of such tests for eventual carcinogenesis. Further studies are required before sister chromatid exchange can be applied for routine "monitoring" of workers.

QUESTION 6

Does fluorescent light exposure cause melanoma?

Although one retrospective study found an association between fluorescent lighting exposure at work and melanoma, no other studies have been reported to date. (Lancet 2:290, 1982). There are no good animal models that have demonstrated hazards of fluorescent lighting and cancer risk. It is clear that patients with melanoma would have marked recall bias so that prospective cohort studies are required. There is a high incidence of melanoma in Australia, and the wave length spectrum in Australia is similar to that of fluorescent lights, thus suggesting a possible association.

QUESTION 7

Is fiberglass exposure associated with mesothelioma and lung cancer?

Peritoneal and pleural injection of fiberglass in rodents has

produced local neoplasms while inhalation studies to date have been negative. Epidemiological studies have also been negative or inconclusive. Cohort studies have not been large enough to detect relatively low risks and have evaluated only workers exposed to a longer fiber than is now common in industrial use. Researchers have reported an association between fiber dimension and tumor induction; this provides a basis for further investigation.

QUESTION 8

Do petro-chemical workers have an increased incidence of brain tumors: aluminum reduction workers an increased incidence of lymphoma?

Epidemiological studies of brain tumors amongst petro-chemical workers have produced conflicting results. These difficulties are due to different methodologies and definitions of exposed and control populations, to differences in historical exposures between the initial or index plant in which a cluster of brain tumors is reported and subsequently studied plants. The most recent series of studies were published in the Journal of National Cancer Institute 70:75, 1983 and in the Journal of Occupational Medicine 25:304 and 25:313, 1983, and further studies are now in progress.

In a major study of aluminum reduction workers reported in the Journal of Occupational Medicine 25:549, 1983, there were

indications of a higher than expected risk of pancreatic cancer, lymphohematopoietic cancers, genital urinary cancer, non-malignant respiratory disease and benign and unspecified neoplasms. Previously reported findings of an increased risk of lung cancer mortality were not confirmed.

QUESTION 9

Would there be a meaningful clinical difference if the current benzene standard was lowered from 10 to 1 ppm?

Epidemiological research performed by NIOSH has found that the 10 fold decrease from 10 ppm to 1 ppm would, in fact, be expected to substantially reduce the number of cancer deaths amongst the exposed work force. In a monograph on benzene published by the International Agency for Research on Cancer, the assessment suggested that the risk of leukemia deaths attributable to benzene exposure could decrease from approximately 14 to 17 per thousand with the proposed reduction in exposure levels. (IARC Monograph No. 29, 1982).

QUESTION 10

Is the difference between statistical significance and medical significance a useful clinical distinction?

Clinical evaluation is most often concerned with a single patient. A variety of information will be significant in diagnosis and management of the patient's condition. This information is derived from the patient's own examination and history, the

scientific literature and the physician's clinical experience. In contrast, statistical significance is a concept used in evaluation of group data to determine whether a specific factor -- as opposed to chance alone -- is associated with a given disease such as occupational cancer. Statistical significance may be used by the physician to judge the value of published studies and thus to improve the scientific basis for medical certainty.

QUESTION 11

Do current cancer and tumor registries provide useful screening services for detecting occupational cancer?

Epidemiological studies have now utilized data from a number of tumor registries. However, the basic problem is to establish an appropriate control group and to define the denominator for the group at risk. Major problems in the use of tumor registries are the lack of information regarding exposures and confounding variables such as smoking and diet. Of special importance in occupational cancer is the long latency period which may produce negative studies if the followup is not of sufficient length.

QUESTION 12

Is diesel fuel exhaust carcinogenic to humans?

The question is not whether diesel fuel is carcinogenic but how much is carcinogenic? Components of diesel fuel exhaust are very active carcinogens in animal modes. Preliminary studies

in transportation workers with long term exposure to diesel fuel exhaust have suggested an increase incidence of bladder cancer. Railroad workers also exposured to diesel fuel have a slight increase in lung cancer.

QUESTION 13

Is the cancer "hit list" of practical use to clinicians?

The agents on the so called "hit list" are clearly recognized as carcinogens in animal models, and in some cases in human studies as well. However, there are many other chemicals for which epidemiological studies have not been performed for which there is animal data or short term bioassay data which suggest that they should be placed on the cancer "hit list".

QUESTION 14

Are current controls for vinyl chloride adequate to prevent malignant disease?

Current controls are adequate to prevent 99.9 percent of employees from developing malignant disease associated with vinyl chloride exposure. Risk assessments such as this must be combined with cost/benefit analysis for a full evaluation of protection levels. In the case of vinyl chloride, it is important to realize that the technology required to decrease exposure levels actually resulted in sufficient recovery of vinyl chloride to increase profits for the industries concerned.

QUESTION 15

What is a "safe level" of radiation exposure to prevent cancer?

There is no such thing as a "safe level" for radiation or any other carcinogen. Instead it would be best to talk of the "safest level" achievable with existing technology. An energetic debate exists as to whether there is a threshold below which radiation does not cause malignant disease. Current models provide insufficient data to predict the hazards of extremely low level radiation exposure. All major scientific agencies and organizations including NIOSH and OSHA have concluded that because there is no evidence for a threshold level for any carcinogen, no "safe" level can be determined.

QUESTION 16

Is sputum cytology a useful way of monitoring workers who have had exposure to agents potentially capable of causing lung cancer?

This question has now been well studied. Sputum cytology is not a useful monitoring tool and its use does not effect the outcome of lung cancer.

QUESTION 17

What is the best hospital health and safety protocol to protect staff from AIDS?

Current data strongly suggests that an infectious agent is involved in AIDS. Intimate sexual or blood contact appears to

be required for transmission, so recommended precautions are similar to those for hepatitis B. Available data does not suggest a risk to routine hospital staff. However, persons handling blood products, caring for AIDS patients, pathologists performing autopsies and individuals who might perform cardiopulmonary resuscitation may be at risk. Individuals intimately in contact with the blood of AIDS victims are particularly high risk and should take all measures to prevent exposure.

QUESTION 18

What are the appropriate methods for allowing research specialties to work safely with carcinogens?

Occupational safety and health has often been neglected in the research laboratory, and carcinogenic substances such as benzene are frequently found in research laboratories. It is important for occupational safety and health committees within the research laboratory environment to catalogue all potential carcinogens and to provide material safety data sheets to all individuals working with a cancer causing agent.

QUESTION 19

Are oncology nurses and physicians at risk by administering oncological agents?

Studies have demonstrated short term bioassay tests for mutagenicity in the urine and sister chromatid exchange to be positive in nurses and pharmacologists handling oncologic

agents. Careful controls of diet and smoking must be used in future studies undertaken to confirm these finding. Nonetheless, the use of laminar flow hoods and careful technique in preparation of oncological agents is required based on these preliminary studies.

QUESTION 20

Should urine mutagen testing be a routine health surveillance?

No surveillance technique should be considered routine. It must be targeted to the exposures identified, administered in a rational way and explained to the workers. Urine mutagen testing is suitable only for research protocols. Special problems of control of diet and smoking also must be controlled in order to appropriately interpret urine mutagen testing.