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CRITERIA FOR CARCINOGENESIS by Emmanuel Farber, M.D., Ph.D., Fels Research Inst., Temple University, Sch. of Med., Philadelphia, Pa.

The induction of cancer by a chemical is a long process that involves the initial interaction of a chemically reative moiety with many of the target cell constituents including DNA, RNA and protein. This initial phase may be ry short, a matter of hours or days and is often irreersible. The subsequent development of cancer, a process often lasting months or years, and one subject to effective modulation by drugs, hormones, etc., is dominated by two important phenomena - cell injury and focal cell proliferation. The most attractive hypothesis views carcinogenesis as a process of cellular evolution eventuating in increasingly malignant cell populations. The imposition by the chemicals of appropriate selection pressures, such as by cytotoxicity, for the selective encouragement of altered putative premalignant cells, could be important. The carcinogenic chemical often triggers a chain reaction and need not be present during the whole process. Based on this view, carcinogenic activity may be monitored by concentrating on one or more of the suspected steps during carcinogenesis. The events used most commonly for assay are the initial and the final ones. Some critical discussion of these and alternate ones will be presented.

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RELATIONSHIP BETWEEN CARCINOGENESIS AND MUTAGENESIS by Joyce McCann and Bruce N. Ames, Dept. of Biochemistry, University of California, Berkeley, CA., 94720

The development of a bacterial test system for the detection of carcinogens and mutagens will be described. The test utilizes specially constructed mutants of Salmonella typhimurium for detection of mutagenic activity and rat(or human) liver microsomes for metabolic conversion of carcinogens to their active mutagenic forms. Chemicals are tested directly on petri plates with the bacterial tester strains and the microsomal activation system. The test is rapid and economical, and is proving extremely efficient in detecting carcinogens. Hundreds of compounds have been tested with our strains and about 75% of the carcinogens can be detected as mutagens and extremely few of the non-rcinogens are mutagenic. We have adapted the method for tection of mutagenic metabolites in urine. The test is being utilized in detecting potential mutagenic/carcinogenic activity of uncharacterized compounds in complex mixtures, and we have detected mutagenic activity in cigarette smoke condensates, and soot from city air. Recently, new tester strains containing resistance transfer factors have been developed which greatly extend the versatility and sensitivity of the test. A number of compounds of environmental importance, such as vinyl chloride and some metabolic products, can be detected in our system.**

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DOSE-RESPONSE RELATIONSHIP AND THRESHOLD CONCEPTS by Paul Kotin, M.D., Johns-Manville, Denver, Colorado

Dose-response relationships and threshold (DRRT) are numerical expressions of the effect of the reaction of an agent(s) with the chemical constituents of living organisms. In multicellular hosts a hierarchy of levels of reaction exists which can be categorized in several ways: anatomical--cellular protein to intact host; biochemical--transitory to persistent; functional--physiological to pathological; clinical--reversible to permanent; and teleological--good to bad. For noncarcinogens the concept of DRRT is universally recognized and has been quantified for many agents. The existence of DRRT for interaction of a carcinogen with the cell is controversial. The question of DRRT for a neoplasm as distinguished from a transformed cell is a critical one. The verification of DRRT for cancer production must include traditional pharmacologic criteria as well as additional factors such as repair mechanisms, the relationship of altered cells to the normal cell population in the host, latency, and the normal frequency distribution extant in heterogeneous populations. The biology of carcinogenesis and cancer duction appears to be compatible with DRRT.

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LABORATORY APPROACHES TO THE IDENTIFICATION OF CARCINOGENS by Richard R. Bates, M.D., NCI Frederick Cancer Research Center, Fort Detrick, Frederick, Maryland.

Occupational cancer results from failure to detect the carcinogenicity of chemicals before human exposure occurs. Chronic exposure of experimental animals is still the only definitive test for carcinogenicity, but high cost and long duration of these tests prevent testing more than a small proportion of environmental chemicals for carcinogenicity. Recommended improvements in bioassay protocols often lead more definitive results for each chemical tested while reasing the number of chemicals which can be tested on a limited budget. More consideration is needed of the optimum balance between test refinements and ability to test more chemicals. Short-term prescreening techniques being developed may permit more effective identification of carcinogens by increasing the proportion of them in environmental chemicals selected for chronic animal bioassays. Approaches to prescreening include identification of electrophilic reactants among environmental chemicals and their metabolites, detection of reaction of chemicals with critical molecular targets in cells and their repair, mutagenesis prescreens, and cell culture transformation tests. Use of in vitro systems requires the development of effective metabolic activation systems to couple with the assays.

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RESPIRATORY DISEASE MORTALITY AMONG URANIUM MINERS by Victor E. Archer, M.D., J. Dean Gillam, M.A. and Joseph K. Wagoner, S.D. Hyg., Natl. Inst. For Occup. Saf. and Health, Salt Lake City, Utah.

A prospective repeat mortality study using a life table method was done on 3366 white and 780 nonwhite (mostly Navajo Indians) underground uranium miners, and about 1231 surface workers. Observed deaths were found to exceed expected from the following causes among both white and Indian underground workers: respiratory cancer, pneumoconiosis and related diseases, tuberculosis, and violent deaths. Both respiratory cancer and pneumoconiosis related diseases exhibit a good exposure-response relationship when plotted against cumulative internal radiation exposure, mostly received from the alpha particles of radon daughters attached to inhaled dust particles. A high proportion of violent deaths were job related. Excesses of both malignant and pneumoconiotic types of respiratory disease were higher among cigaret smokers than nonsmokers, but the latent periods were longer among nonsmokers. Of three factors involved in both malignant and nonmalignant respiratory diseases (radiation, free silica, and cigaret smoking), radiation was considered to be most important. The data suggest that the present standard for Radon daughters (4 Working Level Months per year) probably gives adequate protection.

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ASBESTOS, SMOKING AND LARYNGEAL CARCINOMA. By Robert W. Morgan, M.D., Department of Preventive Medicine University of Toronto, and P. T. Shettigara, M.R.C.V.S., University of Toronto.

This study was designed to examine a previously reported relationship between asbestos exposure and laryngeal cancer. A retrospective case control study of 43 pairs of laryngeal cancer patients and their matched controls examined a number of variables, including smoking, asbestos exposure, and other occupational factors. Cases and controls were matched for age, sex and place of residence. The data indicate a highly significant association between asbestos exposure and laryngeal cancer. Cigarette smoking was also associated with the disease, although the strength of association was not as high as that for asbestos. Exposure to uranium, chromium, nickel, cobalt, arsenic, x-ray, and alcohol did not appear related to later development of carcinoma of the larynx. We therefore conclude that asbestos exposure and cigarette smoking are potent etiologic factors in the development of this disease.

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CONJUGAL ASBESTOS NEOPLASTIC RISK by H. Anderson, M.D., I.J. Selikoff, M.D., R. Lilis, M.D., S. Daum, M.D., A. Fischbein, M.D. and J. Churg, M.D. Mount Sinai School of Medicine, New York

As more industrial substances are found to have neoplastic potential, the risk of associated conjugal tumors should be evaluated. Numerous mesotheliomas among family members of asbestos workers have been reported. However, in the absence of well-defined population bases the actual incidence and extent of risk remains unknown. All the household contacts of 1,446 asbestos workers employed in a factory which produced amosite asbestos products from 1941 to 1954 are currently being traced and examined. Four cases of pleural mesothelioma have so far been discovered. Morbidity experience will be investigated for the cohort. Of the first 210 household members studied, 81 (38.6%) had radiologic evidence of asbestos exposure (pleural, parenchymal). The possible relationship of these changes to tumor induction in the future is presently unknown.

This study demonstrated that for one household substance, amosite asbestos, significant household contamination can and does commonly occur, and may result in characteristic radiological changes as well as in neoplastic disease.

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MORBIDITY AND MORTALITY AMONG HARD ROCK MINERS EXPOSED AN ASBESTIFORM MINERAL by J. Dean Gillam, M.A., Salt Lak City, Utah, Richard A. Lemen, M.S., Cincinnati, Ohio, Vi E. Archer, M.D., Salt Lake City, Joseph K. Wagoner, S.D. Cincinnati, John Dement, M.S., Cincinnati, Ohio, Natl. I for Occup. Safety and Health.

A mortality study and review of chest X-rays of a gro of 439 underground metal miners with exposure to an asbe form mineral found an elevated risk of both malignant an non-malignant respiratory disease, and job related accid Environmental data taken in 1960 showed 39% free silica the airborne dust, while 1974 samples showed 23%. Even t 1960 settled dust samples in areas surrounding the mine ed a .5% arsenic content, current samples showed only .0 concentration in underground airborne dust, and .015% in tled dust. Counts of fibers greater than 5 microns in l averaged 0.24 fibers per milliliter. Seventy deaths were served over 5613 person years. Ten deaths were attribute malignant respiratory disease where 3.3 were expected. malignant diseases of the respiratory system accounted fo five deaths where 1.4 were expected. Eight job related ac dents were observed. The excess malignant neoplasms of t respiratory system may be caused by either arsenic and/or asbestos fiber exposure, while both silica and asbestos f may contribute to the non-malignant respiratory disease.

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HOSPITAL ADMISSION RECORDS: A SOURCE FOR IDENTIFYING OCCUPATIONAL GROUPS AT RISK OF CANCER
by Lorne Houten, Ph.D., Department of Biostatistics, Roswell Park Memorial Institute, Buffalo, N.Y.

In this study the Epidemiology schedules collected at Roswell Park Memorial Institute from 1956-1965 were analyzed for the relationship between occupation and cancer. The patients were subdivided by age, sex, diagnosis, occupation and industry, and length of exposure to occupation. Relative risks were calculated for the various categories described above using clerical workers as a control series. The full tables are to be published as a monograph by the National Institute of Occupational Safety and Health.

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CANCER MORTALITY IN THE STEEL INDUSTRY by Edward P. Radford, M.D., Dept. of Env. Med. Johns Hopkins Univ. School of Hygiene & Public Health, Baltimore, Md. 21205

Extensive studies of mortality by cause among steelworkers have been carried out over several years by Lloyd, Redmond and their coworkers at the University of Pittsburgh. Their results have indicated an excess of respiratory and genito-urinary cancer among coke oven workers; more detailed analysis by Redmond and Breslin indicates that janitors also show an excess of genito-urinary cancers. We have begun an evaluation of mortality of steelworkers at a plant not included in the above study. Results to date are from proportionate mortality only, but indicate that cancer deaths are in excess of those expected based on records for an adjacent urban area, especially for white workers. Principal sites contributing to the excess are respiratory cancer, bladder and kidney cancer, and pancreatic cancer. These excesses are not restricted to the coke oven operation. These preliminary results suggest that carcinogenic agents may be more prevalent in steel-making than has been previously supposed. Some differences between the two study populations which might account for these data will be discussed.

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SPUTUM CYTOLOGY AMONG ALUMINUM POTROOM WORKERS by David P. Discher, M.D., Bryce D. Breitenstein, M.D., and Abraham I. Schweid, M.D., University of Washington, Seattle, Washington.

In addition to a number of other parameters, the cytopathologic findings in sputum from a sample of aluminum potroom workers in the Pacific Northwest were compared with a group of matched controls. The results of this study were as follows:

Classification	Sample	Controls
Negative	0.58	0.63
Atypical	0.26	0.11
Suspicious	0.006	0.0
Positive	0.002	0.0
Unsatisfactory	0.13	0.21
Unknown	0.02	0.05

The morphologic findings were those typically seen in sputa ranging from regular metaplasia to outspoken squamous cancer. The meaning of the differences between the sample and controls remains doubtful.

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CANCER MORTALITY PATTERNS ASSOCIATED WITH EXPOSURE TO METALS by Samuel Milham, Jr., M.D., Washington State Department of Health, Olympia, Washington

An age standardized proportionate mortality (PMR) analysis of the occupational and cause of death information on 300,000 white male death records filed in Washington State in the years 1950-1971, reveals an interesting neoplasia pattern in workers exposed to metals. The occupational groups studied were: boilermakers, copper smelter workers, machinists, metal molders, plumbers, structural metal workers, sheet metal workers, aluminum mill workers, welders, and tool and die makers. Eight of these 10 groups showed PMR increases for respiratory cancers. Four of the 10 groups showed PMR increases for cancer of the urinary bladder. Cancer of the tongue was increased in 3 groups, and cancers of the pancreas and malignant lymphomas were increased in each of 2 groups. Workers in aluminum mills showed PMR increases for cancer of the pancreas (PMR=204) and malignant lymphoma (PMR=250). The respiratory cancer increase seen in nearly all the groups suggests that metals (particles, fumes, etc.) are carcinogenic for humans when inhaled. The aluminum worker neoplasia pattern is different from that of the other groups studied here, suggesting that other agents may be responsible for the neoplasia.

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CANCER MORTALITY PATTERNS IN THE LEAD INDUSTRY
by W. Clark Cooper, M.D. Tabershaw/Cooper Associates, Inc. Berkeley, California

The mortality of 7032 men employed for one or more years in lead production facilities("smelters") or battery plants was observed over a 23-year period, 1947-70. There were 1267 certified deaths. Lead absorption in many members of the cohort was known to have been greatly in excess of accepted standards. The standardized mortality ratio(SMR) for all causes was 107 for smelter workers and 99 for battery plant workers. Deaths from malignant neoplasms were somewhat elevated in both groups, the SMR being 133 for smelter workers and 111 for battery plants. The excesses arose largely from tumors of the digestive organs and the respiratory system. Only 3 deaths are attributed to malignant renal tumors and 7 to tumors of the central nervous system. The latter findings were of interest in view of the experimental production of renal tumors in rats and mice by the injection or oral administration of very large doses of lead salts, and the report by one group of investigators of gliomas in rats fed lead subacetate.

Studies are continuing to characterize more fully the exposures of the above lead workers to substances other than lead. Additional followup of the cohort is also contemplated.

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HISTOLOGIC TYPES OF BRONCHOGENIC CARCINOMA AMONG MEMBERS OF COPPER MINING AND SMELTING COMMUNITIES by John A. Newman, M. D., Victor E. Archer, M. D., Geno Saccomanno, M. D., Marvin Kuschner, M. D., Oscar Auerbach, M. D., Raymond D. Grondahl, M. D. and John C. Wilson, M. A.

An increased incidence of bronchogenic carcinoma is found among men and women of Anaconda, MT., a copper smelter community and among men and women of Butte, MT., a copper mining community. A significantly increased incidence of lung cancer is not noted in the residents of the counties of these cities. Comparison of histologic types of bronchogenic carcinoma shows a significant increase of poorly differentiated epidermoid carcinomas and small cell undifferentiated carcinomas among smelter workers. It is felt that this is due to exposure to arsenic. The miners and control group of "other" males show a histologic type distribution similar to other control groups and to asbestos workers. It is postulated that this may be due to exposure to certain silicates and amphiboles prevalent in the waste rock or gangue of the mines and the sanding, anti-skid material used on the Butte City streets. The histologic type distribution of Butte women is not similar to that of other report series, showing a high incidence of epidermoid carcinoma and a lowered incidence of adenocarcinoma.

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THE IARC PROGRAMME TO EVALUATE THE CARCINOGENIC RISK OF CHEMICALS TO MAN by Lorenzo Tomatis, International Agency for Research on Cancer, Lyon, France

The International Agency for Research on Cancer has initiated a programme to evaluate the carcinogenic risk of chemicals to man. This programme is centered on the production of monographs on individual chemicals, consisting of data on use and production, carcinogenicity in experimental animals, epidemiological studies and case reports, and other biological data such as metabolism and mutagenicity, and ending with a balanced evaluation of all the data made by an international group of experts. Chemicals to be surveyed for the preparation of monographs have so far been selected among those for which some evidence or suspicion of carcinogenicity in experimental animals and/or man exists and for which human exposure is known to occur. Of the 196 compounds already evaluated, 17 have been found to be associated with cancer in man. Ninety-three compounds were definitely carcinogenic in experimental animals and 41 were shown to have a limited carcinogenic effect in experimental animals. A number of the chemicals found carcinogenic in experimental animals are produced in very large quantities. The type of exposure to the 17 chemicals found carcinogenic to man w occupational for 14, medicinal for two and dietary for o

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STATISTICAL EXTRAPOLATION METHODS FOR ESTIMATING RISKS FROM ANIMAL DATA by David G. Hoel, Ph.D., National Institute of Environmental Health Sciences, Research Triangle Park, N. C.

Regulatory standards for the permissible levels of environmental carcinogens often incorporate results from extrapolated animal carcinogenesis studies. Typically, data from a relatively high dose experiment are first extrapolated to obtain a predict response at low dose, which is then followed by the inclusion of a species conversion factor to give an estimate of the response in man. Various statistical models will be discussed with regard to their biological basis, or lack of, and their implications on prediction. Finally, some discussion will be given concerning the effects of experimental design on extrapolated values.

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NEOPLASTIC RISK AMONG VINYL CHLORIDE POLYMERIZATION WORKERS by Richard J. Waxweiler, MSIE, William Stringer, MS, Henry Falk, M.D., Coleman Carter, M.D., James Jones, BSChE, Joseph K. Wagoner, S.D. Hyg., NIOSH, CDC

A retrospective cohort study of mortality among persons orking at four separate polyvinyl chloride polymerization facilities was carried out. Study observations were limited to the period following five years of exposure and ten years since onset of exposure to vinyl chloride (VC). This restriction was imposed to avoid bias due to selection or due to insufficient latency for occupationally induced malignancies to become clinically manifest. An environmental profile indicated areas of VC exposure and the limitations of calculating individual estimated cumulative exposure to VC. Death certificates were obtained for all cohort members known to have died. Hospital records, pathology reports and tissues were collected, when available, for review by an expert panel of pathologists to evaluate the primary site and specific histology of malignancies.

When mortality of the cohort was compared with U.S. white males, results demonstrated a close agreement with previous animal bioassay studies and human epidemiological studies in terms of excess risk of cancer and site distribution of those cancers.

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ONCOGENIC AND MUTAGENIC RISKS IN COMMUNITIES WITH POLYVINYL CHLORIDE PRODUCTION FACILITIES by Peter F. Infante, DDS, Ohio Department of Health, Columbus, Ohio.

The results of a preliminary investigation indicate that residents of the three Ohio communities with polyvinyl chloride production facilities gave birth to a significantly greater number of children with malformations during the period 1970-73, as compared to the expected, based on occurrence in the entire state. The rate of malformations in the index cities also was significantly greater than the rate in the balance of the counties in which these cities were located, $P < 0.001$. Other county-city combinations f similar size revealed no significant differences in lformation rates. Most notable among specific birth anomalies were those involving the Central Nervous System; 5.62 expected versus 17 observed. These preliminary findings do not link the presence of polyvinyl chloride production facilities with the increased occurrence of malformations, but indicate the need for further study of possible contributing factors.

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CANCER AND CONGENITAL ANOMALIES ASSOCIATED WITH ANESTHETICS by Thomas H. Corbett, M.D., University of Michigan Medical Center, Ann Arbor, Michigan.

Survey studies have demonstrated a high incidence of cancer among anesthesia personnel and a high incidence of birth defects among their offspring. Teratogenicity of inhalation anesthetic agents in rodents has been demonstrated previously. Preliminary studies with isoflurane, an alpha-chloro ether inhalation anesthetic agent, suggest the agent is carcinogenic in Swiss/ICR mice. Groups of pregnant mice were exposed to subanesthetic concentrations by inhalation, and offspring further exposed every other day for 25 additional exposures. Controls were exposed to room air. Necropsies were performed at 3, 6, and 9 months of age. Pulmonary adenomas occurred with a higher incidence than in controls at all necropsy times. At 9 months, three liver neoplasms and one uterine malignancy were observed in experimental groups. These observations suggest the need to evaluate the possible carcinogenicity of all the halogenated alkane and ether inhalation anesthetic agents.

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CANCER AMONG BENZOYL CHLORIDE MANUFACTURING WORKERS by Hiroyuki Sakabe, M.D., Hidetsuru Matsushita, Ph.D., and Migezi Koshi, M.D., Natl. Inst. Ind. Health, Kawasaki, JAPAN.

Three lung cancers (2 dead and 1 alive) and one maxillary malignant lymphoma were found in a small plant which had produced benzoyl chloride from 1954 to 1972. The number of employees had usually been 20. These four workers had engaged in the manufacture of benzoyl chloride in the very bad environmental conditions during 6 to 15 years before the onset of disease. Expected value of lung cancer death among benzoyl chloride manufacturing workers is 0.06 and observed 2 ($p=0.0017$). Benzoyl chloride was manufactured by hydrolysis of benzotrichloride which was prepared by chlorination of toluene. These victims had ainly been exposed to toluene, chlorine, hydrogen chloride, enzotrichloride, and benzoyl chloride. Benzotrichloride and/or benzoyl chloride are suspected to be carcinogenic to humans considering that benzyl chloride which has a similar chemical structure to these was reported to be carcinogenic to rats.

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CASE STUDY 3. VINYL CHLORIDE - BEST AVAILABLE TECHNOLOGY by Donald V. Lassiter, Ph.D., Occupational Safety and Health Administration, Washington, D.C.

Promulgation of a standard regulating occupational exposure to vinyl chloride (VC) by OSHA on October 4, 1974, marked the initial Federal attempt to regulate occupational exposure to a carcinogen on the basis of available analytical methodology. Demonstration of carcinogenicity of VC had included experimental animal studies performed by separate investigators and a continuing case list of human cancer in workers occupationally exposed to VC. Although various tumors were observed both in experimental animals and in occupationally exposed workers, the finding of angiosarcoma of the liver in both instances revealed a definite correlation between chemical exposure and induction of cancer. The significance of polyvinyl chloride (PVC) production to the Nation's economy rendered impractical even de facto elimination of this important industry through unattainable controls prescribing "zero" employee exposure to VC. Rather, exposure to VC was limited to one ppm as an 8-hour TWA and 5 minutes as a 15-minute TWA. The one ppm exposure limit was based on recommendations made to OSHA by NIOSH and represented the sensitivity of available analytical methodology for determination of compliance.

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INORGANIC ARSENIC: AMBIENT LEVEL APPROACH TO THE CONTROL OF OCCUPATIONAL CANCERIGENIC EXPOSURES by Hector P. Blejer, M.D., D.I.H., and William Wagner, M.S., National Institute for Occupational Safety and Health, Cincinnati, Ohio

In 1822 the first malignancies reported as due to arsenic exposure were scrotal cancers among smelters. A century later causal relationship between chronic occupational, environmental or medical arsenic exposure and skin cancer was firmly established. Since 1948 data from 9 epidemiological studies have, initially or upon review, demonstrated significant excess of lung cancer mortality among workers of diverse industries with exposure to various inorganic arsenic compounds. Two such studies reported in 1974 also showed significant excess of lymphatic system cancer and/or leukemia mortality. A semi-quantitative study demonstrated a dose-response relationship between arsenic and lung cancer, with a possible contributory role by sulfur dioxide and/or other contaminants; whereas the only quantitative epidemiological study, reported in 1974, revealed a dose-response demonstrating an increased lung cancer mortality risk at arsenic concentrations above 1 $\mu g/M^3$, calculated as the average occupational exposure over a 40-year work life. Given indications of increased cancer mortality resulting from community exposure to inorganic arsenic, and the absence of data documenting a safe level of occupational exposure, the conclusion is drawn that the arsenic body burden of workers should not be occupationally increased above that produced by the highest recorded ambient level.

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ALDRIN AND DIELDRIN SUSPENSION BASED ON EXPERIMENTAL EVIDENCE AND EVALUATION OF SOCIETAL NEEDS. Samuel S. Epstein, M.D. Case Western Reserve University Medical School, Cleveland, Ohio.

The carcinogenicity of Dieldrin has been unequivocally demonstrated in valid independent studies on several strains of mice. While these data largely relate to hepatocarcinogenicity, inter alia as evidenced by pulmonary metastases, other target organs are also clearly involved. Dieldrin is carcinogenic at the lowest dose, 0.1 ppm, tested. More limited studies demonstrate the carcinogenicity of Dieldrin in rats, in which multiple site tumors have been induced. No valid data exist on other species, including man. Dieldrin is poorly degradable and fat soluble and is widely disseminated as an environmental pollutant in air, water, food and human fat. Agricultural uses of Dieldrin have resulted in major economic losses, particularly to the poultry and fish industries. The major agricultural use of Dieldrin is as a prophylactic insecticide and no valid data support contentions for its efficacy as used. Decisions to suspend major agricultural uses of Dieldrin reflect its carcinogenic hazards and the involuntary nature of human exposure, besides its lack of efficacy in a broad societal context.

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TOWARD AN INTEGRATED PROGRAM OF GOVERNMENTAL ACTION by David P. Rall, M.D., Ph.D., Director, National Institute of Environmental Health Sciences; Chairman, DHEW Committee to Coordinate Toxicology and Related Programs, Research Triangle Park, North Carolina.

The elements of a rational program of governmental action on environmental carcinogenesis include: Information - Decision - Action - Followup. I shall concentrate on the first and last. The critical information needs are: What chemical -- with what toxic effects (on laboratory animals or man) -- at what concentration is in contact with what population? The sources of this information include the private sector, the academic community and governmental laboratories. Before a governmental decision is made, it is critical that all information be collected and evaluated. The DHEW Committee to Coordinate Toxicology and Related Programs is in an excellent position to facilitate information collection, evaluation and dissemination from the academic and governmental sectors. Problems may exist in obtaining timely information from the private sector. Followup of a decision and the resulting action is important and has similar elements, emphasizing clinical and epidemiological studies.

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PREVENTION OF OCCUPATIONAL CANCER - PROGRAM OF THE OCCUPATIONAL SAFETY AND HEALTH ADMINISTRATION by Donald V. Lassiter, Ph.D., Occupational Safety and Health Administration, Washington, D.C.

Prevention and control of occupational cancer involves an integrated program of regulatory exposure controls and effective educational and training programs. The Occupational Safety and Health Administration (OSHA) has program activities directed to each area. Of the 16 health standards promulgated by OSHA following the "start up" standards, all have involved chemical substances with carcinogenic properties. Additional regulatory controls have been proposed for substances such as arsenic and benzene. Although mandatory exposure standards are necessary for prevention of occupational cancer, education of workers concerning cancer hazards is also necessary to enable workers to assess their risk of occupational cancer and to recognize exposure hazards in the workplace.

OSHA is working jointly with the Division of Cancer Control and Rehabilitation of the National Cancer Institute, the National Academy of Sciences, and the National Institute for Occupational Safety and Health (NIOSH) to develop an effective training and education program for workers concerning occupational cancer responsive to their particular needs.

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THE FEDERAL ROLE IN PREVENTION OF OCCUPATIONAL CANCER IN MINES AND MILLS by James M. Day, Administrator, Mining Enforcement and Safety Administration, Washington, D. C.

The Mining Enforcement and Safety Administration (MESA) was established in 1973. Its establishment separated from the U. S. Bureau of Mines the administration of the Federal Metal and Nonmetallic Mine Safety Act of 1966, and, except for certain research functions, the Federal Coal Mine Health and Safety Act of 1969. MESA promotes health and safety in the minerals industry through inspection, investigation, and enforcement of Federal standards; technical support, education, training and motivation for State and industry personnel; sponsoring research in health and safety. Lung cancer is known to occur among miners exposed to airborne radiation in uranium and non-uranium mines, and among mill and mine workers with a history of exposure to asbestos. Mines and mills are being surveyed for inorganic arsenic, a possible carcenogen in the mineral industry. Health inspections are conducted on the basis of Federal standards designed to prevent the incidence of cancer. MESA's cooperation and exchange of information with other Federal and State agencies and private professional organizations will contribute to the prevention of occupational cancer.

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CANCER MORTALITY AMONG WORKERS EXPOSED TO CUTTING OIL MIST by Pierre Decoufle, Sc.D., National Institute for Occupational Safety and Health, Rockville, Maryland.

Certain cutting oils have been found to be carcinogenic for the skin among exposed workers. The present study was initiated to determine whether exposure to cutting oils in the form of a mist increased the risk of malignancies of internal organs as well as chronic respiratory disease. Selected for study was a population of 5,189 production workers engaged in metal machining operations where soluble, non-soluble, and synthetic cutting fluids have been used for many years. They were employed between 1938 and 1967 and followed for mortality through 1967. Expected numbers of deaths by cause were computed based on U.S. white male death rates specific for age and calendar year. Total mortality for the group was less than the general population over the entire period of observation. Deaths from cancers of the respiratory and digestive systems were excessive only after 30 years from onset of exposure. When results were examined by duration of exposure and latency, systematic risk patterns were difficult to observe due to the small numbers involved. Death rates for other major causes including non-malignant respiratory disease were lower than those predicted by the general population.

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CANCER EXPERIENCE AMONG COKE BY-PRODUCT WORKERS by Carol M. Redmond, Sc.D., University of Pittsburgh, School of Public Health, Pittsburgh, Pa.

Previous reports on a study of 58,628 men employed in seven Allegheny County steel plants in 1953 show that men employed at the coke ovens in by-product coke plants experienced a high mortality from lung cancer, with the level of the lung cancer risk being directly related to the proximity of the workers to the coke ovens and the length of time employed at the coke ovens. Because of the exposure of the men in the by-product operations of the coke plant to a wide variety of coal tar distillates, this updated report focusses on the cancer experience among workers in the coke plant as a whole, with particular emphasis on the mortality findings for non-oven workers. For all coke workers with 5 or more years experience in the coke plant, excesses in mortality due to lung cancers are seen in oven workers, with excesses in cancers of the kidney and prostate occurring in both oven and non-oven workers. Cancers of the digestive system are shown to be statistically significantly increased in non-oven workers. These observations clearly indicate the need to consider non-oven, as well as oven workers, in evaluating the cancer hazards in the coke plant.

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36. Cancer Mortality Among Rubber Workers, A.J. McMichael, D.A. Andjelkovic, H.A. Tyroler, Occupational Health Studies Group, University of North Carolina, Chapel Hill, N.C.

Several previous epidemiologic studies of the rubber industry-which uses many chemicals-have identified excess mortality from certain specific cancers. In this study, four cohorts of active (aged 40-plus) and retired workers, at four major rubber-tire plants, were identified historically, and followed for ten years. The cancer mortality of these four populations was compared, separately and combined, with that of the general community. For all cancers there was a slight excess above the expected number of deaths, while for some specific cancers (stomach, colorectal, prostate, and neoplasms of the lymphatic and hematopoietic system) there was a marked excess of deaths. Proportional mortality analysis at other, smaller plants revealed similar excesses for these cancers, and some excess for lung, bladder, and CNS cancers. Analysis of detailed individual work-histories reveals an association of certain cancers with specific job exposures - for example, leukemia and solvent exposure, lung cancer and curing room exposure, and stomach cancer and rubber processing. Further analytic studies are currently underway to identify groups of workers at increased risk of other specific cancers.

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LEUKEMIA ASSOCIATED WITH BENZENE EXPOSURE by Enrico C. Vigliani, Clinica del Lavoro "L. Devoto", University of Milan, Italy

Benzene has been known for more than a century as a bone marrow poison, leading to hyporegenerative or aplastic anemia. However, evidence has been accumulating in the last 40 years that benzene can also cause leukemias. More than 150 cases of benzene leukemia are known at present; in many cases leukemia develops as a terminal stage of a hyporegenerative anemia. It is mostly an acute hemocytoblastic or myelobiastic leukemia, sometimes leukopenic, but other types of leukemia are also said to occur after exposure to benzene. The experience of the Institutes of Occupational Health of Milano and Pavia are recorded, showing that more than 50% of the fatal cases of chronic benzene poisoning died of acute leukemia. There may be a latent period extending over several years between cessation of exposure to benzene, with more or less pronounced anemia, and the onset of leukemia. In the cases of anemia ending with acute leukemia, the anemic stage can be considered as a pre-leukemic one. Benzene is known to induce chromosomal aberrations and this might be an important factor in the pathogenesis of leukemia.

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Tyler Asbestos Workers Project-S. Donald Greenberg, M. D. The Program was begun July 1974 in Tyler, Texas(TexasChestHospital) to investigate a cohort of 890 former asbestos workers. Approximately 90% of these men are cigarette smokers. Unique to the program are the sputum cytopathology studies(both aerosol induced and spontaneous early morning sputa specimens, each worker having sputum cytopathology every 6 mos. This report is based on initial study of 500 sputa specimens from 226 workers. 107(47%)had no atypias, 107(57%)had mild atypias, 9(5%)had severe atypias and 1(.4%)had cells of a squamous carcinoma. 75(32%)demonstrated ferrugenous bodies (FB)in their sputa. Only 2(.8%) had unsatisfactory specimens(saliva). The number of FB/specimen(4 Papanicolau stained smears)were counted and reported as "few"(1-14),"moderate" (15-30), and"many"(30+). Of 75 w/FB, 43(57%)had FB in aerosol specimens, 15(20%)showed FB in spontaneous produced specimens, and 17(23%)had FB present in both. The yield of FB in the aerosol induced specimens was almost twice that of the spontaneous specimens. The 19 specimens revealing severe atypias were equally distributed between aerosol induced and spontaneous sputa specimens. In the one patient whose sputa revealed squamous carcinoma cells, the chest roentgenogram showed no localizing lesions; however, fiberoptic bronchoscopy disclosed an ulcerative squamous carcinoma of the bronchus intermedius, proven by washing, brushing & biopsy. It is concluded that sputum cytopathology is an excellent, simple, noninvasive, painless and inexpensive means of early detection of malignant and premalignant lesions of the lung, and that no special techniques are necessary for the detection of FB.

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EARLY INDICES OF CANCER RISK AMONG URANIUM MINERS WITH REFERENCE TO MODIFYING FACTORS
by Geno Saccomanno, M.D., Grand Junction, Colorado

Periodic sputum examinations from uranium miners since 1957 have been studied to demonstrate the cytological development of epidermoid carcinoma of the lung. Many individuals developed atypical squamous cell metaplasia when exposed to cigarette smoke and radon daughter radiation, and many miners developed carcinoma in situ which eventually progressed to invasive carcinoma. Both of these carcinogens cause the premalignant squamous cell metaplasia of the lung when in concert, but the radon daughter carcinogen alone does not significantly add to the incidence of cancer among uranium miners, but cigarette smoking miners have at least a two-fold incidence of cancer of the lung, suggesting promotional or synergistic effect of these carcinogens. Age at start of mining was strongly associated with age of development of cancer of the lung. The period of time that elapsed in each stage of development of carcinoma in situ and the in-situ period varies markedly, but averaged 3.22 yrs. in mild atypia; 3.58 yrs., moderate atypia; 2.94 yrs., marked atypia, and 4.45 yrs. in carcinoma in situ in a population of 34 cases followed through these stages of tumor development.