Abstracts

Lung Cancer Risks of Underground Miners: Cohort and Case-Control Studies.  V.E. Archer.  University of Utah, Salt Lake City, Utah

All underground mines have higher radon levels than are found in surface air. Ventilation is the primary method of controlling radon levels. Fourteen cohort and seven case-control studies done on underground miners are reviewed; they include many types of ore. Only five of the studies deal with more than 100 lung cancer deaths. Variations in the attributable risk are given. Some generalizations can be drawn from these studies: the longer the follow-up, the greater is the attributable risk, even though the relative risk is reasonably constant. The induction-latent period is quite variable but is shortened by high exposure rates, by cigarette smoking, and by increasing age at start of mining. The predominant histological type of lung cancer among miners changed from small-cell undifferentiated for short follow-up time to epidermoid after long follow-up times. With short follow-up time, a multiplicative interaction between smoking and radiation was indicated, but, with long follow-up time, the two factors appear to be simply additive. This difference is probably due to the shortened latent period among cigarette smokers, not to synergism.

This paper appears in full in Yale J Biol Med 61:183–193, 1988.

Models for the Analysis of Radon-Exposed Populations.  J.H. Lubin.  National Cancer Institute, Bethesda, Maryland

Radon-222 is a radioactive decay product of radium-226 and uranium-238, which are found throughout the crust of the earth. Studies of underground miners clearly show that exposure to radon and its decay products increases the risk of developing lung cancer. Data on standardized mortality ratios from eight cohort studies indicate that the radon-lung cancer relationship is statistically homogeneous, even though cohorts are from different types of mines and from different countries.

Regression methods for cohort data based on a Poisson probability model permit a thorough consideration of risk patterns. In this report, we review these methods, wherein the disease rate in each cell of a multi-way table is modeled as a function of the cross-classifying variables. The National Academy of Sciences’ Committee on the Biological Effects of Ionizing Radiation uses the Poisson regression approach to develop a model for age-specific lung cancer risk which depends on cumulative exposure, age at risk, and time since exposure. This model is reviewed and its implications discussed.

The most important determinant of lung cancer is cigarette smoking. The paper discusses relative risk models for analysis of joint exposure to radon and tobacco products. The review of available studies suggests that the joint relationship of radon and smoking with lung cancer is consistent with a multiplicative model, but a submultiplicative relationship is most likely. An additive model is rejected.

This paper appears in full in Yale J Biol Med 61:195–214, 1988.

Case-Control Studies of Residential Radon Exposure and Lung Cancer.  J.B. Schoenberg, J.B. Klotz, H.B. Wilcox, M. Gil-del-Real, G.P. Nicholls, and A. Stemhagen.  New Jersey State Department of Health, Trenton, New Jersey  Z. Hrubec and T.J. Mason.  National Cancer Institute, Bethesda, Maryland

An association between lung cancer and residential radon exposure has been predicted, based on extrapolations from studies of miners, and has been suggested by results of four case-control studies conducted in Sweden and Canada. A study of 994 female lung cancer cases in New Jersey and 995
Experimental Animal Studies of Radon and Lung Cancer: Summary. F.T. Cross. Pacific Northwest Laboratory, Richland, Washington

Several biological effects have been observed in dogs and rodents following the inhalation of radon and radon daughters: primarily, respiratory epithelial carcinoma, pulmonary fibrosis, pulmonary emphysema, and lifespan shortening. Extrapulmonary lesions are generally not a significant finding in these exposures.

Five variables appear to influence the tumorigenic potential of radon daughters in the experimental-animal studies:
- Radon daughter cumulative exposure
- Radon daughter exposure rate
- Radon daughter unattached fraction
- Radon daughter disequilibrium
- Concomitant exposures to cigarette smoke

Tumorigenic potential increases with: (1) increase in WLM exposure until lifespan shortening reverses the trend; (2) decrease in radon daughter exposure rate; and (3) increase in radon daughter unattached fraction and disequilibrium. Although simultaneous exposure to elevated levels of ore dust or diesel-engine exhaust increased the incidence of emphysema and fibrosis, it did not appear to increase the number of tumors produced by high radon daughter exposures. The influence of cigarette smoke depends on the temporal sequence of the exposures. In beagle dogs, alternating cigarette smoke and radon daughter exposures on the same day produced a decrease in lung tumor incidence from that produced by radon daughter exposures alone. Smoke exposures completed before radon daughter exposures did not alter the lung cancer incidence in rats; however, smoke exposures following completed radon daughter exposures produced a synergistic effect. The influence of exposure to other pollutants is unknown at current low radon daughter levels in the mines or in the environment.

Although lung tumor data differ somewhat, the overall incidence data in animals (rats, primarily) are similar to present estimated lung tumor incidence data in man. The derived range in mean lifetime risk coefficient for atmospheres with low percentages of unattached daughters, weekly exposure rates exceeding about 200 WLM (0.7 J h m$^{-3}$), and data uncorrected for lifespan differences from control animals, is about 1 to $5 \times 10^{-4}$ WLM$^{-1}$ (300 to $1,400 \times 10^{-4}$ J h$^{-1}$ m$^{-3}$) between 100 and 5,000 WLM (0.35 and 17 J h m$^{-3}$) exposures. Similar cumulative exposure data from underground miners are also estimated to range between about 1 and $5 \times 10^{-4}$ WLM$^{-1}$. Recent data from rats with 20 to 50 WLM (0.07 to 0.17 J h m$^{-3}$) exposures, at low exposure rates, place the lifetime risk coefficient at about 6 to $8 \times 10^{-4}$ WLM$^{-1}$ (1,700 to 2,300 $\times 10^{-4}$ J h$^{-1}$ m$^{3}$).

Data observed in animals that are not unequivocally demonstrated in human exposures to radon daughters are: (1) the increase in tumor production with increase in radon daughter unattached fraction and disequilibrium, and (2) the importance of the temporal sequence of exposures to cigarette smoke and radon daughters. (The absence of these findings, however, does not constitute proof that similar data might not be obtainable in human exposures but may rather reflect the paucity of this type of human data.)

The similarities in the human and animal data presently outweigh the differences between them. The animal experiments continue to yield valuable information that helps to explain the effects on man of inhaled radon and radon daughters, and associated pollutants, especially in mine environments.

Human T-Cell Lymphotropic Virus Type I and Adult T-Cell Leukemia/Lymphoma Outside Japan and the Caribbean Basin. P.H. Levine, E.S. Jaffe, A. Manns, E.L. Murphy, J. Clark, and W.A. Blattner. National Cancer Institute, Bethesda, Maryland

Ninety-six patients with the diagnosis of adult T-cell leukemia/lymphoma (ATLL) were identified in countries outside Japan and the Caribbean Basin. Seventy-four of these patients were
initially diagnosed in the United States; 25 of 52 patients whose place of birth was known had been born in the United States. The detection of 14 patients born in the southeastern United States, all black, indicates a group deserving particular attention for studies of human T-cell lymphotropic virus type I (HTLV-I), a suspected etiologic agent in most cases of ATLL. Although geographic clustering of ATLL in areas endemic for HTLV-I, particularly southwest Japan and the Caribbean Basin, is a dramatic feature of this disease, a review of the literature indicates that HTLV-I-associated ATLL probably occurs sporadically in a much wider distribution, the disease being diagnosed in native-born African, Chinese, European, and Latin American patients. A registry for ATLL cases is suggested, to assist in the identification of risk factors for this disease and, at the same time, improve case definitions and early diagnosis.

This paper appears in full in Yale J Biol Med 61:215–222, 1988.

**Exposure to Chemotherapeutic Agents and the Risk of a Second Breast Cancer: Preliminary Findings.** P.L. Horn and W.D. Thompson. Yale University School of Medicine, New Haven, Connecticut

Chemotherapeutic treatment for cancer has been successful in prolonging survival but may also lead to the development of second cancers. Two case-control studies presented here suggest, however, that breast cancer patients who receive chemotherapy are at significantly lower risk of a contralateral breast cancer than those who do not. Approximately 300 incident cases of contralateral breast cancer and 300 randomly chosen surviving controls with unilateral breast cancer were identified through the Connecticut Tumor Registry for inclusion in each study. The initial study was based on review of medical records at eight hospitals and indicated that the overall association with chemotherapy was modified by body build. The second study obtained information from in-person interviews, hospital records, and outpatient chemotherapy records from across the state. The preliminary results of this second study confirm the previous findings. Both cytotoxic and hormonal drugs were associated with a reduction in the risk of second breast cancers (OR = 0.5, 95 percent CI: 0.3–1.0; OR = 0.5, 95 percent CI: 0.2–1.2, respectively). Significant interaction with body build was observed for hormonal treatment (ratio of ORs = 5.8, 95 percent CI: 1.0–34.3 for a five-unit change in Quetelet's index), with a nonsignificant but detrimental effect suggested for overweight women (OR = 2.3, 95 percent CI: 0.4–13.9 for a Quetelet's score of 35).

This paper appears in full in Yale J Biol Med 61:223–231, 1988.

**Patterns of Substance Use and Abuse in Inner-City Adolescent Medical Patients.** F. Earls and J. Powell. Washington University School of Medicine, St. Louis, Missouri

Distinct patterns of use and abuse of alcohol and illicit drugs are described in a sample of 2,415 teenage patients using primary health clinics over a two-year period. The sample was obtained in the course of a large-scale study to evaluate the effectiveness of consolidated medical programs directed to predominantly inner-city, minority-group adolescents. Information was obtained in personal interviews using a structured format and professional interviewers. Analysis of data proceeded in two steps. First, the rates of progression from abstention or light use of alcohol and drugs to regular use or abuse, and the reverse of this pattern (i.e., remission) were examined. The second step in the analysis was to examine the degree to which certain psychosocial variables characterized temporal patterns of heavy use. Regular tobacco use had a substantial influence on the progression to substance abuse in male and female patients. The results indicate that about 20 percent of the patients attending these clinics were in some phase of either increasing or decreasing their substance use, another 20 percent engaged in regular use continuously over the two-year period, while the remaining 60 percent of patients stayed at low risk over this same period. These subgroups were rather easy to differentiate on the basis of concurrent behavioral and lifestyle problems.

This paper appears in full in Yale J Biol Med 61:233–242, 1988.
Lifestyle Orientations in Late Adolescence and Patterns of Substance Abuse. L.D. Johnston, P.M. O’Malley, and J.G. Bachman. The University of Michigan, Ann Arbor, Michigan

This paper explores the relationship between various life-style factors and the use of licit and illicit drugs in large, nationally representative samples of American young people, and the extent to which changes in such life-style factors may help to explain observed changes in prevalence of drug use. We conclude that use of licit and illicit drugs is related to a variety of different life-style characteristics, including delinquency and deviant behavior; attitudes toward risk-taking; religious commitment; attachment to and involvement with school (including truancy, liking of school, grades, educational aspiration, and an index of extracurricular involvement); and time spent out of the home (including number of hours spent working, average number of evenings out per week, amount of dating, frequency of attending rock concerts, frequency of going to parties, bars, and out with friends). Controlling for a variety of background factors, including sex, race, parental education, number of parents in home, region, and urbanicity, does not substantially change the relationships. Having a healthy life-style orientation shows a rather limited relationship with drug use, with the important exception of cigarette smoking. The “counter-culture” orientation, which at an earlier time had a strong relationship with some forms of illicit drug use, has a much weaker relationship today.

Drinking in Different Social Contexts Among White, Black, and Hispanic Men. R. Caetano. Medical Research Institute of San Francisco, San Francisco, California D. Herd. University of California, Berkeley, California

This paper describes alcohol use by White, Black, and Hispanic men in eight different social settings. Data were obtained from a multi-stage probability sample of the household population of White, Black, and Hispanic adults aged 18 years and over, residing in the 48 contiguous United States. The response rate was 73 percent for Whites, 76 percent for Blacks, and 72 percent for Hispanics. Results show that Whites go more frequently and drink more frequently than Blacks and Hispanics at restaurants, in clubs or organizational meetings, and in bars. Blacks go more frequently than Whites and Hispanics to public settings such as parks, streets, and parking lots; however, the mean number of drinks consumed in these public places and the proportion of men drinking five or more drinks is higher for Hispanics than for Whites and Blacks. Other places where heavier drinking is common in all three ethnic groups are bars, taverns and cocktail lounges, and parties. In all three ethnic groups, men who are younger and those who are single go more frequently than other men to bars or public places such as streets, parks, and parking lots. Men who are younger and those who are single also have a higher rate of heavy drinking and of drunkenness than other men.

This paper appears in full in Yale J Biol Med 61:243–258, 1988.

Prevalence, Persistence and Sequelae of HIV p24 Antigen in a Cohort of Intravenous Drug Users. D.C. Des Jarlais. New York State Division of Substance Abuse Services, New York, New York D. Mildvan, S. Yancovitz. Beth Israel Medical Center, New York, New York J-P. Allain, M. Lether. Abbott Laboratories, King of Prussia, Pennsylvania S.R. Friedman. Narcotic and Drug Research, Inc., New York, New York M. Marmor. New York University Medical Center, New York, New York S. Beatrice. New York City Department of Health, New York, New York W. El-Sadr. Manhattan Veterans Administration Medical Center, New York, New York

HIV p24 antigen was examined in a cohort of 138 intravenous drug users in New York City. HIV serologic status and lymphocyte subsets were measured in the cohort, over a mean follow-up time of 9.2 months. Measurement of p24 antigen was conducted at Abbott Laboratories, using a test developed there.

Only four subjects had detectable antigen at the start of the study; antigen persisted in these subjects and was detected in one additional subject at follow-up. All five subjects with detectable
ABSTRACTS

Antigen were among the 65 who were initially anti-HIV-positive. Antigen was not detected in the four subjects who seroconverted during the follow-up period. None of the antigen-positive subjects had anti-p24 as measured by an Abbott competitive assay, but three of five did have detectable anti-p24 by Western blot. As expected, the anti-HIV seropositive group showed loss of lymphocytes during the follow-up period, with a median percentage loss of 31 percent for T4 cell count, 23 percent for T8 cell count, 0 percent for B cell count, and 26 percent for total lymphocyte count. The five antigen-positive subjects showed greater percentage losses than the other anti-HIV seropositive subjects in T4 cell counts and B cell counts (p = .02 by Wilcoxon two-sample tests). As of January 1987, five of the original 65 anti-HIV-positive subjects had developed AIDS; two of these were also antigen-positive. Detectable antigen was thus a predictor of developing AIDS among all anti-HIV seropositive subjects (p = .044 by Fisher’s exact test). Among the five antigen-positive subjects, the two who injected drugs at the highest levels during the follow-up period were the two who later developed AIDS (p = .10 by two-tailed Fisher’s exact test).

The prevalence of p24 antigen among anti-HIV intravenous drug users appears to be less than among anti-HIV-positive homosexual/bisexual men. In both groups, however, detectable p24 antigen is associated with progressive immunosuppression and development of clinical AIDS. Detectable p24 antigen also appears compatible with low levels of anti-p24 in the same subjects. Among intravenous drug users, p24 antigen appears to be a relatively specific but not highly sensitive indicator of progressive immunosuppression.

Life Styles and Substance Abuse. L.N. Robins. Washington University School of Medicine, St. Louis, Missouri

The growth of drug abuse and dependence has closely resembled that of the traditional epidemic, with a sudden spurt beginning at an identifiable date (about 1969); confinement prior to that date to specific groups defined by age, sex, and location; a spread afterward throughout the general population of young people; and a dependence of personal contact with affected persons for transmission. Although drug dependence often has alcohol dependence as a co-morbid state, and the two share risk factors (childhood conduct problems, early smoking, parental alcoholism, poor school performance, early sexual experience, and early first use of alcohol and drugs), alcohol dependence has been much less epidemic in character, with a relatively constant prevalence over time and the stability of groups at high risk.

This study contrasts the histories of these two disorders by comparing their associated life styles, using data from the Epidemiologic Catchment Area project, a study of the general adult population in New Haven, Baltimore, St. Louis, Durham, and Los Angeles, from 1981 to 1985. Life-style correlates of drug and alcohol problems in the year prior to interview are examined in approximately 15,000 persons who received a second psychiatric interview. The life-style components available for study are economic, medical, marital, legal, and interpersonal aggression. Periods of depression and suicide attempts were also assessed.

Nine percent of the sample weighted to represent national distributions of age, sex, and race were found to have had one or more alcohol problems in the year preceding the interview, and 2.1 percent had had problems with drugs. Rates were highest among those under the age of 35 for both substances. For young men, 17.0 percent had had an alcohol problem in the preceding year, and 5.9 percent had had a drug problem. Among young women, the rate of alcohol problems was only 4.3 percent, and the rate of drug problems was 3.4 percent. Thus among the young, the male:female ratio for drugs is only 1.7, but for alcohol it is 4.0.

Comparison of life styles of drug and alcohol abusers is limited to persons under 35 because of low drug abuse rates in older persons. Life styles of abusers were compared to those without a history of abuse or heavy use of either substance and were stratified by age. Similarities are more striking than differences in the life styles associated with alcohol and drug abuse. For both alcohol and drug abuse in men and women, there are elevated rates of suicidal thoughts and attempts, depression, arrests for non-traffic offenses, illegal earnings, fighting and weapon use, and spouse battering (all relative risks > 1.5). Hospital admissions, heavy use of medical services (>4 visits), and traffic arrests were similarly elevated for drug and alcohol abuse in men. No strong relationship with low income or household size was apparent for either sex.

Despite these similarities, for men, drug problems are more strongly associated with life style than alcohol problems. For men, only drug abuse is associated with cohabitation (drug and
alcohol abuse are associated with cohabitation for women) and unemployment (neither abuse is associated with cohabitation for women). For men, the proportion of deviant lifestyle indicators is higher in drug than alcohol abusers in 14 of 16 of the indicators (hospital admissions and traffic tickets were equal). For women, the impact of drug and alcohol problems is approximately equal. While only alcohol problems are associated with heavy use of medical services, only drug problems are associated with being single. Comparing proportions involved in deviant life styles, for women, seven life styles are more common in drug abusers, seven in alcohol abusers, and two are equal. For women, alcohol has a notably greater association with frequent medical care, suicidal thoughts, and fighting, while drug abuse has the greater association with never marrying and illegal earnings.

For men, therefore, it appears that lifestyle patterns are similar, but drug abusers are more deviant. For women, the degree of deviance does not vary, but women lead somewhat different life styles, depending on which form of substance abuse they are involved in. While these sex differences are intriguing, they should not obscure the fact that in both sexes most of these deviant life styles are elevated for both alcohol and drug abusers.

Finding little difference in the life styles of young alcoholics from young drug abusers is not surprising, and some respondents had problems with both types of substances. Current lifestyles are the complex result of early social and family history, including factors that may have led to the initiation of substance abuse; of the exposure to substances that affect behavior, education, and therefore capacity to maintain family and economic roles; and of the attitudes of the public toward drug and alcohol abusers, which present the abuser with barriers to marital and job stability. Teasing apart how much can be attributed to pre-substance abuse states, how much to the biological effects of substance abuse, and how much to the differential meanings that society gives alcohol and drug abuse is beyond the capacity of these data but would be necessary for fully understanding how different histories of the spread of illness might be represented in the life styles of the affected persons.

Suicide Attempts in the Epidemiologic Catchment Area Study. E.K. Mościcki, D.S. Rae, B.Z. Locke, and D.A. Regier. National Institute of Mental Health, Rockville, Maryland P. O’Carroll. Centers for Disease Control, Atlanta, Georgia A. Roy. National Institute of Alcohol Abuse and Alcoholism, Bethesda, Maryland

This study examines risk factors for attempted suicide in the general community. Data from the five-site NIMH Epidemiologic Catchment Area (ECA) Study were used to estimate lifetime prevalence and identify risk factors for suicide attempts. Occurrence of suicide attempts and lifetime diagnosis of psychiatric disorder were ascertained, using the NIMH Diagnostic Interview Schedule (DIS). Of 18,571 adult respondents aged 18 and over, 2.9 percent reported that they had attempted suicide at some time in their lives. A weighted logistic regression model was constructed to ascertain significant (p < .0028 with Bonferroni correction) risk factors for attempted suicide. Persons who had a lifetime diagnosis of a psychiatric disorder had the highest risk of attempted suicide (odds ratio [OR] = 8.4). Females (OR = 3.3), separated or divorced persons (OR = 2.5), Whites (OR = 1.7), persons in the two lowest socioeconomic quartiles (ORs = 2.2, 2.3), and respondents from the Los Angeles ECA (OR = 1.8) were also more likely to have attempted suicide. These findings contribute to an understanding of suicide and suicidal behavior in general populations, outside the clinical setting.

This paper appears in full in Yale J Biol Med 61:259–268, 1988.

A Policy to Control the Spread of HIV Infection. L.H. Kuller. University of Pittsburgh, Pittsburgh, Pennsylvania

The prevention of transmission of HIV infection is the most important public health concern of the AIDS epidemic. To date, unfortunately, we have failed to contain the epidemic. The increasingly rapid spread of HIV into the IV drug-abusing population and subsequent heterosexual transmission represent a further failure of the public health system. Current organization of the public health programs, especially the lack of independence and adequate financial and personnel support, is an extremely serious problem. More funding may not be the answer, unless there is better organization. Identification of infected individuals and a vigorous education
program must be implemented. HIV antibody-positive individuals should be followed carefully in order to evaluate the risk factors for AIDS and efficacy of specific interventions.

This paper appears in full in Yale J Biol Med 61:269–276, 1988.

Epidemiologic Observations of the AIDS Epidemic. A Basis for Control Strategies. R. Altman. New Jersey Department of Health, Trenton, New Jersey

When control strategies are not known for a communicable disease, control measures for another disease may be used, often unsuccessfully, because the epidemiology of the two diseases is different. Control measures for AIDS need to be developed, measures that are related to its epidemiology, rather than using methods that have been used for syphilis control with minimal success.

Three epidemics of AIDS are described. The epidemic in homosexual men has caused a terrible tragedy in that community but is not a source of much spread beyond it. The epidemic in intravenous drug abusers may be the key to much of the growth of the U.S. AIDS epidemic and is currently the cause of the heterosexual epidemic, which is largely confined to minorities.

New Jersey is using three control strategies. We are increasing counseling, testing, and contact tracing, aware of their inherent problems and lack of well-documented benefits, as well as increasing the availability of drug abuse treatment and prevention. Education is presently the most important AIDS prevention measure. Education is directed toward several groups, but potentially the most effective is education directed to teenagers to motivate behavioral change toward safer sexual practices and prevention of intravenous drug abuse. We must learn how to reach this group.