AMERICAN JOURNAL OF EPIDEMIOLOGY
Vol. 127, No. 1

Printed in U.S.A.

CASE-CONTROL STUDY OF LUNG CANCER IN CIVILIAN EMPLOYEES AT THE PORTSMOUTH NAVAL SHIPYARD, KITTERY, MAINE[1]

ROBERT A. RINSKY, JAMES M. MELIUS, RICHARD W. HORNUNG, RALPH D. ZUMWALDE, RICHARD J. WAXWEILER, PHILIP J. LANDRIGAN, PHILIP J. BIERBAUM, AND WILLIAM E. MURRAY, JR.

Rinsky, R. A. (National Institute for Occupational Safety and Health, Cincinnati, OH 45226), J. M. Melius, R. W. Hornung, R. D. Zumwalde, R. J. Waxweiler, P. J. Landrigan, P. J. Bierbaum, and W. E. Murray, Jr. Case-control study of lung cancer in civilian employees at the Portsmouth Naval Shipyard, Kittery, Maine. *Am J Epidemiol* 1988;127:55–64.

Case-control analysis of deaths due to lung cancer (*International Classification of Diseases*, Eighth Revision, code 162) among persons who worked at the Portsmouth Naval Shipyard, Kittery, Maine, between 1952 and 1977 found elevated odds ratios for exposures to ionizing radiation, asbestos, and welding byproducts. The radiation-related excess was statistically significant in persons with cumulative lifetime exposures of 1.0–4.999 rem. When asbestos and welding histories were combined into a single risk factor, odds ratios for the combined exposure were significantly elevated for two of three duration-of-exposure categories examined. Further analysis of data on radiation exposure, controlling for exposures to asbestos and welding, found reductions in initial estimates of radiation risk at all levels of radiation exposure. This reduction suggests that radiation workers were more heavily exposed to asbestos and/or welding fumes than were other workers and that those exposures confounded the observed association between radiation and lung cancer. Analysis of mortality by time since first exposure to radiation revealed no pattern of progressive increase as latency increased. By contrast, odds ratios for asbestos/welding increased with latency. Data on cigarette smoking and socioeconomic status were not available. The results of this study do not preclude a possible association between radiation exposure at the Portsmouth Naval Shipyard and excess mortality from lung cancer. However, they provide no evidence in support of such a relation.

asbestos; radiation, ionizing; respiratory tract neoplasms; welding

In May 1978, nuclear workers at the Portsmouth Naval Shipyard in Kittery, Maine, were reported by Najarian and Colton (1) to have experienced a fivefold increase in proportional mortality due to leukemia and a twofold increase due to all cancers combined. Consequently, the United States House of Representatives' Subcommittee on Health and the Environment requested that the Department of Health and Human Services conduct further epidemiologic studies. The National Institute for Occupational Safety and Health was directed to conduct this research and undertook a retrospective cohort mortality study of the entire shipyard population and of radiation workers in particular (2).

Received for publication March 21, 1986, and in final form March 19, 1987.

[1] From the National Institute for Occupational Safety and Health, 4676 Columbia Parkway, Cincinnati, OH 45226. (Reprint requests to Robert A. Rinsky.)

An invited letter by Irwin D. Bross commenting on the present paper by Rinsky et al. appears on pages 202–4 of this issue of the *American Journal of Epidemiology*.

The data from the cohort mortality study did not support the previous findings of increased mortality due either to leukemia or to all cancers combined. In addition, no excess mortality from any cause was observed in shipyard workers with occupational exposure to ionizing radiation (3, 4). The principal explanation for the discrepancies between the two studies appears to have been misclassification of data on radiation exposure histories by the original researchers; this misclassification resulted from failure to elicit accurate work histories from next-of-kin of deceased workers (5).

An unanticipated finding in the cohort mortality study was excess lung cancer deaths among men with cumulative lifetime exposure of at least 1 rem who had experienced initial radiation exposure at least 15 years before death. In that group, 13 lung cancer deaths were observed versus 6.56 expected (standardized mortality ratio = 198). Although no a priori hypothesis postulating such a relation had been established, a decision was made to analyze these deaths further. To simplify the task of coding occupational exposure histories, we used a case-control design. This report presents that analysis.

MATERIALS AND METHODS

Population

The study population, as defined in the previous cohort mortality study (3), consisted of white males who had worked at the Portsmouth Naval Shipyard at any time from January 1, 1952 to August 15, 1977. From this group, any person with an underlying cause of death due to a malignant neoplasm of the trachea, bronchus, or lung (lung cancer) was considered for the present analysis to be a case. Only death certificates in the possession of the National Institute for Occupational Safety and Health by December 1980 were eligible for consideration. Causes of death were coded from death certificate designation by a qualified nosologist.

To select an appropriate number of controls per case, we performed power calculations at various odds ratios and exposure rates. A ratio of three controls to each case was found to provide adequate power for detection of an odds ratio of 1.5 (power = 96 per cent, given a 33 per cent exposure rate). Every member of the cohort was eligible to be selected as a matched control for each case, with the exception that if deceased, a candidate must not have died of a malignant neoplasm. Each case was compared with every other member of the cohort and evaluated for closeness of match by three criteria: 1) absolute difference in dates of birth; 2) absolute difference in dates of first employment; and 3) absolute difference in the durations of employment (from first to last dates of employment). These three differences were then summed to produce a rank. The three candidates with lowest ranks were matched with each respective case. When the lowest ranking score was the same for more than three candidates, the first three candidates encountered (files are ordered by Social Security number) were selected. Each selected control remained in the pool of eligible candidates. In the event that the same person was chosen as a control for more than one case, he was assigned to the case who matched more closely; a new candidate was then selected for the remaining case.

Although recent methodological studies (6, 7) published after this investigation had begun to suggest that it would be better to select controls from the pool of workers at risk at the time the case died, time of death was not considered in this sampling scheme. By matching on date of birth, year first employed, and duration of employment, we assumed under the null hypothesis that the expected proportions of exposed and unexposed controls would be the same as those of the cases.

Environment

The Portsmouth Naval Shipyard is a large industrial complex which employs workers from a number of trades, including welding, insulating, pipe fitting, electrical work, rubber work, and machining. Within any trade, a person may be a "radiation worker," meaning that he is eligible to work in an area in which external exposure to radiation is possible. The radiation sources were the nuclear reactor components (primarily gamma radiation from cobalt 60) and radiographic examination of welds (x-radiation). Regardless of a person's job classification, if he had ever worked in an area with potential radiation exposure, he was monitored for such exposure.

Monitoring of external radiation was by film badge from 1950 until 1974 when film badges were replaced by calcium fluoride thermoluminescent dosimeters. Monitoring of internal radiation, resulting from inhalation or ingestion of radionuclides, has been performed by whole-body monitoring. Although instances of internal radiation exposure have occurred at the shipyard, we believe such exposures were not significant in comparison with external exposures. For each radiation worker, radiation doses have been recorded by the Portsmouth Naval Shipyard and were reported to us as an annual dose.

A study member was considered to be a radiation worker if a history of radiation exposure had been maintained by the Portsmouth Naval Shipyard, even if his recorded lifetime cumulative dose was zero. We verified all recorded radiation values by comparing the annual summaries used in the study with actual source documents ("DD 1141 forms") kept in the medical files at the Portsmouth Naval Shipyard. The forms for each case and each control were reviewed for evidence of internal exposures, errors, and any unusual exposure or medical disqualification from the radiation program. The results of this audit revealed an error rate of less than 0.5 per cent. All errors were corrected before analysis. No instance of internal exposure was found.

Unfortunately, no similarly comprehensive industrial hygiene record system describing the types and extents of other individual occupational exposures was maintained by the Portsmouth Naval Shipyard. Personnel records indicating the specific shops to which a person had been assigned, his job classifications, and the date of each change in employment (either a change in shop or job assignment) were available, however. Job descriptions, some limited Portsmouth Naval Shipyard industrial hygiene data, and reports of several National Institute for Occupational Safety and Health industrial hygiene surveys assisted in the identification and quantification of occupational exposures (3).

For each case and control, a detailed work history was coded. This work history included data on the beginning and ending dates of each job held throughout an employee's entire working career at the Portsmouth Naval Shipyard. Any change in shop assignment or job classification was considered to be a job change. Coding of all job history information was standardized according to a classification system which grouped shops and jobs by commonality of processes, materials handled, and occupational exposures. This classification procedure enabled examination of data by assignment to shop, job performed, or the combination of the two.

Because asbestos, which is a known lung carcinogen, and welding by-products, which are suspected to contain lung carcinogens, were both present in abundance at the Portsmouth Naval Shipyard, they were considered to be potentially confounding risk factors for lung cancer (8, 9). Therefore, shops and job classifications suspected of involving exposure to either asbestos or welding by-products were identified. These determinations were based on available industrial hygiene data. Shop and job classifications in which asbestos exposure was probable were categorized as "probable asbestos exposures." Shop and job classifications in which asbestos exposure was less certain were categorized as "potential asbestos exposures." In like manner, exposures to by-products of welding were categorized as probable and potential asbestos exposures.

Analyses

Odds ratios and corresponding two-tailed 95 per cent confidence intervals were generated for specific "exposed" shops and jobs and for exposure to radiation. Matching was maintained throughout all analyses that generated odds ratios for exposures within a specified universe, and values for chi-square were calculated as described by Mantel and Haenszel for individual exposure variables (10). When simultaneous investigation of multiple exposure variables was desired, conditional logistic regression was employed (11). Use of this model allowed estimation of the odds ratio for radiation exposure while simultaneously controlling for exposure to other carcinogens, as well as for possible interactions.

Analyses were performed for all radiation workers combined (regardless of amount of exposure) as well as separately for each of the following cumulative lifetime exposure categories: 0.0 rem (monitored, but less than the limits of detection), 0.001–0.999 rem, 1.00–4.999 rem, and equal to or greater than 5.00 rem.

Death from lung cancer is generally believed to require a long latency period subsequent to the initiating exposure. Accordingly, analyses were performed in which five, 10, 15, and 20 years were subtracted from the date of death of each case, and the resultant dates were used as the terminal work history date for each person in the matched set. This "lagging" of work histories eliminates from consideration exposures to radiation and asbestos and/or welding which may not have had sufficient latency to be of etiologic importance.

RESULTS

A total of 405 persons were identified in the Portsmouth Naval Shipyard population as having died from malignant neoplasms of the trachea, bronchus, or lung (lung cancer). For those cases, we selected 1,215 controls (three for each case). The mean age at date first employed and date last employed, mean length of employment, date of birth, date first employed, and date last employed were determined for cases and controls (table 1). Comparisons of these means indicate the closeness of matching.

Of the cases, 121 had radiation histories maintained by the Portsmouth Naval Shipyard. Of the controls, 330 had radiation histories. Radiation exposures are summarized in table 2.

Radiation

Lung cancer cases were found to have an odds ratio of 1.23 (95 per cent confidence interval (CI) = 0.91–1.67) for ever having had a history of radiation exposure (table 3). Although not significantly different from 1.0, this odds ratio is higher than the risk of death from lung cancer in radiation workers seen in the previous cohort analy-

TABLE 1

Comparison of mean ages and calendar times between lung cancer deaths and matched controls, Portsmouth Naval Shipyard, Kittery, ME, January 1, 1952 to August 15, 1977

	Cases (*n* = 405)	Controls (*n* = 1,215)
Age at date first employed (years)	37.02	37.07
Age at date last employed (or study end data, if active) (years)	55.29	55.32
Length of employment (years)	14.07	14.41
Date of birth (year)	1906.25	1906.23
Year first employed	1943.31	1943.30
Year last employed	1961.53	1961.55

TABLE 2

Distribution of 405 lung cancer deaths and 1,215 matched controls by cumulative lifetime radiation exposure at Portsmouth Naval Shipyard, Kittery, ME, January 1, 1952 to August 15, 1977

Cumulative lifetime radiation exposure (rem)	Cases		Controls	
	n	% exposed	*n*	% exposed
No history	284	70.1	885	72.8
0.0	21	5.2	60	4.9
0.001–0.029	14	3.5	40	3.3
0.030–0.099	19	4.7	44	3.6
0.100–0.499	14	3.5	77	6.3
0.500–0.999	15	3.7	29	2.4
1.000–4.999	25	6.2	47	3.9
5.000–14.999	8	2.0	20	1.6
≥15.00	5	1.2	13	1.1
Total	405	100	1,215	100

TABLE 3

Mantel-Haenszel odds ratio for cumulative lifetime radiation exposures: 405 lung cancer deaths and 1,215 matched controls, Portsmouth Naval Shipyard, Kittery, ME, January 1, 1952 to August 15, 1977

Cumulative lifetime radiation exposure (rem)	Exposed cases	Exposed controls	Matched odds ratios	95% confidence intervals
Any history	121	330	1.23	0.91–1.67
0.0	21	60	1.17	0.68–2.04
0.001–0.999	62	190	1.11	0.77–1.61
1.0–4.999	25	47	1.81	1.05–3.12
≥5.0	13	33	1.37	0.68–2.78

sis (3). Restricting the analysis to workers with a cumulative lifetime radiation dose of 0.0 rem and to those with exposure of between 0.001 and 0.999 rem compared with those with no radiation history did not appreciably change the odds ratio (odds ratio (OR) = 1.17, 95 per cent CI = 0.68–2.04 and OR = 1.11, 95 per cent CI = 0.77–1.61, respectively). A comparison of workers with cumulative lifetime radiation exposure of 1.00–4.999 rem with those having no history of radiation yielded a statistically significant odds ratio of 1.81 (95 per cent CI = 1.05–3.12). However, a comparison of workers who had a cumulative lifetime exposure of 5.00 rem or greater with those who had no exposure yielded an odds ratio of 1.37, which was not statistically significant (95 per cent CI = 0.68–2.78).

Asbestos

Asbestos exposure was an obvious factor to consider when evaluating lung cancer mortality in a shipyard population (8). Lung cancer cases were found to have an odds ratio of 1.24 for ever having worked in an probable asbestos-classified job (95 per cent CI = 0.92–1.68) (table 4). When a requirement was imposed for a minimum of five years of exposure, the odds ratio increased to 1.53 (95 per cent CI = 0.99–2.36), and with a minimum requirement of 10 years of exposure, the odds ratio was 1.61 (95 per cent CI = 0.94–2.75). Although none of these elevated odds ratios are statistically significant, possibly due to the small number of cases in the latter categories, a progressive increase in odds ratios with increasing duration of exposure is apparent.

A history of ever having worked in a job classified as having either a probable or potential asbestos exposure yielded an odds ratio of 1.25 (95 per cent CI = 0.99–1.58). With a minimum requirement of five years exposure in such jobs, the odds ratio increased to 1.31 (95 per cent CI = 0.97–1.78). However, when a 10-year minimum requirement was imposed, the odds ratio decreased to 1.18 (95 per cent CI = 0.83–1.69).

Almost all employees of shop 56 (Pipe Shop) were classified as having probable or potential asbestos exposure. Odds ratios for ever having worked in shop 56, for working a minimum of five years, and for working a minimum of 10 years were calculated. All of these odds ratios were significantly elevated, and they increased from 1.43 (95 per

TABLE 4

Mantel-Haenszel odds ratios for asbestos exposure: 405 lung cancer deaths and 1,215 matched controls, Portsmouth Naval Shipyard, Kittery, ME, January 1, 1952 to August 15, 1977

Amount of exposure	Exposed cases	Exposed controls	Matched odds ratios	95% confidence intervals
Probable exposure				
Ever exposed	71	178	1.24	0.92–1.68
Minimum 5 years	35	68	1.53	0.99–2.36
Minimum 10 years	24	42	1.61	0.94–2.75
Probable or potential exposure				
Ever exposed	213	576	1.25	0.99–1.58
Minimum 5 years	111	242	1.31	0.97–1.78
Minimum 10 years	73	146	1.18	0.83–1.69
Shop 56 (Pipe Shop)				
Ever exposed	59	131	1.43	1.03–2.00
Minimum 5 years	31	53	1.83	1.14–2.95
Minimum 10 years	21	33	1.99	1.10–3.58

cent CI = 1.03–2.00) for having ever worked in shop 56 to 1.83 (95 per cent CI = 1.14–2.95) for persons with at least five years experience in the shop, and 1.99 (95 per cent CI = 1.10–3.58) for persons with at least 10 years experience.

Welding

Occupational exposures to the by-products of welding have also been associated with increased risk of lung cancer (9). Some odds ratios for welding exposure were elevated, although statistical significance was not demonstrated overall for jobs with probable exposure to welding (table 5).

Significantly elevated odds ratios were present for working in a job with either a probable or potential welding exposure. The odds ratio for ever having worked in such a job was 1.46 (95 per cent CI = 1.17–1.83), that for working a minimum of five years was 1.41 (95 per cent CI = 1.06–1.87), and that for working a minimum of 10 years was 1.24 (95 per cent CI = 0.89–1.74).

TABLE 5

Mantel-Haenszel odds ratios for welding exposure: 405 lung cancer deaths and 1,215 matched controls, Portsmouth Naval Shipyard, Kittery, ME, January 1, 1952 to August 15, 1977

Amount of exposure	Exposed cases	Exposed controls	Matched odds ratios	95% confidence intervals
Probable exposure				
Ever exposed	41	111	1.13	0.76–1.68
Minimum 5 years	28	71	1.20	0.74–1.92
Minimum 10 years	16	49	0.93	0.50–1.72
Probable or potential exposure				
Ever exposed	236	597	1.46	1.17–1.83
Minimum 5 years	143	310	1.41	1.06–1.87
Minimum 10 years	91	190	1.24	0.89–1.74
Shop 26 (Welding Shop)				
Ever exposed	41	111	1.13	0.76–1.68
Minimum 5 years	28	73	1.16	0.73–1.86
Minimum 10 years	16	54	0.83	0.46–1.53

Almost all persons assigned to shop 26 (Welding Shop) were involved in welding. Odds ratios for ever having worked in this shop, for working a minimum of five years, and for working a minimum of 10 years were 1.13, 1.16, and 0.83, respectively. None of these ratios were statistically significant.

Asbestos and welding combination

Because of considerable overlap of study subjects among the categories of asbestos exposure, welding exposure, and assignment to the welding and pipe shops, it is not readily apparent which exposure or interaction of exposures account for the elevated odds ratios. To facilitate the present evaluation, we therefore combined jobs classified as having asbestos and welding exposures and treated them as one exposure category. Lung cancer odds ratios for this combined category are presented in table 6. For ever having had experience in a job classified as having any exposure to asbestos or welding, the odds ratio was 1.43 (95 per cent CI = 1.12–1.81). With a five-year minimum exposure requirement, the odds ratio became 1.50 (95 per cent CI = 1.11–2.04), and for a minimum of 10 years, the ratio was 1.38 (95 per cent CI = 0.97–1.98).

Radiation and possible confounders

To determine if the elevated odds ratios associated with radiation exposure were attributable to radiation exposure itself or if they resulted from an association between radiation and exposure to other known carcinogens, we controlled for asbestos and welding exposure by using conditional logistic regression (11) with both radiation and the combined asbestos/welding exposure variables in the model. Odds ratios and 95 per cent confidence intervals were calculated for ever having a radiation history and for categories corresponding to cumulative radiation histories of 0.0, 0.001–0.999, 1.0–4.999, and equal to or greater than 5.00 rem, all corrected for asbestos/welding. In addition, possible interaction between radiation exposure and asbestos/welding exposure was tested using the conditional logistic model. This model revealed no statistically significant interaction between these exposures. The interaction term was then removed from the model before exposure odds ratios were estimated. The estimated odds ratio for ever having a history of radiation (OR = 1.18, 95 per cent CI = 0.86–1.62), for a dose of 0.0 rem (OR = 1.13, 95 per cent CI = 0.65–1.96), for doses of 0.001–0.999 rem (OR = 1.07, 95 per cent CI = 0.74–1.55), for doses of 1.00–4.999 rem (OR = 1.68, 95 per cent CI = 0.97–2.91), and for doses equal to or greater than 5.00 rem (OR = 1.23, 95 per cent CI = 0.60–2.51) were all nonsignificant (table 7), although the category 1.00–4.999 rem was associated with a higher odds ratio as compared with the other categories. The odds ratio for asbestos/welding exposure (with radiation exposure in the model) was significant (OR = 1.41; 95 per cent CI = 1.10–1.81).

TABLE 6

Mantel-Haenszel odds ratios for all asbestos and welding exposures: 405 lung cancer deaths and 1,215 matched controls, Portsmouth Naval Shipyard, Kittery, ME, January 1, 1952 to August 15, 1977

Amount of exposure	Exposed cases	Exposed controls	Matched odds ratios	95% confidence intervals
Ever exposed	267	706	1.43	1.12–1.81
Minimum 5 years	152	317	1.50	1.11–2.04
Minimum 10 years	96	181	1.38	0.97–1.98

To investigate further the possibility of a higher risk of lung cancer with increased cumulative exposure to radiation, we assessed dose-response relations. Several models were fit to characterize the shape and significance of a potential dose-response curve. The probability of death from lung cancer was modeled as a function of the variable dose, dose + dose^2, and the natural log of dose. All three models were nonsignificant, with the best fit achieved by the log dose model.

Effect of lagging exposures

Meaningful analysis of lung cancer mortality required consideration of induction-latency periods. Because the exact latency period for radiation-induced cancer after prolonged exposure is unknown, exposure was lagged five, 10, 15, and 20 years from the death of each case. In this analysis, odds ratios were not found to be significant for exposure to any amount of radiation or at any of the lag periods examined (table 7). Odds ratios for radiation displayed no pattern of progressive increase as lag intervals became larger. However, the wide confidence intervals observed for the larger lag periods demonstrated that few workers in this population had experienced radiation exposure 15 or more years prior to death of the case. In contrast, all odds ratios for

TABLE 7

Odds ratios (OR) and 95% confidence intervals (CI) for exposures to radiation and to asbestos or welding among lung cancer deaths and controls as determined by conditional logistic regression for selected lag periods, Portsmouth Naval Shipyard, Kittery, ME, January 1, 1952 to August 15, 1977

Exposure (rem)	Lag period (years)									
	0		5		10		15		20	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Any history	1.18	0.86–1.62	0.94	0.68–1.32	0.91	0.62–1.32	1.56	0.98–2.46	1.01	0.40–2.57
0.0	1.13	0.65–1.96	0.74	0.38–1.43	0.83	0.42–1.64	1.82	0.83–3.94	0.00	—*
0.001–0.999	1.07	0.74–1.55	0.88	0.59–1.30	0.84	0.54–1.33	1.72	0.98–2.98	1.64	0.57–4.69
1.00–4.999	1.68	0.97–2.91	1.60	0.90–2.83	1.38	0.73–2.64	1.64	0.71–3.79	0.95	0.10–9.26
≥5.00	1.23	0.60–2.51	0.87	0.40–1.90	0.67	0.36–1.83	0.29	0.04–2.27	0.00	—*
Asbestos/welding	1.41	1.10–1.81	1.47	1.14–1.90	1.60	1.24–2.07	1.58	1.21–2.06	1.63	1.23–2.16

* Not calculable.

asbestos/welding exposure remained significantly elevated across all lag periods. In fact, odds ratios for those exposures increased relative to nonlagged analysis through the five- and 10-year lag periods before leveling off through the 15- and 20-year periods.

Discussion

In this case-control study of 405 lung cancer deaths at the Portsmouth Naval Shipyard, odds ratios for exposure to gamma and x-radiation were elevated, whether exposure was defined as 1) any recorded radiation history, 2) measured cumulative exposure to 0.0 rem, 3) cumulative exposure to 0.001–0.999 rem, 4) cumulative exposure to 1.00–4.999 rem, or 5) cumulative exposure to at least 5.00 rem. The increase was statistically significant for the group with exposure to 1.0–4.999 rem when exposure to other known lung carcinogens was not considered. This finding was not unexpected because this group was, in essence, the same as that identified previously in a retrospective cohort mortality study of this population as having excess mortality from lung cancer (3). The observation of an elevated odds ratio in this group therefore substantiates the results of the standardized mortality ratio study, but does not by itself establish radiation as a factor in the etiology of lung cancer in workers at the Portsmouth Naval Shipyard.

Therefore, further analyses were performed to evaluate whether radiation itself or a combination of occupational exposures was responsible for the observed excess in lung cancer mortality at Portsmouth Naval Shipyard. These analyses revealed increased odds of having worked in areas in which asbestos and/or welding by-products were believed to be present. Separation of the effects of welding from those of asbestos was not possible because most persons with exposure to one of these agents also had exposure to the other. However, analysis of the group with the greatest exposures to asbestos (shop 56 workers) supports the notion that asbestos is responsible for some of the lung cancer risk; the most highly significant odds ratios were seen for this group.

Because exposures to asbestos and welding by-products were both significantly associated with mortality from lung cancer, attempts were made to consider the potential confounding effect of these combined exposures upon the observed association between radiation exposure and lung cancer. In this analysis, odds ratios for radiation exposure decreased for all dose categories examined. Thus, the hypothesis that radiation exposure accounted for the observed excess in lung cancer mortality could not be substantiated. Instead, it appears that exposures to asbestos and/or welding by-products were in large part responsible for the excess risk and confounded the observed association between radiation exposure and lung cancer.

In evaluating these findings, it is important to consider the potential importance for misclassification in the designation of various shops and jobs as having exposure to asbestos or welding by-products. In large part, these designations were subjective determinations based on examination of sparse industrial hygiene data, supplemented by field surveys and discussions with Portsmouth Naval Shipyard personnel. Most asbestos exposures had occurred prior to efforts by the shipyard to curtail them. Efforts were made to reduce misclassification in coding of all work histories by ensuring that all coders were blind to designation of cases and controls. The possibility of misclassification is considerably less likely for radiation exposures, in which there exists a relatively high degree of confidence in the data.

Another possible source of error in this study is selection of controls. Controls were selected and work histories coded in 1980. Since then, a preferred technique for control selection has been suggested (7). This technique calls for selecting controls randomly from the pool of persons alive and at risk of dying from lung cancer at the time the case dies. In an attempt to address the possible effect on the results of our approach to control selection, we conducted a supplementary analysis that restricted the study population by requiring the control to survive the case. With these restrictions, the size of the study population was diminished to 1,307 persons, 387 cases and 920 controls. Odds ratios for radiation categories 0.0 rem (OR = 1.13), 0.001–0.999 rem (OR = 1.09), 1.00–4.999 rem (OR = 1.80), and equal to or greater than 5.00 rem (OR = 1.20) were essentially unchanged in this analysis. In addition, the odds ratio for asbestos/welding exposure continued to show a statistically significant elevation (OR = 1.41, $p = 0.012$).

Radiation exposure has not existed in this shipyard for as many years as exposures to asbestos and welding. For that reason, our results may conceivably change in the future with the accumulation of additional latency.

No smoking histories were available in this study. A differential of smoking habits between workers exposed and those not exposed to radiation could introduce considerable bias on our results because of the well-documented synergistic relation between smoking and asbestos (12). In addition, because the shipyard recruited for job classifications such as planners and estimators from the ranks of the blue-collar tradesmen, there was no way to use job classification (as an indication of socioeconomic status) as a surrogate for smoking. However, we had no evidence indicating that radiation workers smoked either more or less than did other workers in the population. Therefore, throughout our analysis, we have assumed that the proportions of smokers and the number of cigarettes smoked were the same in all groups.

Statistical power calculations conducted at the outset of this investigation were intended to enable selection of an adequate number of controls for optimum study size. The lowest odds ratio considered was 1.5. Detection of odds ratios of less than 1.5 has statistical power considerably lower. For instance, the power of this study to detect a true relative risk of 1.3 was 56 per cent, and that to detect a true relative risk of 1.2 was 31 per cent. It is possible, therefore, that low excess relative risks could exist in this population, but could not be statistically detected. Although there is some disagreement as to the magnitude of excess risk at low levels of gamma and x-radiation, it can be deduced from most studies that the relative risk associated with the average dose in this cohort (<1 rem) would be below 1.1 (13–17). Although we were aware of the low power of this study for detection of slight excess risk at the outset, we were compelled to investigate the findings of the earlier cohort life table analysis (3) in greater detail. Our results are not inconsistent with the body of scientific literature concerning the relation between radiation and lung cancer (13–17).

References

1. Najarian T, Colton T. Mortality from leukemia and cancer in shipyard nuclear workers. Lancet 1978;1:1018–20.
2. National Institute for Occupational Safety and Health. Protocol: epidemiologic study of civilian employees at the Portsmouth Naval Shipyard, Kittery, Maine. Cincinnati, OH: National Institute for Occupational Safety and Health, 1978. US Department of Health and Human Services.
3. Rinsky RA, Zumwalde RD, Waxweiler RJ, et al. Epidemiologic study of civilian employees at the Portsmouth Naval Shipyard, Kittery, Maine. Report to the Director of the National Institute for Occupational Safety and Health, December 1980. Cincinnati, OH: US Department of Health and Human Services.
4. Rinsky RA, Zumwalde RD, Waxweiler RJ, et al. Cancer mortality at a naval nuclear shipyard. Lancet 1981;1:231–5.
5. Greenberg ER, Rosner B, Hennekens C, et al. An investigation of bias in a study of nuclear shipyard workers. Am J Epidemiol 1985;121:301–8.
6. Greenland S, Thomas DC. On the need for the rare disease assumption in case-control studies. Am J Epidemiol 1982;116:547–53.
7. Breslow N, Lubin J, Marek P, et al. Multiplicative models and cohort analysis. J Am Stat Assoc 1983;78:1–12.
8. Selikoff I. Asbestos-associated disease. In: Last JM, ed. Public health and preventive medicine. Norwalk, CT: Appleton-Century-Crofts, 1986: 523–45.
9. Beaumont J, Weiss N. Lung cancer among welders. J Occup Med 1981;23:839–44.
10. Mantel N, Haenszel W. Statistical aspects of the

analysis of data from retrospective studies of disease. JNCI 1959;22:719–48.
11. Kleinbaum D, Kupper L, Morgenstern H. Epidemiologic research: principles and quantitative methods. Belmont, CA: Lifetime Learning Publications, 1982.
12. Hammond E, Selikoff I, Seidman H. Asbestos exposure, cigarette smoking and death rates. Ann NY Acad Sci 1979;330:473–90.
13. National Research Council, Committee on the Biological Effects of Ionizing Radiation (BEIR III). The effects on populations of exposure to low levels of ionizing radiation. Washington, DC: National Academy of Sciences, 1980.
14. Kato H, Schull W. Studies of the mortality of A-bomb survivors. Radiat Res 1982;90:395–432.
15. Smith P, Doll R. Mortality among patients with ankylosing spondylitis after a single treatment course with x-rays. Br Med J 1982;284:449–60.
16. Boice J, Monson R, Rosenstein M. Cancer mortality in women after repeated fluoroscopic examinations of the chest. JNCI 1981;66:863–7.
17. Land C. Estimating cancer risks from low doses of ionizing radiation. Science 1980;209:1197–1203.