American Journal of Public Health

Reprint

Cancer Rates after the Three Mile Island Nuclear Accident and Proximity of Residence to the Plant

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ABSTRACT

Background: In the light of a possible link between stress and cancer promotion or progression, and of previously reported distress in residents near the Three Mile Island (TMI) nuclear power plant, we attempted to evaluate the impact of the March 1979 accident on community cancer rates.

Methods: Proximity of residence to the plant, which related to distress in previous studies, was taken as a possible indicator of accident stress; the postaccident pattern in cancer rates was examined in 69 "study tracts" within a 10-mile radius of TMI, in relation to residential proximity.

Results: A modest association was found between postaccident cancer rates and proximity (OR = 1.4; 95% CI = 1.3, 1.6). After adjusting for a gradient in cancer risk prior to the accident, the odds ratio contrasting those closest to the plant with those living farther out was 1.2 (95% CI = 1.0, 1.4). A postaccident increase in cancer rates near the Three Mile Island plant was notable in 1982, persisted for another year, and then declined. Radiation emissions, as modeled mathematically, did not account for the observed increase.

Conclusion: Interpretation in terms of accident stress is limited by the lack of an individual measure of stress and by uncertainty about whether stress has a biological effect on cancer in humans. An alternative mechanism for the cancer increase near the plant is through changes in care-seeking and diagnostic practice arising from postaccident concern. (*Am J Public Health.* 1991;81:719–724)

Introduction

Shortly after the accident at the Three Mile Island (TMI) nuclear power plant on March 28, 1979, some area residents believed an increase in cancer had occurred, although a detectable excess had not been predicted. In light of the low estimates of radiation emitted, the President's Commission on the Accident at Three Mile Island concluded that the sole health consequence for the population living nearby was mental distress.[1] Because of growing interest in the effects of stress on cancer promotion and progression, we attempted an ecologic test of the relationship between cancer rates and accident stress. Natural disasters have been associated with subsequent cancer risk in previous reports,[2,3] one of which proposed that a similar study be mounted in the Three Mile Island area.[3]

At Three Mile Island, levels of distress among area residents arose immediately after the accident[4–7] and alcohol consumption rose in parallel.[8] While distress levels were elevated, they were generally in the normal range and seemed to abate within nine months, although attitudinal effects such as distrust of authorities and concerns about safety persisted.[4,5] During clean-up and krypton venting at the plant, and restart of the undamaged reactor in October 1985, turmoil at Three Mile Island was ongoing and stress and consequent distress continued or recurred. A year after the accident, a sample of community residents exhibited significantly higher levels of stress hormones and stress symptoms than residents near undamaged nuclear or coal-powered plants although, again, the levels observed were within normal limits[9]; a similar survey five years postaccident found evidence of chronic stress.[10] Periodic resurveys of other cohorts at TMI have also showed persistent distress[11] and even clinical levels of anxiety, depression and hostility, particularly in those living close to the plant.[6,12–14]

In recent years, increased attention has focused on the possibility that stress and other psychosocial factors may affect the carcinogenic process[15–21]—perhaps through the action of corticosteroids on immune function[20,21] or of stress hormones like prolactin on regulation of neoplastic cell growth.[15,19] Indirect mechanisms involving behavioral risk factors also need to be considered, as do possible interactions between stress and other risk factors. While epidemiologic studies have looked for links between psychological states, personality traits, stressful life events and the onset and development of cancer, thus far the evidence is less than conclusive.[22–38] Two recent positive reports are fairly rigorous. In one, survival time for patients with metastatic breast cancer was found to be significantly increased among those randomized to a psychosocial intervention which reduced depression, anxiety, and pain.[39] In the other, severely stressful life events proved to be strongly predictive of a first recurrence of

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Editor's Note: See also related editorial on page 687 of this issue.

breast cancer in carefully matched patients with previously operable tumors.[40]

A biologic rationale connecting stress and cancer does exist. Inconsistent results from research in humans may indicate the lack of a true association, or a lack of understanding about how the neuroendocrine and immune systems mediate between psychosocial factors and cancer. In the present report, we summarize an *a priori*, if crude, test of the impact of an objective stress situation on a community's cancer rates.

Methods

The methods of this record-based geographic study are described in detail elsewhere.[41] Briefly, cancers among residents living within 10 miles of the TMI plant in the period 1975–85 were ascertained by review of patient charts at all local and regional referral hospitals (incident cases) and from vital certificates (deaths). The study area was divided into 69 small "study tracts," built up from census blocks, with populations ranging from 500-9,500 (2,300 on average). Cancers were assigned based on residence at diagnosis or at death, and for each study tract, annual rates of cancer incidence and mortality were calculated for the 11 years of the study period.

Cancer Sites Studied

In terms of the accident as a stressful event, we prespecified certain cancers or groupings of cancers for analysis, although there was little literature to guide us. Four categories were selected:

- *leukemias*, chosen because of their responsiveness to glucocorticoids, one of the "stress" hormones[42];
- *lymphomas*, which also respond to glucocorticoids and, in addition, are associated with immunosuppressive states[43];
- *"hormonally dependent" cancers* (breast, endometrium, ovary, prostate and testis), selected because stress hormones can alter concentrations of other hormones that affect cancer cells[19];
- the grouping *"all cancers"*, because in theory stress can influence the biology of all tumors through changes to the immune system.

Proximity as a Surrogate Measure of Stress

In the absence of any direct measure of stress, we used a surrogate measure supported by findings from the earlier psychosocial research at TMI. The measure is based on residential proximity to the Three Mile Island facility. A postaccident evacuation advisory issued by the Governor had focused public attention sharply on the area within a five-mile radius, with evident effect. Not only were evacuation rates higher in the five-mile radius, but so were rates of demoralization as determined by the President's Commission on Behavioral Effects.[4] Another population survey, by the Pennsylvania Department of Health,[5] found that as proximity increased so did the reported levels of perceived threat, of feeling "upset by the accident," and of psychophysiological symptoms. A study of mothers with young children found that those living in a five-mile radius of the TMI plant were more likely to experience a clinical episode of depression or anxiety than mothers living farther away.[14]

To evaluate residential proximity in the study reported here, we assigned each study tract a value corresponding to the distance between its midpoint and the TMI facility. The study area was also divided into three contiguous concentric rings based on natural breakpoints in the distribution of distances.

Proximity as Distinct from Radiation Emissions

While we treat residential proximity as a surrogate for accident-related stress, others have used it to define exposure to radiation near nuclear installations. Factors like wind direction, terrain, and elevation modify the distribution of exposures, however, and in the Three Mile Island area the terrain northeast and northwest of the plant directed emissions away from residents. In estimating radiation exposures, we developed mathematical models that take such modifying influences into account. Overlap between residential proximity and exposure to radiation emissions modeled mathematically is adjusted for in the analysis. A detailed description of the radiation emissions models is given in a separate report.[41]

Statistical Analyses

Logistic regression based on maximum likelihood estimation[44] was used to examine the age-sex-specific probability of cancer in relation to proximity of residence to the plant. Odds ratios derived from the logistic regression estimates were calculated contrasting median distance in the inner and outer rings. Indicator variables were used to adjust for a maximum of 16 age-sex categories (0–14, 15–24,. . . 65–74, 75 +). No adjustment was made for race since the population is over 96 percent White. Using aggregate data for each of the 69 study tracts, we adjusted for urbanization (population per km^2) and social class (median income; percent high school graduates), treating these measures as continuous variables.

The analyses were performed for both the preaccident period (January 1975-March 1979) and the period immediately following the accident (April 1979-December 1985). Where indicated, we used an unconditional logistic regression procedure to control for underlying heterogeneity among study tracts prior to the accident. This analysis, which is a means of adjusting for baseline risk, incorporates a parameter for each study tract, an indicator variable for period (preaccident or postaccident) and a distance variable coded zero before the accident and according to its assigned value after the accident. A conditional analysis based on a Poisson model gave similar results and is not presented here.

For descriptive purposes, we calculated standardized incidence ratios (SIRs) and standardized mortality ratios (SMRs) for the three rings at distances from the TMI facility of 0–6 km, >6–12 km, and >12 km, using age-sex-specific rates for Whites in the national Surveillance Epidemiology End Results (SEER) program (1978–81, Puerto Rico excluded).[45] However, interpretations are based on the regression analyses, which do not use an external standard.

Results

The distribution of population density, income and education by distance from the TMI plant (Table 1) shows that nearby areas are more urban and of lower socioeconomic status; these factors, as well as age and sex, are controlled in the logistic regression models.

Stress in Proximity to the Plant

For all cancers as a group, there is a statistically significant relationship between incidence rates (Table 2) after the accident and residential proximity to the plant (OR = 1.4; 95% CI = 1.3, 1.6). The association is present in both males (OR = 1.4; 95% CI = 1.2, 1.6) and females (OR = 1.5; 95% CI = 1.3, 1.7). Among the specific cancer categories tested, lymphoma shows the strongest association (OR = 1.9; 95% CI = 1.2, 3.0). Leukemias and hormonal tumors show associations of about the same magnitude as for all cancers. In addition, two common tumors

TABLE 1—Descriptive Data for Areas Defined by Distance of Midpoint from the Three Mile Island (TMI) Nuclear Plant

Distance (median) in kilometers	1980 Population[a]	Density per km^2	Median Income $	% High School Graduates
0–6 (4.3)	16,115	571	17,662	61.9
>6–12 (10.0)	60,654	316	19,452	68.8
>12 (14.2)	82,915	329	20,192	68.9

a) Midyear population estimates; adjustment has been made to the census figures for April 1, 1980.

TABLE 2—Incidence of Cancer and Proximity to TMI: Standardized Incidence Ratios (SIR)* and Odds Ratios (OR)‡ for Specific Cancer Types before and after the Accident

	Distance from Plant			
Cancer Grouping	0-6km SIR (obs)	>6-12km SIR(obs)	>12km SIR(obs)	OR (95% CI)
All Cancer				
Preaccident	0.9 (166)	0.7 (581)	0.7 (975)	1.2 (1.0,1.4)
Postaccident	1.1 (381)	1.0 (1423)	0.9 (1967)	1.4 (1.3,1.6)
Other Prespecified Sites				
Lymphoma				
Preaccident	1.7 (13)	0.7 (25)	1.0 (51)	1.2 (0.6,2.2)
Postaccident	1.5 (21)	0.9 (54)	0.9 (77)	1.9 (1.2,3.0)
Leukemia				
Preaccident	0.7 (4)	0.5 (12)	0.6 (23)	1.1 (0.4,3.0)
Postaccident	0.9 (9)	1.1 (43)	0.8 (51)	1.4 (0.8,2.5)
Hormonal[a]				
Preaccident	0.9 (45)	0.8 (165)	0.9 (298)	1.1 (0.8,1.4)
Postaccident	1.0 (86)	1.1 (408)	1.0 (581)	1.2 (1.0,1.4)
Selected Common Cancers				
Lung				
Preaccident	0.6 (17)	0.5 (61)	0.6 (116)	1.2 (0.8,1.8)
Postaccident	1.3 (67)	1.0 (214)	0.8 (282)	1.7 (1.3,2.1)
Colon				
Preaccident	0.7 (14)	0.8 (70)	0.8 (104)	1.1 (0.7,1.7)
Postaccident	1.7 (56)	1.3 (185)	1.0 (234)	1.7 (1.3,2.2)

*For calculation of SIRs, expectations are based on SEER (1978–81), age-specific rates for whites (excluding Puerto Rico). Number of observed cancers in parentheses.

‡Odds ratios comparing median distance in the inner ring with median distance in the outer ring, derived from logistic analysis adjusted for age, sex, density, median income, and education.

a) Includes breast, endometrium, ovary, prostate, and testis.

(lung and colon) also show associations with proximity to TMI (OR = 1.7 for each). The observed increase in "all cancers" thus seems to be due to increases in several cancer types.

For the "all cancer" grouping, rates in the area close to the plant are higher before the accident as well as afterwards. We corrected for the preaccident pattern by means of the procedure described above; the odds ratio adjusted for risk at baseline was reduced from 1.4 to 1.2 (95% confidence limits = 1.0, 1.4).

In Figure 1 we show incidence rates for all cancers for each year of the study period by proximity to the plant (three distance rings). By 1982, rates in the area closest to TMI were clearly elevated. The numbers of cases among residents of the inner ring rose from a yearly average of less than 50 to a high of 78 (a value that lies outside the 99% CI around 50 (33.7, 71.3), assuming the number of cases to be a Poisson variable). By 1984, the cancer rate had fallen to preaccident levels and by 1985 was lower than the rates in the more distant rings.

Mortality data (Table 3) suggest no general increase in cancer deaths with proximity to the plant in the postaccident period compared to the preaccident period. Neither do mortality rates for all cancers by year show any evidence of a change (data not presented).

Detection Bias

To test for detection bias arising from postaccident concern about cancer risk, we compared the relationship between stage at diagnosis and residential proximity to the plant in the periods before and after the event. Cancers of the breast, lung, colon, and prostate were selected since screening is common for these sites (see Table 4). With breast cancer, a shift in the postaccident period to an earlier stage at diagnosis is seen only among residents of the middle ring. For prostate cancer, residents of the inner ring actually show a decrease in the proportion of tumors diagnosed at an early stage after the accident compared to before. Lung and colon cancer show the reverse: after the accident, a higher proportion of tumors was diagnosed early among those living close to the plant.

Discussion

In an admittedly crude test of an accident-stress hypothesis, we found an increase in cancer following the accident that related to proximity of residence to the Three Mile Island nuclear plant. Cancer rates in those living nearest TMI rose in 1982, three years postaccident, remained raised for another year, and then declined. The relationship with proximity is unlikely to be explained by better case ascertainment for residents of the inner ring since, in the interests of comprehensive case-finding, we reviewed medical records at all hospitals within a 30-mile radius and at regional referral centers.

Residential proximity to the TMI plant was related to cancer rates prior to the accident as well as after, suggesting the presence of risk factors that were not sufficiently controlled by our adjustments for urbanization and social class. As a means of handling the confounding effects of unmeasured factors (e.g. cigarette smoking), we therefore adjusted for baseline risk. With this adjustment, the odds ratio for residential proximity after the accident was reduced to borderline statistical significance. Nonetheless, the postaccident pattern involving a sudden peak of excess cancers in residents near the plant does appear to be distinct from the preaccident pattern, which showed cancer rates in the inner ring to be slightly higher throughout the period.

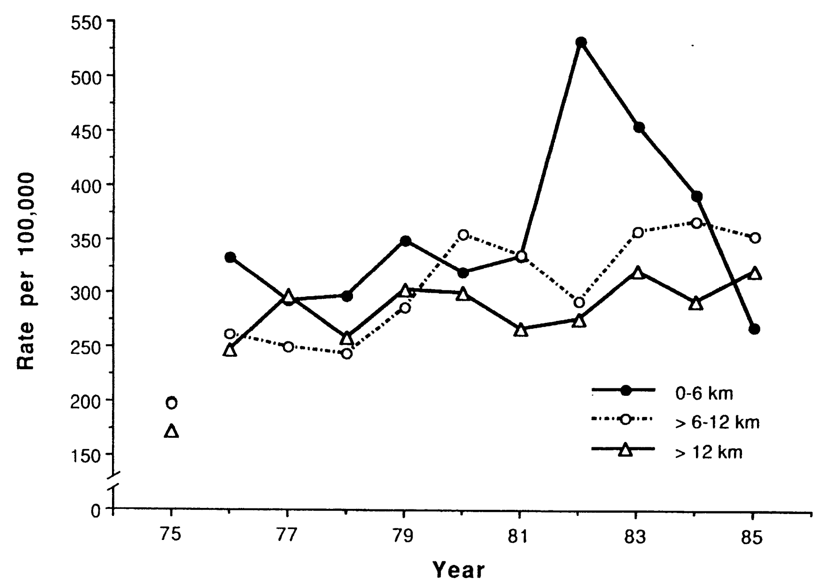

FIGURE 1—Yearly Age-adjusted Incidence Rates (100,000) of all Cancers, 1975-85, for Three Areas Defined by Distance from the TMI Nuclear Plant.

Note: In all three areas, figures were low for 1975, when hospital records were initially computerized.

TABLE 3—Mortality from Cancer and Proximity to TMI: Standarized Mortality Ratios (SMR)[a] and Odds Ratios (OR)[b] for Specific Cancer Types before and after the Accident

	Distance from Plant			
Cancer Grouping	0-6km SMR(obs)	>6-12km SMR(obs)	>12km SMR(obs)	OR (95% CI)
All Cancer				
Preaccident	1.3 (121)	1.0 (396)	1.0 (649)	1.2 (1.0,1.4)
Postaccident	1.0 (156)	1.1 (775)	1.0 (1119)	1.9 (0.9,1.2)
Other Prespecified Sites				
Lymphoma				
Preaccident	2.6 (9)	1.0 (15)	1.1 (28)	1.5 (0.7,3.1)
Postaccident	0.5 (3)	1.0 (27)	0.9 (38)	0.6 (0.3,1.3)
Leukemia				
Preaccident	0.7 (3)	0.6 (12)	1.1 (33)	0.5 (0.3,1.2)
Postaccident	0.8 (6)	1.2 (40)	0.9 (47)	1.0 (0.6,1.9)
Hormonal[c]				
Preaccident	1.2 (21)	1.2 (86)	1.0 (118)	1.4 (0.9,2.0)
Postaccident	0.7 (19)	1.2 (155)	1.2 (229)	0.8 (0.6,1.0)
Selected Common Cancers				
Lung				
Preaccident	1.2 (28)	0.8 (80)	0.9 (135)	1.4 (1.0,2.0)
Postaccident	1.0 (40)	1.0 (164)	0.9 (241)	1.3 (1.0,1.6)
Colon				
Preaccident	0.8 (9)	0.9 (40)	1.2 (84)	0.6 (0.4,1.1)
Postaccident	1.4 (25)	1.0 (80)	1.0 (125)	1.1 (0.8,1.6)

[a]For calculation of SMRs, expectations are based on SEER (1978-81), age-specific rates for whites (excluding Puerto Rico). Number of observed cancers in parentheses.
[b]Odds ratios comparing median distance in the inner ring with median distance in the outer ring, derived from logistic analysis adjusted for age, sex, density, median income, and education.
[c]Includes breast, endometrium, ovary, prostate, and testis.

Why a peak of cancer cases should arise in 1982, three years after the accident is not at all obvious. It could relate to increased cancer surveillance near the plant, particularly as the increase appears to involve several different cancer types. If residents changed their medical care habits following the accident, so that cancer was diagnosed earlier, a "screening effect" could arise, resulting in an initial inflation in cancer rates.[46] We sought and did not find consistent evidence of earlier detection near the plant in our comparison of preaccident and postaccident diagnostic trends. The absence of an increase in mortality rates—particularly for lung cancer which is rapidly fatal—may point to a screening bias, however, as may the dip in the cancer incidence rate near the plant in 1985, the last year of the study period. Distinguishing between improved surveillance, potentially stress-related, and a direct biological effect of stress is difficult with these data, particularly if, as seems likely, stress acts to accelerate the appearance of cancer rather than to initiate new cases.

In terms of a stress hypothesis, the study's major limitation is the lack of any measure of stress at the individual level. Using distance of residence from the plant to indicate stress is bound to introduce measurement error since individuals vary in both their perception of stressful events and response to them. It does seem reasonable to assume, however, that residents living close to the plant experienced more stress on average than residents living farther away. The Governor's evacuation advisory, issued two days after the accident, focused on a five-mile radius, and investigations of possible mental health consequences found that stress responses among area residents were related to distance from the plant.[4,5,9,14] In our study, however, the proximity measure is vulnerable to migration effects: inmigrants will not have been exposed to the stress of the accident but will be considered so in the analysis, and out-migrants may be self-selected for high stress levels. Given these sources of error, if stress does underlie the observed association between proximity to the plant and cancer risk, its effect could be underestimated. On the other hand, ecological associations frequently overestimate the magnitude of effects at the individual level.[47,48] Even if the stress hypothesis holds, the mechanism could be indirect. The stress of the accident could have increased exposure to behavioral risk factors, such as cigarette smoking, but we have no data with which

TABLE 4—Distribution (%) of Selected Cancers by Stage of Diagnosis[a] and Proximity to the Three Mile Island Plant for the Periods before and after the Accident

Stage at Diagnosis	0-6k pre	0-6k post	>6-12k pre	>6-12k post	>12k pre	>12k post
Breast Cancer						
Local	39.3	40.4	39.4	51.8	46.0	48.5
Regional	52.6	42.5	31.3	30.7	32.2	36.5
Distant	8.2	17.0	29.1	17.8	21.7	15.0
Prostate Cancer						
Local	62.2	41.7	56.1	59.8	53.3	60.9
Regional	9.0	13.5	20.2	10.7	17.7	15.6
Distant	28.8	44.9	23.7	29.5	29.0	23.5
Lung Cancer						
Local	30.7	36.9	37.5	24.0	23.6	26.7
Regional	23.9	16.9	13.6	26.2	29.4	25.5
Distant	45.4	46.4	48.9	49.8	47.0	47.9
Colon Cancer						
Local	29.7	39.3	30.9	29.1	27.0	30.8
Regional	43.9	29.9	31.7	34.7	35.9	36.2
Distant	26.4	30.8	37.4	36.2	37.1	33.0

[a]Among those with known stage of diagnosis.

to evaluate this possibility. Whatever the mechanism, a true effect on cancer produced in so short a time could only manifest itself by acting on preexisting cancers.

We carried out statistical analyses to test whether the gradient in cancer risk with residential proximity—present during routine operation of the Three Mile Island plant prior to the accident, as well as after—could possibly be explained by emissions from TMI. Fitting a multivariate regression model with both measures (proximity and plant emissions modeled mathematically) actually strengthens the association of proximity with cancer incidence. Also, the pattern of rise and fall in diagnosed cancers between 1982 and 1984 would not be expected with radiation.

Conclusion

In an analysis examining cancer rates and residential proximity to the Three Mile Island nuclear plant, we observed a modest postaccident increase in cancer near TMI that is unlikely to be explained by radiation emissions. The increase resulted from a small wave of excess cancers in 1982, three years after the 1979 accident. Such a pattern might reflect the impact of accident stress on cancer progression. Our study lacked a direct, individual measure of stress, however, The most plausible alternative explanation is that improved surveillance of cancer near the TMI plant led to the observed increase. Investigations of cancer patterns in communities with future environmental incidents should consider gathering data on stress and stress-related behaviors, including change in medial care-seeking, as well as on exposure to pollutants. □

Acknowledgments

We are indebted to Dr. Myunghee Paik for contributions to statistical analysis, to Christine Johnsen for field work, Hung Tao for computer programming, George Colbert for cartography, and Joyce White for preparation of the manuscript. We thank the Pennsylvania State Health Data Center for providing records of cancer deaths and the 25 participating hospitals for access to records of cancer patients. The research was supported by the Three Mile Island Public Health Fund, a court-supervised fund created to address public health issues of concern to residents of the area surrounding the TMI nuclear facility; we appreciate their support.

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