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# Occupational Exposure to Pesticides and Risk of Adult Brain Tumors

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## Abstract

The authors examined incident glioma and meningioma risk associated with occupational exposure to insecticides and herbicides in a hospital-based, case-control study of brain cancer. Cases were 462 glioma and 195 meningioma patients diagnosed between 1994 and 1998 in three US hospitals. Controls were 765 patients admitted to the same hospitals for nonmalignant conditions. Occupational histories were collected during personal interviews. Exposure to pesticides was estimated by use of a questionnaire, combined with pesticide measurement data abstracted from published sources. Using logistic regression models, the authors found no association between insecticide and herbicide exposures and risk for glioma and meningioma. There was no association between glioma and exposure to insecticides or herbicides, in men or women. Women who reported ever using herbicides had a significantly increased risk for meningioma compared with women who never used herbicides (odds ratio = 2.4, 95% confidence interval: 1.4, 4.3), and there were significant trends of increasing risk with increasing years of herbicide exposure ($p = 0.01$) and increasing cumulative exposure ($p = 0.01$). There was no association between meningioma and herbicide or insecticide exposure among men. These findings highlight the need to go beyond job title to elucidate potential carcinogenic exposures within different occupations.

Tumors of the brain, cranial nerves, and meninges account for 95 percent of tumors of the central nervous system (1) and include some of the most rapidly fatal types of cancer (2). An estimated 20,500 new cases of brain and other nervous system cancers were diagnosed during 2007 in the United States (3). The two most common histologic types of brain tumors are gliomas and meningiomas, and data suggest that gliomas are more common in men, while meningiomas occur more often in women (2).

The etiology of brain cancer is still poorly understood. Exposure to ionizing radiation and certain genetic abnormalities are the only established risk factors for brain tumors (2). Some studies suggest that hormonal factors are related to glioma and meningioma risk (4–7), and others indicate that brain tumors may be related to allergies or autoimmune disorders (8–10). Brain tumors have also been associated with several occupational and environmental exposures, including farming (11–13) and pesticides (2, 13–15). Some pesticides contain

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alkylureas or amines that metabolize to nitroso compounds, which have been associated with neurogenic tumors (15, 16).

Using data from a US hospital-based, case-control study of adult brain tumors conducted from 1994 to 1998, we examined risk of glioma and meningioma associated with occupational exposure to pesticides. Previous analyses of occupation and brain cancer risk in this study revealed a significant association between glioma and work as a general farmer or farmworker (odds ratio (OR) = 2.5, 95 percent confidence interval (CI): 1.4, 4.7) (11) and a nonstatistically significant association between meningioma and work as a general farmer or farmworker (OR = 2.0, 95 percent CI: 0.8, 5.3) (12). These analyses were based primarily on job title and did not include information about specific exposures. In the present study, we extend that work to examine associations between glioma and meningioma and occupational pesticide exposure using job-specific information.

## MATERIALS AND METHODS

This study has previously been described in detail (17). Participants were enrolled between 1994 and 1998 at one of three hospitals specializing in brain tumor treatment in Phoenix, Arizona; Boston, Massachusetts; and Pittsburgh, Pennsylvania. Eligible cases were patients 18 years or older who were newly diagnosed with intracranial glioma or other neuroepithelial neoplasms, meningioma, or acoustic neuroma (*International Classification of Diseases for Oncology*, Second Edition, codes 9380–9473, 9490–9506, 9530–9538, 9560) (18). This analysis focuses on glioma and meningioma. Controls were patients admitted to the same hospitals who were treated for various nonneoplastic conditions: injuries (25 percent), circulatory system disorders (22 percent), musculoskeletal disorders (22 percent), digestive disorders (12 percent), and other nonmalignant illnesses or conditions (19 percent). Study controls were frequency matched to the total case series on the basis of hospital, age (10–year intervals), sex, race/ethnicity, and distance of residence from the hospital. This study was approved by the institutional review boards of the National Cancer Institute and all participating hospitals.

Eligible cases and controls (or their next of kin) were contacted after permission was obtained from treating physicians, and written, informed consent was obtained from each participant. We interviewed 489 glioma patients (92 percent of those eligible), 197 meningioma patients (94 percent), and 799 control patients (86 percent). A structured interview was administered by a trained research nurse to all participants or their proxy respondents. The occupational section of the interview solicited information on each job held for 6 months or longer since the age of 16 years, including the name and location of each employer, type of product/service provided, job title, year started and stopped, full- or part-time work status, and principal activities. For 64 occupations of a priori interest, job-specific modules developed by an industrial hygienist were administered to elicit in-depth information on tasks and exposures for each job held for at least 2 years (19).

### Exposure assessment

We collected information on 8,535 jobs. Each job was assessed for insecticides and herbicides. Of the 64 job modules, only those for general farmer, farmworker, gardener, and janitor contained specific questions about herbicides and insecticides. Information on the types of pesticides used was collected only for farmers. However, there were too few farmers to allow analysis of specific pesticide active ingredients. Exposure assessment for all jobs for which there were no job modules, or for which we did not ask questions about pesticide use, was based on a job exposure matrix (JEM). The JEM was developed by an industrial hygienist (P. A. S.) who reviewed more than 500 published papers on pesticides, of which more than 100 reported dermal measurements. Dermal exposure is thought to contribute 90–95 percent of total exposure (20), so respiratory exposure was not considered.

Dermal pesticide exposure measurements were summarized from the literature to estimate exposure levels for each job/type of crop/method of use or application/decade where available for grain, vegetable, orchard, and animal farmers; exterminators; gardeners; farmworkers; and greenhouse, lawn care, forestry, golf course, and pesticide manufacturing workers. The only measurements used were those taken on unexposed skin or typical clothing, defined as that worn most often by the monitored subjects for each job. Farmers and farmworkers were asked about their typical clothing, and adjustments to the estimates were made on the basis of published protective factors. Based on these measurements, JEMs were developed for insecticides and herbicides, incorporating estimates for exposure metrics of probability, frequency, and intensity, as well as a confidence assigned to each of these exposure variables. JEM metrics were modified on the basis of the questionnaire information.

Each job was assessed for these metrics for insecticides and herbicides. *Probability* was defined as the percentage of people with the same job and industry in the same decade who were likely to have exposure and, based on the JEM, it was assessed as follows: 0 (specifically reported no use, reported <10 hours/year of use of the pesticide class, or 0 percent probability based on the JEM); 1 (>0–33 percent probability); 2 (>33–66 percent probability); 3 (>66–89 percent probability); or 4 (self-reported use or ≥90 percent probability). *Frequency* of exposure was defined as the average number of hours exposed to a pesticide in 1 week (hours per year/52 weeks), and it was categorized as follows: 1 (<2 hours/week); 2 (2–10 hours/week); 3 (11–19 hours/week); or 4 (≥20 hours/week). *Intensity* was defined as the average expected amount of pesticide deposited on the clothing or exposed skin during use and categorized as follows: 1 (<1 mg/hour); 2 (1–9 mg/hour); 3 (10–99 mg/hour); or 4 (≥100 mg/hour). Table 1 summarizes the most frequently assigned values of probability, frequency, and intensity for the most commonly reported jobs ($n$ > 100) and for general and livestock farmers, farmworkers, gardeners, and janitors. The top five most frequently reported jobs included waiter/waitress, sales clerk in grocery and drug stores, cashier in restaurants or food markets, teacher, and cook. About 25 percent of these jobs were categorized as exposed.

We assigned a confidence rating to each job and exposure metric (i.e., probability, frequency, intensity) as follows: 1 (the data were contradictory or no information was available); 2 (the value was based on the JEM); or 3 (the value was based on self-report or, for intensity, measurements were available). For farmworkers, we developed a matrix based upon the application method, the type of crop, and type of task, using the same JEM categories. Intensity for these jobs was modified according to the type of clothing reported as typically worn while working.

## Statistical analysis

We used unconditional logistic regression to estimate odds ratios and calculate 95 percent confidence intervals to examine the association between exposure to insecticides and herbicides and glioma and, for meningioma risk, for men and women separately. We included the following in the analysis: ever versus never exposed, duration exposed (sum of total years exposed), cumulative exposure (exposure intensity × exposure frequency × total years worked, summed across all exposed jobs), cumulative exposure lagged by 10 years, average exposure (cumulative exposure/total years worked in exposed jobs), and total years worked at the job with the highest exposure. Continuous exposure variables were categorized into quartiles or cut at the median, depending upon the total numbers of exposed participants. Cutpoints were based upon the percentile distributions of exposed controls, were gender specific, and were determined for herbicides and insecticides separately.

The covariates in our models were age (18–29, 30–39, 40–49, 50–59, 60–69, 70–79, ≥80 years), education (less than high school, high school diploma, post-high school), race (White/non-White), marital status, hospital location (Phoenix, Arizona; Boston, Massachusetts; Pittsburgh, Pennsylvania), proxy interview (yes/no), distance lived from the hospital (0–5, >5–15, >15–30, >30–50, >50 miles; 1 mile = 1.61 km), and household income in $1,000s (<15.0, 15.0–24.9, 25.0–34.9, 35.0–49.9, 50.0–74.9, ≥75.0). We initially included smoking and history of cranial radiotherapy, but the addition of these variables had little impact on our estimates, so we excluded them. In addition, only 31 patients reported a history of cranial radiotherapy. We evaluated brain tumor risk using six baseline models to account for the combinations of gender, exposure (herbicides, insecticides), and outcome (glioma, meningioma). Tests for trend were computed using the Wald statistic, treating the exposure variable as continuous by entering the median value for each level of the categorical variable among controls. We performed all analyses a second time excluding proxy respondents. We examined risk stratified by age (≤50, >50 years) and, for gliomas, tumor grade (high, low). To evaluate potential bias due to hospital controls, we systematically excluded control subgroups from our analyses. $p$ values were two sided, and statistical significance was set at $p < 0.05$.

We analyzed the data in three different ways to account for the varying levels of confidence associated with the exposure assessment. We initially considered all jobs with a probability of exposure of less than 2 as unexposed. This accounted for the uncertainty of our assigned exposures, but it did not account for the uncertainty of unexposed jobs. In a second analysis, we excluded all subjects who had at least one job, either exposed or unexposed, with low confidence (40 percent of cases; 40 percent of controls). Finally, we retained as many of the data as possible by using all jobs with an exposure probability of greater than 1, regardless of confidence level. Since the patterns of association were similar for all three methods, we report only the results using the full data set, regardless of confidence level.

## RESULTS

We excluded 159 patients missing one or more exposure or sociodemographic variables. A total of 765 controls and 462 glioma and 195 meningioma patients were retained (table 2). Glioma and meningioma patients tended to be slightly older than controls. Glioma patients were predominantly male, and meningioma patients were predominantly female. Patients with tumors tended to be more educated than controls, and the majority of cases and controls were White/non-Hispanic. Approximately 50 percent of the cases and controls were from the Phoenix hospital. There were more proxy interviews (either full proxy or assisted) conducted for glioma patients than for meningioma patients or controls.

### Glioma

There was no association between glioma and ever having been exposed to insecticides among men (OR = 1.0, 95 percent CI: 0.7, 1.5) or women (OR = 0.9, 95 percent CI: 0.6, 1.4) (table 3). For both genders, there was no significant association between glioma and total years of insecticide exposure or cumulative lifetime insecticide exposure. The results did not change appreciably when we lagged cumulative exposure by 10 years, and neither average lifetime exposure nor total years spent at the highest exposed job (data not shown) were associated with risk of glioma. For men, the results were similar for high- and low-grade glioma (table 4). There were too few glioma cases among exposed women to adequately examine risk by tumor grade. Our findings were similar for herbicides (table 3). There was no overall association between ever using herbicides and glioma risk in men (OR = 0.9, 95 percent CI: 0.6, 1.3) or women (OR = 1.3, 95 percent CI: 0.8, 2.0). We observed no association between glioma and total years of herbicide exposure or with cumulative lifetime herbicide exposure. The results did not change appreciably when we lagged cumulative exposure by 10 years, and neither average lifetime herbicide exposure nor total years spent at highest exposed job were associated with risk of glioma (data not shown).

### Meningioma

We observed no consistent association between meningioma and exposure to herbicides or insecticides among men (data not shown). Given that 77 percent of meningioma patients were female, there were only 16 insecticide- and eight herbicide-exposed male meningioma patients. Among women, there was no association between meningioma risk and insecticide exposure. Women who reported ever using herbicides had a significantly increased meningioma risk compared with women who never used herbicides (OR = 2.4, 95 percent CI: 1.4, 4.3) (table 5). We observed significant trends of increasing risk with increasing years of herbicide exposure ($p = 0.01$) and with increasing cumulative exposure ($p = 0.01$), which were somewhat stronger with 10-year lagging.

There were no striking differences in risk by age at interview for men (table 6) for glioma or meningioma. For women, meningioma risks associated with herbicide exposure were higher for women more than 50 years of age. There was an inverse trend in glioma risk among women aged 50 years or less and exposed to insecticides, most pronounced above the median cumulative exposure level of greater than 19.8 mg/hour. The overall trends in risk observed between insecticides and herbicides and both tumor types, in both sexes, did not change when we excluded proxy respondents. Excluding major control subgroups did not change our results.

## DISCUSSION

In this large, multicenter, case-control study of brain tumors, we found no overall association between exposure to insecticides or herbicides and glioma risk in men or women. Likewise, we found no association between exposure to insecticides or herbicides and meningioma risk among men and no association between exposure to insecticides and meningioma among women. Women with occupational herbicide exposure, however, appeared to experience an increased risk for meningioma.

Several studies have examined pesticide exposure and brain tumors as a group, not glioma and meningioma separately. Therefore, there is little published information concerning the association of pesticide exposure and meningioma risk. Most studies of pesticide manufacturing workers have not shown excesses of mortality from brain cancer (21–26), and some reported decreased risks for brain cancer (27–29). Results from studies of licensed pesticide applicators and studies that have examined the association between pesticides and all brain cancers as a group have yielded mixed results, with many reporting excess risks (30, 31), some reporting no excess risks (32, 33), and others reporting reduced risks (34, 35).

Findings from a Swedish cohort study suggested positive associations between glioma and employment as a farm supervisor, forestry supervisor, or horticultural worker; however, occupational exposure to herbicides was not associated with glioma risk (36). Results from an Italian case-control study suggested a fourfold excess risk for glioma among farmers who used insecticides and fungicides and a threefold excess risk among herbicides users (15). A recent case-control study of pesticide use and glioma in Nebraska reported excess glioma risks for ever use of two herbicides and three insecticides, but these risks were attenuated after excluding proxy respondents (37). Findings from an international case-control study of occupation and glioma indicated no association between use of pesticides and either high- or low-grade glioma (38). In a US study, Ruder et al. (39) found no associations between glioma risk and 12 specific pesticides, but they found reduced risks for glioma incidence associated with insecticides, fumigants, and organochlorine insecticides. Provost et al. (40) reported a significantly increased risk for glioma, but not for meningioma, associated with the highest quartile of cumulative occupational exposure to pesticides. The authors reported risks for men and women combined and did not examine risk associated with different classes of pesticides.

In previous analyses of our data, work as a general farmer or farmworker was positively associated with glioma (11) and meningioma (12). These analyses based on job and industry titles assumed that all participants who held the same job in the same industry had similar exposures. Specific exposures underlying the excess risks noted among farmers and farmworkers, such as pesticides, could only be hypothesized. In the present study, only 13 of 81 farmer and 19 of 81 farmworker jobs were classified as exposed to insecticides or herbicides; either participants reported that they had never applied pesticides, or the detailed job information indicated no exposure. It is likely that our exposure assessment method reduced the potential misclassification of exposure status assumed from job titles (19, 41).

To our knowledge, there have been no studies investigating meningioma and pesticide-exposed women. Our finding that women exposed to herbicides experienced increased meningioma risk may be a chance finding, and our results should be interpreted cautiously. Women in the highest exposure category for herbicides ($n$ = 17) were workers in eating places (eight jobs), grocery stores (seven jobs), and hardware stores (one job); a gardener; an apple farm laborer; a mobile home park manager; and a potato processor. Workers in eating places, grocery stores, and the potato processor were likely to have handled produce contaminated with herbicides, while the hardware cashier was likely to have handled contaminated herbicide spray cans.

It is unclear why we observed an inverse association between glioma and cumulative insecticide exposure among younger women; however, this pattern was not consistent across other insecticide exposure metrics. We know of no evidence that suggests that women's susceptibility to these compounds differs from that of men. Hormonal factors have also been associated with meningiomas and gliomas, but results have been inconsistent. In this population, we observed an excess glioma risk associated with older age at menarche (4). Others have also reported this association, while associations reported for hormone replacement therapy use and glioma have been inconsistent (6, 7). For meningioma, some have reported higher risk associated with use of hormone replacement therapy (5, 42), age at menarche and parity (5), and hormonal contraceptives (43) but reduced risk associated with menopause (44) and number of pregnancies (45). Others reported no association with parity and age at first birth (46), age at menarche (45), and oral contraceptive use (5, 42, 45).

Strengths of our study include a large number of histologically confirmed glioma and meningioma brain tumors, high participation rates, rapid identification of incident cancers, detailed exposure information for some jobs, and the extensive pesticide literature, which aided our exposure assessment. Our results may have been affected by differential recall between glioma and meningioma patients, as glioma patients may experience more impaired memory or cognition than do meningioma patients (17). It is unlikely that our results were markedly affected by differential recall between study participants and proxy respondents since our results did not change appreciably after excluding proxies from the analyses. Because we conducted the exposure assessment without knowledge of diagnoses, any potential exposure misclassification was likely to be nondifferential. We also attempted to minimize any referral bias by frequency matching cases and controls on distance between hospital and residence.

We cannot rule out the possibility of chance findings due to small numbers of pesticide-exposed individuals for certain analyses. Other farm exposures, such as zoonotic viruses, dusts, and solvents, may explain the previously reported associations between farming and brain cancers (11). Alternatively, excesses found in some studies may reflect the use of specific pesticides that were not used, or used rarely, by participants in our study. We were unable to examine the effects of individual pesticides because few participants recalled specific pesticide names. We had incomplete data concerning residential pesticide treatments. Levels of household application, however, tend to be substantially lower than what farmers experience during occupational application.

In this large, multicenter, case-control study of glioma and meningioma, we found that women occupationally exposed to herbicides were at increased risk for meningioma, which increased as exposure duration increased. Our examination of pesticide exposure was a follow-up analysis of occupation and brain cancer (11, 12), and we used detailed, job-specific exposure information collected through the administration of job-module questionnaires. Our findings highlight the need to go beyond job title in order to elucidate potential carcinogenic exposures within different occupations.

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## TABLE 1

Most frequently assigned levels of exposure probability, frequency, and intensity for the most frequently reported jobs (*n* > 100) and general/livestock/dairy farmer, farmworker, gardener, and janitor, Phoenix, Arizona, Boston, Massachusetts, and Pittsburgh, Pennsylvania, 1994–1998*

| Occupation (SOC†) | Total no. of jobs | Insecticides | | | | Herbicides | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Total exposed‡ | Probability§ | Frequency¶ | Intensity# | Total exposed‡ | Probability§ | Frequency¶ | Intensity# |
| Waiter/waitress (5213) | 803 | 266 | 3 | 4 | 1 | 0 | | | |
| Sales clerk (4362), grocery and drug stores | 618 | 82 | 3 | 2 | 1 | 43 | 3 | 2 | 1 |
| Cashier (4364), restaurants and food markets | 534 | 108 | 3 | 2 | 1 | 54 | 3 | 2 | 1 |
| Teacher (2300) | 471 | 114 | 2 | 2 | 1 | 0 | | | |
| Cook, except short order (5214) | 306 | 102 | 3 | 4 | 1 | 89 | 3 | 3 | 1 |
| Janitor (5244) | 228 | 43 | 2 | 1 | 1 | 8 | 3 | 2 | 1 |
| Kitchen worker (5217) | 225 | 72 | 3 | 2, 4 | 1 | 69 | 3 | 3 | 1 |
| Stock handler/bagger (8724), grocery stores | 171 | 42 | 3 | 2 | 1 | 31 | 3 | 2 | 1 |
| Carpenter (6422) | 162 | 28 | 4 | 2 | 1 | 0 | | | |
| Miscellaneous food and beverage preparation (5219) | 141 | 47 | 3 | 4 | 1 | 44 | 2 | 3 | 1 |
| Gardener, nonfarm (5622) | 138 | 18 | 4 | 1 | 4 | 22 | 4 | 1 | 4 |
| Farmworker (5612) | 81 | 19 | 4 | 2 | 3 | 9 | 2, 3 | 1, 2, 3 | 2, 3 |
| General farmer (5512) | 81 | 13 | 2, 4 | 1, 2 | 1, 3, 4 | 6 | 4 | 1, 2 | 3, 4 |
| Livestock/dairy farmer (5514) | 36 | 7 | 4 | 1 | 3 | 3 | 4 | 1 | 3, 4 |

*Categories with more than one value indicate jobs for which levels were assigned with equal frequency because of small numbers of exposed jobs.

†SOC, Standard Occupational Classification (a universal occupational classification system produced by the US Department of Labor, Bureau of Labor Statistics (http://www.bls.gov/soc/soc_k9j2.htm).

‡"Total exposed" equals the total number of jobs classified as having any exposure to either insecticides and/or herbicides on the basis of industry, decade, and description of job activities.

§Values for each job represent the most frequent value assigned for probability of exposure to either insecticides or herbicides, using the following scale: 0 (reported no use, reported <10 hours per year of use, or 0% probability based on the job exposure matrix (JEM)); 1 (>0–33% probability based on the JEM); 2 (>33–66% probability based on the JEM); 3 (>66–89% probability based on the JEM); 4 (self-reported use or ≥90% probability based on the JEM).

¶Values for each job represent the most frequent value assigned for frequency of exposure (average number of hours per week in 1 year) to either insecticides or herbicides, using the following scale: 1 (<2 hours/week); 2 (2–10 hours/week); 3 (11–19 hours/week); 4 (≥20 hours/week).

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#Values for each job represent the most frequent value assigned for intensity of exposure (average milligrams per hour of dermal exposure) to either insecticides or herbicides, using the following scale: 1 (<1 mg/hour); 2 (1–9 mg/hour); 3 (10–99 mg/hour); 4 (≥100 mg/hour).

## TABLE 2

Characteristics of study controls and glioma and meningioma cases, Phoenix, Arizona, Boston, Massachusetts, and Pittsburgh, Pennsylvania, 1994–1998

| | Controls ($n$ = 765) | | Glioma ($n$ = 462) | | Meningioma ($n$ = 195) | |
|---|---|---|---|---|---|---|
| | No. | % | No. | % | No. | % |
| Age at interview (years) | | | | | | |
| Median | 49 | | 51 | | 54 | |
| 18–29 | 78 | 10.2 | 45 | 9.7 | 4 | 2.1 |
| 30–39 | 145 | 19.0 | 72 | 15.6 | 28 | 14.5 |
| 40–49 | 164 | 21.4 | 101 | 21.9 | 43 | 22.1 |
| 50–59 | 148 | 19.4 | 74 | 16.0 | 44 | 22.6 |
| 60–69 | 122 | 16.0 | 86 | 18.6 | 39 | 20.0 |
| 70–79 | 85 | 11.1 | 72 | 15.6 | 29 | 14.8 |
| ≥80 | 23 | 3.0 | 12 | 2.6 | | 4.1 |
| Female gender | 415 | 54.3 | 201 | 43.5 | 149 | 76.4 |
| Education | | | | | | |
| Less than high school | 101 | 13.2 | 62 | 13.4 | 23 | 11.8 |
| High school diploma | 230 | 30.1 | 120 | 26.0 | 57 | 29.2 |
| Post-high school | 434 | 56.7 | 280 | 60.6 | 115 | 59.0 |
| Race/ethnicity | | | | | | |
| White, non-Hispanic | 686 | 89.7 | 422 | 91.3 | 162 | 83.1 |
| Other | 79 | 10.3 | 40 | 8.7 | 33 | 16.9 |
| Marital status, married | 441 | 57.7 | 332 | 71.9 | 137 | 70.3 |
| Hospital location | | | | | | |
| Phoenix, AZ | 382 | 49.9 | 232 | 50.2 | 98 | 50.3 |
| Boston, MA | 219 | 28.6 | 142 | 30.7 | 79 | 40.5 |
| Pittsburgh, PA | 164 | 21.4 | 88 | 19.1 | 18 | 9.2 |
| Distance from hospital (miles*) | | | | | | |
| 0–5 | 252 | 32.9 | 118 | 25.5 | 57 | 29.2 |
| >5–15 | 221 | 28.9 | 146 | 31.6 | 56 | 28.7 |
| >15–30 | 157 | 20.5 | 112 | 24.2 | 43 | 22.1 |

| | Controls (*n* = 765) | | Glioma (*n* = 462) | | Meningioma (*n* = 195) | |
|---|---|---|---|---|---|---|
| | **No.** | **%** | **No.** | **%** | **No.** | **%** |
| >30–50 | 56 | 7.3 | 38 | 8.2 | 17 | 8.7 |
| >50 | 79 | 10.3 | 48 | 10.4 | 22 | 11.3 |
| Proxy interview | 22 | 2.4 | 78 | 15.2 | 15 | 7.2 |
| Jewish religion | 27 | 3.5 | 27 | 5.8 | 21 | 10.8 |
| Household income ($1,000s) | | | | | | |
| <15.0 | 118 | 16.4 | 43 | 9.9 | 16 | 9.0 |
| 15.0–24.9 | 110 | 15.3 | 71 | 16.4 | 31 | 17.4 |
| 25.0–34.9 | 101 | 14.1 | 66 | 15.2 | 29 | 16.3 |
| 35.0–49.9 | 128 | 17.8 | 81 | 18.7 | 31 | 17.4 |
| 50.0–74.9 | 143 | 19.9 | 78 | 18.0 | 32 | 18.0 |
| ≥75.0 | 119 | 16.6 | 95 | 21.9 | 39 | 21.9 |

* One mile = 1.61 km.

## TABLE 3

Odds ratios and 95% confidence intervals for glioma and occupational exposure to insecticides and herbicides, Phoenix, Arizona, Boston, Massachusetts, and Pittsburgh, Pennsylvania, 1994–1998

| | Men | | | | | Women | | | |
|---|---|---|---|---|---|---|---|---|---|
| **Occupational exposure (mg)** | **No. of controls (*n* = 350)** | **No. of cases (*n* = 261)** | **Odds ratio** | **95% confidence interval** | | **No. of controls (*n* = 415)** | **No. of cases (*n* = 201)** | **Odds ratio** | **95% confidence interval** |
| | | | | | *Ever exposed* | | | | |
| Insecticides* | 176 | 125 | 1.0 | 0.7, 1.5 | Insecticides† | 225 | 102 | 0.9 | 0.6, 1.4 |
| Herbicides* | 103 | 65 | 0.9 | 0.6, 1.3 | Herbicides† | 71 | 35 | 1.3 | 0.8, 2.0 |
| | | | | | *Total years exposed* | | | | |
| Insecticides (quartiles) | | | | | | | | | |
| Unexposed* | 174 | 136 | 1.0 | | Unexposed† | 190 | 99 | 1.0 | |
| >0–1.2 | 41 | 33 | 1.1 | 0.7, 1.9 | >0–1 | 61 | 34 | 1.1 | 0.6, 1.9 |
| >1.2–3 | 49 | 36 | 1.1 | 0.7, 1.9 | >1–3 | 52 | 19 | 0.8 | 0.4, 1.5 |
| >3–9 | 43 | 23 | 0.8 | 0.5, 1.5 | >3–9.0 | 54 | 24 | 0.9 | 0.5, 1.7 |
| >9 | 43 | 33 | 1.1 | 0.7, 1.9 | >9.0 | 58 | 25 | 0.9 | 0.5, 1.7 |
| | | | $p = 0.87$ | | | | | $p = 0.83$ | |
| Herbicides (quartiles)‡ | | | | | | | | | |
| Unexposed* | 247 | 196 | 1.0 | | Unexposed‡ | 344 | 166 | 1.0 | |
| >0–1 | 37 | 25 | 1.0 | 0.5, 1.7 | >0–2 | 43 | 22 | 1.2 | 0.7, 2.2 |
| >1–2 | 19 | 12 | 1.0 | 0.4, 2.1 | >2 | 28 | 13 | 1.3 | 0.6, 2.7 |
| >2–5 | 21 | 18 | 1.2 | 0.6, 2.4 | | | | | |
| >5 | 26 | 10 | 0.5 | 0.2, 1.0 | | | | | |
| | | | $p = 0.08$ | | | | | $p = 0.45$ | |
| | | | | | *Cumulative lifetime exposure* | | | | |
| Insecticides (quartiles) | | | | | | | | | |
| Unexposed* | 174 | 136 | 1.0 | | Unexposed† | 190 | 99 | 1.0 | |
| >0–5 | 44 | 35 | 1.2 | 0.7,2.0 | >0–2.5 | 61 | 31 | 1.0 | 0.6, 1.8 |
| >5–27 | 42 | 35 | 1.4 | 0.8.2.3 | >2.5–19.8 | 49 | 29 | 1.2 | 0.7, 2.2 |
| >27–90 | 45 | 21 | 0.6 | 0.3, 1.1 | >19.8–75 | 61 | 23 | 0.7 | 0.4, 1.3 |

| Occupational exposure (mg) | Men: No. of controls ($n$ = 350) | Men: No. of cases ($n$ = 261) | Men: Odds ratio | Men: 95% confidence interval | | Women: No. of controls ($n$ = 415) | Women: No. of cases ($n$ = 201) | Women: Odds ratio | Women: 95% confidence interval |
|---|---|---|---|---|---|---|---|---|---|
| >90 | 45 | 34 | 1.1 | 0.6, 1.8 | >75 | 54 | 19 | 0.8 | 0.5, 1.6 |
| | | | | $p$ = 0.97 | | | | | $p$ = 0.48 |
| Insecticides (quartiles), lag 10 years | | | | | | | | | |
| Unexposed* | 199 | 153 | 1.0 | | Unexposed† | 220 | 115 | 1.0 | |
| >0–5 | 41 | 33 | 1.1 | 0.7, 1.9 | >0–2.5 | 54 | 25 | 0.9 | 0.5, 1.6 |
| >5–22.5 | 36 | 27 | 1.2 | 0.7, 2.1 | >2.5–15 | 49 | 19 | 0.8 | 0.4, 1.5 |
| >22.5–68.8 | 36 | 19 | 0.7 | 0.4, 1.4 | >15–63.5 | 44 | 23 | 1.2 | 0.6, 2.1 |
| >68.8 | 38 | 29 | 1.0 | 0.6, 1.8 | >63.5 | 48 | 19 | 0.9 | 0.5, 1.7 |
| | | | | $p$ = 0.92 | | | | | $p$ = 0.90 |
| Herbicides (quartiles)‡ | | | | | | | | | |
| Unexposed* | 247 | 196 | 1.0 | | Unexposed† | 344 | 166 | 1.0 | |
| >0–2.5 | 28 | 20 | 1.0 | 0.5, 1.9 | >0–7.5 | 39 | 23 | 1.6 | 0.8, 2.7 |
| >2.5–9.8 | 22 | 16 | 1.0 | 0.5, 2.1 | >7.5 | 32 | 12 | 1.0 | 0.5, 2.1 |
| >9.8–45 | 27 | 12 | 0.6 | 0.3, 1.3 | | | | | |
| >45 | 26 | 17 | 0.8 | 0.4, 1.6 | | | | | |
| | | | | $p$ = 0.50 | | | | | $p$ = 0.91 |
| Herbicides (quartiles), lag 10 years‡ | | | | | | | | | |
| Unexposed* | 271 | 204 | 1.0 | | Unexposed† | 357 | 172 | 1.0 | |
| >0–2.5 | 22 | 19 | 1.2 | 0.6, 2.4 | >0–2.5 | 30 | 10 | 0.8 | 0.4, 1.8 |
| >2.5–8.1 | 18 | 11 | 0.8 | 0.4, 1.9 | >2.5 | 28 | 19 | 1.7 | 0.9, 3.3 |
| >8.1–40 | 19 | 12 | 1.0 | 0.5, 2.1 | | | | | |
| >40 | 20 | 15 | 0.9 | 0.5, 2.0 | | | | | |
| | | | | $p$ = 0.85 | | | | | $p$ = 0.28 |

*Adjusted for age (18–29, 30–39, 40–49, 50–59, 60–69, 70–79, ≥80 years), hospital location (Phoenix, Boston, Pittsburgh), and proxy interview (yes/no).

†Adjusted for age, hospital location, proxy interview, distance lived from hospital (0–5, >5–15, >15–30, >30–50, >50 miles), and marital status (married/not married). One mile = 1.61 km.

‡Exposure categories for women were cut at the median because of the smaller number of female glioma patients.

## TABLE 4

Odds ratios and 95% confidence intervals for glioma and cumulative exposure to insecticides and herbicides, stratified by tumor grade (men only), Phoenix, Arizona, Boston, Massachusetts, and Pittsburgh, Pennsylvania, 1994–1998*

| Cumulative lifetime exposure (mg) | High grade | | | | Low grade | | | |
|---|---|---|---|---|---|---|---|---|
| | **No. of controls** | **No. of cases** | **Odds ratio** | **95% confidence interval** | **No. of controls** | **No. of cases** | **Odds ratio** | **95% confidence interval** |
| Insecticides (quartiles) | | | | | | | | |
| Unexposed | 174 | 24 | 1.0 | | 174 | 112 | 1.0 | |
| >0–5 | 44 | 10 | 1.3 | 0.5, 3.2 | 44 | 25 | 1.3 | 0.7, 2.3 |
| >5–27 | 42 | 12 | 1.9 | 0.8, 4.6 | 42 | 23 | 1.3 | 0.7, 2.4 |
| >27–90 | 45 | 7 | 0.9 | 0.4, 2.4 | 45 | 14 | 0.6 | 0.3, 1.1 |
| >90 | 45 | 12 | 1.7 | 0.7, 3.9 | 45 | 22 | 0.9 | 0.5, 1.7 |
| | | | | *p* = 0.33 | | | | *p* = 0.60 |
| Herbicides (quartiles) | | | | | | | | |
| Unexposed | 247 | 40 | 1.0 | | 247 | 156 | 1.0 | |
| >0–2.5 | 28 | 8 | 1.0 | 0.4, 2.4 | 28 | 12 | 1.0 | 0.5, 2.2 |
| >2.5–9.83 | 22 | 8 | 1.5 | 0.6, 4.0 | 22 | 8 | 0.9 | 0.4, 2.2 |
| >9.83–45 | 27 | 5 | 0.8 | 0.3, 2.2 | 27 | 7 | 0.6 | 0.2, 1.4 |
| >45 | 26 | 4 | 0.6 | 0.2, 1.8 | 26 | 13 | 1.0 | 0.5, 2.0 |
| | | | | *p* = 0.31 | | | | *p* = 0.89 |

*Adjusted for age (18–29, 30–39, 40–49, 50–59, 60–69, 70–79, ≥80 years), education (less than high school, high school diploma, post-high school), hospital location (Phoenix, Boston, Pittsburgh), proxy interview (yes/no), race (White, non-White), and distance from hospital (0–30, >30 miles). One mile = 1.61 km.

## TABLE 5

Odds ratios and 95% confidence intervals for meningioma and occupational exposure to insecticides and herbicides (women only), Phoenix, Arizona, Boston, Massachusetts, and Pittsburgh, Pennsylvania, 1994–1998*

| Occupational exposure (mg) | No. of controls (*n* = 415) | No. of cases (*n* = 149) | Odds ratio | 95% confidence interval |
|---|---|---|---|---|
| | | *Ever exposed* | | |
| Insecticides | 225 | 80 | 1.3 | 0.8, 2.0 |
| Herbicides | 71 | 33 | 2.4 | 1.4, 4.3 |
| | | *Total years exposed* | | |
| Insecticides (quartiles) | | | | |
| Unexposed | 190 | 69 | 1.0 | |
| >0–1 | 61 | 12 | 0.8 | 0.4, 1.6 |
| >1–3 | 52 | 16 | 0.8 | 0.4, 1.8 |
| >3–9.045 | 54 | 31 | 2.4 | 1.3, 4.5 |
| >9.045 | 58 | 21 | 1.2 | 0.6, 2.4 |
| | | | | $p = 0.21$ |
| Herbicides (quartiles) | | | | |
| Unexposed | 344 | 116 | 1.0 | |
| >0–5 | 31 | 11 | 2.0 | 0.9, 4.6 |
| >5–27 | 12 | 4 | 1.1 | 0.2, 5.7 |
| >27–90 | 13 | 9 | 3.8 | 1.4, 10.3 |
| >90 | 15 | 9 | 3.0 | 1.0, 8.5 |
| | | | | $p = 0.01$ |
| | | *Cumulative lifetime exposure* | | |
| Insecticides (quartiles) | | | | |
| Unexposed | 190 | 69 | 1.0 | |
| >0–2.5 | 61 | 11 | 0.7 | 0.3, 1.5 |
| >2.5–19.8 | 49 | 26 | 1.6 | 0.8, 3.2 |
| >19.8–75.0 | 61 | 23 | 1.4 | 0.7, 2.7 |
| >75.0 | 54 | 20 | 1.5 | 0.8, 2.9 |
| | | | | $p = 0.23$ |
| Insecticides (quartiles), lag 10 years | | | | |
| Unexposed | 220 | 72 | 1.0 | |
| >0–2.5 | 54 | 14 | 1.1 | 0.5, 2.3 |
| >2.5–15 | 49 | 27 | 1.7 | 0.9, 3.3 |
| >15–63.5 | 44 | 20 | 1.3 | 0.7, 2.7 |
| >63.5 | 48 | 16 | 1.3 | 0.7, 2.7 |
| | | | | $p = 0.51$ |
| Herbicides (median) | | | | |
| Unexposed | 344 | 116 | 1.0 | |
| >0–1.25 | 39 | 16 | 2.1 | 1.0, 4.4 |

| Occupational exposure (mg) | No. of controls ($n$ = 415) | No. of cases ($n$ = 149) | Odds ratio | 95% confidence interval |
|---|---|---|---|---|
| >27.125 | 32 | 17 | 2.9 | 1.3, 6.2 |
| | | | | $p = 0.01$ |
| Herbicides (median), lag 10 years | | | | |
| Unexposed | 357 | 117 | 1.0 | |
| >0–2.5 | 30 | 11 | 2.3 | 1.0, 5.2 |
| >2.5 | 28 | 21 | 3.0 | 1.5, 6.2 |
| | | | | $p = 0.004$ |

* Adjusted for age (18–29, 30–39, 40–49, 50–59, 60–69, 70–79, ≥80 years), hospital location (Phoenix, Boston, Pittsburgh), proxy interview (yes/no), race (White, non-White), marital status (married/not married), Jewish religion (yes/no), and household income in $1,000s (<15.0, 15.0–24.9, 25.0–34.9, 35.0–49.9, 50.0–74.9, ≥75.0).

## TABLE 6

Odds ratios and 95% confidence intervals for glioma and meningioma and cumulative exposure to insecticides/herbicides, stratified by age (≤50 vs. >50 years), Phoenix, Arizona, Boston, Massachusetts, and Pittsburgh, Pennsylvania, 1994–1998

| Cumulative lifetime exposure (mg) | Glioma | | | | Meningioma | | | |
|---|---|---|---|---|---|---|---|---|
| | No. of controls | No. of cases | Odds ratio | 95% confidence interval | No. of controls | No. of cases | Odds ratio | 95% confidence interval |
| *Men* | | | | | | | | |
| Inspecticides | | | | | | | | |
| Up to 50 years of age | | | | | | | | |
| Unexposed | 69 | 49 | 1.0* | | 69 | 9 | 1.0* | |
| >0–27 | 53 | 49 | 1.5 | 0.9, 2.6 | 53 | 5 | 0.8 | 0.2, 2.7 |
| >27 | 52 | 29 | 0.8 | 0.5, 1.5 | 52 | 1 | | |
| | | | | $p = 0.22$ | | | | |
| Over 50 years of age | | | | | | | | |
| Unexposed | 105 | 87 | 1.0* | | 105 | 21 | 1.0* | |
| >0–27 | 33 | 21 | 0.9 | 0.5, 1.8 | 33 | 3 | 0.5 | 0.1, 1.8 |
| >27 | 38 | 26 | 0.9 | 0.5, 1.6 | 38 | 7 | 0.9 | 0.3, 2.3 |
| | | | | $p = 0.68$ | | | | $p = 0.97$ |
| Herbicides | | | | | | | | |
| Up to 50 years of age | | | | | | | | |
| Unexposed | 96 | 74 | 1.0* | | 96 | 13 | 1.0† | |
| >0–9.83 | 38 | 34 | 1.3 | 0.7, 2.2 | 38 | 2 | 0.5 | 0.1, 2.4 |
| >9.83 | 40 | 19 | 0.6 | 0.3, 1.2 | 40 | 0 | | |
| | | | | $p = 0.11$ | | | | |
| Over 50 years of age | | | | | | | | |
| Unexposed | 151 | 122 | 1.0* | | 151 | 27 | 1.0† | |
| >0–9.83 | 12 | 2 | 0.2 | 0.1, 1.1 | 12 | 2 | 1.6 | 0.3, 9.6 |
| >9.83 | 13 | 10 | 1.0 | 0.4, 2.4 | 13 | 2 | 0.4 | 0.1, 2.9 |
| | | | | $p = 0.96$ | | | | $p = 0.38$ |
| *Women* | | | | | | | | |
| Insecticides | | | | | | | | |

| Cumulative lifetime exposure (mg) | Glioma | | | | Meningioma | | | |
|---|---|---|---|---|---|---|---|---|
| | No. of controls | No. of cases | Odds ratio | 95% confidence interval | No. of controls | No. of cases | Odds ratio | 95% confidence interval |
| Up to 50 years of age | | | | | | | | |
| Unexposed | 74 | 39 | 1.0[‡] | | 74 | 22 | 1.0[§] | |
| >0–19.8 | 79 | 39 | 0.9 | 0.5, 1.6 | 79 | 20 | 1.0 | 0.5, 2.0 |
| >19.8 | 60 | 13 | 0.4 | 0.2, 0.9 | 60 | 18 | 1.4 | 0.6, 2.9 |
| | | | | $p = 0.02$ | | | | $p = 0.36$ |
| Over 50 years of age | | | | | | | | |
| Unexposed | 116 | 60 | 1.0[‡] | | 116 | 47 | 1.0[§] | |
| >0–19.8 | 31 | 21 | 1.5 | 0.7, 3.0 | 31 | 17 | 1.4 | 0.7, 2.9 |
| >19.8 | 55 | 29 | 1.2 | 0.6, 2.2 | 55 | 25 | 1.2 | 0.6, 2.3 |
| | | | | $p = 0.79$ | | | | $p = 0.72$ |
| Herbicides | | | | | | | | |
| Up to 50 years of age | | | | | | | | |
| Unexposed | 158 | 71 | 1.0[‡] | | 158 | 45 | 1.0[§] | |
| >0–1.25 | 32 | 14 | 1.1 | 0.5, 2.3 | 32 | 8 | 1.4 | 0.5, 3.5 |
| >27.125 | 23 | 6 | 0.6 | 0.2, 1.6 | 23 | 7 | 2.0 | 0.7, 5.9 |
| | | | | $p = 0.27$ | | | | $p = 0.21$ |
| Over 50 years of age | | | | | | | | |
| Unexposed | 186 | 95 | 1.0[‡] | | 186 | 71 | 1.0[§] | |
| >0–1.25 | 7 | 9 | 3.5 | 1.1, 10.9 | 7 | 8 | 5.2 | 1.4, 18.7 |
| >27.125 | 9 | 6 | 1.9 | 0.6, 5,9 | 9 | 10 | 3.9 | 1.2, 12.5 |
| | | | | $p = 0.28$ | | | | $p = 0.02$ |

[*] Adjusted for age (18–29, 30–39,40–49, 50–59, 60–69, 70–79, ≥80 years), hospital location (Phoenix, Boston, Pittsburgh), and proxy interview (yes/no).

[†] Adjusted for age, hospital location, proxy interview, race (White, non-White), marital status (married/not married), and Jewish religion.

[‡] Adjusted for age, hospital location, proxy interview, marital status, and distance lived from hospital (0–5, >5–15, >15–30, >30—50, >50 miles). One mile = 1.61 km.

[§] Adjusted for age, hospital location, proxy interview, race, marital status, Jewish religion (yes/no), and household income in $1,0005 (<15.0, 15.0–24.9, 25.0–34.9, 35.0–49.9, 50.0–74.9, ≥75.0).