CANCER MORTALITY AND BIRTH MALFORMATIONS IN FOUR WHEAT-PRODUCING U.S. STATES

Dina M. Schreinemachers

National Health and Environmental Effects Research Laboratory, Office of Research and Development, U.S. Environmental Protection Agency, Research Triangle Park, NC 27711

Introduction

Newly emerging global patterns of disease have been observed. Environmental exposures, which are involuntary, widespread, and mostly low-dose in nature, have been implicated. Comparisons of populations rather than individuals are needed to identify health effects resulting from these exposures. Population or ecologic studies are fundamental in addressing the associated public health problems[1]. Since lack of null comparison data may complicate population studies, inter-region comparisons may be used instead[2]. While population studies can be the first step in identifying potential hazards, other disciplines ranging from the molecular to the population domain, are required to completely define the association between environmental exposures and health effects[1]. An example of two hazard identification studies is presented here.

Chlorophenoxy herbicides are widely used for broadleaf weed control in grain farming and maintenance of parks, right-of-ways, and home lawns. Previous studies have reported associations between chlorophenoxy herbicides and adverse human health effects. Case-control and cohort studies conducted in Sweden, the U.S. and Canada reported increased risks for soft tissue sarcoma, malignant lymphoma and prostate cancer in association with chlorophenoxy herbicides. Excess birth malformations among 1989-1992 births were reported in Northwestern Minnesota, an agricultural region where wheat is one of the major crops[3]. This excess was observed not only in the offspring of pesticide appliers, but also in the general population, suggesting that exposure was not restricted to pesticide appliers and their families. Another study observed excess mortality from prostate, thyroid, and bone cancer during 1980-1989 in this same Northwestern region of Minnesota[4].

The aim of two recently conducted population studies was to identify the potential health hazards from environmental exposures to chlorophenoxy herbicides and/or contaminants in the general population of rural, agricultural counties of Minnesota (MN), Montana (MT), North Dakota (ND), and South Dakota (SD)[5,6]. These states produce most of the spring and durum wheat grown in the U.S. Over 85% of this wheat acreage is treated with chlorophenoxy herbicides, such as 2,4-dichlorophenoxyacetic acid (2,4-D) and 4-chloro-2-methylphenoxyacetic acid (MCPA). Other major field crops in these four states, such as corn and soybeans, are mostly treated with different herbicides. Because of the crop-specificity of chlorophenoxy herbicides, wheat acreage was proposed as a surrogate measure of exposure to chlorophenoxy herbicides. The association of cancer mortality and birth malformation rates with the level of wheat farming was investigated.

Methods and Materials

Data routinely collected by Federal Agencies and made available to the public were used for these studies. Information on 1980-1989 cancer mortality and 1995-1997 births were obtained from the National Center for Health Statistics. Agricultural data were obtained from the U.S. Department of Agriculture. Counties were selected for study if at least 20% of the available land was dedicated to agriculture, and at least 50% of the population was rural. Only the white population was studied because data on nonwhites were sparse. For the cancer mortality study, counties were grouped into tertiles based on wheat acreage per county (low, medium, high). For each cancer site and gender, age-standardized rates for the second and third tertile were compared to the first tertile, using Mantel-Haenszel methods. For frequent cancers, age-adjusted mortality rates were plotted against wheat acreage per county. Birth malformations were analyzed collectively based on organ system classification, or singularly, provided enough observations were available. Counties were divided into a low- and high-wheat group based on the median percentage of land dedicated to wheat farming. The effect of residency in high-wheat counties on birth malformations was analyzed by logistic regression with adjustment for county of birth. For those malformations where wheat acreage had a significant effect, covariate adjustment for maternal characteristics was performed.

Results and Discussion

Low level environmental exposures to chlorophenoxy herbicides and/or contaminants may be involved in the increased rates of cancer mortality and birth malformations. Exposures may occur via inhalation, ingestion, and absorption. Proximity to wheat crop fields, precipitation, atmospheric transport, indoor house dust, are examples of potential routes of exposure. An association with wheat acreage was observed for cancer mortality at the following sites: stomach, rectum, pancreas, larynx, cervix, ovary, prostate, thyroid, bone, brain, leukemia, eye, nasal cavity, oral cavity (Table 1). In this analysis involving grouped counties as the unit of observation, no effects were observed for stomach cancer, leukemia, and ovarian cancer. However, in analyses where single counties were the unit of observation, effects were observed for these three sites (data not presented). An excess of circulatory/respiratory and muskuloskeletal/- integumental malformations was observed in the high-wheat counties (Table 2). Adjustment for maternal covariates did not change the effect of residency in high-wheat counties (data not presented).

Conclusions

Results of these ecologic studies are of concern because of the widespread use of chlorophenoxy herbicides in the U.S. Since the purpose of these studies was hazard identification, more targeted studies involving chlorophenoxy herbicides and contaminants at levels as they occur in the environment, are needed to confirm the results.

Disclaimer: This document has been reviewed in accordance with U.S. Environmental Protection Agency policy and approved for publication. It does not necessarily reflect EPA policy.

Table 1. Cancer mortality during 1980-1989 in rural agricultural counties of MN, MT, ND, and SD. Age-adjusted rates in low (<23,000 acres), medium (23,000-110,999 acres) and high (≥111,000 acres) wheat counties .

Cancer site	Men Rates /100,000			Women Rates /100,000		
	low	medium	high	low	medium	high
Salivary gland	**0.13**	**0.53***	0.28	---	---	---
Oral cavity	3.08	2.90	3.34	**0.67**	**0.87**	**1.32***
Esophagus	**5.66**	**5.74**	**5.87**	**1.06**	**1.11**	**1.17**
Stomach	10.23	10.05	10.59	**4.20**	**4.39**	**5.61***
Large intestine	26.82	27.43	26.23	19.87	21.13	19.75
Rectum	**4.75**	**4.94**	**6.26***	**2.19**	**3.00***	2.46
Liver, gall bladder	4.62	5.48	5.23	**4.65**	**4.72**	**5.51**
Pancreas	**11.78**	**12.82**	**14.53***	**8.54**	**9.61**	**10.55***
Larynx	**1.75**	**1.95**	**2.69***	—	—	—
Lung	66.69	66.24	66.25	20.97	19.31	22.15
Breast	---	—	—	36.23	35.62	35.52
Cervix uteri	—	—	—	**2.02**	**2.21**	**3.09***
Uterus	—	—	—	4.79	4.81	4.37
Ovary	—	—	—	11.27	10.28	11.95
Prostate	**31.12**	**34.24***	**38.64***	—	—	—
Kidney	**7.04**	**7.10**	**7.28**	3.86	3.42	4.13
Bladder	7.19	6.07	6.36	**1.96**	**2.14**	**2.21**
Malignant melanoma	3.39	2.67	2.68	1.99	2.44	1.48
Nonmelanoma skin	1.26	1.24	1.25	0.43	0.36	0.54
Brain, other CNS	7.48	6.96	8.16	4.66	4.45	5.39
Thyroid	**0.27**	**0.39**	**0.51**	0.49	0.38	0.45
Thymus, endocr.glands	0.32	0.26	0.45	—	—	—
Bone	**0.56**	**0.66**	**1.08**	0.54	0.36	0.64
Connective, soft tissue	1.37	1.00	1.45	1.28	1.65	1.58
Hodgkin's disease	**1.01**	**1.81***	0.80	0.72	0.74	0.62
Other lymphoma	10.83	8.82	9.68	7.71	7.41	7.32
Multiple myeloma	4.96	4.95	3.89	3.47	3.46	3.35
Leukemia	11.90	11.60	13.25	7.20	6.81	6.70
Secondary	14.67	15.77	11.95	**10.53**	**12.48***	11.71
All cancers	**240.88**	**243.23**	**250.05***	**162.65**	**164.44**	**171.34***

Bold text indicates increasing cancer rates for the three tertiles of counties or a statistically significant increased rate (*) for either the second or third tertile.
Average annual population at risk: men , 338,471, 155,468, and 134,419; women, 349,660, 160,200, 134,105 for combined low, medium, and high wheat counties, respectively.

Table 2. Birth malformations in low-wheat (LW) and high-wheat (HW) counties of Minnesota, Montana, North Dakota, and South Dakota, among 1995-1997 live births

Birth Malformation	N_{LW}	N_{HW}	OR[a] (95% CI)
Births with any anomaly	596	213	1.07 (0.87-1.31)
Central nervous system anomalies	50	12	0.81 (0.46-1.42)
Other cns anomalies	20	5	0.79 (0.30-2.11)
Circulatory / respiratory anomalies	74	39	**1.65 (1.07-2.55)**
Heart malformations	40	15	1.23 (0.70-2.17)
Other circ./resp. anomalies	42	27	**2.03 (1.14-3.59)**
Digestive system anomalies	81	24	0.92 (0.55-1.52)
Cleft lip/palate	46	16	1.12 (0.62-2.01)
Urogenital anomalies [b]	112	37	0.97 (0.65-1.44)
Malformed genitalia [b]	25	8	1.03 (0.51-2.09)
Other urogenital anomalies [b]	91	29	0.91 (0.57-1.44)
Musculosk. / integumental anomalies	142	70	**1.50 (1.06-2.12)**
Poly- / syn- / adactyly	19	14	**2.43 (1.26-4.71)**
Club foot	33	9	0.84 (0.39-1.80)
Other musc./integ. anomalies	84	47	**1.70 (1.10-2.62)**
Chromosomal	60	17	0.93 (0.55-1.58)
Down's syndrome	32	10	1.02 (0.52-2.01)
Other chromosomal anomalies	28	7	0.80 (0.33-1.96)
Other congenital anomalies	189	42	0.69 (0.49-0.98)
Infant death from congenital anomalies [b]	23	17	**2.66 (1.52-4.65)**
Total number of births	33,380	10,254	

[a] unadjusted odds ratio
[b] data for boys only
The following birth malformations were included in the aggregate categories, based on organ system classification, but were not analyzed as single categories due to low number of observations: anencephalus, spina bifida/meningocele, hydrocephalus, microcephalus, rectal atresia/stenosis, tracheo-esophageal fistula, omphalocele, other gastrointestinal anomalies, renal agenesis, diaphragmatic hernia.

References

1. Pekkanen, J., Pearce, N; (2001) Environmental Health Perspectives. 109(1), 1.
2. McMichael, A.J; (2002) Lancet. 359, 1145.
3. Garry, V.F., Schreinemachers, D., Harkins, M.E., Griffith, J. (1996) Environ Health Perspect. 104, 394.
4. Schreinemachers, D, Creason, J.P., Garry, V.F.(1999) Environ Health Perspect . 107, 205.
5. Schreinemachers, D. (2000) Environ Health Perspect.108, 873.
6. Schreinemachers, D.(2003) Environ Health Perspect. In press.