

ORIGINAL CONTRIBUTIONS

Soft-Tissue Sarcoma and Non-Hodgkin's Lymphoma Clusters around a Municipal Solid Waste Incinerator with High Dioxin Emission Levels

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Overall evidence from epidemiologic studies in the workplace suggests that dioxin is a human carcinogen, but whether low doses affect the general population remains to be determined. The authors examined the spatial distribution of soft-tissue sarcomas and non-Hodgkin's lymphomas around a French municipal solid waste incinerator with high emission levels of dioxin (16.3 ng international toxic equivalency factor/m³). Not consistently associated with dioxin exposure, Hodgkin's disease served as the control cancer category. Clusters were identified from 1980 to 1995 in the area ("département") of Doubs by applying a spatial scan statistic to 26 electoral wards. The most likely and highly significant clusters found were identical for soft-tissue sarcomas and non-Hodgkin's lymphomas and included the area around the municipal solid waste incinerator; standardized incidence ratios were 1.44 (observed number of cases = 45, focused test *p* value = 0.004) and 1.27 (observed number of cases = 286, focused test *p* value = 0.00003), respectively. Conversely, Hodgkin's disease exhibited no specific spatial distribution. Confounding by socioeconomic status, urbanization, or patterns of medical referral seemed unlikely to explain the clusters. Although consistent, these findings should be confirmed by further investigation (e.g., a case-control study in which dioxins are measured in biologic tissues) before clusters of soft-tissue sarcoma and non-Hodgkin's lymphoma are ascribed to dioxin released by the municipal solid waste incinerator. *Am J Epidemiol* 2000;152:13–19.

cluster analysis; dioxins; incidence; incineration; lymphoma, non-Hodgkin; sarcoma; soft tissue neoplasms; waste management

Dioxin is the name loosely given to a class of chemicals, the chlorinated dioxins and furans formed as a combustion by-product of the burning of several materials (e.g., transformer oil containing polychlorinated biphenyls, wood treated with creosote), a reaction by-product during manufacture of several chemicals (including the herbicides 2,4-dichlorophenoxyacetic acid (2,4-D) and 2,4,5-trichlorophenoxyacetic acid (2,4,5-T)), or a by-product of the chlorine bleaching of pulp and paper. Thus, there are four principal types of sources of dioxin release into the environment: combustion and incineration sources, chemical manufacturing sources, industrial and municipal sources, and reservoir sources (e.g., sediments, soil, and sewage sludge) (1). Of the 73 possible dioxins, 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (2,3,7,8-TCDD) is considered the most potent.

Received for publication December 4, 1998, and accepted for publication September 20, 1999.

Abbreviations: ICD-O, *International Classification of Diseases for Oncology*; I-TEQ, international toxic equivalency factor; MSW, municipal solid waste; 2,3,7,8-TCDD, 2,3,7,8-tetrachlorodibenzo-*p*-dioxin; 2,4,5-T, 2,4,5-trichlorophenoxyacetic acid.

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Because of the steep increase in manufacture and use of chlorinated organic chemicals and plastics and in burning of household trash, municipal solid waste (MSW) incineration is one, if not the top, source of dioxin production. During incineration, thermal breakdown of trace metals, chlorinated compounds, and organic materials takes place. To control formation of dioxin, the flue gas is cooled rapidly by using a spray dryer and a scrubber or some other pollution control device. In ideal conditions, the temperature would change instantaneously and no dioxin would be formed; unfortunately, however, some dioxin develops nevertheless.

Airborne deposition appears to be the most efficient mode of transport for dioxin. Ingestion of contaminated plants and water by farm animals enables the dioxin to enter the food chain. From there, bioaccumulation occurs in the fatty tissue of ruminants. It is estimated that intake from food (e.g., cow's milk, other dairy products, meat) accounts for well over 90 percent of the body burden of dioxin in the general human population (2).

Dioxin has been shown to be a carcinogen, a teratogen, and a reproductive toxicant in animals; available data indicate that high-level human exposure to dioxin produces adverse health effects and that humans are sensitive to the toxic effects of dioxins (3). However, its human carcinogenicity has been a matter of dispute. A 1994 US Environmental Protection Agency risk assessment of dioxin confirmed earlier reports of 1985 and 1988 and concluded that the overall weight of evidence from the epidemiologic

studies suggests that the generally increased risk of cancer in occupationally exposed cohorts is more than likely due to exposure to dioxin (1).

More recently, according to an International Agency for Research on Cancer working group, the strongest evidence for the carcinogenicity of dioxin is for all cancers combined (average relative risk = 1.4), although an increased risk of lung cancer, with about the same relative risk, also was found in the most informative studies (2). This evaluation relied primarily on four cohort studies of herbicide producers, while additional studies of herbicide applicators (both cohort and case-control) and military personnel in Vietnam who had considerably lower exposures to dioxin were not considered critical to the evaluation (2). Other researchers estimated that epidemiologic studies had shown an increased risk of cancer, notably soft-tissue sarcoma and non-Hodgkin's lymphoma, in populations occupationally or accidentally exposed to chemicals contaminated with dioxin (4, 5). This finding is in line with those from a study of the largest overall cohort of 2,3,7,8-TCDD-exposed workers ever followed, whose results were published recently; among these workers, mortality from soft-tissue sarcoma and non-Hodgkin's lymphoma was higher than expected from national mortality rates, although nonsignificantly for the latter type of cancer (6). Nevertheless, whether low doses of dioxin affect the general population remains to be determined (3).

Even though these health risks have been suspected for many years, few standards for dioxin emissions from MSW incinerators were established until recently. In Sweden, Germany, and the Netherlands, strict standards have been in place since the mid-1980s. In 1994, the European Union limited dioxin emission from MSW incinerators to 0.1 ng international toxic equivalency factor (I-TEQ)/m³ (7).

In an April 3, 1998, press release, the French Ministry of Environment revealed that of 71 MSW incinerators processing more than 6 metric tons of material per hour, dioxin emissions from 15 of them were above 10 ng I-TEQ/m³. Only 1 of these 15 (Besançon, emitting 16.3 ng I-TEQ/m³) is located in an area ("département" of Doubs) covered by a population-based general cancer registry. This finding prompted us to examine the spatial distribution of cancer cases that, if located mainly near the incinerator, could have been caused in part by dioxin.

MATERIALS AND METHODS

Study site

The département of Doubs (485,000 inhabitants) is located in eastern France and follows a northeast to southwest direction. It is divided into 29 electoral wards called "cantons" (inhabitants, 2,900–123,000; size, 50–325 km²). Because of changes in the defined boundaries between the 1982 and 1990 censuses, which yielded new cantons that partially overlapped some old ones, we were forced to aggregate some of them to obtain unequivocal and stable spatial units across years. Hence, our study considered 26 statistical units rather than the 29 original cantons (figure 1).

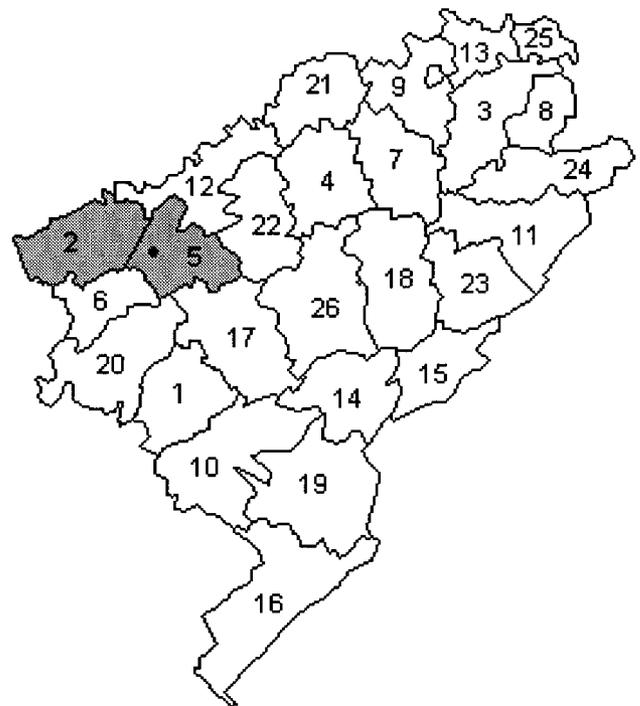


FIGURE 1. The 26 electoral wards of the département of Doubs, France (numbered in alphabetic order). Shaded areas, the most likely cluster for soft-tissue sarcomas and non-Hodgkin's lymphoma (1980–1995); ●, location of the municipal solid waste incinerator. 1, Amancey; 2, Audeux; 3, Audincourt-Pont de Roide-Valentigney; 4, Baume-les-Dames; 5, Besançon; 6, Boussières; 7, Clerval; 8, Hérimoncourt; 9, Isle-sur-le-Doubs; 10, Levier; 11, Maîche; 12, Marchaux; 13, Montbéliard; 14, Montbenoît; 15, Morteau; 16, Mouthe; 17, Ornans; 18, Pierrefontaine-les-Varans; 19, Pontarlier; 20, Quingey; 21, Rougemont; 22, Roulans; 23, Le Russey; 24, Saint-Hippolyte; 25, Sochaux-Grand Charmont-Étupes; 26, Vercel-Villerdiou le Camp.

In the regional capital of Besançon, the MSW incinerator under investigation is located 4 km west of the city center in an urbanized area that comprises, among other buildings, University Hospital. The incinerator began operating in 1971 with combustion chambers 1 and 2 (each with a capacity of 2.1 metric tons per hour). They were complemented in 1976 with combustion chamber 3 (with a capacity of 3 metric tons per hour). In 1998, approximately 67,000 metric tons were processed (unpublished data). It is considered the main point source of pollution since heavily polluting industries, which were replaced two decades ago by small-scale, advanced-technology industries, no longer operate in the area. Compared with the Besançon incinerator, the other major incineration facility in the département, located 80 km away in Montbéliard, seems much cleaner and has a dioxin emission concentration of only 0.1 ng I-TEQ/m³.

Exposure data

On February 6, 1998, the prefect of the département of Doubs ordered the plant's owner to adhere to some legal guidelines for MSW incinerator emissions. In particular,

dust and hydrogen chlorine emission levels were higher than prescribed (combustion chamber 3: 315.6 vs. 30 mg/nm³ and 803.5 vs. 50 mg/nm³, respectively (1997 data)). Moreover, legal residence time (>2 seconds) of exhaust gas at temperatures of more than 850°C (in the presence of at least 6 percent oxygen) was not followed, allowing dioxins to be emitted (which are destroyed only above these thresholds).

Meanwhile (May 30, 1997), yearly measurement of the amount of dioxin emitted by MSW incinerators processing more than 6 metric tons per hour became compulsory nationwide. Subsequently, one dioxin concentration in exhaust gas (from combustion chamber 1) was measured for the first time (in December 1997 but made public on April 3, 1998) and was found to be 16.3 ng I-TEQ/m³.

Then, concentrations of dioxin were determined in cow's milk from farms located within a 3 km radius of the incinerator. Only four farms met the criterion in this urbanized area (with no cattle breeding on one of them); thus, three samples were collected (one per milk tank). Dioxin concentrations (in ng I-TEQ/kg of fat) and distances between the farms and the plant were as follows: 1.03 (0.9 km), 0.59 (1.5 km), and 0.58 (2.0 km). To our knowledge, no other dioxin data were available on tissue levels of residents or soil samples (whatever the time period) or on air concentrations before December 1997.

Cancer cases

The département of Doubs is covered by a cancer registry established in 1976. Its global recognition is demonstrated by its inclusion, from 1982 onward, in the International Agency for Research on Cancer series entitled *Cancer Incidence in Five Continents* (8). To avoid data dredging, we focused on incident cases of soft-tissue sarcoma (*International Classification of Diseases for Oncology* (ICD-O) topology code C49 and morphology code 8800/3) and non-Hodgkin's lymphoma (ICD-O morphology codes 9590/3–9595/3, 9670/3–9723/3, and 9761/3). Lung cancer cases were kept separate, since no relevant analysis could be carried out within the spatial framework of this study. As a matter of fact, such a spatial study is more likely to give an accurate representation of the prevalence of smoking at some time in the past and be of little value in helping to identify other causes or risk factors for lung cancer (9). We decided to include one control cancer category, Hodgkin's disease (ICD-O morphology codes 9650/3–9667/3). Not consistently associated with dioxin exposure, this type of cancer has the same order of incidence rate as the one for soft-tissue sarcomas and follows the same referral pattern as non-Hodgkin's lymphoma (enabling us to shed some light on possible selection bias). To avoid uncertainties in the morphologic classification of this diverse group of neoplasms, all records were reassessed by a medical specialist blind to the location of cases. A special effort was made to exclude chronic lymphocytic leukemia from the non-Hodgkin's lymphoma group. Any case occurring before 1980 was discarded to enhance confidence in the completeness of the registration process.

Statistical analysis

This study relied on a three-step procedure. First, we used a focused test, since there was a prespecified point source (the MSW incinerator) and we aimed at identifying an elevated risk of some cancers around that specific source. Second, we conducted a space-time interaction test to determine whether there was clustering around the Besançon facility throughout the time period. Third, we applied a non-focused cluster detection test to possibly both pinpoint the location and test the significance of other clusters not located near the MSW incinerator. Our a priori reasoning was as follows: If 1) a significant cluster that included the Besançon area (where the MSW incinerator is located) was highlighted by the focused test, 2) a significant space-time interaction involving the recent years was found around the facility (making occurrence of the cluster compatible with a latency period), and 3) no other cluster was noticeable in the remaining area, then these findings would support a relation between plant location and cancer incidence possibly mediated by dioxin emission.

Soft-tissue sarcoma is a rare event. Therefore, units considered in the statistical analyses consisted of the cantons composing the département of Doubs to ensure a sufficient number of cases per zone.

Expected numbers of cases for each canton were computed by applying an internal standard (i.e., incidence rates from the whole département for the same years) to the number of person-years for each area, stratified by gender and 5-year age groups. Population data by canton, gender, and 5-year age groups were obtained from the French Office of Population Censuses for the 1975, 1982, and 1990 censuses.

Clusters can be detected by using a wide variety of statistical methods. Typically, the latter either detect clusters without making any statistical inference or they detect significant clustering without specifying the clusters involved. To test for the presence of disease clusters and to identify their approximate location, we used a recently developed spatial scan statistic (10–13). We assumed the number of incident cases to be Poisson distributed. The method tests the null hypothesis that in each gender and age group, the risk of cancer is the same for all cantons. In other words, the expected incidence rate adjusted for gender and age is constant over the whole area.

The method we used imposed a circular window on the map and allowed its center to move over the area so that, at any given position, the window included different sets of neighboring cantons. If the window contained the centroid of a canton (defined as the location of the main town church), then that whole canton was included in the window. The center of the circular window was positioned at the centroids of the 26 cantons, and the window radius was varied continuously from zero to a maximum so that the window never included more than 30 percent of the total population.

For each location and size of the scanning window, the null hypothesis was that the risk of cancer was the same in all windows (corresponding to complete spatial randomness), whereas the alternative hypothesis was that there was an elevated rate within compared with outside the window. A likelihood function was calculated for each window and

was maximized over all of them, identifying the zone that represented the most likely disease cluster. For hypothesis testing, we used a Monte Carlo procedure to generate 29,999 random replications of the data set under the null hypothesis (scanning over the possible locations and sizes). The maximum likelihood ratio test statistic was calculated for each random replication as well as for the real data set; if the latter was among the 5 percent highest, then the test was significant at the 0.05 level.

We also used two extensions of this spatial scan statistic: a focused test around a point source of pollution (the MSW incinerator) in which the window was positioned at the facility's location only (but the size of the window's radius was allowed to vary) and a focused space-time scan test in which we used a cylindrical window with a circular geographic base and whose height corresponded to time. For the latter, time intervals were 1 year long, and the maximum temporal cluster size was 30 percent of the study period as a whole. No adjustment was made for trends over time. The calculations were performed by using the software program SaTScan, designed specifically to implement the spatial scan statistic (14).

RESULTS

Soft-tissue sarcoma

During the 16-year study period, 110 cases of soft-tissue sarcoma accrued, corresponding to a crude incidence rate of 1.4 per 100,000. Table 1 displays the results of different scan

tests that were conducted for this cancer category. The focused test found a significant cluster ($p = 0.004$) around the MSW incinerator, which was made up of two cantons: Besançon (containing the plant) and Audeux (west and contiguous to the former) (figure 1). An excess of 14 cases was observed, and the standardized incidence ratio was 1.44. When we applied a focused space-time test, the time window 1994–1995 for the canton of Besançon was significant ($p = 0.008$). When a broader alternative that depended on the set of 26 centroids (and not on the facility location only) was used, the same cantons of Besançon and Audeux appeared at high risk, but not significantly so ($p = 0.12$). When we analyzed data according to gender, the location of the most likely cluster was identical but appeared significant only for males (focused $p = 0.004$ and 0.16 for males and females, respectively).

Non-Hodgkin's lymphoma

Between 1980 and 1995, 803 cases of non-Hodgkin's lymphoma were diagnosed, yielding a crude incidence rate of 10.4 per 100,000. Results for this cancer site are shown in table 2. Whatever type of analysis we used, the most likely cluster appeared to be the same, composed of the cantons of Besançon and Audeux, and was highly significant ($p = 0.0003$). In purely spatial analyses, we found an excess of 61 cases (standardized incidence ratio = 1.27); with the space-time approach, the time frame identified corresponded to 1991–1994. These findings were consistent across gender (focused $p = 0.004$ and 0.0004 for males and females, respectively).

TABLE 1. Soft-tissue sarcoma clusters in the département of Doubs, France, 1980–1995 (scan test analyses)

	Census area(s)	Time frame	No. of cases		SIR*	<i>p</i> value
			Observed	Expected		
Spatial cluster around the Besançon MSW* incinerator	Besançon, Audeux		45	31.22	1.44	0.004
Space-time cluster around the Besançon MSW incinerator	Besançon	1994–1995	12	3.49	3.44	0.008
Spatial cluster in the département of Doubs	Besançon, Audeux		45	31.22	1.44	0.12

* SIR, standardized incidence ratio; MSW, municipal solid waste.

TABLE 2. Non-Hodgkin's lymphoma clusters in the département of Doubs, France, 1980–1995 (scan test analyses)

	Census areas	Time frame	No. of cases		SIR*	<i>p</i> value
			Observed	Expected		
Spatial cluster around the Besançon MSW* incinerator	Besançon, Audeux		286	225.25	1.27	0.00003
Space-time cluster around the Besançon MSW incinerator	Besançon, Audeux	1991–1994	109	59.09	1.84	0.00003
Spatial cluster in the département of Doubs	Besançon, Audeux		286	225.25	1.27	0.0003

* SIR, standardized incidence ratio; MSW, municipal solid waste.

Hodgkin's disease

During the study period, 176 cases of Hodgkin's disease were observed; the crude incidence rate was 2.3 per 100,000. Scan test results are summarized in table 3. No cluster was found around the MSW incinerator when a purely spatial approach was used, since its surroundings were located in a low-risk zone (Besançon: observed number of cases = 44, expected number of cases = 47.28). However, when we performed a space-time focused test, the 1992–1993 time window became noticeable, although not significantly so ($p = 0.89$). Finally, the most likely cluster in the whole département consisted of four cantons located south of Besançon (figure 1), but the associated risk was not significant ($p = 0.95$).

DISCUSSION

This study localized incident case clusters of soft-tissue sarcoma and non-Hodgkin's lymphoma to the vicinity of the MSW incinerator in Besançon, which were more pronounced at the end of the study period. It also showed that no other clusters were noticeable in the remaining areas.

Our study has some strengths. First, data were provided by a permanent cancer registry in which cases are identified homogeneously and prospectively, which eliminated a registration bias (to be particularly feared in ad hoc surveys, where higher rates can reflect only more complete registration of cases in areas around installations than elsewhere). Besides, compared with mortality data, morbidity data are not affected by differential survival among areas, and their use alleviates migration effects because the time lag from the exposure is shorter.

Another advantage of our study is that it was hypothesis driven rather than data driven. We started from a highly polluting point source and investigated the most likely outcomes related to that exposure. Hence, the reported spatial clusters were based neither on anecdotal evidence nor on prior identification of a cluster location; a subsequent test was designed for this particular alternative hypothesis.

Finally, the spatial scan statistic we used had four attractive features:

1. It adjusted for the inhomogeneous population density.
2. The test statistic based on the likelihood ratio took multiple testing into account and delivered a single p value for the test of the null hypothesis.
3. If the null hypothesis was rejected, the approximate location of the cluster that caused the rejection could be specified.
4. It performed well even though the "real" cluster was not circular.

That we found lower p values for focused tests is not surprising. Their alternative hypothesis was narrower (they were restricted to the location of interest), entailing a higher statistical power.

We consider the space-time interaction we highlighted for the more recent years to be of limited added value. Upward trends in soft-tissue sarcomas and non-Hodgkin's lymphomas are observed worldwide (15, 16) and cannot be disentangled from a putative exposure with some time lag, which occurred with the Besançon MSW incinerator. Conversely, finding a space-time interaction for the early years would have represented a counterargument for an association between the incinerator and the outcomes under study, since the time gap between the opening of the facility and such a space-time cluster would have been too short considering the latency period generally observed for the cancer sites under study.

As is true of any spatial study, ours has some limitations. Because we dealt with data aggregated to the canton level, we did not have enough resolution to efficiently detect clusters that affected a subpart of a canton. Moreover, even though the Besançon-Audeux area is the most likely cluster, it probably does not coincide exactly with the real cluster; the scan test provided only an estimate for the position and the radius of the latter. (However, it is noteworthy that the MSW incinerator is located west of Besançon and central to the Besançon-Audeux cluster.) Finally, a substantial proportion of persons might have migrated to another geographic

TABLE 3. Hodgkin's disease clusters in the département of Doubs, France, 1980–1995 (scan test analyses)

	Census areas	Time frame	No. of cases		SIR*	p value
			Observed	Expected		
Spatial cluster around the Besançon MSW* incinerator†						
Space-time cluster around the Besançon MSW incinerator	Besançon, Audeux	1992–1993	9	5.99	1.50	0.89
Spatial cluster in the département of Doubs	Amancey, Ornans, Quingey, Boussières		17	11.94	1.42	0.95

* SIR, standardized incidence ratio; MSW, municipal solid waste.

† No cluster could be found in the vicinity of the MSW incinerator, since the number of observed cases was lower than the number of expected cases.

area during the time lag between residence near the point source and occurrence of the disease. However, in- and out-migrations result in a dilution effect, reducing and not overestimating ecologic estimates (17).

To put the present results in a broader context, findings from replication studies around the other high-polluting French MSW incinerators would have been welcome. Unfortunately, absence of a nationwide cancer registry precludes such systematic analysis.

Considering the common dioxin guideline value that western countries use for cow's milk (6 ng I-TEQ/kg of fat), the local results reported in the Exposure Data section of this paper seem reassuring. Nevertheless, these data were very scarce (only three dioxin concentrations), and the sampling frame is questionable. Indeed, according to the wind patterns, only one farm (with the highest dioxin level) is considered to be located under the plume of the incinerator's stacks.

If dioxin is involved, the route of exposure remains to be determined. A number of studies have demonstrated the localized influence of MSW incinerators on the dioxin concentration of the milk of cows grazing nearby (2). Although Audeux is a semirural area, Besançon is densely populated, with very few pastures. Furthermore, dioxins can be carried on tiny specks of fly ash and can be deposited long distances away from the source.

Obviously, there are other known or hypothesized risk factors for soft-tissue sarcoma and non-Hodgkin's lymphoma that we were unable to include in this population-based analysis. Socioeconomic status could be one. People living near an industrial site do not constitute a random sample of the general population. Because of chosen or imposed circumstances (e.g., economic forces, employment, family environment), these people often are subject to social disadvantages (18). Moreover, if the diseases under study show a negative social class gradient, then socioeconomic factors likely explain the apparent relation between disease and proximity to a point source. However, the majority of mortality and incidence data for lymphomas and connective tissue cancer have shown no clear association with social class (19), making socioeconomic confounding unlikely. This conclusion is reinforced by using the deprivation index of Carstairs and Morris (20), which reflects a median level of affluence for Besançon (rank 14 of 26) but the highest socioeconomic status for Audeux.

Cancer clusters in densely populated areas (such as Besançon) raise the issue of urbanization as a confounding factor. Mortality rates for non-Hodgkin's lymphoma are suspected to increase with the level of urbanization (16). However, for two reasons, urbanization could not have confounded our results: the evidence is still controversial, and, to our knowledge, no similar findings have been reported for soft-tissue sarcoma; the standardized incidence ratios for the next three densely populated areas (Montbéliard, Sochaux, and Audincourt) were lower than 1 for both non-Hodgkin's lymphoma and soft-tissue sarcoma.

In fact, the mounting evidence implicating phenoxy herbicides would involve a rural-urban difference rather than an urban-rural gradient for both soft-tissue sarcoma and non-Hodgkin's lymphoma. It is noteworthy that among the phe-

noxy herbicides, 2,4,5-T is known to be contaminated with 2,3,7,8-TCDD. The International Agency for Research on Cancer has extensively reviewed studies of herbicide exposure among farmers, pesticide applicators, and other nonindustrial populations (2). In general, but not consistently, positive associations between occupational exposure to chlorophenoxy herbicides and soft-tissue sarcoma or non-Hodgkin's lymphoma have been found in case-control studies, whereas follow-up studies are less indicative of an association. Hence, the overall evidence is still not conclusive (16), and our study underscoring clusters in an urban area does not add any support to this hypothesis.

The heterogeneity of the French health care system could result in varied patterns of referral based on patients' precise diagnosis, age, mobility, and distance from the center. In France, primary health care is delivered by private physicians, either general practitioners or specialized clinicians. The latter are consulted either directly or by referral from general practitioners. Hospital care is provided in public or private hospitals at the district level, but specialist oncology services and radiotherapy services are more centralized. To make sure that distance from these centers did not act as a confounder (the closer the residence, the wider the access to specialized care and the more frequent the cancer diagnoses), we also considered Hodgkin's disease. For this condition (handled by the same specialized clinicians as those for non-Hodgkin's lymphoma), no cluster was noticeable in the entire study area. Thus, we are inclined to conclude that the clusters of soft-tissue sarcoma and non-Hodgkin's lymphoma observed in the Besançon-Audeux area are not attributable to the presence of University Hospital in the vicinity.

It is also possible that coexposures from the incinerator, instead of dioxin, could be responsible for the clusters we observed. Emissions of dust and hydrogen chloride, which were above the legal limits, could be important provided that exposure really is associated with occurrence of soft-tissue sarcoma and non-Hodgkin's lymphoma.

On the whole, the consistency of our findings for soft-tissue sarcoma and non-Hodgkin's lymphoma is remarkable. Moreover, the fact that we found no specific cluster for the control cancer category of Hodgkin's disease reinforces previous, positive results. These findings, together with the consistency of the results across genders for non-Hodgkin's lymphoma (clusters involving only males would have favored an occupational exposure), make us suspect, at least for this type of cancer, an environmental pathway involving dioxin. However, despite the fact that all preliminary descriptive criteria were met, caution should be exercised before clusters of soft-tissue sarcoma and non-Hodgkin's lymphoma are ascribed to dioxin released by the MSW incinerator. Much remains to be understood about the environmental route, which is clearly worthy of further investigation (e.g., a case-control study in which dioxins are measured in biologic tissues).

Exploring alternatives to possibly harmful emissions, local policy makers wisely implemented the precautionary principle (while ignoring our results) by closing down combustion chamber 1 on December 31, 1998; upgrading the other two; and planning the construction of a cleaner facility.

Furthermore, they produced an environmental impact statement to show how the new combustion chamber will affect the surroundings, giving the public a role in the outcome.

ACKNOWLEDGMENTS

This study was carried out within the framework of a European Community Biomed II Project entitled "A European Initiative in Advanced Methods for Disease Mapping and Risk Assessment." The Doubs Cancer Registry is funded by the French Ministry of Health (Direction Générale de la Santé) and the National Medical Research Institute (INSERM), Paris, France.

The authors are indebted to Dr. Bruno Challier, Dr. Yvonne Kieffer, and Patricia Zanon for their technical assistance.

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