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# Maternal residence near municipal waste incinerators and the risk of urinary tract birth defects

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## See Commentary, p 433

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## ABSTRACT

**Objectives** Waste incineration releases a mixture of chemicals with high embryotoxic potential, including heavy metals and dioxins/furans, into the atmosphere. In a previous ecological study we found an association between the risk of urinary tract birth defects and residence in the vicinity of municipal solid waste incinerators (MSWIs). The objective of the present study was to specifically test this association.

**Methods** A population-based case–control study compared 304 infants with urinary tract birth defects diagnosed in the Rhône-Alpes region (2001–2003) with a random sample of 226 population controls frequency-matched for infant sex and year and district of birth. Exposure to dioxins in early pregnancy at the place of residence, used as a tracer of the mixture released by 21 active waste incinerators, was predicted with second-generation Gaussian modelling (ADMS3 software). Other industrial emissions of dioxins, population density and neighbourhood deprivation were also assessed. Individual risk factors including consumption of local food were obtained by interviews with 62% of the case and all control families.

**Results** Risk was increased for mothers exposed to dioxins above the median at the beginning of pregnancy (OR 2.95, 95% CI 1.47 to 5.92 for dioxin deposits). When only interviewed cases were considered, risk estimates decreased mainly because the non-interviewed cases were more likely to live in exposed residential environments (OR 2.05, 95% CI 0.92 to 4.57). The results suggest that consumption of local food modifies this risk.

**Conclusions** This study confirms our previous observation of a link between the risk of urinary tract birth defects and exposure to MSWI emissions in early pregnancy and illustrates the effect of participation bias on risk estimates of environmental health impacts.

Incineration is an efficient way to dispose of municipal solid waste by reducing landfills and associated nuisances and sometimes producing energy for municipal heating. In France, more than 11 million tons of such waste (26% of the total) was incinerated in 2000. Incineration releases a mixture of persistent toxic chemicals into the atmosphere. In 2001, municipal solid waste incinerators (MSWIs) were by far the largest atmospheric source of dioxins in France, responsible for a total of 202 g I-TEQ (International Toxic Equivalency Factor)/year, 52% of all emissions. Technological improvements and closing obsolete plants reduced this contribution to an estimated 9% in 2006.<sup>1</sup> In addition to dioxins and

## What this paper adds

- ▶ Municipal waste incineration releases into the atmosphere a complex mixture of compounds, several of which, such as dioxins and heavy metals, are known developmental toxicants.
- ▶ Epidemiological studies on the risk of birth defects around these plants have been inconclusive, although our previous ecological study suggested urinary tract birth defects as a potential target.
- ▶ This population-based case–control study confirms that exposure to dioxins (used as a tracer of total emissions) at the maternal residence in early pregnancy, assessed by second-generation Gaussian modelling, was associated with an increased risk of urinary tract birth defects.
- ▶ The findings suggest that consumption of local food modifies the risk, increasing it in exposed areas and decreasing it in unexposed areas, compared with the risk to non-consumers.
- ▶ Modern incinerators do not appear to reach the estimated level of exposure to dioxins from municipal waste incinerators, above which an increased risk is observed, but continued surveillance is recommended.

furans, a number of other compounds are released into the atmosphere, including polychlorobiphenyls, polycyclic aromatic hydrocarbons, metals (arsenic, cadmium, chromium, manganese, mercury, nickel and lead), various volatile organic compounds, particulates (PM<sub>10</sub>), nitrogen and sulphur oxides and hydrochloric acid. The known toxicity of dioxins and other individual components of the mixture and of their possible joint action justifies public concern about the potential health impact of living in the vicinity of MSWIs.

Relatively few epidemiological studies have examined – with contradictory results – the risks of infant deaths and congenital anomalies and the impact on birth weight and sex ratio in populations living around MSWIs.<sup>2–7</sup> Our previous ecological study of birth defect rates in southeastern France near one of the 70 MSWIs functioning for at least 1 year from 1988 to 1997 suggested an increased risk of urinary tract birth defects.<sup>8</sup> It also found that some groups of birth defects, including those of the urinary tract, were associated with high traffic density within 500 m of a city centre.

This initial finding led us to set up a population-based case-control study specifically designed to test the hypothesis that exposure to either MSWI emissions or road traffic or both increases the risk of urinary tract birth defects. We report here the results related to MSWI emissions.

## MATERIALS AND METHODS

The case-control study was conducted in the Rhône-Alpes region in southeastern France, where a registry records birth defects and numerous MSWIs still operate.

### Population

Cases were all live births, stillbirths or medical terminations of pregnancy between January 2001 and December 2003, diagnosed with a renal birth defect (International Classification of Diseases Tenth Edition (ICD-10) codes Q61.0, Q61.4, Q61.5, Q61.8, Q61.9) or obstructive uropathy (ICD-10 Q62) and whose family resided in one of the eight administrative districts of the region. Malformations due to chromosomal aberrations or monogenic syndromes were excluded. Grouping of renal birth defects and other urinary tract anomalies leading to urine flow impairment is justified by the common embryological origin of kidneys and urinary tract from the nephrogenic cord, which develops out of the intermediate mesoderm.<sup>9</sup> A birth defects registry covers the eight administrative districts in the Rhône-Alpes region (southeastern France) with approximately 77 000 annual births. The region includes large metropolitan areas around Lyon, Grenoble and Saint-Etienne, industrial activities (mainly metal, chemistry, plastics and electronics) and agricultural activity (grains, vineyards and orchards). Various medical sources in the region were used to identify cases, including reports from maternity hospitals to the birth defect registry and active searching in the records of the region's five university hospital prenatal diagnosis centres and paediatric surgery departments. In all, 353 cases were identified with some basic data including diagnosis (type, timing), date of conception, date of birth, vital status, sex, birth weight and family address at birth. Incomplete addresses in the medical records prevented us from locating the homes of 49 families. Of the remaining 304 families, 187 mothers (62%) agreed to participate and were interviewed by telephone or completed a questionnaire.

A control group was randomly selected in the region after stratification for sex and year and district of birth, and frequency-matching to the case distributions. The study was presented to families as a general study on the environment and children's health. Controls were selected through computer-assisted telephone interviews by a polling institute from a sampling frame of 3000 phone numbers presumed to belong to families with children. The institute did not reach 460 families (no answer or wrong number), 325 refused the interview (refusals) and 1955 did not meet the eligibility criteria (having a biological child of the right sex and year and district of birth), resulting in 260 full interviews being conducted. A refusal rate ( $325/(3000-460)=12.7\%$ ) was therefore estimated from the total number of families contacted, eligible or not. Of the 260 interviews, 34 were excluded because of residence outside the region during pregnancy ( $n=6$ ), low birth weight ( $<2500$  g) or birth defects ( $n=28$ ). That left 226 control subjects.

All interviewed participants provided informed consent for data collection and the appropriate ethics committees (the national consultative board relative to data treatment in research (CCTIRS) and the French board which enforces law on data protection (CNIL)) approved the study procedures.

### Exposure to MSWI emissions

Exposure to emissions from MSWIs at the family home for the 4-month period from 1 month before conception until the end of the first trimester of pregnancy was modelled for all subjects, without knowledge of case-control status. Including preconception in the exposure period, in addition to the main period of organogenesis of the urinary system, allowed for delayed action of compounds potentially stored in maternal fat tissues.

Between 2001 and 2003, 21 MSWIs operated in the Rhône-Alpes region. For each, we collected technical characteristics (chimney height, chimney diameter, emission temperature, emission speed, distribution between the gaseous and particulate phases) and emission of dioxins/furans and of three groups of metals (PbMnCuCr, NiAs and CdHg, legally required to be measured), measured by the operator or a public body during the relevant time periods. When we lacked detailed measurements by metal groups (at three MSWIs), we used a global metal emission score assigned by an expert group, based on the incinerator's technical characteristics, according to a procedure described previously.<sup>8</sup> The Institut Géographique National provided landscape descriptions (including terrain roughness), and Météo France data on local meteorological conditions (wind speed and direction, rainfall, mean day and night temperatures, and cloud cover). Experts representing operators, public authorities and research institutions consensually defined the distribution of gaseous and particulate phases a priori for each pollutant, according to incinerator type and fume treatment. This varied according to the incinerator technology, but was mainly gaseous for dioxins and particulate for metals. One of us (LAV) modelled atmospheric concentrations and deposits of dioxins and metals from MSWI emissions with a second-generation dispersion model (ADMS3, Cambridge Environmental Research Consultants), with 100-m grid spacing and including all the parameters mentioned above. Pollutant concentrations attributable to a MSWI were considered negligible outside a 10 km zone. Exposure to dioxins and metals 10 km away from the most heavily polluting MSWI was computed and any family exposed to a level below this threshold was considered not exposed. We then classified women as exposed (exposure value above the threshold) or unexposed. Because so few women were considered exposed, the exposed women were classified into two groups only: above or below median exposure.

### Exposure to other industrial dioxin sources

Other possible sources of dioxin in the atmosphere were considered: petroleum refineries, cement and glass production, some chemical and textile industries, metal production and processing industries, and paper industries. Their activities during the period of interest were assessed from the French Registry of Polluting Emissions (<http://www.irep.ecologie.gouv.fr/IREP>). When at least one industry was present in her municipality of residence, a woman was considered potentially exposed to other industrial dioxin sources.

The Rhône-Alpes region contains 70 MSWIs that operated for at least 1 year since 1988. Most had been decommissioned by the time this study started in 2001, but the cumulative dioxin deposits in the municipality of residence the year of each subject's birth were estimated according to a procedure previously described.<sup>8</sup>

### Area-based socioeconomic characteristics

Two area-based socioeconomic characteristics (deprivation, measured by the index described below, and population density) were constructed since they could be defined at the census block

level, as were the exposure indices described above, for all cases and controls with a known address whether they were interviewed or not.

A deprivation index was constructed for the census block (IRIS, the smallest geographical entity for which 2001 census data are available; the average population of these blocks in Rhône-Alpes was 1400 inhabitants) of each family's home, by principal component analysis of 54 socioeconomic measures included in the census data. These indicators covered housing details, employment and unemployment, population characteristics (immigrants, students, retirees, etc), family and household types, and average income in the IRIS, as reported on census forms. The block deprivation was then ranked on a four-point scale: very low (=wealthy), low, moderate, high (=deprived).<sup>10</sup> Population density was measured as inhabitants per square kilometre.

### Individual risk factors

Case families were contacted to obtain information about their social and demographic characteristics, obstetric history, medical and familial history, employment status and residence history during pregnancy, tobacco and alcohol use, and consumption of locally grown food. Families first received a letter explaining the objectives of the study and asking for an appointment for a telephone interview with a physician from the birth defects registry. If no contact was established after three attempts on different days at different times or because of missed appointments, the questionnaire was mailed to the home. The mailed questionnaire was similar to that used in the telephone interview but omitted the most lengthy section, on lodgings. Mail contact was considered preferable to the absence of data. Individual data concerning case families was obtained from 90 phone interviews and 97 mailed questionnaires. The polling institute used the same questionnaire for telephone interviews for the population controls.

Altogether, 187 case families and 226 population control families answered a detailed questionnaire on individual risk factors.

### Statistical analysis

Medical and environmental characteristics were compared between case families who were and were not interviewed. Correlations between different sources of dioxin exposure and the socioeconomic characteristics of the mother's residence were estimated for controls with the Spearman coefficient.

The percentages of exposed cases and controls were compared, as were their levels of exposure to atmospheric dioxins (sum of gaseous and particulate forms) and to dioxin deposits (sum of gaseous and particulate forms). Multivariate logistic regression models were used to estimate the association between dioxin exposure and the risk of urinary tract birth defects. All models were adjusted for stratification variables (child's sex, year and district of birth). Fifteen potential confounders were included in models using backward selection according to Hosmer and Lemeshow's strategy:<sup>11</sup> area-based indicators for the mother's residence (population density, deprivation score, industrial dioxin sources besides MSWIs), maternal age, parental geographical origin, educational level, employment status during pregnancy, treatment for chronic disease during the first trimester, folic acid supplementation, history of urinary tract birth defects in first-degree relatives, parity, obesity (defined as body mass index  $>30 \text{ kg/m}^2$ ), tobacco and alcohol use during pregnancy, and environmental tobacco smoke exposure. All these analyses used SAS statistical software (v 9.1.3; SAS Institute).

## RESULTS

Most cases were identified in Rhône and Isère, and almost 70% were boys. Pregnancy terminations after prenatal diagnosis accounted for a higher percentage of non-interviewed cases (10.3%) than interviewed cases (4.3%). Non-interviewed cases were more often born at the beginning of the inclusion period, in 2001 and lived in more deprived and more heavily populated environments than interviewed cases (table 1). Among interviewed subjects, cases included a higher proportion of families of non-European origin and of mothers who drank more than one glass of alcohol a week, compared with controls.

### Exposure to MSWI emissions and other industrial dioxin sources (table 2)

Nine of the 21 active MSWIs contributed to dioxin exposure above the threshold at the beginning of pregnancy. In all, 88 women (16.6% of the total sample) were considered exposed to atmospheric concentrations of dioxins and 108 (20.4%) to deposits. Median exposures were  $3.0 \times 10^{-3} \text{ pg/m}^3$  and  $1.7 \times 10^{-5} \text{ pg/m}^2/\text{s}$ , respectively. Only 29 women (5.5%) were considered exposed to metals above the threshold from MSWI emissions. Other industrial dioxin sources were present in the neighbourhood of 17.9% of all subjects, and potential exposure from past MSWI activity was considered present for 20.9%. Among case families, those who were not interviewed were exposed to dioxin emissions from active MSWIs more often than those who were interviewed.

All the exposure variables considered were highly correlated (table 3). Except for metal exposure, assessed exposures to environmental pollution were also strongly correlated with both population density and the deprivation score. In other words, exposure to industrial sources of dioxins was associated with poor socioeconomic conditions.

### Associations between exposure to MSWI emissions and risk of urinary tract birth defects

The odds ratios presented in table 4 included the total sample and were adjusted for stratification variables only, since neither population density nor the deprivation score were identified as a confounder in the association between MSWI emission exposure and risk of urinary tract birth defects. They show increases in the risk of these birth defects linked to above-median exposure to emissions from active MSWIs at the beginning of pregnancy, as atmospheric dioxins (OR 2.84, 95% CI 1.32 to 6.09), dioxin deposits (OR 2.95, 95% CI 1.47 to 5.92) or metals (OR 2.30, 95% CI 0.93 to 5.68), compared with lack of exposure. No excess risk was related to exposure to other dioxin sources or past MSWI activity.

When restricting the sample to interviewed subjects, the risk of above-median exposure to dioxin deposits was decreased due to selection of interviewed cases only (OR 2.25, 95% CI 1.04 to 4.87). In addition, four confounders were identified, namely parental geographical origin, family history of urinary tract birth defects, parity and maternal alcohol drinking. The risk was further reduced (OR 2.05, 95% CI 0.92 to 4.57) compared to the total sample. Similar variations were seen for atmospheric dioxins.

Because dioxin exposure is thought to occur mainly through dietary intake, we quantified the impact of self-reported consumption ( $\geq$ once per week) of locally grown animal food (milk products, eggs and poultry) on risk estimates for dioxin deposits. Compared with mothers who did not eat local food and lived in an area exposed below the median (reference category), consumers of local food in the same type of area had a reduced risk of urinary tract birth defects (OR 0.57, 95% CI

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**Table 1** Sociodemographic characteristics of case groups (interviewed or not interviewed) and control group, case-control study, France, 2001–2004

	Cases				p Value*	Controls (n=226)		OR†	95% CI
	Not interviewed (n=117)		Interviewed (n=187)			n	%		
	n	%	n	%					
Deprivation score									
Very low	28	24.8	61	33.2	0.05	73	33.2	Ref	
Low	13	11.5	33	17.9		54	24.6	0.70	0.42 to 1.15
Moderate	31	27.4	49	26.6		45	20.5	1.46	0.90 to 2.35
High	41	36.2	41	22.3		48	21.8	1.40	0.87 to 2.45
Population density (inhabitants/km <sup>2</sup> )									
<100	18	15.6	41	21.9	0.03	44	19.5	Ref	
100–500	20	17.4	46	24.6		64	28.3	1.91	0.75 to 1.90
501–5000	31	27.0	55	29.4		70	31.0	1.30	0.77 to 2.19
>5000	46	40.0	43	24.1		48	21.2	1.84	1.13 to 3.00
Among interviewed women									
Maternal age (mean±SD)			30.2±5.8					29.9±4.1	
Geographical origin									
Europe			159	85.0	–	211	93.4	Ref	
Other			28	15.0		15	6.6	2.48	1.28 to 4.79
Number of years of education									
<13			46	24.9	–	52	23.0	Ref.	
13–14			32	17.3		56	24.8	1.03	0.64 to 1.65
>14			107	57.8		118	52.2	0.65	0.36 to 1.16
Employment at the beginning of pregnancy			153	82.3	–	185	81.9	1.03	0.62 to 1.70
Folic acid supplementation			9	5.0	–	20	8.9	0.54	0.24 to 1.22
Parity									
0			98	52.4	–	97	42.9	Ref	
1			55	29.4		86	38.1	0.63	0.41 to 0.98
≥2			34	18.2		43	19.0	0.78	0.46 to 1.33
First-degree relatives with urinary tract birth defects			8	4.3	–	1	0.4	10.35	1.28 to 83.49
Tobacco smoking at the beginning of pregnancy									
No			105	57.7	–	141	62.4	Ref	
Passive			45	24.7		35	15.5	1.73	1.04 to 2.87
Active			32	17.6		50	22.1	0.86	0.52 to 1.43
Alcohol consumption at the beginning of pregnancy									
≥1 drink/week			22	12.0	–	10	4.4	2.95	1.36 to 6.41

\*Interviewed versus non-interviewed cases.

†All cases versus controls.

0.36 to 0.90). An increased risk, albeit not significant, was seen in consumers of local food living in areas with above-median exposure (OR 1.88, 95% CI 0.55 to 6.35), whereas non-consumers living in exposed areas had an intermediate risk (OR 1.33, 95% CI 0.46 to 3.87). Departure from a multiplicative effect of exposure to dioxin deposits and consumption of local

food was not however statistically significant (p for interaction=0.27).

We also checked the impact of considering workplace exposure at the beginning of pregnancy, with a time-weighted average estimate of exposure to dioxin emissions. For the 155 control subjects for whom we had information about location

**Table 2** Exposure characteristics of case subjects (according to interview status) and control subjects, case-control study, France, 2001–2004

	Cases					
	Not interviewed (n=117)		Interviewed (n=187)		Controls (n=226)	
	n	%	n	%	n	%
Exposure to atmospheric dioxins*	32	27.4	31	16.7	25	11.1
Exposure to dioxin deposits*	39	33.3	36	19.4	33	14.6
Exposure to metals	9	7.7	13	7.0	7	3.1
Presence of other industrial source of dioxin emissions in the mother's place of residence	24	20.5	28	15.0	43	19.0
Past MSWI activity	28	23.9	43	23.0	40	17.7

MSWI, municipal solid waste incinerator.

\*Among 116 non-interviewed cases, 187 interviewed cases and 225 controls because of missing values.

**Table 3** Spearman coefficients of correlation between measures of exposure and socioeconomic characteristics of residence computed from the control group, case-control study, France, 2001–2004

	Exposure to atmospheric dioxins	Exposure to dioxin deposits	Exposure to metals	Other sources of dioxin emissions	Past MSWI activity	Population density
Exposure to atmospheric dioxins	1					
Exposure to dioxin deposits	0.69*	1				
Exposure to metals	0.34*	0.29*	1			
Other sources of dioxin emissions	0.30*	0.18**	−0.09	1		
Past MSWI activity	0.46*	0.40*	0.18**	0.37*	1	
Population density	0.39*	0.39*	0.10	0.40*	0.34*	1
Deprivation score	0.38*	0.36*	0.11	0.47*	0.37*	0.72*

MSWI, municipal solid waste incinerator.

\* $p < 0.0001$ ; \*\* $p < 0.01$ .

and hours of work at the beginning of pregnancy, concordance was high ( $\kappa=0.94$ ) between the exposure classification that considered workplace exposure and the one that did not.

## DISCUSSION

Our results suggest that exposure to MSWI emissions in early pregnancy, with dioxins used as a marker of the mixture, is associated with the risk of urinary tract birth defects. These results are in agreement with the hypothesis generated by our previous ecological study.<sup>8</sup>

This analysis also underlines the correlations of exposure to MSWI emissions and to various other pollution sources with residence in a socioeconomically deprived area. These socioeconomic characteristics are likely to condition the probability of participation in such studies. Omitting the subjects who were not interviewed from the analysis would have resulted in underestimating the relative risk by as much as 24%.

Population controls were meant to be representative of the source population in our study; although 88% of eligible families contacted agreed to participate, we may nevertheless have selected families with a healthier lifestyle, potentially motivated by concern about the health impact of pollution. It is also plausible that non-interviewed controls (ie, eligible controls who could not be contacted or refused) were, like the non-interviewed cases, more likely to live in exposed areas. If we assume that controls have the same ratio of exposure rates between interviewed and non-interviewed as observed among cases, since there is no evidence that case or control status influences this ratio, we estimate that excluding non-interviewed controls would have resulted in an increase of less than 10% of the crude relative risk. An increase of similar magnitude can be expected from failing to contact potential controls. The magnitude of this overestimation is however not sufficient to entirely explain the excess risk observed.

**Table 4** Risk of urinary tract birth defects associated with exposure to MSWI emissions at the beginning of pregnancy, case-control study, France, 2001–2004

	Cases (n = 304)		Controls (n = 226)		OR*	95% CI
	n	%	n	%		
Active MSWIs						
Atmospheric dioxins						
Not exposed	240	79.2	200	88.9	Ref.	
Exposed	63	20.8	25	11.1	1.99	1.17 to 3.40
Below median	30	9.9	15	6.7	1.44	0.72 to 2.87
Above median	33	10.9	10	4.4	2.84	1.32 to 6.09
Dioxin deposits						
Not exposed	228	75.3	192	83.3	Ref.	
Exposed	75	24.7	33	14.6	1.83	1.13 to 2.96
Below median	34	11.2	21	9.3	1.18	0.63 to 2.19
Above median	41	13.5	12	5.3	2.95	1.47 to 5.92
Metals						
Not exposed	282	92.8	219	96.9	Ref.	
Exposed	22	7.2	7	3.1	2.30	0.93 to 5.68
Other industrial sources of dioxin emissions at the mother's place of residence	52	17.1	43	19.0	0.73	0.45 to 1.19
Past MSWI activity	71	23.4	40	17.7	1.31	0.83 to 2.05
Consumption of local food and dioxin deposits (interviewed cases only)						
Non-consumer and not exposed above median	98	56.0	101	44.9	Ref.	
Consumer and not exposed above median	58	33.1	112	49.8	0.57†	0.36 to 0.90
Non-consumer and exposed above median	11	6.3	7	3.1	1.33†	0.46 to 3.87
Consumer and exposed above median	8	4.6	5	2.2	1.88†	0.55 to 6.35

MSWI, municipal solid waste incinerator.

\*Adjusted for child's sex, year and district of birth.

†Additional adjustment for geographical origin, parity, family history and alcohol consumption.

The impact of individual confounders was assessed only among interviewed subjects. Our strategy identified a few confounders, and controlling for them had a minimal impact on the overall risk estimates.

The principal cause of any measurement errors that might have affected exposure assessment differentially is likely to be an erroneous home address at the beginning of pregnancy. For the non-interviewed cases, the only address available was from the medical records and was the address at the child's birth. Various sources (questionnaires, census data, etc) suggest that the percentage of families who moved during pregnancy was in the order of 10%. This type of error would therefore have principally affected the case group, and the direction of the effect is hard to predict. We saw that estimating exposure for place of residence without considering workplace exposure had a minimal impact on estimates. Other measurement errors are due to insufficiently detailed information for modelling, such as the paucity of emission measurements, extrapolation from distant meteorological monitoring stations, or local topographical characteristics that produced dispersion patterns difficult for the software to take into account. We validated the modelling by comparing our predictions of atmospheric emissions and deposits with those obtained by the Institut de Veille Sanitaire, which modelled emissions from one of the same incinerators (Bourgoin, Isère) for a similar time period.<sup>12</sup> All modelling was done without knowledge of case-control status.

Dioxin emissions served as a marker for the entire mixture of compounds generated by incineration, several of which are teratogenic. In mice, effects on the developing urinary tract (hydronephrosis) and palate (cleft palate) are the two most sensitive and reproducible indicators of 2,3,7,8-tetradibenzo-p-dioxin (TCDD) developmental toxicity. Hydronephrosis is induced at doses below those that induce palatal clefting.<sup>13</sup> These effects are also observed when testing complex organic mixtures containing TCDD.<sup>14</sup> Dioxins, even at low doses, are likely to disrupt multiple endocrine pathways, and their toxic effect on the developing urinary tract has been attributed in part to their interaction with hormone and growth factor receptors, such as epidermal growth factor (EGF) receptors.<sup>15</sup>

Our results suggest that exposure during early pregnancy to emissions from some MSWIs operating in southeastern France between 2001 and 2003 increased the background level of a mixture of compounds including dioxins/furans to a level sufficient to induce an excess risk of urinary tract birth defects. For dioxins only, the predicted additional level above which effects were observed was in the range of 0.0015 pg I-TEQ/m<sup>3</sup> for atmospheric concentrations and 10<sup>-5</sup> pg/m<sup>2</sup>/s for dioxin deposits. In our study, no MSWI complying with the regulatory limit of 0.1 ng TEQ/m<sup>3</sup> for dioxin emissions reached this level. It is lower than the atmospheric dioxin concentrations measured in large urban areas and due to various pollution sources,<sup>16</sup> but almost equal to the highest concentration predicted around another French MSWI, that in Besançon (0.0016 I-TEQ/m<sup>3</sup>) where an excess risk of non-Hodgkin's lymphoma was observed.<sup>17</sup>

In the general population, ingestion is generally considered the principal route of dioxin exposure. In our study, the model results for atmospheric dioxins and dioxin deposits resulting from MSWI emissions were closely correlated: the associations observed could not be attributed to one form only. Despite documented emissions at the MSWI stacks, studies measuring serum dioxin levels in nearby populations often fail to show their influence (except for a slight increase among consumers of local animal products),<sup>18</sup> even though modelled exposure is

correlated with air and soil levels when adequate indicators are used.<sup>19, 20</sup> This suggests that serum levels that integrate residents' lifelong history of environmental exposure, including dietary habits and medical, obstetric and physiological characteristics, may not adequately reflect short-term variations in exposure, such as those estimated during pregnancy. This hypothesis is corroborated by an experiment showing that a single bolus dose administered by gavage to pregnant rats on day 15 of gestation resulted in considerably higher (1.7 times) fetal concentrations on day 16 than did low daily doses.<sup>21</sup>

Our data also suggest that dietary exposure to locally grown food plays a specific role: in areas not exposed to MSWI emissions, the risk of urinary tract birth defects is lower among consumers of local food, whereas in exposed areas this risk is higher among those who do than those who do not eat local produce.

Although we considered many characteristics of the study families, it remains possible that this association might be explained by a risk factor other than residence near a MSWI. The interpretation of these results is made more delicate by the relatively low level of the estimated additional exposure attributable to MSWI emissions compared with the atmospheric concentrations reported in some urban areas. Nonetheless, we think that the unique susceptibility of the developing fetus and the unique mixture of embryotoxic agents released by waste incineration must be considered in this situation.

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**Competing interests** None.

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## REFERENCES

1. CITEPA. *Emissions dans l'air en France. Substances relatives à la contamination par les polluants organiques persistants*. Paris: Centre Interprofessionnel Technique d'Etudes de la Pollution Atmosphérique, 2008.
2. Williams FL, Lawson AB, Lloyd OL. Low sex ratios of births in areas at risk from air pollution from incinerators, as shown by geographical analysis and 3-dimensional mapping. *Int J Epidemiol* 1992;**21**:311–9.
3. Rydhstroem H. No obvious spatial clustering of twin births in Sweden between 1973 and 1990. *Environ Res* 1998;**76**:27–31.
4. Lin CM, Li CY, Mao IF. Birth outcomes of infants born in areas with elevated ambient exposure to incinerator generated PCDD/Fs. *Environ Int* 2006;**32**:624–9.
5. Tango T, Fujita T, Tanihata T, et al. Risk of adverse reproductive outcomes associated with proximity to municipal solid waste incinerators with high dioxin emission levels in Japan. *J Epidemiol* 2004;**14**:83–93.
6. ten Tusscher GW, Stam GA, Koppe JG. Open chemical combustions resulting in a local increased incidence of orofacial clefts. *Chemosphere* 2000;**40**:1263–70.
7. Dummer TJ, Dickinson HO, Parker L. Adverse pregnancy outcomes around incinerators and crematoriums in Cumbria, north west England, 1956–93. *J Epidemiol Community Health* 2003;**57**:456–61.
8. Cordier S, Chevrier C, Robert-Gnansia E, et al. Risk of congenital anomalies in the vicinity of municipal solid waste incinerators. *Occup Environ Med* 2004;**61**:8–15.
9. VanAllen M. Urinary tract. In: Stevenson RE, Hall JG, Goodman RM, eds. *Human malformations and related anomalies volume II*. Oxford:Oxford University Press, 1993:501–550.

10. **Havard S**, Deguen S, Bodin J, *et al*. A small-area index of socioeconomic deprivation to capture health inequalities in France. *Soc Sci Med* 2008;**67**:2007–16.
11. **Hosmer D**, Lemeshow S. *Applied logistic regression*, 2nd edn. Wiley, Series in Probability and Statistics, 2000.
12. **Viel JF**, Daniau C, Gorla S, *et al*. Risk for non Hodgkin's lymphoma in the vicinity of French municipal solid waste incinerators. *Environ Health* 2008;**7**:51.
13. **Couture LA**, Abbott BD, Birnbaum LS. A critical review of the developmental toxicity and teratogenicity of 2,3,7,8-tetrachlorodibenzo-p-dioxin: recent advances toward understanding the mechanism. *Teratology* 1990;**42**:619–27.
14. **Silkworth JB**, Cutler DS, Antrim L, *et al*. Teratology of 2,3,7,8-tetrachlorodibenzo-p-dioxin in a complex environmental mixture from the love canal. *Fundam Appl Toxicol* 1989;**13**:1–15.
15. **Abbott BD**, Birnbaum LS. Effects of TCDD on embryonic ureteric epithelial EGF receptor expression and cell proliferation. *Teratology* 1990;**41**:71–84.
16. **IARC**. *IARC monographs on the evaluation of carcinogenic risks to humans Vol. 69 Polychlorinated dibenzo- para-dioxins and polychlorinated dibenzofurans*. IARC: Lyon, France, 1997.
17. **Floret N**, Mauny F, Challier B, *et al*. Dioxin emissions from a solid waste incinerator and risk of non-Hodgkin lymphoma. *Epidemiology* 2003;**14**:392–8.
18. **Chen HL**, Su HJ, Lee CC. Patterns of serum PCDD/Fs affected by vegetarian regime and consumption of local food for residents living near municipal waste incinerators from Taiwan. *Environ Int* 2006;**32**:650–5.
19. **Oh JE**, Choi SD, Lee SJ, *et al*. Influence of a municipal solid waste incinerator on ambient air and soil PCDD/Fs levels. *Chemosphere* 2006;**64**:579–87.
20. **Goovaerts P**, Trinh HT, Demond AH, *et al*. Geostatistical modeling of the spatial distribution of soil dioxin in the vicinity of an incinerator. 2. Verification and calibration study. *Environ Sci Technol* 2008;**42**:3655–61.
21. **JECFA**. Joint FAO/WHO Expert Committee on Food Additives: Summary and Conclusions. Fifty-seventh meeting. Rome, 5-14 June 2001, 2001.