ABSTRACT

Using data from the Nova Scotia Atlee Perinatal Database, rates of adverse birth outcomes were compared among residents of Sydney, Nova Scotia and residents of Cape Breton County, Nova Scotia (excluding Sydney) with birth outcomes among residents of the rest of Nova Scotia. There was a small but statistically significant increase in the rate of major congenital anomalies in Sydney (2.8%) compared to the rest of Nova Scotia (2.3%) (adjusted RR=1.25, 95% CI=1.04-1.51). Rates of anomaly sub-groups were consistently elevated in Sydney compared to the rest of Nova Scotia, but most were not statistically significant. For the most part, the increased rates of congenital anomalies observed among residents of Sydney were not evident in the neighbouring community. Since Sydney and the rest of Cape Breton County share a similar risk factor and socio-demographic profile, other factors likely explain the increased rates observed in Sydney.

ABRÉGÉ

En puisant dans la base de données périnatales Atlee de Nouvelle-Écosse, nous avons comparé les taux d'issues indésirables de la grossesse chez les habitants de Sydney et de Cape Breton County (sauf Sydney) à ceux des habitants du reste de la Nouvelle-Écosse. Nous avons constaté une augmentation faible, mais significative, des taux des principales anomalies congénitales à Sydney (2,8 %) par rapport au reste de la Nouvelle-Écosse (2,3 %) (RR standardisé = 1,25, 95 % IC=1,04-1,51). Les taux des sous-groupes d'anomalies étaient uniformément plus élevés à Sydney, mais dans la plupart des cas, pas de façon significative. Dans l'ensemble, les taux supérieurs d'anomalies congénitales observés chez les habitants de Sydney ne se retrouvaient pas dans la localité voisine. Comme Sydney et le reste de Cape Breton County affichent des facteurs de risque et un profil socio-démographique semblables, d'autres facteurs expliquent sans doute les taux supérieurs observés à Sydney.

Congenital Anomalies and Other Birth Outcomes Among Infants Born to Women Living Near a Hazardous Waste Site in Sydney, Nova Scotia

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Concern about possible adverse health effects for populations living near hazardous waste sites has grown in recent years. It has been reported that one of the largest hazardous waste sites in North America is in Sydney, Nova Scotia. This waste site is largely a result of about 80 years of coke oven operations used to operate one of the country's largest steel operations. The waste site area includes several sources of contamination including the "Tar Ponds", a landfill area, a waste incinerator and sewage outfalls. The "Tar Ponds" were constructed in the 1940s to handle the overflow coal tar and currently contain an estimated 700,000 tons of contaminated sediment. The landfill area was originally used for slag and other wastes from steel production but is now being used for municipal garbage.[1] Contamination is documented in the soil and groundwater in surrounding areas and from air emissions.[2] Some of the chemicals identified in the Sydney site include polycyclic aromatic hydrocarbons, polychlorinated biphenyls, benzene, arsenic, lead and other heavy metals.

Previous reports based on vital statistics and cancer registrations have shown that residents of Cape Breton County (CBC), Nova Scotia have higher rates of certain cancers[3] and higher mortality rates.[4,5] Although no direct cause and effect relationships have been established, environmental and occupational exposure to by-products of steel and coke production are suspected contributors.

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This study was conducted to compare the rates of adverse birth outcomes among residents of Sydney, Nova Scotia compared with residents of the rest of CBC (with similar occupational and lifestyle characteristics) and with Nova Scotia residents outside of Cape Breton County. Whereas excess cancer and mortality may be indicative of historic exposures, increased rates of adverse birth outcomes may reflect more current conditions.

METHODS

Live births and stillbirths among Nova Scotia residents between 1988 and 1998 were identified from the Nova Scotia Atlee Perinatal Database. The Nova Scotia Atlee Perinatal Database, which began province-wide data collection in 1988, is a unique repository of information pertaining to all hospital births of 500 grams and more. The database contains information on maternal and newborn medical conditions, labour and delivery events, mortality and some socio-demographic variables. Maternal residence information was determined from county, municipality and postal code of each woman at the time of the delivery. Information is stored in the database without nominal identifiers, but unique numbers are assigned such that information between mother and her infant(s) is linkable. Ongoing data quality reviews and periodic re-abstraction studies indicate the data are reliable and of good quality.[6] The analyses of congenital anomalies also included information on pregnancy terminations for prenatally diagnosed congenital anomalies, regardless of the fetal weight.

The categories of birth outcomes that were examined included congenital anomalies and outcomes related to fetal weight and gestation. In the analyses of congenital anomalies, only major congenital anomalies

were examined. These were analyzed as all major anomalies combined and by the following anomaly sub-groups: neural tube defects, cardiovascular defects, gastrointestinal defects, respiratory defects, ear/eyes/nose/mouth defects, genito-urinary defects, musculoskeletal defects, chromosomal abnormalities and syndromes not due to chromosomal abnormalities. In the category of all major anomalies combined, infants are counted only once regardless of the number of anomalies they had. However, an infant with several anomalies could be included in more than one system-specific category.

The growth and gestation outcomes, defined for live born infants, included low birthweight (defined as birthweight less than 2500 grams among live born infants), prematurity (defined as delivery before 37 weeks), and intrauterine growth restriction (defined as the bottom 10th percentile for birthweight according to gestational week and sex of the infant).[7]

Comparisons of outcomes were made according to maternal residence at the time of delivery. The outcomes for Nova Scotia residents, excluding CBC, were compared with: 1) the outcomes for residents of Sydney, and 2) the outcomes for residents of CBC (excluding Sydney).

Crude and adjusted rate ratios were estimated from odds ratios using logistic regression models with SAS software.[8] Potential confounders were obtained from the Perinatal Database and included maternal age, parity, infant sex, smoking during pregnancy, gestational diabetes, and pre-existing maternal diabetes. Confounders were eliminated from a model if that factor changed the coefficient pertaining to area of residence by less than 2%.[9] In order to compare results among the same subset of women for each of the anomaly subgroups, the same confounders were controlled for in the final model for each anomaly group. This meant that for some anomaly groups, a factor was included in the final model even though it did not meet the requirement of changing the coefficient pertaining to residence by 2%.

TABLE I
Maternal Risk Factors by Region of Residence, 1988-1998

Risk Factor	# (%) with Factor	Rate Ratio (95% CI)
Maternal Smoking		
N.S. (Exc. CBC)	30,778 (29.5%)	1.0
Sydney	1479 (37.6%)	1.27 (1.22-1.33)
CBC (Exc. Sydney)	4220 (38.5%)	1.31 (1.27-1.34)
Maternal Age<20		
N.S. (Exc. CBC)	8507 (7.8%)	1.0
Sydney	507 (12.4%)	1.58 (1.45-1.71)
CBC (Exc. Sydney)	1436 (12.5%)	1.59 (1.51-1.68)
Maternal Age>35		
N.S. (Exc. CBC)	9578 (8.8%)	1.0
Sydney	386 (9.4%)	1.07 (0.97-1.17)
CBC (Exc. Sydney)	857 (7.5%)	0.84 (0.79-0.90)
No Prenatal Class Attendance: Nulliparous Women Only		
N.S. (Exc. CBC)	11,446 (25.6%)	1.0
Sydney	652 (40.2%)	1.57 (1.48-1.67)
CBC (Exc. Sydney)	2115 (46.4%)	1.82 (1.75-1.88)
Nulliparity		
N.S. (Exc. CBC)	48,299 (44.5%)	1.0
Sydney	1774 (43.2%)	0.97 (0.94-1.01)
CBC (Exc. Sydney)	4815 (41.8%)	0.94 (0.92-0.96)
Infant Sex: Male		
N.S. (Exc. CBC)	55,357 (51.2%)	1.0
Sydney	2067 (50.5%)	0.99 (0.96-1.02)
CBC (Exc. Sydney)	5925 (51.5%)	1.01 (0.99-1.03)
Pre-existing Diabetes		
N.S. (Exc. CBC)	350 (0.32%)	1.0
Sydney	19 (0.46%)	1.44 (0.91-2.28)
CBC (Exc. Sydney)	48 (0.42%)	1.29 (0.96-1.75)
Gestational Diabetes		
N.S. (Exc. CBC)	2514 (2.3%)	1.0
Sydney	186 (4.5%)	1.96 (1.69-2.26)
CBC (Exc. Sydney)	481 (4.2%)	1.80 (1.64-1.99)

RESULTS

During the 11-year study period, there were 4,128 births among Sydney residents, 11,620 births among residents of Cape Breton County (excluding Sydney), and 109,437 births among Nova Scotia residents outside of Cape Breton County. As can be seen in Table I, the rates of maternal smoking, teenage mothers, lack of prenatal class attendance, and gestational diabetes were significantly higher among residents of Sydney and CBC (excluding Sydney) compared to residents of Nova Scotia (excluding CBC).

Table II shows the comparison of the rates of congenital anomalies among the three geographic areas. Anomaly subgroups with fewer than 10 cases in Sydney are not presented. A 25% increase in the rate ratio for all major anomalies was found among residents of Sydney compared to Nova Scotia residents, after adjusting for maternal age and parity (RR=1.25, 95% CI= 1.04-1.51). There was no evidence of an excess of major congenital anomalies in Cape Breton County (excluding Sydney) as compared to the rest of Nova Scotia (RR=1.04, 95% CI= 0.91-1.18).

The rate ratio for neural tube defects among residents of Sydney was significantly increased relative to Nova Scotia (excluding CBC) (RR=1.83, 95% CI= 1.08-3.09), whereas the rate ratio for residents of the rest of CBC was not increased. For the remainder of anomaly sub-groups that were analyzed, there was a non-significant trend of increased rates in Sydney relative to the rest of Nova Scotia. With one exception (musculoskeletal anomalies), the rate ratios for residents of CBC (excluding Sydney) were not different from the rates observed for Nova Scotia residents.

As seen in Table III, there was no evidence that rates of low birthweight differ among residents of Sydney or residents of CBC compared to the rest of Nova Scotia. There was a statistically significant increase in prematurity rates among the residents of CBC (excluding Sydney) relative to the rest of Nova Scotia. The adjusted rate ratios of intrauterine growth restriction were decreased among residents of Sydney and the rest of CBC compared to residents in the rest of Nova Scotia.

DISCUSSION

The results of this report suggest that the rates of major congenital anomalies are

TABLE II
Crude and Adjusted Relative Risks of Congenital Anomalies Related to Area of Residence, 1988-1998

Anomoly Category	# (Rate per 1000 Births)	Crude RR (95% CI)	Adjusted RR* (95% CI)
Major Anomalies			
N.S. (Exc. CBC)	2518 (22.9)	1.0	1.0
Sydney	117 (28.3)	1.24 (1.03-1.50)	1.25 (1.04-1.51)
CBC (Exc. Sydney)	272 (23.4)	1.02 (0.90-1.16)	1.04 (0.91-1.18)
Neural Tube Defects			
N.S. (Exc. CBC)	213 (1.9)	1.0	1.0
Sydney	15 (3.6)	1.87 (1.11-3.16)	1.83 (1.08-3.09)
CBC (Exc. Sydney)	22 (1.9)	0.98 (0.63-1.51)	0.94 (0.61-1.46)
Cardiovascular			
N.S. (Exc. CBC)	843 (7.7)	1.0	1.0
Sydney	40 (9.7)	1.26 (0.92-1.73)	1.27 (0.93-1.75)
CBC (Exc. Sydney)	80 (6.9)	0.90 (0.71-1.13)	0.92 (0.73-1.15)
Genito-urinary			
N.S. (Exc. CBC)	245 (2.2)	1.0	1.0
Sydney	11 (2.7)	1.19 (0.65-2.18)	1.19 (0.65-2.18)
CBC (Exc. Sydney)	13 (1.1)	0.50 (0.29-0.87)	0.50 (0.29-0.87)
Musculoskeletal			
N.S. (Exc. CBC)	665 (6.1)	1.0	1.0
Sydney	29 (7.0)	1.16 (0.80-1.68)	1.16 (0.80-1.69)
CBC (Exc. Sydney)	103 (8.9)	1.47 (1.19-1.81)	1.48 (1.20-1.83)
Ear, Eyes, Nose, Throat			
N.S. (Exc. CBC)	253 (2.3)	1.0	1.0
Sydney	13 (3.1)	1.36 (0.78-2.38)	1.36 (0.78-2.38)
CBC (Exc. Sydney)	21 (1.8)	0.78 (0.50-1.22)	0.78 (0.50-1.23)
Chromosomal			
N.S. (Exc. CBC)	265 (2.4)	1.0	1.0
Sydney	13 (3.1)	1.30 (0.75-2.27)	1.35 (0.77-2.35)
CBC (Exc. Sydney)	19 (1.6)	0.68 (0.42-1.08)	0.74 (0.47-1.19)

* Adjusted for major anomaly, maternal age, maternal smoking, parity

TABLE III
Crude and Adjusted Relative Risks of Low Birthweight, Preterm Delivery and Intrauterine Growth Restriction (IUGR) Related to the Area of Residence, 1988-1998

Outcome	# (%)	Crude RR (95% CI)	Adjusted RR* (95% CI)
Low Birthweight			
N.S. (Exc. CBC)	5874 (5.6%)	1.0	1.0
Sydney	222 (5.6%)	1.01 (0.88-1.16)	0.96 (0.83-1.10)
CBC (Exc. Sydney)	627 (5.7%)	1.02 (0.93-1.11)	0.97 (0.89-1.06)
Preterm Delivery			
N.S. (Exc. CBC)	6538 (6.1%)	1.0	1.0
Sydney	271 (6.6%)	1.09 (0.96-1.24)	1.10 (0.98-1.26)
CBC (Exc. Sydney)	754 (6.6%)	1.10 (1.01-1.19)	1.13 (1.04-1.22)
IUGR			
N.S. (Exc. CBC)	9831 (9.5%)	1.0	1.0
Sydney	369 (9.4%)	0.98 (0.88-1.09)	0.89 (0.80-1.00)
CBC (Exc. Sydney)	1022 (9.4%)	0.99 (0.92-1.06)	0.89 (0.83-0.95)

* Adjusted for major anomaly, maternal age, maternal smoking, parity

25% higher in Sydney compared to the rest of Nova Scotia, whereas there was no excess in the neighbouring communities in Cape Breton County. Yet, the actual difference in the rates of major anomalies in Sydney (2.8%) compared to Nova Scotia (excluding CBC) (2.3%) is relatively small. Our results differ from other studies where excess cancer incidence and excess mortality have been observed among residents of Sydney as well as among residents of Cape Breton County relative to the rest of Nova Scotia.[3-5] Our results suggest that factors contributing to the increased rates of congenital anomalies may be unique to residents of Sydney. Based on information from Statistics Canada and from the Perinatal Database, residents of Sydney and residents of the rest of CBC have similar socioeconomic and risk factor profiles.[10] Therefore, uncontrolled confounding likely does not explain the reason why excess anomaly rates were observed in Sydney but not in the rest of CBC.

Of note in this study is the consistently increased rate ratio for each congenital anomaly category among Sydney residents. Although statistical significance was limited to the categories of all major anomalies and neural tube defects, the rate ratio for each category was at least 20% higher in Sydney compared to the rest of Nova Scotia. However, given the number of statistical comparisons that were made, a Type 1 error cannor be ruled out to explain the statistically significant findings.

Our current understanding of the etiology of birth defects is poor: approximately 65% of birth defects have no known cause.[11] Concern about the effects of exposures to chemical pollutants in the environment is often based on animal studies that suggest adverse effects coupled with the knowledge that the developing embryo is susceptible to external agents. The recognition of the teratogenic potential of drugs and chemicals has led to concerns that environmental exposures may contribute to birth defects of unknown cause, but convincing evidence linking environmental exposures with congenital malformations is lacking.[12]

There is inconsistent support from the literature for a relationship between residence in the vicinity of a hazardous waste site and congenital anomalies. Two recent reviews of health effects associated with residence near hazardous waste sites showed that increases in the risk of birth defects were generally small and that they occurred primarily from studies of multiple waste sites, rather than outcomes associated with residence near a single hazardous waste site.[13,14] Studies of multiple waste sites include large sample sizes and therefore are able to provide sufficient power to detect relatively small increases in risk. The current study appears to be one of the only single site studies to report significant risks of congenital anomalies among women living in proximity to a hazardous waste site.

A limitation of this, and most of the other studies that have evaluated reproductive outcomes related to residence near waste sites, is the ecologic nature of the exposure assessment. Information about the biologically relevant exposure routes

from the toxins in the Sydney waste site is scant. Improved indicators of individual exposures, such as biomarkers, would strengthen conclusions derived from these studies. In the future, as more numbers of cases accumulate, it may be possible to undertake a more refined geographic analysis looking at the risks according to proximity to the site.

There was no evidence of higher rates of low birthweight or intrauterine growth restriction in either Sydney or in the rest of CBC compared to the rest of Nova Scotia. One might expect that if environmental contaminants were an important etiologic factor, effects on intrauterine growth would be observed. Birthweight deficiencies have been noted more consistently than excess anomaly rates among the studies of women living in close proximity to toxic waste sites.[15-18] Other markers of environmental exposures, such as spontaneous abortions or infertility, could not be evaluated in this study because these outcomes are not available in the Perinatal Database.

Residence information was collected at the time of delivery and, for the congenital anomaly outcomes, was a surrogate measure of residence during the early part of the pregnancy. Although the magnitude of residential mis-classification is not known, data from an ongoing case-control study in Nova Scotia indicate that about 10% of women moved between municipalities during pregnancy. The effect of this misclassification would likely bias the risk estimates toward the null.

The strengths of this study include the ability to capture information on birth outcomes and other information on a province-wide basis using consistent methods. In the present study, residence code was from the Perinatal Database, and therefore, not subject to the potential differential bias that occurs when coding of residence for the numerator data (e.g., health outcomes) is from a different source than the denominator data (e.g., total populations). In this study, case ascertainment of congenital anomalies was more complete than in studies that are limited to live or stillbirths because we were able to include data from pregnancy terminations for prenatally diagnosed anomalies.

The results of this report must be interpreted with caution. More research is necessary to determine if the small increase in rates of congenital anomalies observed among Sydney residents is related to the environment. Clean-up efforts in Sydney are proceeding (and should proceed) in spite of the lack of definitive results obtained from health studies to date.

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