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Evaluation of the Association Between Birth Defects and Exposure to Ambient Vinyl Chloride

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ABSTRACT Birth defects incidence for infants born to residents of Shawinigan, Canada in 1966–1979 were significantly higher than in three comparison communities. Since there has been a vinyl chloride polymerization plant in this town since 1943 from which ten cases of angiosarcoma of the liver have been identified, this study explores the possible association between exposure to vinyl chloride monomer (VCM) in ambient air and the occurrence of birth defects in the community. The excess of birth defects fluctuated seasonally in a way that corresponded to changes in VCM concentration in the environment. Mothers who gave birth to malformed children were younger on average in Shawinigan than in the comparison communities. However, there was no excess of still-births in Shawinigan. The excess in birth defects involved most organ systems, and variation in birth-defect rates among school districts could not be accounted for by estimates of VCM in the atmosphere. The occupational and residential histories of parents who gave birth to malformed infants were compared with those of parents of normal infants. The two groups did not differ in occupational exposure or closeness of residence to the vinyl chloride polymerization plant. Some descriptive data from this study raised the hypothesis of an association between VCM in the air and birth defects in the exposed community, but as a whole, within the sample size available, such an association could not be substantiated.

Vinyl chloride monomer (VCM) is carcinogenic in animals (Viola et al., '71; Maltoni and Lefemine, '74,'75) and man (Creech and Johnson, '74; Thomas and Popper, '75; Makk et al., '76; Delorme and Thériault, '78; Monson et al., '74; Waxweiler et al., '76). It is mutagenic in man: Chromosome breaks have been observed in lymphocytes of workers exposed to VCM (Funes-Cravioto et al., '75; Ducatman et al., '75; Fleig and Thiess, '78; Léonard et al., '77; Hansteen et al., '78; Kucerova et al., '79), in microbial tests, in *Drosophila*, in yeast, and in mammalian cells (Drevon and Kuroki, '79; Bartsch and Montesano, '75; Loprieno et al., '76; Magnusson and Ramel, '76). VCM generates mutations primarily through one of its metabolites, chloroethylene oxide, and with the involvement of liver microsomal enzymes (Bartsch and Montesano, '75; Vainio, '78; Rannug et al., '74; Green and Hathway, '78). Although miscarriages and fetal losses among the wives of exposed workers have been suspected (Infante et al., '76), such an effect remains undocumented (MacMahon, '77; Downs et al., '77). VCM teratogenicity has yet to be documented. VCM was present in the fetal and maternal blood and the amniotic fluid of pregnant rats after exposure to contaminated air (Ungvary et al., '78). Two studies of VCM teratogenicity in animals (Ungvary et al., '78; John et al., '77) failed to demonstrate fetal malformations but showed increased fetal mortality rates.

VCM mutagenicity and possible teratogenicity in man raised the question of the origin of birth defects in communities near VCM-emitting plants.

At normal temperature and pressure, VCM is a gas; it liquifies at −13°C. It is processed

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into polyvinyl chloride (PCV, a plastic) through polymerization reactions in autoclaves. The gas is released into the environment during unloading, processing, and autoclave-cleaning operations. The concentration of VCM to which people in the community are exposed depends on production rate, wind direction, wind velocity, and distance from the plant.

In Shawinigan (population 27,000), a vinyl chloride polymerization plant has been in operation since 1943. The plant, which employs about 250 workers, currently produces 25,000 tons/year of PCV. Ten cases of angiosarcoma of the liver have been reported among workers at this plant. In addition, Shawinigan has two other chemical plants, one aluminum electrolysis plant, one carbide plant, and one pulp and paper mill. Several pollutants are discharged into the environment.

This study pursues four objectives. First, to compare the birth-defect and stillbirth rates in Shawinigan with other communities in an attempt to document the high birth-defect rates previously observed in this town; second, to correlate monthly and seasonal variations of birth defects with concentration of VCM in the environment; third, to correlate geographic variation in birth-defect rates with estimates of VCM in the air in the several residential areas; and finally, to compare a group of parents who gave birth to malformed infants with a control group with respect to residential and occupational history, as well as exposure to other risk factors known to generate birth defects.

METHODS

Study population and observation periods

For the assessment of birth-defect rates, the population comprised all women who delivered during the study period and whose residence was within the city limits of the study or the comparison communities at the time of delivery. It extended from January 1, 1966, to December 31, 1979. The starting year 1966 was selected because, due to hospital reorganizations, the information was unobtainable in a suitable form prior to that date. The case-control study was limited to a shorter period (January 1, 1973, to December 31, 1979) because it required information based on the mothers' recollection of events during their pregnancies. It included only Shawinigan mothers who gave birth to a malformed child and their controls.

Definition of a birth defect

A birth defect was defined as a gross physical anomaly present at birth or detected at the hospital during the first days after delivery (within the first 4–6 days). A list of birth defects to be included in the study was drawn beforehand and only those that fit this list were retained.

Two major difficulties were encountered. In birth defects of the cardiovascular system, it soon became apparent that in several hospitals, no diagnoses other than murmurs of the heart were reported, whereas in other hospitals (e.g., Shawinigan), thorough investigations were conducted, leading to precise diagnoses. Consequently only heart murmurs judged severe enough were included in the study, under a separate category. Severity and significance of heart murmurs were assessed by consulting the children's subsequent medical records.

Although such minor defects as metatarsus varus, calcaneum varus and valgus, metatarsus adductus, and abnormal positioning of fingers or toes were not included in the study, foot anomalies which required either a cast or surgery for correction in the year following birth, were considered defects.

Comparison communities

To assess the importance of the excess of birth defects in Shawinigan, three comparison communities were chosen, based on their similarity to Shawinigan in population size and structure, socioeconomic level, and medical-care facilities (Table 1). In order to take into account the influence of environmental pollution, one town with an aluminum plant but no VCM-emitting plant (Baie-Comeau–Hauterive) and two towns with neither a VCM nor an aluminum plant (Drummondville and Rimouski) were chosen as control communities. The recourse to referent communities was necessary because no accurate national or provincial data were available.

Data sources

The Quebec Population Registry provided the annual numbers of births and stillbirths in the communities; as the 1979 data were not available, numbers were estimated from the 3 preceding years. The Quebec Ministry of Social Affairs provided a list of hospitals where women residing in these communities gave birth during the study period. The School Board of Shawinigan furnished the

TABLE 1 Comparisons between Shawinigan and the referent communities

	Shawinigan	Drummondville	Rimouski	Baie-Comeau-Hauterive
Female population (1971)	14,140	16,295	14,115	12,430
% females aged 15-44	44.7	46.9	50.5	50.5
Average annual number of births per 1,000 women aged 15-44	51.4	70.9	82.2	87.9
Average family income ($)	7,881	8,652	9,228	10,954
Ratio of physicians to population	1:689	1:779	1:545	1:1,260
% males employed in manufacturing	43.8	18.7	6.4	38.8
% females employed in manufacturing	15.8	31.1	3.0	5.2

school district boundaries. Birth-defect children and controls were identified and data were collected from several medical files in the hospitals (delivery-room daybooks, birth-defect rosters, discharge lists, mothers' and children's medical files, and birth rosters). For two referent communities (Baie-Comeau–Hauterive and Rimouski) our physician reviewed the files not only of known malformation cases, but of all newborns, to ensure that all cases had been reported.

Identification of cases

Malformed infants born to mothers who resided in the study communities were identified from the birth-defect rosters and the departure lists of the delivery hospitals. A physician reviewed the medical files and decided whether or not each infant met the definition of a birth-defect child. When in doubt, he referred to consultation reports or specialists' advice. In the case-control study, mothers of all affected infants and matched controls were interviewed at home by two medical students.

Selection of controls

Each control was a live-born infant without congenital malformation whose parents resided in Shawinigan and whose birth immediately followed that of the malformed child. Cases and controls were matched by maternal age within 2 years, sex of the infant, and place of residence of the mother (within the city limits of Shawinigan).

Estimates of VCM air concentrations

Two studies were conducted to assess the VCM concentration in ambient air in Shawinigan (Thériault et al., '81). The first consisted in actual measurements of VCM on air samples in several locations in town. Field sampling was done with Bendix BDX 44 Super Sampler pumps, VCM was absorbed on activated charcoal, and samples were analyzed with a Perkin-Elmer model F-42 headspace analyzer gas chromatograph. The desorbent was N,N-dimethylacetamide in water. This first pilot study reached the following conclusions: VCM air concentration varied from nothing to 45 ppb; during winter, VCM accumulated in the snow in the vicinity of the plant; VCM concentration differed between indoor and outdoor samples.

Considering the high cost of a comprehensive air-monitoring program and the results of the first study, ambient VCM concentra-

tion in various locations in Shawinigan was estimated by a consultant firm using a dispersion model. This model used the Pasquill-Gifford equations and allowed the development of isopleths of vinyl chloride concentration over Shawinigan. It employed meteorological variables (such as wind direction and velocity, rainfall, humidity, and temperature), and topographic variables (including buildings), as well as such variables as production, emissions, and plume height.

Statistical analysis

Chi-squared analyses were used to test differences between groups. Degree of significance was based on Bailar and Ederer's ('64) "Ratio of Poisson Variable to its Expectation."

RESULTS

Birth defects in Shawinigan

From January 1966 through December 1979, there were 4,534 live births and 33 stillbirths in Shawinigan. Of the live infants, 150 had birth defects, and of the stillbirths, nine had birth defects. As shown in Table 2, the birth defects reported most frequently were those of the musculoskeletal system, followed by the cardiovascular, central nervous, and urogenital systems. The ages of the mothers at delivery did not differ significantly among the various types of birth defect. The gestation periods were shorter for infants with defects of the central nervous system.

The yearly numbers of malformed children per 100 births varied from 1.68 (in 1969) to 6.84 (in 1973), with an overall ratio of 3.48. Detailed analysis of the monthly distribution of birth defects and the distribution by affected system for the year 1973 showed no single large increase that could account for the high ratio observed that year. Nor did the yearly distribution by system show any particular feature that could account for the annual variation in the overall ratios. Furthermore, birth-defect ratios did not increase or decrease with time.

Shawinigan and the comparison communities

As can be seen in Table 3, the observed numbers of malformed children in Shawinigan were higher than would be expected based on the rates observed in each comparison community or in all three comparison communities together. The excess occurred

TABLE 2. Distribution of malformed children by sex and affected system (Shawinigan, 1966–1979)

Affected system	Males		Females		Total	χ^2
	N	Rate[1]	N	Rate[1]		
Central nervous	13	5.57	17	7.71	30	0.51
Cardiovascular	21	9.00	16	7.27	37	0.23
Gastrointestinal	7	3.00	4	1.82	11	0.26
Urogenital	28	12.00	2	0.91	30	19.64*
Musculoskeletal	18	7.71	31	14.09	49	3.73
Mouth and upper airways	6	2.57	11	5.00	17	1.20
Eye and ear	4	1.71	2	0.91	6	0.11
Chest	1	0.43	2	0.91	3	0.00
Syndromes and other defects	1	0.43	5	2.27	6	1.69
Total number of malformed children	85	36.12	71	31.61	159	0.18

[1]Number of malformed children per 1,000 live births.
*$P < 0.001$

TABLE 3. Number of malformed children observed in Shawinigan compared with expected numbers for the comparison communities (1966–1979)

	Observed in	Expected based on	Expected based on Baie-Comeau	Expected based on	Expected based on all comparison

TABLE 3. *Number of malformed children observed in Shawinigan compared with expected numbers for the comparison communities (1966–1979)*

Affected system	Observed in Shawinigan	Expected based on Drummondville	Expected based on Baie-Comeau–Hauterive	Expected based on Rimouski	Expected based on all comparison communities
Central nervous	30	19.69*	18.18*	15.33**	17.96*
Cardiovascular	37	19.69**	13.94**	43.06	24.29*
Gastrointestinal	11	9.04	9.70	10.95	9.80
Urogenital	30	19.15*	13.94**	13.14**	15.72**
Musculoskeletal	49	36.71	27.88**	40.14	34.70*
Mouth and upper airways	17	6.92**	13.33	13.14	10.82
Eye and ear	6	1.06**	1.82*	—	1.02**
Chest	3	0.53*	—	0.73	0.41*
Syndromes and other defects	6	6.92	9.70	10.95	8.98
Total number of malformed children	159	102.68**	98.80**	124.08**	107.36**

*$P < 0.05$.
**$P < 0.01$.

in the central nervous, cardiovascular, urogenital, and musculoskeletal systems, and in the eye and ear, and the chest.

The malformation rates were greater in all years except 1969 and 1972 (Table 4). The number of stillbirths differed only between Shawinigan and Drummondville, where they were significantly higher (Table 5). The proportion of malformed children among the stillborn was higher in Shawinigan (27.3%) than in the comparison communities (total, 12.4%; Drummondville, 15.3%; Baie-Comeau–Hauterive, 10.0%; Rimouski, 10.2%; chi-square with Yates correction = 4.07, $P = 0.04$). This is consistent with previous findings of an excess of birth defects in Shawinigan.

Mothers who gave birth to malformed children were significantly younger in Shawinigan than in the comparison communities for all malformations combined and for defects of the CNS, mouth and upper airways, and eye and ear. Children in Shawinigan did not differ from those in the comparison communities in mean gestational age at birth.

Seasonal variation in birth-defect rates

Figure 1 compares the monthly birth-defect rates in Shawinigan with those for Drummondville and Rimouski. The Shawinigan curve is V-shaped, with the lowest rates in the summer, whereas the curve for the comparison communities is flatter. Seasonal variation in birth-defect rates was compared between Shawinigan and the other three communities using Edward's method for testing seasonality of events, as modified by Walter (Walter and Elwood, '75). There was a significant seasonal variation in Shawinigan, with the highest rates in March and the lowest in September; no such variation was observed in the comparison communities.

Geographical distribution of birth-defect rates

The geographical distribution of birth defects in Shawinigan with respect to the distance from the VC plant was analyzed using school districts as the units; in no school district did the ratio of observed to expected number of birth defects differ significantly from 1. The district in which the plant was located had approximately the expected number of birth defects.

Birth-defect rates did not differ between school districts with high and low VCM exposure, either for all birth defects or for CNS

TABLE 4. Yearly distribution of malformed children (1966–1979)

Year	Shawinigan	Rate[1]	Comparison communities	Rate	SH/Comparison communities	95% Confidence interval
1966	16	3.54	31	1.82	1.95*	(1.08, 3.52)
1967	13	3.52	33	1.96	1.80	(0.96, 3.39)
1968	8	2.30	24	1.51	1.52	(0.69, 3.34)
1969	6	1.68	27	1.78	0.94	(0.41, 2.18)
1970	15	4.70	24	1.66	2.83*	(1.55, 5.17)
1971	6	2.08	30	2.05	1.01	(0.53, 1.94)
1972	6	2.19	34	2.43	0.90	(0.36, 2.20)
1973	18	6.84	44	3.17	2.16*	(1.28, 3.65)
1974	8	2.97	43	2.81	1.06	(0.48, 2.33)
1975	15	4.40	51	3.10	1.42	(0.81, 2.49)
1976	13	3.98	36	2.20	1.81	(0.93, 3.51)
1977	14	4.56	50	2.76	1.65	(0.93, 2.93)
1978	11	3.33	52	2.88	1.16	(0.61, 2.20)
1979	10	3.11	47	2.69	1.16	(0.60, 2.26)
Total	159	3.48	526	2.35	1.48*	(1.24, 1.77)

[1] Number of malformed children per 100 births
*$P < 0.05$

TABLE 5. Numbers of stillbirths, with and without birth defects, and numbers expected in Shawinigan based on rates in the comparison communities

Condition	Number of stillbirths: With birth defects	Without birth defects	Total	Total number of births
Observed in Shawinigan	9	24	33	4567
Observed in Drummondville	15	83	98	8584
Expected based on Drummondville	7.98	44.16**	52.14**	–
Observed in Baie-Comeau–Hauterive	7	63	70	7535
Expected based on Baie-Comeau–Hauterive	4.24	38.18*	42.42	–
Observed in Rimouski	5	44	49	6257
Expected based on Rimouski	3.65*	32.12	35.77	–
Expected based on all comparison communities	5.51	38.78	44.29	–

*$P < 0.05$.
**$P < 0.01$.

defects (Table 6). Likewise, school districts adjacent to the plant did not differ from the other school districts in numbers of birth defects (total or CNS), nor did districts differ within and beyond a 1-mile radius of the VCM plant.

Case-control study

For the period January 1973 to December 1979, sixty-eight cases of birth defects were identified in Shawinigan and matched with controls (42 male and 26 female pairs). Five of the cases were stillborn; all of the controls were born alive. There was no significant difference between cases and controls in number of weeks' gestation at delivery. The frequencies of previous birth defects in the families of cases and controls did not differ significantly, nor was there a significant difference between case and control mothers in number of previous pregnancies.

Mothers of malformed infants reported no excess of diseases during pregnancy; however, the following diseases suspected to bear a high risk of birth defect were reported by cases only: rubella, hydramnios, epilepsy, nonpsychotic mental disorders, and psychosis (Table 7). Among the mothers of malformed infants, five reported previous occurrences of epilepsy, mental disorders, or both. Their children showed the following birth defects: two cases of hypospadias, one of congenital cataract, one of Down's syndrome, and one interventricular septal de-

MALFORMED CHILDREN PER 100 LIVE BIRTHS

TABLE 6. Compar

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[1] $\chi^2_1 = 0.80$, $P > 0.35$
[2] $\chi^2_1 = 0.10$; $P > 0.70$

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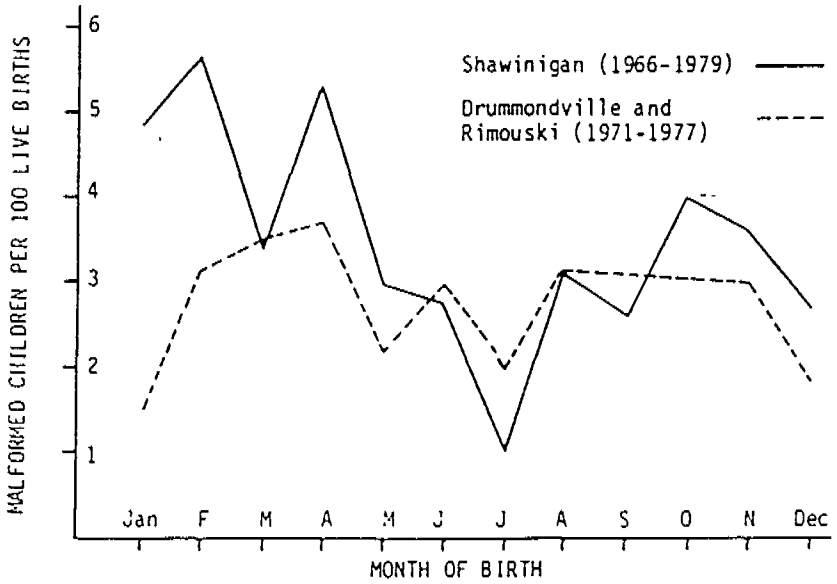

Fig. 1. Monthly distribution of birth-defect rates.

TABLE 6. Comparison of total birth defects[1] and CNS birth defects[2] between school districts with high and low atmospheric vinyl chloride concentration

	School districts with high VCM levels	School districts with low VCM levels	Total
Births with defects	87	70	157
Births without defects	2,285	2,125	4,410
Births with CNS defects	16	13	29
Births without CNS defects	2,356	2,182	4,538
Total births	2,372	2,195	4,567

[1] $\chi^2_1 = 0.80$, $P > 0.35$.
[2] $\chi^2_1 = 0.10$, $P > 0.70$

fect. Two mothers of defective infants reported having used the drug LSD before their pregnancies.

There was no significant difference between case and control mothers in number of previous abortions reported. There was one previous stillbirth among the control mothers and none for the case mothers; there was one previous malformed child in each of the two groups. There was no significant difference between cases and controls in the father's age. No mother (case or control) was exposed to x-rays during the first trimester of pregnancy, and only one case mother was exposed during the second third of pregnancy; exposure during the third trimester did not differ significantly between case and control mothers.

Table 8 summarizes the mothers' occupations before and during their pregnancies. None of the women was ever exposed to VCM at work before or during pregnancy. The working experiences of the case and control mothers before and during pregnancy did not differ, nor did their smoking habits or alcohol consumption. There was no significant difference between cases and controls in the father's occupational exposure to chemicals, and no fathers were ever exposed to vinyl chloride (Table 9). The distance between each mother's place of residence during the first trimester of pregnancy and the VCM plant

TABLE 7. Distribution of cases and controls by diseases of the mothers during pregnancy[1]

Disease	Cases	Controls
None	44	48
Bleeding at the beginning of the pregnancy	6	3
Hypertension	3	6
Rubella	1	0
Lithiasis of the gall bladder	1	1
Renal calculus	1	0
Psychosis	1	0
Premature labor	2	1
Phlebitis	1	0
Hydramnios	2	0
Obesity	0	3
Placenta praevia	0	1
Epilepsy	1	0
Nonpsychotic mental disorders	2	0
Wound	0	1
Infectious or parasitic disease	4	6
Other diseases of the mother	3	2
Total for diseases	24	20
Unknown	0	0
Total	68	68

[1]Partitioning diseases vs. no disease, $\chi^2_1 = 0.54$; $P > 0.45$.

TABLE 8. Distribution of cases and controls by mother's occupation[1]

Mother's occupation	Cases		Control	
	Before pregnancy	During pregnancy	Before pregnancy	During pregnancy
Work outside home without exposure to chemicals	41	22	42	20
Work in VCM industry	0	0	0	0
Work outside home with exposure to chemicals	2	1	2	1
Stay at home	25	45	24	47
Total	68	68	68	68

[1]Partitioning stay at home vs. work outside home before pregnancy: $\chi^2_1 = 0.03$; $P > 0.85$; partioning stay at home vs. work outside home during pregnancy: $\chi^2_1 = 0.13$; $P > 0.71$.

TABLE 9. Distribution of cases and controls by father's occupation[1]

Father's occupation	Cases	Controls
Ever worked in vinyl chloride industry	0	0
Ever worked in industries with exposure to chemicals	20	25
Never worked in industries with exposure to chemicals	43	39
Unknown	5	4
Total	68	68

[1]$\chi^2_1 = 0.73$; $P > 0.39$.

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was measured to ± 100 m, using a map of the city; there was no significant difference between the two groups in distance from the VCM plant.

DISCUSSION

Previous studies

Excess of birth defects in communities in the vicinity of vinyl chloride polymerization plants and the possible association between these birth defects and emissions of vinyl chloride monomer into the atmosphere were first described for three Ohio communities (Infante, '76). The excess was constant between 1970 and 1973. Mothers who gave birth to malformed children were younger in the index communities than in the balance of the three counties. The excess involved mostly the central nervous system (CNS), upper alimentary tract, genital organs, and clubfoot.

In analyzing data collected through the Center for Disease Control's hospital-based birth defects monitoring program, Edmonds et al. ('75) found no increase in CNS defects for one city in Pennsylvania with a PVC plant, but confirmed the excess of anencephaly and spina bifida previously noted in Painesville, Ohio. However, in a case-control study, none of the interviewed parents of affected infants had ever worked at either of the two PVC polymerization plants in Painesville, whereas two fathers of controls had; none of the parents in either group lived within two miles of either plant. Furthermore, a significantly larger proportion of control mothers worked within a 10-mile radius of the PVC plant.

Another study (Infante et al., '76) emphasized fetal losses and miscarriages among women whose husbands worked at PVC plants. Although it concluded that fetal losses were greater among women whose husbands were occupationally exposed to VCM than among controls, this study was criticized for methodological weaknesses.

In a report to the Society of Plastics Industries, MacMahon ('77) concluded that the only evidence so far was to the effect that VCM generates chromosome breakages in workers heavily exposed to it, but that VCM should be regarded as a potential human mutagen and teratogen until better evidence was available. In another report to the Society, Downs et al. ('77) criticized the statistical methods used in vinyl chloride studies and concluded that the existing evidence indicated associations between (1) VCM exposure and lymphocyte aberrations in workers and (2) VCM exposure of workers and fetal wastage among the workers' wives. Those authors found no evidence for an association between VCM exposure and birth defects, but cautioned that such associations may not have been detectable by methods available at the time and that monitoring should continue.

A high incidence of CNS birth defects was found in Kanawha County, West Virginia, from 1970 to 1974 (Edmonds et al., '78). As there is a polyvinyl chloride plant in Kanawha County, a possible relationship between CNS defects and parental exposure to VCM was investigated. In a case-control study, no relationship was found between birth defects and parental occupation. Although the pattern of case-family residences tended to differ from that of controls, it did not correlate with local wind direction and air pollution.

The present study

Some descriptive data from this study raised the hypothesis of an association between VCM in the air and birth defects in the exposed community, but as a whole, within the sample size available, such an association could not be substantiated. Birth-defect rates in Shawinigan were high for the 15-year period, and women who gave birth to malformed children were, on average, younger in Shawinigan than in the comparison communities. These results are consistent with previous findings for three Ohio towns with PVC plants (Infante, '76).

The seasonal variation in birth-defect rates corresponded to variation in atmospheric VCM concentration. No VCM was found in air samples during December, January, and February. It is believed that during these months, VCM tends to accumulate near the plant as a liquid, because the outdoor temperature is below its liquefaction point. This VCM would be released into the air in the spring. Birth-defect rates were lowest in September, which is 8 months after midwinter, corresponding to the time between the first third of pregnancy and delivery. These observations favor an association between VCM concentration in the air and birth defects in the community.

On the other hand, several observations of the present study tend to argue against any association between VCM concentration in the air and birth defects in the community. The geographical distribution of birth defects in Shawinigan was not correlated with esti-

mates of VCM concentrations in the community. Malformation rates were not relatively high either near the plant or in the area where VCM concentrations were estimated to be highest, and the school district with the highest birth-defect rate was far from the plant.

There was no difference in occupational or residential history between the parents who gave birth to malformed infants and the controls. Both groups resided at similar distances from the plant, and none of the parents had worked at the plant. Furthermore, all types of birth defects were in excess in Shawinigan. These results agree with those for the three Ohio cities; however, agents known to be teratogenic in humans and experimental animals have very specific effects, and it seems unlikely that any agent would produce the variety of malformations found in excess in Shawinigan.

Possible explanations of the results as artifactual are not convincing. It is unlikely that Shawinigan's physicians were more inclined to diagnose birth defects than were physicians in the comparision communities since they did not know about such an association when the diagnoses were made (except in 1979, where no difference was seen from previous years). Birth defects were included in this study on the basis of their obviousness, and the birth-defect rates were the same in the three comparison communities. Furthermore, for severe birth defects like those of the CNS, which cannot be misdiagnosed, rates were higher in Shawinigan than in any of the comparison communities. The method by which the data were collected was the same everywhere. It is very unlikely that a bias in the quality of the information from the archives of the regional hospitals could have influenced the results.

The possibility remains that pregnant mothers residing outside Shawinigan, who were at risk of having a malformed child, migrated to the city for delivery, thereby increasing the birth-defect rate for that town. In the case-control study, six mothers (6.7%) were rejected because they had moved to the city of Shawinigan after the first third of pregnancy, and four more cases were untraceable. Thus, as many as 11% of the birth-defect cases observed in Shawinigan might actually have come from elsewhere, reducing the number of observed cases to 142. However, birth-defect rates would still be significantly higher than in the comparison communities, leading us to believe that the excess noted in Shawinigan was real.

Animal studies have shown that exposure to high levels of VCM during pregnancy resulted more often in high rates of fetal loss and miscarriage than in birth defects (Ungvary et al., '78; John et al., '77). However, stillbirth rates were no higher in Shawinigan than in the comparison communities, and in the case-control study, abortion rates reported were not higher for case than for control mothers.

Several industries in Shawinigan emit pollutants into the atmosphere and several of the pollutants may interact to generate potent mutagenic or teratogenic chemicals in the community. A thorough analysis of such an environment and its association with the excess of birth defects was beyond the scope of the present study. However, in the case-control study, there was no difference between the numbers of case and control parents who worked at the aluminum plant, and the comparison community with an aluminum electrolysis plant (Baie-Comeau–Hauterive) had lower birth-defect rates than did Shawinigan. Thus, the aluminum industry probably was not responsible for the excess of birth defects in Shawinigan.

Among risk factors (other than occupational or environmental exposure to a pollutant) known to be associated with birth defects, epilepsy and mental disorders before and during pregnancy and the use of the drug LSD before pregnancy were reported more frequently by mothers of malformed children than by control mothers. Drugs prescribed to control epilepsy have been reported to be associated with birth defects (Smithells, '76) and could account for a few birth defects observed in Shawinigan, as could LSD. These differences, however, could be due to a recall bias whereby the mothers of malformed infants were more aware of exposure to possible etiologic agents during their pregnancy than the mothers of normal children.

In the present study, we were unable to substantiate the presence of an association between VCM in the air and birth defects in the exposed community. In view of the high numbers of angiosarcoma of the liver observed among production workers and the possible large emissions of VCM, it can mean that such an association does not exist. It can also be the result of a small number of observations. The probability of finding an excess

of birth defects in the h
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ones was 80%. This prob
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of birth defects in the highly exposed districts twice as high as in the poorly exposed ones was 80%. This probability would have been 99% had the excess been three times as high.

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