DRAFT

ADVERSE PREGNANCY OUTCOMES IN THE LOVE CANAL AREA

Nicholas J. Vianna, M.D.
Adele K. Polan, M.A.
Ronald Regal, Ph.D.
Stephen Kim, Ph.D.
Glenn E. Haughie, M.D.
Douglas Mitchell, Ph.D.

PROVISIONAL

April, 1980

Adverse Pregnancy Outcomes in the Love Canal Area

Nicholas J. Vianna, M.D. et al

Summary

Among the growing concerns about environmental pollution, the landfill deposition of industrial waste products in close proximity to residential areas poses a potential public health problem of great magnitude. We present evidence that spontaneous abortion and low birth weight might be good initial indicators of human toxicity to multiple chemical agents in this type of setting. Geologic surveys, and comparison of the temporal course of area development with biologic end points, are important in developing hypotheses on possible modes of chemical exposure.

Provisional- April 19 80

The deposition of industrial waste products is an ever-growing problem which might have both immediate and long-term health implications to society. In Niagara County, New York, it is estimated that there are approximately 100 chemical dump sites. Manufacturing, particularly of chemical and allied products, is a major industrial enterprise of the county. According to 1970 data from the New York State Department of Commerce, nine major chemical-producing companies employing a total of 5,267 people are located in the county.

The City of Niagara Falls is located in Niagara County, New York, and had a population of 85,615 in 1970. The Love Canal is a rectangular, 16-acre, below-ground-level landfill site located in a residential section of the southeast corner of the City. In the late 19th Century, the site was excavated as part of a proposed canal linking the Niagara River and Lake Ontario. The Love Canal project was abandoned and subsequently used as a chemical and municipal waste disposal site. The Hooker Chemical Company of Niagara Falls used the site for disposal of chemical wastes, including chlorinated hydrocarbon residues, processed sludges, flyash, and other wastes, for a period of nearly 25 years from about 1930 to about 1953. The City of Niagara Falls also used the site for disposal of municipal waste for many years prior to its concluding in 1953. In the spring of 1953, the site was sold by Hooker Chemical Company to the Board of Education of the City of Niagara Falls. Presently, the site is contained within the area bordered on the north by Colvin Avenue, on the south by Frontier Avenue, on the west by 97th Street, and on the east by 99th Street. Southern and northern sections of the original Love Canal are bordered by the backyards of single-family homes on 97th and 99th Streets, while the middle section is occupied by an elementary school.

On April 25, 1978, after inspecting the Love Canal site, the New York State Commissioner of Health, Dr. Robert P. Whalen, ordered that a fence be erected to limit access to the Canal inasmuch as containers and mounds of chemicals were lying exposed on the surface. Further, he ordered that studies be undertaken to assess

actual or potential health hazards associated with residing in the immediate area. This report presents the results of our initial epidemiological investigations.

Housing Development and Possible Modes of Chemical Spread

The study area extended from 97th Street to 103rd Street and was bounded on the north and south respectively by Colvin and Frontier Avenues (Figure 1). Aerial photographs taken in 1938 show that 97th Street was absent and there were only two houses on what would later be 99th Street. In contrast, 101st, 102nd, and 103rd Streets were occupied by single-family houses and some farms. By 1951, there were still no homes on 97th Street; a few new houses were present on the southeastern section of 99th and 100th through 103rd Streets. The 99th Street School was built in 1954. Housing construction on 97th and 99th Streets proceeded through the 1960's most of the latter street being completed in 1965. In contrast, construction on 97th Street continued through 1973. Backyards of 99 homes on 97th and 99th Streets directly abut the Canal.

Geologic surveys indicate soil strata generally consist of a thin mantle of clay-silt over a sandy-silt or silty-sand texture that rests on a silty-clay with desiccation cracks that extend to the soft clays. The clay strata act as a barrier to movement of water and chemicals below the surface. The accumulation of rain and groundwater facilitated by either natural or manmade activity probably raised the level of chemical wastes to that of higher permeability thus facilitating lateral migration. This slowly overflowing bathtub effect could result in the transport of waste products to adjacent areas.

The most probable mode of exposure is via leachable migration of chemicals through the top soil layer to the basements of houses. Chemicals could then volatilize, producing high local concentrations of agents such as low molecular weight chlorinated organics. Initial air samples taken in the basements of fourteen houses adjacent to the Canal by the United States Environmental Protection

Agency in February, 1978, resulted in the identification of 26 organic compounds also present in the Canal. Thirty-three of 99 houses which abut the Canal tested by the New York State Health Department showed clear evidence of chlorotoluene in basement air. This compound is a good indicator of chemical contamination in the study area since it is not likely to be found in commonly-used household products. In contrast, only four of 256 houses in the outer area showed trace evidence of contamination with this chemical. Similar results were obtained when chlorobenzene was used as an indicator (1).

The possibility that chemicals might have extended beyond adjacent houses through the same or other mechanisms was also considered. Chemicals may have traveled along surficial paths such as the lowlands, (e.g. swamps, ponds, and wetlands) which were present prior to the development of housing in more peripheral areas. The topography of the region under study can be generally characterized as flat, except for three creeks north of the Canal. These creeks contain water year-round. In addition, prior to the development of housing in this area, a number of natural shallow depressions (Figure 1) traversed the area, some of which intersected the Love Canal itself. The location of these depressions, commonly referred to as swales, was determined from aerial photographs taken in 1938, 1951, and 1966, as independently interpreted by the Cornell University School of Civil and Environmental Engineering (2). This group had no knowledge of the hypotheses being tested. These depressions served as drainage ways and produced ponding in certain sections (Figure 1) during times of high water. Additional verification of historically wet areas was obtained from personal interviews, review of photographs and motion pictures, taken by area residents. As the area was developed, the contour and extent of these swales was substantially modified. Development of the area between 1951 and 1956 eliminated the major swale which intersected the Canal as a continuous conduit of surface water flow from the Canal to peripheral areas. In the 1966 aerial photograph, only a small section northeast

of the Canal remained; and at the time of initiation of our study, there was no visible above-ground evidence of these natural depressions. Although the filling of the swales eliminated the potential for chemical migration by surficial flow, it is entirely possible that these natural depressions might conduct leachate from the Canal because of the use of permeable fill.

Recent excavations on the periphery of the Canal on 99th Street indicate that three 4-inch pipes, approximately three feet below the ground extended laterally towards a historic pond area located on the more peripheral streets of the study area. Anecdotally, farmers in these locations used this system to obtain water from the Canal prior to the time that chemical waste products were dumped. Collectively, this information yields a relatively unambiguous topography of the original land surface prior to modification by man. In addition this suggests that at least two potential routes existed for the migration of chemicals from the formal dump site to the more peripheral historic water areas - surface swales (prior to 1950) and underground pipes. Alternatively, chemically contaminated soil may have been used as fill for low level areas during the development of the area. Serial aerial photographs taken between 1951 and 1958 showed that by May 1958, the vast majority of the historical depressions were filled in. During the year 1958, major portions of the ponded sections were filled in. Minutes of the School Board meetings in the 1950's record the transport of fill from the 99th Street School yard to the 93rd Street School properties. This or the hypothetical migration of chemicals along swales and/or through pipes would result in the perferential contamination of historic water areas.

These observations suggested that we dichotomize all houses (other than those directly adjacent to the Canal) into 116 houses built on historically wet properties (water -- either ponds or swales) and 268 houses built on historically dry properties (non-water).

In order to verify further the location of ponds and swales and the extent of chemically contaminated soil, a house-by-house soil boring program has been carried out. Soil sampling information distinguished between undisturbed soil and disturbed soils (fill). By defining houses with at least three feet of fill or houses adjacent to such houses as a fill house, a coefficient of agreement of 0.33 was found between fill houses and water houses ($p < .000001$, chi square = 41.6). Qualitative comparison of a map of fill houses and a map of water houses substantiates the positive correlation between fill houses and water houses. Chemical analyses of soil borings are in progress and will be the subject of a separate report.

Other more general modes of exposures and possible conduits of migration of chemicals were also considered. This neighborhood has been served with a public water supply since 1930. Residents in the whole study area might have been exposed to toxic vapors emanating from the Canal by airborne transmission.

End Points of Human Toxicity

More than 200 chemicals have already been identified at the site by the Division of Laboratories and Research of the New York State Health Department and by the Environmental Protection Agency. Table 1 contains a partial list of compounds found in the Love Canal. Compounds such as benzene (3), toluene (4), benzoic acid (5), lindane (6), trichloroethylene (7), dibromoethane (8), various benzaldehydes (9), methylene chloride (10), carbon tetrachloride (11), and chloroform (12, 13) can produce both acute and chronic toxic responses in man. Although the sensitivity of biologic events such as congenital defects, spontaneous abortions, and low birth weight infants as possible end points of human toxicity to chemicals is not well established, the pre-partum period is characterized by a special susceptibility to certain chemical agents (e.g. Minamata disease and Yusho disease) (14). It is also well established that many chemicals are hazardous to the conceptus of low animals, depending on dosage, route of administration and stage of gestation (15, 16). The importance of examining each of the three end points is dictated by the possibility

that different manifestations of toxicity are likely to be encountered in situations where exposure to a wide variety of chemicals is likely. In addition evaluation of events such as congenital defects might not provide a true indication of the frequency of this end point. The importance of monitoring spontaneous abortions in seeking environmental teratogens is well established since the number and variety of congenital anomalies during gestations is far greater than can be detected in term birth (17). Another advantage in using these three indicators is the shorter induction period than for most adult chronic diseases.

Certain limitations of each of these end points, however, must be appreciated. The frequency of spontaneous abortions, especially those occurring during early pregnancy, is exceedingly difficult to measure. Various congenital malformations such as cardiac abnormalities and mental deficiencies are very difficult to diagnose during the immediate postpartum period and often go unrecognized when birth certificates are filed. Birth weight alone may not be a sufficiently sensitive nor specific measure of toxicity. Accordingly, we decided to examine all three outcomes.

Epidemiologic Hypotheses on Possible Routes of Chemical Migration

Our descriptive study of the temporal patterns of housing development, the topography of the study area, and initial chemical evaluations suggested that many houses directly adjacent to the Love Canal were contaminated. If the more peripheral areas were contaminated, this would most likely have occurred through some general mechanism (e.g. airborne route) affecting broad areas or a more selective route, such as the historic water area.

Based on these considerations, four epidemiologic hypotheses were advanced concerning the possible distribution of spontaneous abortions, congenital defects, and low birth weight infants, in specific sections of the study area:

1) An excess of some or all indicators might be demonstrated only among pregnant females residing in houses on 97th and 99th Streets -- where backyards are directly adjacent to the dump site, and the likelihood of

chemical contamination was greatest. Since temporal factors may be important in the migration of chemicals and the houses on 99th Street were significantly older than those on 97th Street (18), we examined each street separately in all statistical analyses;

2) The entire study area (excluding the two streets adjacent to the Canal) might have an excess of all or some of the biologic indicators. Examination of each indicator by single street might also detect a gradient effect as the distance from the Canal increased. This would support the hypothesis of some general mechanism of contamination;

3) An excess of certain indicators might be demonstrated in historical water areas of the neighborhood, where chemicals might have migrated from the Canal and/or chemically contaminated soil was used for fill prior to construction of houses. In contrast, historical non-water areas might be characterized by a lesser frequency of these markers. Here, too, temporal factors might be important since houses built in water areas are significantly older than those in non-water sections (19); and

4) Regardless of their geographic distribution, the occurrence of indicators such as spontaneous abortions and low birth weight infants and their geographic distribution in various sections of the Love Canal might be related to temporal factors and the nature and the concentration of chemicals to which pregnant females were exposed (20). For example, 99th Street with its close proximity to the dump site and old homes might be characterized by an excess of the worst type of indicator, spontaneous abortions. In contrast, more peripheral sections might have an excess of low birth weight infants.

Selection of Comparison Groups

Initially, expected numbers of spontaneous abortions were obtained from a report by Warburton and Fraser (21). The reasons for selecting this comparison group were that it was a relatively large study illustrating the spontaneous abortion

experience of over 6,000 pregnancies and the frequency of this adverse event was tabulated by both birth order and maternal age at conception. Proband children either had a clear-cut genetic defect, a defect of unknown etiology but with a familial tendency, an undiagnosed defect or series of multiple malformations, or a twin with no defect. The nature of this population suggests that it represents a conservative comparison group. However, possible differences in ascertainment and demographic characteristics of this Canadian population dictated the need for additional comparison groups. Accordingly, a similar distribution table was constructed for residents of houses north of Colvin Avenue (Figure 1). This latter area was selected as a control group for the Love Canal study area for various reasons: it is the most proximate section of the Love Canal (Figure 1); it contains a relatively large population residing in single-family houses in an industrialized community (211 houses, 480 adults, and 190 children); and most importantly, residents were also concerned with the possibility that chemicals from the Love Canal might have migrated into their area. Thus it was anticipated that the degree of participation from these individuals would be comparable to that realized from Love Canal residents. This proved to be true as over 98 percent of the adult residents in each area participated in the investigation.

The potential limitations of this comparison group must also be appreciated. A greater proportion of residents in the north of Colvin region had a college education (15.6 percent) than those in the entire study area (5.6 percent). This was partially overcome by controlling for this factor in statistical analyses. In addition we cannot presently exclude the possibility that the north of Colvin area was also chemically contaminated. If this were proven to be true, it could tend to decrease the excess of confirmed observations in pregnant females from the Love Canal. Finally, a maternal age-parity table was constructed based on the spontaneous abortion experience among females residing in non-water areas. This internal comparison group was employed to evaluate further the hypothesis that an excess of

study indicators might be present in the historic water sections. Here too the possibility of prior chemical contamination cannot be excluded at present. Considering the limitations of each comparison group, the results obtained from all three should be considered in formulating conclusions.

Table two summarizes the pertinent information concerning the age distribution and pregnancy histories of females in four sections of the Love Canal (97th and 99th Streets and the water and non-water sections) and the area north of Colvin Avenue. Over 98 percent of the population in each section was white, and no single ethnic group predominated.

Quality Control of Epidemiologic Data

The same prepared questionnaire was used throughout the investigation. Questions relating to the past medical, therapeutic, social (smoking, drinking and social histories), occupational and pregnancy histories were obtained from all adult residents in a seven month door-to-door survey. The same field teams were used in all areas studied. Investigators had no prior knowledge of the specific hypotheses under evaluation or the areas selected as comparison groups. While in the field, completed questionnaires were reviewed by immediate team supervisors with at least four years of experience to assure standardized data collection. All questionnaires were subsequently reviewed for completeness and possible inconsistencies by two other supervisors, and independently by members of a statistical unit.

The following measures were taken as a validity check on respondents: the interview procedure had a built-in recall mechanism. Certain questions were asked repetitively in the questionnaire; statistical analyses of the low birth weight end point as determined from interview data and birth certificates obtained from the Office of Vital Records, New York State Health Department were done separately, and the results were compared; and an effort was made to confirm all spontaneous abortions through Vital Records, physician interviews and/or medical records.

Keypunching of questionnaires was carried out on a key to disc unit with verification. Programs were checked by hand calculations to guarantee accurate implementation of computational algorithms. Statistical routines of sufficient complexity to prohibit hand checks were run against test data for verification.

Statistical Analyses and Results

Only those indicators occurring among females who resided in the study area as of June 1978, and had lived there during the entire period of pregnancy were included in this investigation. Spontaneous abortions were considered confirmed, and included in our analyses if they were verified through personal physicians, hospital records, or there was evidence of pregnancy with a subsequent history compatible with this outcome. The number of miscarriages claimed by female residents, the number included in the study, and the number excluded for specific reasons (e.g. induced abortion, stillbirth, or the patient was not pregnant according to the private physician) were as follows: 99th Street - 16, 12, 4; 97th Street - 6, 3, 1; historical water area - 27, 25, 2; non-water - 23, 21, 1; and north of Colvin - 18, 11, 4. The remaining events on 97th Street, the non-water and the north of Colvin areas were unconfirmable and were excluded from our analyses.

Women who were ever pregnant at their present address in the study area were categorized according to their age at delivery (minus nine months) and parity (pregnancy order number) for each pregnancy. For each of the areas studied (97th and 99th Streets, and the rest of the Love Canal - individual streets and water and non-water sections), the number of miscarriages observed among the pregnancies was determined. The number of miscarriages expected among these women was calculated by applying the percent miscarriages for each age parity combination of the other control group to the observed number of pregnancies in each cell. The groups used to obtain expected numbers for all study areas were Warburton and Fraser (21) and the north of Colvin area. In addition, the non-water area was used for the water area. The Mantel-Haenzel chi square (22) was used to test the differences between

the observed and expected number of miscarriages.

Of the streets directly adjacent to the Canal, only 99th Street might have had an excess of spontaneous abortions (Table 3). More peripherally, 102nd Street had a significant excess (23) regardless of the comparison group employed. When the whole study area, excluding the 99th and 97th Street houses adjacent to the Love Canal was evaluated, no consistently significant difference was observed. In contrast, statistically significant excesses were observed in the water area when each of the two comparison groups was used (Table 3), and when the non-water area was used to obtain expected numbers ($p = .042$, OBS/Exp. = 1.9). Interestingly, 102nd Street represents a major component of the historical water area (Figure 1). For the north of Colvin comparison group, the highest ratio of observed to expected was on 99th Street, followed by the historic water area. Spontaneous abortions observed in the north of Colvin area did not differ significantly from the numbers derived from either the Warburton-Fraser report or the non-water area.

Table four lists the medically confirmed defects which occurred among children born in the five areas studied. The percent of all live births with birth defects was then calculated for each area studied and the proportion was compared with that for the north of Colvin Avenue area children (difference between two proportions). A significant excess was not found in any of the Love Canal sections studied (Table 5). However, when the water and non-water areas were compared, a statistically significant excess was observed ($p = .024$). The differences in results could be due to the random variation commonly associated with small numbers.

Birth certificate information for all infants born of women from the Love Canal area identified at the interview was obtained from the New York State Office of Vital Records; the address was verified and the birth weight shown on the certificate was recorded. (If the resident address on the certificate was not the same as the address at interview, the birth was not considered in our analyses). Based on the weight stated on the birth certificate, those who weighed five pounds-

eight ounces or less (≤ 2500 grams) were considered low birth weight children. The proportion of all live births which were low birth weight was established for each area studied. The average proportion of all white births which were five pounds-eight ounces or less was determined for New York State excluding New York City (Upstate New York) for the period 1950-1977 (24) and was used as the population proportion, to test whether an area had significantly more low birth weight children than the Upstate proportion.

There was only one low birth weight infant (99th Street) among the 65 live births occurring among residents living directly adjacent to the Canal. The only study area where significant increases in low birth weights were observed was the historic water area (Table 5). The relative risk for this indicator was 2.2 (95 percent confidence limits, 1.23-3.63). This was also true when maternal age was taken into account (chi square test, expected based on Upstate average percent for each age; p = .005).

Children born in the water area also had a generally lower birth weight distribution than those born in the north of Colvin area. For example, 22.9 percent of the 83 water area births compared with 11.8 percent of the 110 north of Colvin births were under 6.25 pounds (10th percentile weight). Conversely, 6.0 percent of the water area and 10.9 percent of the north of Colvin births were 8.75 pounds or over (90th percentile weight) (25).

The results of spontaneous abortion and low birth weight evaluation analyses support the hypotheses (numbers 1 and 3) that chemical contamination might have been maximum on 99th Street adjacent to the Canal and the historical water area. In addition the different patterns for these indicators in these two areas are consistent with the hypothesis (number 4) that dosage might be an important factor in the occurrence indicators evaluated. In contrast we found no statistically significant evidence to support the hypothesis (number 2) of some general mechanism of exposure.

Analysis of variance of the mean age (15 years of age and older) at which

pregnant women had moved into each of the four Love Canal study areas and north of Colvin region showed no significant difference between groups ($p > .05$, range of means 24.1 - 26.0). When the mean years of residence (during ages 15 through 44 years) for the same groups residing in these areas were evaluated, the difference between groups was statistically significant ($p < .01$, mean years: 99th Street - 13.0; 97th Street - 9.4; water - 13.6; non-water - 10.4; north of Colvin - 12.6).

One problem with each of the indicators studied is that mothers can contribute multiple and unequal numbers of outcomes. For example, if some mothers are more prone to miscarriages than others, then using chi square tests to compare raw miscarriage rates in different areas can lead to p-values which are smaller than they should be. Gladen (26) includes a review of some literature on this problem as it relates to toxicological testing on litters of animals. To obviate this potential problem, four methods which take different approaches in analyzing the data with each mother as an observational unit were used: the beta-binomial model (BETA) (27), the jackknifing method (JACK) (26), a t-test on transformed rates for each mother (SQRT) (26), and a comparison involving the percent of ever-pregnant women who had a problem with one of the indicators while residing on the Canal (PER). Water, non-water and the section north of Colvin (North) were compared. Each method had its own limitations and hence the p-values from any one method do not give an adequate interpretation to the data.

Miscarriage rates were significantly higher in the water area than in the North. One-sided p-values for BETA, SQRT, and JACK were all below 0.01 while PER was less than 0.05. Water area miscarriage rates were also higher than non-water rates with p-values between .01 and .05. The non-water area was not significantly different from North ($p > .05$). The significance of water and non-water together against North depended on the test. The p-values for BETA and JACK were around 0.02 while SQRT and PER were not significant ($p > .05$). A part of the difference is that SQRT and PER make no distinction between events such as no miscarriages in one pregnancy and no miscarriages in five pregnancies.

For low birth weights, water was significantly different ($p < .05$) from North and from non-water. Water and non-water areas together or non-water alone was not significantly different from North, although one-sided p-values for water and non-water tended to be around 0.08. The birth defect data showed no significant differences, although the probability values range between 0.07 and 0.08.

Temporal Factors and Adverse Pregnancy Endpoints

No single month or season (winter - December, January and February) predominated for spontaneous abortions when month of event was examined. This was also true when the month of birth was evaluated for children with congenital defects or low birth weights.

Ten spontaneous abortions (50 percent of the pregnancies) on 99th Street adjacent to the Canal, occurred between 1958 and 1964. Of the 12 pregnancies that occurred after 1970, only one resulted in a spontaneous abortion in 1973. The trend of five-year moving averages of the percent of pregnancies which terminated in spontaneous abortion (Figure 2) on 99th Street, adjacent to the Canal, peaked in 1962 (54.6 percent). Using a standard of 15 percent of pregnancies resulting in this end point (21), the binomial probability of this observation or a more extreme one is .003.

We next examined the percent of pregnancies that resulted in spontaneous abortions for each of the past three decades in both the historical water and non-water areas. For the historic water area the percents for the periods 1949 through 1958, 1959 through 1968, and 1969 through 1978 were 4.7 percent, 33.9 percent and 19.2 percent respectively. For the non-water area they were 5.6 percent, 18.6 percent and 14.7 percent. For the period 1959 through 1968, a significant excess ($p = .0004$, observed/expected = 2.1) of this end point was observed when maternal age and parity were controlled for, using the Warburton and Fraser report (23). Significant increases were not found for the two other decades in the historical water area or any of the three decades in the non-water area ($p > .05$ for each).

For the historical water area, the trend of five-year moving averages of the

percent of pregnancies which terminated in spontaneous abortion (Figure 2) showed a high period starting in 1959 (24.0 percent), peaking in 1965 (42.9 percent; binomial probability for 15 percent standard is .002) and ending in 1970 (26.7 percent). In contrast the percents observed for both the non-water and north of Colvin areas during this period fluctuated around 12.5 percent (range 0 percent to 17.9 percent). After 1970, the percent in the historical water area dropped to a low of 7.7 percent in 1975 and was comparable to the two other areas.

The percent of pregnancies which ended in spontaneous abortions from 1959 through 1970 appeared to be higher in both the pond (11/38 = 29.0 percent) and swale (8/24 = 33.3 percent) sections of the historic water area (Figure 1) when compared to the non-water area (9/53 = 17.0 percent). The age of houses on the pond section (mean 31.7 years, median 29.3 years) was somewhat older than those on the historical swale (mean 24.2 years, median 22.7 years).

Analysis of infants with low birth weights and congenital defects in the manner described above was limited by the small number of these events observed (Table 2). Nonetheless using live births as our denominator, the greatest percent of low birth weights and congenital defects occurred in the water area during the years 1949 through 1958 (8/21 = 38.1 percent, versus 1959 through 1968, 8/37 = 21.6 percent and 1969 through 1978, 3/20 = 15.0 percent). In the non-water area the percents from the earliest to the most recent decade were 5.9 percent, 16.2 percent and 11.1 percent respectively. The same pattern was evident when the percent of live births that resulted in low birth weights was examined separately (percent of low birth weights from the earliest to the most recent decades: water - 28.6 percent, 10.8 percent and 10.0 percent; non-water - 5.9 percent, 16.2 percent, and 3.2 percent). The number of infants with low birth weights or congenital defects was too small for further analysis (e.g. five-year moving averages).

Possible Confounding Factors

The apparent excess of spontaneous abortions and low birth weights on 99th Street and the water area might be due to some confounding factor or combination

of factors. Maternal age and/or parity were considered in our analyses of spontaneous abortions and low birth weights. We also examined the possibility that women who had one or more unfavorable pregnancy outcome, while residing in the Love Canal neighborhood, might have had similar outcomes prior to moving into this area. No significant excess of prior spontaneous abortions was found when either the Warburton and Fraser report (21) or the experience in the north of Colvin area was used to generate expected numbers. Prior low birth weights were also not significantly excessive when compared to New York State (excluding New York City) rates. In addition, there were no documented congenital defects among the 57 live births among female residents from 99th Street and the water area prior to moving to the Canal area. This contrasts with 14 among the 122 live births (11.5 percent) while these females resided in these two areas.

Certain occupations, such as operating room attendants (27), and chemical and laboratory operators (28, 29), might also be associated with an excess of spontaneous abortions and congenital malformations. The possible influence of exposure from these sources was also examined among all adults in households from each of the five areas investigated (99th and 97th Streets, water, non-water, and north of Colvin areas). Among households with either a spontaneous abortion and/or a congenital defect, no significant differences were observed (chi square test, df = 4, $p > .05$ for each indicator). Among households with a low birth weight child, the numbers were too small for the five area chi square analysis. However, the water versus the non-water area and water versus the north of Colvin area did not differ significantly (Fisher's exact test, $p > .05$).

Maternal smoking (30, 31) may also influence pregnancy outcome. To control for the possible influence of this factor, we examined the adverse pregnancy experience among women who had never smoked. The proportion who lived in the water area and had an unfavorable event (7/11, 63.6 percent) was significantly higher than those who resided in either the non-water area (10/40, 25.0 percent) or north of Colvin (3/17, 17.7 percent) (Z test, $p < .01$ for each comparison).

Socio-Economic Status (32) might be associated with an increased risk of spontaneous

abortion. Educational level of parents (the higher of the two) of households where pregnancies occurred was used as an indicator of this factor. For households whose educational level was high school graduation but less than college graduation (12 to 15 years), the proportion of women who lived in the water area and had an unfavorable event (24/37, 64.9 percent) was significantly higher than those who resided in either the non-water area (7/19, 31.8 percent) or north of Colvin (11/45, 24.4 percent) ($p < .002$ for each comparison). The proportion of women who lived on 99th Street and had an unfavorable pregnancy outcome (7/19, 36.8 percent) was higher but not significantly different from those who lived in either the non-water or the north of Colvin areas. The numbers in households with other educational levels (less than high school and college graduation or more) were too small for statistical analysis.

Still other factors must be considered. Certain infections (33, 34) such as rubella, mycoplasma, and toxoplasmosis, prior induced spontaneous abortions (17), alcoholism (35), clinical conditions (e.g. maternal diabetes mellitus (36), epilepsy (37), malnutrition (38), maternal exposure to lead (39), methyl mercury (40), and arsenic (41), exposure to ionizing radiation (42) or the ingestion of certain drugs (43) (e.g. androgenic hormones, folic acid antagonists)), might adversely influence the outcome of pregnancy. Past medical histories of females with spontaneous abortions, and children with either congenital defects or low birth weight were reviewed, and with one exception (a pregnant female possibly exposed to rubella during her first trimester whose child was born with a congenital defect) none of these factors could be documented in the Love Canal area.

Variability in interviewer technique and/or respondent recall might account for some of the significant differences we observed. Analysis of the data by individual interviewer did not suggest that the excesses observed were attributable to any one interviewer. We also examined the time interval between the date of interview and the date of spontaneous abortion for the water and non-water areas.

The mean interval was only approximately 2.7 years greater for the water area.

Finally, our validity checks suggested that the accuracy of respondent recall was comparable in the Love Canal and north of Colvin areas. When the low birth weight information as determined by interview data from each area was compared with that obtained from Vital Records, the results were similar. Only the water area had a significant excess of low birth weights ($p = .0009$, relative risk 2.3), when compared with the percent of low birth weights recorded in New York State excluding New York City.

Of all the factors mentioned above mother's age, parity, smoking, drinking and social class as indicated by educational status are probably the most important. House age and duration of residence are also important considerations. Collectively, these factors could conceivably account for the results obtained. This possibility was examined using maximum likelihood linear logistic regression (44). The effects for all variables were assumed to be linear, additive, and the same in all regions. The assumptions are only crudely approximate but should reveal serious confounding problems. A separate constant term or intercept was estimated for each area and comparisons between areas were made in terms of intercepts. The method used was essentially an analysis of covariance approach for binary data. Each pregnancy was treated as a separate, independent event. Hence, differences in rates for different mothers were not accounted for beyond differences in the variables given above. The main conclusion from the logistic analyses is that comparisons of the areas studied were not affected greatly when adjustments were made for those factors listed above as a group.

The p-values from the logistic analyses need to be considered in conjunction with those of BETA, JACK, SQRT, and PER, since the logistic model was necessarily simplified in many respects. A synthesis of the results indicates an excess of miscarriages in the water area over either the north of Colvin or non-water areas. The water area would also appear to have an excess of low birth weights compared to north of Colvin.

Conclusions

Our findings are consistent with the possibility that a slight to moderate excess of spontaneous abortions and/or low birth weights might have occurred on 99th Street and historic water sections of the Love Canal area. Similar pregnancy outcome patterns have been observed among women living in close proximity to a smelter in Northern Sweden which produces a number of metallurgical and chemical products (45). The results obtained with congenital defects were not statistically significant, but the highest percentages were observed on 99th Street adjacent to the Canal and the historic water section. This could be due to the fact that a major portion of the congenitally malformed fetuses are aborted (17). Although these observations could not be explained by the various potentially confounding factors examined, they might be attributed to other variables not considered. The possible deficiencies of each of the comparison groups have already been discussed. The water/non-water dichotomy has certain limitations, particularly with regard to the lateral boundaries of the historical swale. Other obvious limitations are the small numbers involved in certain statistical analyses, and the fact that much of the data obtained for this investigation are based on recall of pregnancy outcomes. This is particularly true for spontaneous abortions due to problems with recognition and ascertainment. Birth weight, since it was obtained from Vital Records, is clearly the more objective and reliable indicator. Finally, and most importantly, we have not yet been able to correlate the geographic distributions of adverse pregnancy outcomes with chemical evidence of exposure. At present, there is no direct evidence of a cause-effect relationship with chemicals from the Canal.

With a great deal of caution we can speculate on the implications of our findings with regard to the possible modes of exposure to Canal chemicals. The hypothesis favoring some general route of exposure to toxins (e.g. modes 1, 4 and 9, Table 6) was not found to be statistically significant. In addition, the water/non-water dichotomy and anecdotal information are not consistent with potential modes of

exposure which are strongly dependent on personal behavior (e.g. modes 5, 6 and 10, Table 6). Our observations appear to be most consistent with hypothetical exposure related to historic low lying areas such as modes 2, 3, 7 and possibly 8 (Table 6).

Dosage and temporal factors might also be important considerations in explaining the different geographic patterns observed for spontaneous abortions and low birth weights. It would seem reasonable that the proximity of houses directly adjacent to the Canal might explain the fact that spontaneous abortion was the most common unfavorable pregnancy outcome observed on 99th Street. The apparent absence of an excessive number of miscarriages on 97th Street, adjacent to the Canal, might be explained partially by the fact that many of the houses were not built until the late 1960's and early 1970's. In contrast the vast majority of spontaneous abortions on 99th Street occurred in the early 1960's.

The historical water area was also characterized by an apparent excess of this end point, particularly during the early 1960's. Interestingly the rise in spontaneous abortions began less than one year after land filling was largely completed in this area. While this observation may well be fortuitous, it tends to support the chemically-contaminated landfill hypothesis (Table 6, Number 7). In contrast, if the historical swales ever provided a surficial conduit for chemicals from the Canal to this area, available evidence suggests that this particular mechanism of transmission ceased by 1956. Finally, the excess of low birth weights in the historical water area and not 99th Street adjacent to the Canal is consistent with the hypothesis that the occurrence of indicators (low birth weights versus spontaneous abortions) might be related to the concentration of chemicals to which pregnant females were exposed.

Epidemiologic studies which attempt to determine whether certain biologic end points might be related to potential exposure to a multiplicity of chemicals, occurring in the past, are exceedingly difficult. The indicators of human toxicity selected might not be sufficiently sensitive. Other health effects, not yet

considered might be more appropriate end points. The methodologic approaches employed might be too insensitive to detect real low level risks. The distinction between exposed and unexposed groups might not be as clear-cut as it is in certain occupational settings. In the absence of supporting environmental data, epidemiologic observations, as described in this report, must be interpreted with great caution. Furthermore, the inherent limitations in attempting to demonstrate an association between chemicals currently found in the study area and certain adverse biologic events, many of which occurred several years ago, must be appreciated.

Despite the current limitations of epidemiology in investigating environmental problems such as the Love Canal, it remains the only direct means of measuring human risk. We believe our observations provide the rationale for several hypotheses dealing with the most likely routes of chemical migration (46).

1. The use of two chemicals as indicators of the spread of contamination in an industrial landfill where over 200 compounds have already been identified has obvious limitations. Nonetheless these initial observations did suggest that houses directly adjacent to the Canal should be examined apart from those in more peripheral areas.

2. Personal communication, Dr. Warren Phillipson
3. N. I. Sax, Dangerous Properties of Industrial Materials (Van Nostrand Reinhold Co., New York, 1975), pp. 440-441.
4. N. I. Sax, Dangerous Properties of Industrial Materials (Van Nostrand Reinhold Co., New York, 1975), p. 1174.
5. N. I. Sax, Dangerous Properties of Industrial Materials (Van Nostrand Reinhold Co., New York, 1975), p. 443.
6. W. C. Hueper, Occupational and Environmental Cancers of the Urinary Tract System (Yale University Press, New Haven, Conn., 1969).
7. N. I. Sax, Dangerous Properties of Industrial Materials (Van Nostrand Reinhold Co., New York, 1975), p. 1186.
8. N. I. Sax, Dangerous Properties of Industrial Materials (Van Nostrand Reinhold Co., New York, 1975), p. 614.
9. N. I. Sax, Dangerous Properties of Industrial Materials (Van Nostrand Reinhold Co., New York, 1975), p. 439.
10. NIOSH Recommended Standard for Occupational Exposure to Methylene Chloride, U.S. Department of Health, Education and Welfare, Public Health Service Center for Disease Control.
11. IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Man, Volume I, p. 53, 1972.
12. P. J. R. Challen, D. E. Hickish, J. Bedford, Brit. J. Indust. Med. 15, 243 (1958).

13. IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Man, Volume I, p. 61, 1972.

14. R. W. Miller, Pediatrics 53, 792 (1974).

15. T. H. Shepard, Catalog of Teratogenic Agents (John Hopkins University Press, Baltimore, 1973).

16. J. Autian, Toxicity and Health Threats of Phthalate Esters: Review of the Literature (Oak Ridge National Laboratory, Oak Ridge, Tennessee, 1972).

17. Z. Stein, M. Susser, D. Warburton, J. Wittes and J. Kline, Am. J. Epid 102, 275 (1975).

18. Considering only those houses with females who were pregnant, 17 of 20 (85.0%) were less than 20 years old on 97th Street. In contrast only 3 of 22 (13.6%) were this old on 99th Street ($p = .00004$, two tail, Z test).

19. For those houses with females who were pregnant, 5 of 49 (10.2%) in the water area and 26 of 98 (26.5%) in the non-water area were less than 20 years of age ($p = .02$, 2 tail, Z test). Houses on 99th Street and the water section did not differ significantly for this parameter ($p = .67$). Another important consideration is the effect of housing development on the extent and contours of historic swales and ponds.

20. The selection of these two indicators was based on several considerations. The true frequency of congenital defects can probably only be determined by a detailed prospective evaluation of spontaneous abortions. The two endpoints selected represent the extremes of pregnancy outcomes. In addition the same chemicals that cause spontaneous abortion might produce low birth weights under different circumstances. In animals the type of outcome appears to be related to the dose and timing of exposure. (H. Kalter in Hollander Chemical Mutagens (Plenum Press, New York, Vol. 1, 1971, pp. 57-69). In man too these factors might be important. (P. A. Buffler, Contr. Epidem. Biostatist. (Marger Basel, Vol. 1, 1979, pp.1118-1137; D. U. Himmelberger, B. W. Brown, Jr.,

E. N. Cohen, Am. J. Epid., Vol. 108, 470, 1978). Temporal factors might also be important with regard to the type(s) of chemicals pregnant females might have been exposed to (e.g. chemical dumping ceased in the early 1950's and various chemicals have different half lives) and available routes of migration.

21. D. Warburton, F. C. Fraser, Am. J. Human Genetics 16, 1 (1963).

22. N. Mantel, W. Haenzel, J. Nat. Cancer Inst. 22, 719 (1959).

23. Using the Warburton and Fraser comparison group, p = .023, O/E = 1.6; using the north of Colvin group, p = .002, O/E = 3.8.

24. New York State Department of Health Annual V.S. Reports 1950 through 1977 (data not available prior to 1950).

25. W. E. Nelson, Textbook of Pediatrics (W. B. Saunders Company, Philadelphia, 1975), pp. 40-41.

26. B. Gladen, JASA 74, 278 (1979).

27. D. A. Williams, Biometrics 31, 949 (1975).

28. R. P. Knill-Jones, B. J. Newman, and A. A. Spence, Lancet 2, 205 (1975).

29. S. Jansa, B. Kallen, J. Tillberg, and H. Wende, Lakartidn 75, 22 (1978).

30. M. Strandberg, K. Sandback, O. Axelson, L. Sundell, Lancet 1, 384 (1978).

31. J. Kline, F. A. Stein, M. Susser, D. Warburton, New Eng. J. Med. 297, 793 (1977).

32. D. U. Himmelberger, B. W. Brown, E. N. Cohen. Am. J. Epid. 108, 470 (1978).

33. F. Pettersson, Epidemiology of Early Pregnancy Wastage (Svenska Bo Kforlaget, Norstedts) 1968.

34. J. G. Lauritsen, Acta. Obst. Gynec. Scand. Supplement 52 (1976).

35. S. W. Sandler, S. African Med. J. 52, 1115 (1977).

36. N. L. Jones, D. W. Smith, A. P. Striessguth, N. C. Myrianthopoulos, Lancet 1, 1076 (1974).

37. K. Karlsson, I. Kjellmer, Am. J. Obstet. Gynec. 112, 213 (1972).

38. R. W. Smithells, Br. Med. Bull. 32, 32 (1976).

39. M. Winick, Clin. Obstet Gynec. 13, 526 (1970).

40. C. R. Angle, M. S. McIntine, Am. J. Dis. Children 108, 436 (1964).

41. J. F. Culfonso, R. R. DeAlvarez, Am. J. Obstet. Gynec. 80, 145 (1960).

42. I. Nordenson, G. Beckman, L. Beckman, and S. Nordstrom, Hereditas 88, 47 (1978).

43. A. S. Dekaban, J. Nucl. Med. 9, 471 (1968).

44. G. Greenberg, W. H. Inman, J. A. C. Weatherall, A. M. Adelstein, and J. C. Haskey, Brit, Med. J. 2, 853 (1977).

45. S. Nordström, L. Beckman, I. Nordenson, Hereditas 90, 291 (1979).

46. We wish to thank the following individuals for their technical assistance: Drs. Peter Greenwald, John Garden, LaVerne Campbell, Dwight Janerich, and Charles Lawrence; Ms. Judith Brady and Mary Conley; Mr. Philip Harper and William Marani. In addition we wish to thank Dr. James Kropelin, numerous community physicians and hospitals for providing medical information required for this investigation.

FIGURE I

Love Canal study area

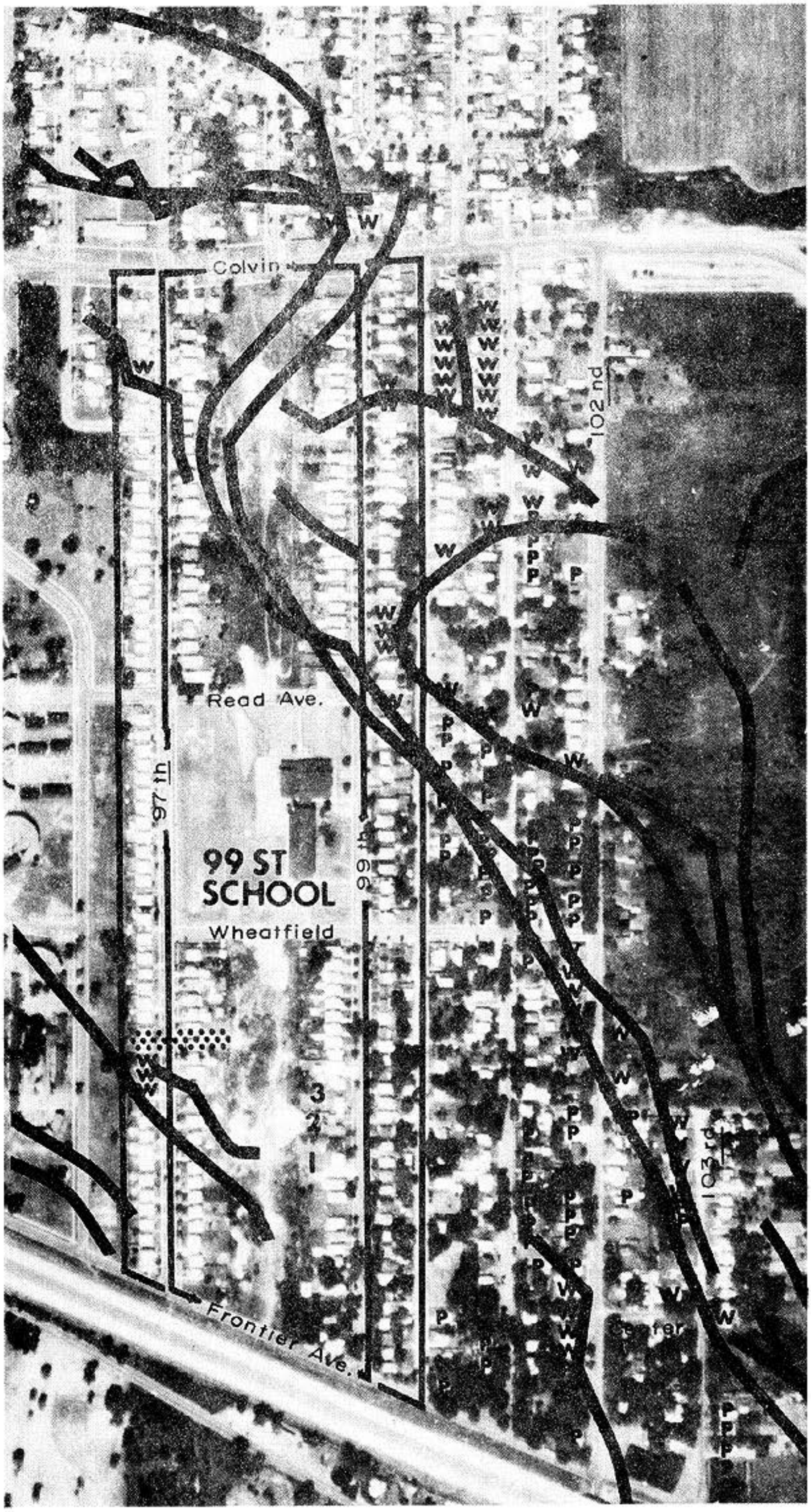

FIGURE II

Percent of pregnancies which terminated in a spontaneous abortion - Five-Year Moving Average

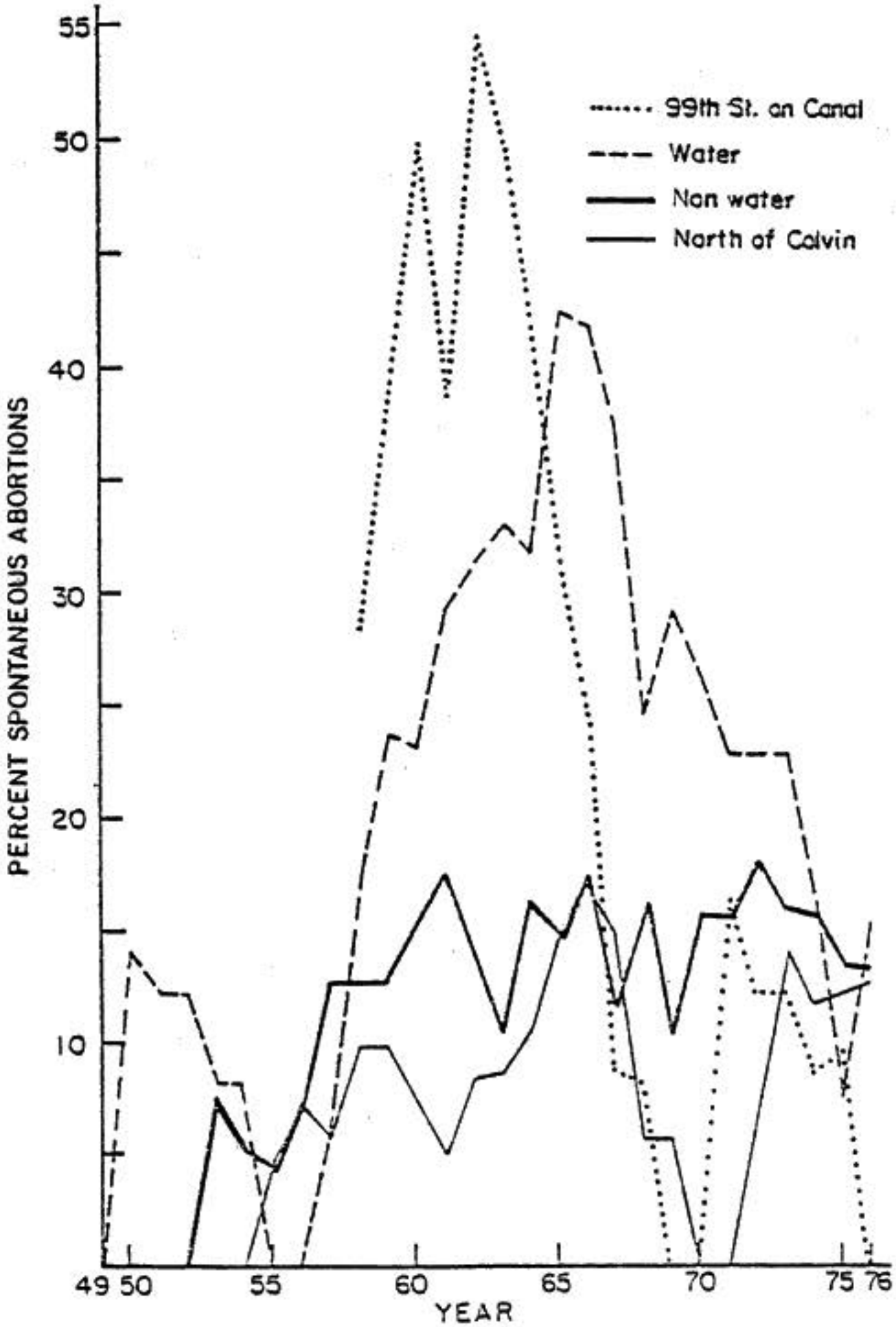

Table 1. Preliminary List of Compounds Found in Love Canal Air or Soil Samples

Chloroform	Tetrachlorobenzene (3 isomers)
Carbon tetrachloride	Benzene
1,1-dichloroethane	Toluene
1,2-dichloroethane	o, m, p, xylenes
1,1,1-trichloroethane	Benzaldehyde
Trichloroethylene	Chlorotoluenes
Tetrachloroethylene	Pentachlorobenzene
Chlorobenzene	Alkyl phenols
Dichlorobenzene (2 isomers)	Hexachlorobenzene
1,2-dichloropropane	BHC's (4 isomers)
Chlorotoluene (2 isomers)	Tetra, penta, hexa chlorinated anthracenes or phenanthraenes**
Chlorobenzaldehyde (isomers)	2,3,7,8 TCDD and other TCDD**
Dichlorotoluene (3 isomers)	Hexachlorodibenzodioxin**
Dichlorobenzaldehyde (isomer)	Dichlorodibenzodioxin**
Trichlorobenzene (3 isomers)	Chlorinated napthalenes** (isomers)
1,2-dibromoethane	Trichloro phenols (isomers)
Trichlorotoluene (5 isomers)	PCB's (2 isomers)
Tetrachlorotoluene (isomers)	Octachlorocyclopentene**

* The first 21 chemicals listed were identified by both the Environmental Protection Agency and the New York State Health Department. The remaining compounds were identified by the New York State Health Department.

** Tentative assignment

Provisional - April, 1980

Table 2. Pregnancy Histories and Age Distribution of Female Residents of Specified Sections of the Love Canal and the North of Colvin Area

Pregnancy History at Present Address	99th*	97th*	Water	Non Water	North of Colvin
Women Ever Pregnant	22	20	49	98	66
Number of Pregnancies**	50	29	108	164	125
(Sets of Twins)	(1)		(2)	(2)	
Women with Live Births	21	19	44	92	64
Number of Live Births	39	26	83	144	110
Women with Miscarriages	7	3	16	16	11
Number of Miscarriages	12	3	25	21	11
Women with Birth Defect Child	4	0	7	7	7
Number of Birth Defect Children	4	0	10	7	8
Women with Low Birth Weight Child	1	0	10	6	3
Number of Low Birth Weight Children	1	0	13	11	3
Women with Stillbirths	0	0	2	1	3
Number of Stillbirths	0	0	2	1	4
Women with No Unfavorable+ Event	14	17	22	70	45
Women with An Unfavorable+ Event	8	3	27	28	21
Age (years) of Females					
Total++	89	90	208	474	343
0-14	26	29	49	138	62
15-29	14	27	65	121	90
30-44	20	17	35	96	62
45-59	21	15	44	73	86
60 and older	8	2	14	45	34

* Houses on the Canal
** Number of Pregnancies = (Live Births + Miscarriages + Stillbirths) Minus Twins.

+ Unfavorable Event: Miscarriage, Birth Defect Child, Stillbirth or Low Birth Weight Child
++ Total Includes Age Unknown

Provisional - April, 1980

Table 3. Spontaneous Abortion Ratios of Observed to Expected Numbers* for Specified Areas of the Love Canal Based on Two Comparison Groups

Area	Warburton & Fraser Comparison Group P	O/E	North of Colvin Comparison Group P+	O/E
99th Street**	.110	1.5	.007	6.0
97th Street**	***	0.7	>.05	1.2
Rest of Love Canal Area	>.05	1.1	.050	2.6
Water	.031	1.5	.007	3.4
Non Water	***	0.8	>.05	2.0

* Standardized for Age and Parity
** Houses on the Canal
*** Observed was less than expected

\+ Mantel-Haensel chi square (one sided test)

Provisional - April, 1980

Table 4. Documented Congenital Defects Among Children Born in Specified Areas of the Love Canal and the Northern Area

Location Type of Malformation	Sex
97th and 99th Streets*	
Congenital deafness	M
Reflux of ureters	F
Cleft palate, deformed ears and teeth, hearing defect, mental retardation, heart defect	F
Club foot	M
Water Area	
Prolapsed mitral valve	M
Non-functioning Rt. hydro-nephrosis	F
Born with 3 ears	M
Ears turned down	F
One kidney	F
Hydrocephalus	M
Club foot	F
Web toes	F
Web toes	M
Web toes	F
Non-Water Area	
Inverted testicle	M
Absence of deciduous teeth	M
Extra toe	M
Obstruction of ureter	M
Disaccharide deficiency	M
No diaphragm	M
Severely retarded, eye defect, teeth defect	F
North of Colvin	
Hypospadias penis	M
Deformed kidney	F
Incomplete left lip	F
Hydrocephalic-slepian eye, deafness	M
Mongolism	F
Diaphramic hernia	M
Immature lungs, pulmonary insufficiency	M
Congenital dysplasia of left hip	F

* Houses on the Love Canal

Provisional - April, 1980

Table 5. Percent of Children with Low Birth Weight or with Congenital Defects, Born in Specified Areas of the Love Canal

Location	Live Births	Children with Low Birth Weight+ Number	Percent	P**	Children with Congenital Defects Number	Percent	P***
99th Street*	39	1	2.56	++	4	10.26	>.05
97th Street*	26	0	0.00	++	0	0.00	++
Rest of Love Canal Area	227	24	10.57	.017	17	7.49	>.05
Water	83	13	15.66	.001	10	12.05	>.05
Non Water	144	11	7.64	>.05	7	4.86	++

* Houses on the Canal

** Normal Approximation, one-sided; sample proportion compared with population proportion 6.97 (Average for period 1950-1977, white births recorded in New York State, excluding New York City)

** Normal Approximation, one-sided, North of Colvin Control (7.27)

\+ Defined as $\leq$ 2500 grams

++ Observed was less than Population or Control

Provisional - April, 1980

Table 6. Possible Modes of Exposure to Toxic Chemicals

Mode	Epidemiological Implications
1) Inhalation of (or skin contact with) ambient air particulates	Incidence of health effects should decrease with increasing distance from Canal
2) Household air particulates from chemical leaching into houses and drying on walls	Expected higher incidence in historic water houses
3) Volatile chemicals in household air, waterborne to the house	As for 2
4) Volatile chemicals in ambient air	As for 1
5) Ingestion of (and skin contact with) Canal soil	Would affect people spending time on the Canal
6) Soil-borne chemicals brought into houses on footwear	Would affect specific families, depending on personal habits
7) Toxic chemicals in transported soil fill used to fill in wet areas	Would affect people living in houses on historically low lying areas
8) Volatile chemicals transported from the Canal to storm sewers to houses via drainage sumps	Would affect only residents of houses with sumps
9) Chemical contamination of town water supply	Would affect a very broad area
10) Ingestion of vegetables grown in contaminated soil	Would affect specific families

NEW YORK STATE
DEPARTMENT OF HEALTH

For release: MONDAY
JUNE 23, 1980

• NEWS RELEASE •

DAVID AXELROD, M.D.
Commissioner

CONTACT: MARVIN G. NAILOR, DIRECTOR OF COMMUNICATIONS (518) 474-5422

Embargoed for release until the conclusion of a scientific briefing scheduled to begin at 1 p.m., June 24, 1980 in the laboratory auditorium of the State Health Department on the Concourse Level of the Tower Building in the Empire State Plaza.

Note to Editors and Reporters:

The attached manuscript describes the New York State Health Department's epidemiologic studies on adverse pregnancy outcomes among Love Canal residents. The studies were conducted from the early summer of 1978 through the spring of 1979.

A scientific briefing by the author and his co-authors will be held beginning at 1 p.m., June 24, 1980 in the laboratory auditorium of the Health Department in Albany.

Release of the manuscript is being embargoed to allow for sufficient review and to ensure, through a scientific briefing, that the findings and conclusions are not misinterpreted.

The decision to release the manuscript before its publication in a scientific journal was made after the Attorney General's Office advised the Department that the paper was not among the Love Canal documents exempted from the Freedom of Information Law (FOIL) in connection with the State's lawsuit against the Hooker Chemical and Plastics Corp. The opinion was sought after the Department received a FOIL request for the manuscript from the chief of the Capitol Bureau of Gannett News Service in Albany.

Because of the widespread interest in the Love Canal and because of the Department's desire not to add to the psychological pressure on the residents of

the Love Canal, the decision was made to make the manuscript generally available while providing an opportunity to news media representatives to question the author and co-authors of the study.

The attached manuscript is being revised for submission to a scientific journal. The revisions will not alter the findings or conclusions contained in the attached version but will respond to questions posed by peer reviewers.

Marvin Nailor
Director of Communications
518 474-5422

-30-

6/23/80-71 PH