VC Research 1976

BIRTH DEFECTS AND VINYL CHLORIDE

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I would like to address the question of vinyl chloride monomer exposure and its possible relationships to birth defects. If there is a relationship between vinyl chloride and birth defects, it could be either a mutagenic effect, prior to conception, or a teratogenic effect after conception.

One of the first reports that vinyl chloride may be related to birth defects in humans was presented in March, 1975, by Dr. Infante at the New York Academy of Science. The study conducted by Dr. Infante, then with the Ohio Department of Health, noted increased rates from 1970 to 1973 in three Ohio communities where polyvinyl chloride plants were located. Anomalies of the central nervous system were of greatest concern and most of the excess was attributed to the city of Painesville, Ohio. The concern was that residential and occupational exposure might be associated with increased rates of CNS defects.

At the Center for Disease Control, data are collected through the Birth Defects Monitoring Program (BDMP). Briefly, the BDMP is a national, hospital-based system for monitoring the incidence of birth defects and other newborn conditions from hospital discharge diagnoses; it consists of approximately 1,200 hospitals monitoring a million births per year from 1970.

The BDMP provided data with which we could further examine the suggested increase in CNS rates in Ohio. We identified two cities which had a polyvinyl chloride plant, and one BDMP hospital believed to serve each community. One hospital was in Pottstown, Pennsylvania, and the other was in Painesville, Ohio.

Selected malformation rates for these two hospitals -- 1970 to 1974 -- were compared with rates for their respective states. The rates seen in Pottstown, Pennsylvania, were 21.6 per 10,000, approximately what was expected from the national BDMP rates. The expected number of defects in Painesville was approximately 11. The observed number of 22 cases was twice the expected.

On the basis of this increase, an investigation was undertaken in Painesville. Painesville, Ohio, is an industrial city on Lake Erie, near Cleveland, with a population of approximately 16,000. There are two polyvinyl chloride plants located in Painesville. They are across the street from each other and about two and a half miles from the center of the city. One of them has been in operation since 1949 and the other since 1967.

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The investigation was a hospital-based study and was limited to cases of anencephaly and spina bifida. The BDMP data were compared to birth certificate data obtained from the Ohio Department of Health. One additional case of anencephaly was found, making a total of 15 cases.

The hospital records were reviewed to confirm the diagnosis and obtain other demographic data. For each case, two controls were selected from the hospital records; the first normal, white birth before and after the case, since all the cases were white.

The physician of each mother in the case group was contacted and permission obtained to interview the parents concerning their past occupational and residential histories. The investigation did confirm increased rates for anencephaly and spina bifida compared to expected statewide rates.

The hospital rates for anencephaly (14.1 per 10,000 births) and for spina bifida (21.2 per 10,000 births) were greater than two times the expected rates, based on the BDMP state data. None of the 14 cases interviewed had ever worked at either of the two polyvinyl chloride plants in Painesville. One set of parents could not be located, but hospital records indicated that they did not work at the plant at the time of their infant's birth.

Among the 30 control parents, two fathers had worked at a polyvinyl chloride plant at the time of their infant's birth. No parent in either case or control group lived within two miles of either plant.

Statistical comparisons on distances varying from one mile to 10 miles of parental residence to the plant indicated that there was no difference between the cases and control.

Local increases in CNS and other malformation rates, such as seen in Painesville, are not uncommon. In this particular study, no association could be found between VC and the higher rates of CNS defects.

A second and similar study was just completed in Kanawha County, West Virginia. Because of the continued concern about the teratogenic potential of vinyl chloride, BDMP data were again reviewed for all counties having a polyvinyl chloride plant and at least one BDMP hospital.

In the earlier study, the selection was limited to cities with only one hospital serving the entire community. At CDC, we identified 17 counties in the U.S. which have a polyvinyl chloride plant and at least one BDMP hospital.

Four of these 17 counties had rates for CNS defects that were significantly higher than rates for the U.S. for the time period,

1970 to 1974. Two of the counties so identified had less than 50 percent of total births in the BDMP and were excluded from this study.

The two remaining counties with increased rates were Lake County, Ohio, (Painesville) the site of the previous study -- and Kanawha County, West Virginia, where 95 percent of county births were monitored. In Kanawha County there were 59 infants born between 1970 and 1974 with CNS defects. The expected number, based on U.S. rates, was 37.

The principal centers of population in Kanawha County include Charleston and South Charleston, which are located along the Kanawha River which meanders through the valley's hilly terrain. The Kanawha River Valley is known for its chemical industry. There are seven major chemical plants and several smaller ones within 10 miles of Charleston. There is one polyvinyl chloride plant, located in South Charleston, bordering Charleston, which began production of polyvinyl chloride in 1935.

Two sources of data were reviewed to identify all cases of central nervous system defects occurring in Kanawha County between January 1, 1970, and December 31, 1974. One source was a case listing obtained from the Birth Defects Monitoring Program which would list the cases occurring in the BDMP hospitals in the county. The second source was vital records. The West Virginia Department of Vital Statistics provided all cases of CNS birth defects occurring between January 1, 1970, and December 31, 1974.

The two lists were combined and the hospital records reviewed to confirm the diagnosis and the place of residence. For each confirmed case, two controls whose parents resided in Kanawha County were selected from vital records. These controls were the first normal, live-born infants whose certificates preceded and followed a case.

The cases and controls were matched according to month of birth, race, paternal education, and maternal age. With the permission of the local physicians, all cases and one randomly chosen control were interviewed. The parents were told that this was a birth defect study and vinyl chloride was not mentioned. The following information was obtained: history of previous pregnancies; five year residential history, prior to and including the time of birth of the affected infant; and five year occupational history of both parents, including the location of work and any possible chemical exposures.

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	BDMP	U.S. Rate
1968	N.A.	
1969	N.A.	
1970	21.8	
1971	22.1	
1972	21.6	
1973	19.9	
1974	18.4	
1975	18.2	
1970-1974	20.6	

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TABLE 1

INCIDENCE OF CNS MALFORMATIONS IN KANAWHA COUNTY, W. VIRGINIA AND THE UNITED STATES, 1968-1975 (RATES PER 10,000 TOTAL BIRTHS)

	BDMP Hospital Data			Vital Statistics		Confirmed Cases	
	U.S.	Kanawha Co.		Kanawha Co.		Kanawha Co.	
	Rate	Case	Rate	Case	Rate	Case	Rate
1968	N.A.	N.A.		(13)	35.4		
1969	N.A.	N.A.		(8)	20.3		
1970	21.8	(12)	35.9	(16)	42.8	(14)	37.5
1971	22.1	(19)	51.7	(13)	34.4	(15)	39.7
1972	21.6	(11)	30.5	(13)	37.9	(12)	34.9
1973	19.9	(11)	28.9	(5)	15.0	(5)	15.0
1974	18.4	(6)	14.4	(1)	3.0	(1)	3.0
1975	18.2	(10)	22.9				
1970-1974	20.6	(59)	31.7	(48)	27.2	(47)	26.7

The BDMP rates are given in the first column of the table. The high Kanawha County rates compared to the U.S. rates are what prompted the investigation. The last column gives the rates for the confirmed cases from 1970 to 1974. As you can see, 1970, 1971, 1972 were the highest years, with the rates starting to decline in 1973 and only one case observed in 1974.

Forty-six cases and their matched controls were located and interviewed. Five cases were not residents of Kanawha County at the time of conception and were eliminated from the study, except in calculation of rates, which are based on residency. Close matching was achieved between the cases and controls for paternal education, maternal age, and the Hollingshead index, which is an indicator of socioeconomic status. Reproductive history revealed that the total number of pregnancies were similar between the cases and controls; 49 for the case group and 48 for the control group. The live birth percentages were also very similar between the two groups. The fetal death rates, which include spontaneous abortions and stillbirths, were 22% for cases and 23% for controls.

Occupational histories revealed that two cases and two control fathers were employed at the vinyl chloride plant at the time of conception. Fathers of three additional controls also had worked at the vinyl chloride plant on a contract basis and may have had possible vinyl chloride monomer exposure. None of the mothers in either the case or control group had worked at the polyvinyl

chloride plant, but few women work in the vinyl chloride industry.

The residences of case and control parents, at conception, were plotted on county maps and the distances from the plant were calculated. Using a chi square test, at one mile intervals, no statistical difference was observed between the cases and controls. Matched pairs of cases and controls were also tested, using a matched-pair T test of significance, and no difference was observed. While no difference was observed in the distance of residence from the plant, inspection of the map suggests that, within the five mile area, cases were concentrated to the northeast of the river, and the controls were concentrated to the southwest.

From the polyvinyl chloride plant, X and Y co-ordinates were determined for the parents' residence, at the time of conception, for each case and control. Cases and controls were then compared for a statistically significant difference in their respective centers of gravity, which is the mean position of the group. The only statistically significant difference (p.02) noted was within the three mile area. There were 10 controls and 9 cases within this area.

Both cases and controls within the three mile area had a higher socioeconomic index than those outside the area. No difference was noted between the cases and controls in regard to occupation or length of residence within the three mile area.

Cases did have an interesting family history of birth defects. One case mother gave birth to two of the cases within the three mile area. Another case mother had had a sister with spina bifida. A third mother in this case group had reported a cousin with a heart defect. While familial components do not exclude environmental cause, they suggest a possibility of a genetic causation.

Atmospheric and environmental data related to vinyl chloride monomer and other chemical emissions in Kanawha County are limited. Some data were provided by the vinyl chloride plant. These data have been collected over the past several years.

On October the 1st, 1974, the largest single emission was noted and the VC levels were measured in the community. The highest atmospheric levels were .1 and .2 parts per million. At that time the wind was from the southwest, and these levels were found to the northeast of the plant.

Additional data were available from the West Virginia Air Pollution Commission. These data, gathered over the past several years, dealt with suspended and settleable particulate matter. They indicate just the opposite of the VC measurements. They indicate that the highest concentrations of the settleable and suspended particulate matter were to the southwest, suggesting a pre-

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In addition to these conflicting data, other data available on wind and temperature data, coupled with the terrain, suggest that Kanawha County in the Kanawha Valley is a veritable mixing bowl for any emissions. There have been identified over a hundred chemicals emitted into the valley. The effect of these chemicals, alone or in combination, is not known, and to attribute this case pattern within three miles to the effect of one chemical plant is unwarranted.

In conclusion, both studies did confirm higher CNS rates than expected during the early 1970's. CNS rates are not significantly different from the U. S. rates at the present time. Occupational histories in both studies revealed no difference between the case and the controls in possible work exposure to vinyl chloride monomer. Residential histories showed no difference between the case and controls when compared at varying distances from the polyvinyl chloride plants.

However, in Kanawha County, we did see a difference in the pattern of residents for cases and controls living within three miles. No explanation of this difference could be found, but the available data suggested no association with vinyl chloride monomer. Further plans are to monitor the counties identified earlier in the birth defect monitoring program. We also are gathering back data from Kanawha County to 1958 in order to determine the CNS rates for these years.

those people with the structural deformity, those fetuses, died. So, you'll have to look at the structural deformities in relation to numbers of abortions in the community, which I did not hear in the study.

I think that when we do these studies, they have to be done with extraordinary care because the stakes are extraordinarily high. Again, I'm not faulting the study. I think that it represents a very serious and important effort. I'm only suggesting that we do need a lot more environmental measurements in the plants and out of the plants.

We do have to define all of the populations at high risk. We do have to carry out studies which will then look at the level at which these populations are affected. As I said before, there is no threshold for most of these things. At every level of environmental contaminants -- in the plant or out of the plant -- someone may be affected. So what we're really talking about when we do careful studies -- and this, I think, is one of the approaches we can take to this problem -- is that we have to look for what are socially acceptable risks. We have to look at dose response relationships and try to come up with some level in the workplace and in the community which will protect virtually all of the population.

If we do this, then we can look at the question of the pregnant woman as a very special case, and make every attempt to protect her without sacrificing her economic status and so on. I think we'll have more to say about that kind of thing in discussion, but I feel that this really is what we're trying to grapple with today and tomorrow.

QUESTIONS, ANSWERS AND COMMENTS

DR. CLARK COOPER: Along with Dr. Carnow, I think we need epidemiological studies concurrent with the actions that we are going to have to take. We have found it very difficult to develop designs for studies that we feel are satisfactory, and I am particularly interested in Dr. Wagoner's report of fetal deaths associated with male exposures to VCM, because this really has been one of the most startling reports that we have had. It was given to us in a very abbreviated form and I am very interested in just how the study was handled, and how data was obtained.

DR. WAGONER: This was a survey in which both male employees exposed to vinyl chloride and unexposed rubber workers in the same facility were questioned concerning the reproductive histories of their spouses. The data were analyzed for potential interviewer bias, and none was found. The data were analyzed, as I indicated in the presentation, with regard to those individuals having two or more miscarriages, three or more miscarriages, or four or more miscarri-

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The complete methodology of the study is included in the paper which was recently published in The Lancet Magazine, where it is available for peer review.

DR. PETER INFANTE: I am also concerned about the results of the CDC study of vinyl chloride, and about the clustering on the northwest side of the plant. I believe the wind direction was predominantly from the southwest in this part of the country.

In fact, recent studies by the Environmental Protection Agency, in which they tagged chlordane isotopes and spread them for agricultural purposes in Dallas, resulted in this chlordane being detected in Cincinnati's water supply. For this reason, I think the predominant direction of the wind is to the southwest, and that is why I'm a little concerned when I see the clustering near the plant, within the three-mile limit on the north side of the plant.

Also, I am concerned about the case control method for the study -- looking at distances from the plant -- given the mobility of the working population. For example, a worker who doesn't work in the plant can work next to the plant but live ten miles away. Should a birth defect or some other anomaly be related to this, it would show up ten miles away when, in fact, the worker spends eight hours a day closer to the plant.

Again, I think these are questions that need to be resolved. In addition, the method of selection in this study requires examination. They looked at 17 communities, with vinyl chloride polymerization facilities, and four of them had a significant excess of central nervous system anomalies.

Now, at the statistically acceptable five percent level, you would expect five out of 100 communities to show significant excess, and yet they found four out of seventeen with a significant excess of central nervous system anomalies. This is of further concern because in two of the communities, the monitoring system ascertained less than 50 percent of the births. Yet they were still able to identify a significant excess of central nervous system anomalies.

I have some information concerning birth defects in a community that was not in the CDC monitoring program. The data was received from the Michigan Department of Health, and it shows the incidence of birth defects in Midland County, Michigan, where there is a large industrial chemical complex, in relation to the rate for the remainder of the state. During the five-year period, 1970-1974, there was an incidence of 21.3 birth defects per thousand live births. That's compared to 9.5 for the state as a whole. So,

again, we see a repeated pattern of birth defects in areas with vinyl chloride polymerization facilities.

As I said a year ago, this certainly does not mean that these observations are causally related to vinyl chloride. But as data continues to come in, I am becoming more concerned about it.

DR. FINKLEA: Thank you very much. I think maybe Dr. Edmonds might want to make a reply. I might add one thing that would be helpful to you. The Environmental Protection Agency did publish a monograph on the air pollution in the Kanawha Valley. And I think if you will look at that, maybe elevation might be just as important here as a location for a plant. That valley acts as a trough and you have frequent inversions, and you have a lot of almost slushing back and forth in that trough. And your air pollution there should follow a little bit different pattern than you would see if your topography were quite level.

MR. EDMONDS: I would just like to make a few comments. First of all, somebody made a comment earlier to the effect that these studies found no association with vinyl chloride. In fact, these studies cannot rule out such an association.

The first thing we compiled was wind data. Dr. Infante said that the predominant winds were out of the southwest. Kanawha Valley is a deep valley. The very top of the valley is an airport, and wind direction at that airport is out of the southwest. Down in the valley there is a different situation. The wind direction is different during the time of day, and time of year. In addition, you cannot ascribe any one wind direction to any one part of the city. We did try to ascertain wind direction at the time of conception for both cases and controls.

The wind blew a little more out of the southwest than out of the northeast -- about 42 percent of the time versus 37 percent of the time. So the difference is very minimal. And difficult to assess. There is very little information on environmental pollutants in the valley. There are a lot of chemicals. I mentioned the VC levels on one day they measured. That one day's measurements were the only levels we could find in Kanawha Valley. The levels were a little bit higher to the northeast, with the winds out of the southwest.

The particulate and settleable matter I told you about has been measured over several years. These measurements are higher to the southwest, and could be reflecting emissions from other industries in the general vicinity.

The environmental and atmospheric data were very confusing. You cannot pinpoint wind direction to any one part of the county. As for selection of the counties, four counties with the highest rates were identified out of the seventeen. Two of them were

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eliminated. In one of them, only three percent of the births were monitored. The other county that was eliminated was a county where 38 percent of the births were monitored between 1970 and 1974, but where the VC plant was not in operation until late 1972. So that community was eliminated, which leaves the two counties of Painesville and Kanawha.

The next comment I would like to make is about the high rates in Midland. I would be interested in knowing what types of defects they are.

DR. INFANTE: The data from Midland County, Michigan, show total defects. With regard to congenital anomalies, thirty-four urogenital defects were observed, whereas only seven were expected; twelve heart anomalies were observed, whereas only four were expected; and fifteen cleft lip and palate defects were observed, whereas five were expected. These observations are highly significant statistically.

MR. EDMONDS: We need to monitor these counties. In Kanawha Valley, we are going to evaluate all birth certificates back to 1958. We still have a concern.

DR. INFANTE: Well, the point I was trying to make is that the population study conducted in the Ohio communities with vinyl chloride polymerization facilities demonstrated a significant excess of birth defects. This study did not conclude that the birth defects were related to vinyl chloride. On the other hand, your study does not rule out the possibility.

DR. GORDON: You cannot rule it out.

DR. INFANTE: In fact, I am more concerned now in that you identify four out of seventeen counties showing a significant excess. To me that is a significant observation.

MS. CLARA SCHIFFER: I am interested in the technologies that are necessary to reduce hazards, and I have two questions. First, I would like to ask Dr. Corbett how much it costs to install a scavenger in an operating room and properly vent it? And, secondly, I know Dr. Gordon was asked to speak on placement and not on what Dow does. But I want to take advantage of his being here to ask him what technological changes Dow is putting in to reduce some of these hazards?

DR. CORBETT: The answer to the first question is that it costs approximately $100 to install the scavenger device on an operating room anesthesia machine. That is, if the existing remainder of the equipment is suitable for removing the gases from the room. In other words, does the operating room ventilation system carry the gases directly outside, as opposed to recirculating the air? If air is recirculated, an alternate form of exhausting is necessary.

Acting Director
Office of Extramural Coordination
and Special Projects

October 7, 1976

called Johnson re. M on

Deputy Director, NIOSH

Vinyl Chloride

Manry Johnson of B. F. Goodrich called today to see what our interpretation of Maltoni's latest findings on VC were. He relayed the following:

# Rats	ppm VC	No. of Rats with Mammary Carcinoma	No. of Rats with Angiosarcoma
120	25	9	3
120	10	11	0
120	5	13	0
120	1	7	0
120	0 (control)	4	0
600			

I don't know the number of rats involved.

Maury said a number of copies of the report were distributed (NCI and others) but, if we can't locate a copy, to call him (216-379-3296) and he'll send a copy to us.

He also asked to be kept appraised of our decisions on this. I assured him we would do this.

/s/ Edward J. Baier

Edward J. Baier

cc: Mr. Vern Rose
Dr. Roscoe Moore
Dr. Bobby Craft

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