

# Cancer Risks and Environmental Exposures in St. Lucie County Florida

Florida Department of Health

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## 1. *Background and Objectives*

From January through December 1998, the Florida Department of Health (DOH) conducted a series of environmental chemistry tests in St. Lucie County Florida. The tests were designed to investigate possible links between environmental contaminants in the air, water, or soil and cases of childhood brain and central nervous system (BCNS) cancer and neuroblastoma. Eight cases of neuroblastoma, a malignant tumor derived from prenatal brain structures, in children age nine or less were diagnosed in the county from 1981 through 1998. Twenty-two cases of BCNS cancer were diagnosed in residents of the county age 19 or less during the same period<sup>1</sup>. Thirteen of the 22 BCNS cancers were diagnosed in 1995 (3), 1996 (5), or 1997 (5). These trends suggested the possibility of elevated rates of these cancers and raised concerns among county residents and local and state health officials that the cases might be associated with exposure to environmental toxins.

The purpose of this analysis is to estimate the increase, if any, in the risk of neuroblastoma or BCNS cancer in individuals who have been exposed to elevated chemical levels. Chemicals found to be associated statistically with an increased risk of cancer will be investigated further for biologic plausibility (e.g. carcinogenicity) and environmental plausibility (e.g. contamination source and individual exposure levels). These investigations, in conjunction with assessments of the social and economic costs, will provide the basis for determining the appropriate public health action. An important limitation of the study is the fact that some of the cancers were diagnosed years in the past. Any environmental contamination that may have contributed to causing these cases may no longer be present in the environment. If this is so, it will tend to reduce the estimates of relative risk for these chemicals, disguising their adverse health impact.

St. Lucie County is located on Florida's east coast, north of Palm Beach and south of Cape Canaveral. The county has approximately 180,000 residents, up from a population of 51,000 in 1970 and 87,000 in 1980, with over 80 percent of recent population growth attributed to migration<sup>2</sup>. The largest cities in the county are Port St. Lucie (pop. 80,000) and Ft. Pierce (pop. 40,000). Residents of St. Lucie County are predominantly white (81 percent) or African-American (17 percent). About 24 percent of the county's residents are under the age of 18. The largest industries in the county in 1994 were services (29 percent of the workforce), retail trade (26 percent), and agriculture (14 percent). The county's unemployment rate was 13.4 percent.

## 2. *Methods*

The study design is case-control. Case-control studies are efficient in situations where the disease is rare. The source population, also known as the population at risk, is the group whose members were selected as cases when diagnosed with BCNS cancer or neuroblastoma. In this study, the source population is persons who were cancer-free, age 19 or less (or unborn) in 1981, and lived in

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<sup>1</sup> Data for cases diagnosed in 1998 are incomplete so additional cases may be reported.

<sup>2</sup> Demographic and economic data are from the Florida Statistical Abstract (1995).

St. Lucie County subsequent to 1981. The cases are all of the members of the source population who were diagnosed with the disease during time period under investigation. The controls are a random sample of the source population used to estimate the frequency of chemical exposure in the source population. Information on the exposure distributions of the cases and controls provides the basis for estimating the increased risk of disease due to exposure.

#### A. Selection of Cases

To be selected as a case for this study, a member of the source population would have had to have been diagnosed with BCNS cancer prior to the age of 20, or neuroblastoma prior to the age of 10. Because there was no way to identify reliably members of the source population who may have been diagnosed after moving away from St. Lucie County, the selected cases were almost entirely limited to those residing in the county at the time of diagnosis. As long as any unidentified out-of-county cases had the same exposure pattern as the identified cases, their exclusion from the study will not bias the results. There were 29 cases selected for the study. Twenty-seven of them lived in St. Lucie County at the time of diagnosis, 20 with BCNS cancer and 7 with neuroblastoma. One BCNS case had permanent residence in neighboring Martin County, but regularly spent the workweek in St. Lucie. Another BCNS case moved from St. Lucie County to Wisconsin three months prior to diagnosis.

#### B. Selection of Controls

Fifteen controls were selected from the current population of St. Lucie County, age 19 or less. Controls were recruited with the assistance of local community groups. Because controls were selected from the current population of minors rather than the source population (which includes historical groups of children), there could be selection bias. This would occur if there were differences in the exposure patterns of the controls compared to the source population. For instance, there may have been changes in population density patterns during the study period so that the controls tend to live in different neighborhoods than the source population. Also, the controls might tend to live in newer homes than the source population as a whole.

The existence and amount of any selection bias is difficult to measure or estimate.

#### C. Exposure Measurement

Cases and controls may have been exposed to environmental chemicals in many places including home, school, work, or recreational areas. In this study, chemical measurements in the home were used to assess exposure. Other sites were excluded since home is where most children spend the largest amount of time and the likelihood of exposure in other locations is low. It is important to remember that these point-in-time environmental chemical measurements may not correspond to the actual exposures experienced by the individuals in the study during the time preceding their illness. An individual's exposure to environmental chemicals depends on their unique behaviors over time as they live, work, and play in their changing environment. To the extent that the environmental testing data misrepresents or misclassifies individual exposures, it will make the cancer risk estimates less reliable<sup>3</sup>.

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<sup>3</sup> Random exposure misclassification among cases and controls will tend to bias the odds ratio estimates towards one, obscuring any effects of chemical exposure on cancer risk. Non-random misclassification could bias the results in either

Two cases spent a great deal of time at the homes of nearby relatives as well as at their own homes. For these cases, tests were conducted in both homes. The highest exposure value from the two sites was used as the exposure measurement.

All of the environmental samples were collected by DOH field staff. Most of the testing was conducted at the DOH Bureau of Laboratories in its Jacksonville facility during the period January through December 1998. Testing of semi-volatile compounds in soil was conducted by the Department of Environmental Protection laboratory.

Of the forty four cases or controls in the sample (29 cases and 15 controls), tests were completed for 10 to 39 of them for each of more than 500 chemicals in the air, water, soil, and dust, plus radon. The chemicals included metals (e.g. lead, mercury, cadmium), pesticides, organic compounds, and PCB's. Many of these are known or suspected carcinogens. The result of each test was reported as a numerical value along with a qualifier code. The qualifier indicates, for example, whether the value could be accurately quantified, whether the value exceeds the state Maximum Contaminant Level (MCL), or if the result should not be used because of possible contamination or other uncertainty. State MCL's are specified for chemicals in drinking water if exposure to levels exceeding the MCL raises the long-term risk of cancer or other diseases. MCLs have not been defined for chemicals in air or soil, although health-based screening criteria have been specified for many chemicals in these media based on the best scientific evidence available. Another important qualifier is the non-detection indicator. If a chemical is not detected, its precise value is unknown, although it does not exceed the method detection level of the test (i.e. the smallest amount that the method can detect). Certain chemicals are tested by more than one method. For these chemicals, the result from the most sensitive test (i.e. lowest method detection level) was used.

Cases and controls were classified as exposed or unexposed to each item based on the results of the lab tests. Exposures were classified in two ways, and the risk associated with exposure was estimated for each exposure definition. A **Level 1 Exposure** was defined as any detectable level of a chemical. Analysis of Level 1 exposures identified many chemicals for which there were few or no exposures in any tested home. Chemicals for which there were three or fewer Level 1 exposures in either cases or controls were eliminated from further analysis. These chemicals were not found in enough locations for them to be plausible causes of the cancers under study.

For the remaining chemicals, a **Level 2 Exposure** was defined as an exposure above the Florida screening criterion for that chemical. The state screening criteria are defined based on evidence of possible increased health risk for intermediate or long-term exposures above those levels. The state screening criteria are at least as stringent as the federal screening criteria where federal standards exist. For chemicals where no federal standard exists, the state screening criterion is determined based on the best toxicological information available. The screening criteria include a safety factor so that Level 2 exposures do not necessarily mean that there is an increased health risk. Level 2 exposures are subject to a more detailed toxicological assessment to determine if there is an elevated health risk. If there were more cases and controls, it would have been possible to define more than two levels of exposure to estimate dose-response effects. However, the study size was too small to produce meaningful risk estimates for any finer categorization of exposures.

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direction depending upon how it affected the cases or controls. The existence and extent of exposure misclassification is difficult to assess.

Water chlorination produces certain carcinogenic byproducts such as bromoform, chloroform, bromodichloromethane, and dibromochloromethane. In this analysis these chemicals, known as trihalomethanes, were screened individually and in total according to the standards in the federal Safe Drinking Water Standards. These regulations specify a standard of 80 ug/L for total trihalomethanes, defined as the sum of the four chemicals listed above.

The chemicals that were tested for Level 2 exposures are listed on the following table. The carcinogenicity categories are determined by federal agencies according to the level of scientific evidence supporting carcinogenic effects. Those "Not Classified" as carcinogens have no accepted evidence supporting carcinogenicity.

Chemical	Matrix	Exposure Screening Criterion	Source of Screening Criterion	Carcinogenicity
1,1,1-Trichloroethane	Air	700 ppbv	6	Not Classified
1,1-Dichloroethylene	Air	20 ppbv	6	Possible
1,2,4 Trimethylbenzene	Air	25 ppmv	11	Not Classified
1,2,4-Trichlorobenzene	Air	5 ppmv	12	Not Classified
1,3,5-Trimethylbenzene	Air	25 ppmv	11	Not Classified
Acetaldehyde	Air	25 ppmv	12	Probable
Acetone	Air	13 ppmv	6, 7	Not Classified
Benzene	Air	4 ppbv	6	Known
Butyraldehyde	Air	Not Available		
Chloroform	Air	50 ppbv	6	Probable
Chloromethane	Air	200 ppbv	6	Not Classified
Chlorpyrifos (Dursban)	Air	0.2 mg/cuM	13	Not Classified
Crotonaldehyde	Air	2 ppmv	11	Possible
Diazinon	Air	9 ug/cuM	6	Not Classified
Dichloromethane (Methylene Chloride)	Air	50 ppbv	11	Probable
Ethylbenzene	Air	200 ppbv	6	Not Classified
Formaldehyde	Air	0.00814 ppmv	6	Probable
Freon 11	Air	Not Available		
Freon 12	Air	Not Available		
G-Chlordane	Air	0.2 ug/cuM	6, 7	Probable
Heptachlor	Air	50 ug/cuM	13	Probable
Hexachlorobutadiene	Air	20 ppbv	11	Possible
Hexanaldehyde	Air	Not Available		
M and/or P Xylenes	Air	700 ppbv (total)	6	Not Classified
Mercury (Vapor Phase)	Air	0.3 ug/M3	8	Not Classified
Mercury (Particulate Phase)	Air	0.3 ug/M3	8	Not Classified
O-Xylene	Air	700 ppbv (total)	6	Not Classified
P-Dichlorobenzene	Air	200 ppbv	6	Possible
Radon	Air	4 pCi/L		Known
Styrene	Air	60 ppbv	7	Possible
Toluene	Air	400 ppbv	7	Not Classified

4,4'-DDD	Soil	Not Available		Probable
4,4'-DDE	Soil	Not Available		Probable
4,4'-DDT	Soil	30 mg/kg	2, 6	Probable
A-Chlordane	Soil	3 mg/kg	1, 3	Probable
Antimony (Dry Weight)	Soil	20 mg/kg	1	Not Classified
Arsenic (Dry Weight)	Soil	20 mg/kg	1, 3	Known
Benzo(A)Anthracene	Soil			Probable
Benzo(A)Pyrene	Soil	0.1 mg/kg	5	Probable
Benzo(B)Fluoranthene	Soil			Probable
Benzo(G,H,I)Perylene	Soil			Probable
Benzo(K)Fluoranthene	Soil			Probable
Beryllium (Dry Weight)	Soil	100 mg/kg	1	Probable
Carbon Disulfide	Soil	5000 mg/kg	1	Not Classified
Chlordane (technical)	Soil	30 mg/kg	1, 3	Probable
Chromium (Dry Weight)	Soil	200 mg/kg	1	Known (Hexavalent form only)
Copper (Dry Weight)	Soil	Not Available		Not Classified
Dibromochloromethane	Soil	Not Available		Not Classified
Dieldrin	Soil	3 mg/kg	1, 3	Probable
G-Chlordane	Soil	30 mg/kg	1, 3	Probable
Lead (Dry Weight)	Soil	400 mg/kg	4	Probable
Manganese (Dry Weight)	Soil	7000 mg/kg	2	Not Classified
Mercury (Dry Weight)	Soil	Not Available		
Methyl Iodide	Soil	Not Available		
Nickel (Dry Weight)	Soil	1000 mg/kg	2	Reasonably Anticipated
Pyrene	Soil	2000 mg/kg	2	Not Classified
Zinc (Dry Weight)	Soil	20,000 mg/kg	1, 2, 3	Not Classified
Aluminum	Water	Not Available	14	Not Classified
Antimony	Water	0.006 mg/L	9	Not Classified
Arsenic	Water	0.05 mg/L	9	Known
Barium	Water	2.0 mg/L	9	Not Classified
Bromodichloromethane	Water	100 ug/L	9	Probable
Calcium	Water	Not Available		Not Classified
Chloride (Total)	Water	Not Available	14	Not Classified
Chloroform	Water	100 ug/L	9	Probable
Chromium	Water	100 ug/L	9	Depends on Valence
Dichlorobromomethane	Water	100 ug/L	9	Probable
Fluoride	Water	4.0 mg/L	9	Not Classified
Hexachlorocyclopentadiene	Water	50 ug/L	9	Not Classified
Iron	Water	Not Available	14	
Lead	Water	0.015 mg/L	9	Probable
Magnesium	Water	Not Available		
Manganese	Water	0.05 mg/L		Not Classified
Methyl-Tert-Butyl-Ether	Water	50 ug/L	9	Not Classified
Molybdenum	Water	0.050 mg/L	2	Not Classified

Nickel	Water	100 ug/L	9	Reasonably Anticipated
Nitrate (Total as N)	Water	10 mg/L	9	Not Classified
Nitrite (Total as N)	Water	1 mg/L	9	Not Classified
Orthophosphate as P	Water	Not Available		
Potassium	Water	Not Available		
Selenium	Water	0.05 mg/L	9	Not Classified
Sodium	Water	160 mg/L	9	Not classified
Sulfate (Total)	Water	Not Available	14	
Tin	Water	4.2 mg/L	10	Not Classified
Total Alkalinity as CaCo3	Water	Not Available		
Total Nitrate + Nitrite	Water	10,000 ug/L	9	Not Classified
Total Trihalomethanes	Water	80 ug/L	9	Probable
Zinc	Water	3.0 mg/L	1, 2, 3	Not Classified

**Sources of Screening Criteria:**

- 1) U.S. Agency for Toxic Substances and Disease Registry (ATSDR) Intermediate (15-365 days) Environmental Media Evaluation Guide for children
- 2) ATSDR Reference Dose Media Evaluation Guide for children
- 3) ATSDR Chronic (> 365 days) Environmental Media Evaluation Guide for children
- 4) Residential Recommendation (EPA) Proposed Health-based Screening Criteria - Section 403 Title IV - Childhood Lead Poisoning Prevention Act 1992
- 5) ATSDR Cancer Risk Evaluation Guide for  $1 \times 10^{-6}$  excess cancer risk
- 6) ATSDR Intermediate (15-365 days) Environmental Media Evaluation Guide
- 7) ATSDR Chronic (> 365 days) Environmental Media Evaluation Guide
- 8) Reference Concentration (U.S. Environmental Protection Agency (EPA)) (safe for life-long exposure)
- 9) Primary Drinking Water Standard (EPA and Florida Department of Environmental Protection (DEP))
- 10) Florida Guidance Concentration (DEP)
- 11) Time weighted average, Threshold limit value ACGIH eight hour shift
- 12) Threshold Limit Value Ceiling, ACGIH eight hour shift
- 13) Time weighted average, Threshold limit value ACGIH short-term limit
- 14) Secondary Drinking Water Standard only. These relate to taste and smell, are not health based, and are not used for screening.

**D. Data Analysis**

For a given chemical exposure, the results of the environmental testing can be summarized in a 2 by 2 table as shown below. In this table, A, B, C, and D are the number of cases or controls falling into each category

	Exposed	Unexposed
Cases	A	B
Controls	C	D

The quantity A divided by C, denoted  $A/C$ , estimates the odds that a member of the source population will develop the disease if exposed. Similarly,  $B/D$  estimates the odds of developing the disease if unexposed. The **odds ratio**  $A/C$  divided by  $B/D$ , which can also be written  $AD/BC$ , estimates the relative risk of developing the disease if exposed. In the following hypothetical example, the point estimate of the odds ratio is  $10 \times 8 / 2 \times 20 = 2.0$ . This means that an exposed

individual is estimated to be twice as likely to develop the disease as an unexposed individual. An odds ratio estimate equal to one means no change in risk due to exposure. An odds ratio estimate less than one means that the exposure reduces the risk of disease.

	Exposed	Unexposed
Cases	10	20
Controls	2	8

Odds ratio estimates are influenced by both real differences in exposure effects and random variation. Random variation arises from the biological complexity of exposure-disease causation, unpredictable short-term fluctuations in the environment, error inherent in any laboratory testing procedure, and sampling error in the selection of controls. Along with sample size, random variation influences the **precision** of the odds ratio estimates. Precision is measured by the confidence interval around the estimate. In this example, the 95 percent confidence interval is [0.31, 22.4]<sup>4</sup>. This interval indicates the range of odds ratios that are reasonably compatible with the data. In this example, an odds ratio as large as 22.4 (indicating a strong causal effect of the exposure) is as compatible with the data as one of 0.31 (indicating a protective effect from exposure). The point estimate of 2.0 is the best estimate of relative risk, but the large confidence interval is a reminder of its lack of precision. As in this example, the estimates in this study are relatively imprecise because of the small sample size.

An assumption implicit in this analytical approach is that all of the cases are the outcome of a single exposure-disease process. It may be, however, that the BCNS cancers are associated with exposure to one chemical and the neuroblastomas are associated with another. Or it could be that the more recent cases differ from the earlier cases. If this is so, analyzing the different types of cases together would tend to obscure the subgroup effects. To explore these possibilities, the analysis described above would be repeated for each of these case subgroups separately, although the relative risk estimates would be even less precise since the sample sizes are even smaller.

There are other statistical methods for quantifying the relationship between exposure and disease in more detail. For example, it is important to consider the effect of possible confounding variables. A confounding variable is a factor that is related to both the exposure and the disease. Such a variable can distort the relative risk estimate unless the statistical analysis adjusts for it. While it is worthwhile to consider the influence of any possible confounding variables on the effect estimates in this study, the small sample size prevented any statistical adjustment for them.

#### E. Multiple Tests and Interpretation of Confidence Intervals

A 95 percent confidence interval will, over many repetitions of the experiment, contain the true (unknown) relative risk 95 percent of the time. This means that if many confidence intervals are computed, five percent of them can be expected to "miss" their target due to random variation. This is of particular concern for confidence intervals that do not include the value one. If, for example, the lower limit of the confidence interval is greater than one, it provides evidence that the

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<sup>4</sup> The appropriate confidence interval is computed using small sample (also known as exact) methods. Asymptotic, or large sample, methods are more familiar, but can provide misleading results when applied to samples of this size. For example, the asymptotic confidence interval for this example is [0.36, 11.2] which is too narrow (see Rothman and Greenland 1998). Exact confidence intervals can be computed using the MEANS procedure in SAS.

exposure causes the disease. However, the probabilistic construction of the confidence interval allows for the possibility that the real effect is much smaller than the estimate, or even nonexistent (i.e. odds ratio equals one). On the other hand, the true effect could be even larger than the upper limit of the confidence interval. Any confidence interval must be interpreted with these probabilistic fundamentals in mind.

This does not imply that valid interpretation of the confidence intervals is impossible. They provide a useful way of quantifying the range of odds-ratio values that is reasonably compatible with the data. Odds ratios further from the point estimate are less compatible with the data than ones close to the estimate. This means that if the lower limit of the confidence interval is far above one, the likelihood that there is no exposure effect is small. This would provide relatively strong evidence of an association between the exposure and the disease. Even if a confidence interval contains the value one, the data may suggest an association worth further investigation if the interval extends far above one.

### 3. *Results*

The results of the environmental testing are presented in Tables 1 through 6. **Tables 1 through 5** show the effects of Level 1 exposures and **Table 6** presents the results for Level 2 exposures to selected chemicals.

The test results for dust were not included in the statistical analysis because the dust was not collected in a controlled setting. The dust was collected from air conditioner filters, for example, but there was no way to determine how much air had passed through the filter leaving the dust behind. This made it impossible to interpret the chemical concentrations in the dust relative to the screening criteria. Direct measurements of the chemical concentration in air provide a more reliable indication of respiratory environment than dust.

**Table 1** lists the 372 chemicals for which none of the cases or controls had any detectable exposure. These chemicals were not present in the environment in detectable amounts at the time of the testing.

**Table 2** includes chemicals for which there were no exposed cases and at least one control with a Level 1 exposure. If there were a high number of exposed controls for a chemical on this table, it would indicate a protective effect of the exposure on the disease. However, each of the seven chemicals on the table had only one exposed control. This does not indicate any systematic pattern of exposure differences between the cases and controls. **Table 3** includes chemicals for which there were no exposed controls and at least one case with a Level 1 exposure. A high number of exposed cases for a chemical on this table indicates a numerical association between the exposure and the disease. Three of the chemicals had 10 or more exposed cases out of 22. These were 1,2,4-trichlorobenzene in air (15 cases exposed), hexachlorobutadiene in air (11 cases exposed), and methyl iodide in soil (10 cases) exposed. Several other chemicals exhibited 5 or more exposed cases. Many of these exposures were at very low levels, below the levels thought to present a health risk. Analysis of Level 2 exposures for the chemical on this table with at least four level 1 exposures is shown on **Table 6**.

**Table 4** contains the odds ratio and confidence interval computations for the chemicals with at least one case and one control in each exposure category for Level 1 exposures. One chemical, fluoride

in water (odds ratio 10.50), had an odds ratio greater than ten, indicating a strong positive statistical association with the disease. Several other chemicals had odds ratios greater than 3, including mercury in soil and the chlorination byproducts bromodichloromethane and chloroform. Further analysis showed that detectable amounts of these chlorination byproducts were found in every house supplied by municipal water, and in almost none of the houses supplied by private wells, regardless of case/control status. Thus the apparent association between these chemicals and cancer is due to the fact that a smaller proportion of the controls happened to use municipal water than is usual for study population. In epidemiologic terms, water source is a confounding variable. When the confounding effect of water source is taken into account, the apparent association between these chemicals and disease status disappears. The same is true for flouride. Analysis of Level 2 exposures to the chlorination byproducts (including total trihalomethanes) and flouride is shown on **Table 6**.

Four chemicals have odds ratios less than 0.2, indicating a strong protective statistical association with the disease. These are barium in water (odds ratio 0.07), 1,3,5-trimethylbenzene in air (odds ratio 0.15), acetone in air (odds ratio 0.15), and freon12 in air (odds ratio 0.19). All of the odds ratios on **Table 4** have confidence intervals that are relatively wide and most include the value one. The wide confidence intervals indicate the high degree of uncertainty in the reliability of the odds ratios due to the small number of cases and controls.

**Table 5** includes chemicals with any other exposure pattern. Most of the chemicals on this table exhibit ubiquitous or almost ubiquitous exposures among both cases and controls, with a small number of unexposed cases or controls. There was no apparent statistical association between any of these chemicals and disease, at least for this exposure categorization. It is possible that the exposure levels differed between cases and controls. Analysis of Level 2 exposures for the chemicals on this table with at least four Level 1 exposures is shown on **Table 6**.

**Table 6** shows the chemicals that were tested against the state screening criterion for Level 2 exposures. There are 64 chemicals listed on the table. Forty-nine, indicated in the top shaded portion, showed no Level 2 exposures for cases or controls. This means that all of the exposures for these chemicals were Level 1, or below the level thought to present a possible health risk. Five chemicals, p-dichlorobenzene in air, mercury in air, and fluoride in water, lead in water, and sodium in water, were found in two homes at Level 2. One or two exposed homes does not indicate any systematic pattern of exposure differences between the cases and controls. Ten chemicals, indicated in the lower shaded portion, showed Level 2 exposures in several case or control homes. This allowed the odds ratio and confidence interval to be computed for these chemicals. The highest odds ratio was for crotonaldehyde in air (OR = 1.40). Most of the odds ratios were very close to 1 indicating no evidence of elevated risk associated with exposure. Benzene and radon both had odds ratios of 0.15 or less, indicating a protective effect of Level 2 exposures. All the chemicals have confidence intervals that are relatively wide. The wide confidence intervals indicate the high degree of uncertainty in the reliability of the odds ratios due to the small number of cases and controls.

#### 4. *Discussion*

The purpose of this investigation was to narrow the list of possible environmental causes of the childhood cancers in St. Lucie County. Three-hundred seventy-two of the 517 chemicals tested were not detected in the environment at any of the homes tested (see **Table 1**). An additional 43

chemicals on **Tables 2-5** were detected in three or fewer homes. These 415 chemicals are probably not associated with an increased risk of BCNS cancer or neuroblastoma in the study population since they were detected in the environment so rarely.

The remaining 102 chemicals on **Tables 3, 4, and 5** were detected in four or more homes. These chemicals were compared to the state screening value where such a value exists. Chemical values that exceed the screening criteria were classified as level 2 exposures. A level 2 exposure does not necessarily correspond to a health risk since the screening values have a built in safety factor. However, Level 2 exposures are subject to further toxicological analysis to determine if a health risk exists. The 64 chemicals shown on **Table 6** were evaluated for Level 2 exposures. Forty-nine of the 64 had no level 2 exposures. An additional 5 had just one or two level 2 exposures. The remaining ten chemicals had more than two level 2 exposures. The odds ratio computations estimate the statistical association of level 2 exposure with the presence of cancer. The chemical with the highest odds ratio, crotonaldehyde in air (odds ratio = 1.40), is a possible carcinogen. This means that the only evidence of carcinogenicity is from animal studies. Two known carcinogens, benzene and radon, exhibited strong protective statistical effects of exposure (i.e. low odds ratios). This is not biologically plausible, however, it illustrates the imprecise nature of any risk estimates derived from this relatively small number of cases and controls.

The data in Tables 1-6 combines the neuroblastoma cases with the BCNS cases. Separate analysis of the two diagnosis categories showed basically the same relations between chemical exposures and disease status. The risk estimates are less precise when subgroups of the cases are analyzed because the number of cases is even smaller.

The confidence interval provides a statistical measure of the degree of uncertainty associated with each odds ratio. The confidence intervals are wide for the vast majority of chemicals, primarily because of the small sample size. This lack of precision in measurement does not mean that the estimates themselves are inherently biased or invalid. A careful review of the statistical results, along with an examination of any possible confounding factors, exposure misclassifications, or other biases, can provide useful guidance for public health investigators and members of the community interested in identifying plausible environmental causes.

On the other hand, even a precise estimate of elevated risk for a chemical would not prove that there is an environmentally meaningful effect. Several chemicals are expected to have odds ratios far above or below the value one by chance alone. An elevated odds ratio is a signal for further investigation. Only a comprehensive assessment of a chemical's carcinogenicity, possible environmental sources, and exposure of individuals can determine what intervention is appropriate, if any.

While **Table 6** does not indicate a cancer pattern associated with exposure to any of these chemicals, the Department of Health has evaluated every Level 2 exposure indicated on the table. This exposure assessment considers the toxicity of the chemical, the exact amount detected in the environment, and an analysis of the likely individual exposures to the environmental chemicals. The fact that a chemical is found in the environment does not necessarily mean that it poses a health risk if the levels are low or moderate and individual exposures are low. The results of these exposure assessments have been communicated to the individuals at the affected households.

## *References*

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