NEW YORK STATE DEPARTMENT OF HEALTH
Bureau of Environmental and Occupational Epidemiology

BIRTH OUTCOMES STUDY: 1978-1991
VILLAGE OF SHERBURNE, CHENANGO COUNTY

BACKGROUND

Sherwood Medical Company, Inc. formerly operated in the Village of Sherburne, Chenango County. The company used ethylene oxide (ETO) to sterilize medical care products from about 1977 until July 1990. ETO is a colorless gas with a sweet, ether-like odor at high concentrations. Products being sterilized were placed into a sealed chamber and ETO was introduced, alone or mixed with other gases. At the end of the sterilization period, the gases were vented to the outside. Between approximately 1977 and 1983, several small sterilizers operated in this manner. Control devices (scrubbers) to limit outdoor emission were put in place in 1983 on stacks 5 and 6 as required by the New York State Department of Environmental Conservation (DEC). During periods in 1987 and 1988, the scrubber on emission point 6 was not used. ETO was emitted without controls on about 200 days between July 1987 and May 1988. Two additional releases of ETO occurred when a control device malfunctioned in late May and early June of 1990. The Sherwood Medical Company stopped operating in the Village in July of 1990.

After processing, the sterilized products were placed in trailers to allow remaining gases to escape. The amount of ETO and other sterilants released to the outside air in this way is unknown but could have contributed to the ETO exposure of residents in the area immediately surrounding Sherwood Medical, Inc. With operating logs obtained from the company and meteorological data from the Syracuse National Weather Station for 1987, DEC modeled the spatial distribution of ETO impacts on the Village of Sherburne. DEC's short-term (one hour) ambient guideline concentration is 18 ug/m^3, while the long-term (annual) guideline is 0.019 micrograms per cubic meter (ug/m^3). During the time that the scrubber for emission point six was not in operation, it is estimated that residents of the Village of Sherburne were exposed to air levels at least 20 times greater than the annual guideline level. Residents in the area very near to Sherwood Medical, Inc. could have been exposed to approximately 10 ug/m^3, more than 500 times the annual guideline concentration.

Concerns have been raised regarding the effect of ETO on reproductive outcomes. ETO causes chromosomal mutations in many animal cell systems. There is also evidence of genetic damage in rats, mice, monkeys, and rabbits exposed to high levels of ETO[4]. Chromosome studies have also been done on workers exposed to ETO, with an increase in chromosomal abnormalities reported in some studies[5-7]. In addition, an increased rate of miscarriage in female hospital workers who were exposed to unmeasured amounts of ETO and other sterilizing gases has been reported[8]. Another study noted an association between paternal occupational exposure to ETO and spontaneous abortion[9].

Limited information exists on chronic health effects of ETO in humans. There is

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evidence in workers that prolonged exposure can cause neurological damage with numbness, weakness, impaired memory and coordination, and seizures[10-14]. Chronic ETO exposures have also been reported to result in cataract formation[15].

ETO causes cancer in rats and monkeys[16,17] and is characterized as a known human carcinogen. Although data on humans are limited, excess leukemia and stomach cancers have been reported in various studies of workers exposed to ETO[18-22]. Other studies have not detected an increased risk of cancer[23-26].

Although the ETO exposure to residents of the Village of Sherburne was not at levels expected to result in acute health effects, the lower limit of chronic exposure levels necessary to cause health effects have not been established. Also, the levels of exposure that affect reproductive outcomes are unknown.

Birth Outcomes Study

The New York State Department of Health (NYS DOH), Bureau of Environmental and Occupational Epidemiology, conducted a study to determine whether or not residents of the Village of Sherburne, an area impacted by ETO emissions from the Sherwood Medical Company, Inc, experienced increases in certain reproductive health outcomes. The health outcomes selected for study are conditions linked to ETO in animal and epidemiological studies for which sufficient data are available to permit statistical evaluation. These include low birthweight, preterm birth and small for gestational age.

Since congenital malformations and neonatal deaths are rare, there were not sufficient data for the relatively small population in the Village of Sherburne to make comparisons possible. In addition, although it has been suggested that exposure to ETO increases the risk of spontaneous abortion, spontaneous abortions are not reported consistently and reliable data are not available for analysis.

METHODS

All births in the state are recorded by NYS Vital Records on birth certificates and include birthweight and gestational age. Data on births for the Village of Sherburne and for Chenango County as a whole and five counties contiguous to Chenango County (Broome, Cortland, Madison, Otsego and Delaware) for the years 1977-1991 were obtained from Vital Records. All cities and towns in New York State, exclusive of New York City, have been assigned to one of five population density categories based on number of residents per square mile. The Village of Sherburne falls into Group 1 (most rural). For the analysis of reproductive outcomes, the reference area was defined as the cities and towns in population density group 1 within the six counties specified. Only data for areas of the six counties having population density similar to the Village of Sherburne were used in this study. The use of areas with similar population density was intended to assure comparability of various socioeconomic and environmental factors. Special attention was paid to the time during which ETO was known to have been released at relatively high levels (1987-1988).

A birthweight of less than 2500 grams was defined as a low birthweight and a gestational

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age of less than 37 completed weeks was considered a preterm birth. Size for gestational age is a common way of assessing both birthweight and gestational age that takes into account the relationship between these two factors. A delivery is considered to be small for gestational age if birthweight is below the tenth percentile of the population birthweight distribution for the week of gestation. For this study, births were classified as small for gestational age based on the birthweight distribution (by week of gestation and sex) for the reference area. However, since the number of births in the reference area was relatively small for certain weeks, a categorization was also made based on the birthweight distribution of births to residents of the United States in 1988.[27]

Data Analysis:

Statistical tests were used to evaluate the incidence of low birthweight, pre-term delivery, and birthweight for gestational age among residents of the Village of Sherburne compared to those for areas of Chenango County and five nearby counties with similar population density. The distribution of potential confounding factors including mother's age, obstetrical history, education, and smoking history were examined to determine need for statistical adjustment.

Results

For the years 1978 to 1991, 873 births were reported to women residing in the Town of Sherburne. Address data were used to identify births to residents within the Village of Sherburne. (Since address information was not available for 1977, births occurring in 1977 were not included in the study.) Of the 873 births, 303 were determined to be births to residents of the Village of Sherburne. Exact address location could not be verified for 378 records: 186 were rural routes and probably not within the village, 44 were missing address information, 87 were post office boxes, and 61 could not be placed for other reasons, e.g., missing street number, unknown street.

A total of 92,953 births was reported for residents of Broome, Chenango, Cortland, Madison, Otsego and Delaware Counties for the years 1978 to 1991. Of these, 47,571 births occurred to residents of the reference area (cities and towns in these counties with population density similar to the Village of Sherburne).

Birthweight and gestational age are known to differ by ethnic background and for multiple births. Due to the small number of Sherburne births for which mother's race was reported to be nonwhite (n=1) or for which there was a multiple birth (n=4), stratification by these factors was not reasonable. Therefore, multiple births and births for which mother's race was nonwhite were not included in the analysis. For the reference area, this resulted in the exclusion of 413 and 1126 births, respectively.

In addition, births with a gestational age of less than 28 weeks and births with a birthweight of less than 500 grams have been inconsistently reported in the past (or may represent errors). For these reasons, births with values below these limits were excluded. This resulted in eight Sherburne births and 1,605 births in the reference area being excluded. A total of 291 Sherburne births and 44,427 births in the reference area were included in the analysis.

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Birthweight and length of gestation as recorded on the birth certificate were compared for Sherburne and the reference area and were found to be very similar. Mother's age and obstetrical history were also observed to be comparable for the two groups (Table 1). In addition, education beyond high school was reported for nearly equal proportions of mothers from the Village of Sherburne and the reference area, 36.5% and 36.6%, respectively. Information on mother's history of smoking during pregnancy was not obtained prior to 1988 and was available for only 28% of births for both Sherburne and the reference area. When data were provided, smoking during pregnancy was reported for 8.6% and 7.5% of births for Sherburne and the reference area, respectively.

The frequencies of low birthweight, preterm and small for gestational age births are shown in Table 2. The proportion of each outcome among births for Sherburne and births for the reference area was very similar and is reflected in odds ratios very near to one. Births during the years 1987 and 1988 were also examined separately. None of the Sherburne births were low birthweight, one was preterm and one was small for gestational age. Based on both the distribution for the reference area and the U.S. distribution, the frequency of each of these outcomes was somewhat less than expected as compared with the reference area, although none of the differences was statistically significant.

Discussion

The frequency of low birthweight, preterm or small for gestational age births was not increased for residents of the Village of Sherburne for the years 1978 to 1991 when compared to the frequencies of these outcomes among births to residents of the reference area (cities and towns in Broome, Chenango, Cortland, Madison, Otsego and Delaware Counties with population density similar to that of the Village of Sherburne). Mother's age, smoking history, number of previous births and number of prenatal visits have been shown to be related to birthweight and gestational age. Mother's education was used as a measure of socioeconomic status which is also related to birth outcome. These factors were examined and were found to be very similar for the Sherburne births and the reference area births. In addition, we looked at data for 1987 and 1988 separately since ETO was known to have been released at relatively high levels during that period. No increases were observed in low birthweight, preterm or small for gestational age births to residents of the Village of Sherburne as compared to the reference area.

In conclusion, a higher than expected number of low birthweight, preterm or small for gestational age births to residents of the Village of Sherburne was not observed to occur for the years 1978 to 1991. Releases of ETO during this period were not associated with an increase in the adverse birth outcomes examined.

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Table 1. Birthweight, gestational age and obstetrical history for births to residents of the Village of Sherburne as compared to residents of the reference area*, 1978 - 1991.

	Sherburne		Reference area	
	Mean	(Std. Dev.**)†	Mean	(Std. Dev.**)†
Birthweight (grams)	3422.1	(547.9)	3444.0	(543.7)
Length of gestation (days)	280.4	(16.5)	281.1	(16.7)
Mother's age	25.2	(5.0)	25.8	(5.3)
No. of previous births	1.3	(1.4)	1.4	(1.4)
No. of prenatal visits	11.5	(3.1)	11.3	(3.2)

* The reference area, as described in the Methods, contains cities and towns in Chenango County and five counties adjacent to Chenango County with population density similar to that of the Village of Sherburne.
** Standard Deviation.
† No significant differences were observed.

Table 2. Associations between birth outcomes and residence in the Village of Sherburne as compared to residence in the reference area*, 1978 - 1991.

	N	%	Odds ratio	(95% confidence interval)
Low birthweight (<2500 g)				
Sherburne	13	4.5	1.04	(0.60,1.82)
Reference area	1903	4.3	Ref.	
Preterm birth (< 37 weeks)				
Sherburne	22	7.6	1.07	(0.69, 1.66)
Reference area	3153	7.1	Ref.	
Small for gestational age based on Reference area distribution				
Sherburne	28	9.6	1.00	(0.68,1.48)
Reference area	4257	9.6	Ref.	
Small for gestational age based on U.S. distribution				
Sherburne	23	7.9	0.96	(0.62,1.47)
Reference area	3651	8.2	Ref.	

* The reference area, as described in the Methods, contains cities and towns in Chenango County and five counties adjacent to Chenango County with population density similar to that of the Village of Sherburne.

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CANCER INCIDENCE IN THE VILLAGE OF SHERBURNE, CHENANGO COUNTY, NEW YORK, 1981-1994

Prepared by the:

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Cancer Surveillance Program
Bureau of Chronic Disease Epidemiology and Surveillance

with the assistance of

New York State Cancer Registry Staff

and

Community Exposure Research Section
Bureau of Environmental and Occupational Epidemiology

For further information contact:
Aura L. Weinstein, M.P.H.
Director, Cancer Surveillance Program

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Background

In August 1994, the Division of Occupational Health and Environmental Epidemiology in the New York State Department of Health, Center for Environmental Health, requested an investigation of cancer incidence among residents of the Village of Sherburne in Chenango County between 1981 and the most recent year for which data were available. This study was requested as part of a health assessment of the area around Sherwood Medical Company, Inc. The company used ethylene oxide (ETO) in processes from about 1977 to 1990 and at various times during this period is known to have released significant quantities of this substance into the environment. As shown on the attached map, the residential area of the Village of Sherburne is concentrated along State Route 12, Main Street, which extends for approximately 1.5 miles through the Village. The Sherwood Medical facility is located on Main Street near the Village's northern boundary, and almost all residences in the Village are within one mile of the facility. Residents of the village, particularly those in the area very near to the company, could have been exposed to ETO in air. ETO causes cancer in rats and monkeys (1, 2) and has been characterized as a human carcinogen (3).

Methods

Study Plan: This investigation was designed to determine whether the number of cases of cancer arising among residents of the study area was unusual. In order to do this, the number of cases actually diagnosed among residents of the study area was compared with the number one would expect to find if cancer rates were the same as in rural areas of New York State, exclusive of New York City.

Study Area and Time Period: The study area was defined as the Village of Sherburne in Chenango County (see attached map). The time period for the investigation was selected as 1981 through 1994, the latest time period the New York State Cancer Registry was considered complete when the study began.

Identification of Observed Incident Cancers: We identified all cases of cancer diagnosed among residents of Sherburne Village between 1981 and 1994. The source for these data was the New York State Cancer Registry. The Cancer Registry contains information on all cases of cancer reported to the New York State Department of Health as mandated by law.

Variation in cancer incidence among different geographic areas reflects not only true differences in cancer incidence, but also the practices of diagnosing, treating, and recording cancers in various areas of the state. The completeness and accuracy of the Cancer Registry depend upon reporting from hospitals. It has been estimated that over 95% of all cancer cases are reported to the Registry (4).

The computerized Cancer Registry files are continuously updated to reflect multiple reports on the same cancer. At the same time, reports on metastatic cancers which have spread from a primary site are eliminated, while true multiple primary cancers are identified. Cancer incidence in this report represents cancer cases

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diagnosed from 1981 through 1994, with additional updates about these cases through July, 1998.

In order to identify all cancer cases within the study area, a listing of all cancer cases with ZIP Code 13460 and a diagnosis of cancer was obtained from the Cancer Registry. The address of each case was examined to determine whether it was located inside the Village limits. All cases with addresses in the Village were grouped by cancer site, sex and age. These are referred to as "observed" cases.

Calculation of Expected New Cases of Cancer: In order to determine whether the number of observed cases was unusual, we calculated the number of cancer cases that would be expected in an area with the same population size, and with the same age and sex composition as the study area. Since cancer patterns are different in urban and rural areas, we also took the degree of urbanization into consideration. We did this by using standard cancer rates based on urbanization to generate expected numbers of cancer cases. All of the ZIP Code areas of New York State, except New York City, have been assigned to one of four urbanization categories. These categories are based on information in the 1990 United States Census. The ZIP Code area containing the Village of Sherburne is in the rural category.

Using the 1980 and 1990 Census, we estimated that the total population of Sherburne Village in 1985 was 1,546 (704 males and 842 females). According to the 1990 census, the total population of the Village was 1,531 (694 males and 837 females). Cancer incidence rates by age and sex for rural areas of New York state were used to calculate the expected numbers of cases. The estimated 1985 population was used for the years 1981-1987. The 1990 population of the Village was used in calculating the expected number of cases for 1988-1994. Expected numbers of cases in the two time periods were then summed to obtain total numbers of cancer cases expected for the period 1981-1994. This procedure adjusts the calculation of expected numbers of cancer cases for a number of factors, including differences in sex and age among Village residents, degree of urbanization and changes in the standard cancer rates that have occurred over time.

Cancer Sites Studied: For this study, we examined total numbers of cancers among males and females, as well as sixteen of the most common types of cancer for males and eighteen of the most common types among females. These included cancers of the lung, colon, rectum, bladder and lymphoma and leukemia. We also included cancers of the breast and female reproductive organs for females and prostate cancer for males.

Statistical Testing: We used statistical testing based on the Poisson model to determine if chance alone could explain whether the observed number of cases was either more or less than expected (5). If the probability of observing an excess or deficit was 0.025 or less, the result was considered to be statistically significant and not likely due to chance. Differences that were not statistically significant were considered to represent random variation in observed patterns of disease.

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Results

In all, we identified 141 cancers among persons residing in the Village between 1981 and 1994. For all anatomic sites combined, 63 cases of cancer were observed among males when 54 were expected, and 78 cases among females when 66 were expected. These observed numbers are not statistically different from the numbers expected. The geographic locations of the residences of the persons diagnosed with cancer were not concentrated in any one area of the Village. To protect confidentiality, we do not provide information pertaining to individuals, including maps of case residences or exact numbers of cases when there are fewer than six in a given category. Table 1 summarizes these results. Because of small numbers, some related cancer sites are combined in Table 1, but statistical testing was done separately for each site.

When individual sites of cancer were examined, the expected number of cases of leukemia and oral cavity cancers in males were significantly different from expected. There were six cases of leukemia observed (2 expected) in males and fewer than six cases of oral cavity cancer (1 expected) in males. For other cancer sites in males, numbers of observed cases were no different from expected. For females, the observed numbers of cases for the individual cancer sites were no different from those expected.

Because multiple myeloma is a rare type of cancer associated with ETO in some studies, we also evaluated multiple myeloma incidence. (Because of its rarity, it is usually included as one type of cancer in a group labeled "other cancers" in cancer incidence studies.) Multiple myeloma was statistically significantly elevated among men or women combined (six observed, one [1.46] expected.)

Discussion

Statistically Significant Findings: We found statistically significant excesses in the number of males diagnosed with leukemia and oral cavity cancer. We found no statistically significant excesses for any individual cancer site among females. We found a statistically significant excess of multiple myeloma in males and females combined. The following presents additional information about these cancer elevations in the context of known and suggested risk factors for these types of cancer. This study's findings are also compared to findings from other studies of populations potentially exposed to ETO.

Leukemia is a family of cancers resulting from abnormal changes in early forms of blood cells arising from bone marrow. Leukemia can affect any type of blood cell but most often develops in either of the two main types of white blood cells – lymphoid (also called lymphocytic) cells or myeloid (collective term for non-lymphoid or non-lymphocytic) cells. When leukemia affects lymphoid cells, it is called lymphocytic leukemia. When non-lymphoid cells are affected, the disease is called myeloid or non-

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lymphocytic leukemia. In all types of leukemia, abnormal blood cells increase in number and suppress the growth of normal blood cells.

Leukemia may be either acute or chronic. In acute leukemia, the abnormal blood cells remain very immature and cannot carry out their normal functions. The numbers increase rapidly, and the disease gets worse quickly. In chronic leukemia, some abnormal blood cells are present, but in general, these cells are more mature and can carry out some of their normal functions. Since the numbers of abnormal cells also increase less rapidly than in acute leukemia, chronic leukemia gets worse gradually. Acute leukemias are diagnosed among all age groups, while chronic forms of leukemia are mainly found among the elderly (6).

Incidence of all types of leukemia is higher among males than females and among whites than blacks. Although certain types of leukemia occur in children, the incidence of most types of leukemia increases with age. In this study, all the males with leukemia were over the age of 20 at the time of diagnosis, and most of the men with leukemia were older than 65 years of age when they were diagnosed. The majority of leukemia diagnoses among men were chronic leukemias, and the chronic leukemias included both myeloid and lymphocytic types. The majority of leukemia diagnoses among men, whether acute or chronic, were myeloid, also called non-lymphocytic, leukemia. Over half of the men diagnosed with leukemia were diagnosed prior to 1988. The observed excess of male leukemia is consistent with the experience of Chenango County, which has an overall higher incidence rate of this cancer among males compared with New York State exclusive of New York City.

In other studies, excess risk of leukemia has been seen among persons exposed to ionizing radiation such as radiologists, x-ray technicians and nuclear industry workers; persons exposed to electrical and magnetic fields such as electricians, power line workers and those employed in electronics; persons exposed to benzene in shoe, leather, rubber and chemical manufacturing; ethylene oxide (ETO) production and sterilization workers; and farmers who may have contact with pesticides and other chemicals used in agriculture (7). None of the males diagnosed with leukemia in this investigation were reported to be employees of Sherwood Medical, although a small number were reported as employed in the pharmaceutical industry.

Cigarette smoking has also been linked to elevated risk for both chronic and acute leukemia, particularly myeloid leukemia. Smoking status, which was available for all of the men with leukemia, showed that almost all were current or former smokers. Almost all of the men with myeloid leukemia were current or former smokers.

A large occupational study suggested in 1993 that the association between ETO and cancer appears to be stronger for two types of cancer originating from lymphoid cells, lymphocytic leukemia and non-Hodgkin's lymphoma (8, 9). Lymphoid cancers also include multiple myeloma, a disease of the plasma cells in the blood, which produce antibodies. In an updated analysis of cancer incidence for this occupational cohort, the investigators expanded the grouping of lymphoid cancers to include multiple

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myeloma. While there was no overall excess of lymphoid or other cancers in this follow-up, there were positive trends associating cumulative exposure levels to lymphoid cancers for males in the cohort. (10)

In contrast to this occupational cohort study, where associations were seen for ETO and lymphoid cancers, in this Sherburne cancer incidence study, the observed excess of leukemia diagnoses included more non-lymphoid than lymphoid leukemias. Again, in contrast to the occupational study's findings, in the Sherburne study, non-Hodgkin's lymphoma was not elevated among men or women. However, for multiple myeloma, the observed number of cases was elevated among both men and women in Sherburne. While not statistically significantly elevated for males or females considered separately, the observed cases were statistically significantly elevated for both sexes considered together. (Lymphoma and multiple myeloma are not shown separately in the attached table because the numbers of observed and expected cases are all below six. They are included in the "other" category.)

Multiple myeloma is a cancer of the blood and blood-forming system that mainly affects older adults. Multiple myeloma is diagnosed more frequently among the African-American population than the white population in the U.S. In epidemiological studies, multiple myeloma has been associated with exposure to radiation and pesticides, or a history of farming, but findings have been inconsistent across studies, perhaps because of the rarity of this type of cancer (11). In this study of cancers among Sherburne residents, we did not have complete information about occupations for the people diagnosed with multiple myeloma, but farming was among the occupations reported. None of the individuals with multiple myeloma were reported to have worked at Sherwood Medical. The men and women diagnosed with multiple myeloma were all over age 70 at the date of diagnosis. Most of the six diagnoses of multiple myeloma occurred in 1988 and 1989.

Cancers of the oral cavity account for almost four percent of all malignancies in the general population. The most commonly involved sites include the tongue, floor of the mouth, lip, tonsil, oropharynx and hypopharynx. Salivary gland tumors are relatively rare. However, in Western countries, the majority of salivary gland tumors arise in the parotid gland. Among Americans, oral cancer is two to three times more common among males than females with a higher overall incidence among black males. Most cases are diagnosed in persons greater than 45 years of age (6).

In this study, the majority of the males diagnosed with oral cavity cancer were over the age of 75. The observed excess of oral cavity cancer in this study is not consistent with the experience of Chenango County which has a lower incidence rate of these cancers among males than New York State exclusive of New York City. In addition, an unusual proportion of the oral cavity cancers were cancers of the parotid gland.

For most types of oral cavity cancer, use of tobacco or alcohol, and especially their combined use, are strongly associated with risk. However, for salivary gland

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cancer, including parotid gland cancer, tobacco and alcohol use do not appear to play a strong role. Occupational exposures may play a role in some types of oral cavity cancers. Cancer of the lip is associated with outdoor occupations such as farming and fishing where there is high exposure to sunlight. Salivary gland cancer has been associated with exposure to ionizing radiation, such as X-rays, and employment in agriculture, rubber manufacturing and auto industry woodworking (15). In this study, some of the males diagnosed with cancer of the oral cavity were reported to have worked in the chemical industry, electronic equipment manufacturing, and lumber industry. Smoking status, which was available for all the men with oral cavity cancer, showed that one-third of the males diagnosed with cancer of the oral cavity were either current or former smokers.

Numbers of women with oral cavity cancer were somewhat greater than expected, but these differences were within the range of chance variation. The specific types of oral cavity cancer among females were different from those reported for males, and all the women with oral cavity cancer were reported to be present smokers.

Comparison with Other Studies of Cancer and Ethylene Oxide Exposures: In a study of cancer incidence and mortality among three groups of workers in Sweden with occupational exposure to ETO, researchers found significant excesses of leukemia and stomach cancer. Although numbers were small, a variety of types of leukemia were represented (12). In this Sherburne study, no excess of stomach cancer was seen. Studies have also suggested that ETO exposure may be associated with elevated risk for breast cancer (13,14). No elevation of breast cancer was observed in the current study. To our knowledge, other studies have not shown an association between ETO exposure and salivary or parotid gland cancer or other cancers of the oral cavity.

Geographic Location and Latency: Address information was available for all the men with leukemia except for one, for whom we had only a post office box as the address. Using addresses at diagnosis for the other five men, most lived within ½ mile of Sherwood Medical at the time of the diagnosis. A small number of men, diagnosed with chronic lymphocytic leukemia, resided at the time of diagnosis very near Sherwood Medical Company, Inc, within one-tenth of a mile. These men living closest to the facility were between the ages of 55 and 75 at diagnosis, and their cancers were diagnosed within a two-year period of each other.

Exposures that initiate or accelerate biological changes that may lead to cancer are estimated to possibly occur from 5 to 40 years prior to the diagnosis of cancer. For exposures to substances such as benzene or ethylene oxide, which cause cellular damage comparable to ionizing radiation, the length of time required from exposure to onset of leukemia may be shorter than the time period for development of solid tumors. Chronic leukemias, which are generally diagnosed among the elderly, are thought to have longer latency than acute leukemias (7). The chronic leukemias diagnosed among men living very close to Sherwood Medical were diagnosed more than five but fewer than ten years after ETO was first used at Sherwood Medical in 1977.

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The number of females diagnosed with leukemia was not different from the number expected. The diagnoses among women were chronic types of leukemia, and the women were over age 75 at diagnosis. (Address information for this small number of women was insufficient for evaluating distance from Sherwood Medical.)

All of the men and women diagnosed with multiple myeloma lived more than ½ mile from the Sherwood plant at the time of diagnosis. Almost all of the multiple myeloma diagnoses occurred more than ten years after the reported introduction of ETO at the Sherwood Medical facility.

Almost all of the people diagnosed with oral cavity cancer lived more than ½ mile from Sherwood Medical at diagnosis. A very small number of the people diagnosed with parotid gland cancer lived in very close proximity to the Sherwood Medical plant at the time of diagnosis, within two-tenths of a mile. The diagnoses of cancer of the oral cavity occurred between seven and 14 years after ETO began to be used at the Sherburne Medical facility.

Study Limitations: Several points need to be made about the methods. First, in making multiple statistical comparisons, it is possible for one or two results to appear statistically significant just due to chance fluctuations in the data.

Second, the ability of a statistical test to identify a true difference, if one exists, is called statistical power. The level of statistical power depends on the number of expected cases. At least 16 cases are required for the statistical test used in this study to have a 90% probability of detecting a cancer rate twice that expected. In this study, only the total number of expected cases in males and females and the expected number of breast cancer cases in females exceeded 16. Therefore, the statistical power of the test to detect a doubling of the cancer, if one existed, was less than 90% for comparisons of the other individual cancer sites.

Third, this study was not able to take into account people who may have moved into or out of the Village shortly before being diagnosed with cancer. The issue of migration may introduce a degree of uncertainty into the conclusions that may be drawn from this analysis.

General Cancer Information

Cancer may result from either genetic or environmental influences or an interaction of both genetics and environment. Examples of possible environmental influences include diet, smoking, other lifestyle factors, and occupation as well as natural and man-made cancer-causing substances in the air, food, or water. The development of cancer is believed to depend on a long-term process involving both the changing of a normal cell into a cancerous cell and the cancer cell then growing out of control. For most types of cancer in adults, diagnoses do not occur until 10 to 30 years after exposure to cancer-causing agents. An agent that promotes the uncontrolled growth of cancer cells may cause cancer symptoms to develop in a shorter time.

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Cancer, unfortunately, is a common disease. One in two men and one in three women will develop cancer during their lifetime (16). The number of people with cancer is increasing in most communities because people are living to older ages, at which cancer is more common, and because more people are surviving due to earlier diagnoses and better treatments.

More research is necessary before the causes of cancer are well understood. We do know that cigarette smoking is a major cause of cancer. Researchers believe that dietary factors, including consumption of high-fat foods and excessive alcohol, also increase the risk of cancer. In fact, it has been estimated that up to two-thirds of all cancer deaths may be due to tobacco use and diet (16). People can also reduce their risk of cancer by avoiding ionizing radiation such as unnecessary X-rays, occupational exposure to cancer-causing agents, and too much exposure to sunlight. Early diagnosis can lead to effective treatment and cure for many cancers. Screening for cancers of the breast, cervix, rectum, colon, and prostate can find problems before symptoms occur, when the chances for a cure are best. Many people could reduce their chance of developing or dying from cancer by adopting a healthier lifestyle and visiting their physician for a checkup that includes cancer screening.

Interpretation

Overall, this investigation showed total numbers of cancers diagnosed among both males and females to be similar to the numbers expected based on rates for similar areas of New York State. Numbers among both males and females were somewhat greater than expected, but these differences were within the range of chance variation. When individual cancer sites were examined, significant excesses of cancer of the oral cavity and leukemia among males, and multiple myeloma among males and females combined, were found, although numbers of cases of these three types of cancer were small.

Although numbers of oral cavity cancers among males were relatively small, an unusual proportion were cancers of the parotid gland. Occupational information showed that a small number of the men with oral cavity cancer had occupations that may have involved exposures associated with parotid gland cancer. Oral cavity cancers have not been associated with ETO exposure in human or animal studies.

Epidemiological studies of workers using ETO for sterilization and in chemical manufacturing have shown an association with leukemia mortality. None of the males diagnosed with leukemia in this investigation were reported to have worked at Sherwood Medical. A small number were reported to have worked in the pharmaceutical industry. Over half of the leukemia diagnoses were chronic leukemia. Early stage chronic leukemia often produces no symptoms and is commonly diagnosed during routine blood testing; therefore, higher incidence rates may reflect good access to health care.

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A small number of the men diagnosed with chronic lymphocytic leukemia diagnosed prior to 1987 lived at the time of diagnosis very near Sherwood Medical Company, where exposure to higher levels of ETO was more likely. Chronic lymphocytic leukemia is generally believed to take ten years or longer to develop while the men living near the plant were diagnosed between five and ten years after Sherwood Medical started using ETO. Epidemiological studies have shown a consistent association between cigarette smoking and both chronic and acute leukemia, particularly myeloid leukemia. Most of the male leukemia cases in this study were of the myeloid type and almost all of these were reported to be current or former smokers.

Conclusion

Some studies of ETO exposure in occupational settings show associations with leukemia, non-Hodgkin's lymphoma, and multiple myeloma mortality. In this community study, some of the men diagnosed with leukemia lived in very close proximity to the Sherwood Medical plant at the time of their diagnoses. However, the study showed no excess of lymphoma among men, and no excess of leukemia or lymphoma among women. The men living near the plant were diagnosed between five and ten years after Sherwood Medical started using ETO. Smoking and occupational exposures may have contributed to the leukemia, multiple myeloma and oral cavity cancer excesses. This type of cancer incidence study is able to assess whether there is an elevation of the occurrence of disease in a specific geographic area, but is not able to determine the cause if an excess is found.

Because of the finding of an excess of leukemia, multiple myeloma, and cancer of the oral cavity, the New York State Cancer Registry was checked for cases of these types of cancer diagnosed among residents of the Village of Sherburne for 1995-1999. The number of leukemia cases observed among Sherburne residents for the years 1995-1999 was greater than the number expected, but the difference was not statistically significant. This means the difference may be due to chance, particularly with such small numbers. The numbers of cases of multiple myeloma and cancer of the oral cavity observed were similar to the numbers expected. For all three types of cancer, the numbers expected and the numbers observed were smaller than six, so are not reported here to preserve confidentiality. The addresses at the time of diagnosis were mapped, and none of the people diagnosed with leukemia, multiple myeloma or cancer of the oral cavity in these more recent years lived within ½ mile of the facility at the time of diagnosis.

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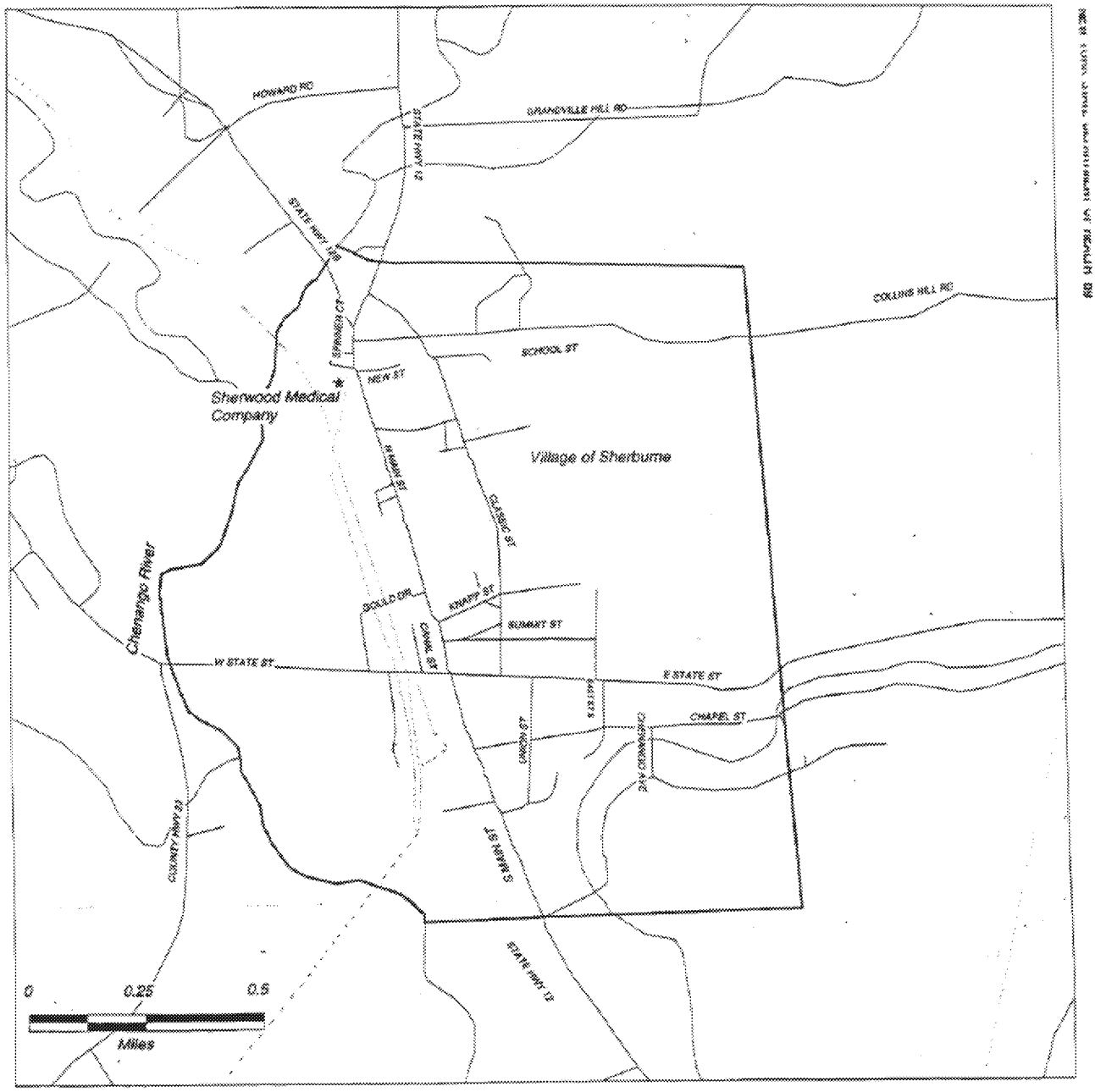
Table 1

BUREAU OF CHRONIC DISEASE EPIDEMIOLOGY AND SURVEILLANCE
NEW YORK STATE DEPARTMENT OF HEALTH

Observed and Expected Numbers of Incident Cancer Cases,
All Sites (140-208), Village of Sherburne,
Chenango County, New York, 1981-1994
Rural Standards 1985 and 1990

SITES (ICD-9)[a]	MALES		FEMALES	
	Observed[b]	Expected[c]	Observed[b]	Expected[c]
All Sites (140-208)	63	54	78	66
Oral Cavity (140-149)	--*[d]	1	--[d]	1
Colon (153)	8	5	12	9
Lung (162)	8	11	7	8
Female Breast (174)	--	--	18	17
Female Reproductive (Uterus, Cervix, Ovary) (179, 180, 182, 183)	--	--	9	8
Prostate (185)	10	13	--	--
Urinary Tract Bladder & Kidney (188,189)	7	6	--[d]	3
Leukemia (204-208)	6*	2	--[d]	2
Other[e]	24	17	32	18

[a]Classification of site is based on International Classification of Diseases, ninth revision.
[b]Data were obtained from the New York State Cancer Registry (database as of July,1998).
[c]Expected numbers are based on cancer incidence rates by age and sex for rural urban-rural areas of New York State, exclusive of New York City. Rates for 1983-1987 were applied to the estimated 1985 population to obtain expected numbers of cases for 1981-1987, and rates for 1988-1992 were applied to the 1990 U.S. Census population to obtain expected numbers of cases for 1988-1994 for Sherburne Village in Chenango County. Individual sites may not sum to total due to rounding.
[d]The number of cases is not shown to protect patient confidentiality. The number of observed cases is added to the "All other sites-observed" cell.
[e]Includes cases not shown above.
*Denotes statistically significant difference from expected at the $p<0.025$ level.

Village of Sherburne,
Chenango County, New York