HEALTH IMPLICATIONS OF ELEVATED NITRATE LEVELS IN DRINKING WATER IN CASS COUNTY, MICHIGAN

by

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ABSTRACT

HEALTH IMPLICATIONS OF NITRATE CONTAMINATED DRINKING WATER IN CASS COUNTY, MICHIGAN

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The effects of nitrate on human health have been widely studied, yet there is little consensus among scientists as to those effects. Methemoglobinanemia (Blue Baby Syndrome) is the outcome most strongly associated with nitrate contaminated drinking water and is the reason for the current federal standard of 10 mg/l. Several studies have found increased incidence of central nervous system (CNS) birth defects in babies born to mothers who were exposed to nitrate contaminated drinking water during pregnancy. Other studies have found a strong association between nitrate levels in drinking water and gastric cancer.

It has been demonstrated that there are high nitrate levels in wells throughout Cass County, Michigan and the residents have concerns regarding the frequency of certain outcomes. The purpose of this study is to assess the health status of the residents of Cass County and to determine if nitrate levels in drinking water are related to the distribution of outcomes.

A house to house survey was conducted. Participants answered questions about their health, eating habits, income

levels, educational background, among others. Drinking water was tested for current nitrate level.

The survey sample was stratified, clustered and random. The sample population was compared to the 1990 census to ascertain that it was representative. X^2 and Odds Ratios were used to estimate risk. This analysis shows that there may indeed be an association between nitrates consumed in drinking water and some of the outcomes reported by participants. The distribution of outcomes and high nitrate concentrations are not independent. However, there appears to be no increase in risk when consuming high levels of nitrate in drinking water and ill-health.

DEDICATION

To my mother, Denise McAnneny and "the aunts" Lucille Blanchette, Lorraine Morse, Adrienne McConnell, Mary Stapleton, Simone Morse, Macy Morse and Pauline Hall. My first and most important teachers.

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CHAPTER I

INTRODUCTION

More than 97% of all rural drinking water in the United States comes from underground sources. According to US census data, this includes more than 30 million people. In 1980, 40% of the US population (74 million people), using public water supplies took their drinking water from groundwater. In the United States, the demand on groundwater resources continues to grow, increasing 158% from 1950-1980 (Lee and Nielsen 1987).

Threats to the quality of groundwater come from many sources: domestic, industrial and agricultural. In 1987, there were 118,000 industrial lagoons or impoundments, 16,000 industrial landfill sites containing hazardous wastes, 18,500 active municipal landfills and 20 million septic systems (Wolfson and D'Itri 1987). In addition, each year US farmers apply 11.5 million tons of nitrogen fertilizers and 1.1 billion tons of animal manure (D'Itri and Wolfson 1987). Contaminants from these sources may find their way into nearby aquifers.

One third of the nation lies over aquifers capable of producing 100,000 gallons per day. The supply of usable water stored within the first 0.8 km of the surface is at least 20 times greater than the amount than the held in all the streams and rivers on the earth (Stafford 1987). If groundwater that is brackish, mineralized, alkaline, bad-tasting or otherwise unfit to drink is included, the total is even greater (Stafford 1987). Yet many parts of the country are facing serious shortages of groundwater while other places are losing their supply to contamination. According to "super-fund" reports, there were 1300 well closings in 1987, 23 of them from nitrate contamination (Stafford 1987).

An area of special concern regarding nitrate contamination is the grain producing region of the United States. Agricultural practices such as irrigation are implicated in the movement of nitrates into groundwater. Many of the same people who use nitrate fertilizers are also exposed to nitrates in their foods and drinking water.

The effects of nitrates on human health have been widely studied. However, there is little consensus among scientists as to these effects. Methemoglobinemia, or "Blue Baby Syndrome" is the disease most strongly associated with nitrate levels in groundwater, although not every baby exposed to high nitrate levels in formula develops this syndrome. Nor does every person who is exposed to nitrate develop cancer, nor every pregnant woman who is exposed have a baby with a central nervous system birth defect, or miscarry a pregnancy. The rate of negative outcomes when compared to the rate of these outcomes among a non-exposed population will help quantify the magnitude of the situation. This study will thus try to establish whether there is a relationship between nitrates in drinking water and adverse health outcomes in Cass County, Michigan.

REVIEW OF LITERATURE

Nitrates

In the conventional nitrogen cycle, NO_3^- is taken up by plants, incorporated into organic substances, and may be later transferred to animals and humans when they consume plants, vegetables or fruits. In an undisturbed system N is returned to the soil in animal excretion products or dead animal or plant material. This cycle is broken when humans remove nutrients from their natural environment (European Chemical Industry Ecology and Toxicology Centre, ECETOC 1988).

All soils contain some organic nitrogen; arable topsoil can contain up to 8,000 kg N/ha, while grassland soils may contain as much as 15,000 kg/ha (ECETOC 1987). Most of the nitrogen is bound up in organic matter (primarily humus). The rate of humus breakdown depends on the climate, degree of soil disturbance and exposure to air. Humus decomposes very slowly and as it does, organic nitrogen is mineralized to ammonia (NH_4^-), which is then nitrified to NO_3^- (Ellis and Olson 1988, ECETOC 1988).

Nitrate ions not taken up by plants or micro-organisms remain in the soil and may move with water. Downward movement predominates in vegetation-free periods; under plant cover water moves upward. Root uptake, evaporation of water and the temperature gradient between soil and atmosphere work together to move water and nitrate to the surface (ECETOC 1988).

Human activities have increased the amount of nitrate in the soil. In the United States use of nitrate fertilizers increased from 2.7 million tons in the 1960's to 11.4 million tons in the 1980's (Goodrich et al 1991, Anderson 1987, Lee and Nielsen 1987). Nitrate, which is the final form of N fertilizers in the soil, is very mobile and can move through the unsaturated zone (Ellis and Olson 1988). If not used by the crop or volatilized, it may eventually move into underlying groundwater (Goodrich et al 1991).

The extent of nitrate contamination of groundwater is illustrated by data collected by the United States Geologic Survey. The USGS National Water Data Storage and Retrieval System (WATSTORE) contains data on NO_3^- levels in water samples collected over 25 years from 87,000 wells throughout the United States. In one third of U.S. counties, 25% of the sampled wells contained NO_3^- levels in excess of 3 mg/l, a level assumed equivalent to background. In 5 percent of counties, 25 percent of sampled wells exceeded 10 mg/l NO_3^- (Fedkiw 1990 USDA Working Group on Water Quality). The Environmental Protection Agency has determined that 10 mg/l of nitrate in drinking water is the minimum level at which there is a risk to human health.

Nitrate contamination of groundwater by agriculture has been documented across the grain belt of the U.S. and Canada (Lee and Nielsen 1987). Nitrate concentrations in excess of 100 mg/l have been found. In drier climates intensive irrigation on sandy soils has also resulted in NO_3^- concentrations exceeding the federal standard for drinking water (Canter 1988). A study of Kansas farmsteads indicated that 29 percent of a statistically representative sample of wells had nitrate levels above the maximum contaminant level (MCL) of 10 mg/l for drinking water (Sophocleous et al 1990).

Conditions under which nitrate movement is facilitated are illustrated in the following studies. Endelman et al (1974) investigated the movement of nitrates in irrigated soils. They tracked the movement of NO_3^- in an irrigated Plainfield loamy sand cropped to potatoes. The experimental fields contained lysimeters. The entire area was irrigated every morning with sprayers that delivered 2.5 cm of water/hour. Nitrate concentrations in water collected in the lysimeters increased over time, with the most marked increase on day four. The maximum was reached eight days after the onset of irrigation. The authors concluded that 2.5 cm of water will move nitrates about 15 to 20 cm in this soil. Assuming a maximum root depth of 45 to 60 cm for crops such as potatoes, a 7.5 to 10 cm rain or irrigation event will move nitrates in the plow zone to depths well below the root zone.

Time or season of application of fertilizers may also be important determinants of the amount of NO_3^- leaching (Hergert 1986). Timing of fertilizer application was studied in Nebraska at the University of Nebraska Sandhills Agricultural Lab on Valentine fine sands. The predominant crop was corn with rooting depths of 90 to 120 cm. Corn, when grown on sandy soils must be irrigated for maximum yields. Irrigation on the experimental fields was at 85 and 130 percent of the evapotranspiration rate. Two hundred kilograms per hectare of N-fertilizer was dispersed through the sprinkler system in 6 equal applications, starting when the corn plants were 30 cm high and ending at the tasseling stage. Soil water that infiltrated below the root zone was collected by extractors in weekly or shorter intervals and analyzed for NO_3^-. Spring fertilizer application produced leachate with NO_3^- concentrations of 40 to 60 mg/l. However, the following spring, before application, after a full season of fertilization, leachates had NO_3^- levels of 100 mg/l. These levels fell off again in summer as plants took up some of the nitrate. Hergert et al (1986) concluded that nitrate leaching could be reduced if: 1. yield goals were consistent with the production capacity of the soil and climatic conditions; 2. pre-planting applications were reduced, and 3.irrigation was based on crop evapotranspiration rates and soil water status.

Artificial drainage of one type or another is used in many areas to make naturally flat areas drier and more suitable for crop production, and represents yet another means by which NO_3^- may be added to the soil water and thus groundwater. Drainage wells are often used and they, in some instances, inject water contaminated with NO_3^- directly into the aquifer below. Baker et al (1985) monitored such water for NO_3^- and showed that 85 percent of samples contained more than 10 mg/l NO_3^-. A survey of farm water supply wells in the vicinity of drainage wells indicated that NO_{3-} contaminated injection water increased NO_3^- levels in the local aquifer (Baker et al 1985).

Manure spreading is a common means of disposing of animal wastes and at the same time increasing the organic matter content of the soil. Gerhart (1986) monitored the appearance of NO_{3-} in groundwater after manuring and rainfall events. He found that nitrate levels increased sharply in spring when plant usage was low and rainfall was frequent.

Nitrates in Michigan Groundwater

There have been several studies on Michigan groundwater that indicate that nitrates are present. For example, a survey of drinking water wells in Grand Traverse County found that 11 percent had NO_3^- levels above 10 mg/l (D'Itri 1987). Application of nitrate fertilizers to fruit orchards in excess of the optimal plant growth requirements has been shown to cause these elevated levels (Ellis and Olson 1988).

In another study of the southern 8 townships of Van Buren County, it was found that 22 percent of wells exceeded drinking water standards for NO_3^-. Fertilizer applications coupled with irrigation were thought to be the primary reasons for this contamination (Ellis and Olson 1987).

D'Itri (1987) noted that there are elevated NO_3^- levels in drinking water in other areas of Michigan. He used Michigan Department of Public Health (MDPH) records of community water supplies and found that wells in 95% of the state, had NO_3^- levels of 2 mg/l or lower. However, the west central, southwestern and northwestern areas of the lower peninsula, showed moderately elevated NO_3^- (highest 6 mg/l) concentrations for the time period 1933-1974. However, for the time period 1974-1985, the highest levels had risen to 10 mg/l and 8% of the sample wells were at this level (Figure 1).

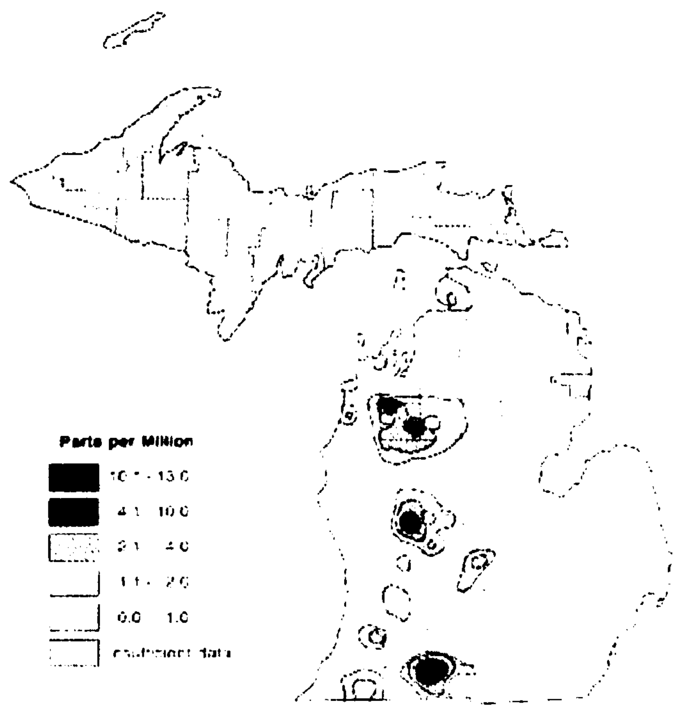

Figure 1 Nitrate Concentrations in Michigan Ground Water
Institute of Water Research, Michigan State University,
Kittleson and Kruska 1991, pp. 40)

Health Effects of Nitrates in Drinking Water

It has been suggested that nitrate exposure is a risk factor in at least three disturbances of human health:

1. Methemoglobinemia results in babies who have been exposed to infant formula made with water containing high nitrate levels (Page 1987, Craun et al 1985, Comly 1945).
2. Neural tube defects occur more frequently in babies whose mothers were exposed to high levels of nitrate in drinking water early in pregnancy (Arbuckle et al 1988, Dorsch et al 1984, Scragg et al 1982).
3. Gastric cancer in adults has been linked to the presence of nitrate in food and water (Packer et al 1989, Forman et al 1983). Prevalence of gastric cancer varies geographically, possibly indicating an environmental cause (Boeing and Frentzel-Beyme 1991, Stillwell et al 1991, Packer et al 1989, Abel et al 1987).

Infant Methemoglobinemia

The process by which nitrates in drinking water cause methemoglobinemia in infants also involves the conversion of nitrate ($NO3_3^-$) to nitrite (NO_3^-) (Page 1987, Shearer et al 1972). Nitrate-reducing bacteria are present in adults, but their numbers and presence in the lower intestinal tract do not usually cause health problems (Page 1987, Fraser and Chilvers 1981). In infants, whose principal food is milk the low acidity of the upper gastrointestinal tract allows nitrate-reducing bacteria to flourish. Infants also consume more fluid per unit body weight than do adults. High levels of nitrates in this fluid are converted to high levels of nitrite. It is thought that nitrite enters the blood stream, wher it is taken up by hemoglobin, making this molecule unavailable to bind oxygen. When methemoglobin reaches concentrations of 5 - 10%, symptoms of clinical cyanosis appear. Severe cases can lead to death by suffocation (Page 1987).

Methemoglobinemia was first recognized by Comly in 1945; he reported two cases of methemoglobinemia in newborns. He recognized that well water mixed with the babies' formula was contaminated with high levels of nitrate. He recommended that the infants' feeding regimens be changed to exclude formula that required large quantities of water. Once this formula was substituted the babies recovered.

The significance of Comly's (1945) study was that it recognized nitrate as the cause of methemoglobinemia in infants fed milk formulas reconstituted or diluted with contaminated well water. Comly solicited information from other physicians about similar cases. He found that other physicians had encountered some of the same problems among their patients. As part of the investigation water from 91 wells was analyzed, and 50 percent of the wells sampled were found to have nitrate levels above current EPA standard of 10 mg/l . Twenty percent had levels of 65 mg/l or more

(Lukens 1987). Since 1945, public health officials have included nitrate measures in their tests of water quality. Despite surveillance and physician education, methemoglobinemia remains a potentially lethal problem for rural infants. The most recent fatality involved an infant in South Dakota who died at 7 weeks of age from progressive cyanosis, that turned out to be unrecognized methemoglobinemia. The formula fed to the baby contained 150 mg/l nitrate or 15 times the national standard (Lukens 1987 Anderson 1986).

As recently as the summer of 1992, the Wisconsin Geologic and Natural History Survey reported a case of methemoglobinemia in a four week old baby (Hennings 1992). This child was drinking water from a well that had less than 50 mg/l nitrate when tested by the Wisconsin Department of Health. The episode was not fatal and continues to be investigated.

Comly's (1945) study described above is largely responsible for the current limit of 10 mg/l of nitrate set by the EPA. Several studies have disputed the need for such a limit. For example, a study in Washington County, Illinois, measured methemoglobin levels in children aged 1 - 8. This study showed that ingestion of water containing nitrate levels of 2 - 11 mg/l NO_{3-} was not related to high or above normal levels of Methemoglobin (Craun et al 1981). However, children 1 year or older are not the population of most concern. Comly (1945) demonstrated that newborns are the most susceptible to nitrate toxicity because of their metabolism, diet, and unique intestinal conditions (Lukens 1987, Shuval and Gruener 1972).

Another study (Shuval and Gruener 1972) has shown that when bottle fed infants ingest elevated levels of nitrate, they have elevated levels of methemoglobin in their blood . In this study a sample of 148 out of a population of 2,473 infants were formula reconstituted with water with nitrate concentrations ranging from 45 to 90 mg/l. The bottle fed infants showed elevated levels of methemoglobin in their blood. The authors argue that the levels were not high enough to be of concern.

Variations in blood levels of methemoglobin in infants have been attributed to factors other than the concentration of nitrate in drinking water. Shearer et al (1972) found that there were age variations in methemoglobin levels independent of nitrate levels in water. Babies younger than 60 days were likely to have higher methemoglobin levels than did older babies. These authors also found that sick babies had higher methemoglobin levels than well babies.

Central Nervous System Birth Defects

Concern with nitrates and CNS birth defects was first raised in Australia. A descriptive study by Scragg et al (1982), reported a localized excess of congenital malformations for the period 1968 - 76 in the Mount Gambier district of South Australia. The rate of perinatal death in this area from congenital malformations was 6.25/1000 compared to 2.79/1000 for the remainder of the southeast Australia (Scragg et al 1982). Neural tube defects were the malformations primarily responsible for the deaths.

The local area lacks surface water; therefore the community depends on rain or ground water for drinking. The local lake which fills from a lower aquifer is known to have at least 15 mg/l NO_3^-, which is much higher than rainwater or water consumed in other communities in Australia (Scragg et al 1982).

In the rural areas surrounding Mt. Gambier, families depend on bore holes for domestic water. This water comes largely from an upper aquifer which has been shown to deliver water with more than 45 mg/l NO_3^-.

A case control study was conducted using all 258 cases of malformations in the southeastern region of Australia, for the period 1951 - 1979. They were matched with normal controls, based on maternal age parity and date of birth. The relative risk for women who drank either water from Blue Lake or a borehole was 2.8 (95% CI 1.6 -5.1), compared to a relative risk for women who drank rainwater of 1.0. If this comparison was restricted to users of borehole water, with nitrate levels of 15 mg/l or higher, the relative risk rose to 4.1 (95% CI 1.7 - 10). The risk for women using low nitrate level borehole water was 1.4 (95% CI 0.6 - 3.4). The relationship held for all three calendar decades (Scragg et al 1982).

In the study by Scragg et al (1982), CNS birth defects were most strongly associated with groundwater use. There were 22 cases of anencephaly, 10 of spina bifida, and 10 of hydrocephaly. When the source of water is ignored, but nitrate level factored in, there is a doubling of the risk from water containing less than 5 mg/l to that containing 5 - 15 mg/l NO_3^-. The association of nitrate concentrations with CNS birth defects suggests a role for nitrates. Animal studies suggest that nitrites can pass through the placenta, and that methemoglobin levels may then be elevated in the fetus (Scragg et al 1982, Shuval and Greuner 1972). However, Scragg et al (1982) caution that there may be other factors, either environmental, social or in the water, for which they did not account.

A later study using the same population found a three fold greater risk for women who drank water containing 5 - 15 mg/l NO_3^- to have babies with CNS birth defects and a fourfold increase in risk in those consuming water with more than 15 mg/l NO_3^- (Dorsch et al 1984). Regression analysis found that there was also a seasonal component to this risk. Babies conceived in autumn were at three times higher risk than those conceived in winter. Babies conceived in spring and summer were at 7 and 6.3 times the risk as winter babies. Confounding factors such as gender, areas of residence, and water supply contributed significantly to the risk (Dorsch et al 1984).

Another study conducted in New Brunswick, Canada found a weak association between the likelihood of delivering a baby with a CNS birth defect and nitrate levels in drinking water (Arbuckle 1988). The relationship was strongest among well water users. Like the Australian studies, water was tested after the fact and it was assumed that nitrate levels post delivery and hence exposure were the same. Unlike the Australian study Arbuckle et al (1988) studied incidence of CNS birth defects, including both morbidity and mortality.

However a study that looked at the relationship between spontaneous abortion and quality of community drinking water found a negative association between nitrate concentration in water and miscarriage (Aschengrau et al 1989). The termination of pregnancy in the first trimester is a common occurrence, and is often related to the viability of the fetus. Yet the authors found no correlation between this outcome and nitrate levels in community water supplies. There was no attempt to assess the actual exposure of their subjects to nitrate, or any of the other substances they included in the analysis. The authors concluded that the reason their study disagreed with those of Scragg et al 1982, Dorsch et al 1984 and Arbuckle et al 1988, is that they were looking at a different outcome. However, the populations used in each of the other studies were largely rural, compared to the women of Aschengrau's study who were patients at the Boston Women's Hospital, Brigham Division and who, for the most part, lived in an urban environment.

Gastric Cancer

Incidence of gastric cancer (GC) varies 25-fold among different countries, suggesting that environmental factors are involved in its etiology. The GC rate is highest in Japan, being eight times the US rate. The rate is also elevated in Chile, Colombia, Germany, and Eastern Europe (Boeing and Fentzel-Beyme 1991, Stillwell et al 1991, Packer et al 1989 and Abel and Becker 1987). Within countries there is a small differnce the GC rate in urban vs rural populations, however the rate is highest among groups of low socio-economic status.

The mechanism by which nitrate acts as an etiologic agent is indirect. Bacteria in the mouth, stomach and sometimes in food act to reduce nitrate to nitrite. Nitrite is less stable and more reactive than NO_3^-. Nitrites react with appropriate substances to form N-nitroso compounds such as nitrosamine and nitrosoamide which are strongly carcinogenic in animals (Forman 1983). Nitrosamides are the most likely etiologic agents because they can be produced in the stomach from nitrites and amides. Amide nitrosation is catalyzed by acid, thus the stomach would be the preferred site for such a conversion. These compounds, unlike nitrosamine, are unstable, therefore they would have to act locally (Mirvish 1983).

In the U.S., nitrate intake is more important in influencing gastric nitrite concentration than is the intake of nitrite itself. Daily intake of nitrate is about 75 mg/day, 85 percent of which comes from vegetables (Mirvish 1983). In urban areas, only a small portion of ingested nitrate comes from drinking water, but in rural areas this can be a major source of nitrate, especially in areas where a domestic water well is the primary source of drinking water. Nitrate is of special concern when nitrate levels exceed the EPA standard of 10 mg/l NO_3^-. Farm supply wells in Illinois have had a median nitrate concentration of 145 mg/l NO_3^-, and well water in Nebraska may contain 50 - 100 mg/l NO_3^- (Mirvish 1983). More than 25% of wells tested in Missouri and Wisconsin had levels exceeding 3 mg/l NO_3^- (Mirvish 1983, Geleperin et al 1976).

A comparison of nitrate intake among 12 countries showed a significant correlation with gastric cancer incidence. This correlation is strong (0.8), even though the methods used and populations studied were different (Mirvish 1983). For example, the high nitrate intake in Japan is thought to be due to consumption of large quantities of vegetables containing high levels of nitrate. The U.S. has fewer cases of gastric cancer than expected on the basis of nitrate intake. This finding may be due to the high intake of fruits and in the U.S. (Mirvish 1983).

Evidence of regional variation of gastric cancer comes from many other sources. In Chile, Armijo and Coulson (1975) describe areas of high prevalence of GC in three central provinces where there is a long tradition of nitrate fertilizer use. Farmers have taken advantage of Chile's natural nitrate deposits and each year have applied 250,000 tons of nitrate to various crops such as corn, rice, beans, peas, wheat, potatoes, vineyards and more than 20 varieties fresh vegetables. The population here can be assumed to have high dietary intake regardless of diet, since any commodity carries a considerable concentration of nitrate (Correa et al 1970). Drinking water samples from these areas show that the groundwater is contaminated with nitrates. However, high gastric cancer mortality rates are associated with high incidence of defective housing, high infant mortality rates and low socio-economic status (Armijo and Coulson 1975).

In a follow up study Armijo et al (1981) tested the hypothesis that early exposure to nitrate is associated with increased incidence of gastric cancer. They recruited subjects from Santiago, who were attending gastroscopy clinics. Interviews took place before any diagnosis was made. Subsequently, cancer patients were matched to controls. Among cancer patients, the authors found longer term residence in the high risk area early in life, and an association between stomach cancer and prior occupation in agriculture, when compared to controls.

The strongest association between exposure to nitrates and gastric cancer is found in the population studied by Armijo. Studies from other countries with lower exposure rates have not produced similar results. Forman et al (1983) examined the incidence of gastric cancer in four regions in the United Kingdom. Two regions were characterized by low and two by high incidence of gastric cancer. The population in the high risk regions had approximately twice the mortality rate as the residents in the low risk areas. Subjects were recruited from hospital visitors. They completed a questionnaire and provided saliva samples which were analyzed for nitrate content. The low risk population had 50 percent more nitrate in their saliva than subjects from the high risk areas. This difference reflected the amount of nitrate in the diet and was not affected by confounding factors such as age, gender, social class, smoking or time of last meal.

The results of this study were confirmed by Knight et al (1990). Four provinces in Great Britain, two each of high and low mortality gastric cancer rates were compared. Again people visiting hospital for other than clinical reasons were recruited. The subjects donated saliva and responded to a dietary questionnaire. The subjects from the low risk regions had slightly higher levels of nitrate in their saliva.

Forman (1985) in another article, and others (Tannenbuam et al 1985, Mirvish 1985 and ECETOC 1988) suggested that the results of these two studies, high dietary nitrates, high salivary nitrates but low risk of mortality from gastric cancer may be due to the high consumption of vegetables. The source of nitrate may have been vegetables, which may, because of their vitamin C content, act in a protective fashion. Ascorbic acid (vitamin C) inhibits the formation of N-nitroso compounds. Questions regarding the usefulness of salivary levels of nitrate were raised by these authors. Nitrate is more readily converted to nitrite in patients with gastritis, hence the amount of nitrate in the saliva of these people may be reduced. If high risk populations have a higher incidence of gastritis, then their saliva nitrate levels will be lower than that of low risk populations (ECETOC 1988, Forman et al 1985, Mirvish 1983).

These results do not suggest a direct role for nitrate in the etiology of gastric cancer or that nitrate is rate limiting in the induction of neoplasms. Rather, they imply that saliva levels of nitrate may not be the best indicator of body burden or of the conversion rate to nitrites (Forman et al 1985, Mirvish 1983). Further, these results do not explain the geographic distribution of gastric cancer seen in the U.S. and elsewhere.

While Forman et al 1985 and Knight et al 1990 ignored the contribution of drinking water to the overall intake of nitrates, others have tried to link gastric cancer mortality rates to nitrate levels in drinking water. Beresford (1985) examined the relationship between nitrate levels in drinking water and gastric cancer mortality. Information on water quality for the period 1969 - 1973 was linked to mortality data for the same period. Two hundred and fifty three urban areas covering 90 percent of all British communities with populations of 50,000 or more were studied. Nitrate levels in drinking water were measured from several sources at the community level. Beresford (1985) found a significant negative correlation between gastric cancer mortality and the nitrate content of community water supplies, for both men and women.

The age adjusted, gender specific mortality rates from certain cancers of the digestive system for the same 238 urban areas were analyzed by type of water source (Carpenter and Beresford 1986). The percent of water supplied by upland rivers best described the pattern of cancer mortality in each site and gender. When adjusted for socioeconomic factors such as income and housing, the regression coefficient for the percentage of upland river supply remained statistically significant only for stomach and intestinal cancer in females (Carpenter and Beresford 1986).

Gilli et al (1984) correlated gastric cancer incidence rates for the period 1976 - 1979 in the 1,199 communes of the Piemonte Region of Italy with the nitrate content of the drinking water for the same period. They found a positive correlation between incidence of gastric cancer and communes having higher levels of nitrate in drinking water. Of the 155 communes with nitrate levels of 20 mg/l, 10 had elevated cancer rates. The remaining 1044 communes had nitrate levels below 20 mg/l and only 5 had elevated cancer rates.

Beresford (1985), Carpenter and Beresford (1986) and Gilli (1984) compared cancer mortality for the same period for which they measured nitrate levels in drinking water, having ignored the time required to develop gastric neoplasms. Agricultural practices have changed drastically over the last 20 years, and this could have affected the level of nitrates in the water source. Concentration of nitrate in drinking water could have been different at the time of critical exposure than at the time of the study (ECETOC 1988).

The relationship between nitrates in food and water and health outcomes has been intensively investigated and debated. Several studies have suggested a link between nitrates in drinking water and gastric cancer (Boeing and Fentzel-Beyme 1991, Knight et al 1990, Abel and Becker 1987, Carpenter et al 1986, Beresford 1985, 1981, Armijo et al 1981, Armijo and Coulson 1975). Others have disputed this link observing that investigators ignored the long time period between exposure and development of disease required by most cancers (ECETOC 1988, Mirvish 1983). Other authors have observed that there are differences in nitrate intake among ethnic groups, based on the proportion of their diet that comes from vegetables, fruit, meat or fish (Moller et al 1989a, 1989b, Packer et al 1989, Mirvish 1983). Some authors have implied that the source of nitrate as well as the amount taken in is important to gastric cancer mortality and prevalence rates (Dutt et al 1989, Packer et al 1989, Mirvish 1983).

Mirvish (1983) observed that in the U.S. intake of nitrates from food is fairly consistent at about 75 mg per day, which constitutes 85% of our intake. However, if this is true, the amount of nitrate taken in can be altered, as shown in Table 1 depending on the concentration in drinking water (Chilvers et al 1984). If nitrate in food is indeed relatively constant, then intake can be dramatically affected by concentration of nitrate in drinking water (ECETOC 1988). In the following Table the contribution of drinking water is calculated using the average daily nitrate (57 mg) intake in food in Europe.

TABLE 1
PROPORTION OF NITRATE INTAKE FROM FOOD AND WATER

Nitrate in Water mg/l	Daily Intake mg nitrate from water	Daily Intake mg nitrate from food	Derived from water %
10	14	57	20
50	71	57	55
75	107	57	65
100	143	57	71
150	214	57	79

(ECETOC 1988)

Attention has also been given to the relationship between the incidence of central nervous system birth defects or spontaneous abortion, and levels of nitrates in drinking water (Arbuckle et al 1989, Aschengrau et al 1989, Dorsch et al 1984, Scragg et al 1982). There is little agreement among the authors of these studies as to nitrates role in these outcomes. Comparison among studies is indeed difficult because authors use different methods to determine exposure to nitrate. For example, inferences have been made regarding exposure to nitrate from drinking water based on levels in community supplies (Knight et al 1990, 1987, Aschengrau et al 1989, Moller et al 1989a, 1989b, Carpenter et al 1986, Beresford 1985). Other studies have measured nitrate at the well or the tap to establish exposure (Arbuckle et al 1988, Chilvers et al 1984. Dorsch et al 1984, Scragg et al 1982). In some cases nitrate contributed by food has been ignored (Arbuckle et al 1988, Dorsch et al, 1984, Scragg et al 1982).

CHAPTER II

METHODOLOGY

The Problem

Cass County, the site of an on going study by the Institute of Water research at Michigan State University has been identified as one of the Michigan counties of concern with regard to nitrates in drinking water (Lusch and Ervin 1990, Kittleson and Kruska 1991). As work by the investigators from the Institute of Water Research has progressed, local citizens have raised the issue of health effects of nitrate contaminated drinking water (Ervin personal communication 1992). Anecdotal evidence from Cass County indicates that there exists an elevated prevalence of all types of neoplasms in the county (Ervin 1992, Wade personal communication 1992). Data from Michigan Department of Public Health, for the year 1989, indicate that mortality from gastric cancer in the state as a whole is low. Deaths from gastric cancer represent only 2.8% of cancer deaths in Michigan. However 4.2% of cancer deaths in Cass County are from digestive organ cancer (MDPH 1990). This rate is higher than the rate for the state as whole.

Simlarly, in Cass County, the 1989 rate of congenital malformations is 2.4 percent of live births in the county, which was slightly higher than the rate for the state as whole (2.1 percent; MDPH 1990). There has been some concern in the county that drinking water may be a source of problems for expectant mothers (Ervin 1992 personal communication).

The low numbers of gastric cancer and CNS birth defects along with the problem of establishing a time sequence for exposure and outcome make determining the relationship between nitrate intake and these outcomes difficult at best. There has been a long established relationship between nitrate contaminated drinking water and methemoglobinemia. The work by Comly in 1945 established the link. Yet this disease is still problematic today. The literature reports few cases, among the most recent, a fatality in South Dakota (ECETOC 1988, Lukens 1987). A recent report from Wisconsin (Hemmings 1992) indicated that an infant had been admitted and treated for methemoglobinemia summer of 1992. Further investigation by the Department of Health revealed that within the last year, there had been at least 3 other cases admitted to hospitals in Wisconsin (Knobeloch personal communication 1992).

Further difficulty in identifying methemoglobinemia cases arises because physicians do not expect to see this disease and are likely to diagnose the problem as something else, such as failure to thrive (Knobeloch 1992).

The problems remain:

--what are the health effects of nitrate-contaminated drinking water

--to what degree does using contaminated drinking water contribute to these outcomes

--how much nitrate is consumed in the form of drinking water at a given concentration.

A personal interview survey will be used to assess and compare the general health status of people using groundwater with different levels of nitrate in Cass County Michigan. This study will also estimate the amount of nitrate consumed from all sources and estimate the contribution of drinking water.

The proposed research hypothesis is that the general health status of well water users in Cass County, exposed to more than 3 mg/l nitrate (the Federal EPA considers this level equivalent to background) in their drinking water will be worse than those whose drinking water contains less than 3 mg/l nitrate. The null hypothesis is that nitrate has no effect on health status of the well water users of Cass County.

The model

The framework shown in Figure 2 will be used structure this study. In this model the primary focus is the interaction between the host and agent. The environment includes all of the people in Cass County and their activities as well as the physical geography of the county. Soils, uses of the soil, and the groundwater are all part of the physical and human structure. Nitrate, the agent, enters this system as a result of agricultural practices, specifically manure spreading, chemical fertilization and to a small degree faulty septic systems. Drinking water serves as the vehicle in this model. The source for most drinking water in Cass County is shallow aquifers. Thus, nitrate is transfered from the environment to the host, with groundwater providing the link. The host population is the users of groundwater for drinking water. In Cass County, this includes virtually the whole population. However, the population of most concern are those households that obtain water on site. These wells are not subject to testing and may contain high levels of nitrate.

The hosts are also subject to factors that can make them more or less susceptible to diseases. These factors are divided into two categories, extrinsic and intrinsic.

RESERVOIR - or source, agricultural inputs/faulty septic systems

AGENT
Nitrates

ENVIRONMENT
1. type of soils
   sandy, droughty
2. agricultural practices
   irrigation, manure spreading, fertilization
3. rural county
   on site water, no testing

VEHICLE
drinking water

HOST

EXTRINSIC FACTORS

1. occupation
2. socioeconomic status
   housing

INTRINSIC FACTORS

1. genetic
   sex, race
2. age
   physiology
   exposure potential
   exposure experience
3. physiologic state
   puberty
   pregnancy
   nutritional status
4. behavioral characteristics

DISEASE
(or not)

Figure 2 Environment, Host and Agent Complex

Extrinsic factors are those that are, to some degree, under the control of the host, such as occupation, socio-economic status, housing, etc. Intrinsic factors are those over which the host has no control; age, sex, and race for example. Try as we might to make this otherwise, age always increases. Sex and ethnic background are determined genetically and there is little that can be done to alter these factors.

The relationship between the host and agent is represented as linear, with the environment acting only on the agent. However, the agent and the host must be close spatially, and share some connection. In the case of Cass County, the reservoir for nitrates is agricultural activities often times performed by the hosts. So while the environment in one sense provides a source of nitrates, the reservoir is maintained as a result of the economic activities of the region. These activities happen to occur on soils and sediments that are especially permeable, and in an area where the aquifers are shallow and used as the local source of drinking water.

The purpose of this study is to investigate the health status of Cass County residents and to investigate the possiblity that nitrates play a role in the health or illness of people in this county. The model is used to provide a conceptual framework for the design of the study. It is especially important in development of the questionnaire, helping to categorize areas of concern so that confounding variables can be identified.

Study Area

Cass County is located in southwest Michigan (Figure 3), within one of the high nitrate regions identified by D'Itri and Wolfson (1987). The physiography of the county is the result of glaciation, specifically the Woodfordian substage of the Wisconsin glaciation (Bowman 1991). The landscape left behind upon retreat of the glacier consists of outwash plains, moraines and small glacial lakes. There are three major outwash plains, extending from the southwest to the northwest. The largest covers most of the southern townships from Porter to Ontwa and a narrow band from Ontwa to Marcellus. The second extends from the western part of Milton township through Volinia and the western part of Marcellus. The third plain covers the northwestern part of Pokagon to Silver Creek township. The soils in the county range from well-drained loamy sand on the outwash plains and moraines to muck soils on old glacial lake beds (Bowman 1991).

The total area of the county is 317,581 acres. In 1991, twenty percent of the land was forested, (Figure 4) less than 5 percent is urban, and 70 percent of the land is used for agriculture (Bowman 1991). About 95 % of agriculture

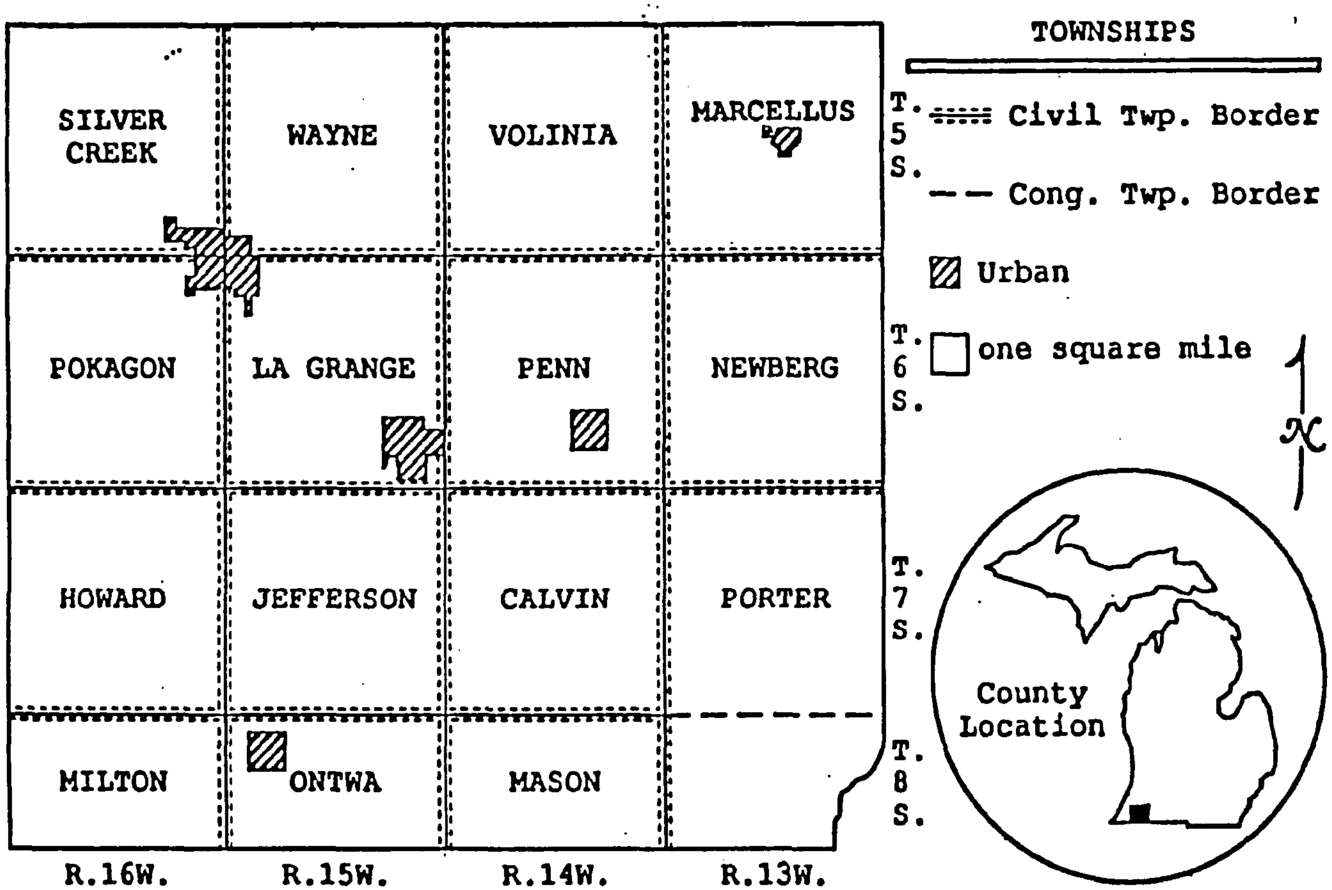

Figure 3 Cass County, Michigan 1988-1990
Plat Book Cass County Soil Conservation District, Cassopolis, MI

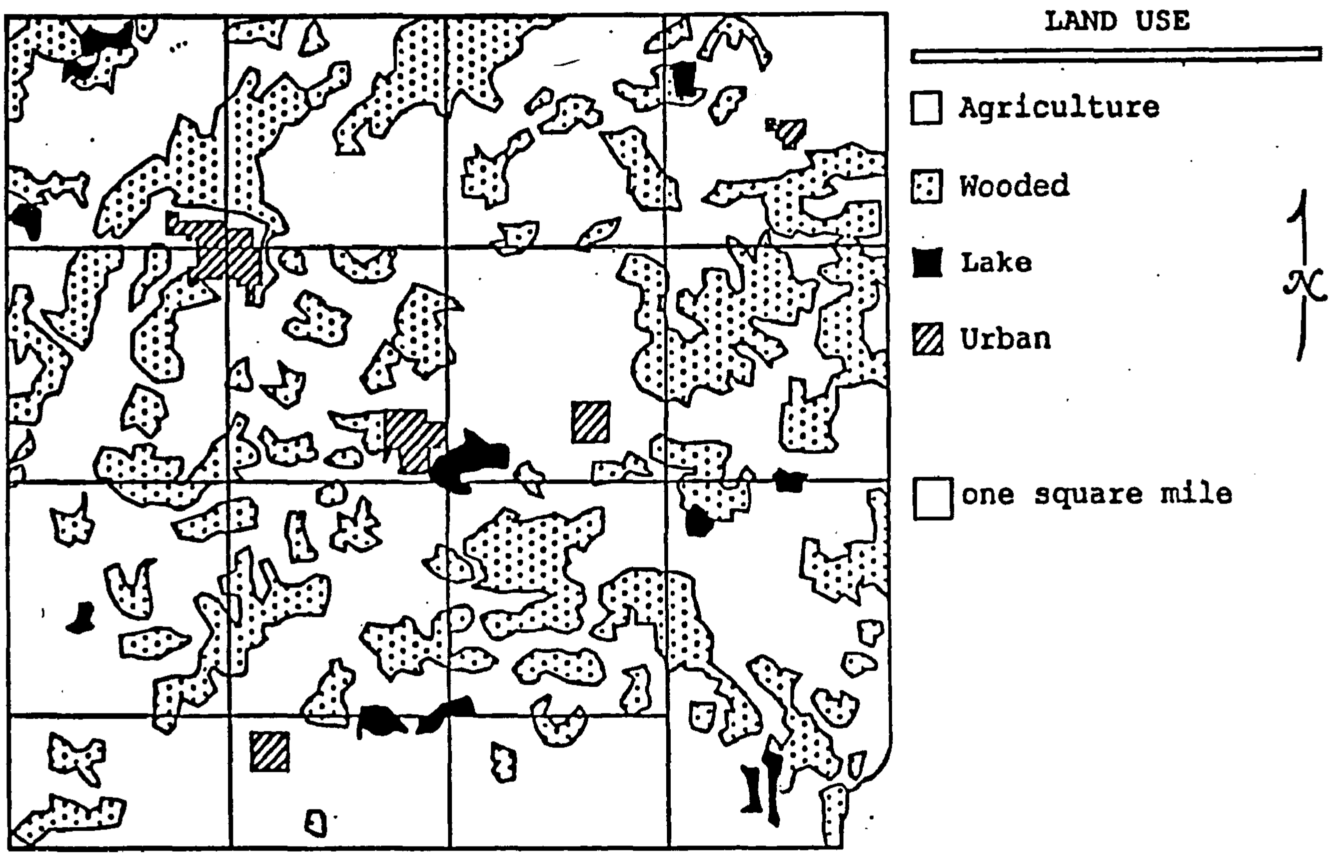

Figure 4 Land Use in Cass County Michigan

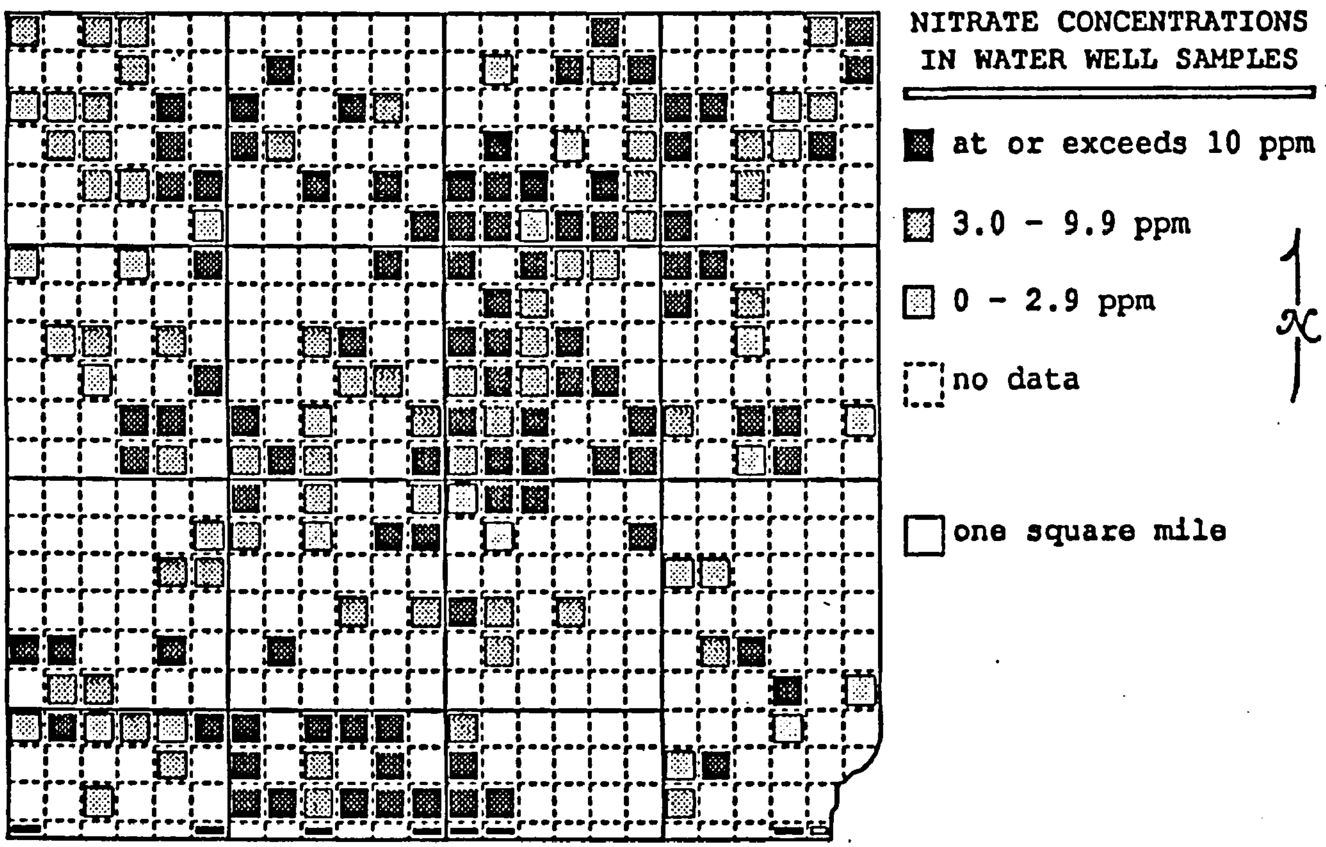

Figure 5 Average Nitrate Concentrations in Well Water in Cass County, Michigan

occurs over vulnerable aquifers (Bowman 1991, Kittleson and Kruska 1987) spreading of manure on the vulnerable sites may lead groundwater contamination (Bowman 1988, Kittleson 1987).

Cass County produces more hogs than any other county in Michigan (Agricultural Statistics 1991). To support the hog population, producers raise their own feed corn (Ervin 1992 personal communication), often on sandy soils that are well drained and somewhat droughty; therefore they must be fertilized and irrigated for maximum production (Hergert 1986). To enrich the soil and as a means of disposing of animal waste, some farmers spread manure, of which they have an ample supply, on the fields (Ervin 1992 personal communication). In other cases, large numbers of hogs are kept and finished in relatively small areas, thereby depositing large amounts of manure on the surface.

Cass County is the subject of an on-going study by the Institute of Water Research at MSU, the purpose of which is to study the movement of nitrate from the surface to groundwater. Concentrations of nitrate in 405 individual wells were abstracted from well logs and data collected by the MDPH, the Cooperative Extension Service, Michigan Farm Bureau, Migrant Health and MSU "Ag Expo". Of 517 sections (Figure 5) in the county, 187 (36%) were sampled (wells varied from 1-20 per section), of these, 99 sections or 53% have average nitrate levels at or above 10 mg/l. This figure represents 20% of total sections in the county (Institute of Water Research, MSU 1990)

Study Population

The study population includes all well users in Cass County. This group includes full-time farmers, rural residents, and lakeside cottage dwellers, and excludes the urban areas of Marcellus, Edwardsburg, Vandalia, Dowagiac and Cassopolis. Passero and Straw (1988) reported that there were 2,421 wells for which there are records in Cass County. According to the 1990 census, there were 22,266 households in Cass County, only 21.9% of these households used a public water supply (all of which have groundwater as their source) and 19.2% are served by public sewer facilities.

Sampling Procedure

To minimize selection bias, participants selected should be representative of the population from which the sample is taken (Stark et al 1990). Therefore, a stratified, clustered, random sample of 114 households was taken. The sample size was based on the following equation:

$n=[\ z(a)*\ (pi*(1-pi))/d^2]$ and $N=n/(1+n/TP)$

where: TP= total population, Pi = population proportion
d= acceptable maximum error in sample proportion (1%)
z=alpha (5%) (Kleinbaum et al 1982)

Prevalence rates of two of the major outcomes (gastric cancer, central nervous system birth defects) were used to

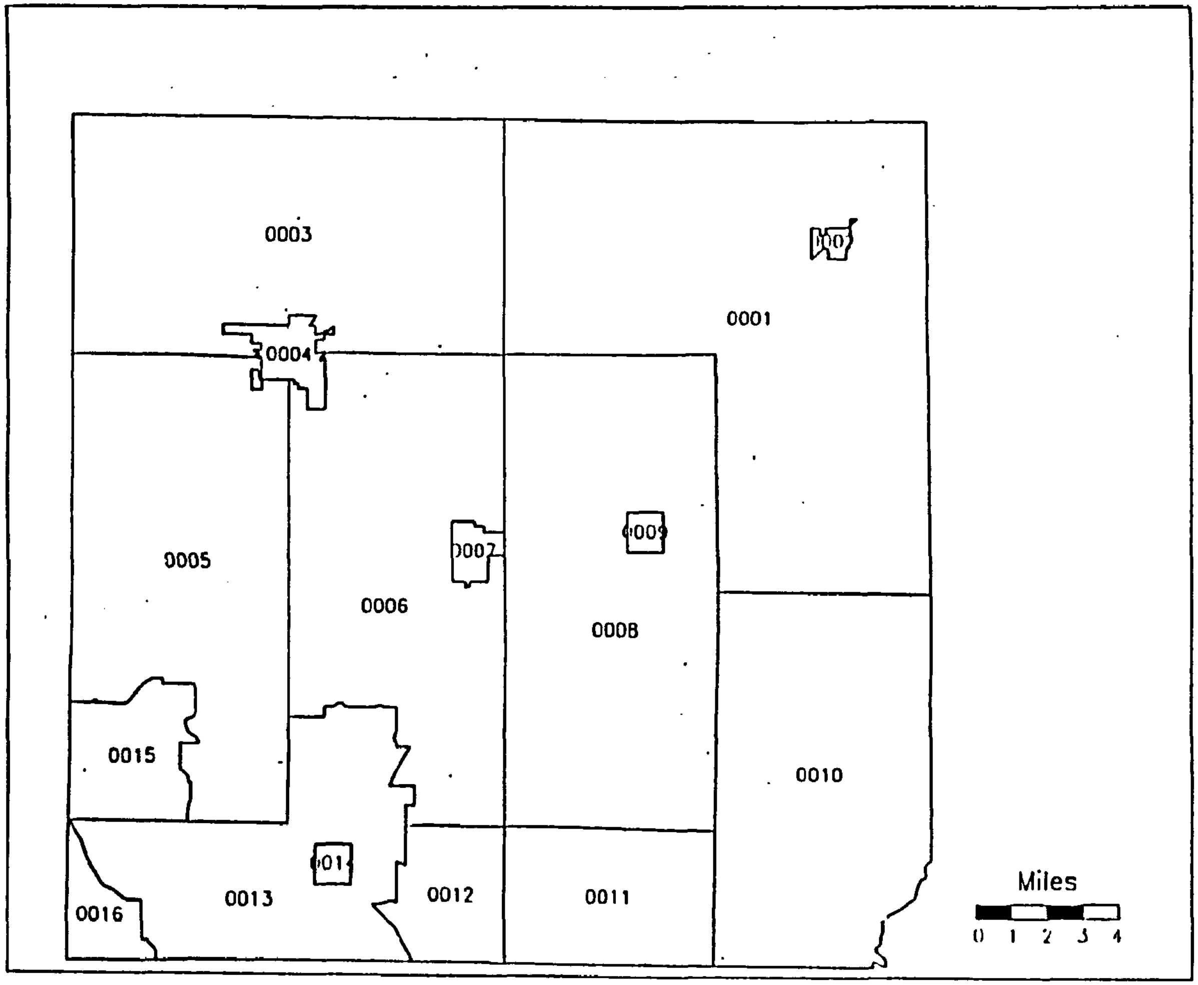

Figure 6 Census Tracts in Cass County, Michigan

calculate the number of subjects needed. The totals were then added together to come up with the total sample needed. Because these numbers seemed low (less than 50 households), the sample size was also estimated using the rule of thumb that 30 observations are needed for each independent variable for statistical significance. The sample size of 100 is a compromise between the two estimates. The compromise is based on time limitations and available resources.

Using Census Blocks established by the 1990 census as the unit of stratification (Figure 6), a proportionate number of interviews were taken in each block. For example, if block 1 has 1,700 households and 75 of them have wells, it has 9.7 percent of all households in the county; but has only 3 percent of households with wells. Thus 3 percent or 3 of all interviews conducted came from this block.

All households, with wells, in any given block will have an equal chance of being selected, and taking proportionate numbers from each block insures that the area with the most wells will be sampled most heavily (Gordis 1988).

Once the number of households to be interviewed in each census block was determined, households were chosen in the following manner:

Selection of Sections:

1. Using a map constructed by the MSU Institute of Water Research (Figure 5) sections were classified as

+ nitrate if the average nitrate value in the sampled wells exceeded 3 mg/liter or - nitrate if the average obtained for that section was less than 3 mg/liter. If there were no data available for a given section then that section was classified as "no data".

2. Within each census tract, every section clasified as + nitrate was available to be used. When possible, adjacent - nitrate or no data sections were used.
3. Sections were also stratified based on level of nitrate contamination. Those with highest average nitrate values and highest populations were given highest priority. Nitrate levels were considered over population, but every effort was made to sample proportionately to population.

Selection of households:

1. The most recent plat and topographic maps were used.
2. Each household on the plat map was numbered using the following procedure:

   Starting in the northeast corner of a section, and proceding south along the eastern border, west along the the southern border and north along the western border and continuing in the same manner towards the center of the section, each house was given a number in sequence starting with 1. The first structure in the northeast corner was designated as 1.

3. A random numbers table was used to select a set of random numbers equal to the number of households in the section.
4. Households were visited in the order of their numbered positions in the set of random numbers. For example if a section had a set of 5 households, and the random number order was 3, 2, 5, 1, 4, household 3 would have been visited first followed by household 2 and so on.
5. Visits were continued until the required number of interviews were obtained or at least 3 attempts had been made to acquire the necessary number within a section. If more than one visit to a section was required, a new set of random numbers was generated for each subsequent visit to the section. Households already interviewed were excluded.
6. Contact was made only at the time of the interview. Only 5 people in the contact area refused to be interviewed, a refusal rate of 4.4 percent. Of those households who refused, two were large hog farms, one was a woman who "just did not want to know about this stuff," and two others were women who were too busy. Four of the five refusals were on the eastern side of the county, but not in the same census tracts, and one was in the south western corner.

The Survey

Recruitment

Participants were selected in the manner described above. However, prior to starting the survey, local civic groups such as the Chamber of Commerce, Kiwanis, the Farm Bureau, Garden Clubs, and Lake Associations were contacted and, when possible visited. The Chamber of Commerce invited me to speak at one of their meetings. This led to favorable publicity in the local press and greatly aided the visibility of this study. In addition, at a conference on water pollution issues, I was introduced and my study described. This also helped make the project known in the community. Announcements about this project were placed in church bulletins and in some cases announced from the pulpit.

As a safety precaution, the Cass County Sherrif's Office was contacted; the Sherrif was provided with a copy of my credentials (letters from Drs. Hunter and Olson verifying my status as a student at MSU) a photograph and the licence and registration materials of my automobile. I checked in periodically to let them know when I was around and basically what my plans were. I felt that this protected me, and could be offered as reassurance to anyone I contacted that I wasn't a water treatment sales person.

Questionnaire

Please see Appendix II for the questionnaire. It was anticipated that the interview would take 20 to 30 minutes. Questions were asked of one member of participant households. However, often other family members were present and contributed to the interview. In many cases spouses were interviewed together.

The questionnaire was designed to cover the variables usually associated with increased morbidity. Age, gender, income, smoking habits, alcohol consumption, length of residence in Cass County, current occupation, past occupation and source of health care were asked of all interviewees. Questions regarding parity, prenatal care, and age of mother at conception were directed to households with children, and excluded in households that have been without children since 1987.

In order to estimate the current consumption of nitrate, a water sample was taken, and tested for nitrate. The water sample was taken from the tap in the kitchen. The water was allowed to run for 1 minute before the test strip was inserted into the stream. A kit developed by *AquaChek*(R) from Environmental Test Systems Inc. of Elkhart, Indiana was used. The colormetric test measures the amount of nitrate in a sample. This test kit was compared to the Michigan Department of Health water tests (Figure 7) and found to perform accurately.

Participants were asked to estimate how much water they drink in all forms at home, and at work. This includes water consumed as coffee, tea (hot and/or iced), fruit juices made from concentrate or powder, other soft drinks such as Kool-Aid(R), lemonade, etc.

Each household was asked to estimate how many times each week the family eats processed meats such as hot dogs, orbacon. Intake of vegetables such as spinach and other leafy types, and potatoes was estimated. The source of such vegetables, whether they are grown locally (by the household, or obtained from local farmers' markets) or bought at a local grocery store was also recorded. Fruit consumption was also estimated. The purpose of these questions is not to conduct an exhaustive food survey, but rather to determine if each household falls within U.S. national norms for consumption of such items. The assumption in the U.S. is that we consume about 75 mg nitrate in our food every day (Mirvish 1983). Standardized estimates of nitrate concentration in various foods were used to evaluate consumption from this source. This allows a better assessment of exposure to nitrate from water among the subjects of the study.

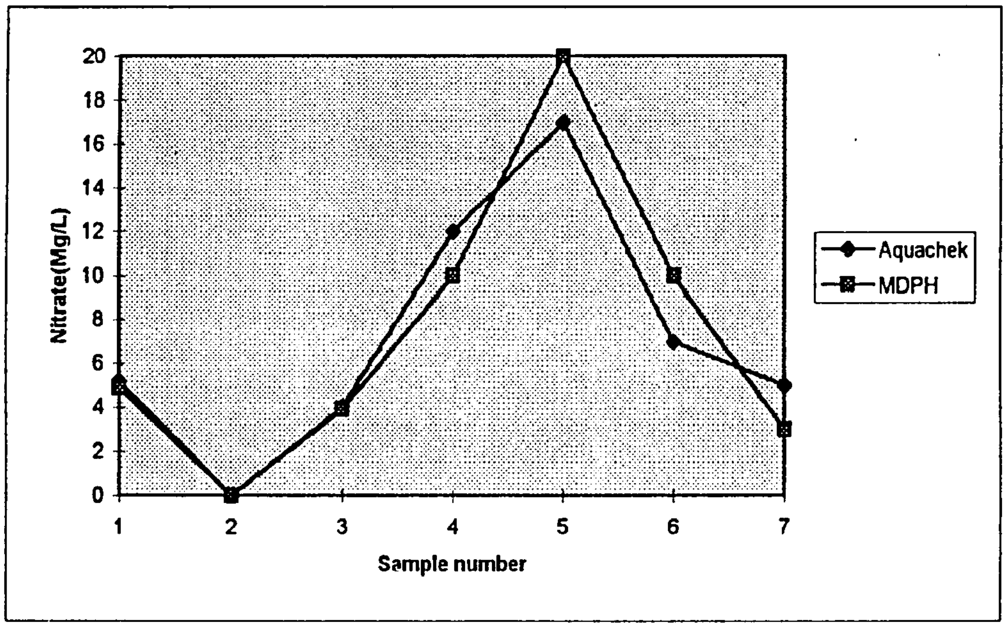

Figure 7 Comparison of Michigan Department of Public Health Nitrate Levels and Results from *AQUACHEK*

All participants were asked about their well, its age, depth and construction and whether the construction has been updated and when. The location and distance of the well relative to cultivated fields and animal pens was noted. Amounts and timing of fertilization and manure spreading was investigated. Activities from nearby farms was also investigated. Manuring, fertilization, types of crops, presence of animals was considered.

Recall bias is always a concern when using a survey (Moller et al 1989a, 1989b, Baker et al 1988). Participants may sometimes be motivated to tell the interviewer what they think she wishes to hear, or to exaggerate exposure to the substance in question if they think some form of compensation may be involved. Unfortunately, recall bias cannot be avoided completely. It was explained clearly to the interviewees that this is a research project from which there will be no financial gain to the investigator or the interviewees. Every effort was made to help the participants estimate accurately their intake of water and foods.

Preview and pretest

The survey instrument was previewed and pretested. Several people who had participated in a groundwater study conducted by Ervin et al (1991) from the MSU Water Reserach Institute were asked to examine the questionnaire and to suggest improvements. Each of the previewer's comments were considered and adjustments made to the questions.

The instrument was then pretested. The population used for this portion of the study were people who actively sought to be included. At each civic group, church and at the water contamination meeting, participants were solicited. They were asked to send their telephone numbers so that an appointment could be made. Thirty-five households were included in this portion of the study. This process afforded the opportunity to test and improve my interview technique.

Physician Interviews

To better characterize the health status of Cass County residents, all 23 local physicians were contacted by letter. The purpose of this study was explained, and an interview requested. Each letter included a self addressed stamped response card with the request that the card be returned indicating whether or not the physician would agree an interview. Of 23 physicians, four responded to the letters, one negatively and three agreed to be interviewed. The offices of each non-responding physician were then contacted by telephone. An interview was requested, usually a request fielded by a member of the office staff. The doctor would be consulted and a return call promised. There were no calls returned from these doctors. However, the physicians who did agree to be interviewed were generous with their time and information. The pathologist from the Barry County Hospital was interviewed by telephone. He also serves as the pathologist for the hospital in Dowagiac.

CHAPTER III

RESULTS:

Location and Distribution of Sampled Households:

In a survey such as this there is always a concern that those who participate are different in some way than the general population. As described in the Methods section above, great care was taken to sample the population of Cass County in a representative manner. A stratified, clustered, random sample was taken. A total of 114 households and 220 people were included in the sample. This represents about 0.6% of the households with domestic wells in Cass County. Figure 8 shows the location of sampled households. The sampling procedure provided fairly extensive coverage of Cass County.

Distribution of Household Nitrate Levels in Survey:

Each household in the survey sample provided water to be tested for nitrate levels. About one third of households in this sample had no detectable nitrate in their drinking water (Table 2). Twenty percent of the sample tested at the maximum contaminant level, 10 mg/l, or higher; 7 percent, tested at 15 to 25 mg/l nitrate, 1.5 to 2.5 times the MCL. Two households tested at 50 mg/l nitrate, 5 times MCL. The distribution of nitrate levels in the survey sample is shown in Figure 8. There are three categories of nitrate levels shown on this map. The *Aquachek*(R) Kit allowed determination of a zero level of nitrate. And it is important to distinguish between these households and those with even low levels of nitrate in drinking water. If a household is using water containing 3 mg/l of nitrate and family members are drinking approximately 2 liters of water each day, something that was commonly reported, then they are getting 6 mg of nitrate from drinking water, about 8 percent of overall consumption.

The average age and depth of the wells in the survey sample are shown in Table 3. It appears that as nitrate levels increase, age increases and depth decreases. The variation in each group is large and when a regression is run with NO_{3-} as the dependent variable, and age and depth as dependent variables, R^2 is low, 0.20.

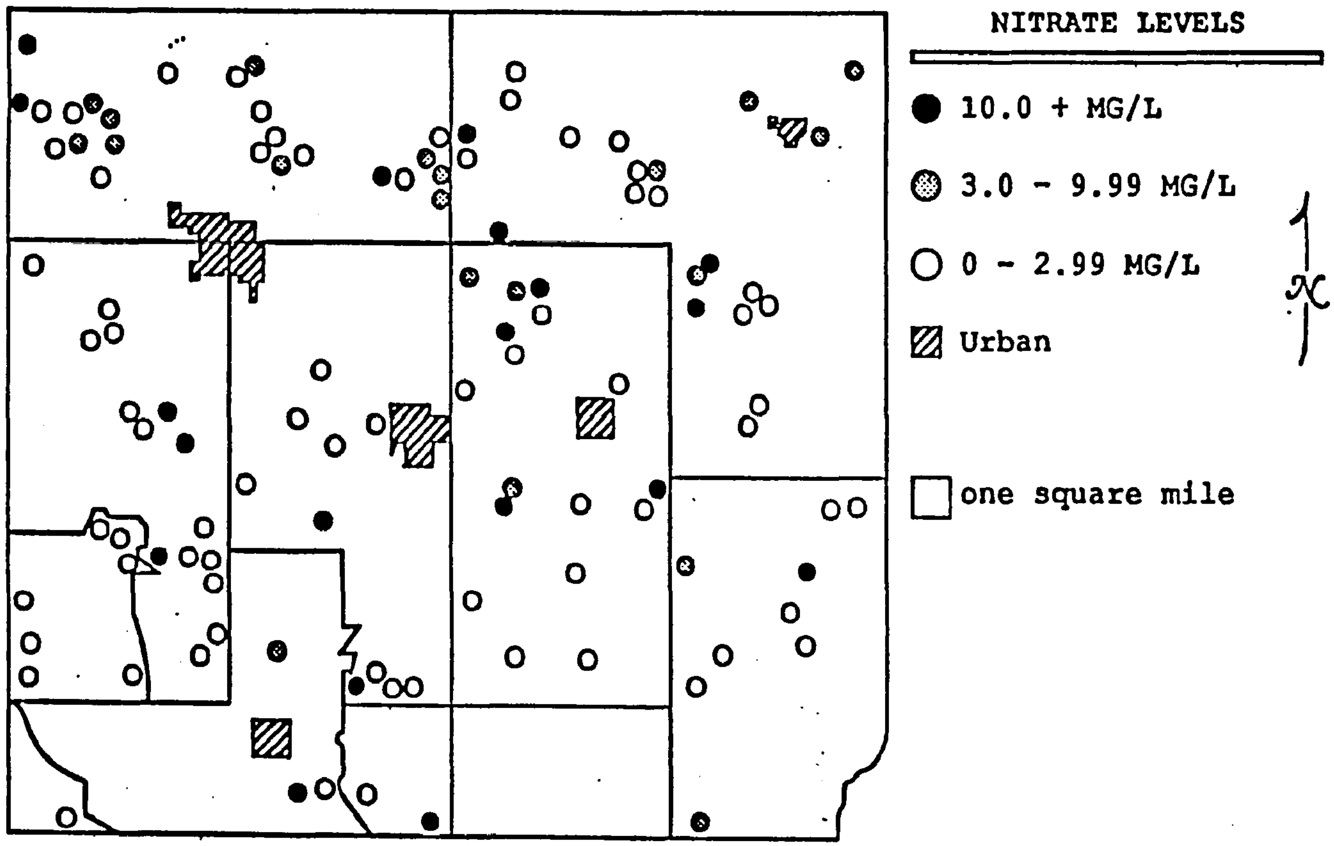

Figure 8 Nitrate levels in sampled households

TABLE 2
FREQUENCY OF NITRATE LEVEL AMONG SAMPLED HOUSEHOLDS

Nitrate (mg/l)	Number	% of Sample
0	37	32.4
1.0 - 2.9	36	31.6
3.0 - 6.9	16	14.0
7.0 9.9	3	2.6
10 +	22	19.3
n=114		

TABLE 3
AVERAGE AGE AND DEPTH OF WELLS BY NITRATE LEVEL IN SURVEY SAMPLE

Nitrate	Age (years)	Depth (Feet)
0	15.4	102.1
	± 12.5	± 82.7
	n = 30	n = 23
1.0 - 2.9	25.8	79.2
	± 19.9	± 41.6
	n = 32	n = 23
3.0 - 9.9	22.6	67.6
	± 19.9	± 48.9
	n = 16	n = 9
10.0 - 19.9	19.1	77.0
	± 16.5	± 32.6
	n = 14	n = 9
20 +	33.2	58.8
	± 29.9	± 25.9
	n = 8	n = 6
Overall	21.7	82.5
	± 18.9	± 55.2
	n =102	n = 84

± = Standard deviation.
$\bar{n}$ does not equal 114 because some subjects did not know either well age, depth or both.

The households were chosen randomly, with clustering based on average nitrate levels in sections determined by the Michigan State University Institute of Water Research, and stratified by population in census tracts (Figure 6). Samples were clustered spatially so that it would be possible to have cases and controls from roughly the same area, perhaps holding constant some unknown environmental exposure. There is a slight over-representation of households on Kalamazoo and Oshtemo soils (Table 4). Together they make up about 45 percent of all soils in Cass County and 63 percent of all households surveyed were on these soil types. Thirty five percent of all households that had nitrate levels above 0 were found on Kalamazoo soils, 22.7 of all households with nitrate levels greater than 10 mg/l were also found on Kalamazoo soils. Oshtemo soils make up 14.9 percent of area in Cass County, and 26.3 percent of the households surveyed are located on these soils. Close to 30% (29.7) of all nitrate contaminated wells are found in this group. Forty one percent of all wells with >10 mg/l of nitrates were found in this soil type.

TABLE 4

DISTRIBUTION OF SAMPLE HOUSEHOLDS AND SOIL TYPES

Soil	% Cass County	%Survey Households
Kalamazoo	29.5	36.8
Oshtemo	14.9	26.3
Spinks	9.2	13.2
Schoolcraft	2.2	2.6
Riddles	2.6	2.6
Spinks/Oshtemo	7.7	6.1
Barry	3.2	0.9
Cassopolis	2.5	1.8
Ormas	3.4	1.8
Bronson	5.9	1.8
Coloma	1.9	2.6
Brady	1.3	0.9
Tedrow	0.4	1.8

% of Cass County = % of total acreage

Comparison of Survey Sample to Cass County Census Data

Age and Sex

Age distribution in the sample is shown in Table 5. The age categories 20 - 24 and 25 - 29 are under represented. This may be due to differences in counting These age groups are counted in the census just as any other age group. However, people in the 20 - 24 age groups not living on their own were excluded from the sample unless they were present and participated in the interview. The older of the two groups, 25 - 29, are, if they are out on their own, perhaps more likely to be at work during the day and therefore unavailable for interview. There is also a slight over representation in the older age groups in the survey sample than in the census. However, the X^2 (29.06, P=.001) value indicates that these distributions are not independent.

The distribution of sexes in the sample as compared to the 1990 census is shown in Table 5 and 7. Females outnumber males in both the survey sample and in the population as represented by the census. The proportion of females in the survey sample is slightly larger than in the census. This may be due to the over representation of the older age groups in the sample (Table 6 and 7).

TABLE 5
AGE DISTRIBUTION IN SAMPLE COMPARED TO 1990 CENSUS

AGE	SURVEY NUMBER	%	CENSUS NUMBER	%
20 - 24	2	0.9	2912	8.4
25 - 29	14	6.4	3528	10.2
30 - 34	21	9.5	3936	11.4
35 - 39	27	12.3	3869	11.2
40 - 44	24	10.9	3597	10.4
45 - 49	22	10.0	3027	8.7
50 - 54	15	6.8	2478	7.1
55 - 59	24	10.9	2378	6.9
60 - 64	18	8.2	2433	6.5
65 - 69	21	9.5	2264	6.5
70 - 74	14	6.4	1641	4.7
75+	18	8.2	2572	7.4

$X^2 = 29.603$ $p = .001$ df 7

TABLE 6
SEX DISTRIBUTION IN SAMPLE COMPARED TO 1990 CENSUS

SEX	SURVEY NUMBER	%	CENSUS NUMBER	%
FEMALE	119	54.1	25,188	50.9
MALE	101	45.9	24,289	49.1

TABLE 7

DISTRIBUTION OF SUBJECTS BY AGE AND SEX IN SURVEY SAMPLE COMPARED TO 1990 CENSUS

	FEMALES						MALES					
	SURVEY			CENSUS			SURVEY			CENSUS		
Age	Number	% Cohort	% Sample	Number	% Cohort	% Sample	Number	% Cohort	% Sample	Number	% Cohort	% Sample
20 - 24	2	100	0.9	1435	49.3	4.1	0	0	0	1477	50.7	4.3
25 - 29	6	42.9	2.7	1856	52.6	5.4	8	57.1	3.6	1672	47.8	4.8
30 - 34	15	71.4	6.8	1955	49.6	5.6	13	28.7	2.7	1981	50.4	5.7
35 - 39	14	51.8	6.4	1979	48.2	5.7	13	48.1	5.9	1890	51.8	5.4
40 - 44	11	45.8	5.0	1827	50.7	5.2	13	54.2	5.9	1770	49.3	5.1
45 - 49	12	54.5	5.4	1545	51.0	4.5	10	45.4	4.5	1482	49.0	4.3
50 - 54	9	60.0	4.1	1216	49.1	3.5	6	40.0	2.7	1262	50.9	3.6
55 - 59	11	45.8	5.0	1229	51.7	3.3	13	54.2	5.9	1149	48.3	3.3
60 - 64	10	55.5	4.5	1235	50.7	3.6	8	44.4	3.6	1198	49.3	3.4
65 - 69	12	66.7	5.4	1195	52.7	3.4	9	42.8	4.1	1069	47.3	3.1
70 - 74	7	50.0	3.2	906	55.2	2.6	7	50.0	3.2	735	44.8	2.1
75 +	10	55.5	4.5	1577	61.3	4.5	8	44.4	3.6	995	39.7	2.9

% Sample based on total number of adults surveyed: 21 and older.
% Census sample based on the number of adults aged 20 and older.
% Cohort in both census and survey is based on the number of adults in population.

Educational Attainment

There appears to some difference between the survey population and the census with regard to educational achievement. The survey sample has a few more college graduates than the population at large (Table 8). There are fewer people in the survey population who have completed less than the ninth grade and slightly more people who completed at least some high school. There are 2 percent more high school graduates in the general population than in the survey sample. However, about 7 percent more people in the survey sample completed at least some college and 4 percent more survey participants completed a Bachelor's degree, while the proportion of professionals holding advanced degrees is about equal in both the census and survey samples.

TABLE 8

EDUCATIONAL ATTAINMENT IN SAMPLE COMPARED TO 1990 CENSUS

YEARS COMPLETED	SURVEY NUMBER	%	CENSUS NUMBER	%
Less than 9th grade	5	2.3	2745	8.6
Some high school	47	21.3	6082	19.1
High school Graduate	78	35.4	12082	37.9
Some college	55	25.0	5887	18.5
Associate degree	6	2.7	2102	6.6
Bachelor's degree	22	10.0	1852	5.8
Graduate or professional	7	3.2	1091	3.4

X^2 28.13 p = .000 df = 6

Survey universe all adults 21 years and older.
Census universe all adults 25 years and older.

Occupations

It appears from these data that the occupations represented in the survey sample are some what different than those represented in the census. Farmers, for example, are over represented, they make up 14.1% of the sample compared to 2.5% of the census (Table 9). This may be due to differences in classification; the census may consider only those who earn a certain percentage of their income as farmers while the survey allowed the participants to define their occupation. Some people may have identified themselves as farmers despite the fact that they worked off farm to earn additional income or some women who would have been identified as homemakers by the census classified themselves as farmers. Also, because this study targeted the non-urban population it stands to reason that there would be a higher proportion of farmers in the sample than in the general population. Interestingly, there are more members of protective services (police) in the survey sample than in the census, 2.3% compared to 0.6% in the census. This maybe due to the odd hours worked by police officers and sheriff's deputies; they are home during the day and thus available to be interviewed. If the refusal rate had been higher than 4%, it could be argued that because the sheriff and his staff may have been aware of my study they were more willing to participate than other members of the community.

Among the occupations under represented in the study group were the managerial, professional specialties, sales and non-household services. Again this may be due to difference in classification. It is more likely however, that these groups work during the usual business hours and are not at home available to be interviewed. The category of unemployed, students, homemakers and retired are represented at about the same rate in the survey population as in the census, 42.7% and 43% respectively (Table 9).

TABLE 9
OCCUPATIONS REPRESENTED IN SAMPLE COMPARED TO 1990 CENSUS

OCCUPATION	SURVEY Number	%	CENSUS Number	%
Executive, Managerial, Administrative	2	0.9	2106	6.0
Professional, Specialty	7	3.6	1896	5.5
Sales	8	3.6	2114	6.2
Administrative support	18	8.1	3098	9.1
Household	8	3.0	56	0.2
Protective Services	5	2.0	212	0.6
Non-household Services	3	2.6	2314	6.8
Machinists, operators, Inspectors	6	2.7	3309	9.7
Transportation	4	1.8	1482	4.4
Handlers	31	14.1	1253	3.7
Farmers	31	14.1	866	2.5
Unemployed, students, homemakers, retired	94	42.7	19265	43.0

calculated as percent of total in sample or total adults in census

Income

In general the survey participants seem to have lower incomes than the population represented in the census (Table 11). Yet the distribution of income in survey and census groups are not independent. With exception of two lowest categories, less than 10,000, 10,000 - 14,999 and the middle group 20,000 - 24,999, the proportion of survey participants in each of the remaining income groups is less than the census. For example, seventeen percent of the survey sample earned less than 10,000 dollars compared to 15 percent of the general population. The proportion earning 10,000 - 14,999 is about the same as the census while those earning 20,000 - 24,999 is 2 percent higher in the survey than the census. In every other category the proportion in the survey is less than those in the census.

Some of this difference may be explained by the option not to answer that question in the survey; 11.2 percent of survey participants chose not to reveal their income or did not know what their income was (Table 10). Other reasons for these differences might include the under representation in the survey population of professionals and higher level administrators or the over representation of farmers in the survey sample compared to the census.

TABLE 10
HOUSEHOLD INCOME IN SAMPLE COMPARED TO CENSUS

INCOME	SURVEY		CENSUS	
	Number	%	Number	%
Less than 10,000	20	17.2	2812	15.0
10,000 - 14,999	11	9.4	1694	9.0
15,000 - 19,999	7	6.0	1792	7.0
20,000 - 24,999	14	12.1	1856	10.1
25,000 - 34,999	17	14.6	3470	19.1
35,000 - 49,999	20	17.2	3478	19.1
More than 50,000	14	12.1	3099	17.0
Refused\Unsure	13	11.2	n/a	n/a

$X^2 = 4.49$, $p = .61$, $df = 6$
n= 116 household in survey and 17,000 households in census

However if the data are income are broken down on the basis of age, we can see that there are some discrepancies (Table 11). For example, participants between the ages of 30 and 44 make up 32 percent of the sample, yet, 6.8 percent of this age cohort earns more than 50,000 dollars and 8.7 percent earns at least 35,000 dollars. Conversely, the cohort older than 60 years also comprises 32 percent of this sample; yet only 2.1 percent of them earn at least 35,000. However, 7.7 percent of this group earns less than 10,000 dollars each year, and 8.4 percent of this population earns between 20,000 and 35,000 dollars.

TABLE 11
HOUSEHOLD INCOME BY AGE

Income* Age	<10	10-19.9	20-34.9	35-50	>50	Refused
20-24	0	0	.4	0	.4	0
25-29	1.4	0	1.4	2.3	1.4	0
30-34	1.8	0.4	1.8	1.4	2.3	0.9
35-39	0	0.9	4.1	3.2	2.7	0
40-44	0.9	0.9	3.2	3.2	2.7	0
45-49	1.4	0	2.3	2.3	1.8	2.3
50-54	0.4	1.3	1.8	0.9	0.9	1.4
55-59	0	1.8	3.2	0.4	0.9	1.8
60-64	2.3	2.2	0.4	1.3	0	1.8
65-69	1.4	2.2	3.2	0	0	0.9
70-74	0.4	1.3	1.8	0.9	0	0.4
75+	3.6	2.7	0.9	0	0	0.9

*Income * 1000. Percent of sample in each age cohort who earn a given income.

Term of Residence

As shown in Table 12 most survey participants have lived in Cass County for more than 5 years. Ninety-five percent of the sample lived in the county for at least 5 years, while 83% of the sample resided in the county for 10 or more years. At least 50 percent of the sample has lived in Cass County for more than 35 years. This could be a function of the population targeted; perhaps farmers are less likely to leave their home county, or perhaps rural people in general are more likely to remain in or close to their family home. The mean residence time in Cass County for the sampled population is 34 years with a standard deviation of 21.8 years, with a range of 0.25 - 89 years.

TABLE 12
RESIDENCE IN CASS COUNTY

Length of residence	number	%
Less than 1 year	7	3.2
1.0 - 4.9	4	1.8
5.0 - 9.9	26	11.8
10.0 - 14.9	14	6.4
15.0 - 19.9	11	5.0
20.0 - 24.9	14	6.4
25.0 - 29.9	26	11.1
30.0 - 34.9	10	4.5
35.0 - 39.9	25	11.4
40.0 - 44.9	19	8.6
45.0 - 49.9	13	5.9
50.0 - 54.9	8	3.6
55.0 - 59.9	11	5.0
60.0 - 64.9	7	3.2
65.0 - 69.9	9	4.1
70.0 - 74.9	7	3.2
75.0 - 79.9	4	1.8
80.0 - 84.9	5	2.3
85.0 +	1	0.4

n = 220 Mean = 34.0 ± 21.6, Range 0.25 - 89 years

It is not surprising then, that the time at current residence in Cass County is also longer (Table 13). For example, 19 percent of participants have lived at their current address less than 5 years, but 35 percent have lived in their current homes between 5 and 20 years. Forty-six percent have lived at their present address for more than 20 years. Again, this may be reflective of the farming/rural community. Families may remain in the family home even if the land is no longer in agriculture or even owned by the family. There were a number of participants who responded that they had lived in Cass County for their entire life. Several others were still living in the house in which they were born. The mean time at current address is 20.1 ± 16.6 years, with a wide range of 0.25 - 75 years.

TABLE 13
TIME AT CURRENT RESIDENCE IN SURVEY

Length of residence			number	%
Less than 1 year			20	9.0
1.0	-	4.9	22	10.0
5.0	-	9.9	34	15.4
10.0	-	14.9	22	10.0
15.0	-	19.9	23	10.4
20.0	-	24.9	13	6.8
25.0	-	29.9	26	11.8
30.0	-	34.9	10	4.5
35.0	-	39.9	22	10.0
40.0	-	44.9	10	4.5
45.0	-	49.9	4	1.8
50.0	-	54.9	4	1.8
55.0	-	59.9	0	0.0
60.0	-	64.9	4	1.8
65.0	+		4	1.8

n = 220, Mean = 20.1 $\pm$ 16.6, Range 0.25 - 75 years

According to the census, 61.7 percent of the population in Cass County lived in the same house since 1987. In the survey sample 65 percent of the respondents have resided in the same house since 1987 (Table 14). Prior to 1987, eighteen percent of the census sample lived in Cass County but in a different house compared to 17 percent of the survey sample. However, 6 percent more of the survey group lived outside of Cass County in 1985 than the census population.

TABLE 14
COMPARISON OF SURVEY AND CENSUS:RESIDENCE IN CASS COUNTY

	Census		Survey	
Residence	Number	%	Number	%
Same house since 1985	28,403	61.7	143	65.0
Different house same county	8,498	18.4	37	16.8
Other than Cass County	9,135	19.8	20	25.9

Universe = 15+ census
21+ survey

It would appear from the data presented in Tables 2 through 14 that the sample population, while not identical to the census population of Cass County, represents a good approximation. It will be possible then to address the issues of health and risk with some confidence. In the following sections, data collected about the health outcomes will be described and analyzed.

Description and Comparison of Health Issues and Outcomes:

There are many ways to look at the overall health of a population; prevalence rates of various diseases (morbidity), or the number of deaths from various causes, (mortality). Such a view tells who among the population is already sick and who has already died. Examination of the variables in common of those who have contracted a disease and those who have died from it can help to understand who may be at risk in the community.

The purpose of this study was to find out who in Cass County is sick and what factors they may share, especially if one of those factors is exposure to elevated levels of nitrate in drinking water. In the model described above (Figure 2), the factors that contribute to the likelihood of illness were divided into several parts. Included is the environment, i.e., Cass County. The distribution of surveyed households with regard to their place in that environment is shown in the maps in Figures 4 - 6 and in Table 5.

Many of the households share a similar soil type and proximity to farms. As discussed above, a large portion of contaminated wells are found on Kalamazoo and Oshtemo soils. As we are considering nitrate to be the agent in this study, its source or reservoir and its mode of ingestion or exposure are also of concern.

In Cass County, among other agriculturally active places in the midwest, nitrates are thought to find their way into the ground water through their use on the soil. The spreading of animal manure and chemical fertilization are thought to be the sources for ultimate ground water contamination. Hence the users of domestic wells that often go untested are at risk of exposure to the agent through the agent, drinking water. This brings us to the host, there are factors associated with the individual that make him or her more likely to develop a disease.

In the model used here, these factors are considered intrinsic and extrinsic. Intrinsic factors are things like age, sex, race and physiologic state. Age can only increase, sex and race are genetically determined and not alterable by the subject. Physiological state is also to some degree beyond the control of the individual. This factor is to some degree linked to behavior, poor eating habits for example may leave clogged arteries, or traces of malnourishment. Eating habits can change and the damage lessened, but not totally reversed.

Extrinsic factors are those that to some degree are under the hosts' control. Occupation, income, education, diet, and risky behaviors such as smoking are choices made by the individual, admittedly within a given framework of social and economic constraints. For example, how often one sees a physician and follows recommended schedules for check-ups are also extrinsic factors and may indicate how concerned an individual is about their health. A major economic constraint may well be insurance coverage. Mammograms are expensive and only recently have been covered by some insurance plans. Pap smears are often not covered. This is a major determining issue for many women when making a judgement.

In the following sections the factors that affect the hosts as well as the rates of diseases are shown and analyzed for association.

Overall, the population of Cass County appears healthy

Most of the survey respondents (74%) do not smoke (Table 15). This agrees well with data presented by Healthy US (1992). According to this estimate, 25 percent of the national population smokes.

TABLE 15
SMOKERS IN SAMPLE

	Number	%
Non-smokers	163	74.2
Smokers	57	25.9

Primary Care and Frequency of Contact

Almost the entire survey population (89%) has a family physician (Table 16) whom they have visited within the year.

TABLE 16
FAMILY PHYSICIAN IN SURVEY SAMPLE

	Number	%
Physician	196	89
No Physician	24	11

Generally, respondents sought primary care, that is care other than basic check-ups from their own doctors (Table 16). Only 4.1 percent report seeking such care from the local emergency room. Ninety - four percent of respondents receive care from their own doctor or from a free standing clinic. Independent practitioners are the most important source of health for the survey respondents.

TABLE 17
SOURCE OF PRIMARY CARE

Source	Number	%
Family Physician	185	84.0
Free Standing Clinic	23	10.4
Hospital Emergency Room	9	4.1
No Primary Care Sought	3	1.4

There does however, seem to be a pattern in claiming a family physician related to age (Table 18). The oldest group has the lowest percentage family doctors, 24 percent, despite representing 32 percent of the population. Twenty-five percent of the next oldest group, 45 - 59 claim a family doctor, while group, aged 30 - 44, which is also the wealthiest age group, 27.2 percent have a doctor.

TABLE 18
FAMILY PHYSICIAN BY AGE

Age	Yes	% Sample	No	% Sample
20 - 24	2	0.9	0	0
25 - 29	12	5.4	2	0.9
30 - 34	14	6.4	3	1.4
35 - 39	23	10.4	4	1.8
40 - 44	23	10.4	1	0.4
45 - 49	20	10.0	2	0.9
50 - 54	11	5.0	4	1.8
55 - 59	22	10.0	2	0.9
60 - 64	17	7.7	1	0.4
65 - 69	20	10.0	1	0.4
70 - 74	14	6.3	0	0
75 +	16	7.3	2	0.9

The data in Table 19 demonstrate the relationship between income and family physician. Of those earning less than \$10,000 per year, 11.4 percent claim a family doctor. Recall from Table 12 that this group is comprised largely of older participants. However the group representing the largest users of family practitioners earn between \$25,000 and $35,000 per year. Of those respondents who earn more than $35,000 per year, 25 percent have a family doctor.

While most participants (89 %) report that they have a family physician (Table 16) as shown in Table 20, only 74 percent of participants visited a doctor within the year and 82 percent report having seen a physician within two years (Table 20).

TABLE 19
FAMILY PHYSICIAN BY INCOME

Income $	Yes	%Sample	No	%Sample
>10,000	25	11.4	5	2.3
10,000 - 14,999	16	7.2	2	0.9
15,000 - 19,999	13	5.9	1	0.4
20,000 - 24,999	22	10.0	6	2.7
25,000 - 34,999	33	15.0	0	0
35,000 - 49,999	28	12.7	0	0
50,000 +	27	12.3	2	0.9

TABLE 20
TIME SINCE LAST PHYSICIAN CONTACT

Years	Number	%
1	163	74.1
2	19	8.6
3	17	7.7
4	14	6.4
5	3	1.4
Unsure	2	0.9
Refused	2	0.9

n=220

However, when compared to the national figures provided by NIHS (Centers for Disease Control/National Center for Health Statistics 1992, Table 71, pp 115), in all but one age category the survey participants visited their doctors less often (Table 21). The 25 - 44 age group visited their physician the least often, 56 percent of people in this age group had contact with their doctor within the year, compared to 73 percent in the NIHS survey. The two groups (65 - 74 and >75) also had contact with the doctor less frequently than those in the same age categories in the national data set. Eighty three percent of each group visited their doctor within the year compared to 86 and 90 percent, respectively in the NIHS data set. The age group 45 - 65 was the only one in which survey participants reported more frequent contact with their doctor than the NIHS subjects (Table 21).

TABLE 21
COMPARISON OF RATES OF PHYSICIAN CONTACT IN SURVEY SAMPLE AND NATIONAL HEALTH INTERVIEW SURVEY

Age	% Survey	%NIHS
25 - 44	56	73
45 - 64	81	78
65 - 74	83	86
75 +	83	90

% = the percent of persons who had contact with a physician within the year. Calculated as the number in each age group who visited a physician divided by the total number in that age group.

When physician contact rates are compared on the basis of age and sex there appears to be a similar pattern (Table 22). Males in the youngest age group, 18 - 44, report the lowest rate of physician contact within a year in both the NHIS and the survey sample. The rate reported by surveyed females in the youngest age group, 67 percent, had contact with a doctor within the year is some what higher than that of surveyed males but still lower than rates reported for this groups in the national survey (84 percent). As age increases the percent of members of an age cohort who report at least one physician contact each year also increases. The exception is in the 45 - 64 age group in the NIHS study. This group reports a slight decrease in the rate of contact 82 percent down from 84 percent in the youngest age group.

The contact rate for men increases steadily with age in both study groups, with closest agreement in the rate of contact in the middle age groups. Males in Cass County report the lowest contact rates when they are young, and highest when they reach 65. It is in these two periods when the discrepancy between the two studies is greatest.

Women in Cass County report more physician contact in the middle years than in the youngest or oldest age groups. (Table 22). Interestingly, women's contact rates exceed those of the men until 65 at which time they are lower.

TABLE 22
PHYSICIAN CONTACT BY AGE AND SEX COMPARED TO DATA FROM THE NATIONAL HEALTH SURVEY

	Females		Males	
Age	%Survey	%NIHS	%Survey	%NIHS
18 - 44	67	84	49	64
45 - 64	88	82	76	73
65 +	72	89	92	85

%Survey = number who contacted a physician within the year divided by total number in the survey in that age-sex group.
%NIHS = number who had contact with a physician within the year divided by the survey population in that age-sex group.

Hospitalization

As shown in Table 23 only a small proportion of the survey population was hospitalized within the last year. That in itself is somewhat different than the rates reported by NIHS (Table 74, pp 120). This study reports that 10.8/1,000 persons were discharged from a hospital in the year of their survey. The hospitalization rate in this survey was 27/220 persons or 121/1,000 persons.

TABLE 23
PARTICIPANTS HOSPITALIZED WITHIN THE LAST YEAR

	Number	%
No Hospital	191	86.8
Hospital	27	12.7

However, the pattern of hospitalization by age and income for the Cass County survey population varies in the same direction as that reported by CDC (Table 74 pp 120). For example, females are hospitalized at a greater rate than are males in every age category except the 65 - 74 group (Table 24). Despite representing a slightly smaller (1.4%) proportion of the sample, males in this age group were hospitalized at a much higher rate, (18.7 percent compared to 10.1 percent) for females of the same age.

TABLE 24
HOSPITALIZATION BY AGE AND SEX

Age	Females Number	Females %	Males Number	Males %
18 - 44	8	16.7	2	4.2
45 - 64	6	14.3	1	2.7
65 +	6	20.7	5	20.8

% = percent of cohort in sample hospitalized at least once within the last year.

In the population surveyed by CDC, women are hospitalized more often than men, except in the under 18 age group. This observation remains consistent if hospitalizations for childbirth are excluded (Table 24).

TABLE 25
SHORT HOSPITAL STAYS REPORTED BY NIHS

Age	Females Number/1,000		Males Number/1,000
>18	2.4	(2.7)	3.0
18 - 44	4.5	(9.7)	3.2
45 - 64	6.2		6.5
65 +	11.4		13.5

() includes hospitalization for deliveries

When rates of hospitalization are compared by income, Cass County residents appear to hospitalized at greater frequency at all income levels (Table 26). The best agreement in hospitalization rates occurs in the 20,000 - 34,999 income group. The Cass County rate exceeds the CDC rate by only 1.5 percent. The highest hospitalization rate is in the lowest income group in both studies. However, the rate in Cass County is much higher than that reported by CDC in the National Interview Health Survey. One possible explanation for this is that this group is least likely to be insured or insured inadequately, and put off seeking health care and therefore require more intensive care when they finally do seek medical attention. This may be true for NIHS group but does not seem to hold true for the Cass County study (Table 27).

TABLE 26
HOSPITALIZATION RATE BY INCOME
COMPARISON OF SURVEY POPULATION AND NATIONAL HEALTH SURVEY RESPONDENTS

Income	% Sample	%NIHS
>10,000	28.6	8.9
10,000 - 19,999	18.7	7.2
20,000 - 34,999	11.5	6.2
35,000 +	14.5	5.0
Refused/Not sure	10.7	na

% = percent of persons in each income category hospitalized in the last year.

Insurance

A surprising 91 percent of subjects are insured and most, 66.8 percent, have coverage from their work place (Table 27). Only 3.6 and 2.7 percent are dependent on either medicaid or medicare, respectively. Of those who have medicare 18.7 percent carry a supplement. Only 7.3 percent carry no insurance. These people were not all unemployed only 3 adults reported being out of work, therefore, the 10 other adults who reported no insurance were employed or retired. For example, one couple could not get insurance, due to illness and were as yet, too young to qualify for medicare.

TABLE 27
INSURANCE IN SAMPLE POPULATION

	Number	%
Not Insured	16	7.3
Insured	201	91.4
Unsure/Refused	3	1.4

TABLE 28
DISTRIBUTION OF INSURANCE CARRIERS IN SAMPLE POPULATION

Insurance Carrier	Number	%
No insurance	16	7.3
Private	149	66.8
Medicaid	8	3.6
Medicare	6	2.7
Medicare + Supplement	41	18.7

Exposure

Nitrate exposure is defined in this study as nitrates consumed in drinking water and food. As will be shown in Figures 9 - 26 and Tables 43 - 46, dietary preferences are about the same for most interviewees and therefore differences nitrate intake probably comes from drinking water. Exposure is calculated as milligrams per day using the total volume of water consumed in liters and the total number of milligrams nitrate per liter as determined by *AquaTest*(R). A base of 75 mg nitrate in food is used and the amount consumed in water is added to 75 mg. The percentage of that taken in water indicates proportion of dietary nitrate that comes from water.

TABLE 29

CONSUMPTION OF NITRATES IN DRINKING WATER

Nitrate in mg	+10	9.9 - 3.0	2.9 - .001	0
Number	31	52	59	70
Percent	15	25	29	34

As shown in Table 29, at least 66 percent of subjects consume some nitrate in their drinking water. As will be shown in the next section the majority of subjects report no illness within the last 5 years despite having been exposed for at least some time, to nitrates. The next section will examine the outcomes reported by the respondents, and the rates of these illness, and whether they are higher than would be expected. Data from the Centers for Disease Control, National Health Interview Survey are used for comparison (Centers of Disease Control/National Center for Health Statistics 1992).

Outcomes

TABLE 30
HEALTH OUTCOMES IN CASS COUNTY SURVEY POPULATION

Outcome	Number	%
No illness	139	63.0
Hypertension	17	7.7
Cancers[1]	12	5.4
Cardiac[2]	8	3.6
Asthma	6	2.7
Kidney[3]	5	2.3
Diabetes	5	2.3
Allergies	4	1.8
Gastrointestinal[4]	4	1.8
Arthritis	4	1.8
Thyroid	3	1.5

1 Cancers of all sites
2 All forms of cardiac illness
3 All kidney ailments
4 All GI illness

As shown in Table 30, the majority (63%) of the sample reported no serious illness within the preceding 5 years. The most frequent illnesses reported were hypertension, cancers, cardiac problems. Kidney problems, diabetes, gastrointestinal illness, allergies, asthma are reported at about the same frequencies.

In Table 31, the various types of cancer reported are shown. Included in this table are the age, sex and amount of nitrate consumed in drinking water by the respondent who reported the illness. Only three cancer patients were female, two of whom have breast cancer and one woman has bladder cancer. One of the youngest victims of cancer, a female at age 37 with breast cancer, also consumes the most nitrate in her drinking water, 36 mg each day. If we assume that she also takes in 75 mg of nitrate each day from food, the proportion of nitrate from drinking water in her diet is 48 percent. However, nitrates have not been implicated in the etiology of breast cancer. As is shown in Table 31 most cancer patients are older, with exception of the 39 year old male with mouth cancer, the 31 one year old male with an undefined malignant tumor and the 37 year old breast cancer patient, the youngest person with a diagnosis of cancer is a 61 year old male with colon cancer. In Table 32, the age specific rates for each type of cancer are presented.

TABLE 31
TYPES OF CANCERS IN SURVEY POPULATION

Cancer	Nitrate in H_2O	Age	Sex
Skin	0	66	Male
Mouth	0	39	Male
Breast	0.7	72	Female
Breast	36.0	37	Female
Prostate	1.4	77	Male
Prostate	0	72	Male
Colon	4.7	84	Male
Colon	0	66	Male
Colon	0	61	Male
Bladder	1.4	89	Female
Lung	4.7	89	Male
Tumor	13.9	31	Male

With the exception of the rate for all cancers in the 75+ age group, the rates are not exceptionally high. When the rates are further broken down by disease and age they remain in the reasonable range and agree with rates published by Healthy U.S. (1992). There are no cases of stomach cancer among the respondents. This agrees with the assessment of Dr. Weimar, who reported seeing no cases of stomach cancer in Cass County, for at least 2 - 3 years (Personal Communication 1992).

Age Specific Rates

TABLE 32
AGE SPECIFIC RATES FOR CANCERS IN SURVEY POPULATION

Ages	Number	Number in age range	Rate/1000
		All Cancers	
18 - 44	1	95	10.5
45 - 64	2	79	28.6
65 - 74	4	34	117.6
75 +	4	18	222.2
		Skin Cancer	
66	1	34	29.4
		Mouth Cancer	
39	1	95	10.5
		Breast Cancer	
72	1	34	29.4
37	1	95	10.5
		Prostate Cancer	
77	1	18	55.6
70	1	34	29.4
		Colon Cancer	
61	1	79	12.6
66	1	34	29.4
84	1	18	55.6
		Bladder Cancer	
89	1	18	55.6
		Lung Cancer	
84	1	18	55.6

The most frequently reported health outcome among survey participants is hypertension; there were 17 cases reported (7.7%). The age rates of hypertension in Cass County are compared to data collected by CDC in the National Interview Health Survey (NIHS 1992 Table 57 pp 83)(Table 34). The rates in Cass County are markedly lower than those reported on a national basis.

TABLE 33
AGE SPECIFIC RATES FOR HYPERTENSION IN SURVEY POPULATION COMPARED TO NATIONAL HEALTH INTERVIEW SURVEY

Age	Number	Rate/1000	NIHS RATE/1000
18 - 44	2 (95)	21.0	46.3
45 - 64	11 (79)	138.9	244.0
65 - 74	3 (35)	8.6	377.6
75 +	1 (18)	55.6	365.5

()= Number in age cohort in Cass County survey

Other outcomes reported by participants include cardiac problems. There were a total of 8 cases reported by survey respondents. This includes all types of cardiac ill health, bypass, congestive heart failure, and valve replacements. As is shown in Table 34 the age specific rates are much lower in Cass County than in the population surveyed in the NIHS study. Age is an important factor with most cases reported in the 45 - 64 age group.

TABLE 34

AGE SPECIFIC RATES OF CARDIAC* PROBLEMS IN SURVEY POPULATION COMPARED TO NATIONAL INTERVIEW HEALTH SURVEY

Age	Number	Rate/1,000	NIHS Rate/1,000
45 - 64	4 (79)	50.6	134.1
65 - 74	3 (35)	90.9	256.4
75 +	1 (18)	55.6	354.3
All ages	8 (220)	36.4	82.6

(NHIS 1992 Table 57 pp. 83)

The age specific rates for diabetes are shown in Table 36. The overall rate for the sample is lower in Cass County than in the NIHS data set. However, rates in the 18 -44 and 45 - 64 age groups are much higher than those reported by NIHS. In the oldest age group, 64 - 74 the rate for Cass County Survey participants is much lower than that reported by NIHS.

TABLE 35

AGE SPECIFIC RATES OF DIABETES IN SURVEY POPULATION COMPARED TO NATIONAL INTERVIEW HEALTH SURVEY

Age	Number	Rate/1,000	NIHS Rate/1000
18 - 44	1 (95)	10.5	1.1
45 - 64	3 (79)	38.5	13.6
64 - 74	1 (35)	28.6	103.8
All ages	5 (220)	31.8	82.6

() = Number in age cohort in Cass County survey

*Includes all Cardiac conditions: bypass, valve replacement and congestive heart failure.

Kidney ailments in general are reported more often by Cass County respondents than by NIHS respondents (Table 37), except the 18 - 44 age group.

TABLE 36

AGE SPECIFIC RATES OF KIDNEY PROBLEMS IN SURVEY POPULATION COMPARED TO NATIONAL INTERVIEW HEALTH SURVEY

Age	Number	Rate/1000	NIHS Rate/1,000
18 - 44	1 (95)	10.5	12.9
65 - 74	4 (35)	114.3	23.9
75 +	1 (18)	55.6	27.6
All	6 (220)	27.2	12.6

() = Number in age cohort in Cass County survey

Thyroid problems are reported at about the same rate in both Cass County and the NIHS surveys (Table 38). However the rate in the 45 - 64 age group is more than double in Cass County than in the NIHS study population.

TABLE 39

AGE SPECIFIC RATES OF THYROID PROBLEMS IN SURVEY POPULATION COMPARED TO NATIONAL INTERVIEW HEALTH SURVEY

Age	Number	Rate/1000	NIHS Rate/1000
45 - 64	3 (79)	38.0	17.3
All ages	3 (220)	13.6	14.8

() = Number in age cohort in Cass County survey

CHAPTER IV

DISCUSSION

As is shown in the preceding section, the rates of various outcomes are lower in Cass County survey participants than in the NIHS sample. The exceptions to this observation are the following rates considered on an age specific basis. Thyroid problems in the 45 - 64 age group (Table 38), kidney problems in the 65+ age groups (Table 37) and diabetes in the 18-44 and 45 - 64 age groups (Table 36). The basic question this study poses is whether nitrate consumption in drinking water contributes to the risk of illness. If nitrates do contribute to risk, the distribution of illness should be different in exposed than non-exposed groups. Using the Chi-square statistic, the distributions of illness in nitrate and non-nitrate exposed groups were tested for independence. A calculated X^2 that is greater than the tabled value at the P level of 0.05, would lead us to reject the hypothesis that the distribution of illness in each of the groups is independent. As is shown in Table 39, there does appear to be a difference in nitrate exposed groups when compared to non-exposed. In the case of all cancers, cardiac, kidney outcomes and diabetes, the distribution in exposed and non-exposed groups is not independent. The tabled X^2 value for 1 degree of freedom at the 0.05 level is 3.84, and in each of these cases is exceeded. There is an association between each of these outcomes and nitrate consumed in drinking water. It should be noted that this result should be treated with care, in the case of cancers for example, there is no distinction made among the various types of cancer, and there are no cases of stomach cancer, the disease thought to be most commonly associated with high nitrate levels. And indeed there is little in the literature to support the idea of an association between diabetes, kidney outcomes and nitrate.

Also in all of the outcomes, the frequency is low, and yet apparently all meet the requirement of no cell with an expected value less than 3 (Clark and Hoskings, 1986). However, because the sample size is small, that is the number of people with a particular outcome is low, the association may not be a strong one.

If nitrates in drinking water are important to the development of any of the health problems described above, then there should be an increase in risk with exposure to nitrates in drinking water. The Odds Ratio is a measurement of association. It can be used to compare the odds of developing a disease among exposed and non-exposed subjects. The odds ratio can be used to determine relative risk when the cases studied are representative of both healthy and ill populations (Gordis 1988). The sample as a whole is fairly representative of the rural population in Cass County, therefore, the odds ratio can be used to estimate risk in this sample. If there is no increase in risk of contracting a disease upon exposure to a pathogen, or environmental contaminant, the odds ratio will be 1 or less. In order to assess the accuracy of the ratio and whether the value is indeed different from 1, a 95% confidence level is calculated. If the range of the limit is narrow, the ratio is accurate, if it contains the null value of 1, the ratio does not indicate increased risk, even if the ratio is greater than 1 (Kleinbaum et al 1982).

TABLE 38
RELATIVE RISK OF SELECTED OUTCOMES RELATED TO NITRATE CONSUMED IN DRINKING WATER

	Exposed		Non-exposed				
Outcome	+	-	+	-	X^2	OR	95%CI
Hypertension	11	139	6	64	2.24	0.84	.21-2.09
All Cancers	8	138	4	70	8.48*	1.00	.26-4.16
Cardiac	7	143	2	68	7.79*	1.15	.69-9.16
Diabetes	3	147	2	68	7.79*	1.66	.30-71.29
Kidney	4	146	1	69	7.79*	1.89	.19-2603415
Thyroid	2	148	1	69	0.32	0.93	.93-1.19

df=1, P =.05, X2 tabled value = 3.841, * X2 values larger than tabled.

From the data presented in Table 39, it is clear that although there are three instances, cardiac, diabetes and kidney, where the odds ratio is greater than 1, there is no increased risk of illness upon nitrate exposure. In every case the confidence limit includes the null value, 1.

If nitrate exposure does not explain the pattern of illness in the county, what other factors could contribute to increased risk for illness? Some authors have reported that occupations such as farming and certain industrial jobs have higher prevalence rates of cancer. Shown in Table 40 are the occupations listed by respondents and the rates of outcomes based on the numbers in each occupational category. Calculation of X^2 reveals that there is an association between occupation and outcome. The calculated value of 36.67, 6 df is larger than the tabled value, 12.592, indicating an association. The most unhealthy occupational group were those who were retired. Twenty-nine percent of the sample listed retired as their occupation yet they account for 52.9 percent of hypertension cases, 88.9 percent of cardiac cases and 75.0 percent of all cancer patients (Table 40). It is probable that the major contributing factor to these numbers is age. However, previous occupation and hence exposure to a variety of compounds may be a risk factor.

Most retirees worked in the following occupations: office (16), factory, (12), farmer (8), homemaker (8), sales (7), truckers (6).

TABLE 39

OUTCOME BY OCCUPATION IN THE SURVEY POPULATION

Occupational groups	Number	%	Healthy	%	Outcome	Number	%
Factory	22	10.0	18	8.2	Hypt	2	0.9
					Diab	1	0.4
					Lump	1	0.4
Farmer	31	14.0	23	10.4	Hypt	2	0.9
					Diab	1	0.4
					Card	1	0.4
					Asth	1	0.4
					Thyr	1	0.4
					Brain AB	1	0.4
					Lump	1	0.4
Retired	64	29.1	22	10.0	Hypt	9	4.1
					Diab	1	0.4
					Card	8	3.6
					Asth	2	0.9
					Stom	2	0.9
				(All)	Canc	9	4.1
					Prostate	2	0.9
					Colon	3	1.3
					GI	1	0.4
					breast	1	0.4
					bladder	1	0.4
					lung	1	0.4
Homemakers	21	9.5	13	5.9	Hypt	2	0.4
					Asth	1	0.4
					Stom	1	0.4
				CA	Breast	1	0.4
					Repro	2	0.8
					Aller	1	0.4
Office/Management	29	13.2	21	9.5	Asth	1	0.4
Sales				CA	Mouth	1	0.4
					Lump	1	0.4
					Aller	1	0.4
					Kidney	2	0.9
					Arth	1	0.4
					Hern	1	0.4
Professional Services	12	5.4	10	4.5	Hypt	1	0.4
					Stom	1	0.4
Other Services	12	5.4	10	4.5	Asth	1	0.4
					Arth	1	0.4

Table 39 continued

Table 39 Continued

Construction/drivers	19	8.6	15	6.8	Hypt	1	0.4
					Thyr	1	0.4
				CA	Tumor	1	0.4
					Aller	1	0.4
Student/Unemployed	9	12.7	4	1.8	Hypt	1	0.4
					Diab	1	0.4
					Aller	1	0.4
					Lump	1	0.4

Number = number of persons declaring this occupation or outcome.
% = percent of sample. Lumps are those that required surgical removal.

TABLE 40
OCCUPATION AND OUTCOME

Occupation	Number	%*	Number Healthy	% '	Number Ill	%'
Factory	22	10.0	18	81.8	4	9.0
Farmer	31	14.1	23	74.2	8	25.8
Retired	64	29.1	22	34.4	44	68.7
Homemakers	21	9.5	13	61.9	8	38.9
Mgmt/Office/sales	29	13.2	21	72.4	7	24.1
Professional Serv	12	5.4	10	83.3	2	16.7
Other Services	12	5.4	10	83.3	2	16.7
Construction	19	8.6	15	78.9	4	21.0
Student/Unemp	9	12.7	4	44.4	5	55.5

* = Percent of sample, ' = Percent of Occupational Group

Others worked as machinists (1), welders (1), general construction (2), nurse (1), railroad (1), clergy (1) and as the county's extension agent (1). Just by virtue of numbers office and factory workers should account for most of the outcomes. Farmers, homemakers, salespeople, truckers should account for the next largest number. In table 41 cases by former occupation are shown. Retired factory workers account for 25 percent of all cancer cases followed by farmers and construction/driver retirees. Age may be the factor that contributes most to these rates.

TABLE 41
FORMER OCCUPATION AND OUTCOME RATES

Former Occupation	Outcomes	% of All Cases
Factory	3 Cancers	25.0
	2 Hypertension	11.8
	1 Cardiac	12.5
	1 Diabetes	20.0
Farmer	2 Cancers	16.7
	2 Hypertension	11.8
	2 Cardiac	25.0
Sales/Mgmt/Office	1 Cancer	8.3
	4 Hypertension	23.5
	1 Diabetes	20.0
	1 Thyroid	20.0
Construction/Drivers	2 Cancers	16.7
	1 Hypertension	5.9
	2 Cardiac	25.0
	1 Diabetes	20.0
	1 Thyroid	33.3
Homemaker	1 Hypertension	5.9
	1 Kidney	20.0

Age is indeed important as a confounding variable in the survey population. In Table 42, the X^2 values for several confounding variables are shown. The distribution of illness and age are not independent. As shown in Table 42, income and sex are also related to the distribution of illness in the survey population. As shown in Tables 4 and 5, the survey population makes less money than the census population, and that many of the poorest subjects were also among the oldest. There is also an indication that the older men get the more contact they have with their physicians perhaps indicating an increase in illness with advancing age.

TABLE 42
INTRINSIC AND EXTRINSIC FACTORS CONTRIBUTING TO ILLNESS

Factor	X^2	df	P value
Age	21.373	3	0.0001
Age	44.036	12	0.00001
Income	21.128	7	0.003
Sex*	5.121	1	0.002

P =0.05, X^2 is calculated for 2 levels for age. Four age groups are used for comparison to NIHS data. 13 groups are comparable to census data. The more degrees of freedom the stronger the association. * An Odds Ratio was calculated for sex, 1.996, 95% CI = 1.09 - 3.66.

Dietary Factors

Among the factors that could be considered confounding when trying to sort out the relationship between environmental exposure and health outcomes are other sources of exposure to the compound in question as well as other compounds that may also cause ill health. In an attempt to control for other sources of nitrate exposure, a set of questions on dietary habits was included in the questionnaire. The purpose of these questions was not to obtain a detailed diet history, but rather to find out in a general way what the respondents eat and with what frequency. For example, cured meats such as ham, bacon and sausage are well known sources of nitrate (Knight et al 1987), participants were asked whether they eat these foods, and how often, once a week, once a month, daily. If the subject consumes bacon once a month, its counted as .25 times per week and is counted as a yes. In Figures 9 - 11 the distribution and frequency of foods consumed is shown.

The survey participants eat a fairly wide variety of foods. Most (76%) eat some form of animal protein every day, primarily beef. Chicken and pork are eaten by about the same number of participants and at the same frequency (Table 43). Fish and venison are also eaten by members of the survey. Fish includes that which is caught locally or in Lake Michigan as well as ocean fish purchased at the grocery.

TABLE 43
FREQUENCY OF FOOD CONSUMPTION BY SURVEY POPULATION

Days/week	Animal Protein	Vegetables	Fruit
5 - 7	82.4	95.0	73.6
3 - 4	11.3	2.2	12.7
1 - 2	4.1	2.1	1.8
0	1.8	0	1.8

Percent of Sample who report consumption at this frequency.

Ninety five percent of the survey sample claims to eat at least one vegetable each day; there was no one who would admit to not eating at least some kind of vegetable even if it was potato in the form of french fries. Corn, green beans potatoes, lettuce and cabbage are the most popular of the vegetables, followed by tomatoes, squash including winter and summer squashes, broccoli cauliflower and assorted greens. Beets are by far the least popular of vegetables. The vegetables listed in Figure 11 are grouped, to increase frequency counts. For example, all greens including spinach, beet, collards and swiss chard are counted as greens. And as noted above, all squashes are counted together, summer,

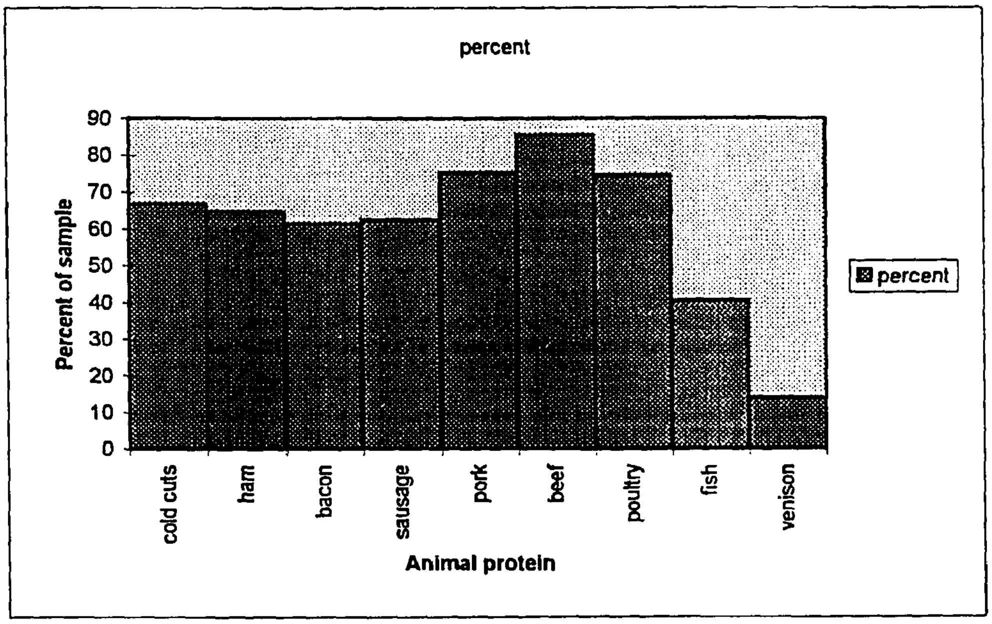

Figure 9 Consumption of Animal Protein by Survey Participants

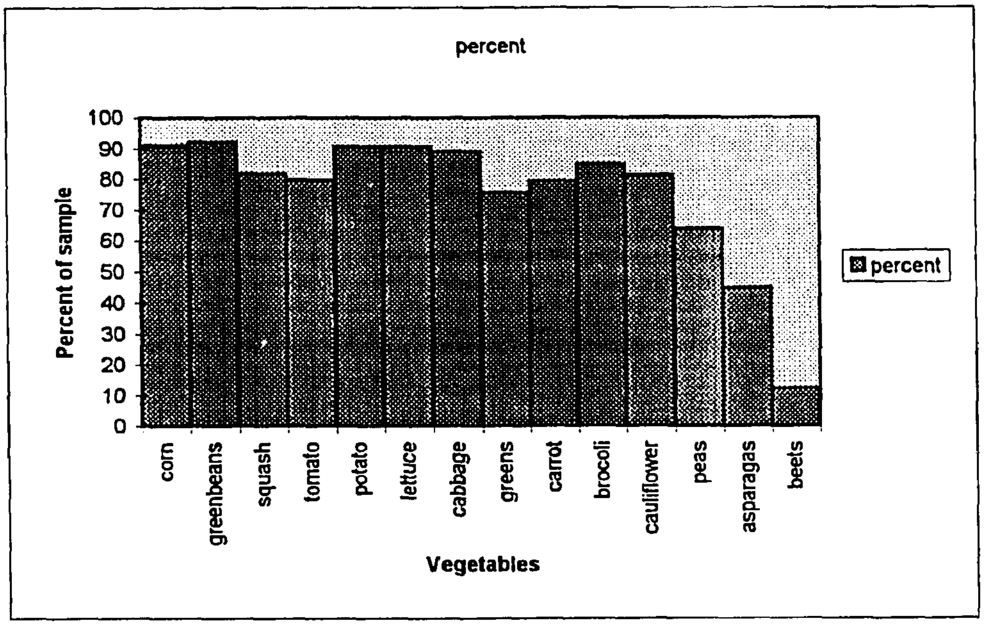

Figure 10 Consumption of Vegetables by Survey Participants

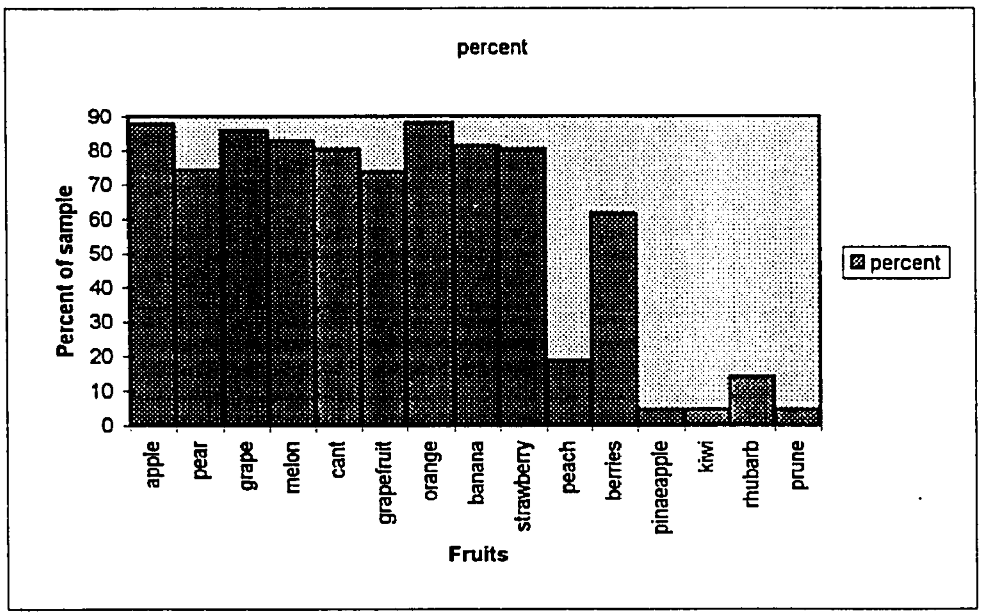

Figure 11 Consumption of Fruits by Survey Participants

zucchini, acorn, butternut etc. Other vegetables were listed by participants such as cucumbers, green peppers, radishes and celery but they are not listed in the figure because the frequency was so low. Many people simply listed salad, which could also include many of these items.

Many participants (68.2%) grew their own vegetables, or had a relative or neighbor who regularly supplied them with fresh vegetables in season. Otherwise most subjects bought vegetables at local stands (79.1%) during the season or at one of the two groceries (90.4%) in the county during the winter.

Fruit consumption is a little more variable. Only 72.7 percent of the sample consume fruit on a daily basis. About 14 percent eat fruit 3 to 5 times per week (Table 43). And a small fraction eat fruit once a week or not at all. Apples were the most popular, and are locally grown and purchased. All types of berries, strawberries, blueberries, raspberries, and blackberries were also very popular, and are local products. Oranges, bananas, melons, grapes, grapefruit were also consumed by most respondents. Citrus fruits were obtained in local grocery markets. Other mentioned fruits were rhubarb, local and in season during the period of the survey, kiwi and pineapple, obviously not locally produced.

The question is whether there are differences among subjects and what they eat. For example, do participants who consume nitrate in their drinking water eat differently than those who do not (Figures 12 - 14 and Table 44). There appear to be some differences, especially in fish consumption (Figure 12) and in certain vegetables (Figure 13). Fruit consumption is more variable, generally, and this is the case when compared on the basis of nitrate consumption (Figure 14).

TABLE 44

FREQUENCY OF CONSUMPTION VS NITRATE CONSUMED IN WATER

Days/week	10+mg/l	9.9 - 3.0mg/l	2.9 - .001mg/l	0mg/l
		Animal Protein		
5 - 7	66.8	78.7	88.2	73.7
3 - 4	15.6	11.5	9.6	3.2
1 - 2	3.1	7.6	0	6.4
0	0	7.6	0	0
		Vegetables		
5 - 7	91.0	95.8	88.7	96.7
3 - 4	3.1	1.9	4.8	0
1 - 2	3.1	1.9	1.6	3.2
0	0	0	0	0
		Fruits		
5 - 7	82.8	67.3	69.9	75.8
3 - 4	11.4	21.1	11.3	9.6
1 - 2	3.1	3.8	12.8	11.3
0	0	3.8	0	0

Percent of participants at each nitrate level

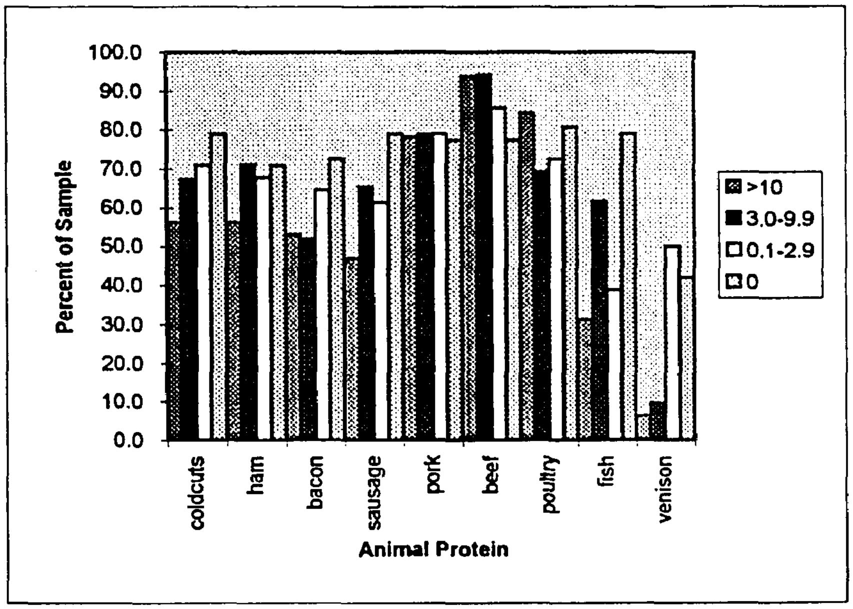

Figure 12 Consumption of Animal Protein Compared to the Nitrate Levels in Drinking Water in the Survey Population

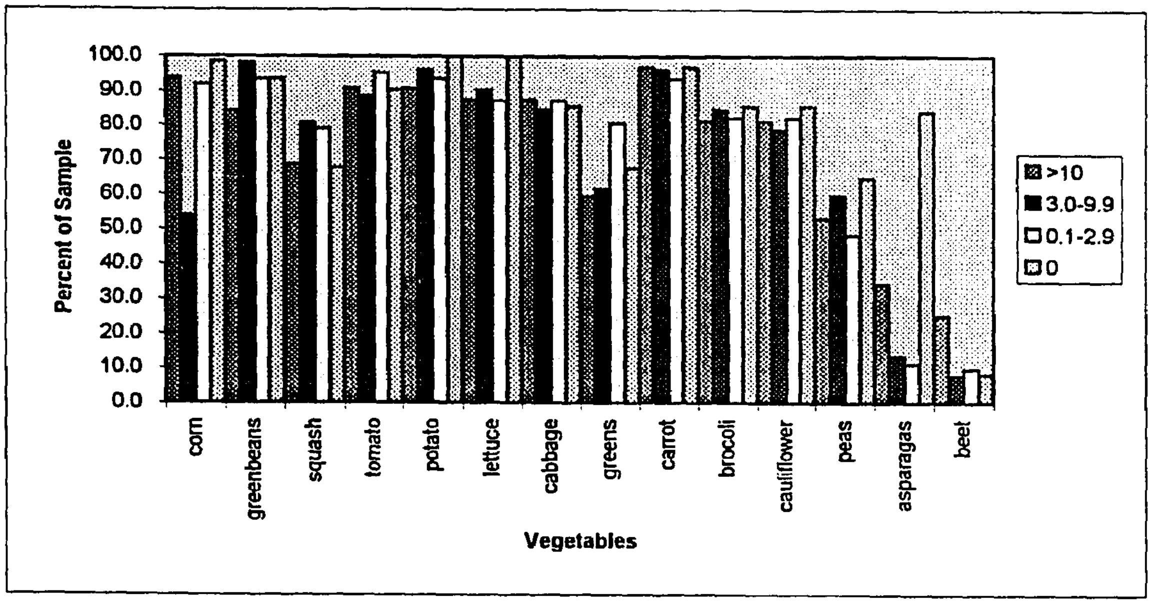

Figure 13 Consumption of Vegetables Compared to the Nitrate Levels in Drinking Water in the Survey Population

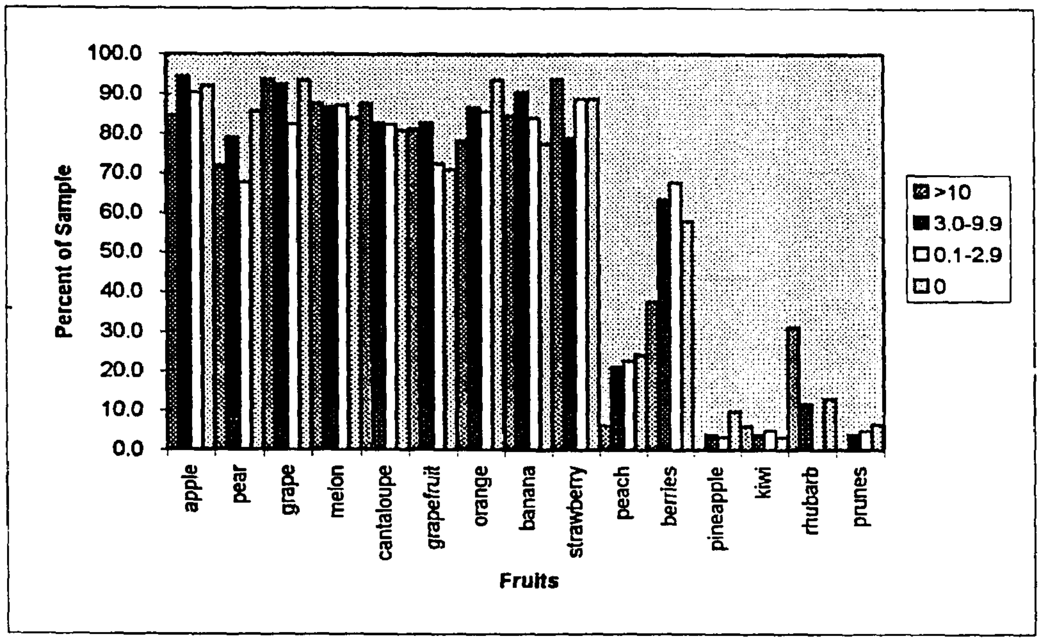

Figure 14 Consumption of Fruit Compared to the Nitrate Levels in Drinking Water in the Survey Population

Is there a difference between healthy and ill subjects in the foods they eat on a regular basis? One striking difference between healthy and ill subjects seems to be in their consumption of fish (Figure 15). More healthy people eat fish than do sick people. Another difference between healthy and ill subjects is that ill subjects report corn as part of their diet more frequently than do healthy subjects (Figure 16). While both ill and healthy people report eating vegetables on a daily basis, slightly fewer sick (77.3) than well (84.9) people report eating meat daily (Table 45).

TABLE 45
FREQUENCY OF CONSUMPTION IN HEALTHY AND ILL PARTICIPANTS

	Animal Protein		Vegetables		Fruit	
Day/Week	Ill	Healthy	Ill	Healthy	Ill	Healthy
5 - 7	77.3	84.9	95.4	94.3	71.2	69.3
3 - 4	10.6	13.3	3.0	2.1	12.1	14.2
1 - 2	9.0	2.9	1.5	3.5	12.1	17.6
0	0	0.2	0	0	3.0	1.4

Percent of healthy and ill subjects who report frequency of consumption.

Age is an important contributing factor in explaining the pattern of health outcomes in the survey population (Table 41). Is there a difference between older and younger respondents in the types of foods and the frequency with which they are consumed? When comparing the types and frequency of foods eaten by various age groups, some differences appear. For example, fewer members of the oldest age group (75+), consume processed meats. In every case, fewer report eating cold cuts, ham, bacon and sausage, than in all other age groups (Figure 21). Comparison of vegetable consumption on the basis of age reveals that the age group 65 - 74 consumes the most vegetables (Figure 22). This appears to be the case as well with regard to fruit consumption (Figure 23). The 65 - 74 age group reports the consumption of fruit more often than any other age group.

TABLE 46

FREQUENCY OF CONSUMPTION OF FOOD GROUPS BY AGE

Days/Week	18 - 44	45 - 64	65 - 74	75+
		Animal Protein		
5 - 7	70.3	86.1	94.3	83.3
3 - 4	8.4	11.4	3.1	0
1 - 2	0	4.3	0	0
0	3.2	2.5	2.9	0
		Vegetables		
5 - 7	78.9	94.9	97.0	88.9
3 - 4	3.2	0	2.9	0
1 - 2	6.4	0	0	0
		Fruits		
5 - 7	48.4	61.9	85.7	61.1
3 - 4	28.4	8.8	2.9	16.7
1 - 2	14.7	8.8	8.6	5.6
0	2.1	1.3	2.9	0

Percent of subjects who report consumption at this frequency.

One means of testing for differences is to use the X^2 statistic on the distribution of foods consumed. The purpose would be to test whether there is an association between the types of food usually eaten and one of the other important factors such as age, illness, (hypertension and cancer, Figures 23 - 28) and nitrate consumed in water. The results of this analysis are shown in Table 47. As is shown in Table 47, in no case does the calculated X^2 exceed the tabled value for the given degrees of freedom and a p = to 0.95.

TABLE 47
X^2 VALUES FOR FOOD DATA

Food	X^2	df	Tabled
	Nitrates in Drinking Water		
Animal Protein	5.673	8	15.507
Vegetables	4.390	13	22.362
Fruit	5.638	11	19.675
	Healthy vs Ill		
Animal Protein	13.667	8	15.507
Vegetables	10.959	13	22.362
Fruit	11.163	11	19.675
	Healthy vs Cancer		
Animal Protein	1.731	7	14.067
Vegetables	1.130	10	18.307
Fruit	5.160	11	19.675
	Healthy vs Hypertension		
Animal Protein	6.410	7	14.067
Vegetables	2.048	13	22.362
Fruit	2.320	10	18.307
	Age		
Animal Protein	16.319	24	36.415
Vegetables	7.122	33	47.636
Fruit	7.241	33	47.636

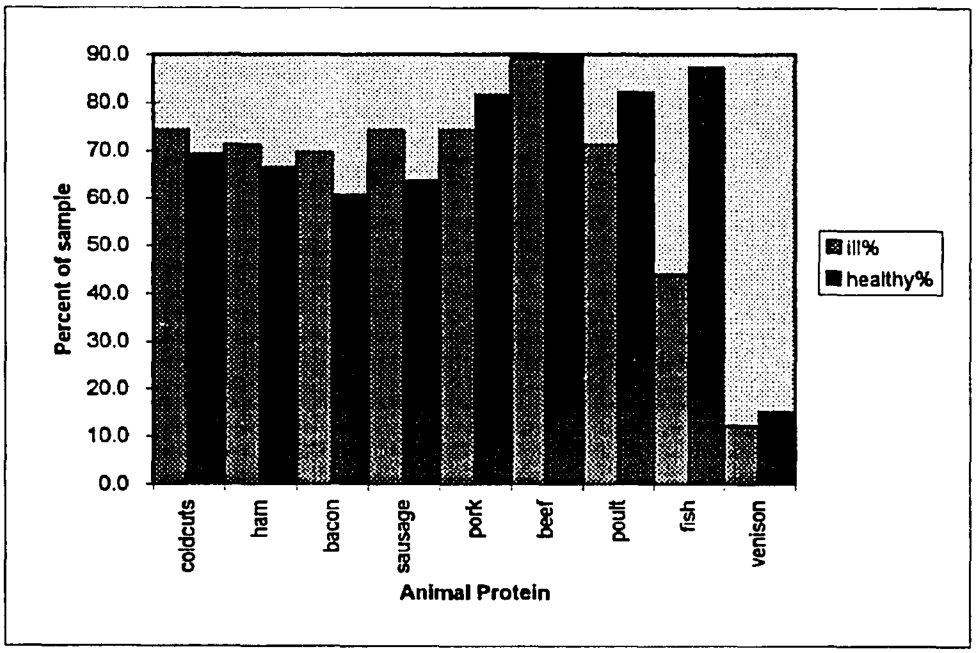

Figure 15 Animal Protein Consumption in Healthy and Ill Survey Participants

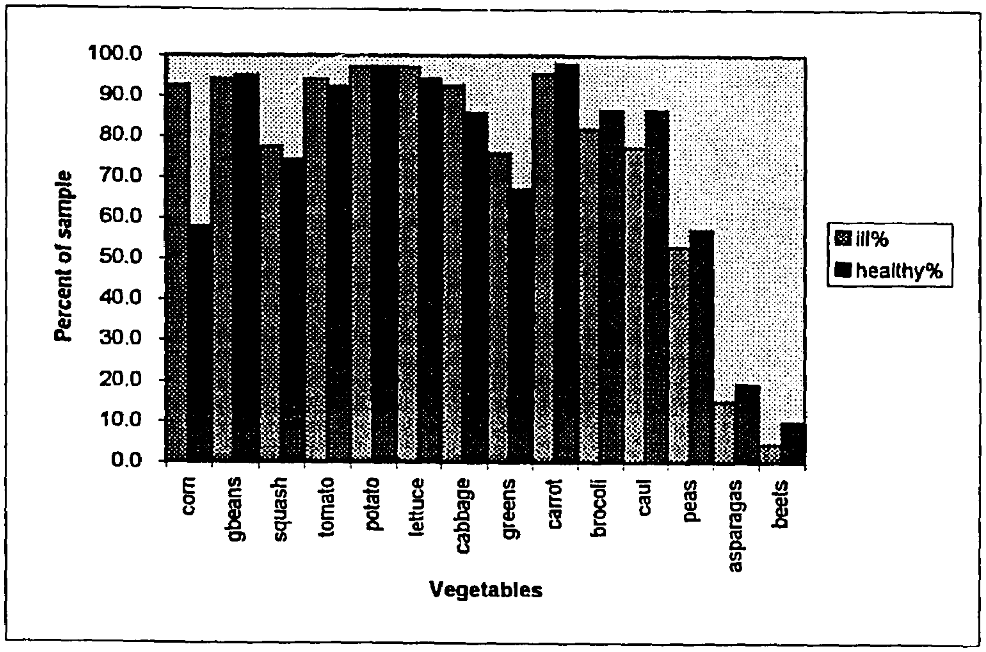

Figure 16 Vegetable Consumption in Healthy and Ill Survey Participants

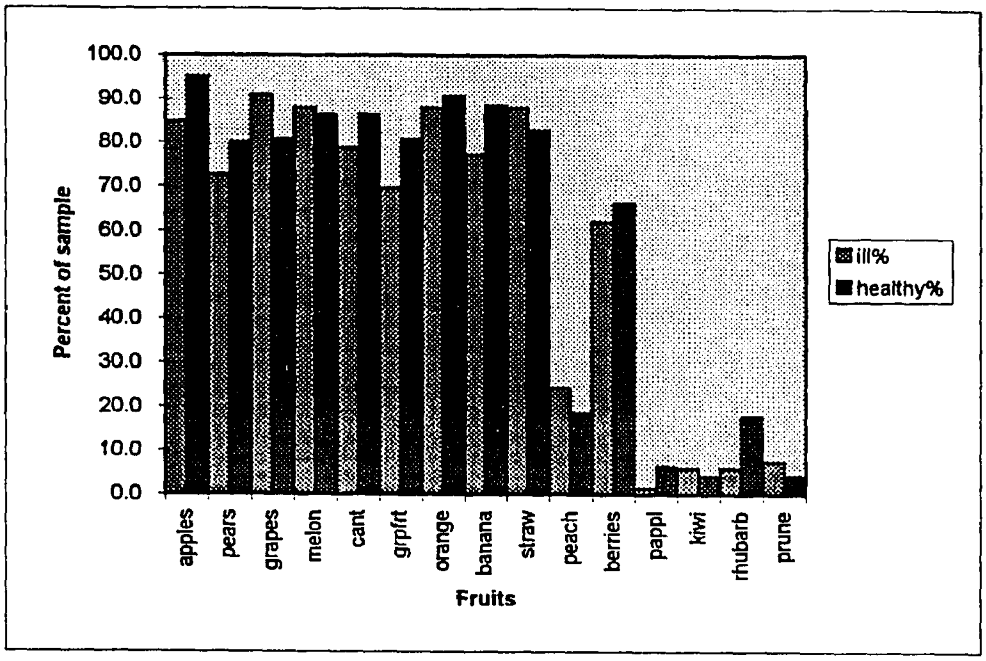

Figure 17 Fruit Consumption in Healthy and Ill survey Participants

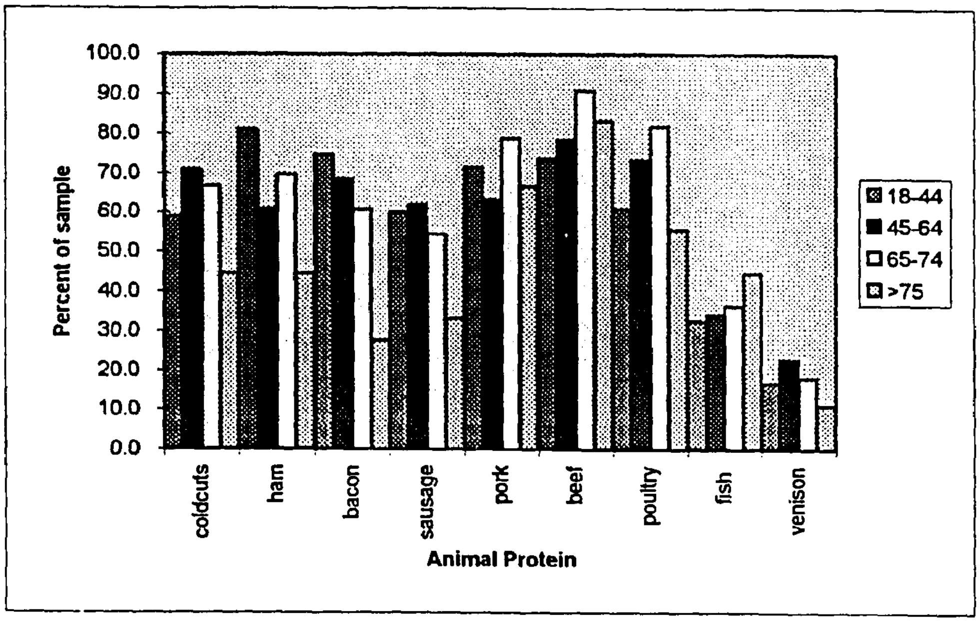

Figure 18 Animal Protein Consumption by Age of Survey Participants

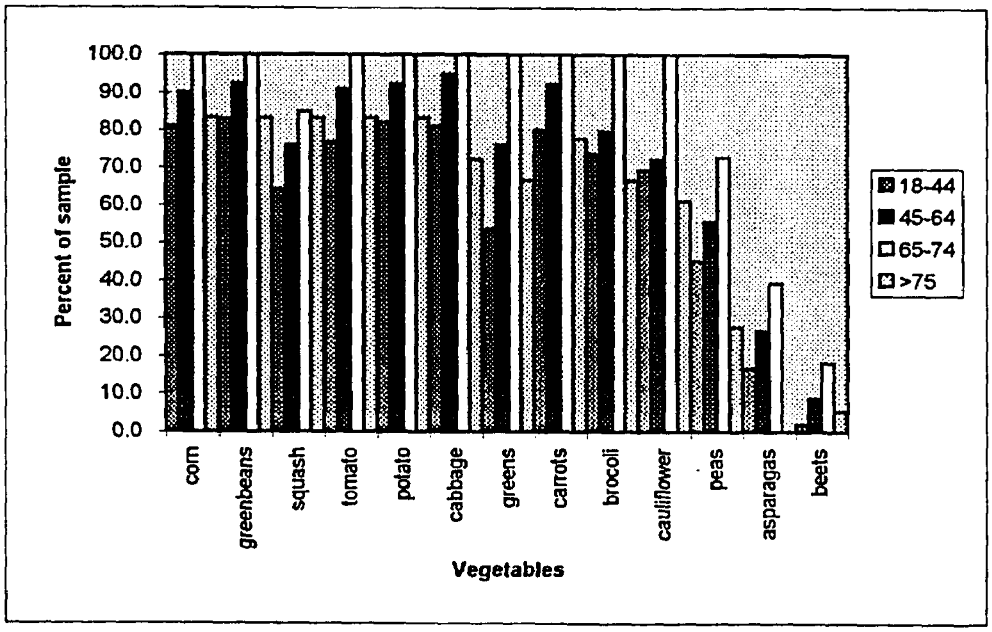

Figure 19 Vegetable Consumption by Age of Survey Participants

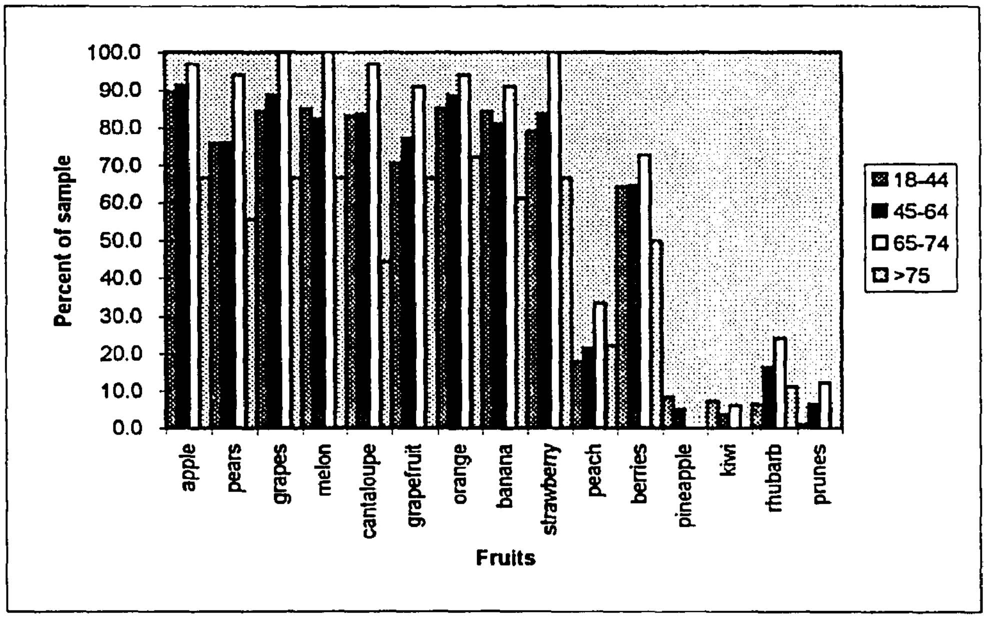

Figure 20 Fruit Consumption by Age of Survey Participants

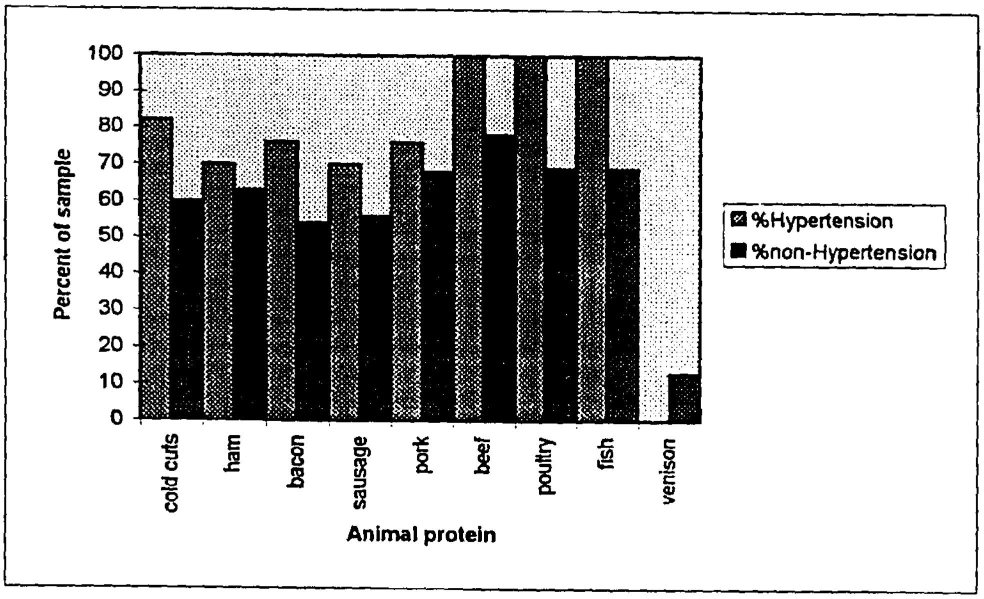

Figure 21 Consumption of Animal Protein by Subjects with and without Hypertension

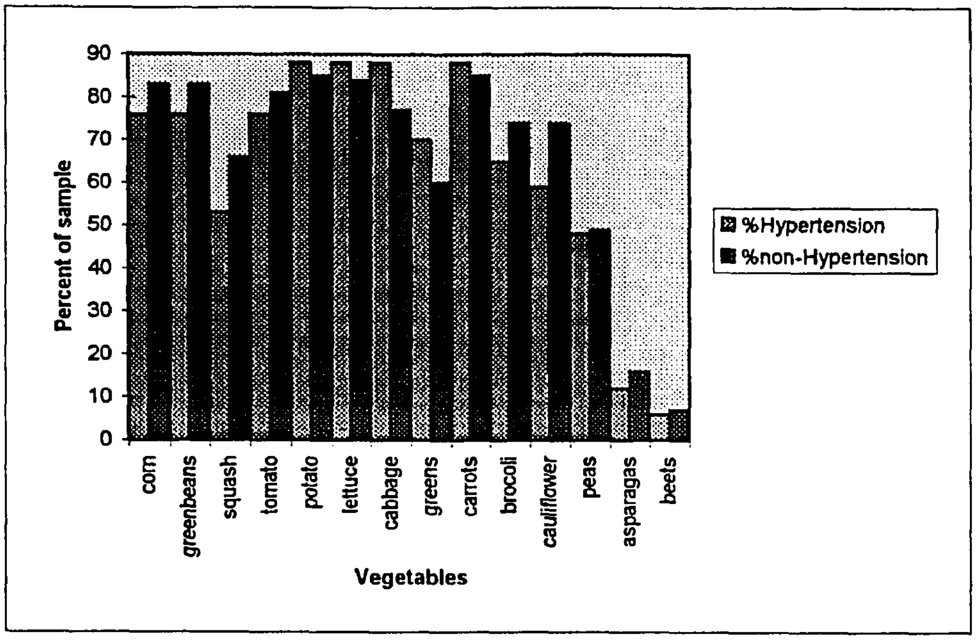

Figure 22 Consumption of Vegetables by Subjects With and Without Hypertension

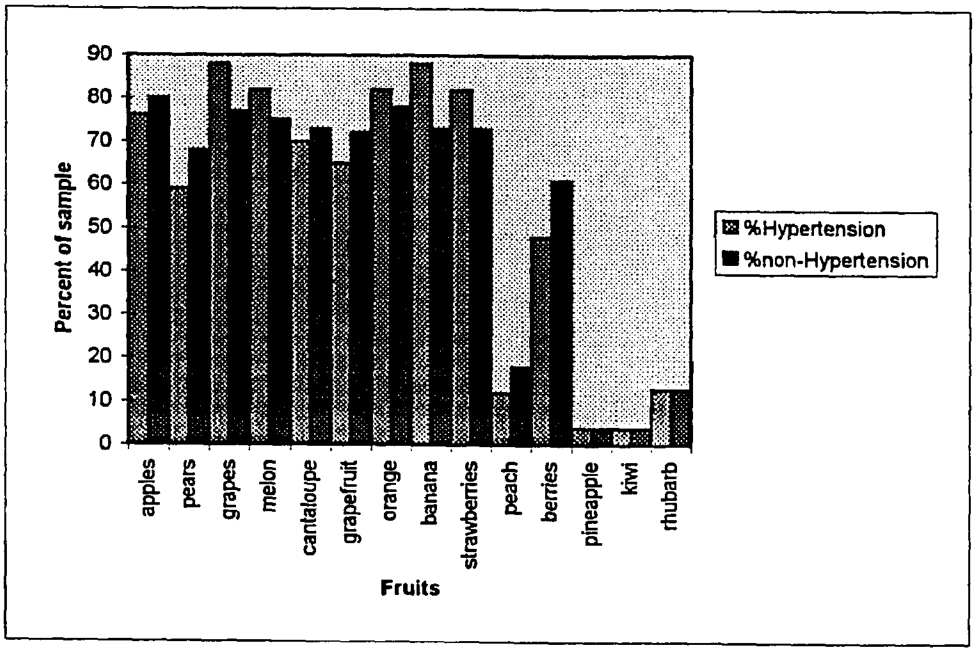

Figure 23 Consumption of Fruit by Subjects With and Without Hypertension

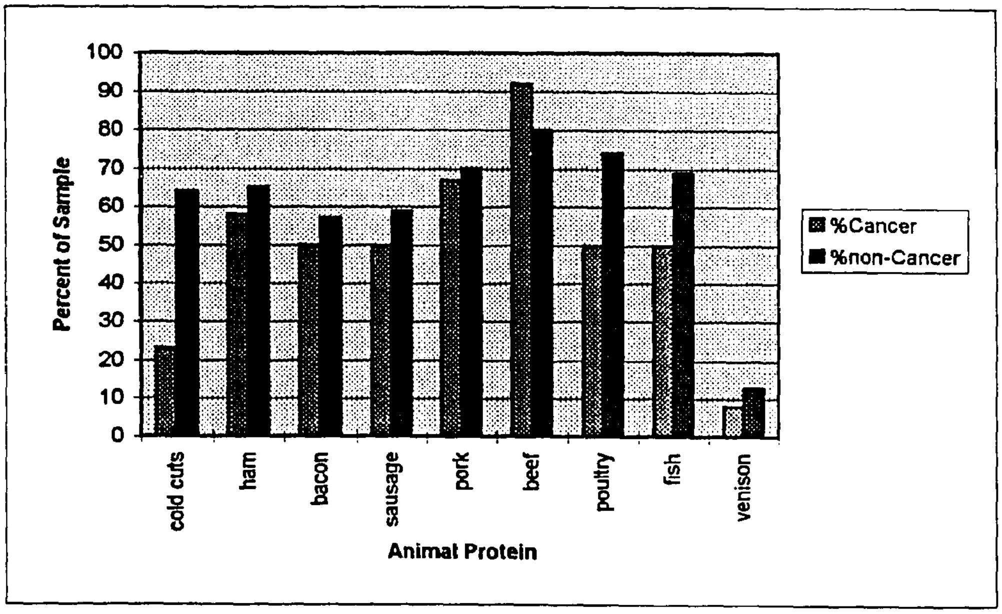

Figure 24 Consumption of Animal Protein by Subjects With and Without Cancer

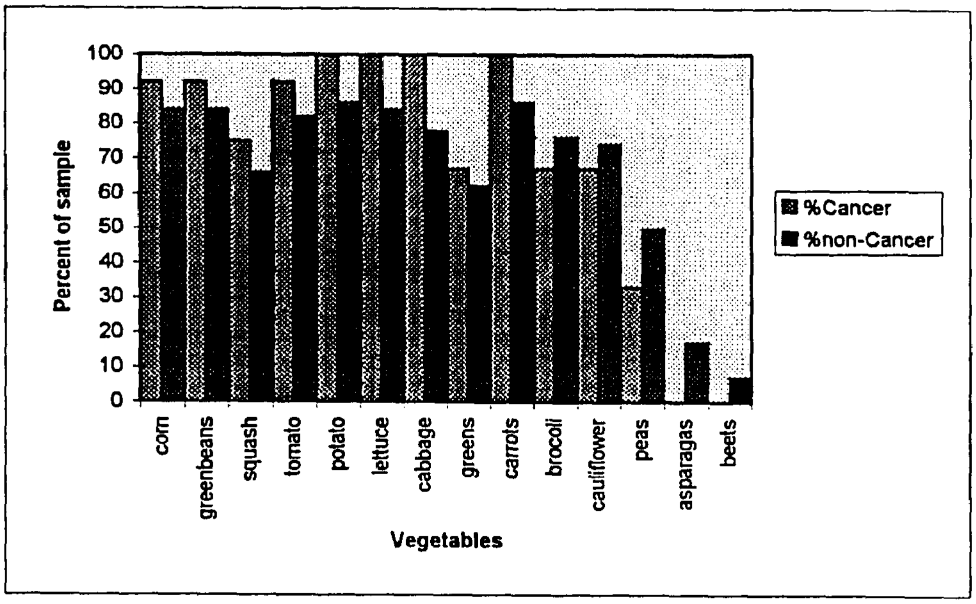

Figure 25 Consumption of Vegetables by Subjects With and Without Cancer

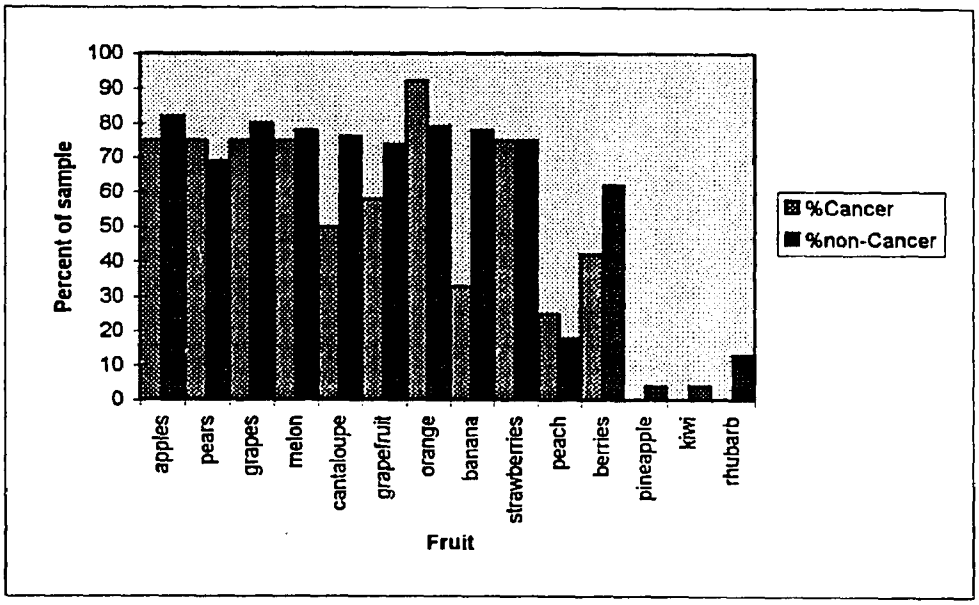

Figure 26 Consumption of Fruit by Subjects With and Without Cancer

This analysis in no way can replace a detailed food analysis. The use of food diaries and duplicate portion studies are still important when trying to establish exacting levels of exposure. However, the expense, and time involved in duplicate portion studies makes them useful on a very limited scale (Salvini et al 1989). Further, the debate among nutritionists about the value of diaries makes them of limited use as well (Jacobson and Bonaa 1990, Persson et al 1990, Margetts et al 1989). The advantages of this type of analysis, are that it is quick, and easy. It gives a general picture of foods consumed in a population as well as the frequency of intake (Margetts et al 1989).

As is shown in Table 47, there appears to be no difference among the various groups with regard to the types and frequency of foods consumed. In no case does the calculated X^2 exceed the tabled value at the 0.05 level. The purpose of the dietary survey was to establish that survey participants are eating a diet that places them well within the range of the norm for other Americans and thus employ the assumption that on average 75 mg nitrate in obtained through the diet. It appears that, while survey respondents may be similar to each other, they are different from the rest of the US population. Patterson et al (1990) report that respondents to the NHANES II study are less likely to report appropriate servings of fruit and vegetables. An estimated 45 percent of this population reported no servings of vegetables or fruit within the last 24 hour period. The respondents to this survey consume both fruit and vegetables with regularity; 95 percent report daily vegetable consumption while 76 percent report daily fruit consumption. It may be that the estimates of nitrates in the American diet are too high if vegetable intake rates are indeed so low. And it may be incorrect to assume such levels for the Cass County respondents. However, one assumption can be maintained; survey respondents have similar diets and nitrate in water is important source in this population of nitrate exposure.

CHAPTER V

SUMMARY AND CONCLUSIONS

The effects of nitrate on human health have been and continue to be debated. Studies have looked at nitrate consumed in food, water and at various times during the life cycle to discover what impact they have on human health. For example, Mirvish (1983) argues that international variation in gastric cancer rates and the strong correlation with nitrate consumption implies a role for nitrate in the etiology of this disease. Other authors have taken a different approach, Knight et al (1990) and Moller et al (1989a &1989b) looked at very small populations, tracing nitrate intake and out go in individuals to estimate body burden of nitrate. Dorsch et al, and Scragg et al report significant levels of risk for babies with central nervous system birth defects among mothers who consume water with elevated nitrates. However, Aschengrau et al (1993) and Arbuckle et al (1988) find a weak link between nitrates and adverse pregnancy outcomes. Comparison among studies is difficult as they are done at different scales and with different populations.

The purpose of this study was to assess the health status of the residents of Cass County and to determine if there is a relationship between nitrate in drinking water and ill health. This study was undertaken partly in response to concerns of Cass County residents, specifically the perception of high and clustered incidence rates of cancer. This area offered the opportunity to look at a population exposed to nitrates, and to work at a scale at which many of the usual confounding factors could controlled. For example, the majority of the population of this county is rural, have lived for a long time in the county and all obtain drinking water from ground water sources.

The survey sample is not identical to the census population, however, it is representative. Use of X^2 and calculation of Odds Ratios to estimate risk is appropriate to assess the association between nitrate and health outcomes (Gordis 1988, Klienbaum 1982). This analysis shows that there may indeed be an association between nitrates and some of the outcomes found among survey respondents. Yet, despite an association between outcome and nitrate consumed in drinking water, the odds ratio reveals that there is no increase in risk of any out come due to elevated nitrate levels.

In order to assure adequate numbers for analysis, cancer cases of all types were grouped. Placing all types of cancer into one category is of course, problematic. It reduces the power of the test by reducing its specificity (Wacholder et al 1989c). However, when interviewing people in both the pretest and the final survey, cancer was always referred to collectively, unless pressed most people did not make any distinction between the various diseases that make up this family. It is partly for this reason, that for analysis, all cancers are classified together and why the disease in this discussion is refereed to collectively. When rates for the various types of cancer are broken out, they are comparable or lower than rates reported at the national level.

Outcomes other than cancer were reported and analyzed for an association with nitrates consumed in drinking water. It was also found that there was is a relationship between nitrates and the prevalence of hypertension, cardiac illness, diabetes and thyroid problems. However, the association is weak, and there is no elevated risk based on the odds ratio. There is no indication in the literature to indicate nitrates in the etiology of these outcomes.

There was only one case of a birth defect found, a case of Downs Syndrome, no analysis was done on this outcome. No instances of methemoglobinemia were found. The only known case was one reported by Dr. Busse' (Personal communication 1993). Another physician interviewed, thought infant methemoglobinemia an "unlikely" diagnosis in Cass County (Jones personal communication 1993).

The ECETOC (1988) argues in their report that the current Maximum Contaminant Level set by WHO is too high given the weak evidence of illnesses associated with nitrates. The authors of this report argue that even methemoglobinemia is so rare that the current standard is too stringent. Other authors have also reported that there is no elevated risk from elevated nitrate levels in drinking water for gastric cancer. Yet the most recent report of methemoglobinemia is from Wisconsin (Henning 1992), indicating that there is still a risk for this outcome. Associations between nitrates and Central Nervous System Birth defects have been shown to be present but weak (Arbuckle 1988). Aschengrau et al (1989) reported no correlation between first trimester spontaneous termination of pregnancy and the nitrate levels in community drinking water supplies.

This study adds to the debate; there is an association found between nitrate levels in drinking water and the most frequent outcomes reported by survey respondents, the distribution of high nitrate levels and ill health are not independent. The difficulty lies in the fact that for many of the outcomes reported factors such as age and income offer explanation for the prevalence and that nitrate concentration in drinking water was measured after diagnosis. All of the outcomes have a latency period of several years, and what role nitrate plays is difficult to discern. However, this study has shown that current nitrate levels and health outcomes may be related. Further, this study has developed a protocol that allows the nitrate consumed in foods and drinking water to be separated. The dietary survey demonstrated that in Cass County most participants consume foods grown and/or purchased locally. The subjects of this study eat remarkably similar diets. While the absolute amounts of each food type is not known, the frequency of consumption and the variety of foods are known. This permits the focus of nitrate consumption to be on drinking water which is easily and cheaply monitored. Thus, this study has provided a framework that can be used to study the relationship between nitrate and drinking water in other counties in Michigan as well as other areas of elevated nitrates throughout the country.

APPENDICES

APPENDIX A

Results From Pilot Study:

TABLE 48
AGE AND SEX DISTRIBUTION IN PILOT STUDY

	Female		Male	
Age	Number	%	Number	%
18 - 44	9	22.5	9	22.5
45 - 64	6	15.0	7	17.5
65 - 74	5	12.5	3	7.5
75 +	0		1	

Average Age = 51 $\pm$ 13.6 n = 40

TABLE 49
NITRATE LEVELS IN THE PILOT STUDY

mg/l Nitrate	Number	Percent
0	8	38.1
.001 - 2.9	3	14.3
3.0 - 6.9	5	23.8
7.0 - 9.9	3	23.8
10.0 +	2	9.5

n = 21 households
mean = 6.5 $\pm$ 12.8 mg/l
range = 0 - 55 mg/l

TABLE 50

EDUCATIONAL ATTAINMENT IN PILOT STUDY

Level Completed	Number	Percent
Less than high school	5	12.8
High School	14	35.9
Tech School	2	5.1
Some College	5	12.8
College	6	15.4
Post Grad/Professional	7	17.0

TABLE 51

HOUSEHOLD INCOME IN PILOT STUDY

Income	Number	%
Less than 10,000	2	9.5
10,000 - 14,999	3	14.3
15,000 - 19,999	0	0
20,000 - 24,999	1	4.8
25,000 - 29,999	3	14.3
30,000 - 34,999	4	19.0
35,000 - 49,000	6	28.6
More than 50,000	1	4.8
Refused/unsure	1	4.8

n = 21

TABLE 52
OCCUPATIONS AMONG PILOT STUDY MEMBERS

Occupational Group	Number	%
Factory	2	4.8
Professionsal Service	10	24.3
Homemakers	6	14.6
Office/Mgmt/Sales	7	17.1
Other Services	3	7.3
Protective Services	1	2.4

Note: There are no farmers in the pilot study.

TABLE 53
RESIDENCE IN CASS COUNTY AND CURRENT ADDRESS

Time in residence	Number	%
Moved to county since 1987	8	20.5
Lived in county before 1987	31	79.5
Mean = 16.9 $\pm$ 21.0 years Range 1.5 - 72		
Moved to current address since 1987	16	41.0
Lived at current address before 1987	23	58.9
Mean 12.96 $\pm$ 12.21 years Range 1.5 - 48		

TABLE 54

INSURANCE IN PILOT STUDY GROUP

Insurance	Number	%
Yes	35	89.7
No	4	10.2
Carrier		
Private	30	76.9
Medicare + Supplement	5	12.8

TABLE 55

OUTCOMES IN PILOT STUDY GROUP

Illness	Number	%
Hypertension	2	5.1
Diabetes	3	7.7
Cancer	3	7.7
Thyroid	1	2.6
Hernia	2	5.2
Gasric	2	5.2

n = 39 12 ill, 30.8%

TABLE 56

OUTCOMES BY AGE,SEX, OCCUPATION AND NITRATE CONSUMED

Illness	Age	Sex	Occupation	Nitrate Consumed
Gall Bladder	43	F	Professor	3.9 (mg)
Gastritis	30	F	Student	0
Hypertension	44	M	Professor	3.9
Hypertension	49	M	Police Officer	10.4
Diabetes	54	F	Retired	0
Diabetes	73	F	Retired	21.1
Thyroid	54	F	Retired	0
Hernia	73	F	Retired	10.4
Hernia	58	F	Sales	0
Cervical Cancer	49	F	Therapist	0
Non-Hodgkins L	61	M	Retired	3.6

Note, that unlike the survey sample most of the respondants with illnesses are female and generally much younger.

TABLE 57
FOOD TYPES IN PILOT GROUP

Food	Number	%
Cold Cuts	14	35.8
Ham	18	46.1
Sausage	18	46.1
Bacon	26	66.7
Beef	26	66.7
Pork	18	46.1
Poultry	18	46.1
Fish	6	15.4
Venison	4	10.3
Corn	20	51.3
Green Bean	20	51.3
Squash	10	25.6
Tomatoes	20	51.3
Potatoes	20	51.3
Lettuce	24	61.5
Cabbage	14	35.9
Greens	10	25.6
Carrots	20	25.6
Brocoli	18	46.1
Cauliflower	16	41.0
Apples	20	51.3
Pears	16	41.0
Grapes	22	56.4
Melon	20	51.3
Cantaloupe	20	51.3
Grapefruit	18	46.1
Oranges	20	51.3
Banana	16	41.0
Strawberries	8	20.5

TABLE 58
FREQUENCY OF FOOD CONSUMPTION

Days/Week	Animal Protein	Vegetables	Friut
5 - 7	76.9	94.9	66.7
3 - 4	15.4	5.1	15.4
1 - 2	5.1	0	5.1
0	0	0	5.1

APPENDIX B

SAMPLE HEALTH QUESTIONNAIRE

I. <u>Household</u>

1. How many men ______ women ______ children ______
   Ages

men	women	children
______	______	______
______	______	______
______	______	______
______	______	______

2.) How long have you lived in Cass County? ________ other members ________, ________, ________.

3.) How long have you lived at your current address? ________ other members ________, ________, ________

4.) What is your current occupation? ________

yourself   other adults

1.employed for wages
2.self employed
4.out of work + 12 months
5.Homemaker
6.student
7.retired
9.refused

5.) How long have you been employed in your current occupation?________, other adults ________, ________, _

6.) If retired what was your occupation before you retired?________, other adults________, ________,

7.) For how long did you work in this occupation?________ other adults, ________, ________, ________.

8.) Education: grade level completed:

yourself   other adults

1. less than eighth grade
2. some high school
3. high school graduate, GED
4. some technical school
5. tech school graduate
6. some college
7. college grad
8. post grad or professional degree
9. refused

9. Are you
   1.married
   2.divorced
   3.widowed
   4.separated
   5.never married,
   6.member of a domestic partnership
   9.refused

II Well Information

10.) What is the age of the well?__________ Recent repairs, casing changes etc?

11.) How deep is the well? ____________

12.) Do you make coffee, tea, juice, soft drinks from well water?_____________

13.) Where is well located? __________

14.) Do you have a septic system?
1. yes 2. no 8.Don't know/not sure 9. refused

15.) What is the approximate location of the leach field?
1 north 2 south 3 east 4 west 8 don't know/not sure
9 refused

III Estimated Consumption

16.) How many glasses of water do you drink each day?______

17.) What size glass you usually use?___________

18.) How many cans/glasses of commercially prepared soda do you drink each day?____________

19.) If you work away from home, how much soda, tea/coffee or water do you consume there?______________

20.) How often do you and your family eat the following?

cold cuts
ham
sauasage
bacon
other types
of pork
hamburger
other types
of beef
vegetables ____/day(1) ____/week(2) ____never(5) _____
Don't know/not sure(8) _____ refused(9) corn
green beans
squash
tomatoes
potatoes
letttuce
cabbage
greens (type)
carrots
other
fruits ____/day(1) ____/week(2) ____never(5) _____
Don't know/not sure(8) _____ refused(9)
apples
pears
grapes
melon
cantalope
grapefruit
oranges
other

21.) Do you grow your own vegetables?
1. yes 2. no 8. Don't know/not sure 9. refused

22.) Do you buy them from a local produce market?
1. yes 2. no 8. Don't know/not sure 9. refused

23.) Do you buy them from a grocery store?
1. yes 2. no 8. Don't know/not sure 9. refused

IV Health Issues

24.) Do you have a family physician?
1. yes 2. no 8. Don't know/not sure 9. refused

25.) If # 39=no, where do you and other members of your household obtain primary care?
1. emergency room 2. free standing clinic 3. don't get primary care 8. don't know/not sure 9. refused

26.) How long since your last check up?
1. 0 - 12 months
2. 13 - 24 months
3. 25 - 60 months
4. 61 + months
5. never
8. don't know/not sure
9. refused
repeat for each household member

27.) Do you have a health care plan?
1. yes 2. no 8. Don't know/not sure 9. refused

28.) Is your health care from a private company or from the public sector?
1. yes 2. no 8. Don't know/not sure 9. refused

29.) Does your health care plan cover all, most some, none of your expenses if hospitalized?
1. all
2. most
3. some
4. none
8. don't know/not sure
9. refused

30.) Does your health care plan cover doctor's visits or preventive measures?
1. all
2. most
3. some
4. none
8. don't know/not sure
9. refused

31.) Has any member of your household been hospitalized within the last 12 months?
1 yes 2 no 8 not sure 9 refused

32.) Who?

33.) What was the diagnosis?

34.) Do you smoke?
1 yes 2 no 8 not sure 9 refused
repeat for household

35.) Have you ever smoked?____________
1 yes 2 no 8 not sure 9 refused
repeat for household

For the following the following questions, please use the following responses.
1. yes, 2. no, 8. not sure/don't know 9. refused

36.) Have you had a baby in the last five years?
If yes # 52, date of birth
Did you/mother receive prenatal care?
1 yes 2 no 8 not sure 9 refused

37.) Was the pregnancy and its outcome normal?
1 yes 2 no 8 not sure 9 refused

38.) Have you/women in household had a miscarriage in the last 5 years?
If yes # 54, Date of miscarriage,

39.) Have had a baby within the last five years that has been diagnosed with:
Hydrocephaly
Anacephaly
Spina bifida
Cleft palate
low birth weight
failure to thrive
methemoglobinemia

40.) Has anyone in this house hold, including your self been diagnosed with any of the following?
stomach cancer
esophageal cancer
bladder cancer
pancreatic cancer
liver cancer
leukemia
non-lymphatic leukemia

41.) Have you/ other members of your household had any other health problems within the last five years?

42.) Household income

1. less than 10,000/year or 833/month, 208/week
2. more than 10,000/year, less than 15,0000/year or 1250/month or 312/week
3. more than 15,000/year, less than 20,000/year or 1667/month or 417/week
4. more than 20,000/year, less than 25,000/year or 2083/month or 729/week
5. more than 25,000/year, less than 35,000/year or 2917/month or 1049/week
6. more than 35,000/year, less than 50,000/year or 4167/month or 1041/week
7. more than 50,000/year
8. don,t know/ not sure
9. refused

BIBLIOGRAPHY

BIBLIOGRAPHY

ABEL U. and Becker N. 1987 Geographical Clusters and Common Patterns in Cancer Mortality of the Federal Republic of Germany. Archives of Environmental Health 42(11) pp. 51 - 57

AICKIN M., Dunn C.N., and Flood T.J., 1991 Estimation of Population Denominators for Public Health Studies at the Tract, Gender and Age-Specific Level. American Jouranl of Public Health. 81 pp. 918-920

ANDERSON J.H., 1987 Agriculture and Natural Resources: The Broadening Horizon. in Rural Groundwater Contamination. D'Itri F.M and Wolfson L.G. editors Lewis Publishers Inc.Chelsea MI 48118

ARBUCKLE T.E., Sherman G.J., Corey P.N., Walters D., and Lo B. 1988 Water Nitrates and CNS Birth Defects: A Population-Based Case-Control Study. Archives of Environmental Health 43(2) pp.162-16

ARMENIAN H.K., 1991 Case Investigation in Epidemiology. American Journal of Epidemiology. 134(10) pp. 1067-1077

ARMIJO R. and Coulson A., 1975 Epidemiology of Stomach Cancer in Chile - The Role of Nitrogen Fertilizers. International Journal of Epidemiology 4(4) pp. 301-309

ARMIJO R., Orellana M., Medina E., Coulson A.H., and Sayre J.W., Detels R., 1981 Epidemiology of Gastric Cancer in Chile: I - Case Control Study. International Journal of Epidemiology. 10(1) pp 53-56

ARMIJO R., Gonzalez A., Orellana M., Coulson A. H., Sayre J.W., and Detels R., 1981 epidemiology of Gastric Cancer in Chile: - II - Nitrate Exposures and Stomach Cancer Frequency. International Journal of Epidemiology 10(1) pp. 57-62

ASCHENGRAU A., Zierler S., and Cohen A., 1993 Quality of Community Drinking Water and the Occurrence of Late Adverse Pregnancy Outcomes. Archives of Environmental Health 48(2) pp. 105-113

ASCHENGRAU A., Zierler S., and Cohen A., 1989 Quality of Drinking Water and the Occurrence of Spontaneous Abortion. Archives of Environmental Health 44(5) pp. 283-290

BAKER D.B., Greenland, S., Mendlein J., and Harmon P., 1988 A Health Study of Two Communities Near the Stringfellow Waste Disposal Site. Archives of Environmental Health 43(5) pp. 325-334

BAKER D.B., 1985 Regional Water Quality Impacts of Intensive Row-Crop Agriculture: A Lake Eire Basin Case Study. Journal of Soil and Water Conservation 40 pp. 125-132

BAKER J.L., Kanwar R.S., and Austin T.A., 1985 Impact of Agricultural Drainage Wells on Groundwater Quality. Journal of Soil and Water Conservation 40 pp 516-520

BEDNAR C.M., and Kies C., 1991 Inorganic Contaminants in Drinking Water Correlated with Disease Occurrence in Nebraska. Water Resources Bulletin. 27(4) pp. 631-635

BERESFORD S.A., 1981 The Relationship between Water Quality and Health in the London Area. International Journal of Epidemiology 10(2) pp. 103-115

BERESFORD S.A., 1985 Is Nitrate in Drinking Water Associated with the Risk of Cancer in the Urban UK? International Journal of Epidemiology 14(1) pp.57-63

BOEING H., and Frentzel-Beyme R., 1991 Regional Risk Factors for Stomach Cancer in the FRG. Environmental Health Perspectives 94 pp. 83-89

BORZELLECA J.F., 1981 Report of the NATO/CCMS Drinking Water Pilot Study on the ASpects of Drinking Water Contaminants. The Science of the Total Environment. 18 pp. 205-217

BOUND J.P., Harvey P.W., and Francis B.J., 1989 Seasonal Prevalence of Major Congenital Malformations in the Flyde of Lancashire. International Journal of Epidemiology and Community Health 43 pp. 330-342

BOUND J.P., Harvey, P.W., Brookes D.M., and Sayers, B.Mc A., 1981 The Incidence of of anencephalus in the Flyde Peninsula 1956-76 and Changes in Water Hardness. Journal of Epidemiology and Community Health 35 pp. 102-205

BOWMAN W.L., 1991 Soil Survey of Cass County, MI Soil Conservation Service, United States Dept. Of Agriculture, U.S. Government Printing Office, Washington, D.C. 20402

BURT T., and Haycock N., 1991 Farming and Nitrate Pollution. Geography 76 (330) pt1 pp.60-63

CAIN D., Helsel D.R., and Ragone S.E., 1989 Preliminary Evaluations of Regional Ground Water Quality. Ground Water 27(2) pp.230-244

CANTER L.W., 1988 Nitrates and Pesticides in Groundwater: An Analysis of a Computer Based Literature Search. pp 153-173 In: Ground Water Quality and Agricultural Practices. Deborah M. Fairchild, editor

CARPENTER L.M. and Beresford, S.A.A. 1986 Cancer Mortality and Type of Water Source: Findings from a Study in the UK. International Journal of Epidemiology 15(3) pp.312-320)

CHILVERS C., Inskip, H., Caygill, C., Bartholomew, B., Fraser, P., and Hill, M., 1984 A Survey of Dietary Nitrate in Well-Water Users. International Journal of Epidemiology 13(3) pp.324-331

COMLY H.H., 1945 Cyanosis in Infants Caused by Nitrates in Well Water. Journal of the American Medical Association, Landmark Article 1987 257(20)

CORREA P., Cuello C., and Duque E., 1970 Carcinoma and Intestinal Metaplasia of the Stomach in Colombian Migrants. Journal of the National Cancer Institute. 44 pp. 297-306

CRAUN G.F., Greathouse D.G., and Gunderson D.H., 1981 Methemoglobin Levels in Young Children Consuming High Nitrate Well Water in the United States. International Journal of Epidemiology 10(4) pp. 309-317

DELEON I.R., Byrne C. J., Peuler E.A. Antoine S.R., Schaffer J., and Murphy R.C. 1986 Trace Organic and Heavy Metal Pollutants In the Mississippi River. Chemosphere 15(6) pp. 795- 805

D'ITRI F.M. and Wolfson L.G., 1987 Rural Groundwater Contamination Lewis Publishers, Chelsea MI 48118

D'ITRI F., Kittleson K.M., and Kruska R.M. 1985 Spatial Analysis of Michigan Department of Public Health Data. Institute of Water Research, Michigan State University, East Lansing MI.

DUTT M.C., Lim H.Y., and Chew R.K.H., 1987 Nitrate consumption and the Incidence of Gastric Cancer in Singapore. Food Chemistry and Toxicology 25(7) pp. 515-520

DORSCH M.M., Scragg R.K.R., McMichael A.J., Baghurst P.A., and Dyer K.F., 1984 Congenital Malformations and Maternal Drinking Water in Rural South Australia: A Case-Control Study. American Journal of Epidemiology 119(4) pp. 473-486

EGBOKA B.C.E., 1984 Nitrate Contamination of Shallow Groundwaters in Ontario, Canada. Science of the Total Environment. 35 pp. 53-70

ELLIS B.G., and Olson R.A., 1988 Nitrates in Water Supplies: Proceedings of Conference on Water Quality: A Realistic Perspective. Ann Arbor MI.

ELWOOD J.M. and Coldman A.J., 1981 Water Compposition in the Etiology of Anencephalus. American Journal of Epidemiology 113(6) pp.681-690

ENDELMAN F.J., Keeney D.R., Gilmour J.T., and Saffigna P.G., 1974 Nitrate and Chloride Movement in the Plainfield Loamy Sand Under Intensive Irrigation. Journal of Environmental Quality 3(2) pp.295-298

ERICSON A., Ericson M., Kallen B., and Meirik O., 1987 Birth Weight Distribution as an Indicator of Environmental Effects on Fetal Development. Scandinavian Journal of Social Medicine. 15 pp. 11-15

ERVIN J.E. 1992 Personal Communication. Michigan State Univesity Institute for Water Research, East Lansing, Michigan

EUROCAT Working Group 1991 Prevalence of Neural Tube Defects in 20 Regions of Europe and the Impact of Prenatal Diagnosis, 1980-1986. Journal of Epidemiology and Community Health 45 pp. 52-58

ECETOC 1988 EUROPEAN CHEMICAL INDUSTRY ECOLOGY AND TOXICOLOGY CENTRE 1988 Technical Report Number 27, Nitrate and Drinking Water.

FEDKIW J., 1990 Nitrate Occurrence in the U.S. Waters Associated with Agriculture. Report by USDA's Working Group on Water Quality.

FLANDERS W.D., Lin L., Pirkle J.L., and Caudill S.P., 1992 Assessing the Direction of Causality in Cross-sectional Studies. American Journal of Epidemiology. 135(8) pp. 926-935

FLATEN T.P. and Bolviken B., 1991 Geographical Associations Between Drinking Water Chemistry and the Mortality and Morbidity of Cancer and Some Other Diseases in Norway. The Science of the Total Environment pp. 75-102

FLIPSE W.J. and Bonner F.T., 1985 Nitrogen-Isotope Ratios of Nitrate in Ground Water Under Fertilized Fields, Long Island, New York. Ground Water 23(1) pp. 59-67

FORMAN D., Al-Dabbagh S., and Doll R., 1983 Nitrates, Nitrites and Gastric Cancer in Great Britain. Nature 313

FRASER P. and Chilvers C. 1981 Health Aspects of Nitrate in Drinking Water. The Science of the Total Environment 18 pp 103-116

FUSSE F. 1993 Personal Communication. Pathologist, Niles Michigan

GELEPERIN A., Moses V.J., and Fox/Chicago G., 1976 Nitrate in Water Supplies and CAncer. Illinois Medical Journal. March pp.251-253

GERHART P., 1986 Ground-Water Recharge and Its Effects on Nitrate Concentrations Beneath a Manured Field Site in Pennsylvania. Ground Water 24(4) pp. 483-489

GILLI G., Corrao G., and Favilli S., 1984 Concentrations of Nitrates in Drinking Water and Incidence of Gastric Carcinomas: First Descriptive Study of the Piemonte Region, Italy. Science of the Total Environment 34(1-2) pp. 35-48

GOODENKAUF O. and Atkinson J.C., 1986 Occurrence of Volatile Organic Chemicals in Nebraska Ground Water. Ground Water 24(2) pp. 231-233

GOODRICH J.A., Lykins B.W., and Clark R.M., 1991 Drinking Water from Agriculturally Contaminated Drinking Water. Journal of Environmental Quality 20(4) pp. 707-717

GORDON J.E. and Shy C.M., 1981 Agricultural Chemical USe and Congenital Cleft Lip and Palate. Archives of Environmental Health. 36(5) pp. 212-221

GORDIS L., 1988 Estimating Risk and Inferring Causality in Epidemiology In: Epidemiology and Health Risk Assessment. Leon Gordis, ed

HAENSZEL W., Kurihara M., Locke F.B., Shimuzu K., and Segi M., 1976 Stomach Cancer in Japan. Journal of the National Cancer Institute. 56(2) pp. 265-274

HAENSZEL W., Kurihara M., Segi M., and Lee R.K.C., 1972 Stomach Cancer Among Japanese in Hawaii. Journal of the National Cancer Institute. 49 pp. 969-988

HALBERG G.R., 1987 Nitrates in Iowa Groundwater. In: Rural Groundwater Contamination. ed. D'Itri F.M. and Wolfson L.M. Lewis Publishers Inc. Chelsea MI 48118

HATHCOCK A.L., Greenberg R.A., and Dakan A.W., 1982 An Analysis of Lung Cancer on a Microgeographical Level. Social Science and Medicine. 16 pp. 1235-1238

HENNINGS R., 1992 Should We Change the Nitrate Level? Editorial in SURVIEW 13(1) pp 2

HERGERT G.W., 1986 Nitrate Leaching Through Sandy Soils as Affected by Sprinkler Irrigation Management. Journal of Environmental Quality 15(3) pp.272-278

Interamerican Group for Research in Environmental Epidemiology 1990 The Health of Latin Americans Exposed to Polluted Rivers: A Triple-Blind Observational Study. International Journal of Epidemiology 18(4) pp. 1091- 1099

ISACSON P., Bean J.A., Splinter R., Olson, D.B., and Kohler, J. 1985 Drinking Water and Cancer Incidence in Iowa III Association of Cancer with Indices of Contamination. American Journal of Epidemiology 121(6) pp. 856-869

ISENSEE A.R., Nash R.G., and Helling C.S. 1990 Effect of Conventional vs. No-Tillage on Pesticide Leaching to Shallow Groundwater. Journal of Environmental Quality 19 pp. 434-440

JACOBSEN B.K. and Bonaa K.H., 1990 The Reproducibility of Dietary Data from a Self-Administered Questionnaire. The Tromso Study. International Journal of Epidemiology 19(2) pp. 349-353

JACOBSEN B.K., Knutsen S.F., and Knutsen R., 1987 The Tromso Heart Study: Comparison of Information from a Short Food Frequency Questionnaire with a Dietary History Survey. Scandinavian Journal of Social Medicine 15 pp 4-47

JOHNSON C.J. and Kross B.C., 1990 Continuing Importance of Nitrate Contamination of Groundwater and wells in Rural Areas. American Journal of Industrial Medicine 18 pp. 449-456

JONES P. 1993 Personal Communication. General Practitioner Dowagiac, Michigan

JORDE L.B., Fineman B.M., and Martin R.A., 1984 Epidemiology of Neural Tube Defects in Utah, 1940-1979. American Journal of Epidemiology 119(4) pp. 487-495

JUNK G.A., Spalding R.F., and Richard J.J., 1980 Areal, Vertical and Temporal Differences in Ground Water Chemistry: II. Organic Constituents. Journal of Environmental Quality 9(3) pp. 479-483

KALLEN B. and Lofkvist E., 1984 Time Trends of Spina Bifida in Sweden 1947-81. Journal of Epidemiology and Community Health 38 pp. 103-107

KHOURY M.J., Erickson J.D., and James L.M., 1982 Etiologic Heterogeneity of Neural Tube Defects: Clues from Epidemiology. American Journal of Epidemiology 115(4) pp. 538-548

KITTLESON K.M. and Kruska R.L., 1987 Spatial Distribution and Analysis of Groundwater Nitrate Contamination in Kalamazoo County, Michigan. Center for Remote Sensing, Michigan State University, East Lansing, MI 48823

KLEINBAUM D.G., Kupper L.L., and Morgenstern H., 1982 Epidemiological Research: Principles and Quantitative Methods. Liftime Learning Publications, Belmont CA

KLEINBAUM D.G., Morgenstern H., and Kupper L.L., 1981 Selection Bias in Epidemiological Studies. American Journal of Epidemiology. 113(4) pp. 452-463

KLEINJANS J.C.S., Albering H.J., Marx A., vanMaanen J.M.S., van Agen B., ten Hoor F., Swaen G.M.H., and Mertens P.L.J.M., 1991 Nitrate Contamination of Drinking Water: Evaluations of Genotoxic Risk In Human Populations. Environmental Health Perspectives 94 pp. 189-193

KLEPPER R., 1978 Nitrogen Fertilizer and Nitrate Concentrations in Tributaries of the Upper Sangamon River in Illinois. Journal of Environmental Quality 7(1) pp.13-22

KNIGHT T.M., Forman D., Al-Dabbagh S.A., and Doll R., 1987 Estimation of Dietary Intake of Nitrate and Nitrites in Great Britain. Food and Chemical Toxicology 25(4) pp. 277-285

KNIGHT T.M., Forman, D., Pirastu R., Comba, P., Iannarilli, Cocco, P.L., Angotz, G., Nino, E., and Schierano, S., 1990 Nitrate and Nitrite Exposure in Different Italian Populations with Different Gastric Cancer Rates. International Journal of Epidemiology 19(3) pp 510-515

KNOBELOCH L., 1993 Personal Comunication. Department of Human Social Services, Madison, Wisconsin

KOIVUSALO M., Jaakkola J.J., Vartiainen T., Hakulinen T., Karjalainen S., Pukkala E., and Tuomisto J., 1994 Drinking Water Mutagenicity and Gastrointestinal and Urinary Tract Cancers: An Ecological Study in Finland. American Journal of Public Health 84 pp. 1223-1228

KROSS B.C., Hallberg G.R. Bruner D.R., Cherryholmes K., and Johnson J.K., 1993 The Nitrate Contamination of Private Well Water in Iowa. American Journal of Public Health. 83 pp. 270-272

LEE L.K. and Nielsen E.G. 1987 The Extent and Costs of Groundwater Contamination by Agriculture. Journal of Soil and Water Conservation 42 pp. 243-248

LOVETT A.A., Gatrell A.C., Bound J.P., Harvey P.W., and Whelan A.R., 1990 Congenital Malformations in the Flyde Region of Lancashire, England 1957-1973. Social Science and Medicine. 30(1) pp. 103-109

LUSCH D.P. and Ervin J.E., 1990 Analyzing and Assesing Risks Through Geographic Information Systems. Conference on Assessing Agricultural Impacts on Groundwater Quality. Agriculture and Natural Resources Week, Michigan State University, East Lansing Michigan.

LUKENS J.N., 1987 The Legacy of Well Water Methemoglobinemia. Journal of the American Medical Association 257(20) pp. 2793-2795

MARGETTS B.M., Cade J.E., and Osmond C., Comparison of a Food Frequency Questionnaire with a Diet Record. International Journal of Epidemiology 18(4) pp.868-873

MACLEAN M.H. and MacLeod A., 1984 Seasonal Variation in the Frequency of Anencephalus and Spina Bifida Births in the United Kingdom. Journal of Epidemiology and Community Health 38 pp. 99-102

MATTHEWS S.A., 1990 Gastric Cancer: an Epidemiologic Review Environmental Geochemistry and Health 12 pp 201-214

MICHIGAN DEPARTMENT OF PUBLIC HEALTH 1990 Michigan Health Statistics, 1988 Office of the State Registrar and Center for Health Statistics, Lansing MI

MIRVISH S.S., 1983 Etiology of Gastric Cancer. Journal of the National Cancer Institute 71(3) pp.631-647

MOLLER H., Landt J., Pedersen E., Jensen P., Autrup, H., and Jensen, O., 1989 Endogenous Nitrosation in Relation to Nitrate Exposure from Drinking Water and Diet in a Danish Rural Population. Cancer Research 49 pp. 3117-3121

MOLLER H., Landt J., Jensen P., Pedersen E., Autrup H., and Jensen O., 1989 Nitrate Exposure from Drinking Water and Diet in a Danish Rural Population. International Journal of Epidemiology 18(1) pp. 206-212

MORIN M.M., Sharret A.R., Bailey K.R., and Fabsitz R.R., 1985 Drinking Water and Source and Mortality in US Cities. International Journal of Epidemiology 14(2) pp.254-264

NAJEM G.R., Thind I.J., Lavenhar M.A., and Louria, D.B., 1983 Gastrointestinal Cancer Mortality in New Jersey Counties, and the Relationship with Environmental Variables. International Journal of Epidemiology 12(3) pp.276-289

NATIONAL WATER SUMMARY 1986 Groundwater Quality: Michigan USGS, Lansing MI

OLSHAN A.F. and Faustman E.M., 1989 Nitrosable Drug Exposure During Preganancy and Adverse Preganancy Outcome. International Journal of Epidemiology 18(4) pp. 891-899

PACKER P.J. Leach S.A., Duncan S.N., Thompson M.H., and Hill M.J., 1989 The Effect of Different Sources Of Nitrate Exposure on Urinary Nitrate Recovery in Humans and its Relevance to the Methods of Estimating Nitrate Exposure in Epidemiological Studies. Carcinogenesis 10(11) pp.1989-1996

PAGE G.W., 1987 Water and Health In: Public Health and the Environment: The United States Experience. ed. M.R. Greenburg. Guilford Press New York 10003

PALDY A., Puskas N., and Farkas I., 1988 Pesticide Use Related to Cancer Incidence as Studied in a Rural District of Hungary. The Science of the Total Environment. 73 pp. 229-244

PASSERO R.N. and Straw W.T., 1988 Groundwater in Southwest MIchigan: A Guide for Citizens and Public Officials Concerned with Protecting Our Underground Drinking Water Supplies pp 1-43 Western Michigan University

PATTERSON B. H., Block G., Rosenberger W.F., Pee D., and Kahle L.L., 1990 Fruit and Vegetables in the American Diet: Data from the NHANES II Survey. American Journal of Public Health 80(12) pp.1443-1449

PEREIRA W.E., Rostad C.E., and Leiker T.J., 1990 Distribution of Agrochemicals in the Lower Mississippi River and Its Tributaries. The Science of the Total Environment 97/98 pp.41-53

PERSSON P-G., Ahlbom A., and Norell S., 1990 Retrospective versus Original Information on Diet: Implications for Epidemiological Studies. International Journal of Epidemiology 19(2) pp. 343-348

SALVINI S., Hunter D.J., Sampson L., Stampfer M.J., Colditz G.A., Rosner B., and Willett W.C., 1989 Food-Based Validation of a Dietary Questionnaire: The Effects of a Week to Week Variation in Food Consumption. International Journal of Epidemiology 18(4) pp. 858-867

POINKE H.B. and Urban J.B., 1985 Effects of Agricultural Land Use on Ground Water Quality in a Small Pennsylvania Watershed. Ground Water 23(1) pp. 68-80

RADEMACHER J.J., Young T.B., and Kanarek M.S., 1992 Gastric Cancer Mortality and Nitrate Levels in Wisconsin Drinking Water. Archives of Environmental Health 47(4) pp. 292-294

RAJAGOPAL R. and Tobin G., 1989 Expert Opinion and Ground-Water Quality Protection: The Case of Nitrate in Drinking Water. Ground Water. 27(6) pp. 835-847

REIF J., Pearce N., and Fraser J., 1989 Cancer Risks In New Zealand Farmers. International Journal of Epidemiology 18(4) pp. 768-774

ROHT L.H., Vernon S.W., Weir F.W., Pier S.M., Sullivan P., and Reed L.J., 1985 Community Exposure to Hazardous waste Disposal Sites: Assessing Reporting Bias. American Journal of Epidemiology. 122(3) pp. 418-433

SAFFIGNA P.G. and Keeney D.R. 1977 Nitrate and Chloride Under Irrigated Agriculture in Central Wisconsin. Ground Water 15(2) pp. 170-177

SCHULMAN J., Selvin S., Shaw G.M., and Malcoe L.H., 1993 Exposure Misclassification Due to Residential Mobility during Pregnancy in Epidemiologic Investigations of Congenital Malformations. Archives of Environmental Health 48(2) pp. 114-119

SCHULMAN J., Selvin S., Shaw G.M., and Malcoe L.H. 1990 Detection of Exess Disease Near an Exposure Point: A Case Study. Archives of Environmental Health 45(3) pp.168-174

SCHWARTZ S., 1994 The Fallacy of the Ecological Fallacy: The Potential Misuse of a Concept and Consequences. American Journal of Public Health 84 pp. 819-824

SCRAGG R.K.R, Dorsch M.M., McMichael A.J., and Baghurst P.A. 1982 Birth Defects and Household Water Supply. Medical Journal of Australia 2 pp.577-579

SHEARER L.A., Goldsmith J.R., Young C., Kearns O.A., and Tamplin B.R., 1972 Methemoglobin Levels in Infants in an Area with High NItrate Water Supply. American Journal of Public Health 62(9) pp. 1174-1180

SHESKIN I.M., 1985 Survey Research for Geographers. Resource Publications in Geography, Association of American Geographers. Washington DC 20009

SHUVAL H.I. and Gruener N., 1972 Epidemiological and Toxicological Aspects of Nitrates and Nitrites in the Environment. American Journal of Public Health 62(8) pp.1045-1052

SOPOCLEOUS M., Townsend, M.A., and Whittemore D.O. 1990 Movement of Atrazine and Bromide in Central Kansas Croplands. Journal of Hydrology 115 pp. 115-137

SPALDING R.F, and Exner M.E., 1980 Areal, Vertical, and Temporal Differences in Ground Water Chemistry: Inorganic Constituents. Journal of Environmental Quality 9(3) pp. 466-478

STAFFORD R.T., 1985 Congressional Initiatives, In: Safe Drinking Water: The Impact of Chemicals on a Limited Resource ed. R.P.Rice Lewis Publishers Chelsea MI

STARK A.D., Chang H., Fitzgerald E.F., Riccardi K., and Stone R.R., 1990 A Retrospective Cohort Study of Cancer Incidence among New York State Farm Bureau Members. Archives of Environmental Health 45(3) pp. 155-162

STILLWELL W.G., Glogowski J., Xu H-X., Wishnok J.S., Zavala D., and Correa M.P., 1991 Urinary Excretion of Nitrate, N-Nitrosoproline, 3-Methyladenine and 7-Methylguanine in a Colombian Population at HIgh Risk for Stomach Cancer. Cancer Research 51 pp.191-194

ST. LEGER A.S., Elwood P.C., and Morton M.S., 1980 Neural Tube Malformations and Trace Elements in Water. Journal of Epidemiology and Community Health. 34 pp. 186-187

STONE D.H., Smalls M.J., Rosenberg K., and Womersley J., 1988 Screening for Neural Tube Defects in a High-risk Area: an Epidemiological Perspective. Journal of Epidemiology and Community Health 42 pp. 272-273

SUPER M., Heese H de V., MacKenzie D., Dempster W.S., du Plessis J., and Ferreira J.J., 1981 An Epidemiolodical Study of Well-Water Nitrates in a Group of South West African/Nambian Infants. Water Research. 15 pp. 1265-1270

TANNENBAUM S.R., Moran D., Rand W., Cuello C., and Correa P., 1979 Gastric Cancer in Colombia.IV. Nitrite and Other Ions in Gastric Contents from a High Risk Region. Journal of the National Cancer Institute. 62(1) pp.9-12

THOMPSON W.D., 1987 Statistical Criteria in the Interpretation of Epidemiological Data. American Journal of Public Health 77(2) pp. 191-194

U.S. Bureau of the Census, Census of Housing, Characteristics of Housing Units, Detailed Housing Characteristics, vol 1, pt. 24 Table 55. U.S. Department of Commerce, U.S. Government Printing Office 20412

U.S. Bureau of the Census, City County Data Book, 1988 U.S. Government Printing Office, Washington DC

U.S. Department of Health and Human Services. 1991 Public Health Services, Centers for Disease Control National Center for Health Statistics. Hyattsville MD

VAN BURKALOW A., 1982 Water Resources and Human Health. Water Resources Bulletin. 18)5) pp. 869-874

VIEL J.F. and Richardson S.T., 1991 Adult Leukemia and Farm Practices: An Alternative Approach for Assessing Geographical Pesticide Exposure. Social Science and Medicine. 32(9) pp. 1067-1073

VENA J.E., Graham S., Freudenheim J., Marshall J., Zeilezny M., Swanson M., and Sufrin G., 1993 Drinking Water, Fluid Intake and Bladder Cancer in Western New York. Archives of Environmental Health 48(3) pp. 191-198

WACHOLDER S., McLaughlin J.K., Silverman D.T., and Mandel J.S., 1992 Selection of Controls in Case-Control Studies. I Principles American Journal of Epidemiology. 135(9) pp. 1019-1028

WACHOLDER S.,Silverman D.T., McLaughlin J.K., and Mandel J.S., 1992 Selection of Controls in Case Control Studies. II Types of Controls. American Journal of Epidemiology. 135(9) pp.1029-1041

WACHOLDER S., Silverman D.T., McLaughlin J.K., and Mandel J.S., 1992 Selection of Controls in Case Control Studies. III Design Options. American Journal of Epidemiology. 135(9) pp.1042-1050

WADE D.M., 1992 Personal Comunication. Michigan Department of Public Health. Lansing Michigan

WAUCHOPE R.D., 1978 The Pesticide Content of Surface Water Draining from Agricultural Fields-A Review. Journal of Environmental Quality 7(4) pp. 459-472

WEHTJE G., Miekle L.N., Leavitt J.R.C., and Schepers J.S. 1984 Leaching of Atrazine in the Root Zone of an Alluvial Soil in Nebraska. Journal of Environmental Quality 13(4) pp. 507-513

WEIL R.R., Weismiller R.A., and Turner R.S., 1990 Nitrate Contamination of Ground Water under Irrigated Coastal Plain Soils. Journal of Environmental Quality 19 pp. 441-448

WEINBERG C.R. and Sandler D.P., 1991 Randomized Recruitment in Case-Control Studies. American Journal of Epidemiology 134(4) pp. 421-432

WESTIN J.B., 1990 Ingestion of Carcinogenic N-Nitrosamines by Infants and Children. Archives of Environmental Health. 45(6) pp.359-363

WHITE F.M.M., Cohen F.G., Sherman G., and McCurdy R., 1988 Chemicals, Birth defects and Stillbirths in New Brunswick: Associations with Agricultural Activity. Canadian Medical Association Journal 138 pp. 117-124

WINNEBERGER J.H.T., 1982 Public Health Significance of Nitrates in Nitrogen, Public Health, and The Environment Ann Arbor Science P.O. Box 1425 Ann Arbor MI 48106

WOLFF I.A. and Wasserman A.E., 1974 Nitrates, Nitrites and Nitrosamines. Science 177(4043) pp. 15-19

WOOLLEY F.R., Schuman K.L., and Lyon J.L., 1982 Neonatal Mortality in Utah. American Journal of Epidemiology 116(3) pp. 541-546

WRENSCH M., Swan S., Murphy P.J., Lipscomb J., Claxton K., Epstein D., and Neutra R., 1990 Hydrogeologic Assessment of Exposure to Solvent-Contaminated Drinking Water: Preganany Outcomes in Realtion to Exposure. Archives of Environmental Health. 45(4) pp.210-216

WU T.L., 1980 Dissipation of Herbicides Atrazine and Alachlor in a Maryland Corn Field. Journal of Environmental Quality 9(3) pp.459-465