

ENVIRONMENTAL HEALTH IN AGRICULTURE

INTRODUCTION

It is well known that farming and agricultural work are associated with high rates of occupational injury, disability and illness. Data from the National Safety Council show that agricultural work has a work accident death rate that is similar to mining and construction and that these three industries are the most dangerous ². Farmers and agricultural workers are at increased risk for a variety of illnesses including respiratory disorders, dermatologic conditions, and cancer ^{73,98,108}. The diagnosis and treatment of acute illness and disorders related to agricultural work is the subject of traditional occupational medicine. The majority of the time we think of these occupational diseases as directly related to work. The farm is a unique workplace however, because it is one of the few situations where the workers and their families often live at the worksite. Thus, farm families may be at risk for disease related to chronic environmental exposures that occur outside the usual definition of work. For example, acute pesticide poisoning during application of pesticides is clearly a work-related event. Chronic exposure to lower levels of pesticides in the environment on the farm (air, water, or food) may also be of concern to the health of farm families.

This chapter is intended to familiarize healthcare providers with environmental health issues that are of particular interest for farm families and agricultural communities. Although environmental health can be broadly defined as including workplace exposures ⁶⁸, the focus of this chapter will be on environmental exposures related to living on or near farms and not on illnesses that are the result of direct work activities (such as acute poisoning or injury). It should be stated that many of the associations between environmental exposures and illness are considered controversial by some authors. Many associations are not controversial however and there is increasing awareness of environmental health problems. The recent passage of the new law regulating livestock confinement operations in the State of Iowa is the direct result of fear about the negative impact of these operations on the health of communities. Healthcare providers may be asked to provide advice, counsel, diagnosis, and management expertise in regards to these environmental health issues. The chapter is divided into four main areas, A) Problem definition; B) Pathophysiology; C) Diagnosis and treatment; and D) Management and regulatory issues.

LEARNING OBJECTIVES

At the completion of this chapter, the healthcare provider will be able to:

- Define the basic requirements for a healthy environment
- Describe the main sources of environmental pollution in farming communities
- Identify health effects and management strategies for environmental-related illness



DEFINITION OF THE PROBLEM

The basic requirements for a healthy environment are said to include, clean air, safe and sufficient water, adequate and safe food, and a safe and peaceful place in which to live¹⁰⁴. Air pollution remains a significant problem in both industrial and undeveloped countries. Air pollution remains a determinant of death rates from respiratory disease even in developed countries. The quality of water is a major determinant of health. The World Health Organization estimates that 80% of all sickness and disease in developing countries is attributable to poor water supplies¹⁰². Undernutrition is a major cause of poor health worldwide. Food contaminated by toxins and chemicals can also be a significant problem.

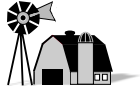
In the context of these environmental health issues, is there evidence that farm families and agricultural communities are at risk of poor health from a lack of clean air, safe water, or food? Our first approach will be to examine evidence for increased illness and health effects that may be due to environmental causes. There is quite a bit of information about the prevalence of respiratory diseases in farming populations. The issues of cancer rates and effects on reproduction in farming populations have also been examined and should give insight into the possibility of significant pollutants in water and food.

Respiratory Disease

There is a high prevalence of respiratory symptoms in farmers. Much of the symptoms reported in large surveys suggest the presence of chronic bronchitis and the occurrence of episodes of acute bronchitis^{28,60,82,94}. The problem goes beyond the mere presence of symptoms. It is apparent that some farming groups have accelerated declines in lung function leading to chronic airflow obstruction^{48,69,70,76,78,92}.

The work environments with the highest risk for chronic bronchitis are those with exposure to grain dust, swine confinement buildings, and poultry housing. Nonsmoking swine confinement workers had a prevalence of symptoms of 25% compared to 12% in other farm workers and 3% in matched non-farming workers²⁵. Acute bronchitis is also described in these same settings^{25,26,94}. These studies highlight the potential for illness due to the poor air quality in livestock confinement operations. One cannot directly extrapolate health effects that occur inside such facilities to health risks outside the facilities, in the community. It is difficult to define dose-response relationships so that one cannot clearly extrapolate from effects of high concentrations of pollutants to effects of lower concentrations. High concentrations of complex mixtures of gasses inside a facility may have effects due to the combination of exposures that may not be present outside where some of the pollutants are greatly modified. In addition, when one considers the health effects in a community one must consider the effects on vulnerable populations such as the elderly, children, asthmatics and other susceptible persons. Thus, it would seem important to study the general population directly.

Some recent studies have examined the prevalence of health effects in communities with intensive livestock operations. Thu and colleagues compared a group of Iowans living within two miles of a 4,000 sow swine operation with a random sample of rural residents living elsewhere⁸⁶. There was an increase in respiratory symptoms (sputum, cough, shortness of breath, chest tightness, and wheezing) in the former group. The pattern of symptoms in the community group was similar to workers in the facility.



Another study evaluated three rural North Carolina communities, one of which was near to a large swine operation¹⁰³. Trained interviewers were used to conduct a survey of health symptoms and measures of quality of life. The residents living near the swine operation reported increased rates of headaches, runny nose, sore throat, excessive coughing, diarrhea, and burning eyes compared to the residents not living near a livestock operation. The quality of life measures were also reduced in the residents near the swine facility. Thus, there is some evidence that release of pollutants from swine operations may affect the respiratory health of community residents.

The prevalence of asthma in the general population is said to be between 5 and 10%. The prevalence of asthma in farm workers has been assessed using survey instruments and lung function studies. A very large study of working age adults, the European Community Respiratory Health Survey, evaluated occupational asthma and found that farmers and agricultural workers had the highest odds ratios for asthma, 2.6 and 1.8 respectively⁵². Other studies have suggested that farmers have an increased risk for asthma morbidity and mortality. A Swedish study found increased mortality from asthma in farmers and farm workers⁸⁷. Evidence for bronchial hyperresponsiveness was found in 10.3% of a group of 741 farmers in France¹¹. In a large study of 1,542 Swiss farmers the prevalence of asthma symptoms was 15.4%. Poultry farmers had the highest rate of symptoms²⁰. A study from New Zealand found that the prevalence of asthma symptoms in farmers overall was 11.8% compared to 15% in a general population⁵¹. However, the New Zealand study also found that workers with animals had higher prevalence rates (18.2% for pig farmers and 17.4% for poultry farmers.) A study from California has found increased rates of asthma in rice farmers⁵⁸. Not all studies have found increased asthma symptoms in farmers. One study of pig farmers found increased chronic bronchitis but not asthma⁹³. Overall, there would appear to be increased risk for asthma or asthma-like symptoms in farmers. As in the discussion above, it is difficult to extrapolate this risk to individuals living on or near farms and livestock operations who may not be directly involved in the day to day work.

Some studies have evaluated the prevalence of asthma in farm families and persons who grew up on farms. A study of Finnish first-year university students found that a childhood farm environment had an odds ratio of 0.63 for risk of asthma compared to urban environments⁵⁰. A Canadian study of 1,199 rural secondary school students, ages 12 to 19 years, found the odds ratios for being raised on a farm were 0.70 for current wheeze, 0.59 for asthma, and 0.58 for atopy³⁸. Adjusting for the difference in the number of siblings did not significantly alter these associations. These and other studies^{12,30,71} have prompted investigators to consider the hypothesis that something in the farm environment such as endotoxin plays a protective role in preventing asthma in children²⁹. It is apparent that there is a paradox when one considers the spectrum of studies that have been performed. Adult farmers have prevalence rates for asthma as high or higher than general populations. Work with animals appears to increase risk. Growing up on a farm does not increase risk and it has been suggested that there is a protective effect.

Cancer

There is ample reason to explore the possibility of increased rates of cancer in agricultural communities. The National Cancer Institute developed a series of maps in the 1970's that displayed mortality patterns for specific cancers in the United States. It was apparent that there was a zone of

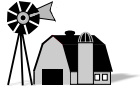


counties with excess rates for leukemia in the Midwest. There were few cities in these counties and it was suggested that agricultural factors were involved ¹⁰. A number of epidemiologic studies have been conducted since then. Farmers appear to experience elevated rates for several cancers, including leukemia, non-Hodgkin's lymphoma, multiple myeloma, soft-tissue sarcoma, and cancers of the skin, lip, stomach, brain, and prostate ¹⁰. It is interesting to note that the overall rate of cancer is lower in farmers than other occupational groups, primarily because of the lower rates of "lifestyle-related" cancers. Farmers tend to smoke less and consume less alcohol. So, the excess cancer rates in some categories is all the more remarkable. Analogous to the comments above about respiratory disease, the extrapolation of risk of cancer from relatively high workplace exposures to the risk from lower exposures in the community may be difficult. It may be difficult to distinguish between effects from exposure from directly working with an agent vs. indirect exposure from living in the vicinity. When Congress formed the EPA it was assumed that there was no lower threshold for the effects of carcinogens. This means that if a high exposure to an agent causes cancer then lower exposures also cause cancer, just less of it. In fact, it is now known that many carcinogens do have a threshold for effects. Meaning, a carcinogen may not have effect unless exposure is above a threshold that overwhelms the body's ability to metabolize it safely.

There have been few studies of overall cancer rates in rural and or agricultural communities. These studies usually include all persons, including those workers with occupational exposure to potential carcinogens. So, there is little data on potentially environmentally related cancers and farm family members and community members. One large study of Norwegian farmers and their spouses evaluated 136,463 men for 1.5 million person-years and 109,641 women for 0.6 million person-years ⁵³. 3333 and 2145 cancer cases were identified, respectively. The overall rates of cancer were low compared to the general population, however, there was a positive association between dairy farming and leukemia in men and pesticide use and multiple myeloma in both men and women. Further study of cancer rates in women was suggested.

Another large study evaluated the association of total pesticide use in California counties with cancer incidence rates ⁵⁹. The investigators found little correlation between total pounds of active ingredient and age-adjusted incidence rates for selected cancers. Some correlations were seen however, primarily in Hispanic males. There was a positive correlation between atrazine and leukemia, 2,4-D and leukemia, captan and leukemia, atrazine and brain cancer, and atrazine and testicular cancer, in Hispanic males. No data about exposure to pesticides at the individual level were available. In addition, there was no assumption of latency between exposure and cancer. Nonetheless, since Hispanic males are often employed as agricultural workers in these counties, there is the suggestion that exposures to pesticides at the worksite is associated with the cancers mentioned.

Drinking water contamination, particularly by atrazine and nitrate, is an important source of exposure to carcinogens. Van Leeuwen et al. evaluated the association between cancer incidence and drinking water contamination with atrazine and nitrate in Ontario, Canada ⁹⁰. Cancer data were obtained from the cancer surveillance program for the entire Ontario population. Exposure data were obtained from the drinking water surveillance program and from the Ontario Landscape Resource Unit. They found that atrazine contamination levels were positively associated with stomach cancer incidence and negatively associated with colon cancer incidence. Nitrate levels were negatively associated with stomach cancer



incidence. They were unable to demonstrate associations for other cancers, including non-Hodgkin's lymphoma (NHL). Another study evaluated the incidence of breast and ovarian cancers in Kentucky in relation to an index of atrazine exposure ⁴⁴. Atrazine exposure was derived from public water measurements, acres of corn planted, and pounds of atrazine sold in 120 counties. A null association was found for atrazine and breast cancer. An inverse association was found for ovarian cancer. The negative associations in these studies are hard to explain on a biologic level. The authors concluded that cancer causation is the result of complex systems where social and biological variables interact.

The majority of the positive data regarding probable carcinogens and cancer in farmers comes from case-control epidemiologic studies. In these studies, cases and appropriate controls are identified and then interviewed for their known exposure to the agents in question, usually pesticides. The majority of studies have evaluated males only. For example, a study of NHL in eastern Nebraska involved 201 new cases and 725 controls ¹⁰⁶. There was a 50% excess of NHL among men who mixed or applied 2,4-D (odds ratio [OR] = 1.5). The risk of NHL increased with the average frequency of use to over threefold for those exposed 20 or more days per year. Adjusting for use of organophosphate insecticides lowered the risk estimate for frequent users (OR = 1.8), but adjustment for fungicide use increased the risk estimate (OR = 4.5). Simultaneous adjustment for organophosphates and fungicides yielded an OR of 3.1 for farmers who mixed or applied 2,4-D more than 20 days per year. Obviously, the data imply a significant increase in risk with increasing occupational exposure.

The same investigators have studied the risk of NHL in women in eastern Nebraska ¹⁰⁷. They found no increased risk of non-Hodgkin's lymphoma in women who had ever lived or worked on a farm (odds ratio [OR] = 1.0). Neither the use of insecticides (OR = 0.8) nor herbicides (OR = 0.7) on the farm was associated with non-Hodgkin's lymphoma; however, the number of women who mixed or applied pesticides was small, particularly in comparison to men on farms. In those women who did personally handle pesticides there was increased risk. It would seem that the case-control studies support associations of cancer with occupational exposure but not with lower, indirect exposures in the farm environment.

Arsenic

Another area of interest to rural communities is the subject of arsenic and cancer. The Safe Drinking Water Act of 1996 required the EPA to revise the existing 50 µg/L standard for arsenic in drinking water. EPA is implementing a 10 µg/L standard for arsenic. Many of the water systems that are not in compliance with the new standard are systems that draw from wells (groundwater systems) in rural areas. For this reason, the issues may be relevant for farm families. One might ask whether farm families are at risk for illness due to arsenic contamination of their drinking water.

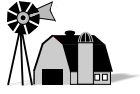
Arsenic is an important environmental carcinogen that is naturally occurring. Drinking water contamination by arsenic is not generally due to industrial or agricultural activities. Inorganic arsenic is the 20th major constituent of the earth's crust and a major constituent of sedimentary and volcanic rock. Drinking water systems that draw from groundwater tend to be at higher risk than surface water systems that draw from rivers, lakes, and reservoirs. The cost of reducing arsenic levels may be quite high and thus the new standard has generated some controversy. It may be helpful for healthcare



providers to be conversant with the issues. When it addressed the problem of arsenic levels the EPA asked for three independent expert panel reviews. These reports were prepared by the National Academy of Sciences, the National Drinking Water Advisory Council, and the EPA Science Advisory Board. The subcommittee of the National Academy of Sciences published their report in September 2001⁸⁸. Human health effects were evaluated from multiple studies. High levels of arsenic exposure are thought to cause reproductive, neurologic, respiratory, hematologic, hepatic, diabetic, and dermal disorders. Some of the data comes from Bangladesh and a study of Millard County, Utah where arsenic levels ranged from several hundred $\mu\text{g/L}$ to several thousand $\mu\text{g/L}$ ⁵⁵. It is hard to demonstrate illness at drinking water levels below 50 $\mu\text{g/L}$ and most of the attention in developing the new standard was focused on cancer. Three large studies, one of effects in Chile and two of effects in Taiwan were used in the cancer estimates. It was concluded that there are clear dose-response effects for arsenic causing bladder and lung cancer. Several methods were used to extrapolate the risk of these cancers for lower exposures, i.e. 3, 10, and 20 $\mu\text{g/L}$ in drinking water. Key issues include which baseline cancer rates are to be used. The estimates of the risk are higher when U.S. baseline cancer rates are used. The mechanism of arsenic carcinogenicity is poorly understood and this also contributes to the difficulty in extrapolating risk from high exposures. They estimated that the 20 $\mu\text{g/L}$ of arsenic would cause an excess lifetime risk of 45 bladder cancers and 27 lung cancers for 10,000 males. The rates were about half of these for the 10 $\mu\text{g/L}$ level (the new standard) in drinking water. These rates would increase the baseline risk for bladder cancer by about 13%. The National Academy report stated that detecting an increase in cancer risk of this magnitude by studying a population exposed to 20 $\mu\text{g/L}$ of arsenic would require a prohibitively large study over many years. It would be even more difficult to detect an increase in lung cancer from epidemiologic methods at these exposure levels since the baseline rate is about ten times that of bladder cancer. Thus, it is very unlikely that we will ever have clear epidemiologic evidence of excess cancer in communities with arsenic levels in the range of 10 to 50 $\mu\text{g/L}$. Additional evidence that any effect of arsenic on cancer rates is small is the fact that the overall rates of lung and bladder cancer are low in farmers¹⁰. Healthcare providers will only be able to discuss the risk to the community and try and put it into perspective. Information is available through the EPA website.

Reproductive health

Many pesticides have been identified as having endocrine and reproductive effects based on animal toxicology studies⁷⁹. The idea that pesticides could cause infertility was brought to attention by the well documented toxicity of dibromochloropropane, a nematocide. Dibromochloropropane caused low sperm counts and infertility in men who were occupationally exposed. The EPA banned this agent in 1979⁷⁹. The issue was raised as to whether environmental exposure to this and other pesticides was affecting fertility rates and/or other endocrine systems. Several studies have been published from Ontario Farm Family Health Study^{19,72}. The authors sampled Ontario farms from the 1986 Canadian Census of Agriculture, identified farm couples, and obtained questionnaire data concerning farm activities, reproductive health experience, and chemical applications. In this retrospective cohort study of farm couples several outcomes were evaluated. In one study the authors looked at the time to pregnancy. There was no strong or consistent pattern of associations of pesticide exposure with time to pregnancy. However, it was found that during time intervals in which women participated in pesticide activities (during most of which the men also participated), 6 of 13 pesticide exposure categories were



associated with a decrease in fecundability (conditional fecundability ratio range = 0.51- 0.80). In another study the authors evaluated pregnancy outcomes. Male farm activities were evaluated in relation to miscarriage, preterm delivery, and small-for-gestational age births. Miscarriage was not associated with chemical activities overall but there was a small association with thiocarbamates. Preterm delivery was not associated with farm chemical activities in general but there was an association with mixing or applying yard herbicides.

Investigators from the University of Iowa have taken another approach in looking at pesticides and reproductive health ⁶². These authors used survey data from Iowa municipal drinking water supplies. The Rathbun rural water system was found to contain elevated levels of triazine herbicides. Rates of low birth weight, prematurity, and intrauterine growth retardation were evaluated in communities served by this water system and compared to other communities in the same counties, but using other water systems. Multiple linear regression analyses revealed that levels of the herbicides atrazine, metolachlor, and cyanazine were each associated with community intrauterine growth retardation rates. There was an overall relative risk of 1.8 for intrauterine growth retardation in communities served by the Rathbun water system. The level of atrazine in the Rathbun water supply averaged 2.2 µg/L, compared to 0.7 µg/L in other surface water supplies in southern Iowa, and to <0.1 µg/L for groundwater systems.

If one tries to summarize these studies, it appears that the retrospective cohort studies do not support the idea that the general use of pesticides on the farm is associated with poor reproductive outcomes. The strongest associations were when the women themselves worked with pesticides directly. The Iowa study of drinking water exposure is concerning in that passive exposure to pesticides through the environment is capable of causing poor pregnancy outcome. The relatively high levels of triazine herbicides in the Rathbun water system in Iowa are fortunately not typical.

Other Health Effects

It has been proposed that environmental agents have other chronic health effects. Effects of pesticides and other agents on child development, cardiovascular health, and other aspects of health have been proposed. Hypotheses are generated from known effects such as neurologic sequelae after severe poisonings by organophosphate pesticides. Studies have not shown any clear relationships between chronic exposures to pesticides and chronic health effects other than those described above. A few studies have looked at general symptoms and mental health issues in relation to livestock confinement facilities. Thu and colleagues evaluated Iowans living with two miles of a 4,000-sow confinement facility ⁸⁶. They did not find evidence of depression or anxiety but did find increased symptoms of nausea, dizziness, headaches, and plugged ears. Schiffman and colleagues evaluated North Carolina residents living in the vicinity of swine confinement operations ⁷⁴. They hypothesized that odors from the swine facility might affect mood. Persons living near the intensive swine operations who experienced the odors reported significantly more tension, more depression, more anger, less vigor, more fatigue, and more confusion than control subjects as measured by the Profile of Mood States. Another study of North Carolina communities used questionnaires to evaluate symptoms and quality of life measures among those living in the vicinity of swine and cattle operations ¹⁰³. Certain respiratory and gastrointestinal problems and mucous membrane irritation were elevated among residents in the

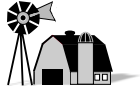


vicinity of the hog operation. Residents in the vicinity of the hog operation reported increased occurrences of headaches, runny nose, sore throat, excessive coughing, diarrhea, and burning eyes as compared to residents of the community with no intensive livestock operations. Quality of life, as indicated by the number of times residents could not open their windows or go outside even in nice weather, was similar in the control and the community in the vicinity of a cattle operation but greatly reduced among residents near a hog operation. While odors may seem to be a relatively minor concern to some they can have significant health effects. Shusterman et al. have studied odors in several industrial settings and write that noxious environmental odors may trigger symptoms by a variety of physiologic mechanisms, including exacerbation of underlying medical conditions, innate odor aversions, aversive conditioning phenomena, stress-induced illness, and possible pheromonal reactions^{80,81}.

Environmental contamination can be considered a form of stress in the community, especially when there is little or no environmental control by the affected community. The situation may be similar to that experienced in areas with industrial contamination or in the Persian Gulf War. Gulf war veterans in Iowa have been studied and found to have more self-reported illness and poorer health quality^{3,21}. This type of mechanism may be a contributor to the adverse health effects reported in communities near large livestock operations. Symptoms such as fibromyalgia, alcohol abuse, anxiety and chronic fatigue are thought to be related to depression and stress and are found in higher prevalence in gulf war veterans. One might wonder whether the poor economic conditions in agricultural communities, especially in times of drought or other hardships that are not under the control of farm families contributes to poor health by similar mechanisms.

Summary

There are a multitude of reasons to be concerned about environmental pollutants and the health of farm families and communities. Air pollution in livestock confinement facilities is a well documented cause of bronchitis and other respiratory complaints. Grain dust and silage are other sources of airway irritants. Some studies of farmers have shown declines in lung function. The evidence that persons who do not directly work in the confinement facilities are affected is less strong. Recent studies would suggest that there are more respiratory symptoms in communities near hog confinement facilities. Evidence for excess rates of some cancers in agricultural communities was first noticed in the 1970's. These excess cancers are notable in the context that farmers have an overall lower rate of cancer compared to other occupational groups. Most of the studies have focused on farmers (so mostly just men) with direct exposure to pesticides and have not examined family members. The evidence that indirect exposure to environmental carcinogens in agricultural communities causes cancer is less strong. Atrazine (and other triazines) contamination of community drinking water has been associated with poorer pregnancy outcome (intrauterine growth retardation). The definition of a healthy environment includes the requirement of a safe and peaceful place to live. The stress of living with environmental concerns and perhaps also with economic stress may also adversely affect the health of the community.



PATHOPHYSIOLOGY

This section will address the mechanisms by which specific environmental pollutants affect health. Air pollutants will be discussed first, followed by a discussion of potential water pollutants including pesticides. Several organizations have recently reviewed the environmental issues surrounding large livestock feeding operations and swine confinement operations in particular. Some of this work was prompted by state governments in anticipation of regulation. The University of Iowa and Iowa State University completed a very complete study of the air quality issues surrounding animal feeding operations and it is available via the internet (<http://www.publichealth.uiowa.edu/ehsrc/CAFOstudy.htm>)³⁶. Other large reviews are available from the E.P.A.

Organic dusts

Organic dusts are the most common respiratory exposures in agricultural work. Toxic organic dusts can occur in association with silage, grain dust, straw, wood chips, and animal confinement buildings. The major toxic components of organic dusts include substances derived from bacterial and fungal contamination such as endotoxin, glucans, and mycotoxins. Endotoxin is a lipopolysaccharide component of the cell wall of Gram-negative bacteria. Gram-negative bacteria are found in air samples from swine barns include *Enterobacter*, *Acinetobacter*, *Enterococcus*, *Moraxella*, *Pseudomonas*, and *E. Coli*^{83: Kiekhaefer, 1995 #220}. Glucans are cell wall components of fungi and molds such as *Aspergillus*, *Scopulariopsis*, *Pencillium*, *Geotrichum*, *Mucor*, and *Fusarium*.

One of the more exciting developments in the area of organic dust induced disease is the characterization of the innate immune system and the mechanisms by which endotoxin and glucans interact with cells⁴. It is now understood that the innate immune response is a first line of defense that allows detection of pathogens, formation of a rapid defensive response, but does not require prior exposure or sensitization. A group of proteins known as the Toll-like family of receptors are expressed on many cells, primarily leukocytes. These receptors recognize conserved motifs on pathogens that are not found in higher organisms. One of these conserved motifs is lipopolysaccharide. Other pathogen-associated motifs are lipoteichoic acid from gram-positive bacteria, glucans from fungi, and zymosan from yeast. A new term has been coined for the conserved motifs, pathogen-associated molecular patterns (PAMPs). The Toll-like family of receptors initiate signaling through a cytoplasmic domain of the molecule that is homologous to that of the IL-1 receptor. Signaling through intermediary molecules can lead to activation of both the AP-1 and NF- κ B transcription factors, which are required for the transcription of immune response genes^{39,40}.

Identification of the Toll-like family of receptors has also facilitated the investigation of variability between individuals in response to inhaled toxins⁶. Arbour et al. have shown that common, co-segregating missense mutations (asp299 to gly; thr399 to ile) in the Toll-like receptor 4 (TLR4) are associated with a blunted response to inhaled lipopolysaccharide⁶. This is one of the first demonstrations of gene-sequence changes that alter the host response to environmental stress.

Grain dusts may also act through the humeral immune system. Mixing of grain dusts with serum activates complement and generates chemotactic factors for neutrophils^{65,97}. Extracts of grain dusts act



as chemoattractants for neutrophils in *in vitro* assays⁹⁶. Exposure of epithelial cells to extracts of grain dusts induces the release of neutrophil chemoattractants⁹⁶. The interaction of grain dusts with such cells may well be due to the Toll-like family of receptors. It is of some interest that the induction of chemotactic factors in epithelial cells by grain dust did not correlate with the concentration of lipopolysaccharide in the dust, suggesting that there are multiple components of organic dust that are active.

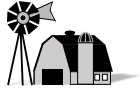
Controlled inhalation of organic dusts has been performed in both animals and humans in the laboratory^{57,95}. Neutrophils are attracted to the lung. Peripheral blood neutrophilia also occurs. The findings are similar to inhalation studies with lipopolysaccharide in mice⁵⁶.

Exposure to organic dusts

The major sources of exposures to organic dusts are situations where farmers or agricultural workers uncap a non-air tight silo, enter a confined space with moldy grain or spoiled hay, or a livestock confinement operation. Farmers are very vulnerable when they enter a silo to remove the top layer of spoiled silage. If this spoiled silage is also dry, tremendous amounts of dust can be created that contain large amounts of bacteria and fungi. Grain workers are exposed whenever dust is generated by loading or unloading grain from grain elevators, train cars, or ships. Grain elevators are designed to store grain with a minimum of spoilage by bacteria and fungi. Nonetheless, significant contamination occurs. Swine confinement operations have significant risk for agricultural workers due to the high levels of dust and bioaerosol. The risk of exposure to persons who do not directly enter these types of closed facilities is harder to estimate but would be significantly lower. Thorne et al. examined concentrations of endotoxin downwind from swine confinement buildings⁸⁴. The levels of endotoxin declined quite rapidly with distance from the buildings. Typical interior concentrations of endotoxin in swine buildings range from 2,190 to 24,100 EU/m³⁸⁵, whereas the concentrations 500 feet downwind ranged from 20 to 142 EU/m³.

Toxic gases

Toxic gases are also of importance in agricultural settings. The production of silage is particularly prone to create toxic gases. Silage is produced by placing green forage crops into silos, that are usually cylinders made of concrete. The forage is covered to reduce the exposure to oxygen and encourage the process called ensilage. Nitrogen dioxide is produced and accumulates above the silage. The levels of nitrogen dioxide may rise quickly after the silo has been filled. When nitrogen dioxide dissolves into water, nitrous acid and nitric acid are formed. Nitrogen dioxide is an irritant to mucous membranes. Less severe exposures cause cough, headache, and dyspnea. After severe exposures acute pulmonary edema may occur. Other sources of toxic gases are those emitted from livestock confinement operations, manure pits, manure lagoons, and from sites of manure land application. The gases are regenerated from urine and feces and also from microbial degeneration of manure. While there are many volatile gases of potential concern²⁴ the main gases of interest are hydrogen sulfide, ammonia, methane, and carbon dioxide. Methane and carbon dioxide are dangerous at very high concentrations and act as asphyxiants. Hydrogen sulfide and ammonia can be toxic at fairly low concentrations and are worth further discussion.

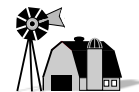


Hydrogen sulfide

Hydrogen sulfide can be immediately toxic and exposure to levels in excess of 100 ppm can cause loss of consciousness and death. The mechanism of this type of poisoning is through effects on the oxygen transport system in mitochondria. The effect is not unlike that of cyanide poisoning. Hydrogen sulfide has an odor like rotten eggs and can be detected by smell at levels below 1 ppm. The odor does not increase as exposure increases above 6 ppm. Hydrogen sulfide is particularly dangerous because at levels above 150 ppm it quickly poisons the olfactory system, hindering the ability to detect high levels through the sense of smell. There have been many documented fatal poisonings where both agricultural workers and rescuers entered closed manure storage containers and could not smell the hydrogen sulfide^{5,66}.

The OSHA permissible exposure limit (PEL) for hydrogen sulfide is 10 ppm. Hydrogen may have important effects at lower concentrations. Bhambhani et al. studied the effects of inhalation of low levels of hydrogen sulfide on healthy volunteers^{8,9}. Levels of 10 ppm and 5 ppm caused alterations of aerobic metabolism during exercise. Several community studies have been reported. Jaakkola and colleagues studied children in a city with significant air pollution including hydrogen sulfide levels of 0.001 ppm⁴⁹. The younger children had a two-fold increase in risk for respiratory infections. Other studies have shown similar risks for mixed air pollution exposures. Inserra and colleagues studied residents of Dakota City, Nebraska. Residents complained of ill effects from the emissions of a waste water treatment plant. 14 residences were monitored and it was found that indoor and outdoor concentrations often exceeded 90 ppb for hydrogen sulfide⁴⁶. These levels were associated with increased hospital visits for asthma a day following peak exposures. Hydrogen sulfide levels often exceed these levels in swine confinement buildings and near manure lagoons. Perturbation of manure lagoons, as in preparation for drainage, can cause local levels to be as high as 1,000 ppm²³. Very few studies of hydrogen sulfide levels in the community or vicinity of these operations have been performed. Some data is available from surveys that the State of Minnesota has conducted relative to their ambient air quality standards for feedlots. The information is available through their website <http://www.pca.state.mn.us/hot/feedlots.html>. The State of Minnesota has a standard of 30 ppb for hydrogen sulfide for a one half hour average not to be exceeded over two in any five consecutive days. The standard applies to air at the property line or area that is accessible to the general public. Surveys in Minnesota have documented many instances where levels exceeded 30 ppb. Swine and dairy facilities were most likely to exceed the limit and the degree of confinement also contributed.

The EPA does not currently have a national standard for ambient levels of hydrogen sulfide. The issue has been left up to the states. Two states, Minnesota and California, have standards for hydrogen sulfide which are 30 ppb for not more than one-half hour for not more than two occurrences in a 5 day period and 50 ppb for not more than one-half hour, and not more than two occurrences per year. The State of Nebraska has an ambient air quality standard for total reduced sulfur (which includes hydrogen sulfide) of 0.1 ppm. The EPA has completed a risk assessment for hydrogen sulfide. For community exposures the EPA recommends a Reference Concentration for a continuous inhalation exposure to humans (including sensitive persons such as those with asthma) that is likely to not have any appreciable adverse effects during a lifetime. The EPA estimates the Reference Concentration from a No-Observed-Adverse-Effect Level (NOAEL) of 0.73 ppm for hydrogen sulfide for nasal irritation and inflammation



in mouse studies⁸⁹. An uncertainty factor of 1000 is used to account for protection of sensitive persons, adjustment for chronicity of exposure, and conversion to human effects. Thus, the Reference Concentration for hydrogen sulfide is 0.7 ppb³⁴. It is hard to estimate what kind of lifetime exposures a person might encounter in the vicinity of feedlots and swine confinement operations but based on the Dakota City data and the Minnesota data there is significant risk that the Reference Concentration is being exceeded in many communities for large amounts of time.

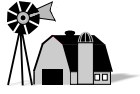
Ammonia

Ammonia is a usual component of manure. The EPA estimates that agricultural operations are responsible for 73 % of the total ammonia air pollution in the United States⁴². The mechanism of toxicity is through damage to airway epithelium. Ammonia is water-soluble and is quickly absorbed into airway secretions. Ammonia concentrations of 50 to 150 ppm will cause severe cough and irritation of mucous membranes. Higher concentrations can cause permanent scarring and massive exposures are fatal. Massive exposures are usually due to accidents with tanks of anhydrous ammonia. Another mechanism of ammonia air pollution is through creation of particulates. Ammonia reacts with acid gases from fossil fuel combustion and forms fine particulate air pollution. Increased fine particulate air pollution in urban areas is associated with increased mortality⁴⁷.

Many studies have documented respiratory illness in agricultural workers exposed to ammonia. Careful studies of swine confinement workers and poultry workers have shown dose-response relationships between exposures and declines in lung function²². These studies have suggested thresholds for exposure to ammonia for declines in lung function of 7 ppm of ammonia for swine workers and 12 ppm for poultry workers. These suggested exposure limits are significantly below the existing OSHA PEL for ammonia of 50 ppm. Some other organizations such as NIOSH and ACHIH have recommended standards of 25 ppm. Similar to the situation for hydrogen sulfide, there is no EPA national standard for ambient air levels of ammonia. There are no state mandated standards either. The EPA has performed a risk assessment for ammonia. Based on occupational studies a NOAEL of 4.3 ppm was estimated. Using an uncertainty factor of 30, they derived a Reference Concentration of 144 ppb for ammonia that should not cause adverse effects over a lifetime exposure³⁵.

Odors

More than 24 odorous chemicals have been identified in the emissions from livestock feeding operations¹⁶. Ammonia and hydrogen sulfide, described above, are odorous. Volatile acids, mercaptans, and amines make up most of the odorous chemicals that are very potently odorous, even at very low concentrations. There is some evidence that strong odors are more of a problem than a neighborhood nuisance. Some of the studies were mentioned above in the discussion of the health effects of living near livestock confinement operations. Schiffman et al found that persons living near intensive swine operations who experienced odors reported significantly more tension, more depression, more anger, less vigor, more fatigue, and more confusion than control subjects⁷⁴. Wing and Wolf found that persons living near a large-scale hog operation experienced decreased quality of life as indicated by the number of times residents could not open their windows or go outside even in nice weather¹⁰³. The mechanisms for effects of odors on health are not well understood. There also has been little research into the



quantification of odors so it is hard to evaluate any dose-response relationship. Several pathways have been proposed for ill-health effects of odors⁷⁵. Odors may cause symptoms in association with combinations of irritants that are also present. Odors may cause symptoms when combined with bioaerosols containing organic dusts. Odors may cause symptoms in the absence of high concentrations of other irritating agents but the mechanism is not clear. The perceived odor and cognitive expectations about the possible chemical associations may influence mood and behavior.

There are no national standards for odors of the types expected from agricultural operations. Only two states, Colorado and Missouri have odor regulations. The regulations are based on sentometry and are 7:1 dilutions at the property line in Colorado and 5.4:1 dilutions in Missouri.

Water Pollution

The EPA conducted a National Water Quality Inventory in 1996 which required individual States to conduct surveys³¹. The States reported that agricultural operations were the most widespread source of water pollution in the U.S. It was estimated that agriculture contributes to the impairment of at least 173,529 river miles, 3,183,159 lake acres, and 2,971 estuary square miles. Twenty two states estimated the impacts of specific agricultural activities and attributed 20 % of the pollution from agriculture to be due to intensive livestock feeding operations. Given these estimates it would appear sensible to examine the potential risks of water pollution to farm families and communities. Sources of pollution include runoff from fields and manure pollution from feedlots and livestock confinement operations. Pollutants contaminate surface water from runoff directly into the river, lake, or reservoir and through percolation into groundwater from which wells draw drinking water. Manure pollution occurs from direct discharges from manure storage, lagoons, stockpiles into surface water and from application of manure onto fields. Knowledge about specific pollutants and the need for testing is particularly important for persons drawing water from private or domestic wells since these wells are generally more shallow and little testing is required. Persons drawing drinking water from public wells are generally at lower risk due to water quality monitoring and treatment requirements. The next few paragraphs will describe the potential health effects of specific pollutants and what is known about dose-response relationships in relation to water quality standards.

Ammonia

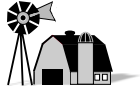
Ammonia (both the ionized form, ammonium, and the un-ionized form) is produced when microorganisms break down organic nitrogen products in manure. Ammonia was discussed above as an air pollutant but it is also very water soluble and is easily transported into surface waters. The impact of ammonia on drinking water quality is mainly indirect. Ammonia is toxic to aquatic life and has been responsible for fish kills. Ammonia is converted easily to nitrate and can lead to nutrient over-enrichment of surface waters. This can lead to nuisance algae blooms which can lead to reduced levels of dissolved oxygen, production of chlorinated byproducts that are carcinogenic, and clogging of water treatment facilities. Drinking water contamination by nitrates is of concern and is discussed below.

**Nitrate**

The process of nitrification occurs in aerobic environments and converts ammonium to nitrite and then to nitrate. Nitrite is toxic to most fish but this is unusual because of the rapid conversion to nitrate. Nitrate is biologically available to plants and is a valuable fertilizer. Nitrate is however associated with health effects in humans. Acute nitrate toxicity is due primarily to its conversion to nitrite, which oxidizes the Fe(+2) form of iron in hemoglobin to the Fe(+3) state. This compound (methemoglobin) does not bind oxygen, resulting in reduced oxygen carrying capacity of the blood. Low levels of methemoglobin occur in normal individuals, with typical values usually ranging from 0.5 to 2.0%. Bacteria are responsible for most of the conversion of nitrate to nitrite in the gastrointestinal system. Consequently, the risk of methemoglobinemia from ingestion of nitrate depends not only on the dose of nitrate, but also on the number and type of enteric bacteria. In healthy adults, available data suggest about 5% of a dose of nitrate is reduced to nitrite by bacteria in the mouth⁷⁷. Conversion of nitrate to nitrite may also occur in the stomach if the pH of the gastric fluid is sufficiently high (above pH 5) to permit bacterial growth. This is of concern in adults with diseases such as achlorhydria or atrophic gastritis. It is also of concern in infants, since the infant gastrointestinal system normally has a high pH that favors the growth of nitrate-reducing bacteria. For this reason, infants (especially age 0-3 months) are generally recognized as being the subpopulation most susceptible to nitrate-induced methemoglobinemia. Walton described a survey performed by the American Public Health Association to identify clinical cases of infantile methemoglobinemia that were associated with ingestion of nitrate-contaminated water⁹⁹. A total of 278 cases of methemoglobinemia were reported. Of 214 cases for which data were available on nitrate levels in water, none occurred in infants consuming water containing <10 mg nitrate-nitrogen/L (1.6 mg nitrate-nitrogen/kg/day). There were 5 cases (2%) in infants exposed to 11-20 mg nitrate-nitrogen/L (1.8-3.2 mg/kg/day), 36 cases (17%) in infants exposed to 21-50 mg/L (3.4-8.0 mg/kg/day), and 173 (81%) in infants exposed to >50 mg/L (>8 mg/kg/day). Based on these studies of nitrate contamination and occurrence of methemoglobin the EPA has set the maximum contaminant level or reference dose for oral intake of 10 mg/l³². This limit should prevent methemoglobinemia in infants. The review is available online through the IRIS database at <http://www.epa.gov/iris/subst/0076.htm>³².

Several epidemiological studies have evaluated the adverse effects of chronic nitrate exposure on birth defects, and the results are inconsistent. Dorsch et al. performed a case-control study and found a statistically significant increase in risk of birth defects in children of women consuming groundwater (which contained 5-15 mg/L of nitrate) compared with women consuming rainwater (which contained <5 mg/L nitrate)²⁷. Arbuckle et al. reported nonstatistically significant increase in the odds ratio for birth defects in children of women exposed to well water (26 mg/L nitrate, equivalent to 0.2 mg nitrate-nitrogen/kg/day) compared with rain water (0.1 mg/L nitrate, equivalent to 0.0008 mg nitrate-nitrogen/kg/day). However, decreased odds ratios (also not statistically significant) were noted for exposure to nitrate in spring water (17 mg/L, equivalent to 0.13 mg nitrate-nitrogen/kg/day) or public water (26 mg/L)⁷.

Nitrates can undergo endogenous reduction to nitrites, and nitrosation of nitrites can form N-nitroso compounds, which are potent carcinogens. A number of recent studies have evaluated nitrate levels in relation to cancer rates. The results are variable. A study from Slovakia found that villages with



medium (10.1-20 mg/L), or high (20.1-50 mg/L) average levels of total nitrate in drinking water had positive association between nitrate in drinking water and non-Hodgkin lymphoma and colorectal cancer. There was a positive trend for an association with stomach cancer⁴¹. A study from Ontario, Canada found no clear associations of nitrates with cancer rates, but the nitrate levels were much lower than in the Slovakian study⁹⁰. In fact, there was a negative association with stomach cancer. A case-control study from Nebraska found that long term exposure to elevated nitrate levels in drinking water may contribute to the risk of NHL¹⁰⁰. The Iowa Women's Health Study analyzed cancer incidence in a cohort of 21,977 Iowa women who were 55-69 years of age at baseline in 1986 and had used the same water supply more than 10 years¹⁰¹. Nitrate exposure was assessed and divided into quartiles (cut points: 0.36, 1.01, and 2.46 mg per liter). For all cancers, there was no association with increasing nitrate in drinking water, nor were there clear and consistent associations for non-Hodgkin lymphoma; leukemia; melanoma; or cancers of the colon, breast, lung, pancreas, or kidney. There were positive associations for bladder cancer and ovarian cancer and inverse associations for uterine cancer and rectal cancer.

Infectious Pathogens

Manure can introduce many organisms into the environment that can impact health. Livestock, aquatic life, and wildlife can be affected in addition to humans. Here we will focus on human health. The table below is a list of potential diseases and pathogenic organisms that can be acquired from manure. It is adapted from a table in the E.P.A. study of feedlots³³. Many of the diseases such as the diarrheal diseases are acquired through contaminated drinking water. Some are acquired through contact with contaminated water as might occur with swimming in a contaminated lake. Some diseases are airborne but nonetheless important for the agricultural community. Table 1 lists the most relevant pathogens that have been identified by the E.P.A.

The E.P.A. has mandated primary drinking water standards for the presence of microorganisms. These apply to public water systems providing water for human consumption through constructed conveyances (pipes or canals) to at least fifteen service connections or an average of twenty-five individuals daily at least 60 days per year. Essentially, there should be no detectable *Cryptosporidium*, *Giardia lamblia*, or *Legionella* in that the Maximum Contaminant Level (MCL) is zero. Public water systems are required to monitor for fecal coliform bacteria as a surrogate for all enteric bacteria. Drinking water should have no more than 5.0% samples positive for total coliforms in a month (for water systems that collect fewer than 40 routine samples per month, no more than one sample can be total coliform-positive per month.) Every sample that has coliforms must be analyzed for either fecal coliforms or *E. coli*. If there are two consecutive total coliform positive samples, and one is also positive for *E.coli* or fecal coliforms, a system has an acute MCL violation.



EPA's surface water treatment rules require systems using surface water or ground water under the direct influence of surface water to (1) disinfect their water, and (2) filter their water or meet criteria for avoiding filtration so that the following contaminants are controlled at the following levels:

Cryptosporidium (as of 1/1/02 for systems serving >10,000 and 1/14/05 for systems serving <10,000) 99% removal.

Giardia lamblia: 99.9% removal/inactivation

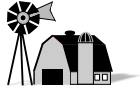
Viruses: 99.99% removal/inactivation

Legionella: No limit, but EPA believes that if *Giardia* and viruses are removed/inactivated, Legionella will also be controlled.

It is apparent that the risk of acquiring an infectious disease from properly monitored public surface water systems is very low. *Cryptosporidium* contamination of public water supplies has occurred due to its resistance to the usual disinfection methods. There was an outbreak of illness in Milwaukee, Wisconsin in 1993^{15,45}. It was estimated that 403,000 persons were affected. The mortality was high in immunocompromised persons. The source of the *Cryptosporidium* oocysts was not definitively identified but runoff from cow manure application sites, wastewater from a slaughterhouse, and municipal wastewater treatment plant effluent were the suspected sources. Properly operated wells that draw from deep groundwater are also very unlikely to be affected due to the filtering nature of the earth. Private wells are at higher risk due to the fact that they tend to be shallower and are thus susceptible to contamination, especially after periods of high rainfall and runoff. Private wells are not subject to monitoring standards as well except if they serve enough people and meet the definition above. A General Accounting Office study that was requested by Congress in 1997 found that 15 to 42% of private wells had occurrences of bacterial contamination each year⁶⁴.

Pesticides

The EPA has classified over 60 of the active ingredients in pesticides as probable carcinogens. Studies of associations of cancer with specific pesticides have shown evidence of cancer in humans for 15 pesticides¹⁰⁵. Thus, it is not unreasonable to examine the potential exposures through drinking water. Pesticides enter drinking water several ways. The most common concern is for runoff from field applications of pesticides to enter surface water systems such as lakes and reservoirs. Well water drawn from deep aquifers is unlikely to be contaminated but more shallow wells are susceptible to contamination by pesticides that leach through the soil and reach the water table. Table 2 is a list of pesticides in current use that have EPA Drinking Water Standards. The potential toxicity is listed in the table. The studies supporting the standards are usually animal studies that can be reviewed through the EPA website. By 2006, under Federal law, EPA must review the safety of all existing tolerances (maximum residue limits) that were in effect as of August 1996. Tolerance reassessment is being accomplished through the pesticide reregistration program, by review of all existing uses of a pesticide when a new use is proposed. The reregistration program is well documented on the EPA website and the reports are an excellent source of toxicology information about pesticides and their risks. Atrazine was discussed above as part of the discussion of cancer rates in agricultural or rural communities. Atrazine is one of the most common herbicides so it is often measured as a general gauge of environmental contamination, thus, we will use atrazine as a focus for discussion and as an example of



the class of agents. Atrazine is a triazine herbicide that is used against broadleaf weeds. It works by inhibiting photosynthesis. It is estimated that 76.4 million pounds of atrazine are used annually in the United States. The major use, 86% of total usage, is on cornfields. Approximately 75% of the corn crop in United States is treated with atrazine. Atrazine is not considered to have much potential for acute toxicity nor mutagenicity. There are both hydroxy and chlorinated metabolites of atrazine. The chlorinated metabolites are thought to be of similar toxicity to atrazine. The hydroxy metabolites are assessed separately but the hydroxy metabolites are not detectable in drinking water. The main effects on rats in chronic feeding studies are on neuroendocrine systems that result in poor weight gain, alterations in neuropeptides levels, and mammary tumors. It is thought that the increase in mammary tumors in female Sprague Dawley rats is secondary to high estrogen and prolactin levels caused by the alterations in pituitary function. Atrazine is not thought to be directly carcinogenic. The chief concern for human consumption of atrazine is thought to be endocrine effects in children that might result in delayed puberty or growth. Atrazine and the chlorinated metabolites are not readily found in foodstuffs and the potential exposure through food is thought to be insignificant. The major source of intake for humans will be in drinking water. Based on modeling from a six-month study in rats of luteinizing hormone levels a recommended maximum dose of 0.018 mg/kg/day was derived. Using models of drinking water consumption a drinking water level of comparison (DWLOC) was estimated to be 12.5 ppb for children. It is somewhat remarkable that this theoretical safe limit for atrazine and its chlorinated metabolites is above the legally mandated MCL of 3 ppb by the EPA.

Quite a bit of water monitoring data for atrazine and chlorotriazines is available since the Safe Drinking Water Act mandates monitoring. The EPA estimates that 29 out of 3670 community water systems using surface water had atrazine levels exceeding safe levels for at least one year. These water systems are located in Illinois, Iowa, Louisiana, Indiana, Kentucky, Missouri, and Ohio. Private, rural wells have also been surveyed but were only sampled once. The wells were chosen for their location in areas of heavy atrazine use. Eight of the 1,505 sampled wells had concentrations exceeding the DWLOC of 12.5 ppb. The highest level was 18 ppb.

DIAGNOSIS AND TREATMENT

A description of the clinical presentations of all the acute respiratory illnesses, poisonings (solvents and pesticides for example), toxicities, and infections that may occur on the farm is beyond the scope of this monograph. There are many resources and textbooks that deal with occupational and environmental medicine and address the diagnosis and management of topics such as acute organophosphate poisoning due to accidental ingestion, for example. In this section we will address the difficulties in identifying the effects of chronic exposures. The most important concept for the health care provider to remember is that environmental exposures should be considered when patients have chronic, puzzling, and/or confusing symptoms and illness. In some cases the environmental exposure history will have to be carefully elicited. Knowledge of the potential toxic agents and illness will help in directing the questioning. In some settings the community will have heightened awareness of potential illness and patients will not fail to mention that they think their cough is due to dust blowing into their house from the large hog barn across the highway. In this case the health care provider will likely have to try and determine the role of the environmental exposure and whether to recommend removal from exposure.

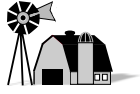
**AIRWAYS DISEASE**

It should be clear from the discussions above that farmers have increased respiratory symptoms and there are many different agents that can cause respiratory disease. The disorders that should prompt some consideration of an environmental cause or trigger are bronchitis, asthma, and asthma-like syndrome. Clues that the environment is contributing are exacerbations of symptoms in relation to specific exposures.

Bronchitis that does not have an apparent infectious cause should prompt some questioning about potential exposures. The key exposures are likely any kind of animal confinement facility and grain or silage storage facilities. Does the subject ever enter such a facility if present and how much exposure do they have to dust? In the absence of clear exacerbations after specific exposures it may be difficult to test for causation. Challenge tests with inhalation of specific agents to diagnose bronchitis are not usually done in clinical settings and are mostly for research purposes. The medical treatment of bronchitis in agricultural workers is not different from other patient groups. Smoking greatly increases the risk of bronchitis in this setting and thus smoking cessation is very important. The important feature of treating these persons will be recognition of the environmental nature of the disease so that protective measures can be taken. Respirators can be used to reduce exposure in animal confinement buildings, but won't be of much use for persons with chronic, low level exposure. Animal confinement buildings can be modified to reduce dust levels. Fully slatted floors, increasing ventilation, increasing the fat in the hog diet, and more frequent washing have all been described as reducing dust levels. Evaluation of farmers, agricultural workers, and farm family members with symptoms of asthma should likely follow the same protocol as one would for occupationally associated asthma¹⁴. The history and physical examination should include an accurate work history. Important components of the history are the temporal relationships between recurrent exposures and disease exacerbations, the circumstances of the exposures, and the severity of the illness. Industrial hygiene data on air monitoring may be available from large operations and employers but will not be available from most farmers. Whether an evaluation of the farm or worksite is needed to assess the degree of exposure is needed depends on the circumstances of the patient and the need for the information.

In some situations challenge tests with antigens or potential agents are indicated. This would be particularly true if the potential causative agent has not been previously described as causing asthma. Protocols and guidelines for bronchoprovocation studies have been published¹³. Peak expiratory flow (PEF) monitoring may be very helpful in evaluating asthma in these settings¹⁴. PEF monitoring has proven to be both sensitive and specific in the evaluation of asthma due to a variety of agents⁶⁷. Allergy testing may be of use in evaluating the possible sensitivity to specific antigens. Pulmonary function tests and nonspecific challenge tests with methacholine are of course used as indicated in the evaluation of asthma and bronchial hyperresponsiveness.

The medical treatment of occupational and environmental asthma is not different from the treatment of nonoccupational asthma. Eliminating or reducing exposure to offending agents is usually the critical area of management of occupational asthma. It can be helpful to determine whether work-related asthma is due to a specific sensitizing antigen or due to irritant-aggravated asthma. In the case of sensitizing antigens it is usually recommended that complete avoidance be achieved. Protective devices



and reduced exposure are not usually sufficient to prevent further deterioration of symptoms and lung function when there is a sensitizing agent in the workplace^{18,61}. Complete removal of the patient from the environment may not be needed in the case of irritant-aggravated asthma. Protective devices and changes in work practices may be enough to avoid high, aggravating exposures. Patients will probably need referral for education and instruction about the use of respirators and protective devices. Unfortunately, the majority of farmers will not have training in or ready access to industrial hygiene services. County extension offices in many states do have information on respiratory protection and many farm supply stores sell the equipment.

There is evidence that some exposures can cause an asthma-like syndrome that does not involve prior sensitization and IgE mediated inflammation. Severe, acute exposures to swine confinement gases and ammonia may cause reactive airways dysfunction syndrome (RADS)^{17,43,91}. Swine confinement workers have increased prevalence of bronchial hyperresponsiveness⁹¹. Supporting the idea that bronchial responsiveness can occur without prior sensitization is the finding that naïve, healthy subjects will develop bronchial responsiveness after exposure in a swine confinement building^{37,54,63}. It is remarkable that this responsiveness occurs after a first time exposure. The diagnosis is dependent on pulmonary function tests demonstrating reversible airflow obstruction or bronchial hyperresponsiveness to methacholine. Treatment is similar to the treatment of asthma and of course reducing exposure or avoidance of further severe exposures. The key exposures are usually animal confinement buildings with swine and poultry being the most common types associated with this type of illness.

CANCER

It will be exceedingly difficult for a health care provider to evaluate a person with a specific cancer for an environmental cause. Unfortunately, subjects with suspicions about environmental exposures will sometimes ask whether their cancer is due to a specific cause, a determination that is usually difficult if not impossible without extensive epidemiologic studies. For most of the cancers that have potential environmental causation the increases in cancer rates are small enough that the excess cases cannot be detected without very large population studies. For cancers such as leukemia and lymphoma it would seem prudent to ask about pesticide use on the farm or home and whether the subject directly works with pesticides. Reducing high exposures, if present, to other family members or workers seems to be common sense.

REPRODUCTIVE HEALTH EFFECTS

Subjects presenting for evaluation of infertility, preterm delivery, and spontaneous abortion may benefit from an occupational and environmental history with the focus on pesticide exposure. There is some epidemiologic evidence of pesticide handling and these outcomes^{19,72}. There is no way of making a case for causation in a specific case however. In addition, there are no studies of the effect of intervention (removing from exposure or stopping pesticide use) on fertility or other outcomes. The health care provider will have to provide advice in the absence of firm information.



OTHER WATERBORNE ILLNESSES

Diarrheal illness and other gastrointestinal disorders due to waterborne infectious agents will be very difficult to clinically differentiate from other causes. Chronic diarrhea in a farmer or family member should be evaluated as for any other person. The use of a private well for drinking water should heighten the suspicion of an infectious disease and prompt the search for stool pathogens such as giardia and cryptosporidiosis. If such an infectious disease is identified the water sources used by the individual may need to be tested. The treatment of infectious diarrhea from the environment is no different than in other settings.

A number of illnesses may suggest an environmental source and prompt an investigation. The alert clinician may be key to this process. There are too many different instances to list here. Examples might be a cluster of symptoms in a family that suggest organophosphate poisoning, skin rashes or diarrhea that suggest contamination of a recreational lake by manure.

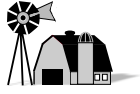
MANAGEMENT ISSUES

The health care provider can play several roles in the diagnosis, management, and prevention of environmental illness in agricultural communities¹. One role is that of educator. Health care providers should be a credible source of information to patients, their families, and communities. Information shared by the provider can inform individuals and communities in their efforts to reduce or eliminate environmental hazards and create a safe home and work environment on the farm. Health care providers may be able to direct persons to the appropriate regulatory agencies and raise awareness of existing regulations. Clinicians should be able to provide accurate diagnosis and know when to pursue environmental causes and thus serve on the frontlines as investigators. A careful environmental history and familiarity with environmental-related disorders are the keys to identifying environmental illness in the community. Health care providers can work with local health agencies to identify trends and contribute to clinical research on agricultural exposures of concern to the rural community. Providers who treat the adverse effects of environmental health hazards can be compelling advocates for more preventive and protective policies at the local, state and national levels. In the next section the regulations and testing available for air and water will be discussed.

REGULATIONS AND TESTING

AIR QUALITY

While there is extensive regulation of certain air pollutants and many industries there is little or no regulation of the hazardous air pollutants produced locally in agricultural operations. Many states have air pollutant emission standards (in addition to national standards) but these usually apply only to industries such as petroleum refineries, smelters, and gasoline distribution facilities. In response to public concerns about large feedlot operations (including swine confinement facilities) some states have begun to regulate air quality near these facilities. Some states have instituted ambient air quality standards for hydrogen sulfide or total reduced sulfur which includes hydrogen sulfide, methyl mercaptan, dimethyl sulfide, and dimethyl disulfide. Nebraska has standards for total reduced sulfur of 0.1 ppm as a 30 minute rolling average and 10 ppm as a one minute maximum. Minnesota and



California have standards for hydrogen sulfide of 30 ppb for not more than one-half hour for not more than two occurrences in a 5 day period and 50 ppb for not more than one-half hour, and not more than two occurrences per year. Some of these regulations apply to air quality at the property line of a facility so the intent is to protect neighbors of such a facility. There is seemingly less protection for those living on the property. If a clinician suspects that there is a problem and the exposure is not easily reduced they might have to resort to help from local and state health departments. Health departments may have information or access to testing labs to further define the problem.

PUBLIC WATER SOURCES

It is very unlikely that clinicians will encounter specific illnesses due to contaminated drinking water from a public water source. This is because our public water supplies are very safe in this regard. Clinicians should be aware of the issues of low level contamination and health effects. An example is the study of pesticide levels in the Rathbun, Iowa water system that was already described⁶². Public drinking water systems, which may be publicly- or privately-owned, serve at least 25 people or 15 service connections for at least 60 days per year. Through the Public Water System Supervision (PWSS) program, the EPA implements and enforces the Safe Drinking Water Act of 1996. Many of the relevant, regulated contaminants have been mentioned already in the discussion of potential hazards in section B of this monograph. The EPA requires regular monitoring of many of the contaminants and the testing results from these water systems can be requested from the water supplier. The EPA also lists the water systems with contaminant level violations on their website at <http://www.epa.gov/safewater/dwinfo.htm>. The annual reports of public water suppliers can also be requested.

PRIVATE WATER SOURCES

The US Geological Survey of 1995 estimated that approximately 42 million people in the U.S. obtain water from their own private drinking water supplies. Most of these supplies are drawn from ground water through wells, but some households also use water from streams or cisterns. The EPA does not oversee or regulate private wells, although some state and local governments do set rules to protect users of these wells. The EPA does provide help with education and encourages these households to take special precautions to ensure the protection and maintenance of their drinking water supplies. EPA has just released a new guide for homeowners entitled "Drinking Water From Household Wells". EPA recommends testing private water supplies at least annually for nitrate and coliform bacteria. Testing for other potential contaminants, such as pesticides, is suggested if problems are suspected. Many laboratories are available to test water quality. The EPA does not test individual homes, and cannot recommend specific labs to test drinking water, but states certify water testing labs. The State Certification Officer can provide a list of certified water testing labs in your state. Some local health departments also test private water for free. Phone numbers for local, county, or state health departments are available under the "health" or "government" listings in the phone book. If a private laboratory is used to conduct the testing, nitrate and coliform bacteria testing will typically cost between \$10 and \$20 to complete. Testing for other contaminants will be more expensive. For example, testing for pesticides or organic chemicals may cost from several hundred to several thousand dollars.

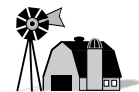


TABLE 1 Infectious Diseases Transmittable to Humans from Manure*

DISEASE	RESPONSIBLE ORGANISM	SYMPTOMS
Bacteria		
Anthrax	<i>Bacillus anthracis</i>	Skin sores, fever, chills, lethargy, headache, nausea, vomiting, shortness of breath, cough, nose/throat congestion, pneumonia, joint stiffness, joint pain
Brucellosis	<i>Brucella abortus</i> , <i>Brucella melitensis</i> , <i>Brucella suis</i>	Weakness, lethargy, fever, chills, sweating, headache
Colibacillosis	<i>Escherichia coli</i> (some serotypes)	Diarrhea, abdominal gas
Coliform mastitis-metritis	<i>Escherichia coli</i> (some stereotypes)	Diarrhea, abdominal gas
Erysipelas	<i>Erysipelothrix</i> <i>Rhusiopathiae</i>	Skin inflammation, rash, facial swelling, fever, chills, seating, joint stiffness, muscle aches, headache, nausea, vomiting
Leptospirosis	<i>Leptospira Pomona</i>	Abdominal pain, muscle pain, vomiting, fever
Listeriosis	<i>Listeria monocytogenes</i>	Fever, fatigue, nausea, vomiting, diarrhea
Salmonellosis	<i>Salmonella species</i>	Abdominal pain, diarrhea, nausea, chills, fever, headache
Tetanus	<i>Clostridium tetani</i>	Violent muscle spasm, “lockjaw” spasm of jaw muscles, difficulty breathing
Tuberculosis	<i>Mycobacterium Tuberculosis</i> <i>Mycobacterium avium</i>	Cough, fatigue, fever, pain in chest, back, and/or kidneys
Rickettsia		
Q Fever	<i>Coxiella Burneti</i>	Fever, headache, muscle pain, joint pain, dry cough, chest pain, abdominal pain, jaundice
Viruses		
Foot and Mouth	<i>Virus</i>	Rash, sore throat, fever
Hog Cholera	<i>Virus</i>	
New Castle	<i>Virus</i>	
Psittacosis	<i>Virus</i>	Pneumonia

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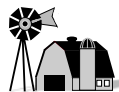


TABLE 1 Continued

DISEASE	RESPONSIBLE ORGANISM	SYMPTOMS
Fungi		
Coccidioidomycosis	<i>Coccidioides immitus</i>	Cough, chest pain, fever, chills, sweating, headaches, muscle stiffness, joint stiffness, rash, wheezing
Histoplasmosis	<i>Histoplasma capsulatum</i>	Fever, chills, muscle ache, muscle stiffness, cough, joint pain, joint stiffness
Ringworm	<i>Various microsporum and trichophyton</i>	Itching, rash
Protozoa		
Balantidiasis	<i>Balatidium coli</i>	Diarrhea, abdominal gas
Coccidiosis	<i>Eimeria species</i>	Diarrhea, abdominal pain, abdominal gas, nausea, vomiting, headache, fever
Cryptosporidiosis	<i>Cryptosporidium species</i>	Watery diarrhea, dehydration, weakness, abdominal cramping
Giardiasis	<i>Giardia lamblia</i>	Diarrhea, abdominal pain, abdominal gas, nausea, vomiting, headache, fever
Toxoplasmosis	<i>Toxoplasma species</i>	Headache, lethargy seizures, reduced cognitive function
Parasites/Metazoa		
Ascariasis	<i>Ascaris lumbricoides</i>	Worms in stool or vomit, fever, cough, abdominal pain, bloody sputum, wheezing, skin rash, shortness of breath.
Sarcocystiasis	<i>Sarcosystis species</i>	Fever, diarrhea, abdominal pain

*Adapted from a report of the EPA, Preliminary Data Summary, Feedlots Point Source Category Study, Dec. 31, 1998, U.S. EPA, Office of Water, Office of Science and Technology, Engineering and Analysis Division, Washington, D.C.³³

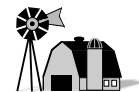


TABLE 2 EPA Drinking Water Standards for Pesticides*

Organic Chemicals	MCLG ¹ (mg/L) ²	MCL ¹ (mg/L) ²	Potential Health Effects from Ingestion of Water	Source of Contaminant in Drinking Water
Alachlor	Zero	0.002	Eye, liver, kidney or spleen problems; anemia; increased risk of cancer	Runoff from herbicide used on row crops
Atrazine	0.003	0.003	Cardiovascular system or reproductive problems	Runoff from herbicide used on row crops
Carbofuron	0.04	0.04	Problems with blood, nervous system, or reproductive system	Leaching of soil fumigant used on rice and alfalfa
2,4-D	0.07	0.07	Kidney, liver, or adrenal gland problems	Runoff from herbicide used on row crops
Dalapon	0.2	0.2	Minor kidney changes	Runoff from herbicide used on row crops
1,2-Dibromo-3-chloro-propane (DBCP)	Zero	0.0002	Reproductive difficulties; increased risk of cancer	Runoff/teaching from soil fumigant used on soybeans, cotton, pineapple, and orchards
Dinoseb	0.007	0.007	Reproductive difficulties	Runoff from herbicide used on soybeans and vegetables
Diquat	0.02	0.02	Cataracts	Runoff from herbicide use
Endothall	0.1	0.1	Stomach and intestinal problems	Runoff from herbicide use
Glyphosate	0.7	0.7	Kidney problems; reproductive difficulties	Runoff from herbicide use
Lindane	0.0002	0.0002	Liver or kidney problems	Runoff/teaching from insecticide used on cattle, lumber, gardens
Methoxychor	0.04	0.04	Reproductive difficulties	Runoff/teaching from insecticide used on fruits, vegetables, alfalfa, livestock
Oxamyl (Vydate)	0.2	0.2	Slight nervous system effects	Runoff/teaching from insecticide used on apples, potatoes, and tomatoes
Picloram	0.5	0.5	Liver problems	Herbicide runoff
Simazine	0.004	0.004	Problems with blood	Herbicide runoff
Toxaphene	Zero	0.0003	Kidney, liver, or thyroid problems; increased risk of cancer	Runoff/teaching from insecticide used on cotton and cattle
2,4,5-TP (Silvex)	0.05	0.05	Liver problems	Residue of banned herbicide

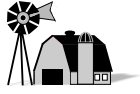
* Adapted from the EPA website which can be seen at <http://www.epa.gov/safewater/mcl.html>

1. Definitions:

MCL – maximum contaminant level, the highest level of a contaminant that is allowed in drinking water. The MCL is set as close to MCLG as feasible using the best available treatment technology. MCLs are enforceable standards.

MCLG – maximum contaminant level goal, the level of a contaminant in drinking water below which there is no known or expected risk to health. MCLGs are non-enforceable public health goals.

2. mg/ml – milligrams per liter, which is equivalent to parts per million, ppm

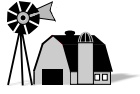


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