

## Concentrated Swine Feeding Operations and Public Health: A Review of Occupational and Community Health Effects

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Recent industry changes in swine-management practices have resulted in a growing controversy surrounding the environmental and public health effects of modern swine production. The numerous wastes produced by intensive swine production not only pose a significant challenge to effective environmental management but also are associated with decreased air quality in confinement houses, potentially transferable antimicrobial resistance patterns, and several infectious agents that can be pathogenic to humans. Published studies have documented a variety of contaminants, microbial agents, and health effects in those occupationally exposed to swine, and these have provided the groundwork for an increasing body of research to evaluate possible community health effects. Nonetheless, several factors limit our ability to define and quantify the potential role of intensive swine-rearing facilities in occupational and community health. Our incomplete understanding and ability to detect specific exposures; the complicated nature of disease etiology, pathogenesis, and surveillance; and the inherent difficulties associated with study design all contribute to the inadequate level of knowledge that currently prevails. However, an evaluation of the published literature, and a recognition of the elements that may be compromising these studies, provides the foundation from which future studies may develop. *Key words:* air quality, air sampling, CAFOs, community health, occupational health, hygiene, industrial wastes, swine production. *Environ Health Perspect* 108:685–699 (2000). [Online 21 June 2000] <http://ehpnet1.niehs.nih.gov/docs/2000/108p685-699cole/abstract.html>

During the last several years most animal husbandry practices in the United States have been industrialized, resulting in an increased number of large corporate and contract livestock operations raising thousands of animals in a single facility. Industrialized farms achieve economies of scale through specialization, increased size, and close confinement that allows high animal densities on relatively small land areas (1,2). These changes in animal production systems, combined with changing community demographics, have considerably narrowed the farm–urban interface and have resulted in growing public concern over the potential occupational, environmental, and community hazards posed by these large concentrated animal feeding operations (CAFOs). Numerous debates and related legislation over this controversial topic have brought to the public forefront several health issues related to modern swine husbandry.

### Swine CAFOs

Most modern swine operations raise thousands of animals in closed confinement buildings. Among other things, closed confinement facilitates climate control and automation of some tasks such as feeding and watering. However, the large number of animals raised in swine CAFOs generate significant amounts

of dusts, dander, and waste materials. Within the confinement buildings, dust particles consisting of swine skin cells, feces, feed, bacteria, and fungi become airborne and contribute to poor indoor air quality (3). The manure and urine produced in these buildings also generate numerous gases that may further decrease the quality of the indoor air. Thousands of gases, particles, and bioaerosol emissions have been documented in swine facilities. Many pollutants present at these facilities do not have occupational exposure limits (OELs).

Swine CAFOs must deal with a substantial amount of waste materials on-site that are associated with significant odors and contain antimicrobials, nutrients, organics, and pathogenic microbes. Raw swine manure can contain 100 million fecal coliform bacteria per gram (4–7). It is estimated that 100 million tons of feces and urine are produced annually by the 60 million hogs raised in the United States (8). Storage and treatment of this waste is typically in wastewater lagoons. Lagoons became popular for the storage and management of swine wastes as production facilities increased in size and efficient storage and treatment of wastes became necessary. The majority of swine lagoons rely principally on anaerobic bacteria (bacteria that do not use oxygen) to decompose the organic matter because more organic matter per unit lagoon

volume can be handled by anaerobic bacteria than by aerobic processes (9,10). In addition, anaerobic lagoons can be deeper, requiring less land area than aerobic lagoons.

Lagoon management has become a significant environmental concern. Contamination of the environment can result from lagoon breaks and the subsequent release of millions of gallons of animal wastes directly into surface water at one time (1) or from seepage losses of lagoon wastewater into the surrounding soil and groundwater (11–13). In addition, land application of liquefied wastes may result in wastes leaching into groundwater or reaching streams as a result of overland flow (4,14). When sprayfields are used to distribute the wastes, aerosolization of particulates may result in contamination over a wide geographic range (15,16).

The widespread application of antimicrobial agents at therapeutic and subtherapeutic levels allows the livestock industry to increase animal densities and feed conversion rates. With greater opportunities for horizontal spread of infectious agents among closely confined animals, antimicrobials are useful to decrease the spread of infectious disease between animals (17,18). The broad application of antimicrobials to farm animals can apply selective pressure to their normal and pathogenic microflora (17–20), resulting in the evolution of groups of resistant organisms that may survive in the environment or pass their resistance properties to other human-associated microbes.

### Identification of Potential Human Health Effects

Historically, human disease resulting from the exposure to gases, aerosols, and infectious

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We thank K. Mottus for assistance in preparing this manuscript.

This research was supported by grant R25-ES08206-04 under the Environmental Justice: Partnerships for Communication program of the NIEHS.

Received 10 January 2000; accepted 10 April 2000.

agents generated or carried by animals and their wastes has been largely limited to those in agricultural occupations (e.g., farmers, food processors, and veterinarians). Consequently, most reports of human-acquired disease from animal husbandry practices focus on occupational exposures. However, even in these high-risk groups, elucidating potential causative agents, dose-response relationships, disease mechanisms, and methods of control is problematic.

In health-effect studies of gases and particulates, it is difficult to identify the cause of occupational illnesses in the absence of specific biomarkers. Similarly, determining which chemicals to sample to evaluate occupational exposures is complicated because it still is not clear which specific contaminants or complex mixtures are responsible for reported symptoms, or even whether all the potentially harmful substances have been evaluated.

Studies of occupational exposure to infectious agents associated with swine production are complicated by the natural history of disease caused by agents of animal origin (zoonoses). The majority of zoonotic diseases that occur in people resolve without specific medical therapy and are not transmitted between people (21). Consequently, large outbreaks or epidemics of disease do not usually occur with zoonoses. Even diseases that do require medical attention can be difficult to diagnose because the symptoms are vague and nonspecific and because traditional human and veterinary surveillance systems are not equipped to detect many of them (22). Consequently, many diagnoses of this type are made only when there is increased suspicion on the part of the medical provider and when special requests are made of the diagnostic laboratory. Even when these requests are made, laboratory technicians unfamiliar with animal diseases may be unprepared for the diagnosis of zoonotic diseases.

Detection of specific exposures and diseases in the communities surrounding swine CAFOs is even more challenging because of the additional complexities of environmental dispersion of agents and human exposure pathways. Furthermore, the susceptibility of community members to contaminants and pathogens may be substantially different from that of workers.

To address some of these issues, we evaluate the evidence related to the adverse exposures and health effects found in occupational studies. Although more susceptible workers may leave their jobs because of adverse health effects, an assessment of the occupational exposures and associated symptoms may provide a template for the approach that studies of potential community problems should take. We discuss the most likely routes of

community exposure to these hazards and the limitations of the published research.

## Identified Hazards of Swine CAFOs

### Air-Associated Contaminants

In the 1970s, researchers described respiratory hazards for workers in swine confinement operations (23,24). Since that time many researchers from the United States, the Netherlands, Sweden, Denmark, Yugoslavia, and Canada have documented symptoms and begun to identify the contaminants and contaminant concentrations associated with the symptoms (25–40). Industrial hygiene studies have measured the concentration of contaminants in the air of swine houses, epidemiologic studies have documented symptoms in workers and contaminant concentrations in air, mechanistic studies have exposed human volunteers to swine dust, and community studies have documented symptoms in residents who live adjacent to swine CAFOs.

The primary airborne contaminants in swine operations can be grouped into three categories: gases and vapors, nonbiologic aerosols, and bioaerosols (24,41,42). Early occupational health studies focused on the gases and nonbiologic aerosols in the indoor air because their adverse health effects generally were well documented and because there were recommended occupational exposure limits for these agents. However, bioaerosols, particularly endotoxins, have emerged as important agents in causing adverse respiratory health effects in swine CAFO workers.

Although the variety of adverse health effects associated with working at a swine CAFO is well documented, it is not clear which agents or mixtures are responsible for the symptoms. For example, health effects have been positively correlated with individual contaminants such as ammonia, dust, and endotoxins, as well as combinations of these (38,43–45). Work practices have also been associated with symptoms seen in workers, such as the types and methods of

feeding the animals, the use of wood shavings for animal bedding, and the use of disinfectants (39,46,47). Holness and Nethercott (46) found that nasal irritation, coughing, wheezing, and dyspnea were frequently associated with floor feeding of hogs and that dizziness was frequently associated with working with liquid manure. The researchers suggested that the high dust levels in their study were because of floor scatter feeding, indoor feed grinding, and the use of high-moisture corn feed.

Epidemiologic studies of workers in swine-production facilities have documented increases in morning phlegm, coughing, scratchy throat, burning eyes, wheezing, shortness of breath, and chronic bronchitis compared to individuals who do not work in these facilities (38,41,42,48).

**Gases and vapors.** The primary gases and vapors of interest to health researchers include ammonia, carbon monoxide, hydrogen sulfide, and methane. The major source of gases and vapors detected in confinement buildings is the manure contained in the storage pits beneath the flooring. The concentrations of specific gases inside swine houses are not usually high enough to be toxic by themselves based on the OELs mandated by the Occupational Safety and Health Administration (OSHA) and recommended by the American Conference of Governmental Industrial Hygienists (ACGIH) and the National Institute for Occupational Safety and Health (NIOSH) (Table 1). However, these guidelines take into account economic as well as health-based considerations (49,50).

Ammonia's effects on the respiratory system include irritation to the eyes, skin, mucous membranes, and upper respiratory system. Ammonia is water-soluble and is absorbed in the upper respiratory tract; however, if there are aerosols and high humidity present in the air, ammonia and other gases can adsorb onto the aerosols and be carried deeper into the lungs. At high concentrations hydrogen sulfide is an eye and respiratory tract irritant. Other chemicals used in swine

**Table 1.** OELs for several agents that are found in swine house air and dust.

Agent	OSHA (249)	ACGIH (250)	NIOSH (251)
Ammonia	50 ppm TWA	25 ppm TWA 35 ppm STEL	25 ppm TWA 35 ppm STEL
Carbon monoxide	35 ppm TWA	25 ppm TWA	35 ppm TWA
Hydrogen sulfide	20 ppm ceiling	10 ppm TWA 15 ppm STEL 5 ppm TWA <sup>a</sup>	200 ppm ceiling 10 ppm ceiling
Particulates			
Inhalable dust	15 mg/m <sup>3</sup> TWA	10 mg/m <sup>3</sup> TWA	—
Respirable dust	5 mg/m <sup>3</sup> TWA	3 mg/m <sup>3</sup> TWA	—
Endotoxins	None	None	—

Abbreviations: STEL, short-term exposure limit; TWA, time-weighted average.

<sup>a</sup>OEL proposed in 1999.

CAFOs that have been implicated in adverse respiratory effects and asthma include quaternary ammonium disinfectants and disinfectants containing aldehydes (glutaraldehyde and formaldehyde) or chloramine (47,51).

In addition to these gases and vapors, thousands of vapors have been identified as being responsible for the odors characteristic of swine CAFOs. Often the odors increase as the animal manure decomposes. Anaerobic

processes can release volatile fatty acids that may be more offensive odorants than ammonia or hydrogen sulfide. Studies show that the odorous compounds in swine CAFOs are adsorbed onto dust particles < 10 microns in size (52). In fact, the odorous air inside swine CAFO buildings was odorless when a respirator equipped with a dust filter was used. When the small dust particles are inhaled they impinge on the moist warm mucous membranes in the nose and the volatile compounds are released—enabling the perception of odor. Researchers have proposed that the most critical factors involved in the release of odorous volatile organic chemicals from the dust particles are the sizes and concentrations of the particles. Table 2 shows characteristic odors for many of the compounds and presents concentrations that have been measured at swine CAFOs. The quantified concentrations of specific contaminants in air are considered low, and it is difficult to evaluate their significance because there are few OELs and associated health effect studies for most chemicals at the level of odor detection.

**Organically derived aerosols.** Nonbiologic aerosols generally consist of dust particles generated from feed, skin cells, hair, and dried feces. Acute exposures to high levels of dust may result in increased phlegm production and pulmonary inflammation 4–10 hr after exposure; these symptoms can last up to 24 hr. Chronic exposures may result in bronchitis and asthma. For industrial hygiene sampling, dust is separated into fractions (total, inspirable, thoracic, and respirable) based on particle size and site of deposition in the lung. Total dust refers to all of the dust particles in the air that can be inhaled or captured on a filter. The inspirable dust fraction is a newer term that refers primarily to materials that are hazardous anywhere in the respiratory tract, particularly in the head airway region. The thoracic fraction is dust that can reach the thoracic airways (past the larynx) or the gas exchange region. The respirable fraction refers only to the size fraction of aerosols that reach deep into the lungs into the gas exchange region—past the terminal bronchioles. Current occupational exposure limits for dust are presented in Table 1.

Pickrell et al. (53) examined the size distribution of aerosols in a swine confinement facility and found that when a certified dust mask was exposed to silica dust, 1% of the dust with an aerodynamic diameter of 0.6–1.0  $\mu\text{m}$  penetrated the mask. However, when the same masks were exposed to swine confinement aerosols, there was 3–25% penetration of the sealed masks. The authors concluded that swine confinement aerosols may have a considerable size distribution

**Table 2.** Odorous chemicals detected in swine house air and dust.

Odor compound	Odor characteristic	Concentrations found	Reference
Organic acids			
3-phenyl-propionic	Cinnamon	Not quantified	(52,228–230)
Acetic	Pungent, sharp, vinegar	3.94–39.81 $\mu\text{g}/\text{m}^3$ 267 $\mu\text{g}/\text{g}$ dust 189 $\mu\text{g}/\text{m}^3$	(231) (232) (233)
Butyric	Sweaty, rancid, sharp, dairy, cheese, butter, fruit nuance	Not quantified 80 $\mu\text{g}/\text{m}^3$ 0.26–11.02 $\mu\text{g}/\text{m}^3$ 73 $\mu\text{g}/\text{g}$ dust 318 $\mu\text{g}/\text{m}^3$	(52,229,230,234,235) (236) (231) (232) (233)
Caproic	Goatlike, mild, sour, fatty	Not quantified 0.15–0.47 $\mu\text{g}/\text{m}^3$ 10 $\mu\text{g}/\text{m}^3$	(52,229,230,234,235) (231) (233)
Isobutyric	Pungent, rancid butter	Not quantified 47 $\mu\text{g}/\text{g}$ dust 40 $\mu\text{g}/\text{m}^3$	(229,230,235) (232) (233)
Isovaleric	Disagreeable, rancid cheese, sour, stinky feet, sweaty	Not quantified 62 $\mu\text{g}/\text{g}$ dust 49 $\mu\text{g}/\text{m}^3$	(229,230,235) (232) (233)
Lauric acid	Heavy, stale	Not quantified	(52,230)
Phenylacetic	Sweet, floral, swine	0.22–0.45 $\mu\text{g}/\text{m}^3$ Not quantified	(231) (52,228,230)
Propionic	Pungent, disagreeable, rancid	0.12–13.08 $\mu\text{g}/\text{m}^3$ 140 $\mu\text{g}/\text{g}$ dust 156 $\mu\text{g}/\text{m}^3$	(231) (232) (233)
Valeric (pentanoic)	Unpleasant, sickening, putrid, fecal, sweaty, rancid	Not quantified 0.21–3.06 $\mu\text{g}/\text{m}^3$ 38 $\mu\text{g}/\text{m}^3$ 35 $\mu\text{g}/\text{m}^3$	(229,230,234) (231) (232) (233)
Phenolics			
Cresols	Medicinal, sweet, tarry	7.3 $\mu\text{g}/\text{m}^3$ 1.17–2.09 $\mu\text{g}/\text{m}^3$ 145 $\mu\text{g}/\text{g}$ dust 39 $\mu\text{g}/\text{m}^3$	(236) (231) (232) (233)
Ethylphenols	Sweet, burned	Not quantified 1.97 $\mu\text{g}/\text{m}^3$ 13 $\mu\text{g}/\text{g}$ dust	(52,228,230,234,237,238) (231) (232)
Phenol	Sweet, tarry, burned	Not quantified 92 $\mu\text{g}/\text{g}$ dust 23 $\mu\text{g}/\text{m}^3$	(52,229,235,237,240) (232) (233)
Nitrogen-containing compounds			
Ammonia	Pungent	Not quantified	(229,230,235)
Dimethyl amine	Pungent, fishy, ammoniacal	2,000 $\mu\text{g}/\text{m}^3$ Not quantified	(233) (237)
Skatole (3-methyl indole)	Fecal odor, nauseating	Not quantified	(52,228–230,235,237)
Trimethyl amine	Ammoniacal, fishy, pungent	2,000 $\mu\text{g}/\text{m}^3$ Not quantified	(233) (229,230,235,240)
Trimethyl-pyrazine	Nutty, musty earthy, powdery cocoa, roasted peanut	0.45 $\mu\text{g}/\text{m}^3$ Not quantified	(236) (230,234)
Tetramethyl-pyrazine	Sweet, musty chocolate, coffee, cocoa, soybean, lard, burnt	0.09 $\mu\text{g}/\text{m}^3$ Not quantified	(236) (230,234)
Indole	Strong moth ball, naphthelene, intense fecal, nauseating	Not quantified	(228–230,235)
Sulfur-containing compounds			
Dimethyl sulfide	Decayed vegetables, putrid	Not quantified	(235,237)
Hydrogen sulfide	Rotten eggs	Not quantified	(229,230,235,241)
Other compounds			
Hexanal	Horseradish, green, fruity, aldehydic, fatty, sweaty	Not quantified 0.40–2.41 $\mu\text{g}/\text{m}^3$	(52) (231)
2-Hexenal	Green plant	0.29–2.58 $\mu\text{g}/\text{m}^3$ Not quantified	(231) (235)

< 1.0  $\mu\text{m}$  in diameter. Therefore, respirable aerosols may be an important size fraction for study in swine CAFOs. A cross-sectional study on respiratory health in swine producers suggested that when workers used dust masks to prevent illness, there was a lower prevalence of chronic and work-related respiratory symptoms (54). Workers who used dust masks preventatively had better lung function indices than those who did not wear masks. However, if workers used dust masks because they were already experiencing symptoms, their lung function was comparable to workers who did not wear dust masks.

**Bioaerosols.** Bioaerosols are particles that contain endotoxins, bacteria, and fungi. Endotoxins are present in dusts as a part of a bacterial cell wall or as fragments of whole bacteria. Endotoxins are fragments of the gram-negative bacterial cell wall that contain lipopolysaccharide as well as the other naturally occurring compounds in the cell wall. In the laboratory, the control standard for endotoxin is chemically pure lipopolysaccharide. When endotoxin is inhaled it can potentially cause chronic respiratory symptoms (cough, phlegm production, and wheezing), pulmonary impairment, malaise, and fever (55–57).

Bioaerosols from swine facilities contain several microbial agents but humidity, temperature, and oxygen content all affect their viability (58,59). Gram-positive bacteria are in the greatest concentration; *Enterococcus* accounts for 68–96% of the total bacteria (60). Total bacteria typically include 7–53% gram-negative bacteria (28,60,61), with only 12–40% of the gram-negative bacteria being adsorbed to respirable particulates (28,60). These gram-negative bacteria are the most susceptible to inactivation by oxygen; therefore they are likely not viable in the environment. Evidence suggests that viruses are more stable on bioaerosols, and it has been proposed that influenza transmission may be attributable, in part, to bioaerosol deposition (58).

### Waste-Associated Contaminants

**Infectious agents.** Swine-associated wastes such as manure, urine, and tissues are associated with numerous microbial pathogens that can be potentially transmissible to humans. These wastes contain bacteria, viruses, and protozoa capable of causing illness in humans even in the absence of physical signs of disease in the swine. Organisms associated with the gastrointestinal tract of swine, such as *Erysipelothrix rhusiopathiae*, *Yersinia enterocolitica*, *Salmonella* species, *Streptococcus suis*, and hepatitis E virus, may be passed to humans by direct contact with either saliva or fecal wastes or by media contaminated with these materials. Alternatively,

contact with infected urine or tissues can result in transmission of organisms such as *Leptospira* or *Brucella* bacteria between animals and humans. Some organisms, such as *S. suis*, influenza virus, and hepatitis E virus, have strains with varying infectivity to human hosts—some strains are species specific and are not capable of infecting humans whereas others do not have such a limited host range. This complicates detection and control of these diseases in humans.

**Antimicrobial resistance.** Some bacteria are naturally resistant to certain antibiotics and others develop resistance by mutation or acquisition from other resistant bacteria when subjected to the selective pressures exerted by antimicrobials (17–19,62). Before 1950 bacteria were largely susceptible to antibiotics (19) but resistance to tetracycline began to be reported in bacterial isolates from market pigs in the United Kingdom starting in 1956 (63). Since then single- and multiple-resistance patterns to virtually every antibiotic have been found in bacteria, including *Escherichia coli*, *Salmonella*, *Campylobacter*, *Enterococcus*, and *Staphylococcus* (18,20,63–76).

Antimicrobial resistance patterns can be transferred between bacteria, and disease does not have to occur in the host to transfer resistance (19,62). The development of resistant strains of bacteria can result in increased infectivity and virulence of pathogens and reduced effectiveness of appropriate therapy. An example is the recently emerged multiply-resistant bacteria, *Salmonella typhimurium* DT104. This strain of *Salmonella*, which emerged in livestock in the United States and the United Kingdom in the 1980s, is resistant to five antimicrobials and is associated with higher morbidity and mortality than antimicrobial-susceptible strains of *Sa. typhimurium* (64,77,78). Direct transmission of this organism from infected animals to their caretakers has been documented (78).

**Nutrients.** Wastes also contain high quantities of many nutrients such as nitrogen and phosphorous. In public health the most notable of these nutrients is nitrogen. Excessive nitrates in water continue to be a cause of methemoglobinemia (blue-baby syndrome)—an underrecognized cause of illness and death in infants (79,80). Some evidence suggests that methemoglobinemia is more likely when nitrate-containing water is also contaminated with bacterial species (as might be expected when groundwater is contaminated with fecal wastes), because the bacteria convert the nitrate to nitrite, causing diarrhea in infants (79). In addition, animal studies and some human studies suggest that reproductive health effects such as central nervous system developmental defects and miscarriages may occur with excessive intake of nitrates (79,81).

## Occupational Health Effect and Exposure Studies of Swine CAFOs

### Air-Associated Contaminants

Epidemiologic studies to evaluate respiratory and other symptoms in swine confinement workers usually compare swine workers with nonfarming control subjects and use questionnaires, lung function tests, and occasionally sputum sample analyses of immune cells. Bacteria and endotoxins have been the primary contaminants measured when symptoms are compared with exposures to air contaminants, total and respirable dust, carbon dioxide, ammonia, hydrogen sulfide, and carbon monoxide. Table 3 lists the levels of contaminants found in the studies cited in this article. The OELs for gases and vapors (Table 1) were rarely exceeded in the studies, and slightly less than half of the studies exceeded the limits for dust. Furthermore, the nuisance dust standard may not be appropriate to apply to swine confinement workers because the dust in these houses is highly biologically active (44). Donham et al. (43) suggested that exposure guidelines should be reduced for total dust and ammonia—to 2.8  $\text{mg}/\text{m}^3$  and 7.5 ppm, respectively. It is difficult to evaluate endotoxin levels because there is no established OEL. Various groups have calculated no-effect levels for endotoxins in several ranges: 170–180 (43,55), 33 (82), and < 1–20  $\text{ng}/\text{m}^3$  (83–87). These no-effect endotoxin levels are similar to the levels observed in nonagricultural and industrial buildings (88), but 12 studies in Table 3 exceeded the highest no-effect level calculated (170–180  $\text{ng}/\text{m}^3$ ).

Swine confinement workers have significantly more symptoms of chronic bronchitis and asthma (35,38,39,89) and more missed work days (43) than controls. Documented symptoms include wheezing, coughing, sinusitis, fever, chest tightness, nasal irritation, phlegm, throat irritation, and sneezing. Some farmers also reported headaches and joint and muscle pain (61). Lung function indices of airflow are significantly lower (35,38,43,44) or no different (89) than nonfarming controls. Swine workers had a significant elevation in macrophages in sputum samples, indicating signs of lower respiratory tract inflammation (89).

Healthy, nonsmoking, previously unexposed volunteers exposed to several hours of swine dust in a swine CAFO experience a variety of symptoms, including cough and nasal stuffiness (90–92), moderate chills (90–94), headaches (90–94), muscle pain (91,92,94,95), mental fatigue (91,95), malaise (93,97), and nausea (93). Third-year veterinary students who visited a swine farm for 3 hr reported eye irritation, headache,



tiredness, cough, nasal and throat irritation, sinus trouble, and flulike symptoms (98). Symptoms generally developed the same day and disappeared within 3 days of the exposure. Thorn and Rylander (99) exposed healthy subjects to bacterial endotoxin; 24 hr after exposure the subjects reported breathlessness, irritation in the throat, dry cough, headache, heaviness in the head, and unusual tiredness.

When comparing health effects to exposures, most studies found a correlation between one or more contaminants and lung function indices and/or respiratory, irritation, and flulike symptoms (Table 4). Endotoxin and ammonia were most often correlated with lung function and symptoms followed by dust.

Donham et al. (43) found that the correlation between exposure and pulmonary function decrements was highest after 6 years of cumulative exposure, with total dust and ammonia being the strongest predictors of response. In a follow-up study with the same cohort, Reynolds et al. (44) found the strongest correlations for workers who had 0–6 years or 10–13 years of exposure. Based on years of exposure, total and respirable endotoxins and ammonia were strongly correlated with response in the 0- to 6-year group; total dust, respirable dust, and ammonia with those in the 10- to 13-year group; and total dust with the > 13-year group. The researchers suggested that although total dust may be an important factor for chronic changes in pulmonary function, endotoxins

may be most important for acute health effects. Zejda et al. (45) found a significant relationship among symptoms, lung function, and the number of hours worked. When a subset of young workers (26–35 years of age) was evaluated, Zejda et al. (35) found that chronic respiratory symptoms were associated with the number of hours worked each day and the number of pigs per barn. The adverse health effects of working in intensive swine operations seen in the subset of workers may be because younger workers spend more time in the barns than older workers. On the other hand, older workers who are symptomatic may have a tendency to leave the industry. Several studies found a positive correlation between lung function and/or symptoms with duration of the use of

**Table 3.** Levels of contaminants found in swine confinement house air.

Total/inhalable dust (mg/m <sup>3</sup> )	Dust fraction (mg/m <sup>3</sup> )	Ammonia (mg/m <sup>3</sup> )	Hydrogen sulfide (ppm)	Carbon monoxide (ppm)	Endotoxin (ng/m <sup>3</sup> or EU/m <sup>3</sup> )	Total bacteria (10 <sup>5</sup> CFU/m <sup>3</sup> )	Bacterial fraction (10 <sup>5</sup> CFU/m <sup>3</sup> )	Reference
3.08 (1.76–5.17) <sup>a,b</sup>	—	—	—	—	120 (40–280) ng/m <sup>3a,c</sup>	—	—	(60)
1.6 ± 0.4 to 8.8 ± 1.7 <sup>a,e</sup>	—	—	—	—	—	1.51 to 5.44 <sup>d</sup>	0.810 to 2.049 <sup>d,f</sup>	(28)
8.5 ± 1.5 to 17 ± 7.2 <sup>a,e</sup>	—	15.5 ± 3.3 to 17.8 ± 2.8 <sup>a</sup>	—	—	7,900 ± 500 to 28,000 ± 10,300 ng/m <sup>3a,g</sup>	—	—	(90)
1.66 to 21.04 <sup>a,e</sup>	—	1.50 to 13.23 <sup>a</sup>	—	—	15.3 (1.6–28.5) ng/m <sup>3a,g</sup>	—	(3–80) <sup>h</sup> (2–60) <sup>i</sup> (0.02–0.2) <sup>j</sup>	(29)
—	—	15.9 to 33.8 <sup>a</sup>	0.44 to 1.4 <sup>a</sup>	3.4 to 9.1 <sup>a</sup>	—	—	—	(242)
—	—	5 <sup>d</sup>	Trace <sup>d</sup>	0.05 <sup>d</sup>	—	—	—	(24)
4.3 ± 2.0 to 6.8 ± 4.5 <sup>a,e</sup>	0.34 ± 0.4 <sup>a,k</sup>	9 ± 5.2 <sup>a</sup>	ND	—	180 ± 100 to 240 ± 200 ng/m <sup>3a,g</sup> 170 ± 150 to 230 ± 200 ng/m <sup>3a,l</sup>	40 ± 20 <sup>a</sup>	—	(38)
4.53 <sup>m,e</sup>	0.23 <sup>m,k</sup>	5.64 <sup>m</sup>	NR	NR	202.35 EU/m <sup>3m,g</sup> 16.59 EU/m <sup>3m,l</sup>	—	—	(43)
4.9 (2.2–15.2) <sup>a,e</sup>	(0.3–1.4) <sup>k</sup>	(10–25)	—	—	(20–1,900) ng/m <sup>3g</sup> (10–30) ng/m <sup>3l</sup>	5.9 <sup>a</sup>	—	(32)
1.57 ± 2.8 <sup>a,n</sup>	—	8.04 ± 2.7 <sup>a</sup>	—	—	24 ± 4 ng/m <sup>3a,o</sup>	—	—	(243)
4.01 ± 1.73 <sup>m,e</sup>	1.31 ± 1.84 <sup>m,p</sup>	6.33 ± 3.55 <sup>m</sup>	—	—	130 ± 1.52 ng/m <sup>3m,q</sup>	1.077 ± 3.37 <sup>m</sup>	0.077 ± 4.48 <sup>m,r</sup>	(61)
2.06 ± 2.5 <sup>m,e</sup>	0.17 ± 3.74 <sup>m,k</sup>	9 <sup>a</sup>	ND	ND	—	—	—	(39,46)
7.4 to 13.8 <sup>a,e</sup>	—	—	—	—	37 to 315 ng/m <sup>3a,g</sup>	—	—	(100)
13.5 (5.6–24.0) <sup>a,e</sup>	—	(2–3)	0.05	—	600 (80–1,300) ng/m <sup>3a,g</sup>	—	—	(97)
23.3 (20.0–29.3) <sup>a,n</sup>	—	—	—	—	1,300 (1,100–1,400) ng/m <sup>3</sup>	—	—	(91)
5.2 ± 1.2 to 9.4 ± 1.7 <sup>a,e</sup>	—	—	—	—	—	9.306 (6.137–12.467) <sup>a</sup>	—	(244) (33)
1.10 ± 0.35 to 3.20 ± 0.38 <sup>a,e</sup>	0.14 ± 0.10 to 0.73 ± 0.10 <sup>a,k</sup>	—	—	—	—	—	—	(245)
4.6 ± 2.2 <sup>m,e</sup>	—	—	—	—	269 ± 4.1 EU/m <sup>3m,g</sup>	—	—	(246)
2.6 ± 1.3 <sup>m,n</sup>	—	2.3 ± 2.3 <sup>m</sup>	—	—	105 ± 1.4 ng/m <sup>3m,o</sup>	—	—	(51)
2.4 ± 1.9 <sup>m,n</sup>	—	—	—	—	92 ± 2.4 ng/m <sup>3o</sup>	—	—	(247)
3.45 ± 2.49 to 3.72 ± 2.49 <sup>m,e</sup>	0.23 ± 2.9 to 0.26 ± 2.24 <sup>m,k</sup>	—	—	—	176.12 ± 3.16 to 202.67 ± 4.33 EU/m <sup>3m,g</sup>	—	—	(44)
—	—	—	—	—	11.86 ± 2.88 to 16.95 ± 2.30 EU/m <sup>3m,l</sup>	—	—	—
2.41 ± 0.09 to 3.8 ± 0.2 <sup>a,e</sup>	—	26.0 ± 0.6 <sup>a</sup>	0.4 ± 0.04 <sup>m</sup>	—	1,873 ± 286.6 to 3,983.5 ± 498.3 EU/m <sup>3m,g</sup>	—	—	(103)
4.00 ± 1.6 <sup>m,e</sup>	0.43 ± 1.6 <sup>m,k</sup>	—	—	—	58.8 ± 2.0 ng/m <sup>3m,g</sup> 4.54 ± 1.8 ng/m <sup>3m,l</sup>	—	—	(248)
2.7 ± 1.3 <sup>m,n</sup>	—	1.7 ± 1.6 <sup>m</sup>	—	—	111 ± 1.5 ng/m <sup>3m,o</sup>	—	—	(47)
22.4 ± 4.7 <sup>a,n</sup>	0.7 ± 0.4 <sup>a,k</sup>	—	—	—	1,200 ± 400 ng/m <sup>3d,o</sup>	—	—	(92)
21 (16–25) <sup>d,n</sup>	—	—	—	—	1,200 (900–1,400) ng/m <sup>3a,o</sup>	—	—	(95)
20.5 (14.6–30) <sup>a,n</sup>	—	—	—	—	1,200 (800–1,400) ng/m <sup>3a,o</sup>	—	—	(94)
23 (20–30) <sup>d,n</sup>	1.0 (0.7–1.2) <sup>d,k</sup>	—	—	—	1,100 (800–1,400) ng/m <sup>3d,o</sup>	—	—	(105)
2.93 ± 0.92 <sup>a,e</sup>	0.13 ± 0.05 <sup>a,k</sup>	11.3 ± 4.2 <sup>a</sup>	—	—	11,322 ± 12,492 EU/m <sup>3a,g</sup>	—	—	(45)

Abbreviations: ND, not detected; NR, not reported.  
<sup>a</sup>Arithmetic mean. <sup>b</sup>Airborne dust. <sup>c</sup>Endotoxin extracted from airborne dust. <sup>d</sup>Median. <sup>e</sup>Total dust. <sup>f</sup>Respirable bacteria. <sup>g</sup>Endotoxin extracted from total dust. <sup>h</sup>Culturable bacteria (25°C). <sup>i</sup>Culturable bacteria (37°C). <sup>j</sup>Culturable bacteria (55°C). <sup>k</sup>Respiratory dust. <sup>l</sup>Endotoxin extracted from respiratory dust. <sup>m</sup>Geometric mean. <sup>n</sup>Inhalable dust. <sup>o</sup>Endotoxin extracted from inhalable dust. <sup>p</sup>Thoracic dust. <sup>q</sup>Endotoxin extracted from thoracic dust. <sup>r</sup>Gram-negative bacteria.

disinfection (47,51). These studies associated the decline in lung function over the years with quaternary ammonium compounds used as disinfectants and with the use of automated dry feeding systems.

**Mechanistic studies.** Although air contaminants have been correlated with lung function indices, changes in traditional lung function tests taken by swine confinement workers are usually only modest compared to the widespread presence of subjective symptoms. Historically, these tests have been used in the field and in volunteer research to evaluate airway obstructions caused by organic dust. However, it is possible that the swine contaminants operate using a different mechanism and the very modest changes in the lung indices are caused by an inflammatory response that would be uncovered using other test methods.

Larsson et al. (100) evaluated lung function, bronchial reactivity (methacholine

challenge), and inflammatory cells in bronchoalveolar lavage (BAL) fluid. Although the lung function and bronchial reactivity tests were similar between farmers and controls, the BAL fluid of the farmers showed elevations in total cell concentrations and in the concentration of neutrophils, granulocytes, albumin, hyaluronan, and fibronectin. These changes are indicative of an inflammatory reaction in the alveoli. These farmers had signs of airway inflammation reaction and activation of the immune system without alteration in lung function or bronchial reactivity (100).

Schwartz et al. (101) reported that swine confinement work is associated with asthma and bronchitis and that the work-related respiratory symptoms are indicative of airway or lung disease. The authors found that swine confinement workers had evidence of early airway injury that may not always be apparent using lung function tests. Although

the lung function tests were normal, symptomatic swine workers tended to have enhanced airway response to inhaled methacholine and had a thickening of the epithelial basement membrane of the lobar bronchi when compared to asymptomatic controls (101). Thickening of the basement membrane is an early and consistent feature of asthma. Carvalho et al. (102) also found that swine CAFO workers had enhanced airway response to inhaled methacholine and had symptoms of chronic bronchitis.

Mechanistic studies have evaluated the upper and lower airway inflammation in swine farmers by exposing healthy, nonsmoking, previously unexposed volunteers to pure endotoxin (lipopolysaccharide) or to several hours of swine dust in a swine CAFO and then assessing nasal lavage and BAL or sputum analysis. The lavage fluids are analyzed for cells involved with inflammatory responses (total count, macrophages, lymphocytes,

**Table 4.** Association of symptoms and lung function with occupational exposures.

S or L	Variable type <sup>a</sup>	Dust	Respirable dust	Ammonia	Carbon dioxide	Endotoxin	Airborne organisms	Exposure (years)	Work/day (hr)	Farming practices <sup>b</sup>	Disinfectant usage	Reference
S	Individual	+	+			+	+ <sup>c</sup> + <sup>d</sup>	+	+			(38)
L	Individual	+	+	+	+	+ <sup>e</sup> - <sup>g</sup> + <sup>g</sup>	+ <sup>f</sup> + <sup>h</sup>	-	+			
L	Individual	+	+	+				+				(43)
L	Multiple	+						+				
L	Individual	-		+		-						(243)
S	Individual			+		+	+					(61)
L	Individual	-	-	-		+ <sup>i</sup>	-					(39)
S	Individual	-	-							+		(39)
L	Individual	-	-									(46)
L	Multiple	-	-									(46)
L	Multiple	-	-									(46)
S	Individual	-		-		-					+	(51)
L	Individual			+		+ <sup>i</sup>					+	
L	Individual	+	+	+		+						(44)
L	Multiple	+						+				
L	Multiple	+				+		+				
L	Multiple	+				+		+				
L	Individual	-		-		-				+	+	(47)
L	Individual									+	+	(249)
S	Individual							+	+			(35)
S	Multiple							+	+			
L	Individual								+			
S	Individual		+	+	+	+			-			(45)
S	Multiple		+			+						
S	Multiple			+		+						
S	Multiple		+						+			
S	Multiple			+					+			
S	Multiple			+		+			+			
S	Multiple			+		+			+			
S	Multiple			+		+			+			
S	Multiple			+		+			+			
S	Multiple			+		+			+			
S	Multiple			+		+			+			
L	Individual		-	-	-	+			-			
L	Multiple		+			+						
L	Multiple			+		+						
L	Multiple		+						+			
L	Multiple			+					+			
L	Multiple			+					+			
L	Multiple				+				+			
L	Multiple					+			+			

For multiple factors, + indicates that when the two factors are tested together the association is stronger than each factor tested individually; - indicates that when the two factors are tested together, the association is not stronger than either factor tested individually. Abbreviations: L, lung function; S, respiratory symptom.

<sup>a</sup>Of factors. <sup>b</sup>Or specific tasks. <sup>c</sup>Mold spores. <sup>d</sup>Total bacteria. <sup>e</sup>Total dust. <sup>f</sup>Bacteria and molds. <sup>g</sup>Respiratory dusts. <sup>h</sup>Total and respiratory microbes. <sup>i</sup>Subgroup.

granulocytes, neutrophils, and eosinophils) (89–91,93,94,97,99,100,103) and/or the proinflammatory cytokines (tumor necrosis factor- $\alpha$ ) (94), interleukins (90,91,103), and other soluble indicators of inflammation (94,97,100). An increase in these cells represents an influx of inflammatory cells in the upper or lower airways. The release of cytokines may be associated with some of the peripheral effects in workers; for example, headaches, malaise, fever, and fatigue. In addition to lavages, blood can be analyzed for inflammatory cells, cytokines, and other soluble factors (90,92–95,97,99,103–106). Methacholine challenge can be used to evaluate bronchial responsiveness. Studies show significant increases in inflammatory cells and cytokines in the lavage fluids and blood and increases in bronchial responsiveness. Tables 5 and 6 show the inflammatory markers in these studies.

### Infectious Agents

Published reports of occupational disease from zoonoses are largely limited to case series and individual case reports. Because of the long history of known transmission of disease between humans and their domesticated animals, numerous accounts are anecdotal and do not appear in the published literature outside of textbook descriptions. A recent study estimated the risk of zoonotic illness among farmers and found an association between increased reported illness and level of contact with different livestock animals (107). Assisting sows with farrowing, for example, was associated with a relative risk of 6.61 for developing pneumonia compared to nonfarmer controls. As is typical of studies of this kind, the report could not confirm animal sources of infection.

Seroprevalence studies are used most commonly in epidemiology to document occupational exposures to zoonoses. Although some of the studies described here have not specifically included swine farmers, the organisms have either been isolated from swine, or swine are considered the main reservoirs of infection.

**Y. enterocolitica.** Porcine and human strains of *Y. enterocolitica* cannot be distinguished from each other (108). In swine, *Y. enterocolitica* is isolated from the tonsils, oral cavity, intestines and feces of 1–83.3% of healthy swine (108–112). Although yersiniosis is primarily considered a foodborne disease associated with the consumption of pork products (108–110,113–115), it has also been recovered from the floors and viscera tables in slaughterhouses and is considered by some researchers to be an occupationally acquired disease (111,112). A study in Finland compared the presence of antibodies to several serotypes of *Y. enterocolitica* in swine farmers and slaughterhouse workers to

grain and berry farmers; swine farmers had an elevated risk of positive serology compared to the other two groups (116). Another study of slaughterhouse workers in Finland reported a higher prevalence of *Y. enterocolitica* antibodies in workers compared to blood donors from the same geographic region (111), and also found a higher rate of enteric disease symptoms among the occupationally exposed compared to the blood donor controls. There are no published reports of direct transmission of *Y. enterocolitica* from pigs to humans (108); however, seroepidemiologic data suggest that transmission does occur in the occupational setting (111,116).

**Salmonella species.** *Salmonella* has been called the universal pathogen because it has been isolated from all tested vertebrates (117). Swine may represent a significant reservoir of *Salmonella* infection for humans (118). Pigs can shed *Salmonella* into the environment without showing signs of disease, or they might display signs of moderate to severe illness (119–121). Four of the most common *Salmonella* serotypes isolated from swine are on the Centers for Disease Control and Prevention (CDC) list of top 10 human isolates (122).

The risk of salmonellosis in occupational settings may be significant considering the presence of published reports of disease after occupational contacts (78,123,124), the prevalence of the organism in swine wastes (84% in some herds) (122,125–127), and the ability of this organism to survive in liquid slurry systems for months (128). Of the estimated 4 million yearly cases of human salmonellosis, however, roughly 1–10% are confirmed and reported to the CDC (123). Consequently, quantifying the risks of disease represented by specific exposures is problematic. Improved surveillance and detection in recent years, however, has resulted in increased success in tracing human infections directly obtained from livestock species other

**Table 5.** Markers of inflammation in lavage fluids that have been altered after exposure to swine confinement house dust.

Markers in lavage	Reference
Total white blood cell count	(90,91,97,100,103)
Monocytes	(94)
Macrophages	(89–91,93,97)
Lymphocytes	(90,91,93,94,97,99)
Granulocytes	(93,94)
Eosinophils	(93,97)
Neutrophils	(90,91,93,97,99,100)
T-cell markers	(93)
IL-1 $\alpha$	(94)
IL-1 $\beta$	(94,103)
IL-6	(94,103)
IL-8	(90,91,103)
Tumor necrosis factor- $\alpha$	(94)
Albumin	(94,97,100)
Fibronectin	(100)
Hyaluronan	(100)

than swine (129–131), and it is anticipated that recognition of this route of transmission will increase in multiple livestock species.

The emergence of *Sa. typhimurium* DT104 as a significant cause of severe diarrheal disease in animals and humans is of particular concern to public health agencies. This organism has been successfully recovered from several livestock species, including swine (132,133), and there is evidence that this strain may have a competitive advantage over other strains of *Sa. typhimurium* (133). Consequently, swine populations may become increasingly infected.

**Leptospira species.** Several human diseases are due to Leptospire organisms. Weil disease (*Leptospira icterohaemorrhagiae*), canicola fever (*Leptospira canicola*), dairy-worker fever (*Leptospira hardjo*), and swineherds disease (*Leptospira pomona*) are all zoonotic diseases associated with occupational exposures (134). Of these, contact with pigs has been most commonly associated with Weil disease and swineherds disease, and direct transmission has been reported (134,135). It is not unusual for detectable antibodies to multiple serovars to be present within an individual animal (136), and the reported prevalence of leptospire antibodies in pigs range from 10 to 46% (135,137).

Human studies of leptospirosis include an epidemiologic study in the United States which found that 58% of sporadic cases could be attributed to meat processing (138). A similar study in Trinidad reported that approximately 6% of human clinical cases were people working on pig farms (137), and several seroprevalence studies confirmed elevated antibody prevalences in farmers and slaughterhouse workers (136,139,140). In addition, there is a positive association between seroprevalence and the number of years of employment as a meat inspector (139). Farmers are considered at the highest risk of leptospirosis (140).

**E. rhusiopathiae.** Disease associated with the pathogen *E. rhusiopathiae* has been recognized in swine occupations since the

**Table 6.** Markers of inflammation in blood that have been altered after exposure to swine confinement house dust.

Markers in blood	Reference
Total white blood cell count	(90,92,95,97,103–105)
Monocytes	(90,92,99)
Lymphocytes	(93,103)
Granulocytes	(92,93,95)
Neutrophils	(90,99,103,104)
IL-1 receptor antagonist	(105)
IL-1 $\beta$	(105)
IL-6	(92,94,95,103,105,106)
Tumor necrosis factor- $\alpha$	(92,105)
Orosomucoid	(97)
C-reactive protein	(97,104)
Fibrinogen	(106)

19th century (141–143). There are three human disease syndromes associated with this pathogen: a cutaneous form (erysiploid), an acute or septicemic form, and a chronic form (141,143,144). *Erysipelothrix* can be isolated from the tonsils, intestines, lymph nodes, gall bladder, joints, and bone marrow of swine (144). This organism is stable in the environment and is associated with pig carcasses and swine fecal slurry (142,143).

Citing the number of reported cases of systemic erysipelas infection in the last 15 years, a recently published case report suggested that the growth of the swine industry in the southern United States was associated with an increase in human infections with *Erysipelothrix* because this number was already equal to the number reported in the preceding 60 years (141). Studies of the seroprevalence of *Erysipelothrix* antibodies in slaughterhouse workers found rates of 16–17% (142). Because erysiploid is the most common form and usually heals spontaneously after a few weeks, this disease may be an underrecognized occupational disease (141,143).

**Brucella suis.** Brucellosis has long been recognized as a serious occupational disease of livestock producers, slaughterhouse workers, and veterinarians. Consequently, it has been the focus of a stringent eradication program in U.S. swine since 1961 (145,146). Estimates vary, but because of the vague clinical signs of disease, the prevalence of subclinical disease, and the difficulty associated with its diagnosis, only 4–50% of cases in the United States are probably reported (146–148). Swine-associated *B. suis* was responsible for most human cases of brucellosis in the 1960s and early 1970s; surprisingly, it continues to be reported as an abattoir-associated disease into the 1990s in spite of its nearly successful eradication in the United States (145,148).

**S. suis.** Since 1968, adult meningitis caused by *S. suis* has been recognized as an occupational disease in those working with swine and swine carcasses (149,150). It has been most commonly reported in Asia and Northern Europe, but recent case reports have come from Canada and New Zealand (149–153). In a study of *S. suis* meningitis in Hong Kong, a crude incidence rate of 0.17 per 100,000 population was calculated, and the majority of human cases were associated with occupational exposures to swine or pork (150). Although it has never been reported in the United States, some researchers assume this is due to the difficulty of bacteriologic diagnosis in human cases and the lack of surveillance for this disease in the United States, because it is found in other countries with intensive pork production and consumption (149,150,152).

There are 35 identified serotypes of *S. suis* in pigs, but not all are associated with disease in swine or humans (149,150,152,154). Only Group R serotype 2 has been isolated in cases of human meningitis (149–153). The organism can cause disease in pigs or can be found in healthy carriers, and many serotypes may be isolated from a single animal (154). Consequently, the risk of infection to workers is difficult to estimate from prevalence studies of the organism in U.S. swine herds.

**Hepatitis E virus.** Historically, there have been two or three strains of human hepatitis E virus (HEV) in the human population—a Mexican strain and one or two Asian/African strains (155). Most U.S. cases of HEV are associated with travel to countries where this virus is endemic, but epidemiologic studies of blood donors have found a seroprevalence rate of 1–2% (up to 28% in some regions of the United States), suggesting a possible unidentified reservoir in this country (156,157). Commercial swine have a high prevalence of HEV antibodies and carry an HEV strain that is similar to the human-isolated HEV (156). Cross-species infection with the human strain and the swine strain of HEV has been successful under experimental conditions (155,156). Recently, a new human strain of HEV has been isolated in the United States from a man with no history of travel, and the strain is molecularly more similar to the swine HEV strain than to the previously identified human strains (155,156,158,159). Together, this new human U.S. strain and the swine HEV are considered a molecularly distinct genotype (155). Consequently, the possibility of zoonotic transmission of this infectious agent between swine and humans is being explored.

**Influenza.** The most widely recognized example of a virus passed between species is the influenza virus. Influenza viruses are usually species specific, but mutation and reassortment of genetic material can allow them to cross species barriers and infect new hosts. Swine are most important in the epidemiology of influenza as the mixing vessel for several viral strains, and simultaneous infection of pigs with avian viruses and swine or human viruses can result in mutation or reassortment of viral genetic material (160–162). Serologic studies of influenza in pigs suggest that pigs may become infected during outbreaks of human disease (163,164). The famous Spanish flu pandemic of 1918 was generated in pigs, and it is anticipated that the next major human pandemic of influenza may again come from swine (160,162,165).

Influenza disease in human hosts, however, is not entirely limited to the human-derived and swine “mixed” strains of virus.

Serology in humans in contact with pigs indicate exposure prevalences to the swine-adapted influenza virus, H1N1, as 8.8–10% (166,167). Although uncommon, the swine-specific influenza virus does cause disease in human hosts and may be more fatal to people than human-adapted strains (165,168–171).

**Cryptosporidium parvum.** *C. parvum* is a coccidian enteric pathogen of mammals that causes clinical disease in numerous species, including swine and humans (172). The prevalence of fecal shedding of *Cryptosporidium* varies significantly among farms, animal species, and animal ages (173–176). Differences in prevalence on swine farms have been related to management practices, with higher shedding and infection rates associated with poor hygienic practices and incomplete waste removal from animal pens (177). In contrast with other livestock species, shedding of *Cryptosporidium* by pigs does not seem to be predominantly restricted to young animals. Prevalence rates in tested swine populations have ranged from 0 to 34.4% (174,175,177). Infected individuals can shed more than 108 oocysts daily for extended periods of time (178,179), and the human infective dose may be as low as 30 oocysts with some strains (180). Direct transmission to humans from animals has been documented, but these reports have not included swine (181–183).

## Antimicrobial Resistance

The role of pigs as reservoirs of bacterial strains with transferable antimicrobial resistance patterns has been studied for many years. A U.K. study of market pigs documented the evolution of antimicrobial resistance to some common antibiotics in *Es. coli* isolates between 1956 and 1979 (63). This study not only documented increasing patterns of resistance in swine isolates, but also reported that up to 95% of some isolated strains of bacteria contained transferable resistance patterns. Since then, numerous studies have isolated transferable single- and multiple-resistant patterns from the bacteria of pigs, some with ribotypes indistinguishable from those found in human isolates (68,72–75,184,185). The percentage of resistant isolates among swine increases with increasing antimicrobial use on farms (69–71,184).

Several studies have demonstrated the potential for transfer of antimicrobial-resistant properties between livestock animals and workers. Exposure to antimicrobial-containing feed and animal wastes and contaminated animal tissues can result in either selective pressure on human bacterial strains or direct transmission of genetic codes for antimicrobial resistance from animals to humans. In 1978 Levy (66) reported the emergence of tetracycline-resistant bacteria



in poultry within 36 hr of the introduction of a tetracycline-containing feed, and within farm personnel between 4 and 6 months after the introduction of antimicrobial-supplemented feed. In 1989 a similar study of poultry and farm personnel (186) documented increased antimicrobial resistance in commercially reared birds compared to free-range village poultry. In this study, similar resistance patterns were isolated among poultry personnel and birds but not in village controls (186). Nijsten et al. (187) demonstrated the ability of fecal *Es. coli* isolated from pigs to directly transfer their resistance patterns to human fecal *Es. coli* strains. In addition, Marshall et al. (188) reported on the stability of resistant strains of bacteria in the environment after experimental inoculation of pigs with a resistant strain of swine *Es. coli* and the subsequent isolation of this strain from water, bedding materials, mice, flies, and a human caretaker within the 4-month test period.

Furthermore, epidemiologic studies have shown that farmers and abattoir workers have higher incidences of antimicrobial-resistant bacteria than other occupational cohorts. A study of pig farmers, slaughterhouse workers, and suburban residents within the same geographic region found that pig farmers have the highest prevalences of antimicrobial resistance in fecal isolates compared to the other cohorts (67). Slaughterhouse workers and pig breeders in Japan have higher prevalences of antimicrobial resistance in fecal microbes than urban controls, and the human patterns were similar to the sampled pigs (65). Ozanne et al. (76) reported that slaughterhouse workers had a higher prevalence ratio of resistance (1.22–1.36) in isolated enteric bacteria than controls when previous antimicrobial exposure was controlled in the study (76). The patterns of resistance in the swine and slaughterhouse workers also indicated circulation of bacterial genetic material between the animals and workers.

### Potential Routes and Effects of Community Exposure to Swine CAFO Hazards

People residing near swine CAFOs may be exposed to hazardous agents through a number of pathways. Airborne contaminants and small microbe-bearing particulates can be distributed into the outdoor air by building ventilation fans and spray application of slurried wastes. In addition, soil transport of microbes and nutrients from land-applied wastes, leaking lagoons, and pit-buried carcasses, as well as overland flow of microbes and nutrients from land-applied wastes, can potentially contaminate ground- and surface water sources and become sources of waterborne disease. Although there is a paucity of research in this

area, there is a potential for, and some evidence of, community health effects.

### Environmental Dispersion of Swine CAFO Hazards

**Airborne.** A limited number of studies have evaluated gases, dusts, bioaerosols, and odors outside swine CAFOs. Particles can be carried in the air long distances from their source (189), and can cause health concerns in the neighboring communities (190,191). If endotoxins are absorbed on particles < 1 µm in diameter, these particles can stay airborne for long distances and periods of time. Mixtures of volatile organic chemicals can also be transported off-site; however, the concentrations are usually orders of magnitude lower than those measured inside a swine house. Furthermore, OELs are not appropriate to use for the community because they assume the exposed population is healthy, exclude children and the elderly, and are based on a limited exposure duration.

Recently, it has been suggested that the unpleasant odors produced by inhalation of volatile organic chemicals can adversely affect the health status of people living near swine CAFOs (191). Shiffman (192) described how airborne emissions can affect health through direct irritant and psychophysiologic mechanisms. Odorous mixtures can cause sensory irritation in the eye, nose, and throat by activating at least five cranial nerves that have receptors in the nasal cavity, oral cavity, and eyes. Irritants can affect respiratory volume (193,194) and can induce inflammatory responses (195,196). People who have pre-existing respiratory problems may be particularly vulnerable to the adverse effects of irritants, and can experience an increase in nasal resistance, respiration rates, and heart rates after exposures (197,198). Odorants positively or adversely affect mood and stress depending on whether the odor is perceived as pleasant or unpleasant (191,199,200).

To determine how far bioaerosols are transported through the air, they were measured inside and outside a swine facility, to a maximum distance of 300 m (59). Air samples were obtained within 1 m of the ground and most air samples contained viable bacteria. At 300 m from the houses, detected bacteria concentrations were approximately 4–10 times lower than concentrations at a distance of 5 m from the houses. There was a dramatic decrease in concentrations at distances > 300 m, although there were several limitations to the study. First, the measurements were taken on a dry and sunny day that could have resulted in low survival of the bacteria. Second, the process of air sampling bioaerosols can kill bacteria by desiccation and result in underestimation of concentrations. Third, the sampling height

may not have been optimal for measuring the plume centerline.

Air samples were obtained 60 m away from four swine facilities and one control (nonlivestock) farm at a height of 2 m. The samples were analyzed for ammonia, hydrogen sulfide, total dust, and endotoxin (201). Outdoor mean ammonia concentrations ranged from 0.086 to 0.214 ppm at the swine facilities compared to nondetected at the control farm. Concentrations of ammonia were always greater downwind of sources than upwind and were significantly higher than concentrations at the control farm. Outdoors, in most cases, concentrations of total dust, endotoxins, and hydrogen sulfide were below detectable levels.

**Waterborne.** Lagoon breaks have resulted in the release of millions of gallons of animal wastes directly into surface water at one time, resulting in eutrophication, fish kills, and high environmental pathogen loads (1). However, the environmental impacts of land application of liquefied wastes, pit burial of carcasses, and chronic lagoon leakage are less documented. Historically, most of the concern and research regarding water pollution from CAFOs has focused on the impact of land application of wastes (4,202). However, a small body of research has also found seepage losses from waste lagoons in several states and excessive nutrient and microbial loading on regional ground and surface waters.

Before the land application of human waste materials, the microbial content of the material must not exceed federally mandated concentrations. No similar regulations apply to the land application of animal wastes, and the microbial content of water runoff from agricultural lands frequently exceeds the standards for recreational water (4,202). In a study of land application of swine wastes on silty clay soil with subsurface drainage, up to 3% of the microbes applied to the land were drained from the soil (4). Periods of rainfall can increase the microbial loading of environmental waters from CAFOs (202). Several of the previously discussed infectious organisms are stable in the environment and can contribute to the contamination of ground and surface waters. One study attributed enteroviral contamination of a major Canadian river to swine-farming activities (203).

Studies in Iowa and North Carolina (11,14,204–206) revealed groundwater contamination resulting from agricultural practices. Moderate to severe seepage losses from lagoons and groundwater pollution with nitrates and microbes, resulting in contamination in excess of drinking water standards, have been documented (11,14,204–206). A voluntary well-testing program conducted by the North Carolina Department of Environmental Health and Natural Resources

(Raleigh, NC) found that 22% of the tested wells in one county had nitrate levels which exceed the no-observed-adverse-effect level (79,207).

### Community Health Effects

There have been few health effect studies to evaluate the physical and mental health of residents living near swine CAFOs. Although outbreaks of *E. coli*, Leptospirosis, and cryptosporidiosis have been traced to contaminated water sources, specific sources of contamination are rarely identified (81). Evidence for the putative role of livestock production in the environmental spread of infectious agents has been limited to reports of increased infection rates in human populations after periods of high rainfall or flooding, and regional animal events such as calving or lambing (139,208,209). Unfortunately, this evidence does not implicate specific exposures. HEV is a waterborne disease in countries where it is endemic, but contamination sources are not clearly defined. Consequently, there is no direct evidence of community outbreaks of infectious disease resulting from microbial contamination from swine facilities.

Antibiotic residues have been found in wastewater specimens (205), and discriminant analysis has identified resistance patterns in bacteria isolated from environmental waters that are distinct from human patterns and have been attributed to agricultural sources (210). However, it is not known whether exposure to antibiotics or resistant bacteria in contaminated waters has any health impacts on surrounding communities.

The incidence of nitrate poisoning in the United States is not known because is not a reportable disease. In addition, in some areas, infant deaths due to nitrate-induced methemoglobinemia are sometimes misdiagnosed as congenital heart disease or sudden infant death syndrome (80). Long associated with well-water usage, nitrate intoxication is considered a disease of rural areas where livestock production, septic systems, and fertilized fields predominate (80,211). Recently, studies have associated excessive nitrate ingestion with developmental abnormalities and miscarriages, and the CDC blamed water contaminated with nitrates from a swine farm for several miscarriages occurring in 1993 and 1994 (79,81).

Several epidemiologic studies have investigated differential reporting of adverse symptoms between communities closely associated with swine CAFOs and other rural communities. One study evaluated the effect of odors from swine facilities on the mental health of people living near the facility (200). Forty-four persons living near the facilities filled out a Profile of Mood States questionnaire on 4 days when the hog odors

could be smelled; an equal number of controls completed the questionnaires for 2 days. Those who lived near the facility and experienced odors had significantly more depression, tension, anger, fatigue, and confusion than controls.

In a study to evaluate both physical and mental health, Thu et al. (212) interviewed 18 people who lived within a 2-mile radius of a swine facility and comparable controls. The subjects near the facility had significantly higher rates of four clusters of physical symptoms compared to controls. These symptoms are consistent with symptoms reported in swine CAFO workers, and include *a*) respiratory effects such as inflammation of the bronchi or bronchioles, wheezing, and cough (associated with air pollution, chronic agricultural dust inhalation, endotoxins, and smoking); *b*) nausea, weakness, dizziness, and fainting (associated with endotoxin exposure); *c*) headaches and plugged ears (25% of swine workers have chronic sinusitis); and *d*) runny nose, scratchy throat, and burning eyes (associated with exposure to irritant gases such as ammonia). There was no significant difference for anxiety or depression between the study and control groups.

A study in North Carolina compared reported physical symptoms and quality-of-life perceptions among 155 individuals from three rural communities: a rural community with no livestock facilities within 2 miles; a similar group of households within 2 miles of a dairy facility; and another group within 2 miles of a swine CAFO (213). The frequencies of reported symptoms in the three groups were compared with adjustment for sex, age, smoking status, and employment. Those living within 2 miles of the swine CAFO reported a significantly greater frequency of headaches, runny nose, sore throat, excessive coughing, burning eyes, and diarrhea than the other two groups. In addition, compared to the other two groups, the residents near the swine CAFO reported significantly more episodes during which they could not open their windows or enjoy the outdoor environment.

### Limitations of Current Evidence

#### Occupational Studies

**Exposure assessment.** One of the limitations of occupational health studies is successfully linking exposures to symptoms and lung function indices. Usually, the environmental measurements are obtained on 1 day, and these limited measurements are then used to compare with symptoms or lung function tests. Air contaminant concentrations vary spatially and by shift, day, week, and season.

Therefore, isolated short-term contaminant measurements are being compared with health effects that may result from long-term exposures. These short-term measurements are probably not representative of the actual exposures over time. Some of the studies obtain personal measurements and some use area samples. Area samples may be poor estimators of personal exposures. One concern when evaluating dose response using these data is the poor ability of area samples to discriminate between workers with lower and higher levels of exposure.

When sampling for endotoxin in particular, the results may not reflect accurate concentrations in air. The conditions under which the endotoxins are collected, extracted, and stored can all affect the accuracy of the analytical results (56,87,214). In a study by Douwes et al. (215), a series of parallel air samples was collected and different methods of collecting and processing the samples were compared. Investigators found a difference of up to 17-fold in endotoxin yield using the different methods of processing the samples. The types of filter and water dramatically impacted the recovery of endotoxin. Freezing and thawing of the samples significantly reduced the activity of endotoxins up to 25%. Additionally, dust samples appeared to be more stable than extracted endotoxins (87).

There are a number of sources of variation and interferences that affect the quantification of endotoxin in the widely used *Limulus* ameobocyte lysate assay (LAL) (216,217). Historically, endotoxin results from this test have been reported in weight/volume or weight/weight units. More recently, standard endotoxin preparations have been developed, and by using these standards, data can be reported in endotoxin units (EUs). The use of EUs allows for comparisons between laboratories and takes into account the variance in biologic activities between endotoxins from different sources. Milton et al. (216) investigated various interferences in the LAL and found that interferences could result in a 136-fold underestimation to a 34-fold overestimation of endotoxin concentration. Preventing the underestimation of concentrations due to endotoxin collection procedures, storage of samples, assay conditions, or interferences present in the sample is particularly important when evaluating community exposures where the levels may be very low.

In epidemiologic studies, exposure misclassification and confounding can reduce the sensitivity of studies to find effects. Exposure misclassification may result from the use of general air rather than personal sampling, failure to characterize specific chemicals or dusts that are most relevant to health outcomes, and inability to characterize temporal

patterns of exposure. Confounding can occur if workers with higher exposures are more exposed to other causes of adverse outcomes, resulting in the observance of an exposure–outcome relationship that may not exist. The opposite problem may also occur. For example, smokers have poorer respiratory function than nonsmokers. Higher smoking among the unexposed group could dilute differences in respiratory function between exposed and unexposed workers. This could happen if smokers are less tolerant of work in confinement operations than nonsmokers.

**Disease detection.** Characterization of human infectious disease depends on the recognition of the pathogenic agents. Most diseases of swine CAFO origin that potentially affect populations at risk cannot be distinguished from more common human-source diseases. In addition, even relatively common zoonoses and intoxications may be significantly underdiagnosed. It has been estimated that only 50% of *Salmonella* cases seek medical attention, and of these only 20% are diagnosed. For parasitic diseases such as cryptosporidiosis clinicians often misunderstand the laboratory protocols that do not include this organism on routine tests, and fail to specifically request it (218). Methemoglobinemia may be misdiagnosed as congenital heart defects or sudden infant death syndrome (79,80). The lack of routine screening for *Yersinia* in U.S. laboratories has been attributed to its low detection rate in this country (114).

In addition, selection factors may decrease disease detection in occupational studies and limit their application to other cohorts. Two types of selection are relevant. First, workers tend to be a generally healthy group compared to the general population, in that they do not include children, the elderly, or persons with chronic diseases who are too ill to work. This is often referred to as the healthy worker effect. Thus, although workers are studied because their exposures are higher, their lower sensitivity to exposure must be considered when adverse health effects are monitored. The second selection issue of concern occurs within the workplace and affects studies that compare exposure levels among workers according to personal monitoring results and/or length of employment [e.g., Reynolds et al. (45)]. In such populations, a healthy worker survivor effect may occur, in which workers who are more sensitive to the adverse effects of occupational exposures leave the workplace at a higher rate than workers who are less sensitive. In this situation, not only is disease detection compromised, but the length of employment (and magnitude of cumulative exposure) is inversely related to health-effect sensitivity. Greater exposure of less-susceptible individuals tends

to dampen dose–response relationships in occupational studies (219,220).

### Community-Based Studies

**Study design.** Community-based health studies suffer from some of the same methodologic problems. Exposure assessment is often very difficult or nonexistent in community-based studies. For example, Thu et al. (212) did not measure exposure but assumed that residents living near hog operations were more exposed than residents further away. Schiffman et al. (200) asked respondents to record survey responses when they smelled odor but there was no independent evaluation of airborne emissions.

Although health symptoms are important outcomes, the responses of participants may be influenced by feelings about the industry created by loss of home values, quality of life, and other adverse social experiences. Experiences of anger or depression may on the one hand influence health outcomes directly, and on the other influence recall in response to survey items, introducing ambiguity in interpretation of results.

Furthermore, community-level disease detection resulting from surveillance systems is probably insufficient to detect changes in disease rates. First, poor access to health care in rural communities limits the ability to detect changes in incidence observed by passive surveillance systems. Second, regional statistics combining urban and rural populations are not sensitive to changes in disease trends in sparse rural populations. Finally, the index of suspicion for diseases possibly associated with swine CAFO exposure must be higher in the regional health care system to detect zoonotic diseases. Consequently, in the absence of specific population-based surveillance, disease trends in rural communities are difficult to measure.

Community-based studies also suffer from small sample sizes, small number of facilities evaluated, and lack of comparability of the evaluated exposures. Thu et al. (212) and Wing and Wolf (213) examined relatively small clusters of individuals in close proximity to a facility of interest, and persons near only one exposure unit were evaluated (i.e., one swine CAFO). Health effects may differ as a function of management systems, facility size, and local factors affecting exposure pathways.

**Environmental injustice.** A disproportionate presence of polluting industries and environmental exposures in communities of poor and people of color has been referred to as environmental injustice. Environmental injustice is not only a concern with regard to specific health effects, but also with regard to general community health, economic development, and disease surveillance. The

presence of intensive swine operations may reduce land values and limit the attractiveness of those locations for other types of economic and social improvements that positively impact both individual and public health.

Environmental injustice has specifically been considered in the North Carolina swine industry. Two N.C. studies showed that in recent years hog production became concentrated in economically distressed counties with high proportions of African Americans (221,222). Another study examined the distribution of intensive hog operations with respect to the economic and racial characteristics of census block groups (areas of approximately 500 households each) and found strong support for the contention that intensive hog operations in North Carolina are located disproportionately in communities where people of color, the poor, and households that use well water are concentrated (223).

Environmental injustice in these regions of swine CAFO concentration further complicates disease detection and public health surveillance. The accumulation of epidemiologic data may be compromised by a lower rate of physician visits by those most affected. For example, a recent study of outpatient visit trends for infectious diseases showed that the visit rate for white populations was 25% higher than the rate for nonwhite populations (224). This difference cannot be explained by differential disease rates: Morbidity and mortality from infectious diseases such as influenza, *Y. enterocolitica*, and *Salmonella* are significantly higher in African-American populations than in white populations (225,226). Clearly, the surveillance of disease trends is compromised by the many economic and social factors that prevent opportunities for physician diagnoses in the populations at risk from CAFOs.

### The Future of Occupational and Community Studies of Swine CAFO Impacts

Although theory and preliminary studies tell us that gases, vapors, aerosols, microbial pathogens, antimicrobial residues and resistance, and nutrients generated at a swine CAFO might reach the community, exposure assessment and disease surveillance are problematic. Future studies in this area need to focus on appropriate exposure measurements, exposure pathways, and the unique characteristics and impacts on the populations at risk.

Future community-based studies should utilize environmental exposure assessment methods and clinical or physiologic measures of health outcomes to improve their sensitivity and specificity. Considering the similarity between the symptoms observed in workers at

swine CAFOs and in community (212,213) studies, endotoxins and ammonia on particles would be candidates for community-level monitoring. One complication with evaluating endotoxins in the home is determining the source or sources (outdoor or indoor). Based on the literature on odors, it would be valuable to use real-time instrumentation that can detect multiple contaminants simultaneously to capture milligram-per-cubic-meter levels of contaminants in air for the signature compounds emanating from nearby swine CAFO facilities.

Exposure pathways need to be identified and contaminants traced through these pathways from the sources of contamination. For microbial pathogens, molecular techniques may prove invaluable in source tracing. The body of literature evaluating molecular technologies that discriminate animal and human sources of microbes is increasing, and may be of particular relevance in environmental epidemiology studies of this kind.

Finally, special attention must be paid to the unique population impacted by the swine industry. Large-scale CAFOs have impacts on the quality of life of neighbors as well as the larger communities in which they are located (227). Although the impacts of reduced quality of life on long-term mental health could be specifically addressed by further research, neighbors are more concerned about immediate threats to their health and well being. The presence of swine CAFOs, especially in poor and underdeveloped regions, may preclude other types of economic development and industrialization and may impact local land ownership, which are critical to keeping profits in local communities. Research in North Carolina suggests that the loss of African-American-owned land is related to the expansion of vertically integrated swine operations in the state (221). There are extensive opportunities for further research into the impacts of swine CAFOs on land values, land ownership, and the ability of communities to attract and maintain educational, industrial, and medical facilities—community resources that are essential to positive public health developments (96).

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