APPENDIX A

Commented [CM1]: Teri, Please restart the page numbers for this Appendix A (1-22) There are references in this Appendix A that refer to other articles listed in this same Appendix.

References

1. Gomes A, Quinteiro-Filho W, Ribeiro A, et al. Overcrowding stress decreases macrophage activity and increases *Salmonella* enteritidis invasion in broiler chickens. *Avian Pathol.* 2014;43(1):82-90.
Link: https://www.ncbi.nlm.nih.gov/pubmed/24350836

This study sought to characterize the immunosuppressive effect of overcrowding stress in broiler chickens. Overcrowding was found to compromise the intestinal immune barrier and integrity of the small intestine, resulting in inflammation and decreased nutrient absorption. The study concludes that animal welfare measures and avoiding overcrowding stress factors in maintaining poultry health and decreased susceptibility to *Salmonella* infection.

2. Rostagno MH. Can stress in farm animals increase food safety risk? *Foodborne pathogens and disease.* 2009;6(7):767-776.
Link: http://online.liebertpub.com/doi/pdf/10.1089/fpd.2009.0315

This study reviewed current knowledge to assess the potential impact of stress-such as that from inadequate nutrition, deprivation of water and/or feed, heat, cold, overcrowding, handling and transport-in farm animals on food safety risk. The review focused on stress mechanisms influencing the colonization and shedding of enteric pathogens in food animals due to the potential for their dissemination into the human food chain, a serious public health and economic concern. The review concluded that there is a growing body of evidence that demonstrates the negative impact of stress on food safety through a variety of potential mechanisms and recommends additional research to optimize animal welfare and minimize production loses and food safety risks.

3. Rule AM, Evans SL, Silbergeld EK. Food animal transport: A potential source of community exposures to health hazards from industrial farming (CAFOs). *Journal of Infection and Public Health.* 2008;1(1):33-39.
Link: https://www.ncbi.nlm.nih.gov/pubmed/20701843

The results of this study support the hypothesis that current methods of food animal transport from farm to slaughterhouse result in the transfer of bacteria, including antibiotic-resistant bacteria, to the vehicles travelling the same road. Bacteria were isolated from air and surface samples from vehicles following open poultry trucks, suggesting a new route of exposure to pathogens and the further dissemination of these pathogens to the general environment.

4. Price LB, Graham JP, Lackey LG, Roess A, Vailes R, Silbergeld E. Elevated risk of carrying gentamicin-resistant *Escherichia coli* among US poultry workers. *Environ Health Perspect.* 2007:1738- 1742.
Link: https://www.ncbi.nlm.nih.gov/pubmed/18087592

Occupational and environmental pathways of human exposure to antimicrobial-resistant bacteria were explored in this study by comparing the relative risk of antimicrobial-resistant *E. coli* among poultry workers compared with community referents. The study concluded that occupational exposure to antimicrobial-resistant bacteria may be an important route of entry for the bacteria into the community, as poultry workers had 32 times the odds of carrying resistant *E. coli* compared to the community referents.

5. Baykov B, Stoyanov M. Microbial air pollution caused by intensive broiler chicken breeding. *FEMS Microbial Ecol.* 1999;29(4):389-392.
Link: https://academic.oup.com/femsec/article/29/4/389/527380/Microbial-air-pollution-caused-by-intensive-broiler-breeding-operations

This study examined the extent of microbial atmospheric pollution caused by industrial broiler breeding operations and found that as birds aged, microbial numbers increased in the indoor air and were spread into the environment to a greater degree. The study also found that microorganisms could be spread by air flow up to 3000 meters from the production buildings.

6. Spencer JL, Guan J. Public health implications related to spread of pathogens in manure from livestock and poultry operations. *Public Health Microbiology: Methods and Protocols.* 2004:503-515.
Link: https://www.ncbi.nlm.nih.gov/pubmed/15156064

Objectionable odors, flies, excessive levels of nitrogen and phosphorus and the potential spread of human pathogens are among the public concerns with the disposal of animal manure and the spread of dust and manure blown from powerful building fans. The study also finds that importance of animal manure in the spread of infectious pathogens is often underestimated despite the linkages between livestock operations and gastroenteritis in humans.

7. Graham JP, Leibler JH, Price LB, et al. The animal-human interface and infectious disease in industrial food animal production: Rethinking biosecurity and biocontainment. *Public Health Rep.* 2008:282-299. Link: https://www.ncbi.nlm.nih.gov/pubmed/19006971

The transition of food animal production from small-scale methods to industrial-scale operations has been accompanied by substantial evidence of the transfer of pathogens between and among industrial food animal facilities, the environment, and exposure to farm workers. This challenges the notion that modem animal production is more biosecure than smaller operations in regards to the introduction and release of pathogens. The study concludes that industrialized food animal production risk factors must be included in strategies to mitigate or prevent the emergence of pandemic avian influenza.
Refer to page 17 of this document for the complete article abstract.

8. Jahne MA, Rogers SW, Holsen TM, Grimberg SJ, Ramler IP. Emission and dispersion of bioaerosols from dairy manure application sites: Human health risk assessment. *Environ Sci Technol.* 2015 ;49(16):9842-9849.
Link: https://www.ncbi.nlm.nih.gov/pubmed/26158489

The risk of human gastrointestinal infection associated with exposure to airborne pathogens following the land application of dairy manure was explored in this study. It was concluded that bioaerosol emissions from manure application sites may present significant public health risks to downwind receptors, and improved manure management practices that include better controls for bioaerosols were recommended to reduce the risk of disease transmission.
Refer to page 12 of this document for the complete article abstract.

9. Casey JA, Curriero FC, Cosgrove SE, Nachman KE, Schwartz **BS.** High-density livestock operations, crop field application of manure, and risk of community-associated methicillin-resistant *Staphylococcus aureus* infection in Pennsylvania. *JAMA Internal Medicine.* 2013;173(21):1980-1990.
Link: https://www .ncbi .nlm .nih .gov/pubmed/24043228

This study assessed the association between exposure to swine and dairy/veal industrial agriculture and the risk of methicillin-resistant *Staphylococcus aureus* (MRSA) infection. The study found that proximity to livestock operations and crop fields treated with swine manure were each associated with MRSA, skin and soft-tissue infection.
Refer to page 16 of this document/or the complete article abstract.

10. Roberts RR, Hota B, Ahmad I, et al. Hospital and societal costs of antimicrobial-resistant infections in a Chicago teaching hospital: Implications for antibiotic stewardship. *Clin Infect Dis.* 2009;49(8): 11751184.
Link: https://academic.oup.com/cid/ miicle/49/8/1175/425330/Hospital-and-Societal-Costs-of-Antimicrobial

Medical and societal costs attributable to antimicrobial-resistant infections are considerable, and important factors in understanding the potential benefits of prevention programs. Medical costs attributable to antimicrobial-resistant infections range from $18,588 to $29,069 per patient, hospital stay durations from 6.4-12.7 days, and mortality of 6.5%. Societal costs were estimated at $10.7-$15 million.

11. Filice GA, Nyman JA, Lexau C, et al. Excess costs and utilization associated with methicillin resistance for patients with *Staphylococcus aureus* infection. *Infection Control & Hospital Epidemiology.* 2010;31(04):365-373.
Link: https://www.ncbi.nlm.nih.gov/pubmed/20184420

Healthcare costs of methicillin-resistant S. *aureus* **(MRSA)** infections and methicillin-susceptible S. *aureus* **(MSSA)** were compared in this study. **MRSA** infections were found to be independently associated with higher costs, more comorbidities, and higher likelihood of death than MSSA infections.

12. Price LB, Lackey LG, Vailes R, Silbergeld E. The persistence of fluoroquinolone-resistant *Campylobacter* in poultry production. *Environ Health Perspect.* 2007:1035-1039. Link: https://www.ncbi.nlm.nih.gov/pmc/miicles/F'MC1913601/

Halting fluoroquinolone use was not found to have an impact on the proportion of fluoroquinolone-resistant *Campylobacter* on products from the conventional producers, indicating that antibiotic-resistant bacteria may persistently contaminate poultry products even after on-farm use of the antibiotic has ceased. Also, *Campylobacter* strains from the conventional producers were more likely to be resistant to fluoroquinolone than those from the antibiotic-free producers, indicating that antibiotic use in food animal production contributes to the develop of antibiotic resistant pathogens.

13. Schulz J, Friese A, Klees S, et al. Longitudinal study of the contamination of air and of soil surfaces in the vicinity of pig barns by livestock-associated methicillin-resistant *Staphylococcus aureus. Appl Environ Microbial.* 2012;78(16):5666-5671.
Link: https://www .ncbi .nlm .nih .gov/pubmed/22685139

This study examined the presence and concentration of **MRSA** in air and soil downwind from swine CAFOs. The results demonstrate regular transmission and deposition of airborne livestock associated MRSA to areas up to at least 300 meters around pig barns that tested positive for MRSA, suggesting that swine CAFOs can expose other farm animals, wildlife, and people to MRSA.

Refer to page 21 of this document for the complete article abstract.

14. Burgos J, Ellington B, Varela M. Presence of multidrug-resistant enteric bacteria in dairy farm topsoil. *J Dairy Sci.* 2005;88(4):1391-1398.
Link: https://www .ncbi.nlm.nih.gov/pubmed/15778307

This study was conducted to better understand how widespread antibiotic-resistant bacteria are in agricultural settings, particularly in dairy farm environments. The study concluded that dairy farm topsoil contains multidrug resistant enteric bacteria and antibiotic-resistant plasmids, and suggests that dairy topsoils serve as a reservoir for the development of bacterial resistance to antibiotics relevant in clinical medicine.
Refer to page 12 of this document for the complete article abstract.

15. Sapkota AR, Curriero FC, Gibson KE, Schwab KJ. Antibiotic-resistant enterococci and fecal indicators in surface water and groundwater impacted by a concentrated swine feeding operation. *Environ Health Perspect.* 2007:1040-1045.
Link: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC19l3567/

Surface and groundwater located up and down gradient from a swine facility was analyzed for the presence of antibiotic-resistant enterococci and other fecal indicators in this study. Both were detected at elevated levels in down gradient water sources relative to the swine facility compared to up-gradient sources, providing evidence that water contaminated with swine manure can contribute to the spread of antibiotic resistance.
Refer to page 20 of this document for the complete article abstract.

16. Graham JP, Evans SL, Price LB, Silbergeld EK. Fate of antimicrobial-resistant enterococci and staphylococci and resistance determinants in stored poultry litter. *Environ Res.* 2009;109(6):682-689.
Link: https://www.ncbi.nlm.nih.gov/pubmed/19541298

This study examined the survival of anti-microbial resistant enterococci and staphylococci and resistance genes in poultry litter to better understand how land application of poultry litter can affect the surrounding populations environment. The study found that poultry litter storage practices do not eliminate drug-resistant bacterial strains, thus allowing the spread of these drug resistant pathogens into and through the environment via land application of poultry litter.

17. United States Environmental Protection Agency. Literature review of contaminants in livestock and poultry manure and implications for water quality. July 2013:1-137.
Link: http://ow.ly/mTDw308gwbZ

This EPA report on the environmental occurrence and potential effects of livestock and poultry manure related contaminants on water quality found that 60-70% of manure nitrogen and phosphorus may not be assimilated by the farmland where it was generated due to the increasing concentration of industrial animal production. The report also notes the variety of pathogens contained in livestock and poultry manure, as well as the potential for their spread to humans when surface and groundwater and food crops come into contact with manure through runoff, spills, and land-application of manure. It also refers to research indicating that antimicrobial use in livestock and poultry production has contributed to the occurrence of anti-microbial resistant pathogens in animal operations and nearby environments. The report also presents that manure discharge to surface waters can occur by various means and have deleterious effects on aquatic

life and contribute to toxic algal blooms harmful to animals, and to humans when exposed via contact with contaminated drinking water or recreational use of contaminated water.

18. Wichmann F, Udikovic-Kolic N, Andrew S, Handelsman J. Diverse antibiotic resistance genes in dairy cow manure. *MBio.* 2014;5(2):e0l0l 7-13.
Link: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3993861/

This study was conducted to better understand the cow microbiome and the role of the land application of cow manure in the spread of antibiotic resistance. The study reports the discovery of new and diverse antibiotic-resistant genes in the cow microbiome, and provides evidence that it is a significant reservoir of antibiotic-resistant genes.
Refer to page 14 of this document for the complete article abstract.

19. Graham JP, Price LB, Evans SL, Graczyk TK, Silbergeld EK. Antibiotic resistant enterococci and staphylococci isolated from flies collected near confined poultry feeding operations. *Sci Total Environ.* 2009;407(8):2701-2710.
Link: https://www.ncbi.nlm.nih.gov/pubmed/19157515

This study examined if and how antibiotic-resistant bacteria are transferred from poultry operations to nearby communities, and found that flies caught near poultry operations carried the same drug-resistant pathogens as those found in poultry litter. The study concludes that flies may be an important vector in the spread of drug-resistant bacteria from poultry operations and may increase human exposure to these resistant pathogens.

20. Heaney CD, Myers K, Wing S, Hall D, Baron D, Stewart JR. Source tracking swine fecal waste in surface water proximal to swine concentrated animal feeding operations. *Sci Total Environ.* 2015;511 :676-683.
Link: https ://www.ncbi.nlm.nih.gov/pubmed/25600418

The microbial quality of surface water proximal to swine CAFOs was investigated in this study to better understand the impact of CAFOs on the surrounding environment. The results demonstrate overall poor water quality in areas with a high density of swine CAFOs, with high fecal indicator bacteria concentrations in waters both up- and down-stream of CAPO lagoon waste land application sites. The swine-specific microbial source tracking markers used in the study were also shown to be useful for tracking off-site conveyance of swine fecal wastes and during rain events.
Refer to page 17 of this document for the complete article abstract.

21. United States Geological Survey (USGS). USGS water use data for the nation. http://waterdata.usgs.gov/nwis/wu. Updated June 8, 2016. Accessed January 31, 2017.

This United States Geological Survey website provides national water use data by area type (aquifer, watershed, county, state), source (rivers or groundwater), and category such as irrigation or public supply.

22. Henderik D, Sigsgaard T, Thome PS, et al. Health effects of airborne exposures from concentrated animal feeding operations. *Environ Health Perspect.* 2007:298-302.
Link: https://www.ncbi.nlm.nih.gov/pmc/atiicles/PMC1817709/

This report from a Conference on Environmental Health Impacts of Concentrated Animal Feeding Operations: Anticipating Hazards -Searching for Solutions working group states that toxic gases, vapors and particles are emitted from CAFOs into the general environment, and that while these agents are known to be harmful to human health, there are few studies that explore the health risks of exposure to these agents for the people living near CAFOs. While there is evidence that psychophysiologic changes may result from exposure to malodors and that microbial exposures are related to deleterious respiratory health effects, the working group concluded that there is great need to study and evaluate the health effects of community exposure to these CAFO related air pollutants to better understand the impact of CAFOs on the health of community members and farm workers.

23. Cambra-Lopez M, Aarnink AJ, Zhao Y, Calvet S, Tones AG. Airborne particulate matter from livestock production systems: A review of an air pollution problem. *Environmental Pollution.* 2010;158(1):1-17.
Link: https://www.ncbi.nlm.nih.gov/pubmed/19656601

This paper reviews research on particulate matter inside and emitted from livestock production system and reports that livestock housing is an important source of particulate matter emissions. The paper recommends additional research to characterize and control particulate matter in livestock houses, as high concentrations such as those found in livestock houses can threaten the environment and the health and welfare of humans and animals.

24. Mirabelli MC, Wing S, Marshall SW, Wilcosky TC. Asthma symptoms among adolescents who attend public schools that are located near confined swine feeding operations. *Pediatrics.* 2006;118(1):e66-75.
Link: http://pediatrics .aappublications .org/content/l l 8/1/e66

The relationship between exposure to airborne effluent from swine CAFOs and asthma symptoms in adolescents age 12-14 years old was assessed in this study to better understand the health effects of living near industrial swine facilities. The study found that estimated exposure to swine CAFO air-pollution was associated with wheezing symptoms in adolescents.
Refer to page 19 of this document for the complete article abstract.

25. Schinasi L, Horton RA, Guidry VT, Wing S, Marshall SW, Morland KB. Air pollution, lung function, and physical symptoms in communities near concentrated swine feeding operations. *Epidemiology.*
2011 ;22(2):208-215.
Link: https://www .ncbi .nlm .nih .gov/pubmed/21228696

This study examined the associations between reported malodor and monitored air pollutants with lung function and physical symptoms in people residing within 1.5 miles of hog operations to better understand the effect of CAFO air pollutants on human health. The study reported that acute physical symptoms, including eye irritation, respiratory symptoms, difficulty breathing, wheezing, declined forced expiratory volume, sore throat, chest tightness, and nausea were related to pollutants measured near hog operations.
Refer to page 21 of this document for the complete article abstract.

26. Hribar C, Schultz M. Understanding concentrated animal feeding operations and their impact on communities. *Bowling Green, **OH:** National Association of Local Boards of Health.* 2010.
Link: https://www.cdc.gov/nceh/ehs/docs/understanding cafos_nalboh.pdf

The National Association of Local Boards of Health produced this report with the support of the Centers for Disease Control and Prevention and the National Center for Environmental Health to assist local board of health members better understand their role in mitigating potential issues with CAPOs. The report concludes that large-scale industrial food animal production can cause numerous public health and environmental problems and should thus be monitored to prevent harm to surrounding communities. Suggested actions include passing ordinances and regulations, and increasing water and air quality monitoring and testing. The report also concludes that local boards of health, in collaboration with state and local agencies, are an appropriate body for instituting these actions due to the local nature of CAPO concerns and risks.

27. Donham KJ, Wing S, Osterberg **D,** et al. Community health and socioeconomic issues surrounding concentrated animal feeding operations. *Environ Health Perspect.* 2007:317-320.
Link: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1817697/

The Workgroup on Community and Socioeconomic Issues examined the impacts of CAPOs on the health of rural communities, using the World Health Organization's definition of health, "a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity." The workgroup recommended more stringent CAPO permitting, limiting animal density per watershed, improving local control, mandating environmental impact statements and considering bonding for manure storage basins.
Refer to page 16 of this document for the complete article abstract.

28. Wing S, Wolf S. Intensive livestock operations, health, and quality of life among eastern North Carolina residents. *Environ Health Perspect.* 2000;108(3):233-238.
Link: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1637983/

Reports of decreased health and quality of life from people who live near industrial animal operations were explored in this study through community surveys in three rural communities, one located near a large swine operation, one near two intensive cattle operations, and one area without nearby livestock operations using liquid waste management systems. Residents near the swine operation reported increased occurrences of poor health, such as headaches, diarrhea, sore throat, excessive coughing and burning eyes and reduced quality of life compared to those in the other two communities.

29. Horton RA, Wing S, Marshall SW, Brownley KA. Malodor as a trigger of stress and negative mood in neighbors of industrial hog operations. Am *J Public Health.* 2009;99(S3): S610-S615.
Link: https://www.ncbi.nlm.nih.gov/pubmed/19890165

The association between malodor and air pollutants from nearby hog CAFOs and reported stress and negative mood was evaluated in this study to better understand the role of CAFOs in human health. The study found that malodor and air pollutants acted as environmental stressors and triggers of negative mood and recommended their inclusion in studies of the health impacts of environmental injustice.
Refer to page 18 of this document for the complete article abstract.

30. Wing S, Horton RA, Rose KM. Air pollution from industrial swine operations and blood pressure of neighboring residents. *Environmental Health Perspectives (Online).* 2013;121(1):92.
Link: https://ehp.niehs.nih.gov/1205109/

The association of air pollution and malodor with stress and blood pressure were assessed in this study to improve understanding of the effects of industrial swine operations on human health. Malodor and some air pollutants were found to be associated with blood pressure increases and reported stress, which could contribute to the development of chronic hypertension.
Refer to page 22 of this document for the complete article abstract.

31. Graham JP, Nachman KE. Managing waste from confined animal feeding operations in the United States: The need for sanitary reform. *Journal a/Water and Health.* 2010;8(4):646-670.
Link: https://www.ncbi.nlm.nih.gov/pubmed/20705978

Trends affecting food animal waste production, risks associated with food-animal wastes, and differences between food-animal waste and human biosolid management practices were examined in this study. The study found that no standards exist for the 335 million tons of food animal waste applied to land in the US, while human biosolids, which make up just 1% of all land-applied wastes, are subject to standards. Hormones, arsenicals, high nutrient loads, antibiotics, and pathogens, including antibiotic-resistant pathogens, are often present in animal waste. The authors made recommendations for improving management of food-animal waste through existing and new policies.

32. Showers WJ, Genna B, McDade T, Bolich R, Fountain JC. Nitrate contamination in groundwater on an urbanized dairy farm. *Environ* Sci *Technol.* 2008;42(13):4683-4688.
Link: https://www.ncbi.nlm.nih.gov/pubmed/186779991

This study sought to identify sources of drinking water well nitrate contamination in a housing development built on a dairy farm site using isotopic compositions of nitrate, ammonia, groundwater and chemical ratios. The results indicate that the elevated nitrate levels were due to the leaching of animal waste from pastures into groundwater during the 35 years of dairy operations. The study suggests enacting statutes requiring well water tests prior to the sale of homes built on urbanized farmland to protect the health of homeowners.
Refer to page 13 of this document for the complete article abstract.

33. Relation between nitrates in water wells and potential sources in the lower Yakima Valley, Washington state. U.S. Environmental Protection Agency, Washington, D.C., 2012. Link: Https://Www3.epa.gov/regionl0/pdv'sites/yakimagw/nitrate in water wells study 9-27-2012.pdf.

This study examined the effectiveness of various techniques to identify specific sources of high nitrate levels in residential drinking water well. Dairy waste was concluded to be a likely source of nitrate contamination in the wells due to isotopic data and contextual evidence such as the historical and current volumes of dairy waste in the area, lack of other potential sources of nitrogen in the area, and soil indicators.
For more detail on this report, refer to page 14 of this document.

34. Burkholder J, Libra B, Weyer P, et al. Impacts of waste from concentrated animal feeding operations on water quality. *Environ Health Perspect.* 2007:308-312.
Link: https://www.ncbi.nlm.nih.gov/pmc/articles/F'MC1817674/

This work-group, part of the Conference on Environmental Health Impacts of Concentrated Animal Feeding Operations: Anticipating Hazards-Searching for Solutions, found that current and generally accepted livestock waste management practices do not protect water resources from the pathogens, pharmaceuticals and excessive nutrients found in animal waste. As concern about

the potential human and environmental health impact of long-term exposure to contaminated water grows, there is greater need for rigorous monitoring of CAFOs, improved understanding of the major toxicants affecting human and environmental health, and a system to enforce these practices.

35. Ward MH. Too much of a good thing? Nitrate from nitrogen fertilizers and cancer. *Rev Environ Health.* 2009;24(4):357-363.
Link: https://www.ncbi.nlm.nih.gov/pmc/atiicles/PMC3068045/

Nitrate, the breakdown product of nitrogen fertilizers, accumulates in groundwater under agricultural land and can spread through waterways due to agricultural field runoff. Nitrates are associated with a range of adverse health effects, including methemoglobinernia, various cancers, negative reproductive outcomes, diabetes, and thyroid conditions. Additional research is needed to further evaluate the health effects of nitrate exposure, especially as environmental exposure to nitrates has increased over the last 50 years and 90% of rural Americans depend on groundwater for drinking water, many relying on private wells, which are not regulated by the Safe Drinking Water Act.

36. Chiu H, Tsai S, Yang C. Nitrate in drinking water and risk of death from bladder cancer: An ecological case-control study in Taiwan. *Journal of Toxicology and Environmental Health, Part* A. 2007;70(12):1000-1004.
Link: https://www.ncbi.nlm.nih.gov/pubmed/17497410

The association between bladder cancer mortality and nitrate exposure from Taiwan drinking water was investigated in this study. The results showed a significant positive relationship between the levels of nitrates in the drinking water and the risk of death from bladder cancer, indicating that environmental exposure to nitrates plays a role in the development of bladder cancer.

37. Ward MH, Kilfoy BA, Weyer PJ, Anderson KE, Folsom AR, Cerhan JR. Nitrate intake and the risk of thyroid cancer and thyroid disease. *Epidemiology.* 2010;21(3):389-395.
Link: https://www.ncbi.nlm.nih.gov/pmc/artic1es/PMC2879161/

This study examined the association between nitrate intake through public water and diet with the risk of thyroid cancer and hypo- and hyperthyroidism. The study found an increased risk of thyroid cancer with high water nitrate levels and with longer consumption of water containing nitrates. The increased intake of dietary nitrate was associated with an increased risk of thyroid cancer, and with the prevalence of hypothyroidism.

38. Gulis G, Czompolyova M, Cerhan JR. An ecologic stu4y of nitrate in municipal drinking water and cancer incidence in Tmava district, Slovakia. *Environ Res.* 2002;88(3):182-187.
Link: https://www.ncbi.nlm.nih.gov/pubmed/12051796

This ecologic study was conducted to assess the association between nitrate levels in drinking water with non-Hodgkin lymphoma and cancers of the digestive and urinary tracts in an agricultural district. The study found is that a higher incidence of some cancers was associated with higher levels of nitrate in drinking water. The trend was found in women for overall cancer cases, stomach cancer, colorectal cancer and non-Hodgkins's lymphoma, and in men for non Hodgkins lymphoma and colorectal cancer.

39. Manassaram DM, Backer LC, Moll DM. A review of nitrates in drinking water: Maternal exposure and adverse reproductive and developmental outcomes. *Environmental Health Perspectives.* 2006.
Link: https://www.ncbi.nlm.nih.gov/pmc/aiticles/PMC1392223/

The relationship between maternal exposure to nitrates through drinking water and adverse reproductive and developmental outcomes was reviewed in this study. Animal studies support the association between nitrate exposure and adverse reproductive effects, and some studies report an association between nitrates in drinking water and spontaneous abortion, intrauterine growth restriction and various birth defects, though a direct exposure-response relationship remains unclear and there is insufficient evidence to establish a causal relationship.

40. Brender JD, Weyer PJ, Romitti PA, et al. Prenatal nitrate intake from drinking water and selected birth defects in offspring of participants in the national birth defects prevention study. *Environ Health Perspect.* 2013;121(9):1083-1089.
Link: https://www.ncbi.nlm.nih.gov/pubmed/23771435

The relationship between prenatal exposure to nitrates in drinking water and birth defects was examined in this study. The study concluded that higher maternal water nitrate consumption was associated with birth defects, including spina bifida, limb deficiency, cleft palate, and cleft lip.

41. Knobeloch L, Salna B, Hogan A, Postle J, Anderson H. Blue babies and nitrate-contaminated well water. *Environ Health Perspect.* 2000;108(7):675-678.
Link: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1638204/

Two cases of infant methemoglobinemia associated with nitrate contaminated private well water were described in this paper. The case studies underscore the danger that this contaminated water poses to infants during the first six months of life, as well as the risks of long-term exposure, which include cancer, thyroid disease and diabetes. Steps to reduce nitrate inputs in groundwater and routine well water testing are recommended to protect health.

42. Heisler J, Glibert PM, Burkholder JM, et al. Eutrophication and harmful algal blooms: A scientific consensus. *Harmful Algae.* 2008;8(1):3-13.
Link: http://www.sciencedirect.corn/science/article/pii/S1568988308001066

The US EPA held a roundtable discussion to develop consensus among academic, federal and state agency representatives on the relationship between eutrophication and harmful algal blooms. Seven statements were adopted during the session, which include acknowledgement of the important role of nutrient pollution and degraded water quality in the development and persistence of many harmful algal blooms.

43. Carmichael WW. Health effects of toxin-producing cyanobacteria: "The CyanoHABs". *Human and Ecological Risk Assessment: An International Journal.* 2001;7(5):1393-1407.
Link: http://www.tandfonline.com/doi/abs/10.1080/20018091095087

Current understandings of cyanobacteria toxin poisonings (CTPs) and their risk to human health were reviewed in this paper. CTPs occur in fresh and brackish waters throughout the world as a result of eutrophication and climate change. Cyanobacteria toxins are responsible for acute lethal, acute, chronic and sub-chronic poisonings of wild and domestic animals and humans. These poisonings result in respiratory and allergic reactions, gastrointestinal disturbances, acute hepatotoxicosis and peracute neurotoxicosis.

44. Paerl FIW, Fulton RS ,3rd, Moisander PH, Dyble J. Harmful freshwater algal blooms, with an emphasis on cyanobacteria. *Scientific World Journal.* 2001;1:76-113.

This paper reviews the effects of harmful freshwater algal blooms, resulting from nutrient oversupply and eutrophication, on water quality. Algal blooms contribute to water quality degradation, including malodor and foul taste, fish kills, toxicity, and food web alterations, while algal bloom toxins can adversely affect human and animal health through exposure to contaminated recreational and drinking water. The control and management of blooms, and their negative outcomes, must include nutrient input constraints, particularly on nitrogen and phosphorus.

45. Fry JP, Laestadius LI, Grechis C, Nachman KE, Neff RA. Investigating the role of state and local health departments in addressing public health concerns related to industrial food animal production sites. *PloS one.* 2013;8(1):e54720.
Link: http:/j ournals .plos .org/plosone/article?id=lO .1371/journal .pone .0054720

The role of local and state health departments in responding to and preventing community concerns with industrial food animal production are explored in this study through qualitative interviews with state and county health department staff and community members in eight states. Political barriers, lack of jurisdiction, and limited resources, expertise and staff all limit health departments' ability to respond to IFAP concerns, while community members reported difficulty in engaging with health departments. These limitations and difficulties contribute to limited health department engagement on these issues.

46. Fry JP, Laestadius LI, Grechis C, Nachman KE, Neff RA. Investigating the role of state permitting and agriculture agencies in addressing public health concerns related to industrial food animal production. *PloS one.* 2014;9(2):e89870.
Link: http://journals.plos.org/plosone/article?id=1O.l 371/journal.pone.0089870

This study explored how state permitting and agriculture agencies respond to environmental public health concerns regarding industrial food animal production through qualitative interviews with state agency staff in seven states. The study found that the agencies were unable to adequately address these environmental public health concerns due to narrow regulations, limited resources and a lack of public health expertise. When these constraints are considered alongside those faced by health departments, significant gaps in the ability to respond to and prevent public health concerns and issues are revealed.

Research Articles Related to Dairy Production

Burgos, J. M., B. A. Ellington, and M. F. Varela. "Presence of multidrug-resistant enteric bacteria in dairy farm topsoil." *Journal of Dairy Science* 88.4 (2005): 1391-1398.
Link: https://www.ncbi.nlm.nih.gov/pubmed/15778307

> In addition to human and veterinary medicine, antibiotics are extensively used in agricultural settings, such as for treatment of infections, growth enhancement, and prophylaxis in food animals, leading to selection of drug and multidrug-resistant bacteria. To help circumvent the problem of bacterial antibiotic resistance, it is first necessary to understand the scope of the problem. However, it is not fully understood how widespread antibiotic-resistant bacteria are in agricultural settings. The lack of such surveillance data is especially evident in dairy farm environments, such as soil. It is also unknown to what extent various physiological modulators, such as salicylate, a component of aspirin and known model modulator of multiple antibiotic resistance (mar) genes, influence bacterial multi-drug resistance. We isolated and identified enteric soil bacteria from local dairy farms within Roosevelt County, NM, determined the resistance profiles to antibiotics associated with mar, such as chloramphenicol, nalidixic acid, penicillin G, and tetracycline. We then purified and characterized plasmid DNA and detected mar phenotypic activity. The minimal inhibitory concentrations (MIC) of antibiotics for the isolates ranged from 6 to >50 microg/mL for chloramphenicol, 2 to 8 microg/mL for nalidixic acid, 25 to >300 microg/mL for penicillin G, and 1 to >80 microg/mL for tetracycline. On the other hand, many of the isolates had significantly enhanced MIC for the same antibiotics in the presence of 5 mM salicylate. Plasmid DNA extracted from 12 randomly chosen isolates ranged in size from 6 to 12.5 kb and, in several cases, conferred resistance to chloramphenicol and penicillin G. It is concluded that enteric bacteria from dairy farm topsoil are multidrug resistant and harbor antibiotic-resistance plasmids. A role for dairy topsoil in zoonoses is suggested, implicating this environment as a reservoir for development of bacterial resistance against clinically relevant antibiotics.

Jahne, Michael A., et al. "Emission and Dispersion of Bioaerosols from Dairy Manure Application Sites: Human Health Risk Assessment." *Environmental Science & Technology* 49.16 (2015): 9842-9849.
Link: http://pubs.acs.org/doi/pdfulus/10.1021/acs.est.5b01981

> In this study, we report the human health risk of gastrointestinal infection associated with inhalation exposure to airborne zoonotic pathogens emitted following application of dairy cattle manure to land. Inverse dispersion modeling with the USEPA's AERMOD dispersion model was used to determine bioaerosol emission rates based on edge-of-field bioaerosol and source material samples analyzed by real-time quantitative polymerase chain reaction (qPCR). Bioaerosol emissions and transport simulated with AERMOD, previously reported viable manure pathogen contents, relevant exposure pathways, and pathogen-specific dose-response relationships were then used to estimate potential downwind risks with a quantitative microbial risk assessment (QMRA) approach. Median 8-h infection risks decreased exponentially with distance from a median of 1:2700 at edge-of-field to 1:13 000 at 100 m and 1:200 000 at 1000 m; peak risks were considerably greater (1:33, 1:170, and 1:2500, respectively). These results indicate that bioaerosols emitted from manure application sites following manure application may present significant public health risks to downwind receptors. Manure management practices should consider improved controls for bioaerosols in order to reduce the risk of disease transmission.

Schmalzried, Hans D., and L. Fleming Fallon Jr. "Proposed Mega-Dairies and Quality-of-Life Concerns: Using Public Health Practices to Engage Neighbors." *Public Health Reports* 125.5 (2010): 754.
Link: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2925014/

> This article describes the steps taken by the Henry County Health Department (Ohio) to engage with concerned community members by collaborating in baseline data collection prior to the arrival of a large-scale dairy operation. Data collection included water quality testing of residential wells neighboring the dairy operation, a fly trapping and counting program, and a review of local property values. As a dairy with 690 cows will have average water requirements of 35,000 gallons/day, the Health Department coordinated a pumping test to assess groundwater levels and found that groundwater volumes were sufficient to supply the needs of the dairy and the surrounding residential wells. Residential wells were tested for coliform bacteria and field-tested for nitrates and hydrogen sulfide gas, and some of the wells tested unsafe for bacteria. In these cases, homeowners were given instructions on how to disinfect their wells and advised to do follow-up testing. The narrative concludes that data obtained prior to operations can be very useful and that local health departments can work with neighbors and facility operators to ensure that appropriate preventive measures are in place before operation to protect the public.

Showers, William J., et al. "Nitrate contamination in groundwater on an urbanized dairy farm." *Environmental Science & Technology* 42.13 (2008): 4683-4688. Link: http://pubs.acs.org/doi/full/10.1021/es07155l t

> Urbanization of rural farmland is a pervasive trend around the globe, and maintaining and protecting adequate water supplies in suburban areas is a growing problem. Identification of the sources of groundwater contamination in urbanized areas is problematic but will become important in areas of rapid population growth and development. The isotopic composition of NO3(815NNO3 and M80 NO3), NH4 (815NNH4), groundwater (62Hwt and 8180wt) and chloride/bromide ratios were used to determine the source of nitrate contamination in drinking water wells in a housing development that was built on the site of a dairy farm in the North Carolina Piedmont, U.S. The 615NNO3 and 6180 NO3 compositions imply that elevated nitrate levels at this site in drinking well water are the result of waste contamination, and that denitrification has not significantly attenuated the groundwater nitrate concentrations. 615NNO3 and 6180NO3compositions in groundwater could not differentiate between septic effluent and animal waste contamination. Chloride/bromide ratios in the most contaminated drinking water wells were similar to ratios found in animal waste application fields and were higher than Cl/Br ratios observed in septic drain fields in the area. 6l 80wt was depleted near the site of a buried waste lagoon without an accompanying shift in 62Hwt suggesting water oxygen exchange with CO2. This water--0O2 exchange resulted from the reduction of buried lagoon organic matter, and oxidation of the released gases in aerobic soils. 6180wt is not depleted in the contaminated drinking water wells, indicating that the buried dairy lagoon is not a source of waste contamination. The isotope and Cl/Br ratios indicate that nitrate contamination in these drinking wells are not from septic systems, but are the result of animal waste leached from pastures into groundwater during 35 years of dairy operations which did not violate any existing regulations. Statutes need to be enacted to protect the health of the homeowners that require well water to be tested prior to the sale of homes built on urbanized farmland.

Wichmann, Fabienne, et al. "Diverse antibiotic resistance genes in dairy cow manure." *MBio* 5.2

(2014): e01017-13.
Link: http://mbio.asm.org/content/5/2/eO1017-13.short

> Application of manure from antibiotic-treated animals to crops facilitates the dissemination of antibiotic resistance determinants into the environment. However, our knowledge of the identity, diversity, and patterns of distribution of these antibiotic resistance determinants remains limited. We used a new combination of methods to examine the resistome of dairy cow manure, a common soil amendment. Metagenomic libraries constructed with DNA extracted from manure were screened for resistance to beta-lactams, phenicols, aminoglycosides, and tetracyclines. Functional screening of fosmid and small insert libraries identified 80 different antibiotic resistance genes whose deduced protein sequences were on average 50 to 60% identical to sequences deposited in GenBank. The resistance genes were frequently found in clusters and originated from a taxonomically diverse set of species, suggesting that some microorganisms in manure harbor multiple resistance genes. Furthermore, amid the great genetic diversity in manure, we discovered a novel Glade of chloramphenicol acetyltransferases. Our study combined functional metagenomics with third generation PacBio sequencing to significantly extend the roster of functional antibiotic resistance genes found in animal gut bacteria, providing a particularly broad resource for understanding the origins and dispersal of antibiotic resistance genes in agriculture and clinical settings. The increasing prevalence of antibiotic resistance among bacteria is one of the most intractable challenges in 21st-century public health. The origins of resistance are complex, and a better understanding of the impacts of antibiotics used on farms would produce a more robust platform for public policy. Microbiomes of farm animals are reservoirs of antibiotic resistance genes, which may affect distribution of antibiotic resistance genes in human pathogens. Previous studies have focused on antibiotic resistance genes in manures of animals subjected to intensive antibiotic use, such as pigs and chickens. Cow manure has received less attention, although it is commonly used in crop production. Here, we report the discovery of novel and diverse antibiotic resistance genes in the cow microbiome, demonstrating that it is a significant reservoir of antibiotic resistance genes. The genomic resource presented here lays the groundwork for understanding the dispersal of antibiotic resistance from the agroecosystem to other settings.

Relation between Nitrates in Water Wells and Potential Sources in the Lower Yakima Valley, Washington State. U.S. Environmental Protection Agency, Washington, D.C., 2012.
Link: https://www3.epa.gov/region10/pdf/sites/yakimagw/nitrate in water wells study 9-27-2012.pdf

> Several investigations relating to nitrate contamination in the Lower Yakima Valley in Washington State have shown nitrate levels in drinking water above the U.S. Environmental Protection Agency (EPA) maximum contaminant level (MCL) of 10 mg/L. From February through April 2010, EPA conducted sampling of drinking water wells and potential sources of nitrate contamination in the Lower

Yakima Valley, in central Washington State. This report presents the results of these sampling efforts. EPA collected over 331 samples from residential drinking water wells for nitrate and bacteria, and multi-parameter sampling on 29 water wells (26 residential drinking water wells and three dairy supply wells), 12 dairy lagoons (15 samples), 11 soil samples (five at dairy application fields and six at irrigated and fertilized crop fields), five dairy manure pile samples, and three wastewater treatment plant (WWTP) influent samples. EPA's data provide some indication of the likely nitrate sources for seven of the 25 residential wells tested- animal waste was determined to be the source for six of the wells, and synthetic fertilizer the source for one of the wells. Given the historic and current volumes of wastes generated and stored by dairies, and the application of nitrogen-rich fertilizers including dairy waste in the Lower Yakima Valley, it is expected that dairies are a likely source of high nitrate levels in downgradient drinking water wells. The total nitrogen, major ions, alkalinity and barium data provide strong evidence that the dairies evaluated in this study are likely sources of the high nitrate levels in the drinking water wells downgradient of the dairies. Additional information that supports this conclusion includes: there are few potential sources of nitrogen located upgradient of the dairies; the dairy lagoons are likely leaking large quantities of nitrogen-rich liquid into the subsurface; and Washington State Department of Agriculture inspectors have reported elevated levels of nitrogen in application fields of the dairies in the study. Evaluating actions to reduce nitrate concentrations in residential drinking water wells was beyond the scope of the EPA's report. EPA concluded that actions to reduce nitrate levels are needed, although it may take many years to reduce nitrates in residential drinking water wells to safe levels because of the extent of the nitrate contamination in the Lower Yakima Valley and the persistence of nitrate in the environment.

Research Articles Related to Swine Production

Casey JA, Curriero FC, Cosgrove SE, Nachman ICE, Schwartz BS. High-Density Livestock Operations, Crop Field Application of Manure, and Risk of Community-Associated Methicillin-Resistant *Staphylococcus aureus* Infection in Pennsylvania. JAMA Intern Med. 2013 Sep 16; 21205(21):1980-90. Link: https://www.ncbi.nlm.nih.gov/pubmed/24043228

> Nearly 80% of antibiotics in the United States are sold for use in livestock feeds. The manure produced by these animals contains antibiotic-resistant bacteria, resistance genes, and antibiotics and is subsequently applied to crop fields, where it may put community members at risk for antibiotic-resistant infections. The objective of this study was to assess the association between individual exposure to swine and dairy/veal industrial agriculture and risk of methicillin-resistant *Staphylococcus aureus* **(MRSA)** infection. This study was a population-based, nested case-control study of primary care patients from a single health care system in Pennsylvania from 2005 to 2010. Incident **MRSA** cases were identified using electronic health records, classified as community-associated MRSA or health care-associated MRSA, and frequency matched to randomly selected controls and patients with skin and soft tissue infection. Nutrient management plans were used to create 2 exposure variables: seasonal crop field manure application and number of livestock animals at the operation. In a sub-study, we collected 200 isolates from patients stratified by location of diagnosis and proximity to livestock operations. The study measured community-associated MRSA, health care-associated MRSA, and skin and soft tissue infection status (with no history of MRSA) compared with controls. From a total population of 446,480 patients, 1,539 community-associated MRSA, 1335 health care-associated MRSA, 2895 skin and soft-tissue infection cases, and 2914 controls were included. After adjustment for MRSA risk factors. the highest quartile of swine crop field exposure was significantly associated with community associated MRSA, health care-associated MRSA. and skin and soft-tissue infection case status (adjusted odds ratios. 1.38 [95% CI. 1.13-1.69]. 1.30 [95% CI. 1.05-1.61], and 1.37 [95% CI. 1.18-1.60]. respectively); and there was a trend of increasing odds across quartiles for each outcome *(P* < .01 for trend in all comparisons). There were similar but weaker associations of swine operations with community-associated MRSA and skin and soft-tissue infection. Molecular testing of 200 isolates identified 31 unique *spa* types, none of which corresponded to CC398 (clonal complex 398), but some have been previously found in swine. Proximity to swine manure application to crop fields and livestock operations each was associated with MRSA and skin and soft-tissue infection. These findings contribute to the growing concern about the potential public health impacts of high density livestock production.

Donham KJ, Wing S, Osterberg D, al et, Flora JL, Hodne C, et al. Community health and socioeconomic issues surrounding concentrated animal feeding operations. Environ Health Perspect. 2007 Feb;l 15(2):317-20.
Link: https ://www.ncbi.nlm.nih.gov/pmc/articles/PMC1817697/

> A consensus of the Workgroup on Community and Socioeconomic Issues was that improving and sustaining healthy rural communities depends on integrating socioeconomic development and environmental protection. The workgroup agreed

that the World Health Organization's definition of health, "a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity," applies to rural communities. These principles are embodied in the following main points agreed upon by this workgroup. Healthy rural communities ensure a) the physical and mental health of individuals, b) financial security for individuals and the greater community, c) social well-being, d) social and environmental justice, and e) political equity and access. This workgroup evaluated impacts of the proliferation of concentrated animal feeding operations (CAFOs) on sustaining the health of rural communities. Recommended policy changes include a more stringent process for issuing permits for CAFOs, considering bonding for manure storage basins, limiting animal density per watershed, enhancing local control, and mandating environmental impact statements.

Graham JP, Leibler JH, Price LB, Otte JM, Pfeiffer DU, Tiensin T, et al. The animal-human interface and infectious disease in industrial food animal production: rethinking biosecurity and biocontainment. Public Health Rep. 2008;123(3):282-99.
Link: https://www.ncbi.nlm.nih.gov/pubmed/19006971

Understanding interactions between animals and humans is critical in preventing outbreaks of zoonotic disease. This is particularly important for avian influenza. Food animal production has been transformed since the 1918 influenza pandemic. Poultry and swine production have changed from small-scale methods to industrial-scale operations. There is substantial evidence of pathogen movement between and among these industrial facilities, release to the external environment, and exposure to farm workers, which challenges the assumption that modem poultry production is more biosecure and biocontained as compared with backyard or small holder operations in preventing introduction and release of pathogens. An analysis of data from the Thai government investigation in 2004 indicates that the odds of H5Nl outbreaks and infections were significantly higher in large-scale commercial poultry operations as compared with backyard flocks. These data suggest that successful strategies to prevent or mitigate the emergence of pandemic avian influenza must consider risk factors specific to modern industrialized food animal production.

Heaney CD, Myers K, Wing S, Hall D, Baron D, Stewart JR. Source tracking swine fecal waste in surface water proximal to swine concentrated animal feeding operations. Sci Total Environ. Elsevier; 2015; 511:676-83,
Link: http://www. sciencedirect. com/science/article/pii/S0048969714017641

Swine farming has gone through many changes in the last few decades, resulting in operations with a high animal density known as confined animal feeding operations (CAFOs). These operations produce a large quantity of fecal waste whose environmental impacts are not well understood. The purpose of this study was to investigate microbial water quality in surface waters proximal to swine CAFOs including microbial source tracking of fecal microbes specific to swine. For one year, surface water samples at up- and downstream sites proximal to swine CAFO lagoon waste land application sites were tested for fecal indicator bacteria (fecal coliforms, Escherichia coli and Enterococcus) and candidate swine-specific microbial source-tracking (MST) markers (Bacteroidales Pig-1-Bac, Pig-2-Bac, and Pig-Bac-2, and methanogen P23-2). Testing of 187 samples showed high fecal indicator bacteria concentrations at both up- and downstream sites. Overall, 40%, 23%, and 61% of samples exceeded state and federal recreational water quality guidelines for fecal coliforms, E. coli, and Enterococcus, respectively. Pig-1 -Bae and Pig-2-Bac showed the highest specificity to swine fecal wastes and were 2.47 (95% confidence interval [CI] =

1.03, 5.94) and 2.30 times (95% CI = 0.90, 5.88) as prevalent proximal down-than proximal upstream of swine CAFOs, respectively. Pig-I-Bae and Pig-2-Bac were also 2.87 (95% CI= 1.21, 6.80) and 3.36 (95% CI= 1.34, 8.41) times as prevalent when 48-hour antecedent rainfall was greater than versus less than the mean, respectively. Results suggest diffuse and overall poor sanitary quality of surface waters where swine CAPO density is high. Pig-1 -Bae and Pig-2-Bac are useful for tracking off-site conveyance of swine fecal wastes into surface waters proximal to and downstream of swine CAFOs and during rain events.

Horton RA, Wing S, Marshall SW, Brownley KA. Malodor as a trigger of stress and negative mood in neighbors of industrial hog operations. Am J Public Health. 2009 Nov;99 Suppl 3:S610-5.
Link: https://www.ncbi.nlm.nih.gov/pubmed/l9890165

Objectives. We evaluated malodor and air pollutants near industrial hog operations as environmental stressors and negative mood triggers.
Methods. We collected data from 101 nonsmoking adults in 16 neighborhoods within 1.5 miles of at least 1 industrial hog operation in eastern North Carolina. Participants rated malodor intensity, stress, and mood for 2 weeks while air pollutants were monitored.
Results. Reported malodor was associated with stress and 4 mood states; odds ratios (ORs) for a 1-unit change on the 0-to-8 odor scale ranged from 1.31 (95% confidence interval [CI]= 1.16, 1.50) to 1.81 (95% CI= 1.63, 2.00). ORs for stress and feeling nervous or anxious were 1.18 (95% CI= 1.08, 1.30) and 1.12 (95% CI = 1.03, 1.22), respectively, for a 1 ppb change in hydrogen sulfide and 1.06 (95% CI= 1.00, 1.11) and 1.10 (95% CI= 1.03, 1.17), respectively, for a 1 $\mu g/m^3$ change in semivolatile particulate matter less than 10 μm in aerodynamic diameter (PM10). *Conclusions.* Hog odor, hydrogen sulfide, and semivolatile **PK**ª are related to stress and negative mood in disproportionately low-income communities near industrial hog operations in eastern North Carolina. Malodor should be considered in studies of health impacts of environmental injustice.

Ma W, Lager KM, Vincent AL, Janke BH, Gramer MR, Richt JA. The role of swine in the generation of novel influenza viruses. Zoonoses Public Health. 2009 Aug;56(6-7):326-37.
Link: https://www.ncbi.nlm.nih.gov/pubmed/19486316

The ecology of influenza A viruses is very complicated, involving multiple host species and viral genes. Avian species have variable susceptibility to influenza A viruses with wild aquatic birds being the reservoir for this group of pathogens. Occasionally, influenza A viruses are transmitted to mammals from avian species, which can lead to the development of human pandemic strains by direct or indirect transmission to man. Because swine are also susceptible to infection with avian and human influenza viruses, genetic reassortment between these viruses and/or swine influenza viruses can occur. The potential to generate novel influenza viruses has resulted in swine being labelled 'mixing vessels'. The mixing vessel theory is one mechanism by which unique viruses can be transmitted from an avian reservoir to man. Although swine can generate novel influenza viruses capable of infecting

man, at present, it is difficult to predict which viruses, if any, will cause a human pandemic. Clearly, the ecology of influenza A viruses is dynamic and can impact human health, companion animals, as well as the health of livestock and poultry for production of valuable protein commodities. For these reasons, influenza is, and will continue to be, a serious threat to the wellbeing of mankind.

Mirabelli MC, Wing S, Marshall SW, Wilcosky TC. Asthma symptoms among adolescents who attend public schools that are located near confined swine feeding operations. Pediatrics. 2006 Jul;118(1):e66- 75.
Link: http://pediatrics.aappublications.org/content/l 18/l/e66

Objectives. Little is known about the health effects of living in close proximity to industrial swine operations. We assessed the relationship between estimated exposure to airborne effluent from confined swine feeding operations and asthma symptoms among adolescents who were aged 12 to 14 years.
Methods. During the 1999-2000 school year, 58,169 adolescents in North Carolina answered questions about their respiratory symptoms, allergies, medications, socioeconomic status, and household environments. To estimate the extent to which these students may have been exposed during the school day to air pollution from confined swine feeding operations, we used publicly available data about schools (n = 265) and swine operations (n = 2343) to generate estimates of exposure for each public school. Prevalence ratios and 95% confidence intervals for wheezing within the past year were estimated using random-intercepts binary regression models, adjusting for potential confounders, including age, race, socioeconomic status, smoking, school exposures, and household exposures. *Results.* The prevalence of wheezing during the past year was slightly higher at schools that were estimated to be exposed to airborne effluent from confined swine feeding operations. For students who reported allergies, the prevalence of wheezing within the past year was 5% higher at schools that were located within 3 miles of an operation relative to those beyond 3 miles and 24% higher at schools in which livestock odor was noticeable indoors twice per month or more relative to those with no odor.
Conclusions. Estimated exposure to airborne pollution from confined swine feeding operations is associated with adolescents' wheezing symptoms.

Rinsky JL, Nadimpalli M, Wing S, Hall D, Baron D, Price LB, et al. Livestock-Associated Methicillin and Multidrug Resistant *Staphylococcus aureus* ls Present among Industrial, Not Antibiotic-Free Livestock Operation Workers in North Carolina. PLoS One. 2013;8(7).
Link: https://www.ncbi.nlm.nih.gov/pubmed/23844044

Objectives. Administration of antibiotics to food animals may select for drug resistant pathogens of clinical significance, such as methicillin-resistant *Staphylococcus aureus* (MRSA). In the United States, studies have examined prevalence of MRSA carriage among individuals exposed to livestock, but prevalence of multidrug-resistant S. *aureus* (MDRSA) carriage and the association with livestock raised with versus without antibiotic selective pressure remains unclear. We aimed to examine prevalence, antibiotic susceptibility, and molecular characteristics of S. *aureus* among industrial livestock operation (ILO) and antibiotic-free livestock operation (AFLO) workers and household members in North Carolina.

Methods. Participants in this cross-sectional study were interviewed and provided a nasal swab for S. *aureus* analysis. Resulting S. *aureus* isolates were assessed for antibiotic susceptibility, multi-locus sequence type, and absence of the sen gene (a marker of livestock association).
Results. Among 99 ILO and 105 AFLO participants, S. *aureus* nasal carriage prevalence was 41% and 40%, respectively. Among ILO and AFLO S. *aureus* carriers, MRSA was detected in 7% (3/41) and 7% (3/42), respectively. Thitty seven percent of 41 ILO versus 19% of 42 AFLO S. aureus-positive participants carried MDRSA. S. *aureus* clonal complex (CC) 398 was observed only among workers and predominated among ILO (13/34) compared with AFLO (1/35) S. aureus-positive workers. Only ILO workers carried sen-negative MRSA CC398 (2/34) and sen-negative MDRSA CC398 (6/34), and all of these isolates were tetracycline resistant.
Conclusions. Despite similar S. *aureus* and MRSA prevalence among ILO and AFLO-exposed individuals, livestock-associated MRSA and MDRSA (tetracycline-resistant, CC398, sen-negative) were only present among ILO exposed individuals. These findings support growing concern about antibiotics use and confinement in livestock production, raising questions about the potential for occupational exposure to an opportunistic and drug-resistant pathogen, which in other settings including hospitals and the community is of broad public health importance.

Sapkota AR, Curriero FC, Gibson KE, Schwab KJ. Antibiotic-resistant enterococci and fecal indicators in surface water and groundwater impacted by a concentrated swine feeding operation. Environ Health Perspect. 2007 Jul;115(7):1040-5.
Link: https://www.ncbi.nlm.nih.gov/pubmed/l 7637920

Background. The nontherapeutic use of antibiotics in swine feed can select for antibiotic resistance in swine enteric bacteria. Leaking swine waste storage pits and the land-application of swine manure can result in the dispersion of resistant bacteria to water sources. However, there are few data comparing levels of resistant bacteria in swine manure-impacted water sources versus unaffected sources. *Objectives.* The goal of this study was to analyze surface water and groundwater situated up and down gradient from a swine facility for antibiotic-resistant enterococci and other fecal indicators.
Methods. Surface water and groundwater samples (n = 28) were collected up and down gradient from a swine facility from 2002 to 2004. Fecal indicators were isolated by membrane filtration, and enterococci (n = 200) were tested for susceptibility to erythromycin, tetracycline, clindamycin, virginiamycin, and vancomycin.
Results. Median concentrations of enterococci, fecal coliforms, and Escherichia coli were 4- to 33-fold higher in down-gradient versus up-gradient surface water and groundwater. We observed higher minimal inhibitory concentrations for four antibiotics in enterococci isolated from down-gradient versus up-gradient surface water and groundwater. Elevated percentages of erythromycin- ($p = 0.02$) and tetracycline-resistant ($p = 0.06$) enterococci were detected in down-gradient surface waters, and higher percentages of tetracycline- ($p = 0.07$) and clindamycin-resistant ($p < 0.001$) enterococci were detected in down-gradient groundwater.
Conclusions. We detected elevated levels of fecal indicators and antibiotic-resistant enterococci in water sources situated down gradient from a swine facility compared with up-gradient sources. These findings provide additional evidence that water contaminated with swine manure could contribute to the spread of antibiotic resistance.

Schinasi L, Horton RA, Guidry VT, Wing S, Marshall SW, Morland KB. Air pollution, lung function, and physical symptoms in communities near concentrated swine feeding operations.

Epidemiology. 2011 Mar;22(2):208-15.
Link: https://www.ncbi.nlm.nih.gov/pubmed/21228696

> *Background.* Concentrated animal feeding operations emit air pollutants that may affect health. We examined associations of reported hog odor and of monitored air pollutants with physical symptoms and lung function in people living within 1.5 miles of hog operations.
> *Methods.* Between September 2003 and September 2005, we measured hydrogen sulfide (H2S), endotoxin, and particulate matter (PMl0, PM2.5, and PM2.5-10) for approximately 2-week periods in each of 16 eastern North Carolina communities. During the same time periods, 101 adults sat outside their homes twice a day for 10 minutes, reported hog odor and physical symptoms, and measured their lung function. Conditional fixed-effects logistic and linear regression models were used to derive estimates of associations.
> *Results.* The log odds (±1 standard error) of acute eye irritation following 10 minutes outdoors increased by 0.53 (±0.06) for every unit increase in odor, by 0.15 (±0.06) per 1 ppb ofH2S, and by 0.36 (+0.11) per 10 µg/m3 of PMl0. Odor and H2S were also associated with irritation and respiratory symptoms in the previous 12 hours. The log odds of difficulty breathing increased by 0.50 (±0.15) per unit of odor. A 10 µg/m3 increase in mean 12-hour PM2.5 was associated with increased log odds of wheezing (0.84 ± 0.29) and declines in forced expiratory volume in 1 second (-0.04 ± 0.02 L). A 10 EU/mg increase in endotoxin was associated with increased log odds of sore throat (0.10 ± 0.05), chest tightness (0.09 ± 0.04), and nausea (0.10 ± 0.05).
> *Conclusions.* Pollutants measured near hog operations are related to acute physical symptoms in a longitudinal study using analyses that preclude confounding by time-invariant characteristics of individuals.

Schulz J, Friese A, Klees S, Tenhagen BA, Fetsch A, Rosier U, et al. Longitudinal study of the contamination of air and of soil surfaces in the vicinity of pig barns by livestock-associated methicillin resistant *Staphylococcus aureus.* Appl Environ Microbiol. 2012 Aug;78(16):5666-71.
Link: http://aem.asm.org/content/78/16/5666.full

> During 1 year, samples were taken on 4 days, one sample in each season, from pigs, the floor, and the air inside pig barns and from the ambient air and soil at different distances outside six commercial livestock-associated methicillin-resistant *Staphylococcus aureus* (LA-MRSA)-positive pig barns in the north and east of Germany. LA-MRSA was isolated from animals, floor, and air samples in the barn, showing a range of airborne LA-MRSA between 6 and 3,619 CFU/m(3) (median, 151 CFU/m(3)). Downwind of the barns, LA-MRSA was detected in low concentrations (11 to 14 CFU/m(3)) at distances of 50 and 150m; all upwind air samples were negative. In contrast, LA-MRSA was found on soil surfaces at distances of 50, 150, and 300m downwind from all barns, but no statistical differences could be observed between the proportions of positive soil surface samples at the three different distances. Upwind of the barns, positive soil surface samples were found only sporadically. Significantly more positive LA-MRSA samples were found in summer than in the other seasons both in air and soil samples upwind and downwind of the pig barns. spa typing was used to confirm the identity of LA-MRSA types found inside and outside the barns. The results show that there is regular airborne LA-MRSA transmission and deposition, which are strongly influenced by wind direction and season, of up to at least 300m around positive pig barns. The described boot sampling method seems suitable to characterize the contamination of the vicinity of LA-MRSA-positive pig barns by the airborne route.

Wing S, Horton RA, Rose KM. Air pollution from industrial swine operations and blood pressure of neighboring residents. Environ Health Perspect. 2013 Jan;121(1):92-6.
Link: https://ehp.niehs.nih.gov/1205109/

Background. Industrial swine operations emit odorant chemicals including ammonia, hydrogen sulfide (H2S), and volatile organic compounds. Malodor and pollutant concentrations have been associated with self-reported stress and altered mood in prior studies.
Objectives: We conducted a repeated-measures study of air pollution, stress, and blood pressure in neighbors of swine operations.
Methods. For approximately 2 weeks, 101 nonsmoking adult volunteers living near industrial swine operations in 16 neighborhoods in eastern North Carolina sat outdoors for 10 min twice daily at preselected times. Afterward, they reported levels of hog odor on a 9- point scale and measured their blood pressure twice using an automated oscillometric device. During the same 2- to 3-week period, we measured ambient levels of H2S and PM10 at a central location in each neighborhood. Associations between systolic and diastolic blood pressure (SBP and DBP, respectively) and pollutant measures were estimated using fixed-effects(conditional) linear regression with adjustment for time of day. *Results.* PMlO showed little association with blood pressure. DBP [13 (SE)] increased 0.23 (0.08) mmHg per unit of reported hog odor during the 10 min outdoors and 0.12 (0.08) mmHg per 1-ppb increase of H2S concentration in the same hour. SBP increased 0.10 (0.12) mmHg per odor unit and 0.29 (0.12) mmHg per 1-ppb increase of H2S in the same hour. Reported stress was strongly associated with BP; adjustment for stress reduced the odor-DBP association, but the H2S-SBP association changed little.
Conclusions. Like noise and other repetitive environmental stressors, malodors may be associated with acute blood pressure increases that could contribute to development of chronic hypertension.