

Antibiotic Resistance and Food Animal Production: a Bibliography of Scientific Studies (1969-2012)

This bibliography lists the latest published scientific and economic literature concerning the contribution of routine antibiotic use in food animals to the growing public health crisis of human antibiotic resistance. Research on how antibiotic use in food animal production contributes to the growing health crisis of antibiotic resistance dates back more than 30 years. As Dr. Frederick J. Angulo, acting associate director of science in the Centers for Disease Control and Prevention's National Center for Environmental Health and the Agency for Toxic Substances and Disease, said in a August 1, 2009, news article in the *Journal of the American Veterinary Medical Association*:

“There is scientific consensus that antibiotic use in food animals contributes to resistance in humans. And there's increasing evidence that such resistance results in adverse human health consequences at the population level. Antibiotics are a finite and precious resource, and we need to promote prudent and judicious antibiotic use.”

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ANTIBIOTIC RESISTANCE IN ANIMAL AGRICULTURE

The impacts of antibiotic resistance in animal agriculture on livestock, the environment and the spreading of infectious diseases.

Joint Committee on the use of antibiotics in animal husbandry and veterinary medicine (“Swann Report”). M.M. Swann, K.L. Blaxter, H.I. Field, J.W. Howie, I.A.M. Lucas, E.L.M. Millar, J.C. Murdoch, J.H. Parsons and E.G. White. Cmnd. 4190. London: Her Majesty’s Stationery Office, 1969.

Summary: Reports on the status of antibiotic use in man and animals. Outlines the uses and amounts consumed for both. Reviews the reasons for which antibiotics are administered to food animals, including disease prevention, use in growth promotion, stress reduction and therapy. States that there are possible dangers to the human population stemming from the administration of antibiotics to animals, such as the rise of antibiotic-resistant strains of bacteria in animals that could cause disease in humans. The resulting infection could then be difficult to treat due to the null effect of antibiotics. Other dangers include the transmission of resistance determinants from animal strains to human strains of bacteria. It is known that such transfers take place and the fear is that resistance may be transferred to normal bacteria that inhabit the human bowel and/or to pathogens that may then cause disease. Discusses the prevalence of multiple antibiotic-resistant strains of bacteria and how they may arise. States that even though there are multiple antibiotics available for treatment of certain diseases, those reserved as a drug of choice may have a number of advantages over alternative treatment. Strains with multidrug resistance pose a greater threat in that the only effective drugs left for treatment in humans may be unsuitable because of toxicity or allergy. These infections are likely to arise where humans and animals share a pathogen such as *Salmonella* and the administration of antimicrobials to animals no doubt encourages the prevalence of resistance in these strains. Concludes that the use of antimicrobials in food animal production, especially when used in growth promotion, is of great concern and that limiting factors should be put in place to secure the use of antibiotics of greatest importance in human administration for therapeutic uses only and in some cases excluded from animal use altogether.

Changes in intestinal flora of farm personnel after introduction of a tetracycline-supplemented feed on a farm. S.B. Levy, G.B. Fitzgerald and A.B. Macone. *New England Journal of Medicine*, 1976. 295(11): 583-588.

Summary: Reports a study to determine if giving animals antibiotics in feed caused changes in intestinal bacterial flora and if workers and neighbors of the farm were affected. Chickens were screened for bacteria before and after a diet that included tetracycline-supplemented feed. Resistance to tetracycline changed dramatically within 36 to 48 hours of changing the diet of the animals. Within two weeks, 90 percent of the chickens were found to excrete essentially all tetracycline-resistant organisms. Within five to six months, there was a large increase in tetracycline-resistant bacteria in farm dwellers while the neighbors showed no change in bacterial count.

An epidemic of resistant *Salmonella* in a nursery: Animal-to-human spread. R.W. Lyons, C.L. Samples, H.N. DeSilva, K.A. Ross, E.M. Julian and P.J. Checko. *Journal of the American Medical Association*, 1980. 243(6): 546-547.

Summary: Studies the case of a pregnant woman, infected with *Salmonella heidelberg*, who worked on her father’s farm until four days before delivery. Her baby subsequently developed mild diarrhea, as did two others sharing the hospital nursery. *Salmonella heidelberg* was isolated

from each and in all cases was resistant to chloramphenicol, sulfamethoxazole and tetracycline. The strain was presumed to originate from a herd of infected dairy cows at the woman's father's farm as those bacteria showed the same resistance pattern as did those collected from the father.

Emergence of multidrug-resistant *Salmonella enterica* serotype Typhimurium DT104 infections in the United States. M.K. Glynn, C. Bopp, W. Dewitt, P. Dabney, M. Mokhtar and F.J. Angulo. *New England Journal of Medicine*, 1998. 338(19): 1333-1338.

Summary: Reviews *Salmonella* data collected by local and state health departments and public health laboratories between 1979 and 1996. Finds that a rapid increase of multidrug-resistant *Salmonella enterica* serotype typhimurium (DT104), a strain widely distributed in food animals and known to cause disease in humans, occurred in this period. The percentage rose from 0.6 percent in 1979–1980 to 34 percent in 1996. Concludes that more prudent use of antibiotics on farms is necessary to reduce the dissemination of multidrug-resistant *Salmonella* and emergence of further resistant strains.

Epidemiologic aspects, control, and importance of multiple-drug resistant *Salmonella typhimurium* DT104 in the United States. J.E. Akkina, A.T. Hogue, F.J. Angulo, R. Johnson, K.E. Petersen, P.K. Saini, P.J. Fedorka-Cray and W.D. Schlosser. *Journal of the American Veterinary Medical Association*, 1999. 214(6): 790-798.

Summary: Studies an animal strain of *Salmonella* and its prevalence of infection in humans. States that multidrug-resistant *Salmonella* DT104 is the second-most-prevalent *Salmonella* organism isolated from humans in England and Wales in the time frame of this study. Gives numerous examples of outbreaks in the U.S., most of which are traced to milk. Cattle, along with pigs, sheep, chickens, turkeys and several other animals, are known carriers of this strain.

Transfer of antibiotic resistant bacteria from animals to man. H.C. Wegener, F.M. Aarestrup, P. Gerner-Smidt and F. Bager. *Acta Veterinaria Scandinavica Supplementum*, 1999. 92: 51-57.

Summary: Describes zoonotic bacterial infections and their treatment. States that most *Salmonella*, *campylobacter*, *yersinia* and entero-haemorrhagic *E. coli* (EHEC) infections do not require antibiotic therapy, but in some cases these tools provide life-saving cures. Increasing levels of resistance in these bacteria, especially fluoroquinolone resistance, give rise for concern when it comes to human infections. Calls for infection control at the herd level and the need for prudent use of antibiotics in food animals.

The use of drugs in food animals: Benefits and risks. Committee on Drug Use in Food Animals, Panel on Animal Health, Food Safety, and Public Health, National Research Council. 1999.

Summary: This review focuses on the following topics associated with antibiotic use in animal agriculture: background and perspectives; production practices and drug use; benefits and risks to human health; drug development, government approval and the regulatory process; drug residues and microbial contamination in food costs of eliminating sub-therapeutic use; and approaches to minimize antibiotic use in food animal production. Primary findings include 60 to 80 percent of livestock and poultry receive antibiotics. This use of antibiotics increases the potential for resistant zoonotic bacteria to impact humans and for resistant genes to be shared by species of bacteria. The review finds an increase cost of \$4.84 to \$9.72 per consumer per year should sub-therapeutic use be banned.

Ceftriaxone-resistant *Salmonella* infection acquired by a child from cattle. P. Fey, T.J. Safranek, M.E. Rupp, E.F. Dunne, E. Ribot, P.C. Iwen, P.A. Bradford, F.J. Angulo and S.H. Hinrichs. *New England Journal of Medicine*, 2000. 342: 1242-1249.

Summary: Reports the case of a 12-year-old boy who lived on a farm in Nebraska and was infected with a ceftriaxone-resistant strain of *Salmonella enterica* serotype typhimurium that was traced to his father's herd of cattle using molecular techniques. States that this finding adds to the growing body of evidence suggesting that the use of antibiotics in livestock is the prominent source of resistance to these agents in *Salmonella* infection.

Appropriate regulation of antibiotics in livestock feed. R.L. Goforth and C.R. Goforth. *Boston College Environmental Affairs Law Review*, 2000. 28(1): 39-77.

Summary: Reviews nontherapeutic uses of antimicrobials in food animals and their impact on human health. States that this practice is creating possibly irreversible effects on the viability of antibiotics used to treat human disease. Concludes that despite short-term economic benefits associated with the widespread use of antibiotics in agriculture, the risk to human health justifies a change in policy.

Antibiotic resistance in *Campylobacter* strains isolated from animals, foods and humans in Spain in 1997–1998. Y. Saenz, M. Zarazaga, M. Lantero, M.J. Gastaneres, F. Baquero and C. Torres. *Antimicrobial Agents and Chemotherapy*, 2000. 44(2): 267-271.

Summary: Studies *Campylobacter* isolated from foods, animals and humans. Finds that a high percentage of *Campylobacter jejuni* contaminates food (54.4 percent), broilers (81 percent) and pigs (88.9 percent). Isolates collected from broilers and pigs showed a 99 percent resistance rate to ciprofloxacin, with only a slightly lower number of human isolates (72 percent) also resistant. High resistance percentages to ampicillin, erythromycin, gentamicin and amikacin also were detected for *C. coli* isolated from these sources. Concludes that “more restrictive policies on the use of antibiotics in animals may result in an improvement of the current situation in the medium term.”

The effect of banning avoparcin on VRE carriage in The Netherlands. A.E. van den Bogaard, N. Bruinsma and E.E. Stobberingh. *Journal of Antimicrobial Chemotherapy*, 2000. 46: 146-148.

Summary: Discusses the removal of avoparcin, an antimicrobial similar to vancomycin, from commercial food animal production in several settings. Sweden, which banned the use of antibiotics as growth promoters in 1986, has not reported any vancomycin-resistant *Enterococci* (VRE). This example strongly suggests that the removal of selective pressure will remove VRE from the human population over time. Denmark also banned the use of avoparcin in 1995 and saw the prevalence of poultry-isolated cases of VRE drop from greater than 80 percent in 1995 to less than 5 percent in 1998.

Epidemiology of resistance to antibiotics: Links between animals and humans. A. Van der Bogaard and E.E. Stobberingh. *International Journal of Antimicrobial Agents*, 2000. 14: 327-335.

Summary: Discusses the ban on avoparcin in food animals in the European Union and resulting significant decreases in resistance to vancomycin (a related drug) in intestinal *Enterococci* bacteria in animals and humans. States that resistant bacteria from animals can infect or reach the human population by direct contact and via food products of animal origin. Shows evidence for transfer of resistant genes between bacteria in humans and animals and recommends reducing the

amount of antibiotics used in food animals in order to protect public health and safeguard the efficacy of antibiotics in veterinary medicine.

Selective pressure by antibiotic use in livestock. W. Witte. *International Journal of Antimicrobial Agents*, 2000. 16: S19-S24

Summary: Describes the selective pressures seen in the use of antibiotics as growth promoters. States that discovery of glycopeptide resistance outside of hospitals in *Enterococcus faecium* is linked to avoparcin use in animals. The review concludes that the spread of resistance is worrisome as mobile genetic elements are seen transferring between bacterial species that could lead to non-resistant pathogens picking up resistance from non-pathogenic strains. It concludes in support of the ban on growth promoters introduced in Europe as this might interfere with treatment in humans.

Quinolone and macrolide resistance in *Campylobacter jejuni* and *C. coli*: Resistance mechanisms and trends in human isolates. J. Engberg, F.M. Aarestrup, D.E. Taylor, P. Gerner-Smidt and I. Nachamkin. *Emerging Infectious Diseases*, 2001. 7(1):24-34.

Summary: Reviews the increasing resistance of *Campylobacter* strains to macrolide and quinolone antibiotics in human clinical isolates with respect to the use of these agents in food animals. Data suggest that while erythromycin and other macrolides should continue to be the antibiotics of choice in most regions, fluoroquinolones may be of limited use in many areas as the overuse of enrofloxacin and other drugs in food animals has caused a sharp upswing in the resistance of *Campylobacter* to these antibiotics.

The need to improve antimicrobial use in agriculture: Ecological and human health consequences. Alliance for the Prudent Use of Antibiotics. *Clinical Infectious Diseases*, 2002 supplement. 34 (S3): S71-144.

Summary: Reviews more than 500 studies relating to agricultural uses of antibiotics and concludes that "elimination of nontherapeutic use of antimicrobials in food animals and agriculture will lower the burden of antimicrobial resistance."

Potential mechanisms of increased disease in humans from antimicrobial resistance in food animals. M. Barza. *Clinical Infectious Diseases*, 2002. 34 (Suppl 3): S123-125.

Summary: Summarizes five potential mechanisms by which antimicrobial resistance may adversely affect human health. Two of the five relate to antimicrobial use in animals: (1) that resistant pathogens acquired by animals as the result of treatment with antibiotics transmit these pathogens through the food chain; and (2) that commensal flora of animals may acquire resistance traits from the previous pool of resistant pathogens, which then may be passed to human commensals and/or pathogens through the food chain.

Antimicrobial residues in animal waste and water resources proximal to large-scale swine and poultry feeding operations. E.R. Campagnolo, K.R. Johnson, A. Karpati, C.S. Rubin, D.W. Kolpin, M.T. Meyer, J.E. Estaban, R.W. Currier, K. Smith, K.M. Thu and M. McGeehin. *The Science of the Total Environment*, 2002. 299: 89-95.

Summary: Reports on data from numerous antimicrobial residues collected from animal wastes, surface water and groundwater proximal to large-scale swine and poultry operations. Data indicate that animal waste applied as fertilizer to the land may serve as a contaminating source of

antimicrobial residues for the environment as a detectable level of antimicrobial compounds was found in waste-storage lagoons and surface and groundwater proximal to these operations.

Antimicrobial use and resistance in animals. S.A. McEwen, and P.J. Fedorka-Cray. *Clinical Infectious Diseases*, 2002. 34 (Suppl 3): S93-106.

Summary: Describes antibiotic use in each animal class. Discusses a 1999 report on the economic effects of banning subtherapeutic antibiotic use in the U.S. Concludes that meat producers following good management practices would not be adversely affected by such a ban. Reviews antimicrobial-resistance-monitoring programs in bacteria of animal origin and the techniques involved. States alternatives to using antibiotics in food animals, such as providing good sanitation, air temperature and clean water, as well as vaccine use and development and use of probiotics that consist of live, beneficial bacteria.

Emergence, spread and environmental effect of antimicrobial resistance: How use of an antimicrobial anywhere can increase resistance to any antimicrobial anywhere else. T.F. O'Brien. *Clinical Infectious Diseases*, 2002. 34(Suppl 3): S78-84.

Summary: Discusses how a bacterial community responds to antimicrobial use by obtaining resistance genes as well as how these genes are spread around the globe and between different bacterial populations. States that in Europe a ban of avoparcin, an antibiotic similar to vancomycin, was implemented in 1997 because of rising concerns that strains of vancomycin-resistant *Enterococci* were being used for growth promotion.

Generally overlooked fundamentals of bacterial genetics and ecology. A.O. Summers. *Clinical Infectious Diseases*, 2002. 34 (Suppl 3): S85-92.

Summary: Reviews how treatment with any given antibiotic may result in resistance to several antibiotics because of the ability of bacteria to obtain genetic elements that code for multidrug resistance. States that the exchange of bacteria between a host and its environment is a continual process and that selective pressure applied to any part of the ecosystem will result in a highly resistant bacterial population. Also states that once resistance is acquired it will be hard to reverse because of molecular mechanisms inherent in bacteria that ensure future generations hold on to resistance characteristics.

Human diseases caused by foodborne pathogens of animal origin. M.N. Swartz. *Clinical Infectious Diseases*, 2002. 34 (Suppl 3): S111-122.

Summary: Evaluates the likelihood that emergence of several resistant strains of bacteria occurred first in animals rather than humans. Reviews studies that correlate antimicrobial use on farms to the occurrence of colonization and infection of farm workers and residents of the surrounding communities. Discusses the trend in antibiotic resistance in commensal microorganisms and their opportunistic infection of hospitalized patients.

Antimicrobial resistance of *Escherichia coli* 0157 isolated from humans, cattle, swine, and food. C.M. Schroeder, C. Zhao, C. DebRoy, J. Torcolini, S. Zhao, D.G. White, D.D. Wagner, P.F. McDermott, R.D. Walker, and J. Meng. *Applied and Environmental Microbiology*. 2002. 68(2): 576-581.

Summary: Examines the prevalence and antimicrobial resistance of Shiga toxin-producing *E. coli* (STEC) 0157 in a collection of samples collected for diagnostic purposes from humans, swine, cattle, and food between 1985 and 2000. Of 361 isolates available to analyze, 210 (58

percent) were STEC 0157. The greatest prevalence of STEC was found in isolates from cattle, followed by humans, food, and swine. Though swine had the smallest prevalence of STEC, isolates from swine demonstrated the highest prevalence of resistance. Prevalence of resistance to ampicillin, sulfamethazole, gentamicin, tetracycline, and trimethoprim-sulfamethoxazole was greater in non-STEC isolates than STEC isolates, however, all isolates were susceptible to ceftriaxone and ceftiofur. Of 191 isolates identified as *E. coli* O157:H7, cattle remained the most frequent source, followed by humans, and food. No O157:H7 was found in swine samples. All isolates from food were susceptible to all antimicrobials tested. Isolates from humans and cattle demonstrated similar resistance prevalence to ampicillin (5 vs. 1 percent), cephalothin (4 vs. 1 percent), chloramphenicol (0 vs. 1 percent), sulfamethoxazole (9 vs. 12 percent), tetracycline (7 vs. 11 percent), and amoxicillin-clavulanic acid (0 vs. 1 percent). Antimicrobial treatment of *E. coli* O157:H7 infection in humans may lead to release of Shiga toxin leading to hemolytic uremic syndrome (HUS). However, clinical trials are underway in which a chemically synthesized analog of Shiga toxin receptor Gb3 is given to patients to absorb the toxin and prevent HUS. If these trials prove successful, antimicrobials may become more important in the treatment of infection from *E. coli* O157:H7. The findings from this study that most STEC isolates were susceptible to all antimicrobials tested is encouraging. However, presence of resistance in isolates from swine and cattle to drugs used in these food-animals suggests that antimicrobial use in these animals contributes to the emergence of resistance in *E. coli* O157:H7.

Antimicrobial resistance in livestock. B. Catry, H. Laevens, L.A. Devriese, G. Opsomer and A. Kruif. *Journal of Veterinary Pharmacology and Therapeutics*, 2003. 26: 81-93.

Summary: Reviews resistance in animals from a veterinary perspective. Notes that resistance could result in economic losses and animal welfare problems for livestock producers and that “the resistance level in a population is directly related to amount of antimicrobial drugs used.” States that commensal bacteria in healthy animals fed or administered antibiotics contain resistance genes that if ingested by humans could colonize the gut and transfer these genes to pathogenic bacteria. This transfer would result in treatment difficulty because of antibiotic resistance.

Emergence of multidrug-resistant *Salmonella enterica* Serotype Newport infections resistant to expanded-spectrum cephalosporins in the United States. A. Gupta, J. Fontana, C. Crowe, B. Bolstorff, A. Stout, S. Van Duyne, M.P. Hoekstra, J.M. Whichard, T.J. Barrett and F.J. Angulo. *Journal of Infectious Diseases*, 2003. 188: 1707-1716.

Summary: Discusses the emergence of new strains of multidrug-resistant *Salmonella* in New England. Reports that isolates of Newport-MDRampC among *Salmonella* serotype Newport from humans rose from 0 percent in 1998 to 53 percent in 2001. This strain shows resistance to amoxicillin/clavulanic acid, cephalothin, cefoxitin and ceftiofur. Concludes that the use of antimicrobial agents in livestock is linked to the emergence of antimicrobial-resistant nontyphoidal *Salmonella* and that the emergence of Newport-MDRampC strains in humans has coincided with the same infections in cattle.

Evidence of an association between use of anti-microbial agents in food animals and antimicrobial resistance among bacteria isolated from humans and the human health consequences of such resistance. F.J. Angulo, V.N. Nargund and T.C. Chiller. *Journal of Veterinary Medicine*, 2004. 51: 374-379.

Summary: Reviews antimicrobial-resistant infections occurring in humans as a result of antibiotic use in food animal production. States that “a review of outbreaks of *Salmonella* infections indicated that outbreaks were more likely to have a food animal source than outbreaks caused by anti-microbial-susceptible *Salmonella*.” Reports that the human health consequences resulting from bacterial resistance include infections caused by resistant pathogens, an increase in treatment failures and increased severity of disease.

Nontherapeutic use of antimicrobial agents in animal agriculture: Implications for pediatrics.

K.M. Shea. *Pediatrics*, 2004. 114(3): 862-868.

Summary: Examines how antimicrobials are used in food animal production and how this practice could contribute to resistance in humans. Notes that children are at greater risk from resistant infections than the general population.

Antibiotic use in agriculture and its impact on the terrestrial environment. K. Kumar, S.C. Gupta, Y. Chander and A.K. Singh. *Advances in Agronomy*, 2005. 87: 1-54.

Summary: Discusses the impact of antibiotic use on disease treatment and growth promotion in animals. States that overuse of antibiotics results in the excretion of drugs that are not absorbed in the animal and that the resulting manure stock may be spread on fields, altering the soil bacteria and contaminating water sources. Notes that the continued prevalent use of antibiotics in agriculture is increasing the emergence of antibiotic-resistant bacteria both in both clinically relevant strains of pathogens and in normal commensal microorganisms. Concludes that “prudent use of antibiotics to a bare minimum along with alternative methods that minimize development and proliferation of resistant bacteria need investigation.”

Agricultural antibiotics and human health: Does antibiotic use in agriculture have a greater impact than hospital use? D.L. Smith, J. Dushoff and J.G. Morris, Jr. *PLoS Medicine*, 2005. 2(8): 731-735.

Summary: Reviews the emergence and spread of antibiotic-resistant bacteria and notes that mathematical models can help with understanding underlying mechanisms and guiding policy responses. Agricultural antibiotic use may generate novel types of antibiotic-resistant bacteria that spread to humans; models can help estimate how much additional disease has been caused by agricultural antibiotic use. Depending on the assumptions used, the model suggests that transmission from agriculture can have a greater impact than hospital transmission on human populations.

Resistant bugs and antibiotic drugs – State and county estimates of antibiotics in agricultural feed and animal waste. K. Florini, R. Denison, T. Stiffler, T. Fitzgerald, and R. Goldberg. *Environmental Defense*, 2005.

Summary: A report on the use of antibiotics in food animal production. States that an estimated 70 percent of the antibiotics used in the U.S. each year are used as feed additives for chickens, hogs and beef cattle. These are used mainly to promote growth and to compensate for poor health conditions. The National Academy of Sciences estimates that a cost estimate of \$4 to \$5 billion is associated with antibiotic-resistant bacteria. The report presents state and county specific estimates of antibiotic use and estimates of the amount of antibiotics excreted as animal waste. Farm families and the surrounding communities where there is greater on-farm antibiotic use may be at a greater risk of exposure to resistant bacteria. Estimates were derived from the U.S. Department of Agriculture’s 2002 Census of Agriculture in conjunction with the Union of

Concerned Scientists per-animal estimates of antibiotic feed-additive use for certain animal groups. North Carolina and Iowa both use an estimated three million pounds of antibiotics annually, which is equal to the estimated amount used for human treatment nationwide. The highest amounts of medically important antibiotics are used in hogs. An estimated 13.5 million pounds of antibiotics are excreted in the form of animal wastes, which is nearly half of the estimated total amount added to animal feeds. Also highlights that food is a pathway for resistance gene spread and that disease such as urinary tract infections may originate from food sources.

The potential role of concentrated animal feeding operations in infectious disease epidemics and antibiotic resistance. M.J. Gilchrist, C. Greko, D.B. Wallinga, G.W. Beran, D.R. Riley and P.S. Thorne. *Environmental Health Perspectives*, 2007. 115(2): 313-316.

Summary: Reports the recommendations of a working group that was part of the 2005 “*Conference on Environmental Health Impacts of Concentrated Animal Feeding Operations: Anticipating Hazards – Searching for Solutions.*” Recommendations include the following: discontinue nontherapeutic use of antibiotics as growth promoters; establish nationwide surveillance programs to fully assess the contribution of antibiotic use in livestock production to the creation of ecological reservoirs of resistance or the transmission of that resistance to humans; identify resistant strains; and establish minimum separation distances for swine and poultry facilities to reduce the risk of influenza outbreaks and municipal-style waste treatment to limit microbial and nutrient contamination of surface and groundwater.

Fluoroquinolone-resistant *Campylobacter* species and the withdrawal of fluoroquinolones from use in poultry: A public health success story. J.M. Nelson, T.M. Chiller, J.H. Powers and F.J. Angulo. *Clinical Infectious Diseases*, 2007. 44: 977-980.

Summary: Reviews fluoroquinolone use and the resulting effect of resistance occurring in the *Campylobacter* that followed the withdrawal of enrofloxacin from use in treating poultry. States that 13 percent of all resistant infections occur from travel abroad, showing that resistance is a global threat and that U.S. regulatory actions are not effective internationally. Concludes that “judicious use of antimicrobial agents should be stressed to preserve the efficacy of these important chemotherapeutic agents.”

Environmental health impacts of concentrated animal feeding operations: Anticipating hazards—searching for solutions. P.S. Thorne. *Environmental Health Perspective*, 2007. 115: 296-297.

Summary: Outlines potential risks to human health from concentrated animal feeding operations (CAFOs) and the research needed to better understand the impact of these operations on public health. Examples of policy change include establishment of a requirement for minimum separation distances, use of solid-waste storage tanks to eliminate the possibility of microbial contamination spreading to water sources and provision of clean water sources for drinking. Expresses concerns over air quality and the need for better surveillance in this area. Expresses a need to phase out the use of antimicrobial agents as growth promotants.

Response of antibiotics and resistance genes to high-intensity and low-intensity manure management. H.N. Storteboom, S-C Kim, K.C. Doesken, K.H. Carlson, J.G. Davis, and A. Pruden. *Journal of Environmental Quality*, 2007. 36: 1695-1703.

Summary: The goal of the study was to understand how antibiotics and antibiotic resistance genes respond to different levels of manure management. Management practices studied were high intensity management and low intensity management. High intensity was defined as amending with alfalfa and dried leaves with regular watering and turning the manure to enhance degradation. Low intensity was defined as piling or windrowing manure, which then received no treatment. A small scale pilot study and a large scale study were performed in which the large scale study focused on feedlot cattle manure and dairy cattle manure. The authors found that high intensity was more successful increasing the rate at which antibiotics degrade but was not a significant factor in reducing levels of resistant genes. Feedlot manure had a significantly higher level of resistant genes than did dairy manure, likely due to the feedlot cattle receiving routine subtherapeutic concentrations of antibiotics. The persistence of resistant genes is speculated to be due to the presence of degraded antibiotics as these products are often still effective and may allow selection pressure to remain. The authors suggest that longer treatment times may be necessary to further reduce levels of antibiotic resistant genes.

Association of antimicrobial resistance in *Campylobacter* isolated from food-producing animals with antimicrobial use on farms. T. Asai, K. Harada, K. Ishihara, A. Kojima, T. Sameshima, Y.

Tamura, and T. Takahashi. *Japanese Journal of Infectious Diseases*. 2007. 60: 290-294.

Summary: This study describes the use of antimicrobials in food-animals in Japan and examines the association between the use of antimicrobials and fluoroquinolone-resistant *Campylobacter*. Fluoroquinolone resistance was of interest because it was approved for therapeutic use in food-production animals in 1991. The most widely used antimicrobials were tetracyclines (7.8 percent), penicillin (6.5 percent), aminoglycosides (4.6 percent), and macrolides and lincosamides (4.3 percent). Fluoroquinolones were used for therapeutic purposes on 1.5 percent of 1,374 operations surveyed. Of operations positive for *C. jejuni*, oxytetracycline (OTC) resistance was present in 57.1 percent of operations using tetracycline antibiotics and on 43.2 percent of operations not using tetracyclines. For *C. coli* positive operations, 92.5 percent using tetracyclines and 74.3 percent not using tetracyclines were resistant to OTC. Enrofloxacin (ERFX) resistance was found in 66.7 percent and 16.7 percent farms reporting fluoroquinolone use for *C. jejuni* and *C. coli*. Farms not reporting use of fluoroquinolones had 15.5 percent and 28.8 percent prevalence of ERFX-resistant *C. jejuni* and *C. coli* respectively. Authors conclude that although fluoroquinolone-resistance in *Campylobacter* arose after approval for use in the treatment of sick animals, ERFX-resistance in *Campylobacter* is able to persist on food-animals operations regardless of use of fluoroquinolones.

Antibiotic resistance in bacteria associated with food animals: A United States perspective of livestock production. A.G. Mathew, R. Cissell, and S. Liamthong. *Foodborne Pathogens and Disease*.

2007. 4(2): 115-133.

Summary: Reviews the debate concerning use of antibiotics in animal production in the U.S. by presenting benefits of use but focusing on the problem of development of antibiotic resistant bacteria. Presents the types of antibiotics used in food-animal production and the main reasons for use including therapeutic, metaphylaxis (short-term treatment of infection), prophylactic, and for growth promotion. The origin of antibiotic resistance and the mechanisms of development and transfer of resistance among bacteria are discussed in detail. Surveillance programs are now present in the U.S. to track resistant bacteria and three are discussed. Based on surveillance and prior research, *Salmonella*, *Campylobacter*, *Listeria*, *Yersinia*, *Enterococcus*, and *Escherichia coli*

are presented as bacteria of concern related to food animal production and human health. Use of antibiotics in the beef cattle, dairy cattle, swine, and poultry industry is discussed. Challenges regulators, the animal production industry, and consumers to take steps in limiting risks based on science-based information.

Associations between antimicrobial resistance genes in fecal generic *Escherichia coli* isolates from cow-calf herds in western Canada. S.P. Gow, C.L. Waldner, J. Harel and P. Boerlin. *Applied and Environmental Microbiology*, 2008. 74(12): 3658-3666.

Summary: Studies antimicrobial-resistance gene distribution among cow-calf herds in western Canada. Finds that 65 percent of the 207 examined isolates of *E. coli* were resistant to at least one antimicrobial. Several patterns emerged from this research, suggesting that when a bacterium acquires resistance to one antimicrobial it is likely to become resistant to others because of the transfer of mobile genetic elements that harbor regions of multiple drug resistance. This suggests that even with careful restriction of antimicrobial use on farms, bacteria may still pick up resistance unrelated to the antimicrobials being used.

Industrial food animal production, antimicrobial resistance, and human health. E.K. Silbergeld, J. Graham and L.B. Price. *Annual Review of Public Health*, 2008. 29: 151-169.

Summary: Reviews the use of antimicrobials in agriculture and presents evidence for resistance stemming from their use in food animals. States that agricultural use of antibiotics can significantly shorten the useful life of these drugs, which are also used to treat disease in humans and animals. Suggests that estimates of nontherapeutic antibiotic use in agriculture fall between 60 percent and 80 percent of total antimicrobial production in the U.S. Concludes that “the use of antimicrobials for nontherapeutic purposes in agriculture is a major factor driving the emergence of antimicrobial resistance globally,” and that “prudent public health policy thus indicates that nontherapeutic uses of antimicrobials in food animal production should stop.”

Effect of subtherapeutic administration of antibiotics on the prevalence of antibiotic-resistant *Escherichia coli* bacteria in feedlot cattle. T.W. Alexander, L.J. Yanke, E. Topp, M.E. Olson, R.R. Read, D.W. Morck, and T.A. McAllister. *Applied and Environmental Microbiology*, 2008. 74(14): 4405-4416.

Summary: A study of *E. coli* resistance in feedlot cattle when they were administered a sub-therapeutic level of antibiotics. Cattle previously not treated with antibiotics were brought to a research feedlot where they were divided into groups each receiving a different regimen of sub-therapeutic antibiotics along with one group as a control not being treated. Cattle were fed two different diets during their treatments, one silage based diet and another grain based. Cattle tested before entering the feedlot (before starting sub-therapeutic treatment) were colonized with *E. coli* resistant to tetracycline (TET) at a rate greater than 40 percent, suggesting a colonization of TET resistant *E. coli* from birth (i.e. there is a high population of *E. coli* in circulation with TET resistance). Additionally the group fed chlortetracycline plus sulfamethazine (TET-SUL) showed an increased rate of TET resistance. A grain-based diet also appeared to increase not only the finding of *E. coli* but also increased the rate of finding TET resistant *E. coli*. Noted is that when antibiotic treatment was stopped for a period of about one to two months during each diet there was not a significant decline in the shedding of resistant *E. coli* except in the TET-SUL group where a slight decline was observed. However, upon starting treatment again the decline was reversed and prevalence of resistance continued to climb. The authors do note that in previous

studies a decline in resistance has been shown when antibiotics (selective pressures) were removed from diets of animals, but this may sometimes take years to see a marked decrease. In summary feeding of certain diets and addition of certain sub-therapeutic levels of antibiotics in feed will increase the rate of resistance in *E. coli*.

The effects of transport and lairage on counts of *Escherichia coli* O157 in the feces and on the hides of individual cattle. N. Fegan, G. Higgs, L. Duffy and R.S. Barlow. *Foodborne Pathogens and Disease*, 2009. 6(9):1113-1120.

Summary: Reports on a study in which *E. coli* O157 rates from feces and from hides of cattle were monitored to determine whether a change occurred during transport from the feedlot to slaughter. Concludes that “transport and lairage did not lead to an increase in the number or isolation rate of *E. coli* O157 from cattle.”

Comparison of the prevalence of bacterial enteropathogens, potentially zoonotic bacteria and bacterial resistance to antimicrobials in organic and conventional poultry, swine and beef production: a systematic review and meta-analysis. I. Young, A. Rajic, B.J. Wilhelm, L. Waddell, S. Parker, and S.A. McEwen. *Epidemiol. Infect.*, 2009. 137: 1217-1232.

Summary: A systematic review of the literature in comparing organic and conventional meats. Finds that the prevalence of *Campylobacter* was higher in organic broiler chickens at slaughter, but a difference was not seen in retail chicken. *Campylobacter* from conventional retail chicken was more likely to be ciprofloxacin resistant. Furthermore, bacteria isolated from conventional food animal production were found to exhibit higher levels of antibiotic resistance. The authors conclude that further research is necessary in this area as this type of data from other food-animal species was limited or inconsistent.

The transformation of U.S. livestock agriculture: Scale, efficiency, and risks. J.M. MacDonald and W.D. McBride. *Economic Information Bulletin Number 43*, United States Department of Agriculture, 2009.

Summary: Report from the United States Department of Agriculture detailing the nature, causes and effects of structural changes in livestock production. States that due to the increase seen in farm size, livestock wastes are becoming geographically concentrated in the US and the application of these wastes to land poses risks to air and water resources. Large-scale operations are more likely to see a rapid spread of disease due to the concentration of animals and tend to administer sub therapeutic doses of antibiotics routinely in feed and water to animals to promote health and prevent disease. These antibiotics may enter the environment through manure application and overuse may contribute to increased resistance in animal and human pathogens. Other technologies, including better sanitation and testing procedures, can be substituted for these practices in some production stages especially in poultry production. These practices, used in most operations not providing their animals sub therapeutic antibiotics, include: the testing of feed for specific pathogens; testing of flocks routinely for disease; cleaning out and sanitizing houses after each flock; and typically were required to have a hazard analysis and critical control point plan in place to direct food safety measures. The farms that do not rely on sub therapeutic antibiotics for disease prevention were nearly twice as likely to follow these procedures as those farms that used sub therapeutic antibiotics.

Fate and transport of antibiotic residues and antibiotic resistance genes following land application of manure waste. J.C. Chee-Sanford, R.I. Mackie, S. Koike, I.G. Krapac, Y.F. Lin, A.C. Yannarell, S. Maxwell and R.I. Aminov. *Journal of Environmental Quality*, 2009. 38: 1086-1108.

Summary: This review article can be broken down into three parts:

1) Dissemination of antimicrobial residues into the environment: Antibiotics fed to food animals are not always fully absorbed and will be excreted in waste. This waste is often applied to the environment as a disposal and fertilization technique. During this process excreted antibiotics that have not broken down during storage of waste are applied to the environment. Numerous studies are cited where antibiotic residues were found in soil and water near or on concentrated animal feeding operations (CAFO).

2) Resistance characteristics and presence of bacteria in CAFO and their transport into the environment: Antibiotic resistance in animals is likely to arise among commensal bacteria as there is a large pool in the gut (often $>10^{14}$) and antibiotic resistance may be selected for each time an antibiotic is administered regardless of the animals health. This is the most likely pathway for the development of pathogen resistance as commensal bacteria may transfer mechanisms of resistance to bacterial pathogens. It is well documented that these bacteria may survive waste treatment methods and are applied to the soil that may have harmful environmental implications.

3) Antibiotic resistance gene transfer in the environment: By applying animal waste to the environment a pool is created that holds a potentially significant amount of resistance genes; however, the transfer of these mechanisms into commensal bacteria of the environment is relatively unknown. Studies are listed showing that the transfer of resistance genes does occur between bacteria of different genera in such areas as soil and groundwater. The authors conclude that although the impacts from antibiotic use in food animal production and the effects on the environment are not completely clear, there are established studies pointing to an increase of incidences in antibiotic resistance.

Sublethal antibiotic treatment leads to multidrug resistance via radical-induced mutagenesis. M.A. Kohanski, M. A. DePristo and J.J. Collins. *Molecular Cell*, 2010. 37:311-320

Summary: Looks at mutation rates of *E. coli* exposed to sublethal doses of different antibiotics. Finds that when sublethal doses of antibiotics were given, cell production of radical oxygen species (ROS) occurred, leading to mutations. ROS can damage DNA, causing a mutation in such a way that the cells may acquire resistance to classes of antibiotics different from those with which they are being treated. Gives a clinical example of incomplete treatment with antibiotics (e.g., a missed pill), but one could postulate that in food animal production, where subtherapeutic levels of antibiotics are given for the purpose of growth promotion, this event may also occur.

Use and environmental occurrence of antibiotics in freestall dairy farms with manured forage fields. N. Watanabe, B.A. Bergamaschi, K.A. Loftin, M.T. Meyer, and T. Harter. *Environmental Science and Technology*, 2010. 44:17 6591-6600.

Summary: Investigates the use and occurrence of antibiotics in concentrated dairy feeding operations to assess their potential transport into first-encountered groundwater. The study finds that wide arrays of antibiotics are used in the farms leading to several hundred grams of antibiotics being excreted per farm per day. Samples containing sulfonamides, tetracyclines and lincomycin were most frequent; however, it appeared that the occurrence of antibiotics in collected samples was limited to farm boundaries and were usually associated with lagoons, hospital pens and calf hutches. There was detection of antibiotics in shallow groundwater 10

meters from lagoons. The authors conclude that these occurrences of antibiotics at the farm surface need closer study as they may affect the ecosystem and microbial community including the development of antibiotic resistance.

The interface between veterinary and human antibiotic use. T.R. Shryock and A. Richwine. *Annals of the New York Academy of Sciences*, 2010. 1-14.

Summary: This review looks at the overlaps between human and veterinary medicine and how current views are redirecting company pipelines in regards to new veterinary antimicrobial drug discovery. The authors state that the listing of “critically important” antibiotics by the World Health Organization has led to a prejudice against the food animal use of specific antimicrobial classes. The authors state several possible remedies to use in parallel or in replacement of these antibiotic classes including novel antibiotic development, vaccines, immunomodulators, bacteriophages and probiotics. A resounding theme is the ever-increasing demand of animal-derived protein and that the current and future availability of novel antimicrobial agents for use in food animal production be considered from this perspective. Other key points addressed include appropriate risk assessment before regulation, as uninformed decisions may discourage innovation of new antibiotics and that industry should apply the use of risk management interventions such as appropriate antibiotic use guidelines.

The effects of moral obligations to others and others’ influence on veterinarians’ attitudes toward and recommendations to utilize antibiotics in feedlot cattle. J-S. Jan, Wm. A. McIntosh, H. M. Scott, and W. Dean. *Journal of Rural Social Sciences*. 2010. 25 (2): 122-148.

Summary: A questionnaire was sent to feedlot veterinarians querying about areas of social pressure that may affect behavior in treatment of animals. Outcomes suggest that pressure from pharmaceutical companies led to a less likely scenario that veterinarians would have a positive attitude toward using antibiotics in acutely sick cattle. The opposite was seen when rule and norm-making organizations such as veterinary professional organizations, the FDA or state licensing boards applied pressure in that veterinarians’ attitudes were positively affected toward the use of antibiotics. Favorability toward using antibiotics was also seen when pressure from feedlot managers and retained owners of cattle was applied but only when moral obligations to these clients were taken into consideration. Otherwise these pressures had little influence on attitudes or recommendations.

Tetracycline and sulfonamide antibiotic resistance genes in livestock lagoons of various operation type, configuration, and antibiotic occurrence. C.W. McKinney, K.A. Loftin, M.T. Meyer, J.G. Davis, and A. Pruden. *Environmental Science & Technology*. 2010. 44: 6102-6109.

Summary: The purpose of this study was to look at waste lagoons among various livestock facilities and examine the behavior of *tet* (tetracyclines) and *sul* (sulfonamide) antibiotic resistance genes (ARGs) over the course of one year. ARG concentrations were significantly higher in lagoon samples from conventional dairy farms compared to organic. Chicken layer operation lagoons had the lowest detectable levels of *tet* and *sul* ARGs, while the highest were in swine lagoons. In general *sul* ARGs were more recalcitrant than *tet* ARGs. The study demonstrated that liquid manure lagoons may show some promise in reducing *tet* ARGs as passing waste through several lagoons decreased *tet* ARGs; however, when compared to sediment samples taken upstream from the facilities, the lagoon water samples still contained three to five times higher *tet* ARGs.

Antibiotic resistance, gene transfer, and water quality patterns observed in waterways near CAFO farms and wastewater treatment facilities. B.M. West, P. Liggit, D.L. Clemans, and S.N. Francoeur. *Water, Air, and Soil Pollution*. 2010.

Summary: In this study, water quality indicators were measured in locations impacted by confined animal feeding operations (CAFOs), nearby reference sites and sites located upstream and downstream of two wastewater treatment facilities. Selected study sites that were impacted by agriculture including three waterways showed levels of phosphorus higher than all other sites, and fecal coliform densities ranged from 70 to >7,900 CFU/100ml. In instances of rain events, densities of fecal coliforms from samples ranged from 700 to “too numerous to count.” Samples containing 70 to 2,300 CFU/100ml were taken from waterways near wastewater treatment plants. Agriculturally impacted sites had a significantly greater proportion of isolates that showed resistance to multiple antibiotics. In assays designed to screen for the transferability of DNA encoding resistance, environmental isolates were found to be very likely to contain elements allowing for this exchange. The authors suggest that testing for antibiotic resistance genes in bacterial strains become part of standard methods when examining water quality in areas at risk for pollution from human and/or animal waste.

CTX-M-type extended-spectrum β -lactamases present in *Escherichia coli* from the feces of cattle in Ohio, United States. T.E. Wittum, D.F. Mollenkopf, J.B. Daniels, A.E. Parkinson, J.L. Mathews, P.R. Fry, M.J. Abley and W.A. Gebreyes. *Foodborne Pathogens and Disease*. 2010.

Summary: CTX-M extended-spectrum β -lactamases are enzymes produced by bacteria that allow them to inhibit the antimicrobial effects of penicillins and cephalosporin drugs. This is of public health concern as expanded-spectrum cephalosporins are the treatment of choice for infections such as salmonellosis in children. In this study, samples from bovine fecal samples were screened for CTX-M producing strains of *E. coli*. Results show that 6 percent (3/50) of fecal samples collected harbored CTX-M genes. It has been hypothesized that ceftiofur use in livestock populations may provide the necessary selection pressure for such resistance genes as CTX-M to disseminate. Results from this study support the hypothesis as *E. coli* harboring CTX-M was isolated from a calf that was recently treated with ceftiofur therapy.

Producer attitudes and practices related to antimicrobial use in beef cattle in Tennessee. A.L. Green, L.R. Carpenter, DE. Edmisson, C.D. Lane, M.G. Welborn, F.M. Hopkins, D.A. Bemis and J.R. Dunn. *JAVMA*. 237 (11): 1292-1298.

Summary: This study involved a sampling by mail of 3,000 beef producers across the state of Tennessee, with 1,042 returned. The results showed 56.3 percent of beef cattle operations reported having used antimicrobials within the past year. Producers with multiple operation types (MOT) were more likely than producers with only cow-calf operations to have administered antibiotics either by mouth or by injection within the past year. The MOT producers were also slightly more likely to agree that antibiotics are not working as effectively than in the past. Herd size also had a positive correlation with antimicrobial use. The authors suggest that beef quality assurance programs should be employed and an effort to reach producers not involved in these programs should be explored. Additionally, efforts to reduce antibiotic use among producers may be found through educational efforts focused on practical, cost and labor effective alternatives such as a focus on bio-security, vaccination and low-stress handling of livestock and decreased stocking density to minimize disease transmission.

Effects of restricted antimicrobial exposure on antimicrobial resistance in fecal *Escherichia coli* from feedlot cattle. P.S. Morley, D.A. Dargatz, D.R. Hyatt, G.A. Dewell, J.G. Patterson, B.A. Burgess and T.E. Wittum. *Foodborne Pathogens and Disease*, 2011. 8-1: 1-12.

Summary: A study on two types of feedlot cattle. Conventional was raised and fed a diet with antibiotics while natural was raised and fed a diet of no antibiotics and were only exposed to antibiotics if disease occurred. The authors conclude that there was no difference in resistance to collected *E. coli* from either group in the study and suggest that conventional feedlot production methods do not predictably increase the prevalence of antimicrobial resistance in *E. coli* when compared to animals raised with restricted exposure to antibiotics.

The study design assigned pens to the natural cattle that may have previously housed cattle fed a conventional diet and no documentation is made on if pens were cleaned before study groups were placed. Cattle from the conventional group were also sometimes clustered in pens adjacent to the natural group to facilitate feeding. Also, after antibiotics were administered to sick cattle they were returned to their previous pens, which may have exposed other cattle in the group to the treated animal's microbial flora. While antibiotic susceptibility testing showed little to no difference (higher resistance to tetracycline and chloramphenicol was observed in conventional cattle) in resistance patterns of collected *E. coli*, the conventional cattle were fed Tylosin, a macrolide antibiotic and there were no macrolides in the susceptibility panel of testing. The authors do not address if the naturally raised cattle could have been exposed to bacteria from previous cattle fed antibiotics that were housed in the same pens.

Also of note is that this study was designed around "natural" raised and "conventional" raised cattle. These definitions are synonymous with the only differences being that "natural" products are minimally processed and do not contain artificial or synthetic ingredients or coloring additives; however, in this study they did attempt to keep the "natural" beef antibiotic free.

Dose imprecision and resistance: Free-choice medicated feeds in industrial food animal production in the United States. D.C. Love, M.F. Davis, A. Bassett, A. Gunther, and K.E. Nachman. *Environmental Health Perspectives*, 2011. 119(3):279-283.

Summary: Food animals in the US are often provided food that includes antibiotics and antiparasitic drugs on a "free choice" basis meaning the animals decide when to eat food and how much of it to consume. This practice is referred to as using free-choice medicated feeds (FCMF) and is shown to result in imprecision of drug intake leading to under and over-medication of animals. Imprecision in dosing of animals can lead to the development of antibiotic-resistant microorganisms or the presence of drug residues in food products. Various factors including labeling, veterinary oversight, feed characteristics, animal and herd behavior, behavior of workers, and drug pharmacokinetics may affect the dose ingested and received by the animal. Little oversight or control of FCMF exists in the US and no federal requirements exist for reporting use of antimicrobial drugs in animal production. This is despite the proposal of the Preservation of Antibiotics for Medical Treatment Act (PAMTA) introduced to Congress in 2009 and a statement from the US Food and Drug Administration (FDA) that "the overall weight of evidence available to date supports the conclusion that using medically important antimicrobial drugs for production purposes is not in the interest of protecting and promoting the public health." The authors conclude that use of FCMF poses an unnecessary risk to public health and that a more appropriate system of medicating animals should be used only when necessary to treat clinically diagnosed disease.

Food animals and antimicrobials: Impacts on human health. B.M. Marshall and S.B. Levy. *Clinical Microbiology Reviews*. 2011, 24(4): 718-733.

Summary: Reviews literature on the link between nontherapeutic antimicrobial (NTA) use in food-animal production, including aquaculture, and the emergence of antibiotic-resistant bacteria in humans and concludes that a wealth of evidence exists to support this link. Use of antibiotics is a powerful force in the selection of resistant bacteria and use anywhere can lead to resistance at point of use and in other areas. Identifies gaps in knowledge related to NTA use highlighting the lack of research regarding genetic infrastructure and spread between commensal and environmental bacteria.

Antibiotic resistance, gene transfer, and water quality patterns observed in waterways near CAFO farms and wastewater treatment facilities. B.M. West, P. Liggitt, D.L. Clemans, and S.N.Francoeur. *Water, Air & Soil Pollution*. 2011. 217(1-4): 473-489.

Summary: Reports findings from a water quality assessment study that sampled up and downstream of waste water treatment plants (WWTP) and locations affected by confined animal feeding operations (CAFO) and reference locations unaffected by CAFOs. Chemical and biological water quality indicators were evaluated. Sites up and downstream of WWTPs met current chemical and biological water quality standards and were considered environmentally healthy. Fecal coliform density ranged from 70-2,300 CFU/100 ml in these locations. High, but similar, levels of drug-resistant fecal coliforms were found up and downstream of WWTPs. In contrast, sites near CAFOs had reduced water quality compliance and fecal coliform levels ranged from 700 CFU/100 ml to too numerous to count. CAFO affected sites had much higher levels of multi-drug resistant bacteria (42 percent) as compared with agricultural sampling sites not affected by CAFOs (17 percent). In laboratory experiment, antibiotic-resistant bacteria collected at all locations demonstrated the ability to transfer resistance genes. Concludes that surface waters may be an important source of human exposure to antibiotic-resistant bacteria and monitoring of antibiotic-resistance should become part of the standard monitoring of waterways.

SWINE

Ways in which swine production affects air, water and farm workers.

An outbreak of multidrug-resistant, quinolone-resistant *Salmonella enterica* serotype typhimurium DT104. K. Molbak, D.L. Baggesen, F.M. Aarestrup, J.M. Ebbesen, J. Engberg, K. Frydendahl, P. Gerner-Smidt, A.M. Petersen, and H.C. Wegener. *New England Journal of Medicine*, 1999. 341: 1420-1425.

Summary: Reviews a 1998 *Salmonella enterica* serotype typhimurium DT104 outbreak in Denmark. The outbreak had 25 confirmed cases, with 11 patients hospitalized and two deaths. Previous cases were resistant to five antibiotics; however, cases in this outbreak also were resistant to nalidixic acid and had reduced susceptibility to fluoroquinolones. Analysis traced the infection to a swine herd delivered to a slaughterhouse and the resulting retail pork was found to be the common food source.

Concentrated swine-feeding operations and public health: A review of occupational and community health effects. D. Cole, L. Todd, and S. Wing. *Environmental Health Perspectives*, 2000. 108: 685-699.

Summary: Reviews the effects of industrial farms on community health. States that there are many potential routes of community exposure to industrial farming hazards and that people residing near swine farms may be exposed to these agents through pathways such as airborne contaminants produced by building ventilation fans, soil transport of microbes from land-applied wastes and leaking lagoons that contaminate groundwater. States that more research is needed to determine the far-reaching effects of industrial farms on community health.

Occurrence and diversity of tetracycline-resistance genes in lagoons and groundwater underlying two swine production facilities. J.C. Chee-Sanford, R.I. Aminov, I.J. Krapac, N. Garrigues-Jeanjean, and R.I. Mackie. *Applied and Environmental Microbiology*, 2001. 67(4): 1494-1502.

Summary: States that 25 percent to 75 percent of antimicrobials administered to food animals are poorly absorbed in the gut and are excreted in feces. These unaltered substances are then applied to land by spreading of manure. Finds that a broad range of tetracycline-resistance genes occurred in two swine-waste lagoons and that upon release into the environment these genes can potentially mobilize and persist. Data suggest that the presence of the resistance genes is due to seepage and movement of groundwater underlying the lagoons and that it may be substantial, as resistance genes were found in a well 250 meters downstream of the lagoon sampled.

Effects of administration of antimicrobials in feed on growth rate and feed efficiency of pigs in multisite production systems. S.S. Dritz, M.D. Tokach, R.D. Goodband, and J.L. Nelssen. *JAVMA* 2002. 220:11 1690-95.

Summary: A study consisting of 10 trials involving a total of 24,099 finishing and nursery pigs. Trials involving pigs feed antimicrobials were selected based on commonly used production system regimens. A control group was also included that was not administered antibiotics unless necessary due to disease and then at a therapeutic dose. When all data were compiled, only nursery pigs showed an increase in average daily gain when given antibiotics in feed. Feed efficiency was lower in all nursery groups given antibiotics in feed compared to the control and feed efficiency was not significantly different in either finishing or nursery groups between control and treated animals. It was concluded that giving antibiotics in feed to finishing pigs had

no effect on average daily gain. The authors note that this study differs from other similar studies, as their noted average daily gains were less than previous reports. Listed explanations include: previous data being biased toward publication of data with positive results; the excellent performance of the control group in the present study; and the fact that current hygienic conditions used exceeded that in previous trials allowing for the control group to perform at a higher level. The authors state that results of the present study indicate that the use of multisite pig production methods greatly reduce pathogen burden on pigs and in turn allows for reduction in use of non-therapeutic antimicrobials.

Productivity and economic effects of antibiotics used for growth promotion in U.S. pork

production. G. Y. Miller, K. A. Algozin, P. E. McNamara, and E. J. Bush. *Journal of Agricultural and Applied Economics*, 2003. 35(3): 469-482.

Summary: Studies the use of growth promoting antibiotics (GPA) in pork production. Finds that when GPA are removed from production operations that use less than four different rations (feed) there is a net decrease in return at sale of nine percent. However, when farms use greater than four different rations there is an increase in feed conversion without the use of antibiotics. Furthermore, when farms used greater than four different rations and applied GPA, feed conversion decreased. The authors state “our results imply that antibiotics used for growth promotion are of value mainly when four or fewer different rations are used in finishing.”

Antimicrobial resistance in commensal flora of pig farmers. H. Aubrey-Damon, K. Grenet, P. Sall-Ndiaye, D. Che, E. Cordeiro, M.E. Bounoux, E. Rigaud, Y. Le Strat, V. Lemanissier, L. Armand-Lefèvre, D. Delzescaux, J.C. Desenclos, M. Liénard, and A. Andreumont. *Emerging Infectious Diseases*, 2004. 10(5): 873-879.

Summary: Compares the carriage rates of antibiotic-resistant bacteria isolated from pig farmers and non-farmers matched for sex, age and county of residence in France. Finds that farmers carry a higher percentage of resistant commensal bacteria than non-farmers. States that the rate of VRE colonization did not differ between farmers and non-farmers and that this finding suggests that the 1997 ban of avoparcin was effective.

Airborne multidrug-resistant bacteria isolated from a concentrated swine feeding operation.

A. Chapin, A. Rule, K. Gibson, T. Buckley, and K. Schwab. *Environmental Health Perspectives*, 2005. 113: 137-142.

Summary: Reports the results of studies air samples taken within confined hog operations for antibiotic-resistant bacteria. Ninety-eight percent of bacteria sampled had resistance to at least two antibiotics used in animal production and a greater potential for worker exposure to resistant bacteria, suggesting that exposure to air from swine operations may allow multidrug-resistant bacteria to be transferred from animals to humans. Notes that “these data are especially relevant to the health of swine CAFO [concentrated animal feeding operations] workers, their direct contacts in the community, and possibly nearby neighbors of swine CAFOs.”

Detection and occurrence of antimicrobially resistant *E. coli* in groundwater on or near swine

farms in eastern North Carolina. M.E. Anderson and M.D. Sobsey. *Water Science and Technology*, 2006. 54(3): 211-218.

Summary: Compares the extent of groundwater contamination from antibiotic-resistant *E. coli* from industrial swine farms and reference sites. Sixty-eight percent of the *E. coli* from the swine

farm sites were resistant to at least one antibiotic, while only one isolate from each of the reference sites showed resistance. Concludes that groundwater on or near swine farms may pose as an environmental pool for antibiotic-resistant *E. coli* and resistance genes.

The effect of subtherapeutic chlortetracycline on antimicrobial resistance in the fecal flora of swine. J.A. Funk, J.T. Lejeune, T.E. Wittum, and P.J. Rajala-Schultz. *Microbial Drug Resistance*, 2006. 12(3): 210-218.

Summary: Studies the occurrence of antimicrobial-resistant *Salmonella* due to the subtherapeutic use of chlortetracycline in the diets of swine. Concludes that "there was a positive association between inclusion of subtherapeutic chlortetracycline in the diet and resistance to multiple antimicrobials."

Isolation of antibiotic-resistant bacteria from the air plume downwind of a swine confined or concentrated animal feeding operation. S.G. Gibbs, C.F. Green, P.M. Tarwater, L.C. Mota, K.D. Mena, and P.V. Scarpino. *Environmental Health Perspectives*, 2006. 114: 1032–1037.

Summary: Studies air samples from upwind, downwind and inside of a confined hog operation. Bacterial samples were tested for antibiotic resistance and *Staphylococcus aureus* was the dominant species recovered. Samples taken within the barn displayed the highest rate of resistance; samples taken up to 150 meters downwind of the barn showed a higher level of resistance than samples taken upwind. Multiple antibiotic-resistant organisms were also found within and around the barn. Concludes that this increase in antimicrobial resistance could have a negative on the health of people who live around these facilities.

Community-acquired MRSA and pig-farming. X.W. Huijsdens, B.J. van Dijke, E. Spalburg, M.G. van Santen-Verheuevel, M.E. Heck, G.N. Pluister, A. Voss, W.J.B. Wannet, and A.J. de Neeling. *Annals of Clinical Microbiology and Antimicrobials*, 2006. 5(26).

Summary: Reports a mother and baby who were found to be carriers of MRSA. A case study followed, finding that the father was a pig farmer, a screening was done to test coworkers, pigs and family members. Three coworkers, eight of 10 pigs and the father were found to be carriers of MRSA. Molecular characterization of the samples clearly revealed transmission of MRSA from pigs to humans. These findings show clonal spread and transmission of MRSA between humans and pigs in the Netherlands.

Are swine workers in the United States at increased risk of infection with zoonotic influenza virus? K.P. Myers, C.W. Olsen, S.F. Setterquist, A.W. Capuano, K.J. Donham, E.L. Thacker, J.A. Merchant and G.C. Gray. *Clinical Infectious Diseases*, 2006. 42: 14-20.

Summary: Studies farmers, meat-processing workers, veterinarians and a control group to determine the extent of exposure to pandemic influenza strains originating from pigs. Finds that farmers are at greatest risk and tend to demonstrate a higher titer to both H1N1 and H1N2 swine influenza virus isolates than control subjects do.

Risk factors for antimicrobial resistance among fecal *Escherichia coli* from residents on forty-three swine farms. T.H. Akwar, C. Poppe, J. Wilson, R.J. Reid-Smith, M. Dyck, J. Waddington, D. Shang, N. Dassie, and S.A. McEwen. *Microbial Drug Resistance*, 2007. 13(1): 69-76.

Summary: Focuses on residents and workers of hog operations that fed antibiotics and those that did not. *E. coli* was obtained from 115 residents and tested for resistance; 25.8 percent of *E. coli*

sampled was resistant to at least one antibiotic. Prevalence of resistant bacteria was higher among workers or residents of the farms where antibiotics were fed to hogs. Results indicate that farmers have an increased occupational hazard of exposure to antibiotic-resistant bacteria when antibiotics are fed to animals.

Monitoring and source tracking of tetracycline resistance genes in lagoons and groundwater adjacent to swine-production facilities over a 3-year period. S. Koike, I.G. Krapac, H.D. Oliver, A.C. Yannarell, J.C. Chee-Sanford, R.I. Aminov, and R.I. Mackie. *Applied and Environmental Microbiology*, 2007. 73(15): 4813-4823.

Summary: Studies the dissemination of tetracycline-resistance genes from lagoons into the surrounding environment. DNA was extracted and analyzed by real-time quantitative PCR showing a similarity of 99.8 percent for a selected resistance gene between collected groundwater sample DNA and that of the lagoons. States that this is clear evidence that animal waste seeping from lagoons can affect the environment by spreading resistance genes through groundwater contamination.

Antibiotic-resistant *Enterococci* and fecal indicators in surface water and groundwater impacted by a concentrated swine feeding operation. A.R. Sapkota, F.R. Curriero, K.E. Gibson, and K.J. Schwab. *Environmental Health Perspectives*, 2007. 115(7): 104-1045.

Summary: Reviews the risks associated with exposure to manure-contaminated water sources by industrial farms. The authors could not obtain specific data on levels of antibiotics in swine feed because it was premixed and delivered by a contracted integrator, which had deemed antibiotic-usage data proprietary information. Reports that elevated levels of fecal indicators and antibiotic-resistant *Enterococci* were detected in water sources situated down-gradient from a swine facility compared with up-gradient surface water and groundwater. Concludes that “the presence of resistant bacteria in both drinking water and surface water sources contaminated by swine farms could contribute to the spread and persistence of both resistant bacteria and antibiotic resistance determinants in humans and the environment.”

Antibiotic resistant bacterial profiles of anaerobic swine-lagoon effluent. J.P. Brooks and M.R. McLaughlin. *Journal of Environmental Quality*, 2009. 38: 2431-2437.

Summary: Focuses on three types of swine farms—farrowing, nursery and finisher. Antibiotic-resistant bacteria were screened for and isolated from all three types of farm lagoons. States that selective pressures appear to have an effect on the amount of resistant isolates recovered from swine-waste lagoons. Nursery lagoons appeared to be most contaminated, with antibiotic-resistant bacteria most likely due to the elevated use of antibiotics in these operations. Finisher farm lagoons contained the lowest concentration, signaling a lower use of antimicrobials in this environment.

Prevalence, numbers and characteristics of *Salmonella* spp. on Irish retail pork. D.M. Prendergast, S.J. Duggan, U. Gonzales-Barron, S. Fanning, F. Butler, M. Cormican, and G. Duffy. *International Journal of Food Microbiology*, 2009. 131: 233-239.

Summary: Explores results of a survey of *Salmonella* in samples of pork from butcher shops and retail markets in Ireland and reports that it was found to contaminate 2.6 percent of samples assayed. *S. Typhimurium* was the dominant serotype found, at a rate of 85 percent; it is also one of the most frequently isolated serotypes from humans in the Irish population. Evidence of cross-

contamination was found between samples, pointing to the need for good hygiene practices at the retail level.

Occurrence and persistence of erythromycin resistance genes (*erm*) and tetracycline resistance genes (*tet*) in waste treatment systems on swine farms. J. Chen, F. C. Michel Jr. S. Sreevatsan, M. Morrison, and Z. Yu. *Microbial Ecology*, 2010.

Summary: This study focuses on how to control antibiotic resistance (AR) that is generated by use of antibiotics in confined animal feeding operations (CAFOs). The authors suggest there are two ways to control AR: reduce the use of antimicrobials on farms or find an effective way to minimize AR dissemination off farms by destroying or containing AR on farms. This study focuses on the latter of those two ways and looks to gain perspective on how well swine farms are containing antibiotic resistance by treating animal manure that is produced in CAFOs before it is being disseminated into the environment. Three swine farms were sampled with different types of waste treatment systems. Upon testing in various stages of waste clean up the authors find that “AR arising from swine-feeding operations can survive typical swine waste treatment processes” and call for treatments that are more functional in destroying AR on farms.

Abundance and diversity of tetracycline resistance genes in soils adjacent to representative swine feedlots in China. N. Wu, M Qiao, B. Zhang, W-D Cheng, and Y-G. Zhu. *Environmental Science and Technology*, 2010.

Summary: Studies the prevalence of tetracycline genes in soil samples from farmlands in the vicinity of nine swine farms located in three cities in China. Finds that 15 tetracycline-resistance genes were commonly detected in soil samples. A strong correlation was found between the concentrations of tetracycline residues, bacterial load and organic matter. Suggests that soils containing bacteria near swine farms may play an important role in the spread of antibiotic resistance and are a large environmental reservoir.

Changes in the use of antimicrobials and the effects on productivity of swine farms in Denmark. F.M. Aarestrup, V.E. Jensen, H-Dorthe Emborg, E. Jacobsen, and H.C. Wegener. *American Journal of Veterinary Research*, 2010. 71:7 726-33.

Summary: Evaluates the changes in antimicrobial use and swine productivity in Denmark between the years 1992 - 2008. In an effort to control the use of antimicrobials in food animal production, Denmark placed a ban on the use of growth promoting antibiotics in January of 2000. In the previous years leading up to the ban, other laws were passed limiting the veterinary profits that could be made on the prescription sale of antibiotics and also included treatment advice for veterinarians to guide the use of antibiotics. The study found there was a greater than 50 percent decrease in the use of antimicrobials per kg of pig produced during the time period from 1992 - 2008 which was associated with the policy to discontinue the use of growth promoting antibiotics. During this time the mortality rate was steady and production increased suggesting that this policy did not have a negative impact on swine production in Denmark.

Ceftiofur use in finishing swine barns and the recovery of fecal *Escherichia coli* or *Salmonella* spp. resistant to ceftriaxone. E.A. Lutz, M.J. McCarty, D.F. Mollenkopf, J.A. Funk, W.A. Gebreyes, and T.E. Wittum. *Foodborne Pathogens and Disease*. 2011. 8(11): 1229-1234.

Summary: Ceftiofur is the only third-generation cephalosporin labeled for veterinary use. It can be used to treat infections from Gram-negative bacteria and is used widely in the swine industry.

The drug of choice to treat human infections from Gram-negative bacteria is another third-generation cephalosporin, ceftriaxone. This study examines the association between antibiotic-resistance in *Salmonella* spp. and *Escherichia coli* swine and ceftiofur use in swine operations in North Carolina. Barns were classified based on ceftiofur use rates as rare, moderate, or common with 579, 648, and 672 fecal samples taken from each category respectively. *E. coli* resistant to ceftriaxone was recovered from 45 percent of samples from rare use barns, 73 percent from moderate use barns, and 68 percent from common use barns. *Salmonella* spp. with resistance to ceftriaxone were found in 4.1 percent of samples from rare use barns, 0.15 percent of samples from moderate use barns, and 6 percent of samples from common use barns. Authors suggest that barns with increased ceftiofur use have greater proportions of *E. coli* and *Salmonella* spp. that are resistance to ceftriaxone.

Detection of the staphylococcal multiresistance gene *cfr* in *Proteus vulgaris* of food animal origin. Y. Wang, Y. Wang, C. Wu, S. Schwarz, Z. Shen, W. Zhang, Q. Zhang, and J. Shen. *Journal of Antimicrobial Chemotherapy*. 2011. 66: 2521-2526.

Summary: Details the presence of a plasmid-borne resistance gene commonly found in gram-positive bacteria in the chromosomal DNA of a gram-negative bacterium taken from a pig. The *cfr* gene has the ability to mediate transfer of resistance to linezolid, an antibiotic used in clinical practice to treat human infections caused by gram-positive bacteria resistant to other antibiotics. In this case *cfr* was found in a *Proteus vulgaris* isolate from the nares of a pig raised on a conventional pig operation in China. This finding supports the claim that selective pressure from the use of antibiotics in pig production may allow for the maintenance and transfer of antibiotic resistance among bacteria.

Prevalence and antimicrobial resistance profile of *Campylobacter* spp. isolated from conventional and antimicrobial-free swine production systems from different US regions. D.A. Tadesse, P.B. Bahnsen, J.A. Funk, S. Thakur, W.E. Morgan Morrow, T. Wittum, F. DeGraves, P. Rajala-Schultz, and W.A. Gebreyes. *Foodborne Pathogens and Disease*. 2011. 8(3): 367-74.

Summary: Investigates the prevalence and antimicrobial resistance patterns of *Campylobacter* among pigs raised in a conventional environment and in antibiotic-free (ABF) environments at various stages of processing from pre-evisceration to post-chill through the collection of fecal and carcass swab samples. Approximately 95 percent (1034/1087) of isolates available for speciation were found to be *C. coli*, and the remainder was not *C. coli* or *C. jejuni*. 58.9 percent of conventional pigs (252/428) and 53.8 percent (220/411) ABF pigs were positive for *Campylobacter*. Prevalence of *Campylobacter* varied at different stages of production with the chill stage demonstrating the highest prevalence for both types of operations in both regions examined. The most common resistance pattern for *Campylobacter* isolated from ABF operations was resistance to tetracycline only (25.2 percent), erythromycin-tetracycline (10.3 percent), and erythromycin-nalidixic acid-tetracycline (10.3 percent). From conventional operations the dominant resistance patterns were erythromycin-tetracycline (33.4 percent), tetracycline (16 percent) and erythromycin (12.6 percent). Conventional and ABF production systems demonstrated 1.2 and 3.7 percent ciprofloxacin resistance. Of all isolates 2.9 percent (37/1257) were resistant to erythromycin and ciprofloxacin, the drugs of choice for treating human *Campylobacter* infection

POULTRY

The effects of poultry production on farm workers, public health and the spread of antibiotic-resistant bacteria.

Direct transmission of *Escherichia coli* from poultry to humans. A.A. Ojeniyi. *Epidemiology and Infection*, 1989. 103(3): 513-522.

Summary: Compares the resistance traits of *E.coli* collected from free-range poultry with those from poultry in a large-scale commercial facility. Reports that resistance to the antibiotics tested occurred only in those samples collected from birds in a commercial setting. Attendants from the commercial facilities also were found to contain resistant bacteria while samples from villagers in the community were negative. The authors also demonstrated that attendants contract bacteria from birds in their care by conducting a study where they infected birds with a known type of resistant *E. coli* and screened the attendants for the same bacteria.

Quinolone resistance in *Campylobacter* isolated from man and poultry following the introduction of fluoroquinolones in veterinary medicine. H.P. Endtz, G.J. Ruijs, B. van Klingeren, W.H. Jansen, T. van der Reyden, and R.P. Mouton. *The Journal of Antimicrobial Chemotherapy*, 1991. 27(2): 199-208.

Summary: Reports the results of tests for quinolone resistance in 883 strains of *Campylobacter* bacteria isolated between 1982 and 1989 from human stool and poultry products. *Campylobacter* isolated from poultry increased in resistance from 0 percent to 14 percent in that time, while resistance in human isolates rose from 0 percent to 11 percent. Results suggest that the increase is mainly due to use of enrofloxacin, a fluoroquinolone, in poultry.

High-frequency recovery of quinupristin-dalfopristin-resistant *Enterococcus faecium* isolates from the poultry-production environment. J.R. Hayes, A.C. McIntosh, S. Qaiumi, J.A. Johnson, L.L. English, L.E. Carr, D.D. Wagner, and S.W. Joseph. *Journal of Clinical Microbiology*, 2001. 39(6): 2298-2299.

Summary: Studies the extent of resistance to quinupristin-dalfopristin, a drug reserved for human use to treat vancomycin-resistant enterococci, in *Enterococcus faecium*. Finds that resistance to this antimicrobial ranged between 51 percent and 78 percent in isolates screened from the food-production environment.

Antibiotic resistance of faecal *Escherichia coli* in poultry, poultry farmers and poultry slaughterers. A.E. van den Bogaard, N. London, C. Driessen, and E.E. Stobberingh. *Journal of Antimicrobial Chemotherapy*, 2001. 47:763-771.

Summary: Reports a survey of *E. coli* in poultry and workers who were in close contact with animals. Finds that the highest resistance rates were in turkeys, closely followed by broilers. Isolates collected from the laying-hen population were much lower, possibly because of the infrequent use of antibiotics in these animals. In the human population the same results followed, with turkey workers' isolates showing greater resistance than those from broilers or laying-hens. Results also strongly suggest the transmission of resistant clones and resistance plasmids of *E. coli* from broilers and turkeys to humans.

The dioxin crisis as experiment to determine poultry-related *Campylobacter enteritis*. A. Vellinga and F. Van Look. *Emerging Infectious Diseases*, 2002. 8(1): 19-22.

Summary: Poultry was withdrawn in Belgium in June 1999 after a contaminant was found in feed. According to a model designed from the sentinel surveillance system, *Campylobacter* infections decreased by 40 percent during that month—from 153 cases per week to 94 cases. States that by using the ban as an epidemiologic tool, the rate of *Campylobacter* infections attributable to poultry was determined to be greater than 40 percent.

The effect of withdrawing growth promoting antibiotics from broiler chickens: A long-term commercial industry study. H.M. Engster, D. Marvil, and B. Stewart-Brown. *The Journal of Applied Poultry Research*, 2002. 431-436.

Summary: A comprehensive study where removal of growth promoting antibiotics (GPA) from broiler chickens was compared with those still receiving GPA. Average reduction of livability was only 0.2 percent on the Delmarva Peninsula (DMV) and 0.14 percent in North Carolina (NC). However, fluctuations were noted in livability from a reduction of 0.5 percent to a positive impact on livability of 0.3 percent. The average reduction in body weight was 0.03 lb on DMV and 0.04 lb in NC but this decline did not start until after the first year of the trial. Feed conversion (weight of food/body weight gain) was not adversely affected in the study for either location. Removal of GPA also resulted in no reports of field outbreaks of disease and total farm condemnations were not affected.

Fluoroquinolone-resistant *Campylobacter* isolates from conventional and antibiotic-free chicken products. L.B. Price, E. Johnson, R. Vailes, and E. Silbergeld. *Environmental Health Perspectives*, 2005. 113: 557-560.

Summary: Concludes that there is no difference in *Campylobacter* contamination between conventionally raised chickens and poultry raised antibiotic-free; however, conventionally raised poultry is more likely to be resistant to antibiotics than chickens raised antibiotic-free. The findings also suggest that fluoroquinolone-resistant isolates of *Campylobacter* may persist after the usage of fluoroquinolones in poultry production has ceased.

Similarity between human and chicken *Escherichia coli* isolates in relation to ciprofloxacin resistance status. J.R. Johnson, M.A. Kuskowski, M. Menard, A. Gajewski, M. Xercavins, and J. Garau. *The Journal of Infectious Diseases*, 2006. 194(1): 71-78.

Summary: Studies the similarities of *E. coli* isolates collected from humans and chickens that were resistant to ciprofloxacin. Finds that resistant *E. coli* in humans appears to have a profile similar to that of resistant *E. coli* collected from chickens, suggesting that the use of antimicrobials in poultry production is leading to resistant *E. coli* that are being transferred to humans, possibly through contaminated meats.

Use of streptogramin growth promoters in poultry and isolation of streptogramin-resistant *Enterococcus faecium* from humans. A.L. Kieke, M.A. Borchardt, B.A. Kieke, S.K. Spencer, M.F. Vandermause, K.E. Smith, S.L. Jawahir, and E.A. Belongia. *The Journal of Infectious Diseases*, 2006. 194(9): 1200-1208.

Summary: Examines virginiamycin use in poultry and its effect on cross-resistance to quinupristin-dalfopristin, a drug also in the streptogramin category that is intended for treating vancomycin-resistant *Enterococcus faecium* infections in humans. The study enrolled patients from hospitals and vegetarians and compared the samples from humans with samples collected from retail poultry meats. Reports that “poultry exposure is associated with a quinupristin-

dalfopristin resistance gene and inducible quinupristin-dalfopristin resistance in human fecal *E. faecium*. The continued use of virginiamycin may increase the potential for streptogramin-resistant *E. faecium* infection in humans.”

Subtherapeutic tylosin phosphate in broiler feed affects *Campylobacter* on carcasses during processing. M.E. Berrang, S.R. Ladely, R.J. Meinersmann, and P.J. Fedorka-Cray. *Poultry Science*, 2007. 86:1229-1233.

Summary: Studies cross-resistance of tylosin and erythromycin (both macrolide drugs). Erythromycin is often the drug of choice for treating campylobacteriosis, and tylosin is approved at subtherapeutic levels for use in broiler feed for growth promotion. Seventy chicks were divided into two groups, half raised on tylosin, half without. Carcasses of broilers fed tylosin had lower numbers of *Campylobacter*, but all the *Campylobacter* found were resistant to erythromycin. No *Campylobacter* isolated from the control carcasses were resistant. Concludes that application of tylosin phosphate in feed results in lower numbers of *Campylobacter*, but those that remain are resistant to erythromycin.

Growth promoting antibiotics in food animal production: An economic analysis. J.P. Graham, J.J. Boland, and E. Silbergeld. *Public Health Reports*, 2007. 122:79-87.

Summary: Examines the economic effect of removing antibiotics used for growth promotion in broiler chickens using data published by Perdue. Positive production changes were associated with use, but were insufficient to offset the cost of the antibiotics. The net effect of using growth-promoting antibiotics was a lost value of \$.0093 per chicken (about 0.45 percent of total cost).

Development of macrolide-resistant *Campylobacter* in broilers administered subtherapeutic or therapeutic concentrations of tylosin. S.R. Ladely, M.A. Harrison, P.J. Fedorka-Cray, M.E. Berrang, M.D. Englen, and R.J. Meinersmann. *Journal of Food Protection*, 2007. 70(8):1915-1951.

Summary: Looks at the impact of antibiotic use on increasing the amount of resistant bacteria in an environment. Poultry were divided into groups of 25 birds: the treatment group was given either therapeutic or subtherapeutic doses of tylosin beginning at two weeks of age while the control group was isolated and not given any antimicrobials. The animals fed subtherapeutic and therapeutic doses of tylosin tested positive for resistant bacteria; no resistant strains were found among the birds that did not get treated with tylosin. The birds treated with subtherapeutic doses of tylosin also showed increased resistance compared with the birds treated with therapeutic doses.

Elevated risk of carrying gentamicin-resistant *Escherichia coli* among U.S. poultry workers. L.B. Price, J.P. Graham, L.G. Lackey, A. Roess, R. Vailes, and E. Silbergeld. *Environmental Health Perspectives*, 2007. 15(12):1738-1742.

Summary: Examines poultry workers and residents on the eastern shore of Maryland and Virginia. Poultry workers had 32 times the odds of being colonized with gentamicin-resistant *E. coli* as community residents; the poultry workers also had an elevated risk of carrying multidrug-resistant *E. coli*. Concludes that “occupational exposure to live animals in the broiler chicken industry may be an important route of entry for antimicrobial-resistant bacteria in to the community.”

Effect of macrolide usage on emergence of erythromycin-resistant *Campylobacter* isolates in chickens. J. Lin, M. Yan, O. Sahin, S. Pereira, Y. Chang, and Q. Zhang. *Antimicrobial Agents and Chemotherapy*. 2007. 51(5): 1678-1686.

Summary: Erythromycin is a macrolide antimicrobial often used to treat *Campylobacter* infection in humans. This article presents information from experiments conducted to determine the emergence of erythromycin-resistant (Ery^r) *Campylobacter jejuni* and *Campylobacter coli* under selection pressure of macrolide use in a laboratory setting. Further discusses mechanisms associated with resistance to erythromycin. Results are presented from three experiments examining treatment of chickens with water containing tylosin, a macrolide-class antibiotic, and two experiments examining treatment of chickens with feed containing tylosin. Experiments show that chickens receiving a three-day therapeutic dose of tylosin in water (0.53 g/liter) shed significantly less *C. jejuni* and *C. coli* during treatment, but when treatment ended, resumed shedding a similar amount of the organisms as the control group that did not receive treatment. No Ery^r mutants were found in the treatment or control group in these experiments. Effects of long-term exposure to tylosin are examined by two experiments one which chickens were inoculated with *C. jejuni* at 3 days of age and one at 17 days of age. Treatment groups in each experiment were given feed containing tylosin at a subtherapeutic dose used for growth promotion (50 mg/kg) and control groups were provided unmedicated feed. Both experiments showed an initial reduction in shedding of *C. jejuni* in the medicated group; however, by day 31 and 17 in the two experiments respectively, Ery^r mutants were observed in chickens receiving medicated feed. No Ery^r mutants were observed in the control group in either experiment. Concludes that *C. jejuni* and *C. coli* have low rates of spontaneous mutation to Ery^r when therapeutic dosing is used but extended use of a macrolide drug as a growth promoter resulted in the emergence of Ery^r *C. jejuni* under laboratory conditions. However, the results presented here may not be used to predict development of antibiotic resistance on poultry farms as many factors may differ between the laboratory and poultry farm setting.

Antimicrobial resistance of old and recent *Staphylococcus aureus* isolates from poultry: First detection of livestock-associated methicillin-resistant strain ST398. M. Nemati, K. Hermans, U. Lipinska, O. Denis, A. Deplano, M. Struelens, L.A. Devriese, F. Pasmans, and F. Haesebrouck. *Antimicrobial Agents and Chemotherapy*, 2008. Oct: 3817-3819.

Summary: Compares the resistance profiles of *Staphylococcus aureus* isolates collected from chickens in the 1970s with profiles from healthy chickens in 2006. Finds that resistant levels to eight of the drugs tested were significantly greater in the 2006 samples.

Food animal transport: A potential source of community exposures to health hazards from industrial farming (CAFOs). A.M. Rule, S.L. Evans, and E.K. Silbergeld. *Journal of Infection and Public Health*, 2008. 1(1): 33-39.

Summary: Compares air samples collected while cars with bacterial-collection equipment were driven behind poultry transport vehicles with background samples taken during normal driving conditions. Twenty-five percent of samples collected while following poultry transport vehicles were resistant at least one antimicrobial, while all background samples were susceptible. Suggests that open-air poultry transport vehicles may play a role in spreading resistant bacteria that originated from the administration of antimicrobials to food animals.

Relationships between multidrug-resistant *Salmonella enterica* Serovar Schwarzengrund and both broiler chickens and retail chicken meats in Japan. T. Asai, K. Murakami, M. Ozawa, R. Koike, and H. Ishikawa. *Japanese Journal of Infectious Diseases*, 2009. 62: 198-200.

Summary: A *Salmonella* strain that causes invasive salmonellosis in humans was isolated from broiler chickens and retail chicken meats in Japan. Numerous isolates showed multidrug resistance.

Fate of antimicrobial-resistant *Enterococci* and *Staphylococci* and resistance determinants in stored poultry litter. J.P. Graham, S.L. Evans, L.B. Price, and E.K. Silbergeld. *Environmental Research*, 2009. 109: 682-689.

Summary: Studies the storage of poultry litter and the stability of bacteria and resistance genes during storage. Finds that over a 120-day period, typical storage practices of poultry litter are not sufficient for eliminating drug-resistant *Enterococci* and *Staphylococci*, which may then be delivered to the environment by land application, aerosolization or water contamination during runoff.

Antibiotic-resistant *Enterococci* and *Staphylococci* isolated from flies collected near confined poultry feeding operations. J.P. Graham, L.B. Price, S.L. Evans, T.K. Graczyk, and E.K. Silbergeld. *Science of the Total Environment*, 2009. 407(8): 2701-2710.

Summary: Investigators collected poultry litter and trapped flies around poultry farms to determine the extent of bacteria present and their resistance-gene profile. Results suggest that flies around poultry operations harbor resistant bacteria in their digestive tracts and exterior surfaces. This could result in human exposure to resistant bacteria that arise from antimicrobial use on poultry farms. Highlights the persistence of resistant genes in the environment and the pool of resistance associated with the use of antibiotics in feed additives.

***Salmonella Heidelberg* Ceftiofur-related resistance in human and retail chicken isolates.** Public Health Agency of Canada. 2009.

Summary: In response to public health concerns about the rise of resistance in isolates of *Salmonella* and *E. coli* to ceftiofur, all broiler chicken hatcheries in Québec voluntarily stopped using ceftiofur in February 2005. This publication reports a decrease in the number of ceftiofur-resistant isolates in both chicken and human *S. heidelberg* isolates and in chicken *Escherichia coli* following the voluntary withdrawal of ceftiofur in hatching and day-old chicks in Québec.

Antibiotic resistance of *Escherichia Coli* isolated from poultry and poultry environment of Bangladesh. M.A. Akond, S.M.R. Hassan, S. Alam, and M. Shirin. *American Journal of Environmental Sciences*, 2009. 5 (1): 47-52.

Summary: A study of *E. coli* isolated from poultry sources in Bangladesh. Resistance was high to many antibiotics including: penicillin, streptomycin, kanamycin, ampicillin and erythromycin. Resistance was not seen to gentamicin. The authors state that the widespread use of antibiotics has led to resistance development that can be transmitted to human pathogens; they suggest that excess use or abuse of antibiotics should be reduced or stopped to ensure public safety.

Ceftiofur resistance in *Salmonella enterica* Serovar Heidelberg from chicken meat and humans, Canada. L. Dutil, R. Irwin, R. Finley, L. King Ng, B. Avery, P. Boerlin, A. Bourgault, L. Cole, D.

Daignault, A. Desruisseau, W. Demczuk, L. Hoang, G.B. Horsman, J. Ismail, F. Jamieson, A. Maki, A. Pacagnella, and D.R. Pillai. *Emerging Infectious Diseases*, 2010. 16(1): 48-54.

Summary: Studies *Salmonella* Heidelberg, a frequently reported cause of infections in North America with sources linked to consumption of poultry, eggs or egg-containing products. Compares resistance rates of *Salmonella* Heidelberg isolates collected from retail chicken to ceftiofur, a third-generation cephalosporin, with rates of human infections that also were resistant to ceftiofur during a period from 2003 to 2008. During this time frame ceftiofur was removed from extralabel use in chicken hatcheries in Québec, resulting in a dramatic decrease in ceftiofur resistance in *Salmonella* Heidelberg and *E. coli* in retail chicken. A similar decrease is shown in resistant human infections of *Salmonella* Heidelberg. Suggests that managing ceftiofur use at the hatchery level may control resistance rates to extended-spectrum cephalosporins. A partial reintroduction of ceftiofur use in hatcheries in 2007 caused a rise in ceftiofur resistance in *E. coli*, but at lower levels than those seen in 2003 to 2004.

Veterinary pharmaceuticals and antibiotic resistance of *Escherichia coli* isolates in poultry litter from commercial farms and controlled feeding trials. V. Furtula, E.G. Farrell, F. Diarrassouba, H. Rempel, J. Pritchard, and M.S. Diarra. *Poultry Science*, 2010. 89:180-188.

Summary: This study found that there were antimicrobial residues in broiler litter from both a controlled environment, where chickens were fed a diet of feed with additives of bacitracin, chlortetracycline, monensin, narasin, nicarbazin, penicillin, salinomycin and virginiamycin and from commercial farms where the same feed additives were also used. Antimicrobials are not fully absorbed by animals in some cases and will be excreted into the litter leaving a residue of antibiotics that may then be applied to soil for crop fertilization. If application occurs, soil microbes will be subjected to these antibiotic pressures and may develop resistance themselves. There is also evidence for plants to uptake antimicrobial agents and can become a source of exposure to such compounds. *E. coli* isolates were collected from poultry litter from commercial farms and were found to be resistant to at least seven different antibiotics. Isolates from commercial farms showed a higher rate of resistance possibly due to the frequent use of feeds that are available with multiple antibiotics incorporated causing increased resistance. Resistance to such antibiotics as trimethoprim-sulfamethoxazole from isolates collected on commercial farms is of concern as this is a leading treatment of urinary tract infections.

Prevalence and distribution of *Salmonella* in organic and conventional broiler poultry farms. W.Q. Alali, S. Thakur, R.D. Berghaus, M.P. Martin, and W.A. Gebreyes. *Foodborne Pathogens and Disease*. 2010. 7(11): 1363-1371.

Summary: Studies the prevalence of *Salmonella* and antimicrobial resistance on one company's USDA-certified organic broiler chicken operations and conventional broiler operations in North Carolina. Samples from fecal floor droppings, the feed hopper, feed lines, house main water line, and in-house drinking nipples were taken from three organic barns and four conventional barns. *Salmonella* was present in 13 of 300 samples (4 percent) taken from organic operations and 115 of 400 samples (29 percent) from conventional operations. Conventional operations demonstrated 11.9 times the prevalence odds of *Salmonella* in fecal samples as compared to organic operations. The prevalence odds ratio for *Salmonella* in feed samples from conventional vs. organic farms was 7.2. Approximately, 25 percent of isolates from organic operations and 1.7 percent of isolates from conventional operations were susceptible to all antimicrobial agents tested. Additionally, 41 percent (5/12) of isolates from organic operations and 62 percent (36/58) of isolates from

conventional operations were resistant to two or more antimicrobial agents. The study demonstrates that within one poultry company in North Carolina, the prevalence of *Salmonella* and antibiotic-resistant *Salmonella* was greater on conventional operations as compared to organic operations. However, as antibiotic resistance was found in both operations this may signal circulation of organisms within a company's farms.

Dutch patients, retail chicken meat and poultry share the same ESBL genes, plasmids and strains.

M.A. Leverstein-van Hall, C.M. Dierikx, J. Cohen Stuart, G.M. Voets, M.P. van den Munckhof, A. van Essen-Zandbergen, T. Platteel, A.C. Fluit, N. van de Sande-Bruinsma, J. Scharinga, M.J.M. Bonten, and D.J. Mevius. *Clinical Microbiology and Infection*. 2011, 17(6):873-880.

Summary: An increase in infections caused by Gram-negative bacteria producing extended spectrum beta-lactamases (ESBL) has been observed globally. In The Netherlands, there is low human use of antibiotics but higher levels of use in poultry production. This study examined the distribution of ESBL genes, plasmids, and strain genotypes in *Escherichia coli* found in retail chicken in 2006, in poultry in 2010, and determined the distribution of isolates from Dutch patients with "poultry associated" (PA) ESBL genes, plasmids, and strains in 2009. Of 98 samples from chicken retail meat, 94 percent contained at least one isolate thought to be positive for ESBL. Of 409 ESBL-positive *E. coli* isolates from humans, 35 percent contained ESBL genes and 19 percent had ESBL genes located on plasmids that were indistinguishable from those found in poultry isolates. The most common genes found in human isolates, *bla*_{CTX-M-1} and *bla*_{TEM-52}, were also the most common genes found in poultry and retail chicken meat and 39 percent of ESBL-producing *E. coli* found in retail meat belonged to genotypes also found in humans. Study results suggest transmission of ESBL-producing *E. coli* between poultry and humans, potentially through contact with retail chicken; however, due to study limitations, further research is required.

RETAIL PRODUCTS

How industrial food animal production affects the food supply.

An evaluation of methods to assess the effect of antimicrobial residues on the human gut flora. D. Corpet. *Veterinary Microbiology*, 1993. 35(3-4):199-212.

Summary: Reviews the effects of antimicrobial residues on the human gut flora and concludes that “most resistant enterobacteria in the human gut of untreated people come from bacterial contamination of raw foods.” This assumption stems from a study previously completed by the author in which a sterile diet was given to seven healthy volunteers with an outcome of reduced antibiotic-resistant bacteria in stools.

Quinoline-resistant *Campylobacter jejuni* infections in Minnesota, 1992–1998. K.E. Smith, J.M. Besser, C.W. Hedberg, F.T. Leano, J.B. Bender, J.H. Wickland, B.P. Johnson, K.A. Moore, and M.T. Osterholm. *New England Journal of Medicine*, 1999. 340(20):1525-1532.

Summary: Reports that ciprofloxacin-resistant *C. jejuni* was isolated from 14 percent of 91 domestic chicken products obtained from retail markets in 1997. The number of quinolone-resistant infections acquired domestically has increased, largely because of the acquisition of resistant strains from poultry. Resulting infections may require additional antimicrobial therapy, as fluoroquinolones such as ciprofloxacin are commonly prescribed for diarrheal illnesses caused by *Campylobacter jejuni*.

Isolation of antimicrobial-resistant *Escherichia coli* from retail meats purchased in Greater Washington, DC, USA. C.M. Schroeder, D.G. White, B. Ge, Y. Zhang, P.F. McDermott, S. Ayers, S. Zhao, and J. Meng. *International Journal of Food Microbiology*, 2003. 85: 197-202.

Summary: Retail meat samples were collected and analyzed from the DC area for presence of *E. coli*. Data on resistance to 11 antimicrobials are given with a large portion showing resistance to such antibiotics as tetracycline (59 percent), sulfamethoxazole (45 percent), streptomycin (44 percent), ampicillin (35 percent) and gentamicin (12 percent). The authors conclude that their findings suggest retail meats may often be contaminated with resistant *E. coli*.

The incidence of antimicrobial-resistant *Salmonella* spp. on freshly processed poultry from US Midwestern processing plants C.M. Logue, J.S. Sherwood, P.A. Olah, L.M. Elijah, and M.R. Dockter. *Journal of Applied Microbiology*, 2003. 94: 16-24

Summary: A study to determine the occurrence of antimicrobial-resistant *Salmonella* spp. on processed turkey at poultry plants in the Midwestern U.S. Samples (surface swabs from carcasses: pre- and post chill and chill water from tanks) were taken from two plants at monthly intervals for one year. Overall incidence of *Salmonella* was around 16.7 percent, with a greater percentage of the pathogen observed on carcasses both pre- and post-chill, with post-chill showing decreased occurrence compared to pre-chill. *Salmonella* from the study had varying levels of antimicrobial resistance. The most common resistance was seen to tetracycline, streptomycin, sulfamethoxazole and ampicillin. Chlorination of chill water is thought to cause this reduction in contamination; however, the authors state that infections would be difficult to treat in the future if chlorine resistance is a factor in promoting selection of bacteria that have other resistance mechanisms.

Concurrent quantitation of total *Campylobacter* and total ciprofloxacin-resistant *Campylobacter* loads in rinses from retail raw chicken carcasses from 2001 to 2003 by direct plating at 42 degrees Celsius. R. Nannapaneni, R. Story, K.C. Wiggins, and M.G. Johnson. *Applied and Environmental Microbiology*, 2005. 71(8): 4510-4515.

Summary: Analyzes the total amount of *Campylobacter* present in retail chicken as well as in ciprofloxacin-resistant isolates. Finds that ciprofloxacin-resistant *Campylobacter* persisted throughout the two-and-a-half-year study, showing a reservoir of resistance in the U.S. food market.

Sulfamethazine uptake by plants from a manure-amended soil. H. Dolliver, K. Kumar, and S. Gupta. *Journal of Environmental Quality*, 2007. 36:1224-1230.

Summary: Studies the uptake of sulfamethazine, an antibiotic extensively used in animal agriculture for therapeutic and subtherapeutic purposes, in corn, lettuce and potatoes when manure-amended soil is used as the growing medium. Following 45 days of growth, all plants tested were contaminated with the antibiotic in varying concentrations.

Antimicrobial drug-resistant *Escherichia coli* from humans and poultry products, Minnesota and Wisconsin, 2002–2004. J.R. Johnson, M.R. Sannes, C. Croy, B. Johnston, C. Clabots, M.A. Kuskowski, J. Bender, K.E. Smith, P.L. Winokur, and E.A. Belongia. *Emerging Infectious Diseases*, 2007, 13(6): 838-846.

Summary: Studies susceptible and resistant *E. coli* collected from hospital patients, healthy vegetarians and poultry that were raised conventionally and without antibiotics. Suggests that many resistant human isolates may originate from poultry. Isolates from healthy vegetarians also follow this pattern, suggesting that avoidance of poultry consumption does not decrease the possibility of carrying drug-resistant *E. coli* from poultry.

The isolation of antibiotic-resistant *Salmonella* from retail ground meats. D.G. White, S. Zhao, R. Sudler, S. Ayers, S. Friedman, S. Chen, P.F. McDermott, S. McDermott, D.D. Wagner, and J. Meng. *New England Journal of Medicine*, 2007. 345(16):1147-1154.

Summary: Researchers tested *Salmonella* from samples of ground chicken, pork, beef and turkey purchased at three supermarkets in the Washington, DC, area. Of 200 samples, 41 (20 percent) contained *Salmonella*. Eighty-four percent of those were resistant to at least one antibiotic and 53 percent were resistant to at least three antibiotics. Sixteen percent were resistant to ceftriaxone, the drug of choice for treating salmonellosis in children.

Antimicrobial-resistant and extraintestinal pathogenic *Escherichia coli* in retail foods. J.R. Johnson, M.A. Kuskowski, K. Smith, T.T. O'Bryan, and S. Tatini. *Journal of Infectious Diseases*. 2005. 191:1040-1049.

Summary: Presents results from a two-year survey of the presence of antimicrobial-resistant *Escherichia coli*, and specifically, extraintestinal pathogenic *E. coli* (ExPEC), in a sampling of foods. To determine differences between retail markets and food types, samples of meat and other foods were systematically taken on a weekly basis from a range of retail markets based on a pre-determined schedule. Approximately 24 percent (396/1648) of samples were positive for *E. coli* with proportions varying by food type (miscellaneous foods: 9 percent; pork: 69 percent; poultry: 92 percent). Among beef and pork being ground was a risk factor for the presence of *E. coli* while natural-store source was associated with a reduction in the presence of the bacteria and

antimicrobial resistance. Antibiotic-free labeling was identified as a risk factor for contamination. ExPEC was found in 4 percent of miscellaneous food, 19 percent of pork, and 46 percent of poultry samples and resistance to at least one antibiotic was present in 27, 85, and 94 percent, respectively. Four of the ExPEC positive isolates from food closely resembled positive isolates from humans. Concludes that retail foods are often contaminated with antibiotic-resistant *E. coli* and ExPEC *E. coli* is also present. Food may serve as an important vehicle for the transmission of antibiotic resistant ExPEC bacteria.

Contamination of retail foods, particularly turkey, from community markets (Minnesota, 1999-2000) with antimicrobial-resistant and extraintestinal pathogenic *Escherichia coli*. J.R. Johnson, P. Delavari, T.T. O'Bryan, K.E. Smith, and S. Tatini. *Foodborne Pathogens and Disease*. 2005. 2(1):38-49.

Summary: Provides results from a one-year retail market survey of the prevalence of antimicrobial-resistant *Escherichia coli* in a range of retail foods. Food products were purchased systematically from 16 retail markets, including large economy and luxury chains, small economy chains, locally owned cooperatives, and farmer's markets (only during the summer). Sixteen percent (35/222) of vegetables sampled were positive for *E. coli*, as well as 5 percent (4/74) of fruit items, 100 percent (10/10) beef, (3/3) pork, (28/28) turkey products, and 89 percent (8/9) chicken products. Ten extraintestinal pathogenic *E. coli* (ExPEC) positive samples containing a range of virulence genes were found in turkey products that differed by type, store, and purchase date. ExPEC isolates were missing several virulence genes commonly found in human clinical *E. coli* isolates; however, four of the ExPEC isolates had virulence profiles, phylogenetic backgrounds, and O antigens that resembled clonal groups associated with human infection. Susceptibility testing for 12 antimicrobial agents demonstrated that resistance to tetracycline and sulfisoxazole was most common, followed by resistance to ampicillin, cefazolin, and gentamicin. No resistance to nitrofurantoin or ciprofloxacin was identified. Resistance was more common in meat products than other products and isolates resistant to more than 4 drugs were recovered from one beef item and 29 percent of turkey items. Suggests meat is more frequently contaminated with *E. coli* and meat-source and produce-source *E. coli* differs in virulence, phylogenetic background, and antimicrobial resistance, and therefore in public health implications. Additionally, turkey may be an important source of human exposure to resistant and potentially pathogenic *E. coli* including ExPEC.

Resistance in bacteria of the food chain: Epidemiology and control strategies. F.M. Aarestrup, H.C. Wegener, and P. Collignon. *Expert Reviews*, 2008. 6(5): 733-750.

Summary: Reviews bacterial resistance due to the use of antimicrobials in food animals and their transferability to humans in the form of pathogens. States that limiting the selective pressure in food animal production, especially those antibiotics that are critically important to human health, will help control the emergence of resistant bacteria most efficiently.

Molecular analysis of *Escherichia coli* from retail meats (2002–2004) from the United States National Antimicrobial Resistance Monitoring System. J.R. Johnson, J.S. McCabe, D.G. White, B. Johnston, M.A. Kuskowski, and P. McDermott. *Clinical Infectious Diseases*, 2009. 49: 195-201.

Summary: Researchers screened 287 *E. coli* isolates collected by the National Antimicrobial Resistance Monitoring System (NARMS) for virulence-associated genes. Resistant and susceptible strains differed minimally based on the assessed virulence factors; however, the four meat types screened showed a great variance as chicken and turkey isolates had consistently

higher virulence scores than beef and pork samples. These results support the hypothesis that antimicrobial-resistant *E. coli* in retail meats emerge from a host species-specific lineage due to the direct effect of selection pressure from use of antimicrobials or as part of the organisms' adaptations to their respective hosts.

Transient intestinal carriage after ingestion of antibiotic-resistant *Enterococcus faecium* from chicken and pork. T.L. Sorensen, M. Blom, D.L. Monnet, N. Frimodt-Moller, R.L. Poulsen, and F. Espersen. *New England Journal of Medicine*, 2009. 345(16): 1161-1166.

Summary: Reports on a study designed to test the ability of *Enterococci* from various meat sources to have sustained viability in the human intestine. Twelve volunteers ingested a suspension of *Enterococci* that originated from either a pig or chicken source that was resistant to at least one antibiotic. None of the 12 volunteers was colonized with resistant *Enterococci* at the onset of the experiment; however, eight of the 12 had antibiotic-resistant *Enterococci* isolated at six days following ingestion, and one had resistant *Enterococci* at 14 days' post ingestion. Concludes that ingestion of resistant *Enterococci* of animal origin leads to detectable concentrations of the same resistant strain in stools for up to 14 days.

Isolation and characterization of Methicillin-resistant *Staphylococcus aureus* strains from Louisiana retail meats. S. Pu, F. Han, and B. Ge. *Applied and Environmental Microbiology*. 2009. 75(1): 265-267.

Summary: Examines the presence of *Staphylococcus aureus* and methicillin-resistant *S. aureus* (MRSA) in raw pork and beef products purchased from retail grocery stores consisting of seven supermarket chains in Baton Rouge, LA. Out of 90 pork samples, 41 were positive for *S. aureus* and 5 of those were found to be MRSA providing a prevalence of MRSA in pork of 6 percent. For beef products, 6/30 samples were positive for *S. aureus* and among those 1 was found to be MRSA for a prevalence of MRSA in beef products of 3 percent. Two of the six MRSA-positive pork samples contained the Pantone-Valentine Leukocidin gene, which is considered the main virulence factor associated with skin and soft tissue infections.

Methicillin-resistant *Staphylococcus aureus* in food products: Cause for concern or complacency? J. A. J. W. Kluytmans. *Clinical Microbiology and Infection*, 2010. 16(1): 11-15.

Summary: A review on an emerging sequence type of MRSA ST398, which has been isolated from various food animals. A recent study in the U.S. observed a contamination rate of 39.2 percent for *S. aureus* on retail meats and in that group 5 percent was MRSA. Studies abroad have shown rates of MRSA contaminating retail meats as high as 11.9 percent. The author suggests that even though ST398 does not appear to spread easily among humans this assumption needs to be confirmed in well-designed studies. The spread of ST398 from animals to humans needs to be monitored as the potential threat from the retail food reservoir has widespread potential implications on human health.

Multidrug-resistant *Salmonella* isolates from retail chicken meat compared with human clinical isolates. N.M. M'ikanatha, C.H. Sandt, A.R. Localio, D. Tewari, S.C. Rankin, J.M. Whichard, S.F. Altekruze, E. Lautenbach, J.P. Folster, A. Russo, T.M. Chiller, S.M. Reynolds, and P.F. McDermott. *Foodborne Pathogens and Disease*, 2010. 7:8 929-934.

Summary: Salmonella isolates from retail chicken were collected in central Pennsylvania from 2006-2007. Overall prevalence rates of Salmonella were 22.2 percent for a combination of open-air market samples, pre-packaged, organic and raised antibiotic free. Prevalence rates were not significantly different between these groups. These isolates were characterized by pulsed-field gel electrophoresis (PFGE) and compared to PulseNet data collected up to 2008. One collected poultry isolate matched directly to a human isolate that was acquired from a 17-year-old Philadelphia resident. The two isolates were collected within five months from each other and poultry consumption was listed as a possible risk factor suggesting that disease was likely caused from contaminated poultry.

Characterization of toxin genes and antimicrobial susceptibility of *Staphylococcus aureus* isolates from Louisiana retail meats. S. Pu, F. Wang, and B. Ge. *Foodborne Pathogens and Disease*, 2010. 1-8.

Summary: This study focuses on *Staphylococcus aureus* collected from retail meats in Louisiana. Isolates characterized included 152 *S. aureus* isolates, with 22 MRSA, for prevalence of 9 enterotoxin and 4 exotoxin genes as well as susceptibility profiles to 20 antimicrobials. Researchers found 85 percent were positive for at least one enterotoxin gene and 66 percent contained 2 to 4 enterotoxin genes. Staphylococcal enterotoxins cause approximately 185,000 food poisoning illnesses annually and occur upon ingestion of the carrier strains with symptoms such as vomiting, nausea, abdominal cramps and diarrhea. Antibiotic resistance was seen most often to penicillin (71 percent), ampicillin (68 percent) and tetracycline (67 percent). Erythromycin resistance (30 percent) and clindamycin resistance (18 percent) were also observed. Multidrug resistance was common in MRSA isolates and those samples from pork. The authors conclude that stringent food safety practice is needed for people who handle raw meat products to prevent food borne infections due to *S. aureus* contamination.

Antimicrobial susceptibility of *Staphylococcus aureus* from retail ground meats. A. Kelman, Y. Soong, N. Dupuy, D. Shafer, W. Richbourg, K. Johnson, T. Brown, E. Kestler, Y. Li, J. Zheng, P. McDermott, and J. Meng. *Journal of Food Protection*, 2011. 24(10). 1625-1629.

Summary: Retail ground beef, pork, and turkey were purchased at grocery stores in the Washington, D.C. area between March and August 2008. Reports 56 percent of 196 ground turkey samples, 28 percent of 198 ground beef samples, and 12 percent of 300 ground pork samples were positive for *Staphylococcus aureus*. Information on resistance to 22 antimicrobial agents is provided. All *S. aureus* from ground turkey, 89 percent from ground pork, and 11 percent from ground beef were resistant to at least one antimicrobial agent. More than half of the *S. aureus* found was resistant to tetracycline. One sample was positive for methicillin-resistant *S. aureus* (MRSA). Concludes that *S. aureus* in retail ground meats is not uncommon and many of these bacteria are resistant to at least one antimicrobial agent.

Multidrug-resistant *Staphylococcus aureus* in U.S. meat and poultry. A.E. Waters, T. Contente-Cuomo, J. Buchhagen, C.M. Liu, L. Watson, K. Pearce, J.T. Foster, J. Bowers, E.M. Driebe, D.M. Engelthaler, P.S. Keim, and L.B. Price. *Clinical Infectious Diseases*, 2011. 52(10). 1227-30.

Summary: Examines the presence and antibiotic-resistance patterns of *Staphylococcus aureus* in meat and poultry products in the U.S. Shows that 77 percent of 26 turkey products, 42 percent of 26 pork products, 41 percent of chicken products, and 37 percent of 38 beef products sampled were positive for *S. aureus*. An evaluation of resistance to 17 antimicrobials is provided and shows that 96 percent of the *S. aureus* positive-samples demonstrated resistance to at least one

antimicrobial agent. Additionally, 52 percent of all *S. aureus* were classified as multidrug resistant, meaning resistant to 3 or more antimicrobial classes. Samples showed resistance to several clinically important antibiotics including ciprofloxacin, quinupristin/dalfopristin, clindamycin, erythromycin, oxacillin, and daptomycin.

Identification and antimicrobial resistance of extraintestinal pathogenic *Escherichia coli* from retail meats. X. Xia, J. Meng, S. Zhao, S. Bodeis-Jones, S.A. Gaines, S.L. Ayers, and P.E. McDermott. *Journal of Food Protection*. 2011. 74(1). 38-44.

Summary: Extraintestinal *Escherichia coli* (ExPEC) is a type of *E. coli* that can cause infections outside of the intestines including urinary tract infections, meningitis, and wound infections. This study determines the prevalence of ExPEC in retail meat purchased in Georgia, Maryland, Oregon, and Tennessee in 2006. Reports 16 percent of 1,275 *E. coli*-positive samples were found to be ExPEC. The authors provide information on the distribution of serotypes and virulence genes found among positive samples. Concludes that many of the strains of ExPEC found in meat samples were of strains that can cause disease in humans and 80 percent were shown to be resistant to at least one antimicrobial agent, many of which are clinically relevant.

Prevalence of *Staphylococcus aureus* and methicillin-resistant *Staphylococcus aureus* (MRSA) on retail meat in Iowa. B.M. Hanson, A.E. Dressler, A.L. Harper, R.P. Scheibel, S.E. Wardyn, L.K. Roberts, J.S. Kroeger, and T.C. Smith. *Journal of Infection and Public Health*. 2011. 4: 169-174.

Summary: Investigates the prevalence and types of *Staphylococcus aureus* present on retail pork, chicken, beef, and turkey products purchased at urban and rural stores across Iowa. Turkey demonstrated the highest prevalence of *S. aureus* with the bacteria found in 7/36 samples (19 percent). Turkey was followed by pork with 10/55 samples (18 percent), chicken with 8/45 samples (18 percent), and beef with 2/29 samples (7 percent) positive for *S. aureus*. Methicillin-resistant *S. aureus* (MRSA) was present in 2/55 pork samples (4 percent) only. Based on molecular methods, 7/27 *S. aureus* positive isolates (26 percent) were identified as ST398 and 4/27 were ST9, both livestock associated types. The two ST8 isolates also carried the Pantone-Valentine Leukocidin virulence gene. Based on antibiotic susceptibility testing 5/27 isolates (19 percent) were susceptible to all antibiotics, 21/27 (78 percent) were resistant to penicillin, 18/27 (67 percent) were resistant to tetracycline, 6/27 were resistant to clindamycin (22 percent), 4/27 (15 percent) were resistant to erythromycin, and 2/27 (7 percent) were resistant to oxacillin. This study was focused on the potential for human contact with *S. aureus* and MRSA through contact with retail meat. For this reason, laboratory methods focused on the presence of these bacteria on the surface of retail meat and did not use more destructive laboratory methods that measure the prevalence of the bacteria anywhere in the meat samples as many other studies have done. Authors conclude that although this study showed lower prevalence of *S. aureus* and MRSA in retail meats than other studies, it shows that *S. aureus* and MRSA are present on the surface of retail meat and may be a source of human exposure.

MRSA

The impacts of methicillin-resistant Staphylococcus aureus (MRSA) on certain areas across the country, veterinarians, health care employees and farmers.

An outbreak of community-acquired foodborne illness caused by Methicillin-resistant *Staphylococcus aureus*. T.F. Jones, M.E. Kellum, S.S. Porter, M. Bell, and W. Schaffner. *Emerging Infectious Diseases*. 2002. 8(1): 82-84.

Summary: Describes an outbreak of acute gastroenteritis caused by methicillin-resistant *Staphylococcus aureus* (MRSA). Three family members consumed coleslaw and barbeque pork purchased from a market-delicatessen and after consuming the products experienced nausea, vomiting, and stomach cramps. Two of the three individuals sought treatment at a hospital. Indistinguishable MRSA isolates were found in a nasal swab from one asymptomatic food preparer at the market-delicatessen, a sample from the coleslaw, and stool cultures from the three patients. This is the first report of gastroenteritis due to MRSA however, *S. aureus* is a common cause of gastrointestinal illness in the US and therefore MRSA may play a larger role than previously thought.

Methicillin-resistant *Staphylococcus aureus* in pig farming. A. Voss, F. Loeffen, J. Bakker, C. Klaassen, and M. Wulf. *Emerging Infectious Diseases*, 2005. 11(12): 1965-1966.

Summary: Examines cases of MRSA colonization resulting from farmers' contact with pigs, how it moved through their families and was transmitted between a hospital patient and nurse. Reports that the frequency of MRSA among the group of regional pig farmers is more than 760 times higher than that among the general Dutch population.

Methicillin-resistant *Staphylococcus aureus* colonization in veterinary personnel. B.A. Hanselman, S.A. Kruth, J. Rousseau, D.E. Low, B.A. Willey, A. McGeer, and J.S. Weese. *Emerging Infectious Diseases*, 2006. 12(12): 1933-1938.

Summary: Reports a comprehensive evaluation of veterinary personnel for carriage of MRSA. Samples were taken from participants who resided in 19 different countries and rates of colonization were determined. Of the volunteers, 6.5 percent were positive for MRSA; those working with larger animals showed higher carriage rates (15.6 percent).

Hospitalizations and deaths caused by methicillin-resistant *Staphylococcus aureus*, United States, 1999–2005. E. Klein, D.L. Smith, and R. Laxminarayan. *Emerging Infectious Diseases*, 2007. 13(12): 1840-1846.

Summary: Reports on trends in MRSA infections between 1999 and 2005. The estimated rise in hospitalizations due to *Staphylococcus aureus* infections during this time was 62 percent, while the rate of MRSA infections more than doubled.

Invasive methicillin-resistant *Staphylococcus aureus* infections in the United States. R.M. Klevens, M.A. Morrison, J. Nadle, S. Petit, K. Gershman, S. Ray, L.H. Harisson, R. Lynfield, G. Dumyati, J.M. Townes, A.S. Craig, E.R. Zell, G.E. Fosheim, L.K. McDougal, R.B. Carey, and S.K. Fridkin. *Journal of the American Medical Association*, 2007. 285(15):1763-1771.

Summary: Finds that MRSA affects certain populations disproportionately, particularly African Americans. After researching invasive MRSA infections reported in hospitals in eight U.S. cities

and the state of Connecticut, the authors estimate that in 2005 more than 94,000 cases of such infections occurred, 18,650 of which were fatal.

Emergence of methicillin-resistant *Staphylococcus aureus* of animal origin in humans. I. van Loo, X. Huijsdens, E. Tuemersma, A. de Neeling, N. van de Sande-Bruinsma, D. Beaujean, A. Voss, and J. Kluytmans. *Emerging Infectious Diseases*, 2007. 13(12):1834-1839.

Summary: Reports that a new type of MRSA from an animal reservoir (pigs in the Netherlands) has recently entered the human population and is now responsible for greater than 20 percent of all MRSA in the Netherlands. As most nontypable MRSA isolates are resistant to doxycycline, the spread of MRSA may be facilitated by the abundant use of tetracyclines in pig and cattle farming.

Methicillin-resistant *Staphylococcus aureus* ST398 in humans and animals, Central Europe. W. Witte, B. Strommenger, C. Stanek, and C. Cuny. *Emerging Infectious Diseases*, 2007. 13(2): 255-258.

Summary: Studies recent human colonization by MRSA ST398, which in previous years had not been seen in humans. Animal-to-human transmission may occur with this strain; for example, a dog being treated for a wound infection transmitted ST398 to the staff of the veterinary practice where the dog was treated. Concludes that “MRSA exhibiting ST398 may colonize and cause infections in humans and in certain animal species such as dogs, horses and pigs.”

Methicillin-resistant *Staphylococcus aureus* colonization in pigs and pig farmers. T. Khanna, R. Friendship, D. Dewey, and J.S. Weese. *Veterinary Microbiology*, 2008. 128:298-303.

Summary: This study, the first of MRSA and pig farms in Canada, found that the prevalence of MRSA colonization on pig farms was 45 percent; prevalence in pig farmers was 20 percent. Humans residing on farms where pigs were free of MRSA also tested negative for MRSA. The authors note another study in which MRSA was identified in food products intended for human consumption, but none originated in pigs. This study adds support to the hypothesis that MRSA can be transmitted between pigs and humans.

Pigs as source of methicillin-resistant *Staphylococcus aureus* CC398 infections in humans, Denmark. H.C. Lewis, K. Molbak, C. Reese, F.M. Aarestrup, M. Selchau, M. Sorum, and R.L. Skov. *Emerging Infectious Diseases*, 2008. 14(9): 1383-1389.

Summary: Provides evidence that persons exposed to animals on farms in Denmark, particularly pig farms, have an increased chance of being colonized or infected with MRSA CC398.

Methicillin-resistant and -susceptible *Staphylococcus aureus* sequence type 398 in pigs and humans. A. van Belkum, D.C. Melles, J.K. Peeters, W.B. van Leeuwen, E. van Duijkeren, X.W. Huijsdens, E. Spalburg, A.J. de Neeling, and H.A. Verbrugh. *Emerging Infectious Diseases*, 2008. 14(3):479-483.

Summary: Reports that MRSA ST398, primarily a pathogen of pigs, appears to be quite virulent and can cause bacteremia in humans. States that if MRSA ST398 obtains this pathogenicity, care should be taken not to introduce this strain into humans.

Transmission of methicillin-resistant *Staphylococcus aureus* strains between different kinds of pig farms. E. van Duijkeren, R. Ikawaty, M.J. Broekhuizen-Stins, M.D. Jansen, E.C. Spalburg, A.J. de Neeling, J.G. Allaart, A. van Nes, J.A. Wagenaar, and A.C. Fluit. *Veterinary Microbiology*, 2008. 126: 383-389.

Summary: MRSA strains were found in 23 percent of the farms tested. States that the use of standard antimicrobials “seems to be a risk factor for finding MRSA-positive pigs on a farm. Pig farms on which the pigs were treated with antimicrobials as group medication had a higher risk of being MRSA positive, whereas farms on which antimicrobials were used restrictively had a much lower chance of being MRSA positive.”

Increase in a Dutch hospital of methicillin-resistant *Staphylococcus aureus* related to animal farming. M.M.L. van Rijen, P.H. Van Keulen, and J.A. Kluytmans. *Clinical Infectious Diseases*, 2008. 16:261-263.

Summary: Reports on a study 2002–2006 in the Netherlands involving hospital patients who had MRSA. Patients exposed to pigs or veal calves were shown to be at higher risk for MRSA as there was an emergence of nontypable MRSA during this time. Nontypable MRSA is assumed to stem from pigs and calves.

Methicillin-resistant *Staphylococcus aureus* (MRSA) strain ST398 is present in Midwestern U.S. swine and swine workers. T.C. Smith, M.J. Male, A.L. Harper, J.S. Kroeger, G.P. Tinkler, E.D. Moritz, A.W. Capuano, L.A. Herwaldt, and D.J. Diekema. *PLoS ONE*, 2009. 4(1): e4258.

Summary: Investigates MRSA in the Midwestern U.S. Samples were taken from swine and production workers in two commercial operations. MRSA prevalence was 49 percent in swine and 45 percent in workers. Results show that MRSA is common in swine production in the U.S. and that these animals could be harboring the bacterium.

Methicillin-resistant *Staphylococcus aureus*: A new zoonotic agent? B. Springer, U. Orendi, P. Much, G. Hoger, W. Ruppitsch, K. Krziwanek, S. Metz-Gercek, and H. Mittermayer. *The Middle European Journal of Medicine*, 2009. 121: 86-90.

Summary: Discusses changes in MRSA over the past decade. Once known almost completely as a hospital pathogen, MRSA is now emerging in the community in persons without hospital-related risk factors. Recent evidence also has shown a link between livestock colonization and MRSA infections in persons working with these animals. Identifies three potential transmission routes of MRSA: from animal origin into the population; human-to-human contact from farm workers to the community; via food or by environmental contamination.

Methicillin-resistant *Staphylococcus aureus* (MRSA) strain ST398 is present in Midwestern swine and swine workers. T.C. Smith, M.J. Male, A.L. Harper, J.S. Kroeger, G.P. Tinkler, E.D. Mortiz, A.W. Capuano, L.A. Herwaldt, and D.J. Diekema. *PLoS One*. 2009. 4(1).

Summary: Establishes evidence of methicillin-resistant *Staphylococcus aureus* (MRSA) ST398 in swine and humans in the U.S. Swine and humans from two conventional swine production systems in Iowa and Illinois participated. MRSA was found in swine and humans working in close contact with the swine on one of the swine operations, the other operation had no MRSA-positive swine or employees. On the operation where MRSA was isolated, an inverse association between MRSA colonization of the nostrils of swine and age was observed with swine 15 weeks old or younger having higher odds of MRSA colonization than adult swine. Of 14 participating employees in close contact with swine, 9 were found to carry MRSA. Risk factors including age, gender, use of tobacco products, use of antimicrobial agents in the prior 3 months, having MRSA in the prior 12 months, and duration of employment were not associated with MRSA colonization. All MRSA isolated was confirmed to be ST398 and negative for the Pantom-

Valentine Leukocidin virulence gene. All MRSA isolates were resistant to penicillin, oxacillin, and tetracycline.

Methicillin resistant *Staphylococcus aureus* ST398 in veal calf farming: Human MRSA carriage related with animal antimicrobial usage and farm hygiene. H. Graveland, J.A. Wagenaar, H. Heesterbeek, D. Mevius, E. van Duijkeren, and D. Heederik. *PLoS One*, 2010. 5(6): 1-6.

Summary: Studies MRSA ST398 carriage in veal calves, farmers, their family members and employees. A large sampling size of veal calf farms in the Netherlands was selected at random to be screened for ST398. All participants were given a questionnaire to fill in describing their contact and role on the farm as well as how farm operations were conducted. Samples from both humans and veal calves were cultured and categorized using molecular techniques. The data presented show that direct associations between human and animal carriage of MRSA ST398 exist and that carriage was shown to increase in calves as antibiotic use on the farm increased. Duration of contact to veal calves showed a highly elevated risk of MRSA ST398 carriage in humans and a decrease in MRSA was seen in farms with better hygiene practices (ie cleaning of stables before new calves were brought on the farm). Disinfection was applied in less than 20 percent of the farms in the study and was not associated with prevalence of MRSA carriage in calves. Overall the prevalence of MRSA was 15.9 percent in participants who lived or worked on veal calf farms, which is far greater than the general population carriage rate in the Netherlands estimated to be below 1 percent.

ANTIMICROBIAL-RESISTANT INFECTIONS

Infections arising with implications toward the use of antimicrobials in food animal production.

Molecular epidemiology of antibiotic resistance in *Salmonella* from animals and human beings in the United States. T.F. O'Brien, J.D. Hopkins, E.S. Gilleece, A.A. Medeiros, R.L. Kent, B.O. Blackburn, M.B. Holmes, J.P. Reardon, J.M. Vergeront, W.L. Schell, E. Christenson, M.L. Bisset, and E.V. Morse. *New England Journal of Medicine* 1982. 307:8 1-6.

Summary: Restriction-endonuclease digestion (a method by which DNA is cleaved at specific locations, then these digestion patterns are observed by gel-electrophoresis to compare similarity between samples) was used to analyze plasmids from *Salmonella* isolates collected from animals and humans. Results show that identical or nearly identical antibiotic resistance gene carrying plasmids are found between human and animal strains of *Salmonella*. Plasmid fragments were found not to cluster by human or animal grouping, rather they are intermixed suggesting that the strains developed in one host then were spread to the other, as both share similar characteristics. The infected patients observed had no prior farm exposure, this leaves meat or food preparation as a plausible route for infection, and also points toward the spread of disease from animals to humans.

Widespread distribution of urinary tract infections caused by a multidrug-resistant *Escherichia coli* clonal group. A.R. Manges, J.R. Johnson, B. Foxman, T.T. O'Bryan, K.E. Fullerton, and L.W. Riley. *New England Journal of Medicine*, 2001. 345(14): 1007-1013.

Summary: Studies urinary tract infections (UTIs) in the U.S. caused by *E. coli* resistant to trimethoprim-sulfamethoxazole as well as other antibiotics. Concludes that UTIs may be caused by contaminated foods, as the outbreaks appear to follow a pattern similar to that of *E. coli* O157 as they spread throughout a community.

De Novo acquisition of resistance to three antibiotics by *Escherichia coli*. M.A. van der Horst, J.M. Schuurmans, M.C. Smid, B.B. Koenders, and B.H. ter Kuile. *Microbial Drug Resistance*. 2001, 17(2): 141-147.

Summary: Explores *de novo* acquisition of resistance by *Escherichia coli* bacteria after varying levels of exposure to three antibiotics – amoxicillin, enrofloxacin, and tetracycline. *E. coli* samples were exposed to sub-lethal concentrations of each antibiotic. If normal growth occurred, colonies were selected and re-plated and exposed to a concentration of the antibiotic at a level doubling the previous exposure. *E. coli* grown in the absence of the amoxicillin had a minimum inhibitory concentration (MIC) that varied between 4 and 8 µg/ml. When grown with 1.25 or 2.5 µg/ml, the MIC reached a maximum of 32 µg/ml, and when grown for another 15 days without antibiotics, the MIC returned to control levels. However, colonies exposed to increasing amounts of amoxicillin reached a maximum MIC of 512 µg/ml and maintained a MIC of 256 µg/ml when grown without antibiotics for another 15 days demonstrating the ability to maintain resistance to amoxicillin. *E. coli* grown in the presence of tetracycline had increasing MIC levels with those exposed to increasing levels of tetracycline demonstrating a maximum MIC of 32 µg/ml. However, all MICs returned to control level when tetracycline was removed. Resistance among *E. coli* exposed to levels of enrofloxacin below the susceptible MIC built quickly, increasing by a factor of up to 100. The increased MIC remained after 15 days of growth in the absence of enrofloxacin. Growth rate of *E. coli* was also examined for each scenario. Differences in resistance and growth rate between the three antibiotics may be due to differences in resistance

mechanisms. Moderate amounts of cross-resistance to all three antibiotics were also detected. Concludes that exposure to low levels of antibiotics poses a risk and resistance selected for in the agricultural sector will transfer to the human sector over time and this transfer is already occurring.

Fluoroquinolone resistance in *Campylobacter* absent from isolates, Australia. L. Unicomb, J. Ferguson, T.V. Riley, and P. Collignon. *Emerging Infectious Diseases*, 2003. 9(11): 1482-1483.

Summary: Reports on a study of fluoroquinolone resistance in New South Wales, Australia, over a three-year period. Only 12 *Campylobacter* isolates were found to be resistant to fluoroquinolones. Ten of these were related to travel; travel status of the other two is unknown. Australia has never allowed the use of fluoroquinolones in food animal production, a policy that may have impacts on human health for countries with fluoroquinolone-resistant cases of *Campylobacter*.

Antibiotic selection pressure and resistance in *Streptococcus pneumoniae* and *Streptococcus pyogenes*. W.C. Albrich, D.L. Monnet, and S. Harbarth. *Emerging Infectious Diseases*, 2004. 10:3 514-517.

Summary: Study designed to assess emerging antibiotic resistance in *Streptococcus pneumoniae* and *Streptococcus pyogenes* in 20 countries by comparing resistance rates to the dose of antibiotics given to outpatients. The authors find that resistance to penicillin and macrolides in these species in outpatients is directly correlated with increased antibiotic selection pressure on a national level and suggest that these findings lend support to policymakers and professional organizations to discourage the overuse of antibiotics in the community.

Possible animal origin of human-associated, multidrug-resistant, uropathogenic *Escherichia coli*. M. Ramchandi, A.R. Manges, C. DeRoy, S.P. Smith, J.R. Johnson, and L.W. Riley. *Clinical Infectious Disease*, 2005. 40: 251-257.

Summary: Reviews a collection of 495 animal and environmental *E. coli* isolates collected by the Gastroenteric Disease Center and determines that 26 percent had indistinguishable characteristics from human isolates. Concludes that the data suggest that drug-resistant, uropathogenic, human-associated *E. coli* strains may have an animal origin and that drug-resistant urinary tract infections in humans could be derived from foodborne illnesses.

The rising influx of multidrug-resistant gram-negative bacilli into a tertiary care hospital. A.E. Pop-Vicas, E. M. and C. D'Agata. *Clinical Infectious Diseases*, 2005. 40: 1792-8.

Summary: Studies multi-drug resistant (MDR) *E. coli*, *Klebsiella* species, *Enterobacter cloacae*, and *Pseudomonas aeruginosa* isolates from patients harboring these bacteria upon entering a hospital in Israel (within 48 hours of admittance). Finds that between 1998 and 2003 the prevalence of MDR isolates of all listed species increased significantly except *Pseudomonas aeruginosa*. Of the 464 isolates collected 12 percent, 35 percent and 53 percent were resistant to 5, 4 and 3 antimicrobial groups, respectively.

Analysis of a uropathogenic *Escherichia coli* clonal group by multilocus sequence typing. S.Y. Tartof, O.D. Solberg, A.R. Manges, and L.W. Riley. *Journal of Clinical Microbiology*, 2005. 5860-5864.

Summary: Forty-five strains of uropathogenic *E. coli* were analyzed by a molecular typing method called multi-locus sequence typing (MLST). The research shows that one sample from a

cow grouped with other human isolates collected from urinary tract infections and bacteremia . This shows that *E. coli* from animals may be a cause of UTIs and bacteremia in humans.

Low-level fluoroquinolone resistance among *Campylobacter jejuni* isolates in Australia. L. Unicomb, J. Ferguson, R.J. Stafford, R. Ashbolt, M.D. Kirk, N.G. Becker, M.S. Patel, G.G. Gilbert, M. Valcanis, and L. Mickan. *Clinical Infectious Diseases*, 2006. 42: 1368-1374.

Summary: Reports a study from five Australian states between 2001 and 2002 that looked into the susceptibility patterns of *Campylobacter jejuni*. Only two percent of isolates from locally acquired infections were resistant to ciprofloxacin, likely reflecting Australia's policy of restricting the use of fluoroquinolones in food production animals.

First report of the emergence of CTX-M-type extended spectrum β -Lactamases (ESBLs) as the predominant ESBL isolated in a U.S. health care system. J. S. Lewis II, M. Herrera, B. Wickes, J.E. Patterson, and J. H. Jorgensen. *Antimicrobial Agents and Chemotherapy*, 2007. 51(11): 4015-4021.

Summary: A study on Extended spectrum beta-lactamases (ESBLs) from a clinic in San Antonio Texas. ESBLs are enzymes produced by bacteria that can negate the use of certain newer antibiotics used in treating infections of *E. coli* or similar bacteria. The new ESBL enzyme described here as seen for the first time in the U.S. is located on a plasmid (a mobile element of DNA) within the bacterium. As plasmids can be readily passed between bacteria this new finding could have a wide health impact. The authors state "a worrisome trend with the emergence of these enzymes has been an increasing frequency of *E. coli* isolates from outpatients or patients hospitalized for a very brief period, suggesting community acquisition of these strains."

Endemic and epidemic lineages of *Escherichia coli* that cause urinary tract infections. A.R. Manges, H. Tabor, P. Tellis, C. Vincent, and P. Tellier. *Emerging Infectious Diseases*, 2008. 14(10): 1575-1583.

Summary: Studies urinary tract infections (UTI) in women from California and Canada. Relatedness of the infections is apparent, as the profiles of the bacteria are identical. Multidrug-resistant *E. coli* outbreaks are the causative agent of the disease, and how these bacteria are acquired by the gut is unclear; however, the authors cite a previous study indicating that poultry and pork consumption may lead to the development of drug-resistant UTIs.

Temporal changes in the prevalence of community-acquired antimicrobial-resistant urinary tract infection affected by *Escherichia coli* clonal group composition. S.P. Smith, A.R. Manges, and L.W. Riley. *Clinical Infectious Diseases*, 2008. 46: 689-695.

Summary: Reports on urinary tract infections (UTIs) from 1,667 patients over the course of 6 years. *E. coli* specimens were collected and characterized by molecular methods. Twelve percent of human UTI samples collected were found to be from a specific group, which from previous work has been shown to include *E. coli* that had been collected from food animals or retail poultry products. The collected human isolates were also shown to be resistant to trimethoprim-sulfamethoxazole at a rate of 49 percent. The authors suggest that contaminated food products may be a source of drug resistant UTIs.

Hospital and societal costs of antimicrobial-resistant infections in a Chicago teaching hospital: Implications for antibiotic stewardship. R.R. Roberts, B. Hota, I. Ahmad, R.D. Scott II, S.D. Foster, F. Abbasi, S. Schabowski, L.M. Kampe, G.G. Ciavarella, M. Supino, J. Naples, R. Cordell, S.B. Levy, and R.A. Weinstein. *Clinical Infectious Diseases*, 2009. 49: 1175-1184.

Summary: Assesses the attributable cost associated with antimicrobial-resistant infections (ARI). Data were collected from patients admitted to a public teaching hospital in the Chicago area in the year 2000. Of 188 patients that met eligibility of ARI, the attributable medical cost of treatment ranged from \$18,588 to \$29,069 per patient. Social costs were \$10.7 to \$15.0 million, and total cost corrected to 2008 dollars was \$13.35 million.

World health organization ranking of antimicrobials according to their importance in human medicine: A critical step for developing risk management strategies for the use of antimicrobials in food production animals. P. Collignon, J.H. Powers, T.M. Chiller, A. Aidara-Kane, and F.M.Aarestrup. *Clinical Infectious Diseases*. 2009. 49: 132-41.

Summary: Presents information regarding antimicrobial agents used to treat disease in humans. Ranks antimicrobial agents and classes as critically important, highly important, and important to human health and reviews changes in the rankings made in 2007. Antimicrobial rankings are based on two main criteria: 1) the agent or class is the sole therapy or one of few alternatives to treat serious human disease; 2) the antimicrobial agent or class is used to treat diseases caused by organisms that may be transmitted via nonhuman sources or diseases caused by organisms that may acquire resistance genes from nonhuman sources. Within the list of critically important antimicrobial agents a committee designated quinolones, third- and fourth-generation cephalosporins and macrolides as the classes for which immediate action should be taken to reduce unnecessary use in food animals and humans.

Antibiotic management of Staphylococcus aureus infections in US children's hospitals, 1999-2008. J.C. Herigon, A.L. Hersh, J.S. Gerber, T.E. Zaoutis, and J.G. Newland. *Pediatrics*, 2010. 125:e1294-e1300.

Summary: This study focuses on the rates of *S. aureus* infection in children under the age of 18 from 1999 until 2008. The authors also track the trend of antimicrobial use during that time period. Finds that *S. aureus* infections increased by a rate of more than 10-fold over the course of 10 years from 14.8 per 1000 admissions in 1999 to 35.7 per 1000 admissions in 2008. MRSA infections also increased 10-fold during the same period from 2.0 cases per 1000 admissions in 1999 to 20.7 cases per 1000 admissions in 2008. Increased use of clindamycin was most substantial (21 percent in 1999 to 63 percent in 2008) while linezolid also saw increased use between 2001 (when it became available) and 2008. The substantial use of clindamycin may lead to greater resistance and ineffective treatment of future *S. aureus* infections. The authors note that continuous monitoring of local *S. aureus* susceptibility patterns is needed as treatment patterns have changed over the past decade due to the emergence of community-associated MRSA.

Genetic identity of aminoglycoside-resistance genes in Escherichia coli isolates from human and animal sources. P. Ho, R.C. Wong, S.W. Lo, K. Chow, S.S. Wong, and T. Que. *Journal of Medical Microbiology*, 2010. 59: 702-707.

Summary: A study in Hong Kong on *E. coli* isolates collected from food producing animals and humans (most from urinary tract infections). The group looked at the aminoglycoside (gentamicin) resistance characteristics of these isolates and found the main source of resistance was due to a gene called aacC2. The aacC2 gene was shown to exist in both human and animal *E. coli*. This suggests that gentamicin resistance in human *E. coli* urinary isolates can be attributed to resistance genes that are present in food-producing animals. Study illustrates when humans are

in close contact with contaminated food, there is a risk of picking up antibiotic resistant *E. coli* that could lead to UTIs that are more difficult to treat.

Food reservoir for *Escherichia coli* causing urinary tract infections. C. Vincent, P. Boerlin, D. Daignault, C.M. Dozois, L. Dutil, C. Galanakis, R.J. Reid-Smith, P-P. Tellier, P.A. Tellis, K. Ziebell, and A.R. Manges. *Emerging Infectious Diseases*, 2010. 16(1):88-95.

Summary: The design of this study was to see if a food reservoir exists for *E. coli* that may cause urinary tract infections. Sampling for *E. coli* was completed between 2005 and 2007 comprising clinical UTI samples, retail meats and restaurant/ready-to-eat foods. Upon comparison of these collected isolates by molecular methods the author's report that *E. coli* identified from retail chicken and other food sources are identical or nearly the same as those from human UTIs.

***Escherichia coli* isolates from broiler chicken meat, broiler chickens, pork, and pigs share phylogroups and antimicrobial resistance with community-dwelling humans and patients with urinary tract infection.** L. Jakobsen, A. Kurbasic, L. Skjøt-Rasmussen, K. Ejrnaes, L.J. Porsbo, K. Pedersen, L.B. Jensen, H.D. Emborg, Y. Agero, K.E.P. Olsen, F.M. Aarestrup, N.Frimodt-Moller, and A.M. Hammerum. *Foodborne Pathogens and Disease*, 2010. 7:5 537-547

Summary: Study in Denmark comparing phylogroups and antimicrobial resistance patterns among *E. coli* collected from UTI patients, community-dwelling humans, broiler chicken meat, broiler chickens, pork meat and pigs. The study finds that the presence of specific *E. coli* phylogroups, that are the main cause of UTIs, exist in samples of animal origin. The collected animal isolates also have similar antibiotic-resistance patterns as those collected from UTI patients and community-dwelling humans suggesting that food animals and meat may be a source of such isolates to humans. Samples from humans were predominantly B2, which is the most commonly found type in UTIs, most likely due to virulence factors associated with the group allowing colonization in humans. Only 6 to 15 percent of isolates of animal origin were found to fall into group B2, but these may still pose a risk for acquiring uropathogenic *E. coli*.

Risk factors for antibiotic-resistant *Escherichia coli* carriage in young children in Peru: Community –based cross sectional prevalence study. H.D. Kalter, R.H. Gilman, L.H. Moulton, A.R. Cullotta, L. Cabrera, and B. Velapatiño . *American Journal of Tropical Medicine and Hygiene*, 2010.

Summary: A study in Peru focused on the carriage and antimicrobial resistance characteristics of *E. coli* from children and their living environments that included animals, market chickens and mothers' hands. The study concludes that data from surveys and sampling for *E. coli* in several regions of Peru shows there were four main factors contributing to antibiotic-resistant *E. coli* carriage in children. Use of antibiotics by anyone in the household increased risk. Residing in an area where a larger proportion of households served home-raised chicken seemed to protect against resistant bacteria, however residing in an area that served market-raised chicken was a risk factor for carriage of resistant *E. coli*. Also, living in environments contaminated with a higher level of multi-drug resistant bacteria were found to increase the risk of carriage of resistant *E. coli*.

Emergence of a new antibiotic resistance mechanism in India, Pakistan, and the UK: A molecular, biological, and epidemiological study. K.K. Kumarasamy, M.A. Toleman, T.R. Walsh, J. Bagaria, F. Butt, R. Balakrishnan, U. Chaudhary, M. Doumith, C.G., Giske, S. Irfan, P. Krishnan, A.V. Kumar, S.

Maharjan, S. Mushtaq, T. Noorie, D.L. Paterson, A. Pearson, C. Perry, R. Pike, B. Rao, U. Ray, J.B. Sarma, M. Sharma, E. Sheridan, M.A. Thirunarayan, J. Turton, S. Upadhyay, M. Warner, W. Welfare, D.M. Livermore, and N. Woodford. *The Lancet*, 2010. 10(9): 597-602.

Summary: Presents information about antibiotic resistance in gram-negative bacteria. Fewer antibiotic agents exist to treat gram-negative bacterial infections and therefore resistance to antibiotics among these bacteria may be especially concerning. Antibiotic-resistance is shared by bacteria mainly through the transfer of plasmids (a mobile piece of DNA). After the discovery of CTX-M-15 extended-spectrum β -lactamase (ESBL), which confers resistance to cephalosporins, was reported in India, a greater reliance on carbapenems to treat infection has been observed. The article presents molecular and epidemiologic information on New Delhi metallo- β -lactamase 1 (NDM-1) positive Enterobacteriaceae in India, Pakistan, and the United Kingdom in 2008 and 2009. NDM-1 is a recently identified carbapenem resistance gene which has been shown to readily transfer between bacteria in vitro. Of 3,521 Enterobacteriaceae recovered in Chennai in 2009, 141 were carbapenem resistant, and 44 were positive for NDM-1 (1 percent of all isolates). In Haryana, 47 of 198 isolates were carbapenem resistant and 26 of those were positive for NDM-1. In addition, 32 NDM-1 positive isolates from 73 carbapenem-resistant isolates were identified in the United Kingdom. An additional 73 isolates from other locations in India and Pakistan were determined to be NDM-1 positive. All 44 isolates from Chennai were resistant to all β -lactam antibiotics, fluoroquinolones, and aminoglycosides (except two susceptible to gentamicin) and came from community acquired urinary tract infections, pneumonia, and blood-stream infections. Isolates from the UK were mostly from samples from urine, blood, burn or wound, sputum, central line tip, and throat swabs. All UK NDM-1 positive isolates were resistant to imipenem and ertapenem. A majority of NDM-1 positive isolates from the UK and Chennai carried the NDM-1 gene on plasmids that could be transferred between bacteria. Isolates from Haryana were not transferable. The authors conclude Enterobacteriaceae with the NDM-1 enzyme are resistant to many antibiotic classes and may present a great deal of difficulty in treating Gram-negative infections with available drugs.

Association between antimicrobial resistance in *Escherichia coli* isolates from food animals and blood stream isolates from humans in Europe: An ecological study. A.R. Vieria, P. Collignon, F.M. Aarestrup, S.A. McEwen, R.S. Hendriksen, T. Hald, and H.C. Wegener. *Foodborne Pathogens and Disease*. 2011. Sep 1. [Epub ahead of print].

Summary: Estimates the correlation between antimicrobial resistance of *Escherichia coli* from human blood stream infections and from *E. coli* isolated from poultry, pigs, and cattle in eleven European countries. Reports strong correlations between antimicrobial resistance found in *E. coli* from human blood stream infections and poultry and human blood stream infections and pigs. States that in addition to contributions from human use of antimicrobials, a proportion of resistant *E. coli* implicated in human blood infections may be from food animal sources.

Selection of resistant bacteria at very low antibiotic concentrations. E. Gullberg, S. Cao, O.G. Berg, C. Ilbäck, L. Sandegren, D. Hughes, and D.I. Anderson. *PLoS Pathogens*. 2011. 7(7). E1002158.

Summary: Demonstrates through experiments with *Escherichia coli* and *Salmonella enterica* that the presence of levels of tetracycline and streptomycin several-hundred fold lower than previously considered important, may lead to selection for resistant strains of these bacteria over susceptible strains. The authors state that very low levels of antibiotics, which can be found in the

environment or in the human body when undergoing treatment, are important in the development and maintenance of antibiotic resistance in pathogens.

Antibiotic resistance in foodborne pathogens: Evidence of the need for a risk management strategy. (CSPI White Paper). C. Smith DeWaal, C. Roberts, and C. Catella. Center for Science in the Public Interest, January 25, 2011.

Summary: Provides general background concerning the use of antibiotics in food animal-production and documents foodborne outbreaks due to antibiotic resistant bacteria. Focuses on documenting outbreaks due to antibiotic-resistant bacteria as antibiotic resistance is not required to be reported to other agencies in the U.S. Notes an increase in outbreaks due to antibiotic-resistant pathogens over the past several decades, although it is not clear whether this is due to a true increase or an increase in testing and reporting. A total of 35 outbreaks due to antibiotic-resistant pathogens were documented between 1973 and 2009. Source of the outbreaks were dairy products (34 percent), ground beef (26 percent), and poultry, pork, produce, and seafood (6 percent each), as well as eggs and multi-ingredient food (3 percent each). Outbreaks lead to 19,897 sick, 3,061 hospitalizations, and 26 deaths. *Salmonella typhimurium* was the most common pathogen implicated in outbreaks. Other *Salmonella* species were the causative agent in outbreaks as well as *Escherichia coli*, *Campylobacter jejuni*, and *Staphylococcus aureus*. These bacteria demonstrated a range of resistance patterns that included resistance to a total of 14 antibiotics including seven classified as “critically important” to human medicine by the World Health Organization.

For additional information on the Pew Campaign on Human Health and Industrial Farming, or on any of these studies, please contact Laura Rogers, project director, Pew Health Group, at (202) 552-2018 or lrogers@pewtrusts.org.