INSTITUTE FOR AGRICULTURE AND TRADE POLICY

Healthy Food Action

No Time to Lose

147 STUDIES SUPPORTING PUBLIC HEALTH ACTION TO REDUCE ANTIBIOTIC OVERUSE IN FOOD ANIMALS*

1. Antibiotic resistance and why it occurs

Health professionals in training learn the basics of antibiotic resistance summarized, for example, in Levy (1999, 2002),[1,2] Tenover (2006)[3] and Courvalin (2006).[4]

As science evolves, it has become clear that resistance is fundamentally an ecological problem, spread via bacteria mutating or acquiring resistance from environmental reservoirs and then thriving.[5,6,7,8,9] Promiscuous bacteria can swap genetic "determinants" of resistance with other, often unrelated bacteria in the environment, between and within hospitals and communities, on farms, and in the guts of animals and humans.[7,10,11] Mothers may pass antibiotic-resistant bacteria from their own gut into their children.[12]

To expend energy for resistance genes, bacteria must derive some advantage. That advantage is explained by the huge volume of antibiotics used, and the selection pressure it exerts.[13] Pharmaceutical sales data (2010) collected by the Food and Drug Administration (FDA) indicate more than 80 percent of U.S. antimicrobials, over 29 million pounds, are sold for use in animal agriculture;[14] 90 percent are added to water or animal feed not to treat sick animals but to promote growth, feed efficiency, or to control disease in otherwise healthy animals being raised in crowded or unhygienic conditions that promote disease.[15] Exposure to antibiotics changes the microbial ecology in the animal gut, as it does in humans.[16]

Selection for resistant bacteria is now known to occur at antibiotic concentrations hundreds of times lower than those previously thought significant;[17] the lower levels of antibiotics put into animal feed compared to injections for sick animals therefore offer little basis for complacency. New science suggests feed antibiotics also can spur the spread of resistance by promoting new genetic mutations, which can give rise to it,[18] as well as by promoting the transfer among gut bacteria of genes (including, potentially, antibiotic resistance genes) via phages.[19] Transformation from benign to dangerous, multidrug-resistant bacteria can happen quickly, since resistance to a dozen or more drugs often sits—physically linked—on the same strand of transferable DNA.[20]

2. Why should we care?

There are rising numbers of disease-causing bacteria for which few, if any, antibiotics exist that might be effective treatments, nor are such treatments being newly developed.[21]

KEEP ANTIBIOTICS WORKING — The Campaign to End Antibiotic Overuse

*Prepared, in part, from a bibliography by the Keep Antibiotics Working coalition, of which IATP is a founding member.

INSTITUTE FOR AGRICULTURE AND TRADE POLICY
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An estimated 900,000 antibiotic-resistant infections occur yearly, including 94,000 infections and 18,650 deaths from methicillin-resistant *Staphylococcus aureus* (MRSA) alone.[22,23] Ten-fold more MRSA infections afflict children in U.S. hospitals than in 1999.[24] Resistant infections generally cause more and longer hospitalizations—costing $18–29,000 per patient to treat—and more deaths.[25,26] Resistant infections cost $20 billion annually in direct treatment costs,[19] with an additional $35 billion or so in missed work or other costs to society.[23] More resistant infections mean more patients now receive antibiotics previously held in reserve that may be less potent or convenient, or inherently more toxic—like vancomycin.[27]

Ever-strengthening science—hundreds of studies to date—ties the spreading epidemic of resistant infections in humans to routine antibiotic use in food animals. This is a select summary of that science, across several critical strands of evidence. (Web links indicate freely available studies; PubMed.org abstracts indicate non-public studies.)

Medical experts and public health agencies therefore agree: Routine antibiotic use in food animal production likely worsens the epidemic of resistance and action must be taken to reduce it. [28,29,30,31]

3. Connecting animal agriculture and antibiotic resistance

- Aarestrup FM, Wegener HC, Collignon P. **Resistance in bacteria of the food chain: epidemiology and control strategies.** *Expert Rev Anti Infect Ther.* 2008;6(5):733-750.

  Our favorite review article of bacterial resistance due to antimicrobial use in food animals, and its transferability to humans.

- Collignon P. Antibiotic resistance in human Salmonella isolates are related to animal strains. *Proc Biol Sci.* 2012;279(1740):2922-2923. Available at http://rspb.royalsocietypublishing.org/content/279/1740/2922.long.

- Hammerum AM. **Enterococci of animal origin and their significance for public health.** *Clin Microbiol Infect.* 2012 Jul;18(7):619-25.

- Davis MF, Price LB, Liu CM, et al. **An ecological perspective on U.S. industrial poultry production: the role of anthropogenic ecosystems in the emergence of drug-resistant bacteria from agricultural environments.** *Curr Opin Microbiol.* 2011;14(3):244-250.

  Rampant use of antibiotics in industrial food animal production has led to both an increased pressure on microbial populations as well as alterations of the ecosystems where antibiotics and bacteria interact.

- Marshall BM, Levy SB. **Food animals and antimicrobials: impacts on human health.** *Clin Microbiol Rev.* 2011 Oct;24(4):718-33. doi: 10.1128/CMR.00002-11.

- Silbergeld EK, Graham J, Price LB. **Industrial food animal production, antimicrobial resistance, and human health.** *Annu Rev Public Health.* 2008;29:151-169.

  Reviews four reasons why agricultural antimicrobial use is a major driver of resistance globally: agriculture is the primary use of antimicrobials; much of agricultural use results in subtherapeutic exposures for bacteria; drugs of every important clinical class are utilized in agriculture; and humans are exposed to resistant pathogens via consumption of animal products, and via widespread release into the environment.

- Barza M. Potential mechanisms of increased disease in humans from antimicrobial resistance in food animals. *Clin Infect Dis.* 2002;34(Suppl 3):S123-125.

  Summarizes five mechanisms by which resistance may adversely affect human health—two of which directly relate to animal antibiotic use. Available at http://cid.oxfordjournals.org/content/34/Supplement_3/S123.full.

Additional studies

- Cogliani C, Goossens H, Greko C. Restricting antimicrobial use in food animals: lessons from Europe. *Microbe Magazine.* 2011;6(6):274-279.

  A review showing that nontherapeutic use of antibiotics in livestock results in greater selection pressure for resistance genes. Available at http://www.tufts.edu/med/apua/news/press_room_34_846139138.pdf.

- Love DC, Davis MF, Bassett A, et al. Dose imprecision and resistance: free-choice medicated feeds in industrial food animal production in the United States. *Environ Health Perspect.* 2011;119(3):279-283. Available at http://ehp03.niehs.nih.gov/article/info:doi/10.1289/ehp.1002625.

- Jackson CR, Lombard JE, Dargatz DA, et al. **Prevalence, species distribution and antimicrobial resistance of enterococci isolated from US dairy cattle.** *Lett Appl Microbiol.* 2011;52(1):41-48.

  Fecal enterococci isolated from 122 dairy cattle operations demonstrated widespread resistance, highest percentage to lincomycin (92.3%), flavomycin (71.9%) and tetracycline (24.5%).

- Diarra MS, Rempel H, Champagne J, et al. Distribution of antimicrobial resistance and virulence genes in Enterococcus spp. and characterization of isolates from broiler chickens. *Appl Environ Microbiol.* 2010;76(24):8033-8043.

  Sixty-nine enterococci isolated from nine commercial poultry farms were analyzed for antibiotic susceptibility. Multidrug resistance of public health significance was evident in *E. faecium* and *E. faecalis* isolates, most commonly of the phenotype Bac Ery Tyl Lin Str Gen Tet Cip. Available at http://aem.asm.org/content/76/24/8033.long.

- Kohanski MA, DePristo MA, Collins JJ. Sublethal antibiotic treatment leads to multidrug resistance via radical-induced mutagenesis. *Mol Cell.* 2010;37(3):311-320.

  Exposed to sublethal doses of antibiotics, such as are put into animal feed, cell production of radical oxygen species (ROS) occurred, leading to increased rate of mutation in *E. coli*. Such mutations potentially could confer resistance, including to antibiotics different from those being administered. Available at http://www.sciencedirect.com/science/article/pii/S1097276510000286.

- Haenni M, Saras E, Châtre P, et al. **vanA in *Enterococcus faecium, Enterococcus faecalis, and Enterococcus casseliflavus* detected in French cattle.** *Foodborne Pathog Dis.* 2009;6(9):1107-1111.

  This study proves *Enterococcus* bacteria in French cattle continued to acquire glycopeptide (VanA)-resistant genes a decade after the glycopeptide, avoparcin, was banned as a feed additive. Because French calves are recurrently exposed to antibiotics, it may signify glycopeptide resistance is reemerging due to co-selection via physical linkage of resistance genes for glycopeptide and other antibiotics.

- Lynne AM, Kaldhone P, David D, et al. **Characterization of antimicrobial resistance in *Salmonella enterica* serotype Heidelberg isolated from food animals.** *Foodborne Pathog Dis.* 2009;6(2):207-215.

  Seventy-two percent of 58 *S. enterica* serovar Heidelberg isolates from food animals displayed resistance, with 24 percent resistant to eight or more antimicrobial agents. Tetracycline resistance was the most commonly observed.

- Price LB, Lackey LG, Vailes R, et al. The persistence of fluoroquinolone-resistant *Campylobacter* in poultry production. *Environ Health Perspect.* 2007;115(7):1035-39.

  Indicates fluoroquinolone (FQ)-resistant *Campylobacter* may persist as contaminants of poultry products after on-farm FQ use has ceased. FDA's ban on FQ use in poultry may be insufficient to reduce FQ-res *Campylobacter* in poultry products. Available at http://ehp03.niehs.nih.gov/article/info:doi/10.1289/ehp.10050.

- Garcia-Migura L, Liebana E, Jensen LB, et al. **A longitudinal study to assess the persistence of vancomycin-resistant *Enterococcus faecium* (VREF) on an intensive broiler farm in the United Kingdom.** *FEMS Microbiol Lett.* 2007;275(2):319-325.

  Avoparcin, an antibiotic feed additive related to vancomycin, was used and then banned in Europe. Seven years post-ban, Van-res *E. faecium* persist in multiple broiler flocks from two UK production facilities, 99 percent of them resistant to at least five antibiotics.

- Gilchrist MJ, Greko C, Wallinga DB, et al. The potential role of concentrated animal feeding operations in infectious disease epidemics and antibiotic resistance. *Environ Health Perspect.* 2007;115(2):313-316. Available at http://ehp03.niehs.nih.gov/article/info:doi/10.1289/ehp.8837.

- Miranda JM, Guarddon M, Mondragon A, et al. **Antimicrobial resistance in *Enterococcus* spp. strains isolated from organic chicken, conventional chicken, and turkey meat: a comparative survey.** *J Food Prot.* 2007;7(4):1021-1024.

  Enterococcus bacteria from organic and conventional chicken and turkey meat in Spain were tested for resistance to eight different antibiotics. Bacteria counts were higher on organic chicken meat, but resistance and multidrug resistance was higher in isolates from conventional chicken or turkey meat than from organic chicken.

- Kieke AL, Borchardt MA, Kieke BA, et al. Use of streptogramin growth promoters in poultry and isolation of streptogramin-resistant *Enterococcus faecium* from humans. *J Infect Dis.* 2006;194(9):1200-1208.

  Examines virginiamycin use in poultry and its effect on cross-resistance to quinupristin-dalfopristin, another streptogramin intended for treating vancomycin-resistant *E. faecium* infections in humans. "[C]ontinued use of virginiamycin may increase the potential for streptogramin-resistant *E. faecium* infection in humans." Available at http://jid.oxfordjournals.org/content/194/9/1200.full.

- Angulo FJ, Nargund VN, Chiller TC. Evidence of an association between use of antimicrobial agents in food animals and antimicrobial resistance among bacteria isolated from humans and the human health consequences of such resistance. *J Vet Med B.* 2004;51:374-379.

  Veterinary review states "[A] review of outbreaks of *Salmonella* infections indicated that outbreaks caused by antimicrobial-resistant *Salmonella* were more likely to have a food animal source than outbreaks caused by antimicrobial-susceptible *Salmonella*." Available at http://www.colby.edu/biology/BI402B/Angulo%20et%20al%202004.pdf.

- Gupta A, Fontana J, Crowe C, et al. Emergence of multidrug-resistant *Salmonella enterica* serotype Newport infections resistant to expanded-spectrum cephalosporins in the United States. *J Infect Dis.* 2003;188(11):1707-1716.

  CDC investigation into a multi-state outbreak found exposure to a dairy farm or food contaminated from the farm was the major risk factor for acquiring multidrug-resistant *Salmonella* infection. Available at http://jid.oxfordjournals.org/content/188/11/1707.full.

- Swartz MN. Human diseases caused by foodborne pathogens of animal origin. *Clin Infect Dis.* 2002;34(Suppl 3):S111-S1122.

  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. Available at http://cid.oxfordjournals.org/content/34/Supplement_3/S111.full.

- Vellinga A, Van Loock F. The dioxin crisis as experiment to determine poultry-related *Campylobacter enteritis*. *Emerg Infect Dis.* 2002;8(1):19-22.

  Poultry was withdrawn in Belgium in June 1999 after a contaminant was found in feed. By using the ban as an epidemiologic tool, the rate of *Campylobacter* infections attributable to poultry was determined to be greater than 40 percent. Available at http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2730260.

- Engberg J, Aarestrup FM, Taylor DE, et al. Quinolone and macrolide resistance in *Campylobacter jejuni* and *C. coli*: resistance mechanisms and trends in human isolates. *Emerg Infect Dis.* 2001;7(1):24-34.

  Review of macrolide and quinolone resistance in *Campylobacter* strains and tracking of the resistance trends in human clinical isolates in relation to use of these agents in food animals. Good synopsis of when antibiotics were licensed in many countries (for food animals) with a bar graph depicting resistances in many countries. Available at http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2631682/.

- Aarestrup FM. **Occurrence, selection and spread of resistance to antimicrobial agents used for growth promotion for food animals in Denmark.** *APMIS Suppl.* 2000;101:1-48.

- van den Bogaard AE, Stobberingh EE. **Antibiotic usage in animals: impact on bacterial resistance and public health.** *Drugs.*1999;58(4):589-607.

  This review article finds that use of antimicrobial growth promoters greatly influences the prevalence of resistance in animal bacteria and poses a risk factor for emergence of antibiotic resistance in human pathogens. Resistance genes can be transferred from animal bacteria to human pathogens in the intestinal flora of humans.

Studies On Farms Comparing Animals Fed and Not Fed Antibiotics

- Mirzaagha P, Louie M, Sharma R, et al. Distribution and characterization of ampicillin- and tetracycline-resistant *Escherichia coli* from feedlot cattle fed subtherapeutic antimicrobials. *BMC Microbiology.* 2011;11:78.

  E. coli were isolated from cattle fed or not fed subtherapeutic levels of chlortetracycline, chlortetracycline and sulfamethazine (SMX), or virginiamycin over 9 months. Results: Administering chlortetracycline alone can lead to emergence of resistance to SMX, and to other antibiotics including ampicillin and chloramphenicol. Multidrug resistant strains were more frequently isolated from steers fed multiple, as opposed to single, antibiotics. Available at http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3103423/.

- Jackson CR, Lombard JE, Dargatz DA, et al. **Prevalence, species distribution and antimicrobial resistance of enterococci isolated from US dairy cattle.** *Lett Appl Microbiol.* 2011;52(1):41-48.

  Enterococci from 700+ fecal samples from 122 dairy cattle operations demonstrated widespread resistance, with the highest percentage of resistant isolates to lincomycin (92.3%), flavomycin (71.9%) and tetracycline (24.5%).

- Morley PS, Dargatz DA, Hyatt DR, et al. **Effects of restricted antimicrobial exposure on antimicrobial resistance in fecal *Escherichia coli* from feedlot cattle.** *Foodborne Pathog Dis.* 2011;8(1):87-98.

  Among *E. coli* collected from two feedlot cattle populations raised with and without antibiotics, no difference was found in resistance.

- Davis MA, Besser TE, Orfe LH, et al Genotypic-phenotypic discrepancies between antibiotic resistance characteristics of *Escherichia coli* isolates from calves in management settings with high and low antibiotic use. *Appl Environ Microbiol.* 2011 May;77(10):3293-9. Available at http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3126435/?tool=pubmed.

- Alexander TW, Inglis GD, Yanke LJ, et al. **Farm-to-fork characterization of *Escherichia coli* associated with feedlot cattle with a known history of antimicrobial use.** *Int J Food Microbiol.* 2010;31;137(1):40-8.

  Compared to control animals fed no antibiotics, prevalence of amp- and tet-resistant *E. coli* was three-fold and four-fold greater, respectively, in feces from cattle fed diets containing chlortetracycline plus sulfamethazine.

- Harvey R, Funk J, Wittum TE, et al. **A metagenomic approach for determining prevalence of tetracycline resistance genes in the fecal flora of conventionally raised feedlot steers and feedlot steers raised without antimicrobials.** *Am J Vet Res.* 2009 Feb;70(2):198-202.

  Comparing feedlot steers raised conventionally and without antibiotics, the prevalence of fecal samples with 11 tet-resistant genes was significantly higher in the former (35/61, or 57%) than in the latter (16/61, or 26%).

- Vieira AR, Houe H, Wegener HC, et al. **Association between tetracycline consumption and tetracycline resistance in *Escherichia coli* from healthy Danish slaughter pigs.** *Foodborne Pathog Dis.* 2009 Jan-Feb;6(1):99-109.

  Study demonstrated the longer the time since the last administration of tetracycline, the lower the likelihood of isolating a tet-resistant *E. coli* from a pig's intestinal tract.

- Ladely SR, Harrison MA, Fedorka-Cray PJ, et al. **Development of macrolide-resistant *Campylobacter* in broilers administered subtherapeutic or therapeutic concentrations of tylosin.** *J Food Prot.* 2007;70(8)1945-1951.

  Chickens fed subtherapeutic and therapeutic doses of tylosin tested positive for resistant bacteria, but no resistant strains were found among tylosin-free flocks. Increased tylosin resistance was associated with birds given subtherapeutic relative to therapeutic doses.

Pathogens Newly Tied to Food Animal Production – MRSA

- Price LB, Stegger M, Hasman H, et al. Staphylococcus aureus CC398: host adaptation and emergence of methicillin resistance in livestock. *MBio.* 2012;3(1):e00305-e00311.

  Whole genome sequence typing of 89 isolates from 19 countries suggests livestock-associated methicillin-resistant *Staphylococcus aureus* (MRSA) CC398 most likely originated as methicillin susceptible *S. aureus* in humans and jumped to livestock where it acquired tetracycline and methicillin resistance. Available at http://mbio.asm.org/content/3/1/e00305-11.long.

- Waters AE, Contente-Cuomo T, Buchhagen J, et al. Multidrug-resistant Staphylococcus aureus in US meat and poultry. *Clin Infect Dis.* 2011;52(10):1227-1230. Available at http://cid.oxfordjournals.org/content/52/10/1227.full.

Additional studies

- Bos ME, Graveland H, Portengen L, et al. **Livestock-associated MRSA prevalence in veal calf production is associated with farm hygiene, use of antimicrobials, and age of the calves.** *Prev Vet Med.* 2012;105(1-2):155-159.

  Reviewed factors associated with the high prevalence of livestock-associated MRSA in Dutch pork and veal production; herd treatment with antimicrobials appears to pose a risk.

- Broens EM, Espinosa-Gongora C, Graat EA, et al. Longitudinal study on transmission of MRSA CC398 within pig herds. *BMC Vet Res.* 2012;8(1):58.

  Longitudinal study of two Danish and four Dutch pig herds finds that livestock-associated MRSA CC398 is endemic and able to spread and persist in herds. Use of antimicrobials as well as the age of pigs is found to affect transmission rates. Available at http://www.biomedcentral.com/content/pdf/1746-6148-8-58.pdf.

- Cuny C, Friederich AW, Witte W. **Absence of livestock-associated methicillin-resistant *Staphylococcus aureus* clonal complex CC398 as a nasal colonizer of pigs raised in an alternative system.** *Appl Environ Microbiol.* 2012;78(4):1296-1297.

  Nasal swabs of 178 pigs and 89 humans working on 25 pig farms not using antibiotics failed to detect livestock-associated ST398 previously found in conventional farm settings.

- Kadlec K, Feßler AT, Hauschild T, et al. **Novel and uncommon antimicrobial resistance genes in livestock-associated methicillin-resistant *Staphylococcus aureus*.** *Clin Microbiol Infect.* 2012;18:745-755.

  Analysis of resistance genes among livestock-associated MRSA (LA-MRSA) isolates reveals most were located on multiresistance plasmids. Co-selection enables LA-MRSA to both receive and donate multiple antimicrobial resistance genes with other Gram-positive organisms.

- Köck R, Loth B, Köksal M, et al. **Persistence of nasal colonization with livestock-associated methicillin-resistant *Staphylococcus aureus* in pig farmers after holidays from pig exposure.** *Appl Environ Microbiol.* 2012;78(11):4046-4047.

  Among 35 pig farmers already colonized with LA-MRSA, colonization persisted among 59 percent even during periods of prolonged absence with the majority spending 7–14 days away from pig contact.

- Richter A, Sting R, Popp C, et al. Prevalence of types of methicillin-resistant *Staphylococcus aureus* in turkey flocks and personnel attending the animals. *Epidemiol Infect*. 2012;10:1-10.

  Among turkey farms in Germany, 18/20 (90%) flocks and 22/59 turkey workers (37.3%) tested positive for MRSA. Livestock-associated MRSA (CC 398) was detectable in most flocks. Available at http://journals.cambridge.org/action/displayAbstract?fromPage=online&aid=8488404.

- Weese JS, Hannon SJ, Booker CW, et al. **The prevalence of methicillin-resistant *Staphylococcus aureus* colonization in feedlot cattle.** *Zoonoses Public Health.* 2012;59(2):144-147.

  Screening in four feedlots in Alberta, Canada of 491 feedlot cattle shortly before slaughter failed to isolate any MRSA.

- Alt K, Fetsch A, Schroeter A, et al. Factors associated with the occurrence of MRSA CC398 in herds of fattening pigs in Germany. *BMC Vet Res.* 2011;7:69.

  Over half (152/290) of German finisher pig farms tested positive for MRSA. All isolates were resistant to tetracycline. Farm size was strongly correlated with risk of MRSA (OR 5.4). Available at http://www.biomedcentral.com/1746-6148/7/69.

- Cavaco LM, Hasman H, Aarestrup FM. Zinc resistance of *Staphylococcus aureus* of animal origin is strongly associated with methicillin resistance. *Vet Microbiol.* 2011;150(3-4):344-348.

  Among several hundred porcine MRSA CC398 isolates from Europe and Canada, zinc resistance was observed in 74 percent, nearly all coding for the czrC resistance gene. The study concludes zinc in animal feed may have contributed to the emergence of livestock-associated MRSA. Available at http://www.biomedcentral.com/1746-6148/7/69.

- García-Álvarez L, Holden MT, Lindsay H, et al. Methicillin-resistant *Staphylococcus aureus* with a novel *mecA* homologue in human and bovine populations in the UK and Denmark: a descriptive study. *Lancet Infect Dis.* 2011;11(8):595-603. Available at http://www.thelancet.com/journals/laninf/article/PIIS1473-3099%2811%2970126-8/fulltext.

- Graveland H, Duim B, van Duijkeren E, et al. **Livestock-associated methicillin-resistant *Staphylococcus aureus* in animals and humans.** *Int J Med Microbiol.* 2011;301(8):630-634.

  This review article summarizes information about livestock-associated MRSA in Europe, China and North America. It concludes that MRSA control in animals should include farm hygiene and reductions in antimicrobial use, both of which contribute to MRSA occurrence on farms.

- Kelman A, Soong YA, Dupuy N, et al. **Antimicrobial susceptibility of *Staphylococcus aureus* from retail ground meats.** *J Food Prot.* 2011;74(10):1625-1629.

  Among retail meats purchased in Washington, D.C. from March to August of 2008, 56 percent of 196 ground turkey samples, 28 percent of 198 ground beef samples and 12 percent of 300 ground pork samples tested positive for *S. aureus*. Concludes that *S. aureus* in retail ground meats is not uncommon, and 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. One sample was MRSA positive.

- Mendes RE, Smith TC, Deshpande L, et al. **Plasmid-borne vga(A)-encoding gene in methicillin-resistant *Staphylococcus aureus* ST398 recovered from swine and a swine farmer in the United States.** *Diagn Microbiol Infect Dis.* 2011;71(2):177-180.

  Reports on a new vga(A) found in livestock-associated MRSA in U.S. swine and swine farmers.

- Pu S, Wang F, Ge B. **Characterization of toxin genes and antimicrobial susceptibility of *Staphylococcus aureus* isolates from Louisiana retail meats.** *Foodborne Pathog Dis.* 2011;8(2):299-306.

  152 *S. aureus* isolates, including 22 MRSA, isolated from Louisiana retail meat, were analyzed for antimicrobial susceptibility, as well as the prevalence of enterotoxin and exotoxin genes.

- Golding GR, Bryden L, Levett PN, et al. Livestock-associated methicillin-resistant *Staphylococcus aureus* sequence type 398 in humans, Canada. *Emerg Infect Dis.* 2010;16(4):587-594.

  Of 3687 MRSA isolates from persons in two Canadian provinces, five were identified as livestock-associated MRSA. Available at http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3321955/.

- Graveland H, Wagenaar JA, Heesterbeek H, et al. Methicillin-resistant *Staphylococcus aureus* ST398 in veal calf farming: human MRSA carriage related with animal antimicrobial usage and farm hygiene. *PLoS One.* 2010;5(6):e10990.

  Human MRSA carriage in veal farmers is strongly associated with the number of MRSA-positive calves on the farm, and with intensity of animal contact. Farm hygiene appeared to lower MRSA prevalence among calves, while antibiotic use raised it. Available at http://www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0010990.

- Harper AL, Ferguson DD, Leedom Larson KR, et al. **An overview of livestock-associated MRSA in agriculture.** *J Agromedicine.* 2010;15(2):101-104.

  Summary of presentations at a 2009 Iowa conference elucidating the picture of livestock-associated MRSA in the American Midwest.

- Kluytmans JA. Methicillin-resistant *Staphylococcus aureus* in food products: cause for concern or complacency. *Clin Microbiol Infect.* 2010;16(1):11-15.

  A review of an emerging sequence type of MRSA ST398, which has been isolated from various food animals observes that in a recent U.S. study, *S. aureus* contamination was found in 39.2 percent of retail meats and in that group 5 percent was MRSA. 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. Available at http://onlinelibrary.wiley.com/doi/10.1111/j.1469-0691.2009.03110.x/full.

- Weese JS, Reid-Smith R, Rousseau J, et al. Methicillin-resistant *Staphylococcus aureus* (MRSA) contamination of retail pork. *Can Vet J.* 2010;51(7):749-752.

  Among 402 samples of retail pork from four Canadian provinces, MRSA was isolated in 31 samples; 39 percent (12/31) were the most common Canadian epidemic clone, CMRSA, widely identified in horses and horse personnel but not in pigs. Thirty-two percent or 10/31, belonged to spa 539/t034, a clone associated with food animals internationally. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2885117/.

- Köck R, Harlizius J, Bressan N, et al. Prevalence and molecular characteristics of methicillin-resistant *Staphylococcus aureus* (MRSA) among pigs on German farms and import of livestock-related MRSA into hospitals. *Eur J Clin Microbiol Infect Dis.* 2009;28(11):1375-1382.

  Among hospital patients admitted with MRSA sequence type ST398, independent risk factors include pig, cattle contact. MRSA-carrying pigs were identified on 70 percent of 40 German pig farms, all ST398. Available at http://www.springerlink.com/content/d07291v16185374t/.

- Nemati M, Hermans K, Lipinska U, et al. Antimicrobial resistance of old and recent *Staphylococcus aureus* isolates from poultry: first detection of livestock-associated methicillin-resistant strain ST398. *Antimicrob Agents Chemother.* 2008;52(10):3817-3819.

  Finds that among *S. aureus* isolated from chickens in the 1970s compared to healthy chickens in 2006, resistance levels to eight of the drugs tested were significantly greater in 2006 samples. Available at http://aac.asm.org/content/52/10/3817.full.

- van Rijen MM, Van Keulen PH, Kluytmans JA. Increase in a Dutch hospital of methicillin-resistant *Staphylococcus aureus* related to animal farming. *Clin Infect Dis.* 2008;46(2):261-263.

  Among Dutch patients identified as having had exposure to pigs or veal calves, up to 32 percent in some hospitals were positive for MRSA. Available at http://cid.oxfordjournals.org/content/46/2/261.full.

- van Belkum A, Melles DC, Peeters JK, et al. Methicillin-resistant and -susceptible *Staphylococcus aureus* sequence type 398 in pigs and humans. *Emerg Infect Dis.* 2008;14(3):479-483.

  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. Available at http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2570802/.

- van Loo I, Huijsdens X, Tiemersma E, et al. Emergence of methicillin-resistant *Staphylococcus aureus* of animal origin in humans. *Emerg Infect Dis.* 2007;13(12):1834-1839.

  Reports a new animal-associated MRSA strain that has entered the human population and is accounting 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. Available at http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2876750/.

Pathogens Newly Tied to Food Animal Production – ExPEC E coli

- Bergeron CR, Prussing C, Boerlin P, et al. Chicken as reservoir for extraintestinal pathogenic *Escherichia coli* in humans, Canada. *Emerg Infec Dis.* 2012;18(3):415-421.

  Extraintestinal pathogenic *E. coli* (ExPEC) strains cause more than 85 percent of the several million community acquired urinary tract infections (UTIs) annually. Comparison of *E. coli* from humans with UTIs and from animals in slaughterhouses suggests ExPEC from the latter—most probably chickens—could be causing UTIs. Available at http://www.cdc.gov/eid/article/18/3/11-1099_article.htm.

- Manges AR, Johnson JR. **Food-borne origins of *Escherichia coli* causing extraintestinal infections.** *Clin Infect Dis.* 2012.

  A review suggesting many ExPEC strains responsible for UTIs, sepsis, and other extraintestinal infections may be transmitted from food animals or the food supply to humans, especially antimicrobial-resistant ExPEC.

Additional studies

- Johnson TJ, Logue CM, Johnson JR. **Associations between multidrug resistance, plasmid content, and virulence potential among extraintestinal pathogenic and commensal *Escherichia coli* from humans and poultry.** *Foodborne Pathog Dis.* 2012;9(1):37-46.

Using antimicrobial susceptibility profiles for over 2202 human and avian *E. coli* isolates, this study finds that in ExPEC *E. coli*, multidrug resistance is most commonly associated with plasmids, and these are frequently found in *E. coli* from poultry production systems.

- Tadesse DA, Zhao S, Tong E, et al. Antimicrobial drug resistance in *Escherichia coli* from humans and food animals, United States, 1950–2002. *Emerg Infect Dis.* 2012;18(5):741-749. Available at http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3358085/.

- Vieira AR, Collignon P, Aarestrup FM, et al. **Association between antimicrobial resistance in *Escherichia coli* isolates from food animals and blood stream isolates from humans in Europe: an ecological study.** *Foodborne Pathog Dis.* 2011;8(12):1295-1301.

  Antimicrobial resistance in *E. coli* from human blood stream infections strongly correlates with that in *E. coli* from poultry and pigs in 11 European countries.

- Xia X, Meng J, Zhao S, et al. **Identification and antimicrobial resistance of extraintestinal pathogenic *Escherichia coli* from retail meats.** *J Food Prot.* 2011;74(1):38-44.

  Among nearly 1300 *E. coli* isolated from ground beef, turkey, chicken breasts and pork chops, about 16 percent overall were identified as ExPEC, including 23.5 percent of those in ground turkey and 20.2 percent in chicken breasts.

- Xia X, Meng J, McDermott PF, et al. ***Escherichia coli* from retail meats carry genes associated with uropathogenic *Escherichia coli*, but are weakly invasive in human bladder cell culture.** *J Appl Microbiol.* 2011;110(5):1166-1176.

  A small proportion of *E. coli* isolates from retail meats carry uropathogenic associated virulence genes and therefore may serve as a reservoir of these genes to uropathogenic *E. coli* in the human intestine.

- Vincent C, Boerlin P, Daignault D, et al. Food reservoir for *Escherichia coli* causing urinary tract infections. *Emerg Infect Dis.* 2010;16(1):88-95.

  The design of this study was to see if a food reservoir exists for *E. coli* that may cause UTIs. Sampling for *E. coli* from 2005 to 2007 comprised of clinical UTI samples, retail meats and restaurant/ready-to-eat foods. Upon comparison of these collected isolates by molecular methods, the authors report that *E. coli* identified from retail chicken and other food sources are identical or nearly the same as those from human UTIs. Available at http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2874376/.

- Gow SP, Waldner CL, Harel J, Boerlin P. Associations between antimicrobial resistance genes in fecal generic *Escherichia coli* isolates from cow-calf herds in western Canada. *Appl Environ Microbiol.* 2008 Jun;74(12):3658-66.

  Sixty-five percent of 207 *E. coli* isolates from cow-calf herds in western Canada were resistant to at least one antimicrobial. Patterns in this research suggest that when a bacterium acquires resistance to one antimicrobial, it likely becomes resistant to others because of the transfer of mobile genetic elements that harbor regions of multiple drug resistance. Available at http://aem.asm.org/content/74/12/3658.full.

- Smith SP, Manges AR, Riley LW. Temporal changes in the prevalence of community-acquired antimicrobial-resistant urinary tract infection affected by *Escherichia coli* clonal group composition. *Clin Infect Dis.* 2008;46(5):689-695.

  Reports on UTIs from 1,667 patients over the course of six 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* 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. Available at http://cid.oxfordjournals.org/content/46/5/689.full.

- Smith JL, Fratamico PM, Gunther NW. **Extraintestinal pathogenic *Escherichia coli*.** *Foodborne Pathog Dis.* 2007;4(2):134-163.

  Given that ExPEC in meat may represent a new class of foodborne illness, this USDA study reviews various aspects of ExPEC prevalence, virulence, zoonotic properties and diseases association with it.

- Johnson JR, Kuskowski MA, Menard M, et al. Similarity between human and chicken *Escherichia coli* isolates in relation to ciprofloxacin resistance status. J *Infect Dis.* 2006;194(1):71-78.

  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 though contaminated meats. Available at http://jid.oxfordjournals.org/content/194/1/71.full.

- Ramchandani M, Manges AR, DebRoy C, et al. Possible animal origin of human-associated, multidrug-resistant, uropathogenic *Escherichia coli*. *Clin Infect Dis.* 2005;40(2):251-7.

  In response to a multistate outbreak of drug resistant UTI infections, the authors examined *E. coli* from animals and found the identical strain supporting the view that the bacteria were transmitted from animal to people through food. Available at http://cid.oxfordjournals.org/content/40/2/251.full.

- Manges AR, Johnson JR, Foxman B, et al. Widespread distribution of urinary tract infections caused by a multi-drug-resistant *Escherichia coli* clonal group. *N Engl J Med.* 2001;345(14):1007-1013.

  Studies community 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. Available at http://www.nejm.org/doi/full/10.1056/NEJMoa011265.

Transmission of resistance via retail meat

- Cohen Stuart J, van den Munckhof T, Voets G, et al. **Comparison of ESBL contamination in organic and conventional retail chicken meat.** *Int J Food Microbiol.* 2012;154(3):212-214.

  Retail chicken contaminated with ESBL-producing bacteria likely contributes to the increasing incidence of human infection with these bacteria.

- Zhao S, Blickenstaff K, Bodeis-Jones S, et al. Comparison of the prevalences and antimicrobial resistances of *Escherichia coli* isolates from different retail meats in the United States, 2002 to 2008. *Appl Environ Microbiol.* 2012;78(6):1701-1707. Available at http://aem.asm.org/content/early/2012/01/06/AEM.07522-11.full.pdf+html.

- Dutil L, Irwin R, Finley R, et al. Ceftiofur resistance in *Salmonella enterica* serovar Heidelberg from chicken meat and humans, Canada. *Emerg Infect Dis.* 2010;16(1):48-54.

  From 2003 to 2008, ceftiofur, a 3rd-generation cephalosporin antibiotic, was removed from extra-label use in chicken hatcheries in Québec, coinciding with a dramatic decrease in ceftiofur resistance in *S.* Heidelberg and *E. coli* in retail chicken and a similar decrease in resistance in *S.* Heidelberg infections in humans. Reintroduction of ceftiofur into hatcheries in 2007 caused a rise in ceftiofur resistance in *E. coli*, but at lower levels than those seen in 2003-04. Available at http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2874360/.

- Zhao S, White DG, Friedman SL, et al. Antimicrobial resistance in *Salmonella enterica* serovar Heidelberg isolates from retail meats, including poultry, from 2002 to 2006. *Appl Environ Microbiol.* 2008;74(21):6656-6662.

  From more than 20,000 retail meat samples over four years, the FDA finds that multidrug-resistant strains of ***S. enterica*** serotype Heidelberg were common isolates. Available at http://aem.asm.org/content/74/21/6656.long.

- O'Brien AM, Hanson BM, Farina SA, et al. MRSA in conventional and alternative retail pork products. *PLoS One.* 2012;7(1):e300092.

  The largest sampling of retail pork to date found 64.8 percent with *S. aureus* and 6.6 percent with MRSA. 26.5 percent of MRSA had spa types associated with MRSA ST398. Available at http://www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0030092.

Additional studies

- Aslam M, Diarra MS, Checkley S, et al. **Characterization of antimicrobial resistance and virulence genes in *Enterococcus* spp. isolated from retail meats in Alberta, Canada.** *Int J Food Microbiol.* 2012;156(3):222-230.

  E. faecalis was found in over 94 percent of poultry samples, about 73 percent of beef and 86 percent of pork samples. Resistance to three or more antimicrobials was more common in *E. faecalis* from chicken and turkey (91%) than from pork (45%) or beef (14%). Resistance to aminoglycosides, macrolides, tetracyclines, streptogramin, bacitracin and lincosamide were most common.

- Hammerum AM, Lester CH, Heuer OE. **Antimicrobial-resistant enterococci in animals and meat: a human health hazard?** *Foodborne Pathog Dis.* 2010;7(10):1137-46.

- Hayes JR, McIntosh AC, Qaiyumi S, et al. High-frequency recovery of quinupristin-dalfopristin-resistant *Enterococcus faecium* isolates from the poultry-production environment. *J Clin Microbiol.* 2001;39(6):2298-2299.

  Among *E. faecium* isolated from a poultry production environment, the extent of resistance found to quinupristin-dalfopristin, a drug reserved for human use to treat vancomycin-resistant enterococci, ranged from 51 percent to 78 percent. Available at http://jcm.asm.org/content/39/6/2298.full.

- ***Salmonella* Heidelberg ceftiofur-related resistance in human and retail chicken isolates.** Ottawa, Ontario: Public Health Agency of Canada; 2009. Available at http://www.phac-aspc.gc.ca/cipars-picra/heidelberg/heidelberg-eng.php (2007 report); http://www.phac-aspc.gc.ca/cipars-picra/heidelberg/heidelberg_090326-eng.php (2009 update).

- Aarestrup FM, Hendriksen RS, Lockett J, et al. International spread of multidrug-resistant *Salmonella* Schwarzengrund in food products. *Emerg Infect Dis.* 2007;13(5):726-731.

  This study of 581 *Salmonella enterica* serotype Schwarzengrund isolates from persons, food and food animals suggests the bacteria pass from chickens to persons in Thailand, and from imported Thai food products to persons in Denmark and the United States. Available at http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2738437.

- Parveen S, Taabodi M, Schwarz JG, et al. **Prevalence and antimicrobial resistance of *Salmonella* recovered from processed poultry.** *J Food Prot.* 2007;70(11):2466-2472.

  Salmonella was highly prevalent in more than 88 percent and over 84 percent of 480 pre- and post-chill whole chicken carcasses, respectively. 79.8 percent were resistant to at least one antimicrobial; 53.4 percent to three or more.

- Skov MN, Andersen JS, Aabo S, et al. Antimicrobial drug resistance of *Salmonella* isolates from meat and humans, Denmark. *Emerg Infect Dis.* 2007;13(4):638-641.

  Comparison of more than 8,000 isolates from meat in Denmark shows higher rates of resistance, including multi-drug resistance, in *Salmonella* from imported vs. domestic meat. Available at http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2725957/.

- White DG, Zhao S, Sudler R, et al. The isolation of antibiotic-resistant *Salmonella* from retail ground meats. *N Engl J Med.* 2007;345(16):1147-1154.

  Salmonella were isolated from 41 out of 200 (20%) of samples of ground chicken, pork, beef, and turkey purchased in Washington, DC. Eighty-four percent of *Salmonella* were resistant to one or more antibiotics; 53 percent were resistant to three or more antibiotics. Sixteen percent were resistant to ceftriaxone, drug of choice for treating salmonellosis in children. Available at http://www.nejm.org/doi/full/10.1056/NEJMoa010315#t=article.

- Logue CM, Sherwood JS, Olah PA, et al. The incidence of antimicrobial-resistant *Salmonella* spp. on freshly processed poultry from US Midwestern processing plants. *J Appl Microbiol.* 2003;94(1):16-24.

  Sixteen percent of samples taken from processed turkey plants in the Midwest over the course of a year detected *Salmonella*, which in turn demonstrated varying levels of antimicrobial resistance. The most common resistance was seen to tetracycline, streptomycin, sulfamethoxazole and ampicillin. Available at http://onlinelibrary.wiley.com/doi/10.1046/j.1365-2672.2003.01815.x/full.

- Thakur S, Zhao S, McDermott PF, et al. **Antimicrobial resistance, virulence, and genotypic profile comparison of *Campylobacter jejuni* and *Campylobacter coli* isolated from humans and retail meats.** *Foodborne Pathog Dis.* 2010;7(7):835-844.

  Campylobacter from humans and retail meats showed limited overlap, suggesting retail meat is not a unique route of *Campylobacter* transmission.

- Young I, Rajić A, Wilhelm BJ, et al. **Comparison of the prevalence of bacterial entero-pathogens, potentially zoonotic bacteria and bacterial resistance to antimicrobials in organic and conventional poultry, swine and beef production: a systematic review and meta-analysis.** *Epidemiol Infect.* 2009;137(9):1217-1232.

  Review article finding that *Campylobacter* is higher in organic compared to conventional broiler chickens at slaughter, but not in retail chicken. However, *Campylobacter* from conventional retail chicken was more likely ciprofloxacin-resistant. Also, bacteria isolated from conventional food animal production exhibit higher levels of antibiotic resistance.

- Berrang ME, Ladely SR, Meinersmann RJ, et al. Subtherapeutic tylosin phosphate in broiler feed affects *Campylobacter* on carcasses during processing. *Poult Sci.* 2007;86(6):1229-1233.

  Erythromycin is often the drug of choice for treating campylobacteriosis, while the similar macrolide antibiotic, tylosin, is FDA-approved in chicken feed at subtherapeutic levels to promote growth. In this feeding study, where chicks were raised with or without tylosin, it was found that tylosin in feed results in lower numbers of *Campylobacter*, but those remaining were erythromycin-resistant. Available at http://ps.fass.org/content/86/6/1229.full.

- Nannapaneni R, Story R, Wiggins KC, et al. 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°C. *Appl Environ Microbiol.* 2005;71(8):4510-4515.

  Demonstrated a reservoir of *Campylobacter* resistance in U.S. retail chicken. Available at http://aem.asm.org/content/71/8/4510.long.

- Price LB, Johnson E, Vailes R, Silbergeld **E.** Fluoroquinolone-resistant *Campylobacter* isolates from conventional and antibiotic-free chicken products. *Environ Health Perspect.* 2005;113(5):557-560.

  Finds that while *Campylobacter* contamination does not significantly differ in poultry raised conventionally versus antibiotic-free, the former were more likely to harbor bacteria that were antibiotic-resistant. Available at http://ehp03.niehs.nih.gov/article/info:doi/10.1289/ehp.7647.

- Jakobsen L, Kurbasic A, Skjøt-Rasmussen L, et al. ***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.** *Foodborne Pathog Dis.* 2010;7(5):537-547.

  Specific *E. coli* phylogroups which are the main cause of UTIs in Denmark, also exist in *E. coli* samples of animal origin, such as from broiler chicken meat, pork meat, chickens and pigs. Animal isolates 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.

- Hannah EL, Johnson JR, Angulo F, et al. Molecular analysis of antimicrobial-susceptible and -resistant *Escherichia coli* from retail meats and human stool and clinical specimens in a rural community setting. *Foodborne Pathog Dis.* 2009;6(3):285-295.

  Of 340 antimicrobial-resistant and -susceptible *E. coli* isolates from retail meat and human stool in a single community, nearly 20 percent of meat-source resistant *E. coli* represented ExPEC. Resistant isolates from stool were more similar to resistance isolates from meat than to susceptible *E. coli* from stool, suggesting foodborne transmission. Available at http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3186705/.

- Johnson JR, McCabe JS, White DG, et al. Molecular analysis of *Escherichia coli* from retail meats (2002–2004) from the United States National Antimicrobial Resistance Monitoring System. *Clin Infect Dis.* 2009;49(2):195-201.

  Resistant and susceptible *E. coli* from NARMS retail meats demonstrated great variance by meat type, with chicken and turkey isolates having consistently higher virulence scores than beef and pork isolates. Supports 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. Available at http://cid.oxfordjournals.org/content/49/2/195.full.

- Smith SP, Manges AR, Riley LW. Temporal changes in the prevalence of community-acquired antimicrobial-resistant urinary tract infection affected by *Escherichia coli* clonal group composition. *Clin Infect Dis.* 2008;46(5):689-695.

  Among *E. coli* isolated from 1,667 patients over six years with UTIs, 49 percent were resistant to trimethoprim-sulfamethoxazole at a rate of 49 percent. Twelve percent were found to be from a specific group previously collected from food animals or retail poultry products as well, suggesting contaminated food may be a source of drug-resistant UTIs. Available at http://cid.oxfordjournals.org/content/46/5/689.full.

- Johnson JR, Sannes MR, Croy C, et al. Antimicrobial drug-resistant *Escherichia coli* from humans and poultry products, Minnesota and Wisconsin, 2002-2004. *Emerg Infect Dis.* 2007;13(6):838-846.

  Comparison of susceptible and resistant *E. coli* collected from hospital patients, healthy vegetarians, and poultry that were raised conventionally and without antibiotics suggests many resistant human isolates may originate from poultry. Available at http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2792839/.

- Schroeder CM, White DG, Ge B, et al. **Isolation of antimicrobial-resistant *Escherichia coli* from retail meats purchased in Greater Washington, DC, USA.** *Int J Food Microbiol.* 2003;85(1-2):197-202.

  Concludes that retail meats often are contaminated with resistant *E. coli*. A large portion of samples demonstrate *E. coli* resistant to tetracycline (59%), sulfamethoxazole (45%), streptomycin (44%), ampicillin (35%) and gentamicin (12%).

Transmission via farmers, workers, veterinarians

- Gilbert MJ, Bos ME, Duim B, et al. **Livestock-associated MRSA ST398 carriage in pig slaughterhouse workers related to quantitative environmental exposure.** *Occup Environ Med.* 2012;69(7):472-478.

  Of 341 Dutch pig slaughterhouse workers tested, 3.2 percent carried MRSA, of which 75 percent was the livestock-associated MRSA ST398 strain. Workers at the start of the slaughter line were at higher risk than those further down the line.

- Smith TC, Male MJ, Harper AL, et al. Methicillin-resistant *Staphyloccus aureus* (MRSA) strain ST398 is present in Midwestern U.S. swine and swine workers. *PLoS ONE.* 2009; 4(1): e4258.

  Prevalence of MRSA was 49 percent in swine and 45 percent in workers in two Midwest swine production operations. Available at http://www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0004258.

- Price LB, Graham JP, Lackey LG, et al. Elevated risk of carrying gentamicin-resistant *Escherichia coli* among U.S. poultry workers. *Environ Health Perspect.* 2007;15(12):1738-1742.

  Poultry workers examined were 32 times more likely to be colonized with gentamicin-resistant *E. coli* as community residents. Poultry workers also had an elevated risk of carrying multidrug-resistant *E. coli*. Available at http://ehp03.niehs.nih.gov/article/info:doi/10.1289/ehp.10191.

Additional studies

- Aslam M, Diarra MS, Service C, Rempel H. **Characterization of antimicrobial resistance in *Enterococcus* spp. recovered from a commercial beef processing plant.** *Foodborne Pathog Dis.* 2010;7(3):235-241.

  Enterococci bacteria appear prevalent in commercial beef processing plant settings and include a pool of resistance genes.

- Garcia-Graells C, Antoine J, Larsen J, et al. **Livestock veterinarians at high risk of acquiring methicillin-resistant *Staphylococcus aureus* ST398.** *Epidemiol Infect.* 2012;140(3):383-389.

  7.5 percent of Belgian and 1.4 percent of Danish veterinarians were colonized with livestock-associated MRSA (ST398), highlighting the importance of preventive measures.

- Bisdorff B, Scholhölter JL, Claußen K, et al. **MRSA-ST398 in livestock farmers and neighbouring residents in a rural area in Germany**. *Epidemiol Infect.* 2011; *FirstView* Article:1-9. Available at http://journals.cambridge.org/abstract_S0950268811002378.

- Graveland H, Wagenaar JA, Bergs K, et al. **Persistence of livestock associated MRSA CC398 in humans is dependent on intensity of animal contact**. *PLoS One.* 2011;6(7):e16830.

  Livestock-associated MRSA in farmers is strongly related to intensity and duration of animal contact. The fact that current LA-MRSA strains poorly colonize most humans is important for MRSA control strategies. Available at http://www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0016830.

- Mendes RE, Smith TC, Deshpande L, Diekema DJ, Sader HS, Jones RN. **Plasmid-borne vga(A)-encoding gene in methicillin-resistant *Staphylococcus aureus* ST398 recovered from swine and a swine farmer in the United States.** *Diagn Microbiol Infect Dis.* 2011;71(2):177-180.

- van Cleef BA, Graveland H, Haenen AP, et al. **Persistence of livestock-associated methicillin-resistant *Staphylococcus aureus* in field workers after short-term occupational exposure to pigs and veal calves**. *J Clin Microbiol.* 2011;49(3):1030-1033.

  An estimated 25 to 35 percent of pig and veal calf farmers in the Netherlands carry MRSA. MRSA-negative field workers were tested for MRSA before and after visiting MRSA-positive pig and veal farms. Seventeen percent of such visits resulted in workers converting to MRSA-positive status, but in most cases, workers lost the MRSA strain within 24 hours. Available at http://jcm.asm.org/content/49/3/1030.long.

- Leedom Larson KR, Smith TC, Donham KJ. **Self-reported methicillin-resistant Staphylococcus aureus infection in USA pork producers**. *Ann Agric Environ Med.* 2010;17(2):331-334.

  3.7 percent of pork producers selected from the National Pork Board`s producer database reported being diagnosed with a MRSA infection. Available at http://www.aaem.pl/pdf/17331.htm.

- Khanna T, Friendship R, Dewey C, Weese JS. **Methicillin-resistant *Staphylococcus aureus* colonization in pigs and pig farmers**. *Vet Microbiol.* 2008;128(3-4):298-303.

  Prevalence of MRSA colonization was 20 percent in farmers and 45 percent of pigs in Canadian pig farms studied. Humans residents of MRSA-free pig farms also were MRSA-negative. Available at http://www.apuabrasil.org.br/arquivos/veterinaria06.pdf.

- Lewis HC, Mølbak K, Reese C, et al. **Pigs as a source of methicillin-resistant *Staphylococcus aureus* CC398 in pigs and humans**. *Emerg Infect Dis.* 2008;14(9):1383-1389.

  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. Available at http://wwwnc.cdc.gov/eid/article/14/9/07-1576_article.htm.

- Hanselman BA, Kruth SA, Rousseau J, et al. **Methicillin-resistant *Staphylococcus aureus* colonization in veterinary personnel**. *Emerg Infect Dis.* 2006;12(12):1933-1938.

  Reports a comprehensive evaluation of veterinary personnel for carriage of MRSA. Samples from veterinary personnel volunteers, from 19 different countries, indicated 6.5 percent were MRSA-positive; among those working with larger animals, prevalence was 15.6 percent. Available at http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3291342/.

- Huijsdens XW, van Dijke BJ, Spalburg E, et al. **Community-acquired MRSA and pig-farming**. *Ann Clin Microbiol Antimicrob.* 2006;5:26.

  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. Available at http://www.biomedcentral.com/1476-0711/5/26.

- Voss A, Loeffen F, Bakker J, et al. **Methicillin-resistant *Staphylococcus aureus* in pig farming**. *Emerg Infect Dis.* 2005;11(12):1965-1966.

  Study showed transmission of MRSA between pig and human, between family members, and between a nurse and patient in a hospital. This is consistent with other studies that have found pig farmers to be at higher risk of MRSA. 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. Available at http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3367632/.

- Aubry-Damon H, Grenet K, Sall-Ndiaye P, et al. Antimicrobial resistance in commensal flora of pig farmers. *Emerg Infect Dis.* 2005;10(5):873-879.

  Study compared pig farmers to matched group of non-farmers and found farmers at greater risk of being colonized with *Staphylococcus aureus* and at greater risk for resistant *Staphylococcus aureus*. Available at http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3323198/.

- Akwar TH, Poppe C, Wilson J, et al. **Risk factors for antimicrobial resistance among fecal *Escherichia coli* from residents on forty-three swine farms.** *Microb Drug Resist.* 2007;13(1):69-76.

  Resistant bacteria were more prevalent among residents or workers on farms where hogs were fed antibiotics. *E. coli* was obtained from 115 residents on 43 farms; 25.8 percent were resistant to at least one antibiotic. Farmers feeding antibiotics to animals appear to have a heightened occupational hazard from exposure to resistant bacteria.

- van den Bogaard AE, London N, Driessen C, et al. Antibiotic resistance of faecal *Escherichia coli* in poultry, poultry farmers, and poultry slaughterers. *J Antimicrob Chemother.* 2001;47(6):763-771.

  A survey of *E. coli* in poultry and in workers in close contact with animals strongly supports the transmission of resistant clones and resistance plasmids of *E. coli* from broilers and turkeys to humans. Available at http://jac.oxfordjournals.org/content/47/6/763.full.

Transmission via the broader environment (air, water, soil)

- McKinney CW, Loftin KA, Meyer MT, et al. ***tet* and *sul* antibiotic resistance genes in livestock lagoons of various operation type, configuration, and antibiotic occurrence.** *Environ Sci Technol.* 2010;44(16):6102-6109.

  Water samples from the manure lagoons of various livestock facilities (dairy, chicken layer, swine) contained three to five times higher tetracycline resistance genes than did sediment samples upstream of such facilities.

- Chee-Sanford JC, Mackie RI, Koike S, et al. Fate and transport of antibiotic residues and antibiotic resistance genes following land application of manure waste. J *Environ Qual.* 2009;38:1086-1108.

  Feeding of antibiotics to food animals disseminates residues into the environment, and also likely leads to antibiotic resistance arising among commensal bacteria in the animal gut. Applying animal waste to the environment creates a reservoir of potentially significant antibiotic resistant genes in the area. Available at https://www.agronomy.org/publications/jeq/articles/38/3/1086.

- Gibbs SG, Green CF, Tarwater PM, et al. Isolation of antibiotic-resistant bacteria from the air plume downwind of a swine confined or concentrated animal feeding operation. *Environ Health Perspect.* 2006;114(7):1032-1037.

  Bacteria isolated from upwind, downwind and inside a confined hog operation revealed multidrug-resistant organisms; those inside the facility were most resistant. Available at http://ehp03.niehs.nih.gov/article/info%3Adoi%2F10.1289%2Fehp.8910.

Additional studies

- West BM, Liggit P, Clemans DL, Francoeur SN. **Antibiotic resistance, gene transfer, and water quality patterns observed in waterways near CAFO farms and wastewater treatment facilities.** *Water Air Soil Pollut.* 2011;217(1-4):473-489.

  In measurement of water quality from locations impacted by confined animal feeding operations (CAFOs) compared to reference sites and sites located upstream and downstream of wastewater treatment facilities, agriculturally impacted sites had a significantly greater proportion of isolates that showed resistance to multiple antibiotics. Available at http://www.nocafos.org/EMUstudy.pdf.

- Wittum TE, Mollenkopf DF, Daniels JB, et al. **CTX-M-type extended-spectrum ß-lactamases present in *Escherichia coli* from the feces of cattle in Ohio, United States.** *Foodborne Pathog Dis.* 2010;7(12):1575-1579.

  Bovine fecal samples were screened for *E. coli* strains producing CTX-M, extended-spectrum ß-lactamase enzymes that allow them to inhibit the antimicrobial effects of penicillins and cephalosporins. Six percent (3/50) of fecal samples harbored CTX-M genes. Ceftiofur use in cattle may provide the selection pressure for CTX-M genes to disseminate.

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