The APUA "FAAIR Report"

Complete list of references cited.

(1993). "Nosocomial enterococci resistant to vancomycin --- United States, 1989-1993." MMWR **42**: 597-9.

(1997). "Salmonellosis --- Kentucky." MMWR **26**: 239.

(1998). National Antimicrobial Susceptibility Monitoring Program: Veterinary Isolates, FDA/USDSA/CDC.

(1998). Veterinary Values, 5th edition, Veterinary Medicine Publishing Group.

(1998). Merck Veterinary Manual, 8th edition. Philadelphia, National Publishing Inc.

(1999). Salmonella serotypes isolated from raw meat and poultry, US Department of Agriculture. **1999**.

(2000). "Salmonellosis associated with chicks and ducklings --- Michigan and Missouri, Spring, 1999." MMWR **49**(14): 297-9.

(2000). US Census 2000. **2001**.

(2001). Agri-Mycin® 17. Crop Protection Reference, 17th ed. New York, NY, Chemical and Pharmaceutical Press**:** 1928-30.

(2001). Mycoshield®. Crop Protection Reference, 17th ed. New York, NY, Chemical and Pharmaceutical Press**:** 2086-7.

Aarestrup, F., F. Bager, et al. (1998). "Surveillance of antimicrobial resistance in bacteria isolated from food animals to antimicrobial growth promoters and related therapeutic agents in Denmark." APMIS **106**: 606-22.

Aarestrup, F. M., A. M. Seyfarth, et al. (2001). "Effect of abolishment of the use of antimicrobial agents for growth promotion on occurrence of antimicrobial resistance in fecal enterococci from food animals in Denmark." Antimicrob Agents Chemother **45**(7): 2054-9.

Ackers, M.-L., N. Puhr, et al. (2000). "Laboratory-based surveillance of Salmonella serotype typhi infections in the United States: Antimicrobial resistance on the rise." JAMA **283**: 2668-73.

Adak, G., J. Cowden, et al. (1995). "The Public Health Laboratory Service national case-control study of primary indigenous sporadic cases of campylobacter infection." Epidemiol Infect **115**: 15-22.

Adams, C., B. Austin, et al. (1998). "Molecular characterization of plasmid-mediated oxytetracycline resistance in *Aeromonas salmonicida*." App Environ Microbiol **64**: 4194-201.

Adler, J., R. Anderson, et al. (1970). "A protracted hospital-associated outbreak of salmonellosis

due to a multiple-antibiotic resistant strain of Salmonella indiana." J Pediatr **77**: 970-5.

Advisory Committee on the Microbiological Safety of Food (ACMSF) (1999). Report on microbial antibiotic resistance in relation to food safety. London, The Stationary Office.

Ahmed, M., L. Lyass, et al. (1995). "Two highly similar multidrug transporters of *Bacillus subtilis* whose expression is differentially regulated." J Bacteriol **177**: 3904-10.

Akkina, J. E., A. T. Hogue, et al. (1999). "Epidemiologic aspects, control, and importance of multiple-drug resistant *Salmonella Typhimurium* DT104 in the United States." J Am Vet Med Assoc **214**(6): 790-8.

Altekruse, S., N. Stern, et al. (1999). "Campylobacter jejuni--an emerging foodborne pathogen." Emerg Inf Dis **5**: 28-35.

Alvarez-Olmos, M. and R. Oberhelman (2001). "Probiotic agents and infectious diseases: a modern perspective on a traditional therapy [review]." Clin Infect Dis **32**: 1567-76.

American Association of Avian Pathologists (2000). Guidelines to judicious therapeutic use of antimicrobials in poultry. **2001**.

American Association of Swine Veterinarians (2000). "Basic Guidelines of Judicious Therapeutic Use of Antimicrobials in Pork Production." Journal of Swine Health and Production **8**(2).

American Veterinary Medical Association (AVMA) (1998). Judicious Therapeutic Use of Antimicrobials, American Veterinary Medical Association. **2001**.

Anderson, E. S. (1968). "Drug resistance in *Salmonella typhimurium* and its implications." BMJ **2**: 333-9.

Anderson, J., W. Gillispie, et al. (1973). "Chemotherapy and antibiotic resistance transfer between enterobacteria in the human gastro-intestinal tract." J Med Microbiol **6**: 461-73.

Anderson, J., L. C. Ingram, et al. (1973). "Studies on the nature of plasmids arising from the conjugation in the human gastro-intestinal tract." J Med Microbiol **6**: 475-486.

Angulo, F. J., K. R. Johnson, et al. (2000). "Origins and consequences of antimicrobial-resistant nontyphoidal Salmonella: implications for the use of fluoroquinolones in food animals." Microb Drug Resist **6**(1): 77-83.
Human Salmonella infections are common; most infections are self- limiting, however severe disease may occur. Antimicrobial agents, while not essential for the treatment of Salmonella gastroenteritis, are essential for the treatment of thousands of patients each year with invasive infections. Fluoroquinolones and third-generation cephalosporins are the drugs-of-choice for invasive Salmonella infections in humans; alternative antimicrobial choices are limited by increasing antimicrobial resistance, limited efficacy, and less desirable pharmacodynamic properties. Antimicrobial-resistant Salmonella results from the use of antimicrobial agents in food animals, and these antimicrobial resistant Salmonella are subsequently transmitted to humans, usually through the food supply. The antimicrobial resistance patterns of isolates collected from

persons with Salmonella infections show more resistance to antimicrobial agents used in agriculture than to antimicrobial agents used for the treatment of Salmonella infections in humans. Because of the adverse health consequences in humans and animals associated with the increasing prevalence of antimicrobial-resistant Salmonella, there is an urgent need to emphasize non-antimicrobial infection control strategies, such as improved sanitation and hygiene, to develop guidelines for the prudent usage of antimicrobial agents, and establishment of adequate public health safeguards to minimize the development and dissemination of antimicrobial resistance and dissemination of Salmonella resistant to these agents.

Animal and Plant Health Inspection Service (APHIS) (1995). Swine '95. Part I: Reference of 1995 swine management practices, USDA.

Animal and Plant Health Inspection Service (APHIS) (1996). Dairy '96. Part III: Reference of 1996 dairy health and health management, USDA.

Animal and Plant Health Inspection Service (APHIS) (1997). Cattle and calves death loss 1995, USDA.

Animal and Plant Health Inspection Service (APHIS) (1997). Swine '95. Part III: Changes in the U.S. pork industry 1990-1995, USDA.

Animal and Plant Health Inspection Service (APHIS) (1997). Catfish '97. Part II: Reference of 1996 U.S. catfish management practices, USDA.

Animal and Plant Health Inspection Service (APHIS) (2000). Changes in the U.S. feedlot industry: 1994-1999, USDA.

Animal and Plant Health Inspection Service (APHIS) (2000). Feedlot '99. Part III: health management and biosecurity in U.S. feedlots, 1999, USDA.

Animal and Plant Health Inspection Service (APHIS) (2001). Swine 2000. Part I: Reference of 2000 swine management practices, USDA.

Animal Health Institute (AHI) (2000). Survey indicates most antibiotics used in animals are used for treating and preventing disease. Washington, D.C., Animal Health Institute.

Ariza, R., S. Cohen, et al. (1994). "Repressor mutations in the *marRAB* operon that activate oxidative stress genes and multiple antibiotic resistance in *Escherichia coli*." J Bacteriol **176**: 143-8.

Atwood, K. C., L. K. Schneider, et al. (1951). "Periodic selection in *Escherichia coli*." Proc. Natl. Acad. Sci. **37**: 146-155.

Austen, R. and T. Trust (1981). "Plasmid specification of resistance to antibacterial compounds in environmental *Citrobacter freundii*." Can J Microbiol **27**: 343-9.

Bager, F. (2000). "DANMAP: monitoring antimicrobial resistance in Denmark." Int J Antimicrob Agents **14**: 271-4.

Bager, F., M. Madsen, et al. (1997). "Avoparcin used as a growth promotor is associated with the occurrence of vancomycin-resistant *Enterococcus faecium* on Danish poultry and pig farms." Prev Vet Med **31**: 95-112.

Bager, G., F. Aarestrup, et al. (1999). "Glycopeptide resistance in *Enterococcus faecium* from broilers following discontinued use of avoparcin." Microb Drug Resist **5**: 53-6.

Bailey, J. S. (1987). "Factors affecting microbial competitive exclusion in poultry." Food Technology **47**: 88-92.

Bailey, J. S., N. A. Cox, et al. (1992). "Effect of competitive exclusion microflora on the distribution of *Salmonella* serotypes in an integrated poultry operation." Poult Sci **71**(Supplement 1).

Baquero, F., M. C. Negri, et al. (1997). "The antibiotic selective process: concentration-specific amplification of low-level resistant populations." Ciba Found Symp **207**: 93-105.
The biochemistry and genetics of antibiotic resistance are far better known than the equally important events underlying the selection of resistant populations. The hidden selection of low-level resistant variants may be a key process in the emergence of high-level antibiotic resistance. Different low-level resistant bacterial subpopulations may be specifically selected by different low antibiotic concentrations. The space in the environment (human body) where a given selective concentration exists represents the selective compartment. For pharmacokinetic reasons, low antibiotic concentrations occur in a larger selective compartment and persist longer than high antibiotic concentrations. The specific selection of low-level variants by low concentrations of antibiotic can be reproduced in experimental in vitro models using mixtures of susceptible and low-level resistant populations. We demonstrated this in Escherichia coli strains harbouring TEM-1, TEM-12 and TEM-10 beta-lactamases challenged by cefotaxime, and also Streptococcus pneumoniae strains with various levels of penicillin resistance challenged by amoxicillin or cefotaxime. In both cases, four hours of antibiotic challenge produced selective peaks of low-level resistant variant populations at low-level antibiotic concentrations. We conclude that variants with small decreases in antibiotic susceptibility may be fully selectable under in vivo circumstances; on the other hand, low-level antibiotic concentrations may have a considerable selective effect on the emergence of antibiotic resistance.

Baranova, N., A. Danchin, et al. (1999). "Mta, a global MerR-type regulator of the Bacillus subtilis multidrug-efflux transporters." Mol Microbiol **31**: 1549-59.

Barnes, E. M., C. S. Impey, et al. (1980). "Competitive exclusion of *Salmonella* from newly hatched chicks." Vet Rec **160**: 61-65.

Barragry, T. (1994). Veterinary Drug Therapy. Philadelphia, Lea & Febiger.

Barrow, P. and K. Page (2000). "Inhibition of colonisation of the alimentary tract in young chickens with Campylobacter jejuni by pre-colonisation with strains of C. jejuni." FEMS Microbiol Lett **182**: 87-91.

Barrow, P., J. Tucker, et al. (1987). "Inhibition of colonization of the chicken alimentary tract with

Salmonella typhiumurium gram-negative facultatively anaerobic bacteria." Epidemiol Infect **98**: 311-22.

Barrow, P. A. and T. S. Wallis (2000). Vaccination against *Salmonella* infections in food animals: rationale, theoretical basis and practical application. *Salmonella* in Domestic Animals. C. Wray and A. Wray. New York, CABI**:** 323-340.

Barza, M., M. Giuliano, et al. (1987). "Effect of broad-spectrum parenteral antibiotics on "colonization resistance" of intestinal microflora of humans." Antimicrob Agents Chemother **31**: 723-7.

Bates, J., J. Jordens, et al. (1994). "Farm animals as a putative reservoir for vancomycin-resistant enterococcal infection in man." J Antimicrob Chemother **34**: 507-14.

Bayer Corporation (2001). Bayer's Submission of Facts, Information and Analysis in Response to the Notice of Opportunity for Hearing. Shawnee Mission, KS, Bayer Corporation.

Beran, G. W. and J. H. Steele (1994). Biosecurity. Handbook of Zooneses: Bacteria, Vol. I, 2nd Edition, CRC Press.

Berndtson, E. (1996). *Campylobacter* in broiler chickens. Dissertation at the Swedish University of Agricultural Sciences, Uppsala, Sweden.

Besser, T., M. Goldoft, et al. (2000). "Multiresistant *Salmonella Typhimuriium* DT 104 infections of humans and domestic animals in the Pacific Northwest of the United States." Epidemiol Infect **124**: 193-200.

Bezoen, A., W. van Haren, et al. (2001). Emergence of a Debate: AGPs and Public Health Human Health and Antibiotic Growth Promoters (AGPs): Reassessing the Risk, Heidelberg Appeal Netherlands Foundation. **2001**.

Bhutta, Z., S. Haqvi, et al. (1991). "Multidrug-resistant typhoid in children: presentation and clinical features." Rev Infect Dis **13**: 832-6.

Bjorkman, J., D. Hughes, et al. (1998). "Virulence of antibiotic-resistant *Salmonella typhimurium*." Proc Natl Acad Sci USA **95**: 3949-53.

Blankenship, L. C., J. S. Bailey, et al. (1993). "Two-step mucosal competitive exclusion flora treatment to diminish *Salmonella* in commercial broiler chickens." Poult Sci **72**: 1667-72.

Blaser, M. J. and R. A. Feldman (1981). "*Salmonella* bacteremia: reports to the Centers for Disease Control, 1968-1979." J Infect Dis **143**: 743-6.

Blaser, M. J. and L. S. Newman (1982). "A review of human salmonellosis. I. Infective dose." Rev Infect Dis **4**: 1096-106.

Blaser, M. J., D. N. Taylor, et al. (1983). "Epidemiology of *Campylobacter jejuni* infections." Epidemiol Rev **5**: 157-76.

Bolton, L., L. Kelley, et al. (1999). "Detection of multidrug-resistant *Salmonella enterica* serotype *typhimurium* DT104 based on a gene which confers cross-resistance to florfenicol and chloramphenicol." J Clin Microbiol **37**: 1348-51.

Bonhoff, M., B. Drake, et al. (1954). "The effect of streptomycin on the susceptibility of the intestinal tract to experimental salmonella infections." Proc Soc Exptl Biol Med **86**: 132-7.

Bonhoff, M. and C. Miller (1962). "Enhanced susceptibility to salmonella infection in streptomycin treated mice." J Infect Dis **111**: 117.

Boyle, J., S. Soumakis, et al. (1993). "Epidemiological analysis and genotypic characterization of a nosocomial outbreak of vancomycin-resistant Enterococci." J Clin Microbiol **31**: 1280-5.

Brenner, F., R. Villar, et al. (2000). "Salmonella nomenclature." J Clin Microbiol **38**: 2465-7.

Bridges, K. and E. Lowbury (1977). "Drug resistance in relation to use of silver sulphadiazine cream in a burns unit." J Clin Pathol **30**: 160-4.

Brown, N., D. Rouch, et al. (1992). "Copper resistance determinants in bacteria [review]." Plasmid **27**: 41-51.

Burr, T. and J. Norelli (1990). Antibiotics. Methods in phytobacteriology. Z. Klement, K. Rudolph and D. Sands. Budapest, Akademiai Kiado**:** 327-31.

Burrows, G. E., R. J. Morton, et al. (1993). "Microdilution antimicrobial susceptibilities of selected gram-negative veterinary bacterial isolates." J Vet Diagn Invest **5**: 541-7.

Butaye, P., L. Devriese, et al. (2001). "Differences in antibiotic resistance patterns of *Enterococcus faecalis* and *Enterococcus faecium* strains isolated from farm and pet animals." Antimicrob Agents Chemother **45**: 1374-8.

Bywater, R. and M. Casewell (2000). "An assessment of the impact of antibiotic resistance in different bacterial species and of the contribution of animal sources to resistance in human infections [letter]." J Antimicrob Chemother **46**: 643-5.

Caprioli, A., L. Busani, et al. (2000). "Monitoring of antibiotic resistance in bacteria of animal origin: epidemiological and microbiological methodologies." Int J Antimicrob Agents **14**: 295-301.

Carter, A., A. Borczyk, et al. (1987). "A severe outbreak of Escherichia coli O157:H7--associated hemorrhagic colitis in a nursing home." N Engl J Med **317**: 1496-500.

Centers for Disease Control and Prevention (1999). National Antimicrobial Resistance Monitoring System (NARMS) for Enteric Bacteria (1996-1999). Atlanta, US Centers for Disease Control.

Centers for Disease Control and Prevention (1999). FoodNet – Foodborne diseases active surveillance network. CDC s emerging infections program – 1999 surveillance results. Atlanta, CDC.

Centers for Disease Control and Prevention (1999). CDC summary of outbreaks of *Escherichia coli* 0157 and other Shiga toxin-producing *E. coli* reported to CDC in 1999., CDC. **2001**.

Centers for Disease Control and Prevention (2000). CDC National Salmonella Surveillance System, CDC.

Chalker, R. and M. Blaser (1988). "A review of human salmonellosis: III. Magnitude of *Salmonella* infection in the United States [review]." Rev Infect Dis **10**: 111-24.

Chatfield, S., L. J. L. Li, et al. (1992). Salmonella genetics and vaccine development. Molecular Biology of Bacteria Infections: Current Status and Future Perspectives. C. E. Hoermache, C. W. Penn and C. J. Smyth. Cambridge, Cambridge University Press**:** 299-312.

Chee-Sanford, J. C., R. I. Aminov, et al. (2001). "Nucleotide occurrence and diversity of tetracycline resistance genes in lagoons and groundwater underlying two swine production facilities." App Environ Microbiol **67**(4): 1494-1502.

Chiew, Y.-F., S.-F. Yeo, et al. (1998). "Can susceptibility to an antimicrobial be restored by halting its use? The case of streptomycin versus Enterobacteriaceae." J Antimicrob Chemother **41**: 247-51.

Clark, R. C. and C. L. Gyles (1993). *Salmonella*. Pathogenesis of Bacterial Infection in Animals, 2nd edition. C. L. Gyles and C. O. Thoen. Ames, IA, Iowa State University Press**:** 133-153.

Cody, S., S. Abbott, et al. (1999). "Two outbreaks of multidrug resistant Salmonella serotype typhimurium DT104 infections linked to raw-milk cheese in Northern California." JAMA **281**: 1805-10.

Coe, N. and R. L. Wood (1991). "The effect of exposure to a cya/crp mutant of *Salmonella typhimurium* on the subsequent colonization of swine by the wild-type parent strain." Veterinary Microbiology **31**: 207-220.

Cohen, M. (1992). "Epidemiology of drug resistance: implications for a post-antimicrobial era [review]." Science **257**: 1050-5.

Cohen, M. and R. Tauxe (1986). "Drug resistant Salmonella in the United States: An epidemiological perspective." Science **234**: 964-9.

Collis, C. and R. Hall (1992). "Gene cassettes from the insert region of integrons are excised as covalently closed circles." Mol Microbiol **6**: 2875-85.

Committee on the Institutional Means for Assessment of Risks to Public Health Commission on Life Sciences National Research Council (1983). Risk Assessment in the Federal Government: Managing the Process. Washington, D.C., National Academy Press.

Cooksey, D. and H. Azad (1992). "Accumulation of copper and other metals by copper-resistant plant pathogenic and saprophytic pseudomonads." Appl Environ Microbiol **58**: 274-8.

Coque, T., J. Tomayko, et al. (1996). "Vancomycin-resistant enterococci from nosocomial, community and animal sources in the United States." Antimicrob Agents Chemother **40**: 2605-9.

Corpet, D. (1993). "Antibiotic resistance from food [letter]." N Engl J Med **318**: 1206-7.

Cote, S., J. Harel, et al. (1991). "Resistance to antimicrobial agents and prevalence of R plasmids in *Pasteurella multocida* from swine." Am J Vet Res **52**(10): 1653-1657.
Twenty-nine field isolates of porcine Pasteurella multocida were characterized for their capsular and somatic types and were evaluated for their susceptibility to 10 antimicrobial agents. Plasmid DNA-screening experiments were conducted to determine whether a relationship existed between the presence of plasmids and antibiotic resistance. Field isolates of P multocida were susceptible to most of the antimicrobials tested, but all isolates were resistant to clindamycin. Eleven isolates of serogroup D were resistant to 1 or 2 antimicrobial agents. Resistance to sulfonamides and streptomycin was observed in 7 isolates. These isolates contained R plasmids conferring resistance to streptomycin and sulfonamides. The R plasmids belonged to 2 groups, one of 5.6 kilobase and the other of 5.9 kilobase. Restriction endonuclease mapping and DNA hybridization revealed that these R plasmids were related to RSF1010 from Salmonella panama, which also confers resistance to streptomycin and sulfonamides.

Courvalin, P. (1996). "Molecular and epidemiologic aspects of the resistance to antibiotics: example of glycopeptides on enterococci." C R Seances Soc Biol Fil **190**(4): 467-9.
The emergence of glycopeptide resistance in enterococci results in a severe clinical problem. Efforts to limit the spread of glycopeptide- resistant enterococci are now considered essential. The many ways in which the resistant strains can disseminate, both in the community and in hospitals, are a source of difficulty in reaching that goal.

Cox, L. and D. Popken (*in press*). "A simulation model of human health risks from chicken-borne *Campylobacter jejuni*." Technology.

Cox, N. A., J. S. Bailey, et al. (1990). "Presence and impact of Salmonella contamination in commercial broiler hatcheries." Poult Sci **69**: 1606-9.

Cunningham-Rundles, S., S. Ahrne, et al. (2000). "Probiotics and immune response." American Journal of Gastroenterology **95**: S22-S25.

Curtiss, R., III and S. M. Kelly (1987). "*Salmonella typhimurium* deletion mutants lacking adenylate cyclase and cyclic AMP receptor protein are avirulent and immunogenic." Infection and Immunity **55**: 3025-3043.

Dahl, K. H., G. S. Simonsen, et al. (1999). "Heterogeneity in the vanB gene cluster of genomically diverse clinical strains of vancomycin-resistant enterococci." Antimicrob Agents Chemother **43**(5): 1105-10.
Molecular analysis of 17 genomically unrelated clinical VanB-type vancomycin-resistant enterococcus isolates from hospital patients in Germany, Norway, Sweden, the United Kingdom and the United States revealed three subtypes of the vanB gene cluster-vanB1, vanB2, and vanB3-which was in accordance with previous subtyping of the ligase gene sequence. There was no correlation between vanB subtype and levels of vancomycin resistance. All strains studied carried a structurally conserved vanB gene cluster as shown by long-range PCR (long PCR) covering 5,959

bp of the published sequence in vanB1 strain V583. Restriction analysis of long PCR amplicons displayed one unique vanB1 pattern and a second vanB2- and vanB3-specific pattern. The vanSB-vanYB intergenic sequences with flanking coding regions were identical within each vanB subtype with one exception. A U.S. vanB2 isolate had a 789-bp enlargement of this region containing a putative open reading frame (ORF) with substantial homology to an ORF in the Clostridium perfringens IS1469 insertion element. The molecular heterogeneity within the vanB gene cluster has implications for the selection of PCR primers, as the primers must ensure detection of all vanB subtypes, and is of importance when considering reservoirs and dissemination of vanB resistance. The molecular identity within the vanB1 and the vanB2 subtype indicates horizontal transmission of both gene clusters between isolates in different geographical areas. Restriction analysis of long PCR vanB amplicons may reveal specific varieties that can be used as epidemiological markers for mobile determinants conferring VanB-type resistance. The finding of three distinct vanB gene clusters should encourage a search for different environmental reservoirs of vanB resistance determinants.

Dargatz, D. A., P. J. Fedorka-Cray, et al. (*in press*). "Survey of *Salmonella* serotypes shed in feces of beef cows and their antimicrobial susceptibility patterns." Am J Vet Res.

Daughton, C. and T. Ternes (1999). "Pharmaceuticals and personal care products in the environment: agents of subtle change?" Environ Health Perspect **107 [suppl 6]**: 907-38.

Davies, J. (1997). Origins, acquisition and dissemination of antibiotic resistance determinants. Antibiotic resistance: Origins, evolution, selection and spread. D. Chadwick and J. Goode. New York, John Wiley & Sons**:** 15-27.

Davies, J. E. (1997). Antibiotic resistance: origins, evolution, selection and spread. Ciba Foundation Symposium, London, John Wiley and Sons, Ltd.

Davies, R. H. and C. Wray (1997). Distribution of *Salmonella* on 23 pig farms in the UK. Proceedings of the 2nd International Symposium on Epidemiology and Control of Salmonella in Pork. Copenhagen, Denmark, 20-22 August**:** 137-141.

Dawson, K. A., B. E. Langlois, et al. (1984). "Antibiotic resistance in anaerobic and coliform bacteria from the intestinal tract of swine fed therapeutic and subtherapeutic concentrations of chlortetracycline." J Anim Sci **58**: 123-31.

de Vries, J., P. Meier, et al. (2001). "The natural transformation of the soil bacteria Pseudomonas stutzeri and Acinetobacter sp. by transgenic plant DNA strictly depends on homologous sequences in the recipient cells." FEMS Microbiol Lett **195**: 211-5.

DeSchrijver, R., A. Moreels, et al. (1990). "Supplementing salinomycin to diets for growing-finish." DTW Dtsch Tierarztl Wochenschr **97**(12): 520-523.

Devriese, L., M. Ieven, et al. (1996). "Presence of vancomycin-resistant enterococci in farm and pet animals." Antimicrob Agents Chemother **40**: 2285-7.

Dewey, C. E., B. D. Cox, et al. (1997). "Associations between off-label feed additives and farm size, veterinary consult use, and animal age." Prev Vet Med **31**: 133-46.

Dewey, C. E., B. D. Cox, et al. (1999). "Use of antimicrobials in swine feeds in the United States." Swine Health and Production **7**(1): 19-25.

Dhakephalkar, P. and B. Chopade (1994). "High levels of multiple metal resistance and its correlation to antibiotic resistance in environmental isolates of *Acinetobacter*." BioMetals **7**: 67-74.

Doern, G. V., M. A. Pfaller, et al. (1998). "Prevalence of antiimicrobial resistance among respiratory tract isolates of *Streptococcus pneumoniae* in North America: 1997 results from the SENTRY antimicrobial surveillance program." Clin Infect Dis **27**: 764-70.

Donskey, C., T. Chowdhry, et al. (2000). "Effect of antibiotic therapy on the density of vancomycin-resistant enterococci in the stool of colonized patients." N Engl J Med **343**: 1925-32.

Donskey, C. J., T. K. Chowdhry, et al. (2000). "Effect of antibiotic therapy on the density of vancomycin-resistant enterococci in the stool of colonized patients." N Engl J Med **343**(26): 1925-32.
BACKGROUND: Colonization and infection with vancomycin-resistant enterococci have been associated with exposure to antibiotics that are active against anaerobes. In mice that have intestinal colonization with vancomycin-resistant enterococci, these agents promote high- density colonization, whereas antibiotics with minimal antianaerobic activity do not. METHODS: We conducted a seven-month prospective study of 51 patients who were colonized with vancomycin-resistant enterococci, as evidenced by the presence of the bacteria in stool. We examined the density of vancomycin-resistant enterococci in stool during and after therapy with antibiotic regimens and compared the effect on this density of antianaerobic agents and agents with minimal antianaerobic activity. In a subgroup of 10 patients, cultures of environmental specimens (e.g., from bedding and clothing) were obtained. RESULTS: During treatment with 40 of 42 antianaerobic- antibiotic regimens (95 percent), high-density colonization with vancomycin-resistant enterococci was maintained (mean [+/-SD] number of organisms, 7.8+/-1.5 log per gram of stool). The density of colonization decreased after these regimens were discontinued. Among patients who had not received antianaerobic antibiotics for at least one week, 10 of 13 patients who began such regimens had an increase in the number of organisms of more than 1.0 log per gram (mean increase, 2.2 log per gram), whereas among 10 patients who began regimens of antibiotics with minimal antianaerobic activity, there was a mean decrease in the number of enterococci of 0.6 log per gram (P=0.006 for the difference between groups). When the density of vancomycin-resistant enterococci in stool was at least 4 log per gram, 10 of 12 sets of cultures of environmental specimens had at least one positive sample, as compared with 1 of 9 sets from patients with a mean number of organisms in stool of less than 4 log per gram (P=0.002). CONCLUSIONS: For patients with vancomycin-resistant enterococci in stool, treatment with antianaerobic antibiotics promotes high-density colonization. Limiting the use of such agents in these patients may help decrease the spread of vancomycin-resistant enterococci.

Dowson, C., T. Coffey, et al. (1994). "Origin and molecular epidemiology of penicillin-binding protein-mediated resistance to beta-lactam antibiotics." Trends Microbiol **2**: 361-6.

Drasar, B. and M. Hill (1974). Human intestinal flora. New York, Academic Press.

Dubois, R., R. W. Scheduler, et al. (1965). "Indigenous, normal, and autochthonous flora of the

gastrointestinal tract." J Exp Med **122**: 67-76.

Dunlop, R. H., S. A. McEwen, et al. (1998). "Associations among antimicrobial drug treatments and antimicrobial resistance of fecal *Escherichia coli* of swine of 34 farrow to finish farms in Ontario, Canada." Prev Vet Med **34**: 283-305.

Dunlop, R. H., S. A. McEwen, et al. (1998). "Antimicrobial drug use and related management practices among Ontario swine producers." Canadian Veterinary Journal **39**: 87-96.

Dunne, E., P. Fey, et al. (2000). "Emergence of domestically acquired ceftriaxone-resistant Salmonella infections associated with AmpC beta-lactamase." JAMA **284**: 3151-6.

Dunne, E., P. Fey, et al. (2000). "Emergence of domestically acquired ceftriaxone-resistant Salmonella infections associated with AmpC beta-lactamase." JAMA **284**: 3151-6.

DuPont, H. and J. Steele (1987). "Use of antimicrobial agents in animal feeds: implications for human health." Rev Infect Dis **9**: 447-60.

Ebner, P. D. and A. G. Mathew (2000). "Effects of antibiotic regimens on the fecal shedding patterns of pigs infected with *Salmonella Typhimurium*." J Food Prot **63**(6): 709-14.

Edel, W., P. Guinee, et al. (1967). "*Salmonella* infection in pigs fattened with pellets and unpelleted meal." Zentralblatt fur Veterinarian mediznie **14**: 393-401.

Effler, P., M. Ieong, et al. (2001). "Sporadic Campylobacter jejuni infections in Hawaii: associations with prior antibiotic use and commercially prepared chicken." J Infect Dis **183**: 1152-5.

Eliopoulos, G. M., C. B. Wennersten, et al. (1998). "Characterization of vancomycin-resistant *Enterococcus faecium* isolates from the United States and their susceptibility in vitro to dalfopristin-quinupristin." Antimicrob Agents Chemother **42**: 1088-92.

Emborg, H.-D., A. K. Ersboll, et al. (2001). "The effect of discontinuing the use of antimicrobial growth promoters on productivity in Danish broiler production." Prev Vet Med **50**: 53-70.

Endtz, H. P., G. J. Ruijs, et al. (1991). "Quinolone resistance in *campylobacter* isolated from man and poultry following the introduction of fluoroquinolones in veterinary medicine." J Antimicrob Chemother **27**: 199-208.

Enne, V. I., D. M. Livermore, et al. (2001). "Persistence of sulphonamide resistance in *Escherichia coli* in the U.K. despite national prescribing restriction." Lancet **357**: 1325-8.

Environmental Protection Agency (EPA) (1992). R.E.D. Facts: Streptomycin and streptomycin sulfate, U.S. Environmental Protection Agency**:** 5.

Environmental Protection Agency (EPA) (1993). R.E.D. Facts: Hydroxytetracycline monohydrochloride and oxytetracycline calcium, U.S. Environmental Protection Agency**:** 5.

Erskine, R. J. (2000). Antimicrobial drug use in bovine mastitis. Antimicrobial therapy in veterinary medicine, 3rd edition. J. F. Prescott, J. D. Baggot and R. D. Walker. Ames, IA, Iowa State University Press**:** 712-34.

European Commission (2001). Commission regulation of amending council directive 70/524/EEC concerning additivies to feeding stuffs as regards withdrawal of the authorization of certain antibiotics. Brussels, Belgium, European Commission, Brussels, Belgium.

Evangelisti, D. G., A. R. English, et al. (1975). "Influence of subtherapeutic levels of oxytetracycline on *Salmonella typhimurium* in swine, calves, and chickens." Antimicrob Agents Chemother **8**: 664-72.

Evers, S., B. Casadewall, et al. (1996). "Evolution of structure and substrate specificity in D-alanine:D-alanine ligases and related enzymes." J Mol Evol **42**(6): 706-12.
The D-alanine:D-alanine-ligase-related enzymes can have three preferential substrate specificities. Usually, these enzymes synthesize D-alanyl-D-alanine. In vancomycin-resistant Gram-positive bacteria, structurally related enzymes synthesize D-alanyl-D-lactate or d-alanyl- d-serine. The sequence of internal fragments of eight structural d- alanine:d-alanine ligase genes from enterococci has been determined. Alignment of the deduced amino acid sequences with those of other related enzymes from Gram-negative and Gram-positive bacteria revealed the presence of four distinct sequence patterns in the putative substrate-binding sites, each correlating with specificity to a particular substrate (D-alanine:D-lactate ligases exhibited two patterns). Phylogenetic analysis showed different clusters. The enterococcal subtree was largely superimposable on that derived from 16S rRNA sequences. In lactic acid bacteria, structural divergence due to differences in substrate specificity was observed. Glycopeptide resistance proteins VanA and VanB, the VanC-type ligases, and DdlA and DdlB from enteric bacteria and Haemophilus influenzae constituted separate clusters.

Exponent (2000). Effect of the use of antimicrobials in food-producing animals on pathogen load: systematic review of the published literature. Rockville, MD, Center for Veterinary Medicine, Food and Drug Administration.

Fales, W. H., L. G. Morehouse, et al. (1989). "Antimicrobial susceptibility and serotypes of *Actinobacillus (Haemophilus) pleuropneumoniae* recovered from Missouri swine." J Vet Diagn Invest **1**(1): 16-19.

Famularo, G., S. Moretti, et al. (1997). Stimulation of immunity by probiotics. Probiotics 2: Applications and practical aspects. R. Fuller. London, Chapman and Hill**:** 133-61.

Fedorka-Cray, P. J., J. S. Bailey, et al. (1999). "Mucosal competitive exclusion to reduce *Salmonella* in swine." J Food Prot **62**: 1376-1380.

Fedorka-Cray, P. J., A. Hogg, et al. (1997). "Feed trucks as a source of *Salmonella* contamination." Swine Health and Production **5**: 189-193.

Fedorka-Cray, P. J., L. C. Kelley, et al. (1995). "Alternate routes of invasion may affect pathogenesis of *Salmonella typhimurium* in swine." Infect Immun **63**: 2658-64.

Fedorka-Cray, P. J., L. C. Kelley, et al. (1995). "Alternate routes of invasion may affect the pathogenesis of *Salmonella typhimurium* in swine, calves, and chickens." Antimicrob Agents Chemother **8**: 664-672.

Fedorka-Cray, P. J., S. Ladely, et al. (2001). "Colonization of broiler chickens by *S.* Typhimurium definite phage type 104." J Food Prot **11**: 1698-1704.

Fey, P., T. Safranek, et al. (2000). "Ceftriaxone-resistant Salmonella infection acquired by a child from cattle." N Engl J Med **342**: 1242-9.

Finegold, S. M., V. Sutter, et al. (1983). Normal indigenous intestinal flora. Human Intestinal Microflora in Health and Disease. D. Hentges. New York, Academic Press**:** 3-32.

Fiorentino, T., Rossiter, et al. (2000). Phage type and antimicrobial resistance trends among human Salmonella serotype Typhimurium isolates in NARMS 1997-1998; continued dominance of DT-104 R-type ACSSu T. International Conference on Emerging Infectious Diseases 2000, Atlanta, GA.

Fish, N., M. Finlayson, et al. (1967). "Salmonellosis: report of a human case following direct contact with infected cattle." Can Med Assoc J **96**: 1163-5.

Food and Drug Administration Center for Veterinary Medicine (1998). A proposed framework for evaluating and assuring the human safety of the microbial effects of antimicrobial new animal drugs intended for use in food-producing animals, Food and Drug Administration Center for Veterinary Medicine.

Food and Drug Administration Center for Veterinary Medicine (1999). Consideration of the Human Health Impact of the Microbial Effects of Antimicrobial New Animal Drugs Intended for Use in Food-Producing Animals, Food and Drug Administration. **2001**.

Food and Drug Administration Center for Veterinary Medicine (2000). An approach for establishing thresholds in association with the use of antimicrobial drugs in food-producing animals, Food and Drug Administration Center for Veterinary Medicine.

Food and Drug Administration Center for Veterinary Medicine (2001). Human Health Impact of Fluoroquinolone Resistant *Campylobacter* Attributed to Consumption of Chicken, Food and Drug Administration, Center for Veterinary Medicine. **2001**.

Frebourg, N., B. Cauliez, et al. (1999). "Evidence for nasal carriage of methicillin-resistant staphylococci colonizing intravascular devices." J Clin Microbiol **37**: 1182-5.

Freifelder, D. (1987). Microbial Genetics. Boston, Jones and Barlett Publishers, Inc.

Friendship, R. (2000). Antimicrobial drug use in swine. Antimicrobial therapy in veterinary medicine. J. F. Prescott, J. D. Baggot and R. D. Walker. Ames, IA, Iowa State University Press**:** 602-16.

Frost, D., L. Overby, et al. (1955). "Studies with arsanilic acid and related compounds." J Agric

Food Chem **3**: 235-43.

Garau, J., M. Xercavins, et al. (1999). "Emergence and dissemination of quinolone-resistant Escherichia coli in the community." Antimicrob Agents Chemother **43**(11): 2736-41.

Gaudreau, C. and H. Gilbert (1998). "Antimicrobial resistance of clinical strains of *Campylobacter jejuni* subsp. *jejuni* isolated from 1985 to 1997 in Quebec, Canada." Antimicrob Agents Chemother **42**: 2106-8.

Gaunt, P. and L. Piddock (1996). "Ciprofloxacin resistant Campylobacter spp. in humans: an epidemiological and laboratory study." J Antimicrob Chemother **37**: 747-57.

Gebhard, F. and K. Smalla (1998). "Transformation of *Acinetobacter* sp. strain BD413 by transgenic sugar beet DNA." Appl Environ Microbiol **64**: 1550-5.

Genovese, K. J., R. C. Anderson, et al. (2000). "Competitive exclusion treatment reduces the mortality and fecal shedding associated with enterotoxigenic *Escherichia coli* infection in nursery-raised neonatal pigs." Can J Vet Res **64**(4): 204-7.

Glynn, M. K., C. Bopp, et al. (1998). "Emergence of multidrug-resistant *Salmonella enterica* serotype typhimurium DT104 infections in the United States." N Engl J Med **338**: 1333-8.

Goni-Urriza, M., M. Capdepuy, et al. (2000). "Impact of an urban effluent on antibiotic resistance of riverine *Enterobacteriaceae* and *Aeromonas* spp." Appl Environ Microbiol **66**: 125-32.

Gootz, T. and B. Martin (1991). "Characterization of high-level quinolone resistance in *Campylobacter jejuni*." Antimicrob Agents Chemother **35**: 840-5.

Gorbach, S. L. (2000). "Probiotics and gastrointestinal health." American Journal of Gastroenterology **95**: S2-S4.

Goren, E. W., A. deJong, et al. (1988). "Reduction of *Salmonella* infection of broiler by spray application of intestinal microflora: a longitudinal study." Vet Q **10**: 249-255.

Gray, J. and P. Fedorka-Cray (2001). "Survival and infectivity of *Salmonella choleraesuis* in swine feces." J Food Prot **64**: 945-9.

Gray, J. T., P. J. Fedorka-Cray, et al. (1995). "Influence of inoculation route on the carrier state of *Salmonella choleraesuis* in swine." Vet Microbiol **47**(1-2): 43-59.

Gray, J. T., P. J. Fedorka-Cray, et al. (1996). "Natural transmission of *Salmonella choleraesuis* in swine." Appl Environ Microbiol **62**(1): 141-6.

Gray, J. T., T. J. Stabel, et al. (1996). "Effect of dose on the immune response and persistence of *Salmonella choleraesuis* infection in swine." Am J Vet Res **57**(3): 313-9.

Grecko, C. (2000). Sweden and the European union: what is happening in relation to antibiotics in feed? Annual Conference proceedings of Australian Veterinarians in Industry and Australian

Veterinarians in Public Health, Perth, Western Australia, Australian Veterinary Association Annual Conference.

Greene, C. (2000). U.S. organic agriculture gaining ground. Agricultural Outlook, USDA Economic Research Service**:** 9-14.

Guardabassi, L., A. Petersen, et al. (1998). "Antibiotic resistance in *Acinetobacter* spp. isolated from sewers receiving waste effluent from a hospital and a pharmaceutical plant." Appl Environ Microbiol **64**: 3499-502.

Guinee, P. (1965). "Transfer of multiple drug resistance from *Escherichia coli* to *Salmonella typhi murium* in the mouse intestine." Antonie van Leeuwenhoek **31**: 314-22.

Guinee, P., N. Ugueto, et al. (1970). "*Escherichia coli* with resistance factors in vegetarians, babies, and non-vegetarians." Appl Microbiol **20**: 531-5.

Guthrie, R. K. (1992). *Salmonella*. Boca Raton, FL, CRC Press, Inc.

Hagedorn, C., S. Robinson, et al. (1999). "Determining sources of fecal pollution in a rural Virginia watershed with antibiotic resistance patterns in fecal streptococci." Appl Environ Microbiol **65**: 5522-31.

Hald, B. and M. Madsen (1997). "Healthy puppies and kittens as carriers of Campylobacter spp., with special reference to *Campylobacter upsaliensis*." J Clin Microbiol **35**: 3351-2.

Hall, R. and C. Collis (1995). "Mobile gene casettes and integrons, capture and spread of genes by site-specific recombination." Molecular Microbiology **15**: 593-600.

Hall, R. and H. Stokes (1993). "Integrons: novel DNA elements which capture genes by site-specific recombination [review]." Genetica **90**: 115-32.

Halling-Sorenson, B., S. N. Nielsen, et al. (1998). "Occurrence, fate, and effects of pharmaceutical substances in the environment -- a review." Chemosphere **36**: 357-93.

Hammerum, A. M., L. B. Jensen, et al. (1998). "Detection of the satA gene and transferability of virginiamycin resistance in *Enterococcus faecium* from food-animals." FEMS Microbiol Lett **168**: 145-51.

Harris, I. T., P. J. Fedorka-Cray, et al. (1997). "Prevalence of *Salmonella* organisms in swine feed." J Am Vet Med Assoc **210**: 382-5.

Hartmann, A., A. C. Adler, et al. (1998). "Identification of fluoroquinolone antibiotics as the main source of *umuC* genotoxicity in native hospital wastewater." Environmental Toxicology and Chemistry **17**: 377-382.

Hartmann, F. A. and S. E. West (1995). "Antimicrobial susceptibility profiles of multidrug-resistant *Salmonella anatum* isolated from horses." J Vet Diagn Invest **7**: 159-61.

Harwood, V., J. Whitlock, et al. (2000). "Classification of antibiotic resistance patterns of indicator bacteria by discriminant analysis: use in predicting the source of fecal contamination in subtropical waters." Appl Environ Microbiol **66**: 3698-704.

Hayes, D. J., H. H. Jensen, et al. (1999). Economic impact of a ban on the use of over-the-counter antibiotics in U.S. swine rations. Ames, IA, Center for Agricultural and Rural Developement, Iowa State University.

Heinemann, J., R. Ankenbauer, et al. (2000). "Do antibiotics maintain antibiotic resistance?" Drug Discov Today **5**: 195-204.

Henzler, D. J. and H. M. Opitz (1992). "The role of mice in the epizootiology of *Salmonella enteritidis* infection on chicken layer farms." Avian Dis **36**: 625-31.

Herwig, R., J. Gray, et al. (1997). "Antibacterial resistant bacteria in surficial sediments near salmon net-cage farms in Puget Sound, Washington." Aquaculture **149**: 263-83.

Hird, D., D. Casebold, et al. (1986). "Risk factors for salmonellosis in hospitalized horses." JAVMA **188**(2): 173-7.

Hirsch, R., T. Ternes, et al. (1999). "Occurrence of antibiotics in the aquatic environment." Sci Total Environ **225**: 109-18.

Holcomb, H. L. (1997). Antibiotic resistance of *Salmonella* in Swine. Ames, IA, Iowa State University.

Holmberg, S., M. Osterholm, et al. (1984). "Drug-resistant Salmonella from animals fed antimicrobials." N Engl J Med **311**: 617-22.

Holmberg, S., S. Solomon, et al. (1987). " Health and economic impacts of antimicrobial resistance." J Infect Dis **9**: 1065-78.

Hook, E. W. (1990). *Salmonella* species (including typhoid fever). Principles and practices of infectious diseases. G. L. Mandell, R. G. Douglas and J. E. Bennett. New York, Churchill Livingston**:** 1700-1722.

Hopkins, J. D., T. F. O'Brien, et al. (1988). "Functional and structural map of pLST1000: a multiresistance plasmid widely distributed in *Enterobacteriaceae*." Plasmid **20**(2): 163-6. pLST1000, an 80-kb plasmid found in Enterobacteriaceae in North and South America, harbors the aadB and several other resistance genes. We suggested earlier that, because of its widespread distribution, pLST1000 could act as a carrier plasmid, bringing the aadB gene to new locations. This paper presents the restriction enzyme recognition site and functional map of the plasmid. The resistance genes lie in a discreet region. The aadB and aadA genes form an operon with the aadB gene promoter proximal. This operon is flanked by bla-TEM and bla-OXA2 genes, the former located in a functional Tn3-like transposon. This arrangement is similar to that of relatives of the transposon TN21, where additional resistance genes are precisely inserted in recombinational "hot spot" sequences that flank the aadA gene. We were not able to demonstrate transposition of the aadB gene in Escherichia coli. A sul gene and mer operon lie beyond the bla-OXA2 gene. The

transfer genes form a single region, defined by insertions of Tn5-132 that give the Tra- phenotype.

Hopkins, R., R. Olmstead, et al. (1984). "Epidemic *Camplylobacter jejuni* infection in Colorado: identified risk factors." Am J Public Health **74**: 249-50.

House of Lords (UK) (1998). Resistance to antibiotics and other antimicrobial agents. Seventh report of the House of Lords' Select Committee on Science and Technology: 1997-98. London, The Stationary Office.

Hughes, V. M. and N. Datta (1983). "Conjugative plasmids in bacteria of the 'pre-antibiotic' era." Nature **302**(5910): 725-6.
Antibiotic resistance is common in bacteria that cause disease in man and animals and is usually determined by plasmids. The prevalence of such plasmids, and the range of drugs to which they confer resistance, have increased greatly in the past 25 yr. It has become clear from work in many laboratories that plasmids have acquired resistance genes, of ultimately unknown origin, as insertions into their circular DNA. The intensive use of antibiotics since their introduction in the 1940s can explain the spread of plasmids that have acquired such genes but little is known of the incidence of plasmids in pathogenic bacteria before the widespread use of antibiotics in medicine. E.D.G. Murray collected strains of Enterobacteriaceae from 1917 to 1954; we now report that 24% of these encode information for the transfer of DNA from one bacterium to another. From at least 19% of the strains, conjugative plasmids carrying no antibiotic resistance were transferred to Escherichia coli K-12.

Hummel, R., H. Tschape, et al. (1986). "Spread of plasmid-mediated nourseothricin resistance due to antibiotic use in animal husbandry." J Basic Microbiol **26**: 461-6.

Humphrey, T. J., A. Henley, et al. (1993). "The colonization of broiler chickens with *Campylobacter jejuni*: some epidemiological investigations." Epidemiol Infect **110**: 601-7.

Ikeda, K. and S. Umezawa (1999). Aminoglycoside antibiotics. Naturally occuring glycosides. R. Ikan. Chichester, England, John Wiley**:** 1-42.

Institute of Medicine (1989). The Effects on Human Health of Subtherapeutic Use of Antimicrobials in Animal Feeds. Washington, DC, National Academy Press.

Institute of Medicine (IOM) (1989). Human Health Risks with the Subtherapeutic Use of Penicillin or Tetracyclines in Animal Feeds. Washington, DC, National Academy Press.

Jacob-Rietsma, W. (1994). Epidemiology of *Campylobacter* in poultry. PhD dissertation at Landbouwuniversiteit Wageningen, Switzerland.

Jacob-Rietsma, W., C. A. Kan, et al. (1994). "The induction of quinolone resistance in *Campylobacter* bacteria in broilers by quinolone treatment." Letters of Applied Biology **19**: 228-31.

Jensen, L. B. (1998). "Differences in the occurrence of two base pair variants of Tn1546 from vancomycin-resistant enterococci from humans, pigs, and poultry [letter]." Antimicrob Agents Chemother **42**(9): 2463-4.

Jensen, L. B., P. Ahrens, et al. (1998). "Molecular analysis of Tn1546 in *Enterococcus faecium* isolated from animals and humans." J Clin Microbiol **36**(2): 437-42.
The internal areas and the position of integration of the glycopeptide resistance element Tn1546 were characterized by using PCR fragment length polymorphism, sequencing, and DNA hybridization techniques with 38 high-level vancomycin-resistant Enterococcus faecium isolates of human and animal origins from Europe and the United States. Only minor variations in the coding regions within Tn1546 were found, suggesting high genetic stability. The isolates originated from broilers (n = 5), a chicken (n = 1), a duck (n = 1), a turkey (n = 1), pigs (n = 8), a pony (n = 1), and humans (n = 23). A total of 13 different types were defined based on a single-nucleotide difference in the vanX gene, the presence of insertion sequences, and hybridization patterns. For some types more than one isolate were found. For type 1, 10 isolates of both human and animal origins were found. All were indistinguishable from the reference strain, BM4147. For type 2, 11 isolates of human and animal origins were found. Six human isolates from England were all of type 3. Two human isolates from the United States, indistinguishable from each other, were type 9. These results showed that vancomycin- resistant E. faecium of animal and human origins can contain indistinguishable genetic elements coding for vancomycin resistance, indicating either horizontal gene transfer between E. faecium organisms of human and animal origins or the existence of a common reservoir for glycopeptide resistance.

Johnson, K., N. Marano, et al. (2000). The antimicrobial resistance patterns of Escherichia coli 0157:H7 --- NARMS, 1996-1999. International Conference on Emerging Infectious Diseases 2000, Atlanta, GA.

Johnson, K. and V. Stockwell (1998). "Management of fire blight: a case study in microbial ecology." Annu Rev Phytopathol **36**: 227-48.

Joint Expert Technical Advisory Committee on Antibiotic Resistance (JETACAR) (1999). The use of antibiotics in food-producing animals: antibiotic-resistant bacteria in animals and humans. Canberra, Australia, Commonwealth Department of Health and Aged Care and Commonwealth Department of Agriculture, Fisheries and Forestry-- Australia.

Jones, A. (1982). Chemical control of phytopathogenic prokaryotes. Phytopathogenic prokaryotes. M. Mount and G. Lacy. NY, Academic Press**:** 399-414.

Joyce, K., P. Mahar, et al. (2000). Emergence of a multidrug-resistance strain of Salmonella serotype Newport in the United States: NARMS 1997-1999. International Conference on Emerging Infectious Diseases 2000, Atlanta, GA.

Jukes, T. (1986). "Effects of low levels of antibiotics in livestock feed." Effects of Antibiotics in Livestock Feeds **10**: 112-126.

Kaneene, J. B. and R. Miller (1992). "Description and evaluation of the influence of veterinary presence on the use of antibiotics and sulfonamides in dairy herds." JAVMA **201**(1): 68-76.

Kapperud, G., E. Skjerve, et al. (1992). "Risk factors for sporadic *Campylobacter* infections: results of a case-control study in southeastern Norway." J Clin Microbiol **30**: 3117-21.

Kashuba, A., A. Nafziger, et al. (1999). "Optimizing aminoglycoside therapy for nosocomial pneumonia caused by gram-negative bacteria." Antimicrob Agents Chemother **43**: 623-9.

Kassenborg, H., K. Smith, et al. (July, 2000). Eating chicken or turkey outside the home associated with domestically acquired fluoroquinolone-resistant campylobacter infections: a FoodNet case-control study. International Conference on Emerging Infectious Diseases 2000, Atlanta, GA.

Kelch, W. J. and J. S. Lee (1978). "Antibiotic resistance patterns of gram-negative bacteria isolated from environmental sources." Appl Environ Microbiol **36**: 450-6.

Kelch, W. J. and J. C. New (1993). "The reported use of drugs to prevet diseases in beef cattle in Tennessee." Prev Vet Med **15**: 291-302.

Kelly, J., O. Dideberg, et al. (1986). "On the origin of bacterial resistance to penicillin: comparison of a beta-lactamase and a penicillin target." Science **231**: 1429-31.

Kelly, S. M., B. A. Bosecker, et al. (1992). "Characterization and protective properties of attenuated mutants of *Salmonella choleraesuis*." Infection and Immunity **60**: 4881-4890.

Khachatourians, G. G. (1998). "Agricultural use of antibiotics and the evolution and transfer of antibiotic-resistant bacteria." CMAJ **159**: 1129-36.

Kirst, H., D. Thompson, et al. (1998). "Historical yearly usage of vancomycin [letter]." Antimicrob Agents Chemother **42**: 1303-4.

Klare, I., D. Badstubner, et al. (1999). "Decreased incidence of VanA-type vancomycin-resistant enterococci isolated from poultry meat and from fecal samples of humans in the community after discontinuation of avoparcin usage in animal husbandry." Microb Drug Resist **5**: 45-52.

Klare, I., H. Heier, et al. (1995). "van A mediated high-level glycopeptide resistance in Enterococcus faecium from animal husbandry." FEMS Microbiol Lett **125**: 165-71.

Kramer, T. T., J. Rhiner, et al. (1994). Comparison of IgG ELISA and bacteriologic diagnosis in experimental swine salmonellosis. Proceedings of the 75th Annual Conference Research Workers in Animal Disease.

Kruse, H., B. K. Johansen, et al. (1999). "The use of avoparcin as a growth promoter and the occurrence of vancomycin-resistant Enterococcus species in Norwegian poultry and swine production." Microb Drug Resist **5**(2): 135-9.
This study documents a strong and statistically significant association between the use of the glycopeptide avoparcin as a growth promoter in Norwegian poultry production and the occurrence of vancomycin-resistant Enterococcus species (VRE). Avoparcin was approved as a feed additive for broilers and turkeys in Norway in 1986 and was banned from June 1, 1995. In a survey conducted in Norway between June, 1995 and March, 1997, VRE were isolated from fecal samples from 106 out of 109 poultry houses previously exposed to avoparcin (97%) and from six out of 33 poultry houses never exposed to avoparcin (18%) (RR = 5.35). Samples from previously exposed poultry houses were collected in three time periods. The proportion of positive samples remained high (96-98%), in all three time periods indicating a persistence of vancomycin resistance among

enterococci for more than a year and a half after the withdrawal of avoparcin. VRE were also isolated from six out of 10 poultry farmers living on farms previously exposed to avoparcin, and from none of 16 farmers living on farms never exposed to avoparcin. Moreover, VRE were isolated from 68 out of the 225 broiler carcasses investigated (30%). The resistance to vancomycin was a high-level type (MIC > or = 256 microg/ml) mediated by the vanA gene. For comparison, VRE could only be isolated from two out of 147 fecal samples from Norwegian flocks of swine (1%). Because avoparcin never has been used in Norwegian swine production, this observation strengthens the association between the use of avoparcin in animal husbandry and the occurrence of VRE.

Lahellec, C. and P. Colin (1985). "Relationship between serotypes of Salmonellae from hatcheries and rearing farms and those from processed poultry carcasses." Br Poult Sci **26**: 179-86.

Langlois, B. E., G. L. Cromwell, et al. (1983). "Antibiotic resistance of fecal coliforms after long-term withdrawal of therpeutic and subtherapeutic antibiotic use in a swine herd." Appl Environ Microbiol **46**: 1433-4.

Langlois, B. E., K. A. Dawson, et al. (1988). "Antimicrobial resistance of fecal coliforms from pigs in a herd not exposed to antimicrobial agents for 126 months." Vet Microbiol **18**: 147-53.

Lawrence, K. (2000). Growth promoters in swine. Proceedings of the 15th IVPS Congress, Birmingham, England, 5-9 July 1998.

Leclercq, R., E. Derlot, et al. (1988). "Plasmid-mediated resistance to vancomycin and teicoplanin in Enterococcus faecium." N Engl J Med **319**: 157-61.

Lee, L., N. Puhr, et al. (1994). "Increase in antimicrobial-resistant Salmonella infections in the United States, 1989-1990." J Infect Dis **170**: 128-34.

Lee, M. D. and J. J. Maurer (2000). "The genetic basis for emerging antibiotic resistance in veterinary pathogens." Annals of the New York Academy of Sciences **916**: 643-645.

Leeson, S. and J. D. Summers (2000). Broiler Breeder Production. Guelph, Ontario, University Books.

Lehnherr, H. and M. Yarmolinsky (1995). "Addiction protein Phd of plasmid prophage P1 is a substrate of the ClpXp serine-protease of *Escherichia coli*." Proc Natl Acad Sci USA **92**: 3274-7.

Lenski, R. E. (1997). The cost of antibiotic resistance-from the perspective of a bacterium. Antibiotic resistance: origins,evolution, selection and spread. D. J. Chadwick and J. Goode. Chicester, John Wiley and Sons. **207:** 93-111.

Lenski, R. E., S. C. Simpson, et al. (1994). "Genetic analysis of a plasmid-encoded, host genotype-specific enhancement of bacterial fitness." J Bacteriol **176**: 3140-7.

Levetin, E. (1997). Aerobiology of agricultural pathogens. Manual of Environmental Microbiology. C. Hurst, G. Knudson, M. McInerney, L. Stetzenbach and M. Walter. Washington, DC, ASM Press**:** 693-702.

Levine, M. M., C. Ferreccio, et al. (1989). "Progress in vaccines against typhoid fever." Review of Infectious Disease **11**: S552-S567.

Levy, S. (1987). "Antibiotic use for growth promotion in animals: ecologic and public health consequences." J Food Prot **50**: 616-20.

Levy, S. (1992). The antibiotic paradox: how miracle drugs are destroying the miracle. NY, Plenum Press.

Levy, S., G. Fitzgerald, et al. (1986). "Changes in intestinal flora of farm personnel after introduction of a tetracycline-supplemented feed on a farm." N Engl J Med **295**: 583-8.

Levy, S., B. Marshall, et al. (1988). "High frequency of antimicrobial resistance in human fecal flora." Antimicrob Agents Chemother **32**: 1801-6.

Levy, S. B. (1998). "The challenge of antibiotic resistance." Sci Am **278**: 46-53.

Levy, S. B., G. B. FitzGerald, et al. (1976). "Spread of antibiotic-resistant plasmids from chicken to chicken and from chicken to man." Nature **260**: 40-42.

Liebert, C., R. Hall, et al. (1999). "Transposon Tn*21*, flagship of the floating genome [review]." Microbiol Mol Biol Rev **63**: 507-22.

Liebert, C. A., R. M. Hall, et al. (1999). "Transposon Tn21, flagship of the floating genome." Microbiol Mol Biol Rev **63**(3): 507-22.
The transposon Tn21 and a group of closely related transposons (the Tn21 family) are involved in the global dissemination of antibiotic resistance determinants in gram-negative facultative bacteria. The molecular basis for their involvement is carriage by the Tn21 family of a mobile DNA element (the integron) encoding a site-specific system for the acquisition of multiple antibiotic resistance genes. The paradigm example, Tn21, also carries genes for its own transposition and a mercury resistance (mer) operon. We have compiled the entire 19,671-bp sequence of Tn21 and assessed the possible origins and functions of the genes it contains. Our assessment adds molecular detail to previous models of the evolution of Tn21 and is consistent with the insertion of the integron In2 into an ancestral Tn501-like mer transposon. Codon usage analysis indicates distinct host origins for the ancestral mer operon, the integron, and the gene cassette and two insertion sequences which lie within the integron. The sole gene of unknown function in the integron, orf5, resembles a puromycin-modifying enzyme from an antibiotic producing bacterium. A possible seventh gene in the mer operon (merE), perhaps with a role in Hg(II) transport, lies in the junction between the integron and the mer operon. Analysis of the region interrupted by insertion of the integron suggests that the putative transposition regulator, tnpM, is the C-terminal vestige of a tyrosine kinase sensor present in the ancestral mer transposon. The extensive dissemination of the Tn21 family may have resulted from the fortuitous association of a genetic element for accumulating multiple antibiotic resistances (the integron) with one conferring resistance to a toxic metal at a time when clinical, agricultural, and industrial practices were rapidly increasing the exposure to both types of selective agents. The compendium offered here will provide a reference point for ongoing observations of related elements in multiply resistant strains emerging worldwide.

Lindow, S., G. McGourty, et al. (1996). "Interactions of antibiotics with Pseudomonas fluorescens strain A506 in the control of fire blight and frost injury of pear." Phytopathology **86**: 841-8.

Ling, J., Y.-W. Hui, et al. (1992). "Development of trimethoprim-resistance in *Salmonella typhi* during therapy." Pathology **24**: 190-3.

Linton, A. H., K. Howe, et al. (1975). "The effects of feeding tetracycline, nitrovin and quindoxin on the drug-resistance of coli-aerogenes bacteria from calves and pigs." J Appl Bacteriol **38**(3): 255-75.

Linton, A. H., N. E. Jennett, et al. (1970). "Multiplication of *Salmonella* in liquid feed and its influence on the duration of excretion in pigs." Res Vet Sci **11**: 452-7.

Linz, B., M. Schenker, et al. (2000). "Frequent interspecific genetic exchange between commensal neisseriae and *Neisseria meningitidis*." Mol Microbiol **36**: 1049-58.

Lipsitch, M., C. Bergstrom, et al. (2000). "The epidemiology of antibiotic resistance in hospitals: paradoxes and prescriptions." Proc Natl Acad Sci USA **97**: 1938-43.

Low, J., G. Hopkins, et al. (1996). "Antibiotic resistant *Salmonella* Typhimurium DT104 in cattle [letter]." Vet Rec **138**: 650-1.

Low, J. C., M. Angus, et al. (1997). "Antimicrobial resistance of *Salmonella enterica Typhimurium* DT104 isolates and investigation of strains with transferable apramycin resistance." Epidemiol Infect **118**: 97-103.

Luby, S., M. Faizan, et al. (1998). "Risk factors for typhoid fever in an endemic setting, Karachi, Pakistan." Epidemiol Infect **120**: 129-38.

Lucey, B., D. Crowley, et al. (2000). "Integronlike structures in *Campylobacter* spp. of human and animal origin." Emerg Infect Dis **6**: 50-5.

Lyons, R., C. Samples, et al. (1980). "An epidemic of resistant Salmonella in a nursery: animal-to-human spread." JAMA **243**: 546-7.

MacDonald, K., M. Cohen, et al. (1987). "Changes in antimicrobial resistance of Salmonella isolated from humans in the United States." JAMA **258**: 1496-9.

Maiden, M. C., J. A. Bygraves, et al. (1998). "Multilocus sequence typing: a portable approach to the identification of clones within populations of pathogenic microorganisms." Proc Natl Acad Sci U S A **95**(6): 3140-5.
Traditional and molecular typing schemes for the characterization of pathogenic microorganisms are poorly portable because they index variation that is difficult to compare among laboratories. To overcome these problems, we propose multilocus sequence typing (MLST), which exploits the unambiguous nature and electronic portability of nucleotide sequence data for the characterization of microorganisms. To evaluate MLST, we determined the sequences of approximately 470-bp fragments from 11 housekeeping genes in a reference set of 107 isolates of Neisseria meningitidis from invasive disease and healthy carriers. For each locus, alleles were assigned arbitrary numbers

and dendrograms were constructed from the pairwise differences in multilocus allelic profiles by cluster analysis. The strain associations obtained were consistent with clonal groupings previously determined by multilocus enzyme electrophoresis. A subset of six gene fragments was chosen that retained the resolution and congruence achieved by using all 11 loci. Most isolates from hyper-virulent lineages of serogroups A, B, and C meningococci were identical for all loci or differed from the majority type at only a single locus. MLST using six loci therefore reliably identified the major meningococcal lineages associated with invasive disease. MLST can be applied to almost all bacterial species and other haploid organisms, including those that are difficult to cultivate. The overwhelming advantage of MLST over other molecular typing methods is that sequence data are truly portable between laboratories, permitting one expanding global database per species to be placed on a World-Wide Web site, thus enabling exchange of molecular typing data for global epidemiology via the Internet.

Manges, A., J. Johnson, et al. (2001). "Widespread distribution of urinary tract infections caused by a multi-drug resistant E. coli clonal group." N Engl J Med **345**(14): 1055-7.

Manulis, S., D. Zutra, et al. (1999). Streptomycin resistance of *Erwinia amylovora* in Israel and occurrence of fire blight in pear orchards in the autumn. VIII International Workshop on Fire Blight, Kusadasi, Turkey, ISHS.

Marano, N., D. Vugia, et al. (2000). Fluoroquinolone-resistant *Campylobacter* causes longer duration of diarrhea than fluoroquinolone-susceptible *Campylobacter* strains in FoodNet sites. International Conference on Emerging Infectious Disease, Atlanta, GA.

Marshall, B., D. Petrowski, et al. (1990). "Inter-and intraspecies spread of *Escherichia coli* in a farm environment in the absence of antibiotic usage." Proc Natl Acad Sci USA **87**: 6609-13.

Marshall, B., C. Tachibana, et al. (1983). "Frequency of tetracycline resistance determinant classes among lactose-fermenting coliforms." Antimicrob Agents Chemother **24**: 835-40.

Martel, J. and M. Coudert (1993). "Bacterial resistance monitoring in animals: the French national experiences of surveillance schemes." Vet Microbiol **35**: 321-38.

Marteniuk, J. V., A. S. Ahl, et al. (1988). "Compliance with recommended drug withdrawal requirements for dairy cows sent to market in Michigan." JAVMA **193**(4): 404-407.

Martone, W. J. (1998). "Spread of vancomycin-resistant enterococci: why did it happen in the United States?" Infect Control Hosp Epidemiol **19**(8): 539-45.
The question of why vancomycin-resistant enterococci (VRE) became epidemic in the United States can be answered on at least three basic levels: (1) molecular and genetic, (2) factors affecting host-microbe interactions, and (3) epidemiological. This article will address the epidemiological issues and seek to defend the assertion that, once VRE had evolved, its spread throughout hospitals in the United States was all but assured. Nosocomial VRE outbreaks were reported first in the mid- and late-1980s. Since that time, scientific reports of VRE have increased over 20-fold. Among hospitals participating in the National Nosocomial Infection Surveillance System from 1989 to 1997, the percentage of enterococci reported as resistant to vancomycin increased from 0.4% to 23.2% in intensive-care settings and from 0.3% to 15.4% in non-intensive-care settings. Factors leading to the spread of VRE in US hospitals include (1) antimicrobial pressure, (2) sub-optimal

clinical laboratory recognition and reporting, (3) unrecognized "silent" carriage and prolonged fecal carriage, (4) environmental contamination and survival, (5) intrahospital and interhospital transfer of colonized patients, (6) introduction of unrecognized carriers from community settings such as nursing homes, and (7) inadequate compliance with hand washing and barrier precautions. Guidelines developed by the Centers for Disease Control and Prevention's Hospital Infection Control Practices Advisory Committee address each of these factors. The impact of these guidelines on the spread of VRE within individual institutions has been variable, and the overall impact of the guidelines nationally is unknown.

Marx, M. (1969). "The effect of interspecies contact upon diarrhea morbidity and salmonellosis in children." J Infect Dis **120**: 202-9.

Matthews, K. H., Jr. (2001). Antimicrobial drug and veterinary costs in U.S. livestock production. Washington, D.C., USDA, Economic Research Service.

Mazel, D., B. Dychinco, et al. (2000). "Antibiotic resistance in the ECOR collection: integrons and identification of a novel *aad* gene." Antimicrob Agents Chemother **44**: 1568-74.

McCartney, A., W. Wenzhi, et al. (1996). "Molecular analysis of the composition of the bifidobacterial and lactobacillus microflora of humans." Appl Environ Microbiol **62**: 4608-13.

McChesney, D. G., G. Kaplan, et al. (1995). FDA survey determines *Salmonella* contamination. Feedstuffs. Minnetonka, MN**:** 20-23.

McDonald, L. C., F. J. Chen, et al. (2001). "Emergence of reduced susceptibility and resistance to fluoroquinolones in *Escherichia coli* in Taiwan and contributions of distinct selective pressure." Antimicrob Agents Chemother **45**(11): 3084-91.

McDonald, L. C., S. Rossiter, et al. (2001). "Quinupristin-dalfopristin-resistant *Enterococcus faecium* on chicken and in human stool specimens." N Engl J Med **345**: 1155-60.

McGowan, J., Jr (2000). "Strategies for study of the role of cycling on antimicrobial use and resistance [review]." Infect Control Hosp Epidemiol **21**(Suppl): S36-43.

McHugh, G., R. Moellering, et al. (1975). "Salmonella typhimurium resistant to silver nitrate, chloramphenicol, and ampicillin." Lancet **1**: 235-40.

McManus, P. (2000). "Antibiotic use and microbial resistance in plant agriculture." ASM News **66**: 448-9.

McManus, P. and V. Stockwell (2000). Antibiotics for Plant Disease Control: Silver Bullets or Rusty Sabers?, ASPnet. **2000**.

Mead, P., L. Slutsker, et al. (1999). "Food-related illness and death in the United States [review]." Emerg Inf Dis **5**: 607-25.

Medeiros, A. A. (1997). "Evolution and dissemination of beta-lactamases accelerated by generations of beta-lactam antibiotics." Clin Infect Dis **24 Suppl 1**: S19-45.

beta-Lactamases are the principal mechanism of bacterial resistance to beta-lactam antibiotics. In recent years the number and variety of new beta-lactamases detected has risen at an alarming rate, apparently in response to the clinical use of novel classes of beta-lactam antibiotics. This paper reviews the structure and evolution of beta- lactamases in an attempt to understand the pressures that have contributed to their emergence.

Mellon, M., C. Benbrook, et al. (2001). Hogging it: estimates of antimicrobial abuse in livestock. Cambridge, MA, UCS Publications.

Meynell, C. (1955). "Some factors affecting the resistance of mice to oral infection by Salmonella typhimurium." Proc R Soc Med **48**: 916.

Meynell, C. and T. Sabbaiah (1963). "Antibacterial mechanisms of the mouse gut. I. Kinetics of infection by salmonella typhimurium in normal and streptomycin-treated mice studied with abortive transductants." Br J Exptl Path **44**: 197-208.

Miki, T., A. Easton, et al. (1978). "Mapping of the resistance genes of the R plasmid NR1." Mol Gen Genet **158**: 217-24.

Millar, M., T. Walsh, et al. (2001). "Carriage of antibiotic-resistant bacteria by healthy children." J Antimicrob Chemother **47**: 605-10.

Miller, C. and M. Bohnhoff (1963). "Changes in the mouse's enteric microflora associated with enhanced susceptibility to salmonella infection following streptomycin treatment." J Infect Dis **113**: 59-66.

Miller, M. A. (1999). "Quality control and safety of animal products." Canadian Journal of Animal Science **79**: 533-8.

Miller, M. A. and W. T. Flynn (2000). Regulation of antibiotic use in animals. Antimicrobial therapy in veterinary medicine. J. F. Prescott, J. D. Baggot and R. D. Walker. Ames, IA, Iowa State University Press**:** 760-73.

Miller, W. G., A. H. Bates, et al. (2000). "Detection on surfaces and in Caco-2 cells of *Campylobacter jejuni* cells transformed with new gfp, yfp, and cfp marker plasmids." App Environ Microbiol **66**(12): 5426-36.

Molbak, K., D. Baggesen, et al. (1999). "An outbreak of multidrug resistant, quinolone resistance Salmonella enterica serotype typhimurium DT104." N Engl J Med **341**: 1420-5.

Monroe, S. and R. Polk (2000). "Antimicrobial use and bacterial resistance [review]." Curr Opin Microbiol **3**: 496-501.

Moreno, M. A., L. Dominguez, et al. (2000). "Antibiotic resistance monitoring: the Spanish programme." Int J Antimicrob Agents **14**: 285-90.

Mundy, L., D. Sahm, et al. (2000). "Relationships between enterococcal virulence and antimicrobial resistance [review]." Clin Microbiol Rev **13**: 513-22.

Murphy, T. (2001). Arsenic use in horticulture. A. Summers. Athens, GA.

National Academy of Sciences Committee on Drug Use in Food Animals (1999). The Use of Drugs in Food Animals: Benefits and Risks. Washington, DC, National Academy Press.

Neal, K., S. Brij, et al. (1994). "Recent treatment with H2 antagonists and antibiotics and gastric surgery as risk factors for salmonella infection." Brit Med J **308**: 176.

Negri, M. C., M. Lipsitch, et al. (2000). "Concentration-dependent selection of small phenotypic differences in TEM beta-lactamase-mediated antibiotic resistance." Antimicrob Agents Chemother **44**(9): 2485-91.
In this paper, the first robust experimental evidence of in vitro and in vivo concentration-dependent selection of low-level antibiotic- resistant genetic variants is described. The work is based on the study of an asymmetric competition assay with pairs of isogenic Escherichia coli strains, differing only (apart from a neutral chromosomal marker) in a single amino acid replacement in a plasmid-mediated TEM-1 beta- lactamase enzyme, which results in the new TEM-12 beta-lactamase. The mixture was challenged by different antibiotic concentrations, both in vitro and in the animal model, and the selective process of the variant population was carefully monitored. A mathematical model was constructed to test the hypothesis that measured growth and killing rates of the individual TEM variants at different antibiotic concentrations could be used to predict quantitatively the strength of selection for TEM-12 observed in competition experiments at these different concentrations.

Neu, H. (1992). "The crisis in antibiotic resistance [review]." Science **257**: 1064-73.

Nikolich, M., G. Hong, et al. (1994). "Evidence for natural horizontal transfer of *tetQ* between bacteria that normally colonize humans and bacteria that normally colonize livestock." Appl Environ Microbiol **60**: 3255-60.

Nisbet, D. J., G. I. Tellez, et al. (1998). "Effect of a commercial competitive exclusion culture (Preempt) on mortality and horizontal transmission of *Salmonella gallinarum* in broiler chickens." Avian Dis **42**(4): 651-6.

Noble, W. C. and R. P. Allaker (1992). "Staphylococci on the skin of pigs: isolates from two farms with different antibiotic policies." Vet Rec **130**: 466-468.

Nunes-Düby, S., H. Kwon, et al. (1998). "Similarities and differences among 105 members of the Int family of site-specific recombinases." Nucleic Acids Res **26**: 391-406.

Nurmi, E. and M. Rantala (1973). "New aspects of *Salmonella* infection in broiler production." Nature **214**: 210-211.

Nÿsten, R., N. London, et al. (1994). "Resistance in faecal *Escherichia coli* isolated from pig farmers and abbatoir workers." Epidemiol Infect **113**: 45-52.

Nÿsten, R., N. London, et al. (1996). "Antibiotic resistance among *Escherichia coli* isolated from faecal samples of pig farmers and pigs." J Antimicrob Chemother **37**: 1131-40.

Nÿsten, R., N. London, et al. (1996). "In-vitro transfer of antibiotic resistance between faecal *Escherichia coli* strains isolated from pig farmers and pigs." J Antimicrob Chemother **37**: 1141-54.

O'Brien, T., M. Pla, et al. (1985). "Intercontinental spread of a new antibiotic resistance gene on an epidemic plasmid." Science **230**: 87-8.

O'Brien, T. F., J. D. Hopkins, et al. (1982). "Molecular epidemiology of antibiotic resistance in salmonella from animals and human beings in the United States." N Engl J Med **307**(1): 1-6.
We collected serotyped isolates of salmonella from reference laboratories in the United States, tested their susceptibility to antibiotics, and extracted plasmids from isolates that were resistant to a different combination of antibiotics from each of three serotypes. Restriction-endonuclease digestion showed that within each of the three groups, plasmid molecules from animal and human isolates were often identical or nearly identical. One serotype-plasmid combination appeared to be endemic in cattle in 20 states and infected 26 persons in two states. The human cases, which were not recognizably related except for their common plasmids, appeared to be clustered in time but geographically dispersed, like cases in previous outbreaks spread by food products. These findings suggest that resistance plasmids may be extensively shared between animal and human bacteria, and that spread of multiresistant strains of salmonella among animals and human beings, as observed in Britain, may have been undetected in the United States for lack of comparable surveillance.

O'Brien, T. F., M. P. Pla, et al. (1985). "Intercontinental spread of a new antibiotic resistance gene on an epidemic plasmid." Science **230**(4721): 87-8.
Bacteria of different genera isolated at nine medical centers in different parts of the United States and at one center in Venezuela during the first decade of gentamicin usage carried the gentamicin resistance gene 2"-aminoglycoside nucleotidyltransferase on the same transferable plasmid. Such widespread dissemination of a newly observed resistance gene on one plasmid suggests that a new resistance gene may emerge once on a single plasmid, which then carries it to other centers and other plasmids. The resistance gene might, therefore, be contained if detected early.

Ochman, H., J. Lawrence, et al. (2000). "Lateral gene transfer and the nature of bacterial innovation [review]." Nature **405**: 299-304.

Oliver, A., R. Canton, et al. (2000). "High frequency of hypermutable *Pseudomonas aeruginosa* in cystic fibrosis lung infection." Science **288**: 391-2.

Olsen, S., R. Bishop, et al. (2001). "The changing epidemiology of salmonella: trends in serotypes isolated from humans in the United States, 1987-1997." J Infect Dis **183**: 753-61.

Olsen, S., C. Blackmore, et al. (2000). Emergence of fluoroquinolone-resistant Salmonella infections in the United States: nosocomial outbreaks suggest a changing epidemiology. International Conference on Emerging Infectious Diseases 2000, Atlanta, GA.

Olsen, S., E. DeBess, et al. (2001). "A nosocomial outbreak of fluoroquinolone-resistant salmonella infection." N Engl J Med **344**: 1572-9.

Ottolenghi, A. and V. Hamparian (1987). "Multiyear study of sludge application to farmland:

prevalence of bacterial enteric pathogens and antibody status of farm families." Appl Environ Microbiol **53**: 1118-24.

Partridge, I. G. (2000). "Vancomycin-resistant enterococci and use of avoparcin in animal feed: is there a link?" Med J Aust **172**(1): 43-4.

Parveen, S., R. Murphree, et al. (1997). "Association of multiple-antibiotic-resistance profiles with point and nonpoint sources of *Escherichia coli* in Apalachicola Bay." Appl Environ Microbiol **63**: 2607-12.

Paulsen, I., T. Littlejohn, et al. (1993). "The 3' conserved segment of integrons contains a gene associated with multidrug resistance to antiseptics and disinfectants." Antimicrob Agents Chemother **37**: 761-8.

Pavia, A., L. Shipman, et al. (1990). "Epidemiologic evidence that prior antimicrobial exposure decreases resistance to
infection by antimicrobial-sensitive Salmonella." J Infect Dis **161**: 255-60.

Perez-Trallero, E. and C. Zigorraga (1995). "Resistance to antimicrobial agents as a public health problem: importance of the use of antibiotics in animals." Int J Antimicrob Agents **6**: 59-63.

Perreten, V., F. Schwarz, et al. (1997). "Antibiotic resistance spread in food [letter]." Nature **389**: 801-2.

Peryea, F. (1998). Historical use of lead arsenate insecticides, resulting soil contamination and implications for soil remediation. 16th World Congress of Soil Science, Montpellier, France.

Petrocheilou, V., M. Richmond, et al. (1979). "Persistence of plasmid-carrying tetracycline-resistant Escherichia coli in a married couple, one of whom was receiving antibiotics." Antimicrob Agents Chemother **16**: 225-30.

Pohronezny, K., M. Sommerfeld, et al. (1994). "Streptomycin resistance and copper tolerance among strains of *Pseudomonas cichorii* in celery seedbeds." Plant Dis **78**: 150-3.

Pradel, N., K. Boukhors, et al. (2001). "Heterogeneity of Shiga toxin-producing *Escherichia coli* strains isolated from hemolytic-uremic syndrome patients, cattle, and food samples in central France." Appl Environ Microbiol **67**: 2460-8.

Radostits, O. M. and J. H. Arundel (2000). Veterinary medicine: a textbook of the diseases of cattle, sheep, pigs, goats and horses. London, Saunders.

Rantala, M. and E. Nurmi (1973). "Prevention of the growth of *Salmonella infantis* in chicks by the flora of the alimentary tract of chickens." British Poultry Science **14**: 627-630.

Recchia, G. and R. Hall (1995). "Plasmid evolution by acquistion of mobile gene cassettes: plasmid pIE723 contains the aadB gene cassette precisely inserted at a secondary site in the IncQ plasmid RSF1010." Mol Microbiol **15**: 179-87.

Ribeiro, C. and J. Frost (2000). "Family clusters of campylobacter infection." Commun Dis Public Health **3**: 274-6.

Ribeiro de Lima, F., T. S. Stahly, et al. (1981). "Effects of copper, with and without ferrous sulfide, and antibiotics on the performance of pigs." Journal of Animal Science **52**(2): 241-247.

Rice, W. and A. Chippindale (2001). "Sexual recombination and the power of natural selection." Science **294**: 555-559.

Richmond, M. and M. John (1964). "Co-transduction by a staphylococcal phage of the genes responsible for penicillinase synthesis and resistance to mercury salts." Nature **202**: 1360-1.

Riley, L., M. Cohen, et al. (1984). "Importance of host factors in human salmonellosis caused by multi-resistant strains of Salmonella." J Infect Dis **149**: 878-83.

Robertson, R. E., E. Lansburgh, et al. (1999). Food safety: the agricultural use of antibiotics and its implications for public health, US General Accounting Office.

Robertson-Welsh, D. and V. Wheelock (2000). Food safety and pig production in Denmark (Report commissioned by the Danish Bacon and Meat Council). Yorkshire, England, Verner Wheelock Associates, Ltd.**:** 35.

Rolland, R., G. Hausfater, et al. (1985). "Antibiotic-resistant bacteria in wild primates: increased prevalence in baboons feeding on human refuse." Appl Environ Microbiol **49**: 791-4.

Roloff, J. (1998). "Drugged waters." Science News **153**: 187-189.

Rossiter, S., K. Joyce, et al. (May, 2000). High prevalence of antimicrobial-resistant, including fluoroquinolone-resistant, Campylobacter on chicken in U.S. grocery stores. ASM 100th General Meeting, Los Angeles, CA.

Rowe, B., E. J. Threlfall, et al. (1979). "International spread of multiresistant strains of *Salmonella typhimurium* phage types 204 and 193 from Britain to Europe." Vet Rec **105**: 468-9.

Rowe-Magnus, D., A.-M. Guerout, et al. (2001). "The evolutionary history of chromosomal super-integrons provides an ancestry for multiresistant integrons." Proc Natl Acad Sci USA **98**: 652-7.

Ryan, C., M. Nickels, et al. (1987). "Massive outbreak of antimicrobial-resistant salmonellosis traced to pasteurized milk." JAMA **258**: 3269-74.

Salyers, A. (2000). A. Vidaver. Lincoln, NE.

Salyers, A. A., (ed.) (1995). Antibiotic resistance transfer in the mammalian intestinal tract: implications for human health, food safety and biotechnology. New York, NY, Springer-Verlag.

Salyers, A. A. and N. B. Shoemaker (1997). "Conjugative transposons." Genet Eng (NY) **19**: 89-90.

Salyers, A. A., N. B. Shoemaker, et al. (1999). Conjugative transposons: Transmissable resistance islands. Pathogenicity Islands and Other Mobile Virulence Elements. J. B. Kaper and J. Hacker. Washington, DC, American Society for Microbiology**:** 331-45.

Salyers, A. A., N. B. Shoemaker, et al. (1995). "Conjugative transposons: an unusual and diverse set of integrated gene transfer elements." Microbiol Rev **59**: 579-90.

Salzman, T. and L. Klemm (1968). "Transfer of antibiotic resistance (R factor) in the mouse intestine." Proc Soc Exptl Biol Med **128**: 392-4.

Saphra, I. and J. Winter (1957). "Clinical manifestations of salmonellosis in man: an evaluation of 7779 human infections identified at the New York *Salmonella* center." N Engl J Med **256**: 1128-3.

Sarwari, A., L. Magder, et al. (2001). "Serotype distribution of *Salmonella* isolates from food animals after slaughter differs from that of isolates found in humans." J Infect Dis **183**: 1295-9.

Sauer, F. and R. Teather (1987). "Changes in oxidation reduction potentials and volatile fatty acid production by rumen bacteria when methane synthesis is inhibited." J. Dairy Sci **70**: 1835-40.

Scheck, H., J. Pscheidt, et al. (1996). "Copper and streptomycin resistance in strains of *Pseudomonas syringae* from Pacific Northwest Nurseries." Plant Dis **80**: 1034-9.

Schiffrin, E. J., F. Rochat, et al. (1995). "Immunomodulation of human blood cells following the ingestion of lactic acid bacteria." J Dairy Sci **78**: 491-7.

Schnabel, E. and A. Jones (1999). "Distribution of tetracycline resistance genes and transposons among phylloplane bacteria in Michigan apple orchards." Appl Environ Microbiol **65**: 4898-907.

Schwarz, S., C. Werckenthin, et al. (2000). "Identification of a plasmid-borne chloramphenicol-florfenicol resistance gene in *Staphlyococcus sciuri*." Antimicrob Agents Chemother **44**: 2530-3.

Segreti, J., T. Gootz, et al. (1992). "High-level quinolone resistance in clinical isolates of *Campylobacter jejuni*." J Infect Dis **165**: 667-70.

Seo, K., P. Holt, et al. (2000). "Combined effect of antibiotic and competitive exclusion treatment on *Salmonella* enteritidis fecal shedding in molted laying hens." J Food Prot **63**: 545-8.

Seppala, H., T. Klaukka, et al. (1995). "Outpatient use of erythromycin: link to increased erythromycin resistance in group A streptococci." Clin Infect Dis **21**: 1378-85.

Shaffer, W. and R. Goodman (1969). "Effectiveness of an extended *Agri-Mycin-17* spray schedule against fireblight." Plant Disease Reporter **53**: 669-75.

Shoemaker, N., H. Vlamakis, et al. (2001). "Evidence for extensive resistance gene transfer among *Bacteroides* spp. and among *Bacteroides* and other genera in the human colon." Appl Environ Microbiol **67**: 561-8.

Shulman, J. A., P. M. Terry, et al. (1971). "Colonization with gentamicin-resistant *Pseudomonas*

aeruginosa, pyocin type 5, in a burn unit." J Infect Dis **124 [Suppl]**.

Silver, S. (1998). "Genes for all metals--a bacterial view of the periodic table. The 1996 Thom Award Lecture." J Ind Microbiol Biotechnol **20**: 1-12.

Silverman, J., L. Thal, et al. (1998). "Epidemiologic evaluation of antimicrobial resistant in community acquired enterococci." J Clin Microbiol **36**: 830-2.

Simondsen, G., H. Haakeim, et al. (1997). Glycopeptide resistant enterococci (GRE) at avoparcin-using farms; possible transmission of strains and the van A gene cluster between chicken and humans. Danish Veterinary Association, Sundvolden, Norway.

Skurray, R. A. and N. Firth (1997). Molecular evolution of multiply-antibiotic-resistant staphylococci. Chichester, John Wiley and Sons.

Skurray, R. A., D. A. Rouch, et al. (1988). "Multiresistant *Staphylococcus aureus*: genetics and evolution of epidemic Australian strains." J Antimicrob Chemother **21 Suppl C**: 19-39. Molecular and genetic analysis of multiresistant isolates of Staphylococcus aureus from widely separated hospitals in Australia has demonstrated that these are clearly related, and that the predominant strains possess up to three different plasmids, which fall into the following classes: (i) small 1.6 kb plasmids, such as pSK3, which are phenotypically cryptic, (ii) 4.5 kb chloramphenicol resistance plasmids, such as pSK2, and (iii) the pSK1 family of multiresistance plasmids, which range in size from 20 to 42 kb and variously encode resistance to antiseptics and disinfectants, trimethoprim (Tpr), penicillin (Pcr) and the aminoglycosides gentamicin, tobramycin and kanamycin (Gmr Tmr Kmr). Gmr Tmr Kmr is encoded on the pSK1 family plasmids by transposon Tn4001, which was also detected on the chromosomes of some clinical isolates. Tn4001 is composed of inverted repeats of the insertion sequence IS256; these repeats flank a Gmr Tmr Kmr sequence encoding for a 57,000 dalton bifunctional protein with aminoglycoside acetyltransferase [AAC(6')] and phosphotransferase [APH(2")] activities. A Tn4001-like structure, which is defective in transposition but encodes for a Gmr Tmr Kmr determinant homologous with that on Tn4001, occurs on conjugative plasmids from strains isolated in North America. Physical studies indicate that Pcr, via a beta- lactamase, and Tpr, via a trimethoprim-insensitive dihydrofolate reductase (DHFR), are also encoded on the pSK1 family by transposons; these transposons have been designated Tn4002 and Tn4003, respectively. Tn4003 is flanked by direct repeats of the insertion sequence IS257. The evolution of the pSK1 family of multiresistance plasmids is traced through the transposition and genetic rearrangement of resistance determinants. Transposition and genetic rearrangement have also contributed to the evolution of a multiresistant chromosome in Staph. aureus. In the majority of contemporary multiply resistant Staph. aureus strains the determinants for resistance to erythromycin (Emr), fusidic acid, methicillin (Mcr), minocycline, rifampicin, spectinomycin, streptomycin, sulphonamides, tetracycline (Tcr), cadmium (Cdr), and mercury (Hgr) are chromosomally encoded; these strains also possess chromosomally encoded Pcr, via a beta-lactamase. Evidence indicates that some of these determinants, Pcr, Cdr, Hgr, and Tcr, were plasmid encoded in isolates collected from Australian hospitals prior to 1970. Through transposition and site-specific integration, they have since been acquired by the chromosome in more recent Staph. aureus strains.(ABSTRACT TRUNCATED AT 400 WORDS)

Smith, B. P., M. Reina-Guerra, et al. (1984). "Aromatic-dependent *Salmonella syphimurium* as modified live vaccines for calves." American Journal of Veterinary Research **45**: 59-66.

Smith, H. (1969). "Transfer of antibiotic resistance from animal and human strains of Escherichia coli to resident E. coli in the alimentary tract of man." Lancet **1**: 1174-6.

Smith, H. W. and J. F. Tucker (1978). "Oral administration of neomycin to chickens experimentally infected with *Salmonella typhimurium*." Vet Rec **102**: 354-6.

Smith, H. W. and J. F. Tucker (1978). "The effect of antimicrobial feed additives on the colonization of the alimentary tract of chickens by *Salmonella typhimurium*." J Hyg **80**: 217-31.

Smith, H. W. and J. F. Tucker (1980). "Further observations on the effect of feeding diets containing avoparcin, bacitracin and sodium arsenilate on the colonization of the alimentary tract of poultry by *Salmonella* organisms." J Hyg **84**: 137-50.

Smith, K., J. Besser, et al. (1999). "Quinolone-resistant *Campylobacter jejuni* infections in Minnesota, 1992-1998." N Engl J Med **340**: 1525-32.

Snydman, D., N. Jacobus, et al. (1999). "Multicenter study of in vitro susceptibility of *Bacteroides fragilis* group, 1995 to 1996, with comparison of resistance trends from 1990 to 1996." Antimicrob Agents Chemother **43**: 2417-22.

Soares, S., K. Kristinsson, et al. (1993). "Evidence for the introduction of a multiresistant clone of serotype 6B Streptococcus pneumoniae from Spain to Iceland in the late 1980s." J. Infect Dis **168**: 158-63.

Sorensen, T. L., M. Blom, et al. (2001). "Transient intestinal carriage after ingestion of antibiotic-resistant *Enterococcus faecium* from chicken and pork." N Engl J Med **345**: 1161-6.

Sorensen, T. L. and D. L. Monnet (2000). "Control of antibiotic use in the community: the Danish experience." Infect Control Hosp Epidemiol **21**: 387-9.

Sorum, H. (2000). "Farming of Atlantic salmon - an experience from Norway." Acta Veterinaria Scandinavica **93**(Supplement): 129-134.

Spika, J., S. Waterman, et al. (1987). "Chloramphenicol-resistant Salmonella newport traced through hamburger to dairy farms: a major persisting source of human salmonellosis in California." N Engl J Med **316**: 565-70.

Stabel, T. J., J. E. Mayfield, et al. (1990). "Oral immunization of mice with attenuated *Salmonella typhimurium* containing a recombinant plasmid which codes for production of a 31-kilodalton protein of *Brucella abortus*." Infection and Immunity **59**: 2941-2947.

Stahly, T. S., G. L. Cromwell, et al. (1980). "Effects of the dietary inclusion of copper and/or antibiotics on the performance of weanling pigs." Journal of Animal Science **51**(6): 1347-51.

Stamey, K., S. Abbott, et al. (2000). Emerging antimicrobial resistance among human Salmonella isolates to clinically important antimicrobial agents, NARMS 1996-1999. International Conference on Emerging Infectious Diseases 2000, Atlanta, GA.

Statens Serum Institut (2001). DANMAP 2000-- Consumption of antimicrobial agents and occurrence of antimicrobial resistance in bacteria from food animals, foods, and humans in Denmark. Copenhagen, Denmark, Danish Veterinary and Food Administration, Danish Medicines Agency, Danish Veterinary Lab.

Stern, N. J., P. J. Fedorka-Cray, et al. (2001). "Distribution of Campylobacter spp. in selected U.S. poultry production and processing operations." J Food Prot **64**(11): 1705-10.

Stetzenbach, L. (1997). Introduction to aerobiology. Manual of Environmental Microbiology. C. Hurst, G. Knudson, M. McInerney, L. Stetzenbach and M. Walter. Washington, DC, ASM Press**:** 619-28.

Stewart, C. and A. Richardson (1989). "Enhanced resistance of anaerobic rumen fungi to the ionophores monensin and lasolacid in the presence of methanogenic bacteria." J Appl Bacteriol **66**: 85-93.

Stobberingh, E., A. van den Bogaard, et al. (1999). "Enterococci with glycopeptide resistance in turkeys, turkey farmers, turkey slaughterers, and (sub) urban residents in the south of the Netherlands: Evidence for transmission of vancomycin resistance from animals to humans." Antimicrob Agents Chemother **43**: 2215-21.

Stockwell, V., K. Johnson, et al. (1996). "Compatibility of bacterial antagonists of Erwinia amylovora with antibiotics used for fire blight control." Phytopathology **86**: 834-40.

Summers, A., J. Wireman, et al. (1993). "Mercury released from dental "silver" fillings provokes an increase in mercury and antibiotic resistant bacteria in the oral and intestinal flora of primates." Antimicrob Agents Chemother **37**: 825-34.

Sundin, G. and C. Bender (1996). "Dissemination of the strA-strB streptomycin-resistance genes among commensal and pathogenic bacteria from humans, animals, and plants." Mol Ecol **5**: 133-43.

Sundin, G. and C. Bender (1996). Molecular genetics and ecology of transposon-encoded streptomycin resistance in plant pathogenic bacteria. Molecular genetics and evolution of pesticide resistance. T. Brown. Washington, DC, American Chemical Society.

Suppola, J. P., E. Kolho, et al. (1999). "vanA and vanB incorporate into an endemic ampicillin-resistant vancomycin-sensitive Enterococcus faecium strain: effect on interpretation of clonality." J Clin Microbiol **37**(12): 3934-9.
Clonal spread and horizontal transfer in the spread of vancomycin resistance genes were investigated. Multiplex PCR, pulsed-field gel electrophoresis (PFGE), hybridization of enterococcal plasmids with the vanA and vanB probes, and sequencing of a fragment of vanB were used in the analysis. Before May 1996, 12 vancomycin-resistant Enterococcus faecium (VRE) isolates were found in Finland. Between May 1996 and October 1997, 156 VRE isolates were found in the Helsinki area. Between December 1997 and April 1998, fecal samples from 359 patients were cultured for VRE. One new case of colonization with VRE was found. During the outbreak period, 88% (137 of 155) of the VRE isolates belonged to two strains (VRE types I and

II), as determined by PFGE. Each VRE type I isolate possessed vanB, and five isolates also had vanA. Of the 34 VRE type II isolates, 27 possessed vanA and 7 possessed vanB. Fifteen of 21 (71%) ampicillin-resistant, vancomycin-sensitive E. faecium (VSE) isolates found during and after the outbreak period in one ward were also of type II. Two VSE type II isolates were found in the hospital before the outbreak in 1995. By PFGE, the three groups (vanA, vanB, or no van gene) of type II shared the same band differences with the main type of VRE type II with vanA. None of the differences was specific to or determinative for any of the groups. Our material suggests that vanA and vanB incorporate into an endemic ampicillin-resistant VSE strain.

Swann, M. (1969). Report of joint committee on the use of antibiotics in animal husbandry and veterinary medicine. London, Her Majesty's Stationery Office.

Swartz, M. (1994). "Hospital-acquired infections: diseases with increasingly limited therapies [review]." Proc Natl Acad Sci USA **91**: 2430-7.

Syspälä, H., T. Klaukka, et al. (1997). "The effect of changes in the consumption of macrolide antibiotics on erythromycin resistance in group A streptococci in Finland." N Engl J Med **337**: 441-6.

Talbot, H., Jr, D. Yamamoto, et al. (1980). "Antibiotic resistance and its transfer among clinical and nonclinical *Klebsiella* strains in botanical environments." Appl Environ Microbiol **39**: 97-104.

Tanner, A. C. (2000). Antimicrobial drug use in poultry. Antimicrobial therapy in veterinary medicine, 3rd edition. J. F. Prescott, J. D. Baggot and R. D. Walker. Ames, IA, Iowa State University Press**:** 637-55.

Tannock, G. (1995). Normal Microflora: An introduction to the microbes inhabiting the human body. London, Chapman & Hall.

Tauxe, R. V. (1997). "Emerging foodborne diseases: an evolving public health challenge." Emerg Infect Dis **3**(4): 425-34.
The epidemiology of foodborne disease is changing. New pathogens have emerged, and some have spread worldwide. Many, including Salmonella, Escherichia coli O157:H7, Campylobacter, and Yersinia enterocolitica, have reservoirs in healthy food animals, from which they spread to an increasing variety of foods. These pathogens cause millions of cases of sporadic illness and chronic complications, as well as large and challenging outbreaks over many states and nations. Improved surveillance that combines rapid subtyping methods, cluster identification, and collaborative epidemiologic investigation can identify and halt large, dispersed outbreaks. Outbreak investigations and case-control studies of sporadic cases can identify sources of infection and guide the development of specific prevention strategies. Better understanding of how pathogens persist in animal reservoirs is also critical to successful long-term prevention. In the past, the central challenge of foodborne disease lay in preventing the contamination of human food with sewage or animal manure. In the future, prevention of foodborne disease will increasingly depend on controlling contamination of feed and water consumed by the animals themselves.

Taylor, D., L.-K. Ng, et al. (1985). "Susceptibility of *Campylobacter* species to nalidixic acid, enoxacin, and other DNA gyrase inhibitors." Antimicrob Agents Chemother **28**: 708-10.

Taylor, J., D. Dwyer, et al. (1993). "Simultaneous outbreak of *Salmonella enteritidis* and *Salmonella schwarzengrund* in a nursing home: association of *S. enteritidis* with bacteremia and hospitalization [letter]." J Infect Dis **167**: 781-2.

Teuber, M., L. Meile, et al. (1999). "Acquired antibiotic resistance in lactic acid bacteria from food [review]." Antonie Van Leeuwenhoek **76**: 115-37.

Thomson, S., S. Gouk, et al. (1993). The presence of streptomycin resistant strains of *Erwinia amylovora* in New Zealand. VI International Workshop on Fireblight, Athens, Greece, ISHS.

Threlfall, E., J. Frost, et al. (1994). "Epidemic in cattle and humans of *Salmonella typhimurium* DT104 with chromosomally integrated multiple drug resistance." Vet Rec **134**: 577.

Threlfall, E., J. Frost, et al. (1996). "Increasing spectrum of resistance in multiresistant *Salmonella typhimurium* [letter]." Lancet **347**: 1053-4.

Threlfall, E., B. Rowe, et al. (1993). "A comparison of multiple drug resistance in salmonellas from humans and food animals in England and Wales, 1981 and 1990." Epidemiol Infect **111**: 189-97.

Threlfall, E., L. Ward, et al. (1997). "Increasing incidence of resistance to trimethoprim and ciprofloxacin in epidemic *Salmonella typhimurium* DT104 in England and Wales." Eurosurveillance **2**: 81-4.

Threlfall, E. J., L. R. Ward, et al. (2000). "Spread of resistance from food animals to man--the UK experience." Acta Vet Scand Suppl **93**: 63-8.
Since 1990 there have been dramatic increase in the occurrence multiply drug-resistant strains of zoonotic pathogens causing infections in humans in many developed countries. Of particular note has been the epidemic spread of MR strains of S. typhimurium DT 104, which now appear to have an almost world-wide distribution. Within DT104 the increasing spectrum of resistance is of considerable concern, with strains with decreased susceptibility to ciprofloxacin increasing in incidence in the United Kingdom and also causing serious disease in humans in other countries. For campylobacters the incidence of ciprofloxacin-resistant organisms is also increasing, with reports of such isolates from numerous countries throughout the world. For VTEC 0157, although resistance is increasing, multiple resistance and resistance to ciprofloxacin remains rare. Drug resistance in food-borne pathogens is an unfortunate but almost inevitable consequence of the use of antimicrobials in food animals. Although for some pathogens-- e.g., Campylobacter spp., the use of antimicrobials in human medicine is also an important factor (Smith el al 1999), it is the use of antimicrobials in food animals which has been a major factor in the development of decreased susceptibility to antibiotics such as ciprofloxacin in zoonotically-transmitted salmonellas. Such use is quite legitimate. However it is regrettable that recommendations such as propounded in 1992 in the UK by the Expert Group on Animal Feedingstuffs--the Lamming Committee, that any new antibiotics with cross resistance to those used in human medicine should not be used for prophylaxis in animal husbandry, were not accepted (Anonymous, 1992). Although the clock cannot be turned back, to combat the development of resistance to such important drugs as the fluoroquinolones it is hoped that a Code of Practice for their use in food animals will soon be internationally implemented.

Threlfall, E. J., L. R. Ward, et al. (1997). "Increase in multiple antibiotic resistance in nontyphoidal

salmonellas from humans in England and Wales: a comparison of data for 1994 and 1996." Microb Drug Resist **3**(3): 263-6.
The incidence of multiple drug resistance (to four or more antimicrobials) in salmonellas from humans in England and Wales in 1996 has been compared with corresponding data for 1994. For Salmonella enteritidis multiple resistance has remained rare, although a high proportion of isolates of phage type 6A have shown resistance to ampicillin. For S. typhimurium multiple resistance has continued to increase, with 81% of isolates now multiresistant. Of particular importance in S. typhimurium has been the continued epidemic of multiresistant DT 104 and the increasing occurrence of strains of this phage type with additional resistance to trimethoprim and/or ciprofloxacin. For S. virchow, a 10% increase in multiple resistance is mainly concentrated in two phage types common in returning travellers. For S. hadar, there has been a substantial increase in the incidence of multiple resistance with over 50% of isolates now multiresistant. Substantial increases in the incidence of resistance to ciprofloxacin in multiresistant S. typhimurium DT 104, S. virchow, and S. hadar since 1993, when the fluoroquinolone antibiotic enrofloxacin was licensed for veterinary use in the UK, are of particular concern.

Tielen, M. J. M., F. W. van Schie, et al. (1997). Risk factors and contol measures for subclinical infection in pig herds. Proceedings of the 2nd International Symposium on Epidemology and Control in Pork, Copenhagen, Denmark.

Tollefson, L. (1996). "FDA reveals plans for antimicrobial susceptibility monitoring." J Am Vet Med Assoc **208**: 459-60.

Tolmasky, M. E. and J. H. Crosa (1987). "Tn1331, a novel multiresistance transposon encoding resistance to amikacin and ampicillin in *Klebsiella pneumoniae*." Antimicrob Agents Chemother **31**(12): 1955-60.
A 7.5-kilobase-pair multiresistance transposon, Tn1331, harboring amikacin resistance was identified as part of Klebsiella pneumoniae plasmid pJHCMW1. Restriction mapping, hybridization, and transposition complementation experiments demonstrated that Tn1331 belongs to the Tn3 family. Its structure is similar to that of Tn3 with the insertion of a DNA fragment encoding resistance to amikacin, kanamycin, and tobramycin.

Tomasz, A. (1997). "Antibiotic resistance in Streptococcus pneumoniae." Clin Infect Dis **24 Suppl 1**: S85-8.
Pneumococci were once among the most highly penicillin-susceptible bacteria. However, reports of multidrug-resistant strains have been published since the late 1970s. The rapid spread of resistant clones and the emergence of new variants of resistance mechanisms call for effective surveillance systems and collaboration among clinicians, scientists, the pharmaceutical industry, and regulatory and public health agencies.

Uchiya, K., M. Barbieri, et al. (1999). "A Salmonella virulence protein that inhibits cellular trafficking." EMBO J **18**: 3924-33.

United States Department of Agriculture (USDA) (2000). USDA agricultural chemical usage1999: fruit and nut summary, United States Department of Agriculture, National Statistics Service**:** 212.

University of Minnesota College of Veterinary Medicine MinnCERT. **2001**.

US Department of Agriculture-- National Agricultural Statistics Service (2000). Meat animals production, disposition, and income chart, USDA. **2001**.

USDA Food Safety and Inspection Service (2001). Pathogen reduction/HACCP & HACCP implementation. **2001**.

Vaillancourt, J.-P., R. Higgins, et al. (1988). "Changes in the susceptibility of *Actinobacillus pleuropneumoniae* to antimicrobial agents in Quebec (1981-1986)." J Am Vet Med Assoc **193**(4): 470-473.

Van De Giessen, A. W. (1996). Epidemiology and control of *Salmonella enteritidis* and *Campylobacter* spp. in poultry flocks. PhD dissertation at Universiteit Utrecht.

van den Bogaard, A., L. Jensen, et al. (1997). "Vancomycin-resistant enterococci in turkeys and farmers [letter]." N Engl J Med **337**: 1558-9.

van den Bogaard, A., P. Mertens, et al. (1997). "High prevalence of colonization with vancomycin- and pristinamycin-resistant enterococci in healthy humans and pigs in The Netherlands: is the addition of antibiotics to animal feeds to blame? [letter]." J Antimicrob Chemother **40**: 454-6.

van den Bogaard, A. and E. Stobberingh (2000). "Epidemiology of resistance to antibiotics: links between animals and humans." Int J Antimicrob Agents **14**: 327-35.

Van den Braak, N., A. van Belkum, et al. (1998). "Molecular characterization of vancomycin-resistant enterococci from hospitalized patients and poultry products in the Netherlands." J Clin Microbiol **36**: 1927-32.

Van der Waaij, D., J. M. Berghuis-de Vries, et al. (1971). "Colonization resistance of the digestive tract in conventional and antibiotic-treated mice." J Hyg **69**: 405-11.

van Treeck, U., F. Schmidt, et al. (1981). "Molecular nature of a streptomycin and sulfonamide resistance plasmid (pBP1) prevalent in clinical Escherichia coli strains and integration of an ampicillin resistance transposon (TnA)." Antimicrob Agents Chemother **19**(3): 371-80.
A small, nonconjugative plasmid, designated pBP1, was originally found in different fecal Escherichia coli serotypes isolated from a healthy proband. Of a total number of 130 hospital strains of E. coli subsequently studied, 8.5% yielded plasmid of the pBP1 type. This R plasmid specifies resistance to streptomycin (Sm) and sulfonamides (Su) and has a mass of 4.0 megadaltons. Inactivation of streptomycin is due to the aminoglycoside phosphotransferase APH-(3 "). A physical map was constructed by analysis with restriction endonucleases. Another small plasmid, pBP1-1, was isolated from one of the hospital strains and characterized as an enlarged pBP1 replicon containing an additional deoxyribonucleic acid sequence identified as a transposable element for ampicillin resistance (TnA). Plasmid pBP1-1 was cleaved by restriction enzymes for identification of the transposon sequence which codes for a TEM 1 beta-lactamase. The sequence organizations in the Sm Su plasmids RSF1010 and pBP1 were shown to be identical for regions specifying streptomycin and sulfonamide resistance, but different for the region containing the origin of replication and genes for replicative functions. Thus, RSF1010, which has been considered as the prototype of Sm Su plasmids, and pBP1, which is at least as frequent in clinical isolates as RSF1010, do not have a single common ancestor.

Velazquez, J. B., A. Jimenez, et al. (1995). "Incidence and transmission of antibiotic resistance in *Campylobacter jejuni* and *Campylobacter coli*." J Antimicrob Chemother **35**: 173-8.

Vidaver, A. K. (2001). Horticultural and other uses of antibiotics. Royal Society of Medicine Symposium, Washington, DC, RSM Press.

Visek, W. (1978). "The mode of growth promotion by antibiotics." Journal of Animal Science **46**(5): 1447-1469.

Walker, R. (2000). "The use of fluoroquinolones for companion animal antimicrobial therapy [review]." Aust Vet J **78**: 84-90.

Wall, P. G., S. Davis, et al. (1995). "Chronic carriage of multidrug resistant *Salmonella typhimurium* in a cat." J Small Anim Pract **36**: 279-81.

Wall, P. G., D. Morgan, et al. (1995). "Transmission of multi-resistant strains of *Salmonella typhimurium* from cattle to man." Vet Rec **136**: 591-2.

Wall, P. G., D. Morgan, et al. (1994). "A case control study of infection with an epidemic strain of multi-resistant *Salmonella typhimurium* DT104 in England and Wales." Commun Dis Rep CDR Rev **4**: R130-5.

Wall, P. G., E. J. Threlfall, et al. (1996). "Multiresistant *Salmonella typhimurium* DT104 in cats: a public health risk." Lancet **348**: 471.

Walton, J. R. (1966). "In vivo transfer of infectious drug resistance." Nature **211**: 312-3.

Watts, J. L., S. A. Salmon, et al. (1995). "Antimicrobial susceptibility of microorganisms isolated from the mammary glands of dairy heifers." J Dairy Sci **78**: 1637-48.

Wegener, H. C., F. M. Aarestrup, et al. (1999). "Use of antimicrobial growth promoters in food animals and Enterococcus faecium resistance to therapeutic antimicrobial drugs in Europe." Emerg Infect Dis **5**(3): 329-35.
Supplementing animal feed with antimicrobial agents to enhance growth has been common practice for more than 30 years and is estimated to constitute more than half the total antimicrobial use worldwide. The potential public health consequences of this use have been debated; however, until recently, clear evidence of a health risk was not available. Accumulating evidence now indicates that the use of the glycopeptide avoparcin as a growth promoter has created in food animals a major reservoir of Enterococcus faecium, which contains the high level glycopeptide resistance determinant vanA, located on the Tn1546 transposon. Furthermore, glycopeptide-resistant strains, as well as resistance determinants, can be transmitted from animals to humans. Two antimicrobial classes expected to provide the future therapeutic options for treatment of infections with vancomycin-resistant enterococci have analogues among the growth promoters, and a huge animal reservoir of resistant E. faecium has already been created, posing a new public health problem.

Wells, S. J., P. J. Fedorka-Cray, et al. (2001). "*Salmonella* fecal shedding by dairy cows on-farm

and at cull cow markets." J. Food Protect. **64**: 3-11.

Welton, L. A., L. A. Thal, et al. (1998). "Antimicrobial resistance in enterococci isolated from turkey flocks fed virginiamycin." Antimicrob Agents Chemother **42**: 705-8.

White, D. G., S. Zhao, et al. (2001). "The isolation of antibiotic-resistant salmonella from retail ground meats." N Engl J Med **345**: 1147-54.

Wiggins, B. A. (1996). "Discriminant analysis of antibiotic resistance patterns in fecal *Streptococci*, a method to differentiate human and animal sources of fecal pollution in natural waters." Appl Environ Microbiol **62**: 3997-4002.

Wiggins, B. A., R. W. Andrews, et al. (1999). "Use of antibiotic resistance analysis to identify nonpoint sources of fecal pollution." Appl Environ Microbiol **65**: 3483-6.

Williams, L. P., Jr, J. B. Vaughn, et al. (1969). "A ten- month study on salmonella contamination in animal protein meals." J Am Vet Med Assoc **155**: 167-74.

Williams, R. E. O. (1959). "Epidemic staphylococci." Lancet **1**: 190-5.

Wills, R. W., J. T. Gray, et al. (2000). "Synergism between porcine reproductive and respiratory syndrome virus (PRRSV) and *Salmonella choleraesuis*." Vet Microbiol **71**: 177-192.

Wilson, K. H. and R. B. Blitchington (1996). "Human colonic biota studied by ribosomal DNA sequence analysis." Appl Environ Microbiol **62**: 2273-8.

Wireman, J., C. A. Liebert, et al. (1997). "Association of mercury resistance and antibiotic resistance in the Gram negative fecal bacteria of primates." Appl Environ Microbiol **63**: 4494-503.

Witte, W. (2000). "Ecological impact of antibiotic use in animals on different complex microflora: environment [review]." Int J Antimicrob Agents **14**: 321-5.

World Health Organization (1997). The medical impact of the use of antimicrobials in food animals. Report from a WHO meeting held in Berlin, Germany. Berlin, Germany, World Health Organization.

World Health Organization (1998). Use of quinolones in food animals and potential impact on human health. Report of a WHO meeting held in Geneva, Switzerland. Geneva, Switzerland, World Health Organization.

World Health Organization (1999). Containing antimicrobial resistance: review of the literature and report of a WHO workshop on the development of a global strategy for the containment of antimicrobial resistance. Geneva, Switzerland, 4-5 February 1999. Geneva, Switzerland, World Health Organization.

World Health Organization (2000). WHO global principles for the containment of antimicrobial resistance in animals intended for food. Report of a WHO consultation. Geneva, Switzerland, World Health Organization.

Wray, C. and J.-C. Gnanou (2000). "Antibiotic resistance monitoring in bacteria of animal origin: analysis of national monitoring programmes." Int J Antimicrob Agents **14**: 291-4.

Wray, C., N. Todd, et al. (1990). "The epidemiology of salmonella infection in calves: the role of dealers." Epidemiology and Infection **105**: 295-305.

Zhao, T., M. P. Doyle, et al. (1998). "Reduction of carriage of enterohemorrhagic *Escherichia coli* O157:H7 in cattle by inoculation with probiotic bacteria." J Clin Microbiol **36**(3): 641-7.

Zhou, D., M. S. Mooseker, et al. (1999). "Role of the *S. typhimurium* actin-binding protein SipA in bacterial internalization." Science **283**: 2092-5.

Zuccato, E., D. Calamari, et al. (2000). "Presence of therapeutic drugs in the environment [letter]." Lancet **355**: 1789-90.