REACH Notes

Recent Developments to Promote Judicious Antibiotic Prescribing

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Antibiotics Resistance and Animal Husbandry in the U.S.

Animal husbandry consumes 20 million pounds annually in the U.S. alone. Sixteen million pounds are mixed into feed as growth promoters, or placed into water supplies for disease prevention. This is to offset the stunted growth and increased infection that has accompanied large scale production of livestock in crowded and often unsanitary conditions.

To date, the Food and Drug Administration has approved a number of antibiotics including tetracycline, penicillin, streptomycin, sulfonamides, nitrofurans, virginiamycin, and fluoroquinolones for use in animals despite their concurrent use for human disease.

Salmonella and Fluoroquinolone Resistance

In the U.S., 1% of beef, 8.7% of swine, and 20% of poultry carcasses are contaminated with salmonella.[i] Antibiotic-resistant salmonella is readily isolated from supermarket meats.[ii] More concerningly, analysis of U.S. human salmonella strains from 1976 to 1996 showed the new emergence of *S. typhimurium* DT104,[iii] a strain that was a major cause of diarrheal illness in Europe before spreading to the U.S. The strain is resistant to 5 antibiotics (ampicillin, chloramphenical, streptomycin, sulfonamides, and tetracycline) and recently linked to a dairy farm outbreak in Vermont.[iv] Treatment of DT104 and other highly-resistant strains of salmonella is limited to 3rd generation cephalosporins and fluoroquinolones. Resistance to the latter has emerged in the UK, and is expected to emerge in the U.S. since the licensing of fluoroquinolones in poultry in 1995.

Campylobacter and Fluoroquinolone Resistance

Campylobacter has been isolated from 4% of beef, 31.5% of swine, and 88% of broiler chicken carcasses.[v] Quinolone-resistant campylobacter has also been increasing following the 1995 U.S. licensing of quinolones in poultry, and the 1998 licensing in cattle. In fact, quinolone-resistant human infection was non-existent in the absence of quinolone exposure until the widespread use of the antibiotic in poultry feed[vi]. By 1998, 13.5% of campylobacter isolated from chicken carcasses were fluoroquinolone resistant[vii]. Human *Campylobacter jejuni* isolates in Minnesota from 1992 to 1998 demonstrated increasing quinolone resistance from 1.3% in 1992 to 10.2% in 1998 [viii]. Overall, all species of campylobacter were 20% resistant to quinolones. Since 1997, U.S. animal quinolone use has been limited to therapeutic indications requiring veterinary prescription. Thus, rising resistance in campylobacter suggests that resistance can emerge from therapeutic uses alone, in spite of bans on use for growth promotion and prophylaxis.

Streptogramin Resistance

Even antibiotics limited to animal use alone can result in unforeseen future public health issues. Currently, the newest human antibiotic agents (e.g. streptogramins (i.e. quinupristin,dalfopristin), oxazolidinones (i.e. Linezolid) are derivatives of antibiotics solely used in animals in previous decades. Not surprisingly, resistance already existed prior to licensing (e.g. streptogramins [6], up to 50%). Recent studies show that quinupristin-dalfopristin-resistant *Enterococcus faecium* can be isolated from 58% of chickens sold in U.S. supermarkets, and is beginning to appear in some stool samples from outpatients.[ix] [x]

For more information, see the website from the Alliance for the Prudent Use of Antibiotics: www.apua.org

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[i] Guidance for Industry #78. U.S.. Department of Health and Human Service. Food and Drug Administration. Center for Veterinary Medicine. http://www.fda.gov/cvm/fda/TOCs/guidad78.html.

[ii] White DG, Zhao S, Sudler R, Ayers S, Friedman S, Chen S, et al. The isolation of antibiotic-resistant salmonella from retail ground meats. NEJM; 345(16): 1147-54.

[iii] Glynn MK, Bopp C, Dewitt W, et al. Emergence of multidrug-resistant *Salmonella enterica* serotype typhimurium DT104 infections in the United States. NEJM. 1998, 338(19), 1333-37.

[iv] FDA response to comments (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.). December 1999. www.fda.org.

[v] Guidance for Industry #78. U.S.. Department of Health and Human Service. Food and Drug Administration. Center for Veterinary Medicine. http://www.fda.gov/cvm/fda/TOCs/guidad78.html.

[vi] Witte W. Medical consequences of antibiotic use in agriculture. Science. 1998, Feb. 279:996-7.

[vii] U.S. National Antimicrobial Resistance Monitoring System (NARMS). http://www.fda.gov/cvm.

[viii] Smith KE, Besser JM, Hedberg CW et al. Quinolone-resistance *Campylobacter jejeuni* infections in Minnesota, 1992-1998. NEJM 1999. 340:20, 1525-32.

[ix] McDonald LC, Rossiter S, Mackinson C, Wang YY, Johnson S, Sullivan M. Quinupristin-dalfopristin-resistant *Enterococcus faecium* on chicken and in human stool specimens. NEJM; 345(16): 1155-60.

[x] Sorensen TL, Blom M, Monnet D, Frimodt-Moller N, Poulsen RL, Espersen F. Transient intestinal carriage after ingestion of antibiotic-resistant *Enterococcus faecium* from chicken and pork. NEJM; 345(16): 1161-66.