Correspondence


Journal of Antimicrobial Chemotherapy
DOI: 10.1093/jac/dkh264
Advance Access publication 12 May 2004

Does the use of antibiotics in food animals pose a risk to human health? An unbiased review?

Vibeke Frøkjær Jensen1,*, Jakob Neimann1, Anette M. Hammerum2, Kåre Mølbak2 and Henrik C. Wegener1

1 Danish Institute for Food and Veterinary Research, Mørkhøj Bygade 19, DK-2860 Søborg; 2 Statens Serum Institut, Artillerivej 5, DK-2300 Copenhagen S, Denmark

Keywords: antibiotic resistance, zoonosis, animal antibiotic use, human health risk

*Corresponding author. E-mail: vfj@dsvf.dk

Sir,

The review by Phillips et al.1 is an insight into the reasoning of the scientific advisors of the animal drug industry. We hope that the industry discounts this bad advice. It would be alarming if preventive action to control resistant human pathogens in the food supply should be taken only when sufficient numbers of humans had been harmed, to enable indisputable epidemiological proof of a ‘devastating clinical effect’.

Phillips et al.1 state that there might be disadvantages to human health and to animal health in the discontinuation of the use of antimicrobial growth promoters (AGP), but do not make a convincing plea. Their argument that in Denmark the ban of AGP may have caused an increase in the incidence of salmonellosis and campylobacteriosis is not correct. The pathogen load has decreased (Salmonella) or remained at a constant level (Campylobacter).2 The AGP ban in Denmark in 1998 in no way affected the yearly increase in the incidence of human campylobacteriosis, of ~20% in 1993–1999 (except for 1997), 5% in 1999–2002 and a decrease of 17% in 2003. The authors repeatedly refer to a small increase in human salmonellosis in 2001, but fail to mention that the incidence has decreased markedly since 1997. This contradictory argument compromises the credibility of the paper.

Based on a Danish finding of a higher prevalence of resistance in Campylobacter jejuni isolates in human infections than in Danish chicken isolates, the authors falsely conclude ‘chicken is not the major source of Campylobacter in humans’. In Denmark, some 27% of the poultry products are imported. The high level of resistance in the imported products explains the higher levels of resistance in Campylobacter isolated from humans, as compared with domestic products.

Yet another example of misquoting and misinterpreting scientific results is in Table 2:1 only one of the references has contributed and it does not support the heading—that there is international evidence of chicken consumption being a protective factor for C. jejuni illness. Selectively citing the finding of ‘eating chicken legs’ as a ‘protective’ factor—when all other chicken cuts came out as risk factors in the same study—is hardly scientific! Neimann et al.4 do not support the statement ‘Case-control studies that fail to consider alternative hypotheses frequently find chicken consumption to be a major risk factor’. Chicken meat remains the most consistently identified risk factor for campylobacteriosis throughout the scientific literature.

The authors state, ‘The realization that VRE infections are largely confined to clinical units in which glycopeptides are heavily used… suggested that such usage in humans might be the driving factor’. Agreed, but VRE do not emerge spontaneously in hospitals; they are introduced from external sources. Numerous studies show that VRE is common in the general population, in food, animals and in the environment because of the use of avoparcin for growth promotion.

Enterococci are highly heterogeneous bacteria, and the probability of isolating identical DNA subtypes of VRE from animals and humans is consequently low in population-based surveys. The authors5 interpretation of this is that transmission between animals and humans is uncommon. This is false. While the isolation of identical types provides strong evidence of transmission, the rate of transmission cannot be assessed. Dendrogramatic analyses of amplified fragment length polymorphism (AFLP) patterns show that human strains and strains causing infections in hospitals belong to the same clusters as strains in animals, food and healthy humans in the community.5,6

It has been shown experimentally that animal enterococci can transiently colonize the gut, and studies suggest that gene transfer can take place in the intestine following transient colonization.7 Nevertheless, Phillips et al.1 conclude ‘The truth about gene transfer from animal isolates….remains beyond our grasp’, misinterpreting the study by Sørensen et al.8 and ignoring Berchieli.9 Phillips et al.1 point out that no transconjugants were detected in the ingestion experiment of Enterococcus faecium8 and suggest that it is ‘not a common event in vivo’. This study was not designed to select for transconjugants. With a transfer rate of 10-7 transconjugants/donor, 1609 isolates should have been tested to obtain an 80% power to find at least one transconjugant.

The authors repeated call for good old ‘shoe leather epidemiology’ is amusing considering the difficulty the industry advisors have in accepting the current strong epidemiological evidence, which rests on the four solid pillars of microbial epidemiology: bacterial isolation, bacterial typing, descriptive epidemiology and analytical epidemiology.

References


Correspondence

Tom M. Chiller*, Timothy Barrett and Frederick J. Angulo

Centers for Disease Control and Prevention, Atlanta, GA, USA

Keywords: antimicrobial resistance, food animals

*Corresponding author. E-mail: tnc3@cdc.gov

Sir,

Several studies conducted by the Centers for Disease Control and Prevention (CDC) were cited in the recent article in JAC by Phillips et al. Unfortunately, Phillips et al. have incorrectly linked these studies to statements that do not summarize the conclusions of the authors. Among several examples, we would like to describe three incorrect summaries.

Phillips et al. cite a CDC article in the New England Journal of Medicine on the emergence of multidrug-resistant Salmonella to support the statement: ‘the resistance prevalence varies from time to time and place to place with no obvious relationship to current antibiotic usage patterns in humans or animals’. To the contrary, the article by Glynn et al., which concerns Salmonella serotype Typhimurium DT104 R-type ACSSuT, states ‘the proportion of isolates with five-drug pattern of resistance has increased from less than 1 percent in 1979–80 to 34 percent in 1996’, and therefore describes increasing, not variable, prevalence. The article also states, ‘the emergence of antimicrobial-drug resistance in Salmonella isolates is associated with the therapeutic use and non-therapeutic use of antimicrobial agents in food animals. Prudent use of antimicrobial agents in farm animals and more effective disease prevention on farms is necessary to reduce the dissemination of five-drug-resistant Typhimurium DT104 and to slow the evolution of resistance to additional agents in this and other strains of Salmonella’. This statement was made based on the direct relationship between use of antimicrobial agents in food animals and the emergence of antimicrobial-resistant Salmonella, which results in increased transmission of these resistant pathogens to humans and increased likelihood of compromising treatment options. This relationship and its consequences are supported by numerous lines of evidence.

In citing CDC authored articles in the Journal of Infectious Diseases and Review of Infectious Diseases, Phillips et al. write: ‘it might be thought that antibiotic-resistant salmonellae would have a devastating clinical effect, but this is rarely the case in developed countries’. However, neither of these articles support this statement. In the first article, Lee et al. reported that patients with antimicrobial-resistant Salmonella infections were more likely to be hospitalized than those with susceptible infections, concluding that ‘these data show that treatment of Salmonella infections may be complicated by growing resistance to clinically important antimicrobial agents and by increasing frequencies of extraintestinal complications’. In the second article, Holmberg et al. evaluated investigations of Salmonella outbreaks and found that the data ‘show higher rates of hospitalization and mortality associated with drug resistant than with drug-susceptible strains’. Although Phillips et al. do not define ‘devastating’, we assume they would agree that excess hospitalization and mortality would merit such characterization and, rare or not, would not be a consequence that should be dismissed.

Phillips et al. cite a CDC abstract from the 2000 International Conference on Emerging Infectious Diseases to support the statement: ‘Marano et al. reported a 4 day decrease in the duration of diarrhoea (from 12 to 8 days) for patients infected with fluoroquinolone-resistant strains treated with ciprofloxacin (but paradoxically no decrease for susceptible strains—6 days for both treated and untreated patients)’. This statement does not represent conclusions from the study. In fact, Marano et al. reported that patients with ciprofloxacin-resistant Campylobacter infections had a longer duration of diarrhoea than those with susceptible infections and that the longer duration occurred both among patients who took ciprofloxacin and those who did not.

There are many opportunities to reduce the overuse and misuse of antimicrobial agents in food animals. Reductions in overuse and misuse now and in the future would benefit human health by slowing the emergence and spread of resistant food-borne infections.

References