The association of antimicrobial resistance patterns and reported usage of antimicrobials in commercial growing pig production.

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**Introduction**

The relationship between microbial use and the development of resistance to antimicrobials has been demonstrated through both external models and has been observed clinically. However, the strength of this relationship in practical production systems has not been clearly quantified. We designed this study to examine the strength of the relationship between use of antimicrobials and the occurrence of antimicrobial resistance among *Salmonella* spp. collected from the same groups of growing pig.

**Materials and Methods**

As part of a larger study on risk factors associated with *Salmonella* shedding (1) and antimicrobial resistance (3) we collected fecal samples on 50 farms from slaughter age pigs over a two year period. Fecal samples were collected from each of 15 individually identified pigs 48 hours or less before slaughter. Cecal contents, rectal contents and caudal mesenteric lymph nodes were collected at slaughter. All samples were individually cultured for *Salmonella* spp. using conventional techniques. Positive isolates were serotyped. Antimicrobial sensitivity of isolates was assayed (2). The use of antimicrobials was described by a survey conducted by interview, with written follow-up to provide clarification when necessary.

Data were summarized to describe antimicrobial use and the prevalence of resistance. The association between reported antimicrobial use and detected antimicrobial resistance was tested by ANOVA, weighted for the number of *Salmonella* isolates per herd. Categories with fewer than four observations were omitted from the analysis. The antimicrobials / resistance pairs tested were penicillin use / ampicillin resistance, use of tetracyclines / tetracycline resistance, and sulfonamide use / sulfamethoxazole resistance.

**Results**

A total of 2174 samples were collected, from which 352 *Salmonellae* were isolated. One or more *Salmonella* were detected among 36 of the 50 herds (62%). Isolation rate was highest for cecal content and lowest for rectal content collected at the slaughter plant. In declining order, prevalence estimate by tissue was cecal content (25.6%), mesenteric lymph node (18.0%), fecal samples collected at the farm (6.3%), and rectal content at the plant (5.2%), similar to the findings of the superset 70 herds (3).

Complete surveys responses were available from 46 of the 50 farms. Twenty-nine farms had both a complete survey and one or more *Salmonella* isolates. Of these 29 farms, 24 raised pigs from birth to market, while five had no breeding stock, raising growing pigs only. Among farms with breeding stock, the mean number of breeding age females was 879.

Respondents reported use of nine antimicrobials for therapy and/or growth promotion, either alone or in combination with another antimicrobial. 240 courses of antimicrobial were reported by any method of application (feed, water, or injection) for all stages of growth from weaning until slaughter. Growth promotion was reported as the reason for 96 courses of antimicrobial. In the final stage of growth, the most commonly used antibiotic was tetracyclines (26 herds, 57%). In declining order of use, other antibiotics reported used were bacitracin (25, 54%), tylosin (24, 52%), penicillin (21, 46%), liacymycin (8, 17%) and sulfa compounds (5, 11%).

Antimicrobial resistance varied widely, and are reported in full for the larger dataset (2). Several antimicrobials had no detected resistance, including amikacin, ciprofloxacain, ceftriaxone, trimethoprim/sulfamethoxazole. Antimicrobials with the highest percentage of resistance were novobiocin (100%), tetracycline (47.7%), sulfamethoxazole (29.0%), neomycin (11.1%), ampicillin and ticarcillin (both 10.5%).

Among the three antimicrobial use / resistance pairs tested, a statistically significant relationship (p<0.05) was found only for use of tetracyclines. Herds reporting therapeutic use of tetracyclines in the final growing phase had higher proportion of resistant *Salmonella* isolates (68.3%) than did herds that did not report use of tetracyclines (48.3%) (p=0.049).
Discussion

Antimicrobial use was common among these farms; however, only a few categories of antibiotics represented the majority of use. The most commonly applied antibiotic, tetracycline, was also the antibiotic showing the highest percentage of resistance overall.

Tetracycline resistance was higher among herds using tetracyclines for therapy. Although a causal link cannot be proven by this analysis, one likely explanation is that therapeutic use of tetracyclines selected for a increased proportion of tetracycline resistant organisms. It is, however, possible that tetracycline use in the final stage of growth may be correlated with other factors that contribute to tetracycline resistance. For example, tetracycline use in late stages of growth may be correlated with tetracycline use in earlier stages of growth.

We did not record the length of time between the slaughter and last use of tetracyclines. Although producers are not required withdraw the use of chlorotetracycline before slaughter, they commonly observe the short industry standard voluntary withdrawal period before slaughter. Because of this short withdrawal period, it is likely that tetracycline use was continued later than either sulfa compounds or penicillin for these farms, increasing the likelihood of finding tetracycline resistance organisms at the time of slaughter. Finally, it should be recalled that since tetracycline use reported in this study was predominately for therapeutic purpose, the results of this study cannot be generalized to subtherapeutic use of the drug.

Although no relationship was found for penicillin and sulfonamide use, several limitations of this study must be highlighted. First, although ampicillin use was not reported in these herds, we tested for ampicillin resistance, not penicillin resistance. Although the development of cross-resistance is possible, it is likely that penicillin resistance would have differed from the ampicillin resistance we report. Second, the use of sulfa drugs was uncommon in the last stage of growth. Finally, use of both of these compounds in common in early stages of growth, possibly leading to resistant organisms that are retained until the time of slaughter. In combination, these factors reduced the likelihood that this study would detect relationships between antimicrobial use and corresponding resistance.

References

