PEER REVIEWED

Dairy veterinarians' views on antimicrobial use, resistance and treatment practices

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Abstract

Veterinarians are being asked to provide more oversight of antibiotics used on dairies and promote stewardship of these drugs because of the risk for development of antimicrobial resistance. As organizations work to develop stewardship guidelines, gathering data on veterinarians' views and actual use can better inform those guidelines. The purpose of this project was to survey dairy veterinarians to understand current antimicrobial use practices and views on antimicrobial resistance. A 50-question online survey was developed and a link sent to members of the Academy of Dairy Veterinary Consultants. The final response rate of 41% (58 of 143) included only practicing veterinarians. Fifty-nine percent did not believe that the current use of antimicrobials on dairy farms contributed to antimicrobial resistance in human pathogens. Most of the respondents (83%) felt that there was unnecessary use of antimicrobials on dairies, particularly in pre-weaned calves, primarily due to protocol non-compliance and farmers' or employees' misidentification of healthy animals as sick and treatment of them with antimicrobials. About half the respondents always had written treatment protocols for their clients, and 40% always provided training on those protocols. Blanket dry-cow therapy was recommended by 65% of the practitioners. The results of this survey provide a baseline of western, large dairy herd veterinary antimicrobial use and recommendations. Responses indicated opportunities for dairy practitioners to improve some antimicrobial stewardship practices that could reduce antimicrobial use.

Key words: antimicrobials, dairy, treatments, survey

Résumé

On demande aux vétérinaires de surveiller plus attentivement les antibiotiques utilisés dans les fermes laitières et de promouvoir l'intendance de ces drogues en raison du risque de développement de la résistance antimicrobienne. Alors que les organisations développent des lignes directrices relatives à l'intendance, l'obtention de données sur le point de vue des vétérinaires et leur utilisation réelle des antibiotiques peut mieux éclairer ces lignes directrices. Le but de ce projet était de sonder les vétérinaires des fermes laitières pour mieux comprendre les pratiques courantes d'utilisation des antimicrobiens et les points de vue sur la résistance antimicrobienne. Un sondage en ligne de 50 questions a été développé et un lien a été envoyé aux membres de l'Académie des consultants vétérinaires laitiers. Le taux final de réponse était de 41% (58 sur 143) et n'incluait que les vétérinaires pratiquants. Parmi les répondants, 59% ne croyaient pas que l'utilisation actuelle des antimicrobiens dans les fermes laitières contribuait à la résistance antimicrobienne pour les pathogènes humains. La majorité des répondants (83%) sentait qu'il y avait une utilisation inutile des antimicrobiens dans les fermes laitières, particulièrement chez les veaux avant sevrage, en raison essentiellement du non-respect des protocoles et parce que les producteurs ou leurs employés donnaient des antimicrobiens à des animaux sains faussement identifiés comme malades. Près de la moitié des répondants fournissaient toujours des protocoles écrits à leurs clients et 40% donnaient toujours une formation pour ces protocoles. Une thérapie de couverture pour les vaches taries était recommandée par 65% des vétérinaires. Les résultats de ce sondage fournissent une base de référence sur l'utilisation et les recommandations pour les antimicrobiens vétérinaires dans de grands troupeaux de laitiers occidentaux. Les réponses donnaient des pistes de solution pour les vétérinaires de fermes laitières afin d'améliorer certaines pratiques d'intendance des antimicrobiens qui pourraient réduire l'utilisation des antimicrobiens.

Introduction

Veterinarians are being asked by the US Food and Drug Administration to increase their oversight of antimicrobial use (AMU) in food animals.[8,10] Although the risk of human pathogen resistance being the direct result of AMU in food animals is smaller than that for human medical AMU,[12] there

is emerging evidence that decreased veterinary AMU has led to reduced resistant commensal *E. coli* in livestock.[5] These resistant *E. coli* can serve as a reservoir for resistance genes for animal and, potentially, human pathogens.[34,41] To reduce AMU and potentially curb antimicrobial resistance (AMR), the US Food and Drug Administration (FDA) developed the Veterinary Feed Directive rule to regulate the use of antimicrobials in animal feed and eliminate in-feed antimicrobials for growth promotion purposes.[8] Producers must have a valid veterinary-client-patient relationship (VCPR) and a directive from their veterinarian to feed antimicrobials for treatment or control of bacterial disease.[9] In addition to this rule, stricter legislation in 1 state[a] eliminated the use of over-the-counter sales of antimicrobials to animal owners, and requires that all antibiotics be used only under veterinary prescription for therapeutic purposes, and that stewardship and AMR continuing education be met before a veterinarian's license can be renewed. The Center for Veterinary Medicine of the US FDA recently released a set of goals for 2019-2023, focused on supporting antimicrobial stewardship (AMS) in veterinary settings.[10] In order to foster AMS, veterinarians need to recognize what constitutes judicious use and what practices promote stewardship.

Antimicrobial stewardship is a coordinated program to promote responsible use, 1 part of which is reduced AMU and changing practitioner prescribing habits. The major routine uses of antimicrobials in the dairy industry are for dry-cow therapy, clinical mastitis therapy, metritis, respiratory illness, gastrointestinal disease, as well as lameness,[37,35,23,36] and in the US antimicrobials are administered primarily by the farmer or farm employee. With the request for increased veterinary oversight, some consultation and instruction by the veterinarian is needed for making on-farm AMU decisions. Sawant and others investigated the use of antibiotics in Pennsylvania dairy herds and found that only about 21% of dairy producers had written treatment protocols, and only 32% consulted with a veterinarian before treating animals with antimicrobials.[37] From a 2006 Washington state survey of dairy producers, only about 25% of respondents had written treatment protocols.[35] In a more recent study, about 45% of producers in a Tennessee study had written treatment protocols.[18] In a UK study of dairy farmers, more responsible treatment choices were associated with the frequency of veterinary contact.[23] Although the FDA suggests that the use of medically important drugs in food animals requires veterinary oversight[8] and that written treatment protocols are needed for drug residue prevention,[31] many producers report little veterinary consultation and no written treatment protocols.

Veterinary surveys of prescribing practices and antimicrobial stewardship are limited, have had very different emphases, and have asked very different questions. Studies done in Ohio, Ontario, Europe, Ireland, and New Zealand have been conducted in regions with mostly small herd sizes (<100 cows).[7,26,14,19,28] Because the roles and responsibilities of dairy veterinarians might be different in regions with large herd sizes due to layers of management and employees responsible for administering treatments,[39] establishing a baseline of AMU by these veterinarians is needed to evaluate progress towards AMU reduction and improved AMS.

The objective of this study was to examine primarily western US dairy veterinarians' attitudes and practices regarding the use of antimicrobials, treatment protocols, and training. The overall goal was to gain a broader understanding of current dairy veterinarian AMU that might inform continuing education needs.

Materials and Methods

Study Population

Practicing veterinarians who were members of the Academy of Dairy Veterinary Consultants (ADVC) were the target of the survey. The study population represented a convenience sample of dairy-focused veterinarians. The organization included about 180 members from private practice, industry, academia as well as veterinary students, with the majority residing in the western United States. An email list, maintained for ADVC by the University of California, Davis, Information and Educational Technology group, was used for delivery of the survey.

Study and Survey Design

This was a cross-sectional study and consisted of a 50-question, online questionnaire. The survey was created using the secure Qualtrics online survey software[b] available through Washington State University. The questions were grouped into the following sections: (1) Antimicrobial Protocol Development, (2) Protocol Training, (3) Protocol Follow-up and Compliance, (4) Antimicrobial use following Surgery and Medical Procedures, (5) Therapeutic use of antimicrobials, and (6) Demographics. Questions were designed and evaluated using guidelines from Dillman.[15] The project was reviewed and provided exempt status from the WSU Institutional Review Board (#16300). Based on Dilman's online survey design method, an invitation email (cover letter) requesting participation in the survey was sent to members of the ADVC list serve on August 7, 2017 and remained open until September 18, 2017. Six weekly reminders were emailed to ADVC members to encourage participation. In order to filter responses from members not in private or clinical practice, the first question asked for practice type. If 'private practice' was selected, the respondent was allowed to complete the survey (see Appendix).

Data Management and Analysis

Results from the survey were acquired from WSU Qualtrics software internal website and exported into a spreadsheet format. Further analysis of the results and descriptive statistics were achieved by use of the spreadsheet software.[c] Odds ratios and Chi squared analyses were calculated using

an online statistical calculator.[d] Comparisons were made for responses to questions based on veterinary school graduation before the year 2000 and after 1999, as well as comparisons of AMU practices based on attitudes about AMR.

Results

Demographics

There were 143 members on the ADVC list serve. A total of 92 members initiated the survey, and of those, 58 were in private practice, resulting in a usable survey response rate of 41%. Not all practitioners responded to every question. Respondents represented in the study primarily practiced in the northwestern and southwestern United States (88%), with veterinary school graduation years ranging from 1973 to 2016 (median = 1999).

A preponderance of respondents (90%) indicated that the proportion of dairy cattle work in their practice was greater than 75%. About 70% of the 49 participants serviced herds that averaged 1,000 to 5,000 cows (Table 1). When asked about services offered to clients, 74% of 49 respondents offered at least 11 different services from a list of 16 services including mastitis/milk quality, obstetrics, farm employee training, record analysis, reproduction, treatment protocols, heifer management, necropsy, surgery, calf management, and disease diagnosis and treatment (Figure 1). Other services offered included facility consulting, biosecurity, nutrition, financial consulting and embryo transfer, and/or other advanced reproductive technologies.

Table 1. Average dairy herd size for practitioners responding to a survey on antimicrobial use.

Herd size	%	Number
<100	0.0	0
100-500	2.0	1
500-1,000	14.3	7
1,000-5,000	69.4	34
5,000-10,000	10.2	5
>10,000	4.1	2
Total		49

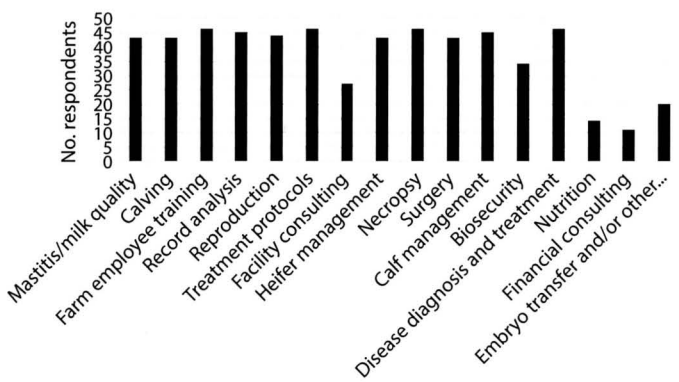

Figure 1. Different veterinary services offered to dairy clients by 53 practitioners.

Views on Antimicrobial Use

More than half (59%) of 49 respondents disagreed with the statement "Do you believe the current use of antimicrobials on dairy farms contributes to antimicrobial resistance in human pathogens?" There was no association between disagreement with this statement and the year of graduation from veterinary college before the year 2000 or after 1999. Only 12.9% of 54 respondents always recommended or tried a non-antibiotic treatment (such as fluids or probiotics depending on the disease) before recommending treatment with an antibiotic. Over 85% of 51 practitioners reported that they always followed AMDUCA guidelines when recommending a drug to be used in an extra-label fashion. There was no association between those who do not believe the current use of antimicrobials on dairies contributes to AMR in human pathogens and those who *sometimes* followed AMDUCA guidelines ($P > 0.4$). When recommending an antimicrobial treatment, 17% of respondents *never* tried to avoid using drugs (or used them as a last resort) that are of high human importance. There was no association between those who do not believe the current use of antimicrobials on dairies contributes to antimicrobial resistance in human pathogens and those who never consciously tried to avoid using drugs that are of "high human importance"[11] when recommending an antimicrobial treatment ($P > 0.2$). However, of those who responded that they *never* tried to avoid using drugs that are of high human importance when recommending an antimicrobial treatment, none believed that the current use of antimicrobials on dairy farms contributed to antimicrobial resistance in human pathogens.

We asked the question, "Do you believe there is unnecessary use of antimicrobials in any of the following areas on any of your clients' farms?" with the potential responses being different stages of the production cycle on the farm. Most of 53 respondents (74%) believed that unnecessary use of antimicrobials existed in pre-weaned calves and 34% believed unnecessary use of antimicrobials existed in growing heifers (Table 2). A set of five possible responses was provided for a question asking why respondents thought there might be unnecessary use of antimicrobials in cattle. The majority responded with "dairy staff not following protocols" and "other" (Figure 2). The major themes within the open-ended responses for "other" included personal beliefs about treatment needs by the farm and personnel (N=9), outside influencers (such as the pharmaceutical industry) on drug use (N=4), concern by dairy personnel about animal welfare (N=3), and the high costs associated with selective treatment (N=2).

Treatment Protocols and Training

Four of 55 (7%) respondents *never* wrote treatment protocols (Table 3). More than half (53%) of the respondents

Table 2. Responses by 53 dairy practitioners to the question "Do you believe there is unnecessary use of antimicrobials in any of the following areas on any of your clients' farms?"

Animal group	%	Number
Pre-weaned calves/hutches	73.6	39
Growing heifers	34.0	18
Cows in the hospital	37.7	20
Cows in fresh pen	28.3	15
Dry-cow therapy	47.7	25
Prophylactically in cows (i.e. after surgeries, prevention of digital dermatitis)	15.1	8

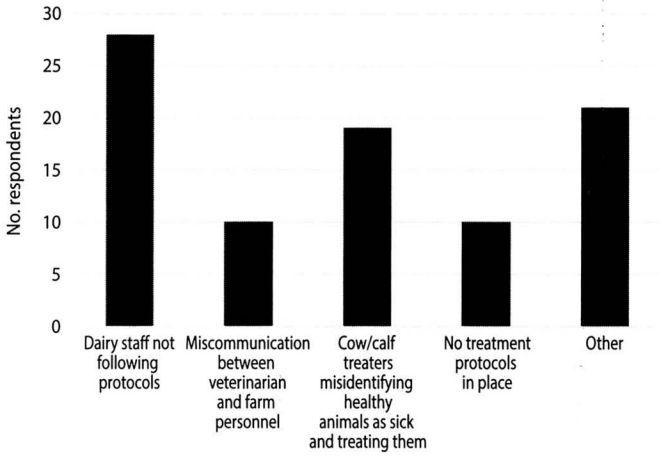

Figure 2. Primary reasons for unnecessary use of antimicrobials in cattle provided by 53 dairy practitioners.

always had written protocols for their clients that outlined when an animal required a treatment with antimicrobials, whereas 40% *sometimes* had written protocols for their clients. When developing treatment protocols, the 49 respondents to this question typically discussed the protocol with the dairy manager (90%), dairy owner (84%), hospital crew (67%), and the cow and/or calf treatment crew (73%).

About 40% of 54 respondents *always* provided training to the treatment crew and 68% of these trainings were offered in both English and Spanish. During these trainings the veterinarians would either give verbal examples as to what to look for (35%), walk around with the treatment crew and point out animals that need to be treated (38%), and/or provide pictures of specific clinical signs to look for to identify animals that need to be treated (26%). Most of 54 respondents (93%) would review treatment protocols at least yearly on some farms (51%) or all farms (41%) while 7% did not review protocols on client farms. The majority of respondents followed up on their treatment protocols by observing the treatment crew (32%), while others reviewed treatment records (25%), met with the dairy owner (17%), or did a combination of all three. About 19% of 54 respondents

Table 3. Responses by 55 practitioners to a question on the groups of cattle for which they wrote treatment protocols.

Age group	%	Number
Pre-weaned calves	85	47
Growing heifers	84	46
Adult cows	85	47
I do not write treatment protocols	7	4
Total		55

visited the drug storage area to look at inventory and labeling at least weekly; however, 41% did this monthly, 30% annually, and 10% never visited the drug storage area. Fifty percent of 54 respondents reported that daily, permanent treatment records were being maintained on *all* of their client farms.

Specific Drug Uses

In response to the question, "Do you use the same amount of drug to treat a first lactation heifer that you would to treat a 3+ lactation cow?", 18% of 53 practitioners responded 'never', 69% 'sometimes', and 11% 'always'. About 4% of 53 respondents *always* sampled for mastitis pathogens to establish a culture-based treatment for clinical mastitis while 85% said 'sometimes' and 11% never did. About 4% of 53 respondents also *never* did necropsies to evaluate diagnoses and treatments done by farm personnel, 94% reported that they *sometimes* did necropsies, and 1 reported *always*.

Questions on very specific antimicrobial uses were asked. When asked about placing antimicrobials into the abdomen after performing a cesarean section, 19% of 53 respondents reported that they always placed antimicrobials in the abdomen (Table 4). There was a tendency for more veterinarians who graduated before the year 2000 to *always* or *sometimes* put antimicrobials in the abdomen, compared to those graduating after 1999 (81% vs 56%; $P = 0.08$). After performing a surgery to correct a left- or right-displaced abomasum, 4% of respondents *always* and 15 % *sometimes* placed antimicrobials in the abdomen. After surgically correcting a uterine prolapse, 42% of 54 respondents *always* used or recommended an antimicrobial treatment. After performing a fetotomy, about half (49%) of 53 respondents *always* recommended putting the cow on antimicrobial treatment and 49% *sometimes* did. Eighteen percent of 49 respondents *always*, and 69% *sometimes*, used or recommended antimicrobials for cows with retained placentas.

Specific questions asked for case definitions and drug uses for metritis, calf diarrhea, calf pneumonia and older heifer pneumonia, in addition to information regarding mastitis diagnostics and preventive treatment. Forty-seven of the practitioners responded to the open-ended question "What is your definition of metritis?" The most common terms used to define metritis included fetid, foul smelling, purulent, malodorous discharge (91% of respondents used 1 or more

Table 4. Specific antimicrobial uses reported by dairy practitioners.

Antimicrobial use	Number (percent)			
	Never	Sometimes	Always	Total
After performing a C-section do you place antimicrobials in the abdomen?	18 (34)	25 (47.1)	10 (18.9)	53
After performing a left/right displaced abomasum surgery do you place antimicrobials in the abdomen?	42 (80.8)	8 (15.4)	2 (3.8%	52
After surgically correcting a prolapse do you use or recommend antimicrobials?	4 (7.6)	27 (50.9)	22 (41.5)	53
After performing a fetotomy do you use or recommend antimicrobials?	1 (1.3)	26 (50)	25 (48.1)	52
Do you use or prescribe the use of an antimicrobial for retained placentas?	6 (12.2)	34 (69.4)	9 (18.4)	49

of these terms), with or without fever (62%), off feed, inappetence, anorexia (19%), and an enlarged uterus (13%). A few practitioners included a time period of 'days in lactation' when this would occur or not resolve by. Eleven different responses were offered for drugs and ways to treat metritis. Many practitioners reported using a number of different drugs and ways to treat this disorder (Figure 3). The most common drugs used included ceftiofur hydrochloride,[e] followed by ampicillin trihydrate,[f] and ceftiofur crystaline free acid.[g]

When asked to define calf diarrhea, the most common terms used included liquid, watery, or loose stools (73% of respondents), dehydrated (16%), fever (13%), and/or depressed (13%). Practitioners were also asked for their calf diarrhea treatment protocol (Figure 4). Of the 44 that responded, the most common treatments included oral electrolytes (70%), IV fluids (57%), and 25 (57%) reported an antimicrobial. Fifteen (35%) of the 44 responses included information on severity and symptom of disease as criteria for different treatments.

Practitioners were asked how they determined if a pre-weaned calf or post-weaned heifer had pneumonia. The majority (31% of 48) selected the Modified California Bovine Respiratory Disease (BRD) Scoring System,[27] followed by the McGuirk[29] (Wisconsin) Clinical Scoring System for BRD (29%). While many practitioners selected "other: please specify" (40%), their responses all included multiple components of both referenced scoring systems including fever, rapid or labored breathing, lung auscultation, nasal discharge and a complete physical exam. A number of drugs were listed for practitioners to select from for their recommended treatments of pneumonia. Many practitioners selected multiple drugs. The most common drugs selected to treat pre-weaned calf pneumonia were; florfenicol[h] (81%), followed by tulathromycin[i] (69%), and enrofloxacin[j] (63%). In regards to older (post-weaned) heifer pneumonia, the most common drugs selected were the same: florfenicol (85%), followed by tulathromycin (79%), and enrofloxacin (42%).

When asked about establishing culture-based treatments for clinical mastitis, 81% of 47 practitioners reported that they *sometimes* established culture-based treatments, while 11% *always* did, and 8% *never* did. More than a third (37%) of 49 respondents reported *always* using mastitis severity scoring to determine treatments for clinical mastitis, while 51% *sometimes* used severity scoring and 12% *never* used severity scoring. The primary dry-cow therapy (DCT) protocol that 49 respondents recommended for prevention of mastitis was blanket antibiotic dry-cow therapy (65%), followed by using cow records upon which to base dry-cow antibiotic treatment (6%), and recommending a culture-based dry-cow antibiotic treatment (4%). Many (20%) selected 'other' and specified that it depended on their cli-

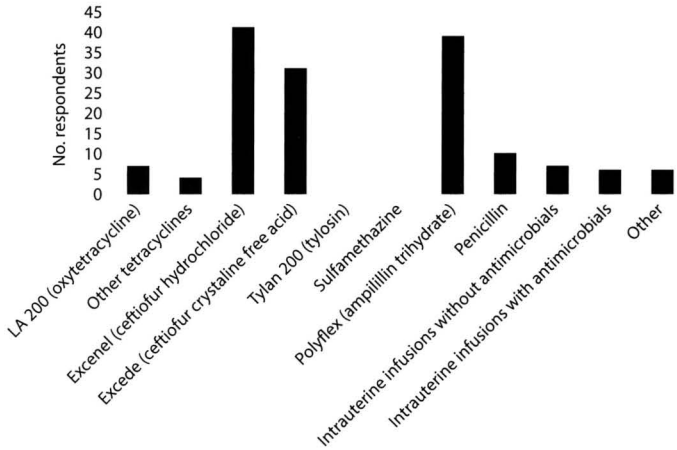

Figure 3. Drugs used to treat metritis selected by 47 practitioners.

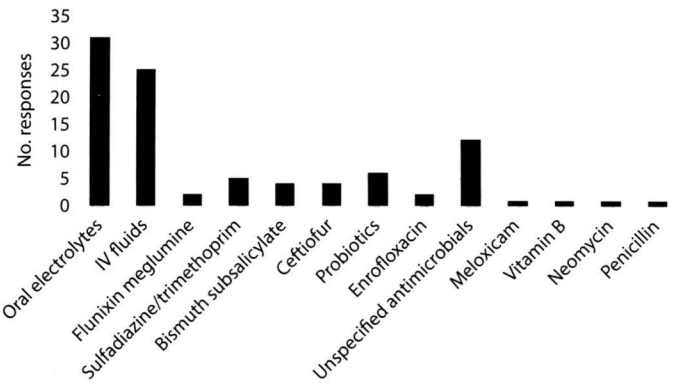

Figure 4. Treatments included in 44 practitioners' calf diarrhea protocols.

ents. Practitioners who graduated before 2000 had 4 times greater odds to recommend blanket DCT compared to those graduating after 1999 (OR = 4.6, 95% CI 1.2, 16.4; $P = 0.02$).

Discussion

The majority of respondents believed that the current use of antimicrobials on dairy farms did not contribute to antimicrobial resistance in human pathogens. In a 2001 Canadian study, 86% of dairy practitioners had some level of disagreement with this concept, while 81% agreed that AMU in the dairy industry is contributing to decreased antimicrobial efficacy in cattle.[26] In Italy, bovine veterinarians were aware of the problem of AMR, but half believed that new antimicrobials were going to be available to replace the less-effective ones.[4] In an Australian study, over 60% of veterinarians thought that their individual AMU had minimal to no effect on AMR in human pathogens, but about the same percentage felt that overall veterinary AMU had moderate to strong contributions to AMR in human pathogens.[22] However, if veterinary practitioners were concerned about the role of veterinary AMU and AMR in people, they were more likely to engage in antimicrobial stewardship programs.[22] Similarly, dairy producers had a higher threshold for treating with antimicrobials if they expressed greater concern for the public health impact of livestock AMU.[20] Although the risk from food animal AMU is not as large as that from human medical use,[12] there is still an incompletely understood risk from food animal AMU to AMR in both animal and human pathogens.[24,41] Education on the actual risks from livestock AMU for AMR in human pathogens is essential to discuss AMU reduction in food animal practice and engage practitioners in stewardship programs.

Although not necessarily believing in the risks for human pathogen AMR from farm AMU, the participating practitioners believed that there was unnecessary use of antimicrobials on at least 1 of their client farms, with preweaned calves the most common group of concern. The primary reasons for unnecessary AMU cited by veterinarians in our study were 'dairy staff not following protocols' and 'cow/calf treaters misidentifying animals as sick and treating them'. In a study of US employee treatment-decision motivation for calf care, most calf care personnel based their decision to treat on their personal beliefs and values.[13] Beliefs and values must be addressed when discussing treatment options with clients and their employees in addition to training on sick calf identification.

Having veterinary oversight of on-farm AMU implies that the veterinarian is helping farmers with treatment decisions. One way to understand and control AMU on the farm is through use of written treatment protocols. Just over half the respondents in our study indicated they *always* had written protocols for their clients that outlined when an animal required therapeutic treatment with antimicrobials, significantly more than what has been reported in past studies, but maybe not the ultimate target. About 28% of Canadian dairy practitioners provided a written protocol for use of antimicrobials for lactating cows[26] and about one-fourth of Ohio practitioners reported consistently providing written protocols.[7] To use antimicrobials judiciously, veterinarians should be working together with the dairy owner, manager, hospital crew, and calf treatment crew to write protocols to help assure that the correct animal is treated with the appropriate antimicrobial, correct dose, and appropriate route of administration, frequency, and duration. Accurate dosing is important, but more than 10% of our respondents claimed that they *always* recommended the same amount of antimicrobial to treat a first-lactation heifer that they would use to treat an older cow, and 69% of respondents *sometimes* recommended this. We did not specify the disease, so there could have been some confusion about this question. However, without correctly knowing the body weight an animal may be under or overdosed. However, most people treating cattle do not always have a way to accurately get a weight on each animal and are left to estimate the animal's weight and associated drug dose. Visually assessing the weight of the animal tends to result in underdosing large-sized animals, and overdosing smaller animals.[43]

Veterinary oversight of on-farm AMU would also include training farmers and/or employees on treatment protocols.[1] Only 40% of respondents *always* provided training to those treating sick animals. Once individuals are trained, there is a need to evaluate compliance with the protocols as well as protocol efficacy. The American Association of Bovine Practitioners recommends practitioners review treatment records every 6 months and assess drug inventory in relation to treatment protocols and on-farm antimicrobial drug dispensing.[2] The majority of respondents in our survey reviewed treatment protocols at least yearly, but not on all client farms. Eighty-nine percent of respondents assessed drug inventory at least annually. By routinely assessing drug inventory, reviewing treatment records and working with people responsible for treatment, practitioners can better understand which drugs are actually being used, the dairy's compliance with treatment protocols, whether the protocols are working, and make sure drugs are not expired.

The most common dairy farm uses of antimicrobials include therapy for mastitis (particularly blanket DCT), metritis, and diarrhea and respiratory disease in calves. A wide range of therapies were reported for metritis treatment. Ceftiofur was the most common drug selected by practitioners to treat metritis in dairy cattle. It was also selected as a treatment for heifers with pneumonia. Third-generation cephalosporins (such as ceftiofur) are drugs valued by physicians to treat serious, life-threatening diseases in people but there are benefits to its use for metritis treatment.[21] Perhaps more important is that the veterinarian educate the hospital or treatment crew to properly identify sick animals to prevent ceftiofur overuse and potential emergence of resistant bacteria to ceftiofur and other third-generation cephalosporins.

Chances of successful respiratory disease treatment in calves requires early detection.[27] Over half the respondents used a clinical scoring system for BRD to identify calves needing treatment.[27,29] With the use of clinical scoring systems for BRD, practitioners can likely prevent the use of antimicrobials in animals who truly do not have BRD. Unfortunately, our survey did not identify whether farm employees were trained on the use of these scoring systems.

More than half of those reporting treatment protocols for calf diarrhea recommended an antibiotic as well as some form of fluids. Two primary reasons to justify AMU for calf diarrhea are to prevent bacteremia as well as reduce overgrowth of coliform bacteria in the small intestine.[40] To reduce AMU for calfhood diarrhea it is recommended to only use antimicrobials when diarrheic calves also express systemic signs (depression, decreased appetite, dehydration, fever) and to continue to closely monitor calves with uncomplicated diarrhea.[40]

The average cost of a case of mastitis is significant, estimated to be around $444, including the cost of antimicrobials, diagnostics, nonsalable milk, veterinary costs, lower milk production, losses associated with poor reproduction, and the costs of replacements.[45] Over 80% of our respondents *sometimes* established culture-based treatments. A study of New York dairy herds included culturing cows with mild to moderate clinical mastitis and only treating cows that were positive for coagulase negative *Staphylococcus*, *Streptococcus* group G and/or group C, *Streptococcus uberis*, *Streptococcus dysgalactiae*, and *Enterococcus* spp. Selectively treating these cows for mastitis resulted in a 67% reduction of intramammary antimicrobial use, and over $30,000 increased cash flow per 1,000 cows.[45]

Blanket DCT has been recommended to dairy farmers for decades as a means of preventing new intramammary infections (IMI), but because of the total volume of drug used, this practice has come under scrutiny as potentially not judicious use.[38] In the most recent USDA National Animal Health Monitoring System (NAHMS) dairy study, 80% of all dairy operations used blanket DCT to aid in the prevention and treatment of mastitis. In our study, almost two-thirds of respondents recommended blanket DCT to their clients, while 6% recommended DCT based on cow somatic cell counts (SCC), and 4% recommended therapy based on milk cultures.[42] A previous study looked at a selective DCT where cows received intramammary antibiotics based on their last SCC test alone. Although there was an 85% reduction in the use of antimicrobials, there was an increase in the incidence of mastitis following the dry period.[38] The Netherlands changed policies from blanket DCT to selective DCT at the end of 2012, with a pre-dry-off SCC level to trigger antimicrobial DCT of 150,000 cells/mL for primiparous cows and 50,000 cells/mL for multiparous cows.[44] This policy led to a dramatic reduction in AMU and did not appear to significantly increase new IMI or mean percent cured IMI during the dry period. Selection of cows for DCT using a Petrifilm-based on-farm culture showed a 21% reduction in antimicrobial use for dry-cow therapy, and the risk for IMI following the dry period was comparable to blanket DCT.[6] Blanket DCT will likely be a target for reducing AMU, and through a combination of management and diagnostic interventions, selective DCT represents a feasible opportunity.[33] Veterinarians serving large dairy herds should evaluate this policy that could potentially reduce drug costs and AMR.

Specific veterinary antimicrobial uses were requested of practitioners in our survey. A number of practitioners indicated that they *always* place antimicrobials in the abdomen after performing a cesarean section, or after surgically correcting a displaced abomasum. Although there are no antimicrobials that are labeled for intra-abdominal administration, Newman noted that after performing a cesarean section in cattle some practitioners may lavage the abdomen with ceftiofur hydrochloride, potassium penicillin, and/or oxytetracyclines to reduce the risk of adhesion formation.[32] Use of ceftiofur in this manner would be an extra-label route of administration which is not currently allowed in the US. In the Netherlands, where a recent efficacy study was done, the only antimicrobial labeled for use as a surgical prophylaxis in cattle in that country was ampicillin-sodium given intravaneously.[25] In human studies, the use of antibiotic-infused collagen sponges intraoperatively during abdominal surgeries actually increased the risk of surgical site infections.[3] In a controlled study looking at antimicrobial administration given perioperatively in cats and dogs during clean-contaminated surgeries, there was no difference in postoperative infection rates between groups that received cephalexin and those receiving a placebo.[3] In a university veterinary hospital setting, investigators conducted a randomized clinical trial comparing the use of prophylactic antimicrobials in cattle undergoing cesarean surgery or exploratory laparotomy. They found that the post-surgery use of antimicrobials after abdominal surgeries could be reduced. They estimated that for every 29 cows receiving prophylactic antimicrobials after a cesarean surgery 1 cow was prevented from developing a serious surgery-related complication, and for every 53 cows receiving prophylactic antimicrobials after an exploratory laparotomy 1 cow was prevented from developing a serious surgery-related complication.[25] However, in a university hospital there may be a lower chance for surgery site or abdomen contamination compared to field surgeries. Prophylactic AMU would be considered prudent given surgeries with a high risk of significant bowel leakage or likelihood for anaerobic bacteria to be present.[22]

The majority of respondents *sometimes* or *always* recommended placing the cow on antimicrobials following a fetotomy, surgical correction of a prolapse, and for cows with retained placentas (RP). Dystocias, uterine prolapses, and retained placentas put cows at a greater risk for developing metritis.[17] Giving systemic antimicrobials after fetotomies and prolapses are indicated because these procedures put the cow at risk for developing metritis and/or endometritis.[30] Drillich

found that systemic antibiotic treatment of all cows with RP was not superior to a selective antibiotic treatment of cows with RP and a fever.[16] Although ceftiofur is not labeled for the treatment of RP it can be used at the labeled dose and route if the veterinarian believes that it is necessary treatment for selective cases, particularly if there were other complications.

Practitioners are asked to avoid using or reduce the use of classes of drugs important to human medicine. According to WHO the "Highest Priority Critically Important Antimicrobials" are: quinolones, third and higher-generation cephalosporins, macrolides and ketolides, glycopeptides, and polymyxins.[46] The issue with restricting use of these drugs is that alternative drugs for food animal medicine are few. The focus should perhaps be on overall reduction in AMU. Reduction in AMU on dairy farms should begin with disease prevention. One drawback to this study is that specific prevention practices were not surveyed. However, practitioners noted a variety of herd health services they offered that included some preventive medicine services such as heifer management, nutrition, facility consulting, calf management and mastitis, and milk quality consultation services. A review of all preventive medicine services with each client and strengthening those would be 1 way to assist clients in curbing AMU.

Conclusions

This survey highlighted some of the AMU practices by dairy veterinarians in the west who serve predominantly large herd clients. It also uncovered some needs for continuing education and research including the need for treatment protocol training, and providing practitioners with methods and strategies for evaluating protocol compliance and assessment of treatment efficacy, including the legitimate risk for development of AMR from AMU in cattle. In addition, some practitioners might appreciate some guidelines for training dairy farm employees. Most practitioners are engaged in providing herd health programs, but could potentially reevaluate the strength and effectiveness of their preventive medicine practices to reduce the use of antimicrobials.

Endnotes

[a] California Senate Bill 27, sponsored by Hill, 2015
[b] Qualtrics[XM], https://www.qualtrics.com/research-core/survey-software/
[c] Excel, Microsoft, Redmond, WA
[d] OpenEpi: Open Source Epidemiologic Statistics for Public Health, Version 3.01. www.OpenEpi.com
[e] Excenel®, Zoetis Animal Health, Florham Park, NJ
[f] Polyflex®, Boehringer Ingelheim Vetmedica, St. Joseph, MO
[g] Excede®, Zoetis Animal Health, Florham Park, NJ
[h] Nuflor®, Merck Animal Health, Madison, NJ
[i] Draxxin®, Zoetis Animal Health, Florham Park, NJ
[j] Baytril®, Bayer Animal Health, Shawnee, KS

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Appendix

Survey

We are being asked as a profession to consider antimicrobial stewardship in our treatments and the treatment protocols we provide to clients, and to provide greater oversight of antimicrobial use on our clients' farms. This survey is intended to gather baseline information about specific antimicrobial uses in dairy practice. The survey is anonymous and only summary results will be provided. We appreciate your participation by completing every question in this questionnaire. Your input is very valuable to us and the profession so that we can help develop more relevant antimicrobial stewardship education. Thank you.

What is your practice type?

- o Private Practice
- o Industry
- o Academia
- o Other: please indicate

(If not in private practice, skip to Thank you, you are done!)

Protocol Development

Do you have written protocols for your dairy/ calf ranch clients that outline when an animal requires antibiotic treatment?

- o Never
- o Sometimes
- o Always

For what dairy cattle do you write treatment protocols? (Check all that apply)

- o Pre-weaned calves
- o Growing heifers
- o Adult cows
- o I do not write treatment protocols

If you do not write your own treatment protocols who does?

- o No protocols are in place
- o Dairy owner
- o Herdsman
- o Hired consultant
- o Other: please specify

When developing a treatment protocol, with whom do you discuss the protocol? (Check all that apply)

- o I do not write treatment protocols
- o Dairy owner
- o Dairy manager
- o Hospital crew
- o Cow/calf treaters
- o No on-farm personnel

Do you recommend or try a non-antibiotic treatment (i.e. fluids or probiotics) before recommending treating the animal with an antibiotic (depending on the disease)?

- o Never
- o Sometimes
- o Always

Do you follow AMDUCA guidelines when recommending a drug to be used in an extra-label fashion?

- o Never
- o Sometimes
- o Always

Do you use the same amount of drug to treat a first-lactation heifer that you would to treat a 3+ lactation cow?

- o Never
- o Sometimes
- o Always

When developing a treatment protocol do you consciously try to avoid using drugs (or use them as a last resort) that are of high human importance?

- o Never
- o Sometimes
- o Always

Protocol Training

Do you provide training to those who will be treating sick animals?

- o Never
- o Sometimes
- o Always

In what language are these trainings?

- o I do not provide training for treatments
- o English
- o English and Spanish
- o Spanish

When training people to identify sick animals do you (check all that apply)

- o Give verbal examples as to what to look for
- o Walk with the treatment personnel and point out animals that need to be treated
- o Provide pictures of specific clinical signs for individuals to look for to identify sick animals
- o I do not provide training on sick animal identification

Protocol Follow-up/Compliance

Do you review your treatment protocols at least yearly?

- o No
- o On some farms
- o On all farms

How are follow-ups of treatment protocols being done?

- o I do not review the treatment protocols
- o I review the treatment records
- o I observe the treatment crew
- o I have a meeting with the owner
- o Other: please specify

Do you sample for pathogens to establish a culture-based treatment?

- o Never
- o Sometimes
- o Always

Do you do necropsies to evaluate diagnoses and treatments done by farm personnel?

- o Never
- o Sometimes
- o Always

How often do you visit the drug storage area to look at the inventory of drugs (to see if the drugs have a label, if any drugs are expired, etc.)?

- o Weekly
- o Monthly
- o Yearly
- o Never

Are daily, permanent treatment records being maintained?

- o On none of my farms
- o On some of my farms
- o On all of my farms

Surgery Uses of Antimicrobials

After performing a C-section do you place antimicrobials in the abdomen?

- o Never
- o Sometimes
- o Always

After performing a left/right displaced abomasum surgery do you place antimicrobials in the abdomen?

- o Never
- o Sometimes
- o Always

After surgically correcting a prolapse do you use or recommend antimicrobials?

- o Never
- o Sometimes
- o Always

After performing a fetotomy do you use antimicrobials?

- o Never
- o Sometimes
- o Always

Therapeutic Use of Antimicrobials

Do you prescribe the use of an antimicrobial for a retained placenta?

- o Never
- o Sometimes
- o Always

What is your definition of metritis?

- o

Which drugs do you choose to treat metritis? (Check all that apply)

- o LA 200 (oxytetracycline)
- o Other tetracycline
- o Excenel (ceftiofur hydrochloride)
- o Excede (ceftiofur crystalline free acid)
- o Tylan 200 (tylosin)
- o Sulfamethazine
- o Polyflex (ampicillin trihydrate)
- o Penicillin
- o Intrauterine infusions without antimicrobials
- o Intrauterine infusions with antimicrobials

How do you determine if a calf has pneumonia?

- o Modified California BRD Scoring System
- o McGuirk (Wisconsin) Clinical Scoring System for BRD
- o Other: please specify

Which drug(s) do you use to treat pre-weaned calf pneumonia?

- o LA 200 (oxytetracycline)
- o Micotil (tilmicosin)
- o Draxxin (tulathromycin)
- o Nuflor (florfenicol)
- o Baytril (enrofloxacin)
- o Ceftiflex (ceftiofur sodium)
- o Ampicillin
- o Polyflex (ampicilin trihydrate)
- o Naxcel (ceftiofur sodium)
- o Zuprevo (tildipirosin)
- o Excede (ceftiofur crystalline free acid)
- o Gentamicin
- o In-feed tetracycline

Which drug(s) do you use to treat older heifer pneumonia?

- o LA 200 (oxytetracycline)
- o Micotil (tilmicosin)
- o Draxxin (tulathromycin)
- o Nuflor (florfenicol)
- o Baytril (enrofloxacin)
- o Ceftiflex (ceftiofur sodium)
- o Ampicillin
- o Polyflex (ampicillin trihydrate)
- o Naxcel (ceftiofur sodium)
- o Zuprevo (tildipirosin)
- o Excede (ceftiofur crystalline free acid)
- o Gentamicin
- o In-feed tetracycline

Do you establish culture-based treatment protocols for clinical mastitis?

- o Never
- o Sometimes
- o Always

Do you use a clinical severity score to determine a treatment protocol for clinical mastitis?

- o Never
- o Sometimes
- o Always

What dry cow protocol do you **primarily** recommend as a preventive measure for mastitis?

- o Recommend blanket antibiotic treatment
- o Recommend blanket non-antibiotic treatment
- o Recommend culture-based antibiotic treatment
- o Recommend records-based antibiotic treatment (SCC)
- o Don't have a dry cow protocol
- o Other (please specify)

How do you define diarrhea in calves?

- o _____

What is your primary calf diarrhea protocol?

- o _____

Do you believe the current use of antimicrobials on dairy farms contributes to antimicrobial resistance in human pathogens?

- o Strongly agree
- o Agree
- o Neutral
- o Disagree
- o Strongly disagree

Do you believe there is unnecessary use of antimicrobials in any of the following areas on any of your clients' farms?

- o Pre-weaned calves/hutches
- o Growing heifers
- o Cows in the hospital
- o Cows in fresh pen
- o Dry-cow therapy
- o Prophylactically in cows (i.e. after surgeries, prevention of digital dermatitis)

Do you feel that unnecessary use of antimicrobials in cattle is primarily due to:

- o Dairy staff not following protocols
- o Miscommunication between veterinarian and farm personnel
- o Cow/calf treaters misidentifying healthy animals as sick and treating them
- o No treatment protocols in place
- o Other (Please specify)

Demographics

Year of gradation

Veterinary school

Region of country

- o Northwest
- o Southwest
- o Midwest
- o Southeast
- o Northeast

Proportion of practice that is dairy work

- o >75%
- o 75-50%
- o 50-25%
- o <25%

Services offered in your practice (Check all that apply)

- o Mastitis/milk quality
- o Calving
- o Farm employee training
- o Record analysis
- o Reproduction
- o Treatment protocols
- o Facility consulting
- o Heifer management
- o Necropsy
- o Surgery
- o Calf management
- o Biosecurity
- o Disease diagnosis and treatment
- o Nutrition
- o Financial consulting

- Embryo transfer and/or other advanced reproductive technologies
- Other: please indicate

Average dairy size in your practice

- <100
- 100-500
- 500-1,000
- 1,000-5,000
- 5,000-10,000
- >10,000

Thank you for your valuable input.

ZACTRAN®
(gamithromycin)

150 mg/mL ANTIMICROBIAL

NADA 141-328, Approved by FDA

For subcutaneous injection in beef and non-lactating dairy cattle only. Not for use in female dairy cattle 20 months of age or older or in calves to be processed for veal.

Caution: Federal (USA) law restricts this drug to use by or on the order of a licensed veterinarian.

READ ENTIRE BROCHURE CAREFULLY BEFORE USING THIS PRODUCT.

INDICATIONS

ZACTRAN is indicated for the treatment of bovine respiratory disease (BRD) associated with *Mannheimia haemolytica*, *Pasteurella multocida*, *Histophilus somni* and *Mycoplasma bovis* in beef and non-lactating dairy cattle. ZACTRAN is also indicated for the control of respiratory disease in beef and non-lactating dairy cattle at high risk of developing BRD associated with *Mannheimia haemolytica* and *Pasteurella multocida*.

CONTRAINDICATIONS

As with all drugs, the use of ZACTRAN is contraindicated in animals previously found to be hypersensitive to this drug.

WARNING: FOR USE IN CATTLE ONLY. NOT FOR USE IN HUMANS. KEEP THIS AND ALL DRUGS OUT OF REACH OF CHILDREN. NOT FOR USE IN CHICKENS OR TURKEYS.

The material safety data sheet (MSDS) contains more detailed occupational safety information. To report adverse effects, obtain an MSDS or for assistance, contact Merial at 1-888-637-4251.

RESIDUE WARNINGS: Do not treat cattle within 35 days of slaughter. Because a discard time in milk has not been established, do not use in female dairy cattle 20 months of age or older. A withdrawal period has not been established for this product in pre-ruminating calves. Do not use in calves to be processed for veal.

PRECAUTIONS

The effects of ZACTRAN on bovine reproductive performance, pregnancy, and lactation have not been determined. Subcutaneous injection of ZACTRAN may cause a transient local tissue reaction in some cattle that may result in trim loss of edible tissues at slaughter.

ADVERSE REACTIONS

Transient animal discomfort and mild to moderate injection site swelling may be seen in cattle treated with ZACTRAN.

EFFECTIVENESS

The effectiveness of ZACTRAN for the treatment of BRD associated with *Mannheimia haemolytica*, *Pasteurella multocida* and *Histophilus somni* was demonstrated in a field study conducted at four geographic locations in the United States. A total of 497 cattle exhibiting clinical signs of BRD were enrolled in the study. Cattle were administered ZACTRAN (6 mg/kg BW) or an equivalent volume of sterile saline as a subcutaneous injection once on Day 0. Cattle were observed daily for clinical signs of BRD and were evaluated for clinical success on Day 10. The percentage of successes in cattle treated with ZACTRAN (58%) was statistically significantly higher ($p<0.05$) than the percentage of successes in the cattle treated with saline (19%).

The effectiveness of ZACTRAN for the treatment of BRD associated with *M. bovis* was demonstrated independently at two U.S. study sites. A total of 502 cattle exhibiting clinical signs of BRD were enrolled in the studies. Cattle were administered ZACTRAN (6 mg/kg BW) or an equivalent volume of sterile saline as a subcutaneous injection once on Day 0. At each site, the percentage of successes in cattle treated with ZACTRAN on Day 10 was statistically significantly higher than the percentage of successes in the cattle treated with saline (74.4% vs. 24% [$p <0.001$], and 67.4% vs. 46.2% [$p = 0.002$]). In addition, in the group of calves treated with gamithromycin that were confirmed positive for *M. bovis* (pre-treatment nasopharyngeal swabs), there were more calves at each site (45 of 57 calves, and 5 of 6 calves) classified as successes than as failures.

The effectiveness of ZACTRAN for the control of respiratory disease in cattle at high risk of developing BRD associated with Mannheim*ia haemolytica* and *Pasteurella multocida* was demonstrated in two independent studies conducted in the United States. A total of 467 crossbred beef cattle at high risk of developing BRD were enrolled in the study. ZACTRAN (6 mg/kg BW) or an equivalent volume of sterile saline was administered as a single subcutaneous injection within one day after arrival. Cattle were observed daily for clinical signs of BRD and were evaluated for clinical success on Day 10 post-treatment. In each of the two studies, the percentage of successes in the cattle treated with ZACTRAN (86% and 78%) was statistically significantly higher ($p = 0.0019$ and $p = 0.0016$) than the percentage of successes in the cattle treated with saline (36% and 58%).

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ZACTRAN®
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BOTTOM LINE:

ZACTRAN

STOPS BRD FROM HITTING YOURS.

Zactran® (gamithromycin) helps wipe out bovine respiratory disease (BRD), so cattle pack on pounds and you keep your hard-earned profits. Visit ZACTRAN.com.

IMPORTANT SAFETY INFORMATION: Do not treat cattle within 35 days of slaughter. Do not use in female dairy cattle 20 months of age or older, or in calves to be processed for veal. Subcutaneous injection may cause a transient local tissue reaction in some cattle that may result in trim loss of edible tissues at slaughter. NOT FOR USE IN HUMANS.

24-HOUR response.[1]

10-DAYS of therapy.[2]

ONE economical dose.

ZACTRAN® (gamithromycin)

[1] Sifferman RL, Wolff WA, Holste JE, et al. Field efficacy evaluation of gamithromycin for treatment of bovine respiratory disease in cattle at feedlots. Intern J Appl Res Vet Med. 2011;9(2):171-180.
[2] ZACTRAN product label.