Metritis diagnosis and treatment practices in 45 dairy farms in California

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ABSTRACT

Minimizing the risk of antimicrobial-resistant organisms and antimicrobial residues in dairy and dairy beef products is a topic of nationwide interest. To design an effective outreach program on judicious use of antimicrobials, it is imperative to describe actual practices on dairies. Thus, our objective was to report current practices for metritis treatment in 45 dairies in California. Data were collected using a survey tool that included questions on systemic antimicrobial treatments, intrauterine treatments, supportive treatments, and treatment records. Researchers collected information based on cow-side observations and responses from fresh cow evaluators. Most dairies ($n = 33$; 70%) performed rectal exams for vaginal discharge (VD) evaluation and based systemic antimicrobial administration on the presence of (a) abnormal VD (fetid and nonfetid), regardless of fever ($n = 11$; 25%); (b) fever regardless of the odor of abnormal VD ($n = 11$; 25%); (c) fetid VD and fever ($n = 1$; 2%); (d) fetid VD ($n = 3$; 9%); or (e) fetid VD or fever ($n = 3$; 9%). Some dairies ($n = 11$; 24%) only detected abnormal VD if visible on tail, vulva, or floor; treatment decisions were based on the presence of abnormal VD ($n = 9$; 20%) or abnormal VD and fever ($n = 2$; 4%). On 3 (6%) dairies, VD characteristics were evaluated after rectal palpation, but no systemic treatments were administered. Cows exhibiting 1 nonspecific sign of health disorder (depressed general appearance, lack of appetite, or drop in milk yield) plus fever ($n = 13$; 29%), or even regardless of fever ($n = 6$; 13%), were treated with systemic antimicrobials. Overall, 8 (18%) dairies justified systemic antimicrobial treatment based on fever alone. Systemic antimicrobials used were ceftiofur products [ceftiofur hydrochloride ($n = 26$; 55%), ceftiofur sodium ($n = 3$; 7%), and ceftiofur crystalline-free acid ($n = 8$; 18%)], penicillin procaine ($n = 8$; 18%), and ampicillin ($n = 3$; 7%). Intrauterine infusions were done with penicillin procaine ($n = 1$;

2%) or oxytetracycline ($n = 12$; 27%). The dose and treatment length varied across dairies for i.m. ceftiofur hydrochloride (15 to 45 mL/d for 3 to 5 d), s.c. ceftiofur crystalline-free acid (20 to 25 mL once or twice), i.m. ceftiofur sodium (15 to 30 mL/d for 3 to 5 d), i.m. penicillin procaine (20 to 60 mL/d for 3 to 6 d), and i.m. ampicillin (25 to 35 mL/d for 3 to 6 d). The antimicrobial drug of choice, the dose, and the treatment length for metritis varied across the study dairies. Based on accepted industry best-management practices for metritis, a need exists to educate fresh cow evaluators on signs of health disorder indicative of metritis and on appropriate antimicrobial treatment regimens.

Key words: metritis, antimicrobial treatments, signs of health disorder

INTRODUCTION

Puerperal metritis is an important herd health concern in postpartum dairy cows that can affect 5 to 20% of cows in a herd (LeBlanc, 2014). At present, we lack a validated diagnostic criteria to identify cows with this disease. However, Sheldon et al. (2006) proposed defining puerperal metritis as an inflammation of the uterus that results in fetid red-brown watery vaginal discharge (**VD**), fever ($>39.5^{\circ}\text{C}$), and signs of systemic illness such as decreased milk yield, dullness, or other signs of toxemia. The economic losses associated with this disease are estimated at approximately \$358 per case, including treatment cost, reduction in milk yield, and an increase in culling (Overton and Fetrow, 2008).

Bacteria isolated from cows with uterine disease are very diverse, including *Trueperella pyogenes*, *Escherichia coli*, *Fusobacterium necrophorum*, and *Prevotella* spp. (Sheldon and Dobson, 2004; Williams et al., 2005). Thus, broad-spectrum antimicrobials are warranted as treatment options for metritis. Recommended treatments include systemic penicillin and ampicillin as well as intrauterine oxytetracycline (Gustafsson, 1984; Smith et al., 1998). However, currently in the United States, only ceftiofur hydrochloride (**CHCl**), ceftiofur crystalline-free acid (**CCFA**), and an injectable oxytetracycline are labeled as treatment options for metritis.

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Limited information is available on industry practices for metritis treatment, including signs of disease used as a guideline for treatment options as well as the type, the dosage, and the length of treatments. Current information available on antimicrobial choices for metritis treatment is based on questionnaires addressed to dairy producers (Zwald et al., 2004; Sawant et al., 2005; Pol and Ruegg, 2007). Results from those questionnaires indicated that ceftiofur, tetracycline, ampicillin, penicillin, and sulfonamides were treatment choices for metritis on US dairies. However, no information has been reported on what signs of health disorder were treated and the length and dose of treatment.

Over the years, antimicrobials have been proven to be efficacious for the treatment of infectious diseases. Nonetheless, antimicrobial resistance has become a worldwide health concern. Judicious use of antimicrobials in veterinary medicine has been proposed as a strategy to slow the emergence of antimicrobial-resistant bacteria and reduce unsuccessful treatment of illness caused by those pathogens. To support this strategy, the State of California (2015) has implemented Senate Bill 27, "Livestock: Use of antimicrobial drugs" (SB-27; 2015), effective January 1, 2018. As of that date, all injectable antimicrobial drugs administered to livestock, including those previously available over the counter (i.e., tetracycline, penicillin procaine), require a veterinary prescription.

On large dairy operations, the identification and treatment of sick animals is mostly performed by dairy employees (Espadamala et al., 2016). A better understanding of the attitudes and practices of fresh cow evaluators regarding metritis treatment will help to develop effective measures to reduce the use of antimicrobial drugs in US dairies. Thus, our objective was to provide baseline information of current diagnosis criteria and treatment practices for metritis on 45 dairies in California.

MATERIALS AND METHODS

We acquired an exemption from the University of California, Davis Institutional Review Board before conducting field visits. General herd information and description of how data were collected was previously reported in Espadamala et al. (2016). A convenience sample of 45 dairies from the San Joaquin Valley of California was identified by California county extension advisors, dairy veterinarians, and dairy consultants. Dairy visits were conducted from February to August 2015. Enrolled dairies were numbered from 1 (9,500 cows) to 45 (450 cows) based on herd size (larger to smaller). To collect information, a survey tool was designed with questions on systemic antimicrobial

treatments, intrauterine treatments with antimicrobial and nonantimicrobial components, supportive therapy, and treatment records (Table 1). On 38 of the visited dairies, researchers (A. Espadamala and P. Pallarés) were able to observe how fresh cow evaluators treated metritis; however, on 7 dairies fresh cow evaluators did not detect any fresh cow with clinical signs of metritis. During each herd visit, researchers initially focused on observing fresh cow evaluators and on taking written notes of their actions. As the assessment progressed, they formulated questions while fresh cow evaluators carried out their work. At the end of each fresh cow evaluation, both researchers interviewed the fresh cow evaluator using the survey tool to compile all the information necessary to describe metritis treatments. The survey tool was initially β -tested on 5 dairies and modified afterward to gather information on second treatment choices.

To minimize behavioral changes or reactivity during the assessment, fresh cow evaluators were assured that data would be collected for research purposes only. To increase data accuracy, questions were asked twice at different times during the interview process. Furthermore, when possible, responses were corroborated with observations. If disagreements were noted between field observations and the responses obtained from fresh cow evaluators, only observations were included in the final data set. Each day upon returning from the field visit, A. Espadamala and P. Pallarés met for 2 to 3 h to compare their field notes, write a report, and enter data into spreadsheets for analysis (Microsoft Office Excel 2010, Microsoft Corp., Redmond, WA). Reported percentages were rounded to the nearest whole percentage point.

RESULTS AND DISCUSSION

The baseline information provided in our study about current diagnostic criteria and treatment practices for metritis should be carefully interpreted, as it includes a limited number of dairies ($n = 45$) from a single region (central valley of California); therefore, our results might not necessarily represent industry practices elsewhere. On the study dairies, nonsupervisor employees ($n = 29$), supervisor employees ($n = 13$), or dairy owners ($n = 3$) were in charge of identifying and treating cows with metritis. Based on the testimony from fresh cow evaluators, on most dairies veterinarians had little direct involvement on fresh cow evaluations ($n = 33$) or were limited to endometritis screening at 3 to 4 wk postpartum ($n = 11$). However, on dairy 30, the veterinarian performed fresh cow evaluations once a week; he advised on treatment protocols and performed nonantimicrobial intrauterine flushings.

Table 1. Survey tool on metritis treatment used on 45 dairies in California

Question	Answer
1. When are systemic antimicrobials used to treat metritis?	a. Foul-smelling vaginal discharge b. No foul-smelling abnormal vaginal discharge c. Fever d. Depressed general appearance Open-ended
2. What is the type, dose and length of systemic antimicrobials used as first choice?	a. Foul-smelling vaginal discharge b. No foul-smelling abnormal vaginal discharge c. Fever d. Depressed general appearance e. Ineffective systemic antimicrobials Open-ended
3. When are intrauterine infusions used to treat metritis?	a. Penicillin procaine b. Oxytetracycline c. Antiseptic d. Carvacrol Open-ended
4. Are intrauterine infusions used as a first or second treatment choice?	Open-ended
5. What type of solutions are infused in the uterus?	a. Penicillin procaine b. Oxytetracycline c. Antiseptic d. Carvacrol Open-ended
6. Are intrauterine infusions combined with systemic antimicrobials?	Open-ended
7. How often are the intrauterine infusions used?	Open-ended
8. Are supportive treatments for metritis administered?	Open-ended
9. How are treatment records for metritis kept?	Open-ended

Signs of Metritis Leading to Systemic Antimicrobial Treatment

Signs of a health disorder associated with metritis leading to systemic antimicrobial treatment included fever, nonfetid VD that appeared abnormal to fresh cow evaluators based on color and viscosity, fetid VD, dull-depressed attitude, or a combination of these signs (Figure 1). The methodology and the frequency of how those signs of health disorder were evaluated has been described elsewhere (Espadamala et al., 2016).

Rectal palpation was commonly used to evaluate VD characteristics before administration of systemic antimicrobials ($n = 33$; 70%) or other treatments ($n = 3$; 6%). Despite the high acceptance of this practice among fresh cow evaluators, rectal palpation is a subjective screening method that lacks sensitivity (Okano and Tomizuka, 1987; LeBlanc et al., 2002). On 11 (24%) dairies, VD evaluation was performed only if visually detected on tail, vulva, or floor.

After rectal palpation, some dairies followed a liberal approach and treated cows with systemic antimicrobials whenever abnormal VD (fetid and nonfetid) was detected regardless of fever ($n = 11$; 25%). Other dairies followed a more conservative approach and limited treatment to cows with fetid VD and fever ($n = 1$; 2%) or just fetid VD ($n = 3$; 6%). Two dairies reduced antimicrobial use by choosing nonantimicrobial intrauterine infusions as the first treatment option or by delaying treatment of cows with abnormal VD after cows were >7 DIM. Delaying systemic antimicrobial therapy might be a desirable strategy, as Sannmann et al. (2013) found that 21.8% of the cows with metritis

(fetid VD and fever) self-recovered within the first 4 d after calving. Similarly, McLaughlin et al. (2012) observed that 55.3% of untreated cows showed clinical cure at 14 DIM. On dairies where rectal palpation was not performed, systemic antimicrobials were administered based on the presence of abnormal VD regardless of odor, with ($n = 2$; 4%) or without fever ($n = 9$; 20%).

Cows exhibiting nonspecific signs of disease (i.e., depressed general appearance, lack of appetite, or drop in milk yield) were treated only if febrile ($n = 13$; 29%), but some dairies treated them regardless of fever ($n = 6$; 13%). On 8 (18%) dairies, systemic antimicrobials were administered to febrile cows even when this was the only sign of health disorder detected; all those dairies performed scheduled daily monitoring programs up to 3 to 15 DIM (Espadamala et al., 2016). This treatment decision should be re-evaluated, considering that 44 to 68% of healthy postpartum cows have at least 1 elevated temperature during the first 10 DIM (Kristula et al., 2001; Wenz et al., 2011).

The present study illustrates the lack of agreement across dairies on signs of health disorder that indicate metritis. Previous research studies have used various definitions for this postpartum disease, such as rectal temperature $>39.5^{\circ}\text{C}$ (Drillich et al., 2001; Chenault et al., 2004; McLaughlin et al., 2012; Lima et al., 2014), rectal temperature above 39.2°C with fetid watery VD within the first 21 DIM (Smith et al., 1998), presence of fetid VD regardless of rectal temperature (Giuliodoro et al., 2013; Lima et al., 2014), watery-purulent fetid VD with a flaccid nonretractable uterus (Smith et al., 1998; Goshen and Shpigel, 2006), and depressed milk yield from 3 to 20 DIM (<7.4 kg at a.m. milk-

Dairies	Observation of Abnormal VD		Rectal Palpation				Depressed and/or anorexic		Only Fever
	FeverN	FeverY	Non-Fetid Abnormal VD		Fetid Abnormal VD		FeverN	FeverY	
			FeverN	FeverY	FeverN	FeverY			
1	<div></div>	<div></div>	<div></div>	<div></div>	<div></div>	<div></div>	<div></div>	<div></div>	<div></div>
3	<div></div>	<div></div>	<div></div>	<div></div>	<div></div>	<div></div>	<div></div>	<div></div>	<div></div>
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18	<div></div>	<div></div>	<div></div>	<div></div>	<div></div>	<div></div>	<div></div>	<div></div>	<div></div>
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31	<div></div>	<div></div>	<div></div>	<div></div>	<div></div>	<div></div>	<div></div>	<div></div>	<div></div>
36	<div></div>	<div></div>	<div></div>	<div></div>	<div></div>	<div></div>	<div></div>	<div></div>	<div></div>
43	<div></div>	<div></div>	<div></div>	<div></div>	<div></div>	<div></div>	<div></div>	<div></div>	<div></div>
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Figure 1. First antimicrobial treatment option in 45 dairies in California after observing signs of health disorder indicative of metritis [dark gray/blue, ceftiofur products (ceftiofur hydrochloride, ceftiofur sodium, and ceftiofur crystalline free acid); black/green, penicillin procaine and ampicillin; light gray/yellow, intrauterine infusions with oxytetracycline]. Signs of health disorder evaluated were vaginal discharge (VD) characteristics based on appearance (color and viscosity) and odor (fetid or nonfetid), fever (FeverY) based on rectal temperature or arm feeling during rectal palpation, no fever or fever not measured (FeverN), depressed attitude (sunken eyes, fallen ears, abnormal body position), or anorexic (no appetite or low rumen fill). Eleven dairies did not perform rectal examination; those dairies treated cows if abnormal VD (fetid and nonfetid) was observed in vulva, perineum, tail, or floor. Color version available online.

ing; Smith et al.,1998). In an attempt to unify criteria and facilitate metritis screening under field conditions, Sheldon et al. (2006) proposed to define acute puerperal metritis as an abnormally enlarged uterus with fetid

red-brown watery VD accompanied by fever ($>39.5^{\circ}\text{C}$) and signs of systemic illness such as decreased milk yield, dullness, or other signs of toxemia. Based on the aforementioned definition, LeBlanc (2008) suggested

limiting antimicrobial treatment to cows who had at least 2 clinical signs of metritis. Our results suggest that these industry guidelines have had poor adoption in California dairies, as most fresh cow evaluators overtreated cows. However, limited evidence exists for a benefit of antimicrobial therapy beyond resolving fever or improving VD characteristics (Drillich et al., 2001; McLaughlin et al., 2012). Moreover, the implementation of the proposed industry guidelines for metritis diagnosis is also limited by the lack of validated screening tools to objectively assess VD characteristics or to appraise signs of systemic illness. As reported by Espadamala et al. (2016), important differences exist in how signs of health disorders were screened across dairies.

Antimicrobial Treatments

The type of antimicrobial drug used for first and second choice, and the treatment dose and duration are shown on Table 2. The most common systemic antimicrobials used were ceftiofur products, specifically i.m. CHCl (Excenel, Zoetis, Kalamazoo, MI; $n = 30$), i.m. ceftiofur sodium (CNa; Naxcel, Zoetis, $n = 2$; or Ceftiflex, Med-Pharmex Inc., Pomona, CA, $n = 1$), s.c. CCFA (Excede, Zoetis; $n = 11$). Also, i.m. penicillin procaine (multiple manufacturers, $n = 19$) and i.m. ampicillin (Polyflex, Boehringer Ingelheim Vetmedica, Inc., St. Joseph, MO; $n = 17$) were used. Intrauterine infusions with penicillin ($n = 1$) or oxytetracycline (multiple manufacturers, $n = 12$) were also used to treat metritis. Systemic antimicrobials used as a first treatment option included CHCl ($n = 26$), CNa ($n = 3$), CCFA ($n = 8$), penicillin ($n = 8$), and ampicillin ($n = 3$).

On 9 dairies, fresh cow evaluators selected the type of antimicrobial drug after considering the severity of the case, the withhold period, or the likelihood that the animal would be culled. Dairy 29 used CHCl to treat febrile cows ($\geq 39.5^\circ\text{C}$), but if fever reached $\geq 40.3^\circ\text{C}$ a single dose of CCFA was used; dairy 45 treated cows with nonfetid VD with CHCl and cows with fetid VD

with penicillin; dairy 30 treated febrile cows with CHCl, but if fever persisted for 2 d the treatment of choice was penicillin (primiparous) or ampicillin (multiparous); dairy 11 treated nonfetid VD with CHCl and fetid VD with penicillin and oxytetracycline intrauterine infusions. Dairy 33 and 27 treated multiparous cows with CHCl and primiparous cows with CCFA (dairy 33) or penicillin (dairy 27); dairy 10 treated cows with CCFA, but if cow recovery was dubious the drug of choice was CHCl. In dairy 6, several criteria were used to decide on the antimicrobial of choice: fetid VD was treated with CHCl, but when moderate or severe signs of systemic disease were observed ampicillin or penicillin was used. Moreover, if cows had poor body condition, the treatment of choice was ampicillin, as penicillin was perceived to delay recovery time on thin cows. On dairy 22, CHCl and penicillin were used to treat metritis; however, due to the high cost of CHCl, the dairy had limited inventory of this drug and most cows were treated with penicillin.

In our study, most systemic ceftiofur drugs were labeled for puerperal metritis treatment, except for CNa, which was used on 3 dairies. Ceftiofur products were widely adopted ($n = 37$; 82%) as a first-choice treatment for cows with metritis; on 2 dairies they were the only systemic antimicrobial drugs in inventory. A 2004 study reported that 41.4% of dairies from Wisconsin, Minnesota, Michigan, and New York choose ceftiofur for metritis and retained fetal membrane treatment (Zwald et al., 2004). A total of 85% of Wisconsin herds reported treating metritis with ceftiofur drugs (Pol and Ruegg, 2007). The popularity of ceftiofur products is most likely explained by their broad antimicrobial spectrum and the economic and food safety incentive of drugs with zero days in milk withdrawal period.

Other drugs commonly used to treat metritis were ampicillin and penicillin. They were used as the first treatment choice on 10 dairies and as a second treatment choice on 19 dairies. The choice to use extra-label penicillin was based on the lower cost and on the perception that they had better efficacy than label ceftio-

Table 2. First and second systemic antimicrobial choices for metritis treatments in 45 dairies in California

Item	Drug	Dose (mL/d)	Duration	Dairies (n)
First option	Ceftiofur hydrochloride	15 to 45	3 to 5 d	27
	Ceftiofur crystalline free acid	20 (1 or 2 d)	at 72 h	10
	Ceftiofur sodium	20 to 30	3 to 5 d	3
	Penicillin	20 to 60	3 to 6 d	8
	Ampicillin	25 to 35	3 to 6 d	3
Second option	Ceftiofur hydrochloride	15 to 20	3 to 5	3
	Ceftiofur crystalline free acid	20 (1 or 2 d)	at 72 h	2
	Penicillin	20 to 60	3 to 6	12
	Ampicillin	25 to 35	3 to 6	15

fur products. Indeed, it has been shown that ampicillin administration results in a faster improvement of VD characteristics and fever remission than ceftiofur; however, this improvement in clinical signs had no implications on cure at 12 d after treatment or fertility at first breeding (Lima et al., 2014). It should be noted that any use of extra-label drugs in livestock, including over-the-counter drugs such as penicillin, requires veterinary oversight and imposes on management, as cows need to be segregated to facilitate milk disposal.

Intrauterine infusions of tetracycline were used on 2 dairies as the only antimicrobial choice for first treatment option. Fresh cow evaluators on both dairies expressed high confidence in the efficacy of this treatment and only one of those dairies tried a second treatment with systemic penicillin if intrauterine infusions failed. Seven dairies combined systemic antimicrobials (CHCl or penicillin) with intrauterine tetracycline when VD was fetid ($n = 3$), cows had fever ($n = 1$), cows had fever and fetid VD ($n = 2$), or when cows had nonfetid abnormal VD ($n = 1$). Four of these dairies used intrauterine tetracycline as the first and only antimicrobial treatment when cows had fetid VD but no fever ($n = 3$) or when cows had fever but nonfetid VD ($n = 1$). Research studies found that cows undergoing metritis benefitted from intrauterine antimicrobial treatments compared with control cows (Goshen and Shpigel, 2006), but extra-label intrauterine antimicrobial infusions were not superior to systemic antimicrobial therapy (Smith et al., 1998; Drillich et al., 2001). In the United States, intrauterine tetracycline administration is an extra-label therapy and it must be prescribed by a veterinarian. In our study, 10 (22%) dairies opted for this treatment route in metritis cases either as first, second, or third treatment option. Fresh cow evaluators choosing intrauterine tetracycline as a treatment option for metritis perceived this treatment was more likely to improve the VD characteristics. The choice of intrauterine oxytetracycline (previously available over the counter) as a treatment for metritis may change in California with SB 27 implementation.

Treatment Dose and Duration of Systemic Antimicrobial Drugs and Treatment Records

The dose and duration of systemic antimicrobial treatments varied greatly across dairies (Table 2). The label dose for CHCl (2.2 mg/kg of BW) is ≈ 30 mL for Holsteins (675 kg of BW) and ≈ 20 mL for Jerseys (450 kg of BW) for 5 d. However, the treatment dose for CHCl ranged from 15 to 45 mL/d for 3 to 5 d, with 20 mL as the most common dose. On 6 dairies, the dose used differed between primiparous and multiparous

cows: two dairies used 15 versus 20 mL/d ($n = 2$); two dairies used 25 versus 30 mL ($n = 2$); one dairy used 25 versus 35 mL/d ($n = 1$); and one dairy used 35 versus 45 mL/d ($n = 1$). Most dairies treated for 3 d, but only dairy 6 reported completing a 5-d treatment. The high cost of CHCl may have discouraged fresh cow evaluators and managers from treating cows beyond 3 d, especially if signs of improvement were observed. Ten herds of Holsteins were treated with CCFA. Per label recommendation, the dose for mature Holstein cows should be ≈ 23 mL of CCFA (6.6 mg/kg of BW) by s.c. route, with a second dose after 72 h. The dose used was 20 mL except at 1 dairy that used 25 mL. Only 1 dairy reported it always administered a second dose after 72 h, whereas 3 dairies decided on the second dose based on disease progression. Although CNa is not labeled for metritis, 3 Holstein herds used this drug to treat this condition. The recommended label dose for CNa is ≈ 15 to 30 mL (1.1 to 2.2 mg/kg of BW) for 3 d and all dairies followed the dose recommendation, but the treatment length was either 3 ($n = 1$) or 5 d ($n = 2$). It should be noted that ceftiofur products (CHCl, CCFA, and CNa) are cephalosporins, and these drugs can only be obtained through a veterinary prescription. Their extra-label use is prohibited, except for disease indication, as long as it follows a labeled dosage regimen (i.e., dose, route, frequency, and duration of administration) approved for dairy cattle (US Government Publishing Office, 2017; 21 CFR Part 530.41).

Penicillin procaine was used at doses that ranged from 20 to 60 mL/d for 3 to 6 d. The label of penicillin procaine dosage (6,600 U/kg) is based on a 1992 Food and Drug Administration approval (NADA 065-010, FDA, 2010): ≈ 15 mL for mature Holstein and 10 mL for Jersey cows. However, evidence exists that higher doses than those indicated on the label are needed to maintain therapeutic tissue and blood concentrations (Prescott, 2000). Meat and milk withdrawal periods for extra-label doses (28,000 IU/kg) have been studied elsewhere (Dubreuil et al., 2001). Ampicillin was used on 3 dairies as the first treatment option, ranging from 25 to 35 mL/d for 3 to 6 d. Based on label recommendations, ampicillin dose (4.4 to 11.1 mg/kg) of mature cows should be ≈ 30 (Holstein) or 20 mL (Jersey) for 2 to 3 d without exceeding 7 d. At the time the present study was conducted, penicillin procaine was available over the counter. However, the implementation of SB 27 might change the use of penicillin for metritis treatments. Moreover, as most dairies administered CHCl and CCFA at doses below label recommendations (especially for multiparous cows), it is important to educate fresh cow evaluators on the dosing regimen and the recommended duration of antimicrobial treatments.

Record-Keeping of Antimicrobial Treatments

All dairies recorded metritis treatments on cow's hide except for dairy 25. These records were easily visible during fresh cow evaluations. Most dairies also kept electronic ($n = 34$) or paper ($n = 4$) records of antimicrobial treatments without milk withdrawal period. On some dairies, ceftiofur products were only recorded on cow's hide ($n = 5$), electronically for CCFA but not for CHCl ($n = 1$), or not recorded ($n = 1$). However, when antimicrobial treatments had milk withdrawal period, records were kept in all enrolled dairies either electronically ($n = 43$) or on paper ($n = 2$).

In our study, record-keeping of antimicrobial drug treatments seems to have improved relative to a decade earlier; in 2006 in Wisconsin 66% of the dairies kept treatment records of antimicrobial drugs (Hoe and Ruegg, 2006), and in 2005 in Pennsylvania 50% of dairies kept treatment records (Sawant et al., 2005). The current surveillance system for antimicrobial residues in milk and meat is likely a major reason for the improvement. However, opportunities still exist to improve record-keeping of antimicrobials without milk withdrawal period.

Nonantimicrobial Intrauterine Treatments

In 18 (40%) dairies, nonantimicrobial intrauterine treatments were administered alone or in combination with systemic antimicrobials based on VD characteristics and the presence of fever. The active compounds included chlorhexidine ($n = 7$), iodine ($n = 5$), carvacrol ($n = 4$), or an unlabeled veterinarian formulation with an iodine base ($n = 2$). Six dairies chose nonantimicrobial intrauterine treatments as the first treatment option in combination with systemic antimicrobials. On dairy 4, iodine intrauterine infusions of cows with abnormal VD started at 5 DIM, but cows were treated with penicillin intrauterine infusions if after 3 infusions improvement was observed. Dairy 22 infused cows with chlorhexidine (abnormal VD) or oxytetracycline (fetid VD). On dairy 42 carvacrol pills were used for intrauterine treatment of metritis. On most dairies, the frequency of nonantimicrobial intrauterine treatments was based on the VD characteristics progression. Nevertheless, 6 dairies had scheduled nonantimicrobial intrauterine treatments 1 ($n = 2$), 2 ($n = 3$), or 3 ($n = 2$) times a week. Dairy 14 opted to infuse all cows at least 2 to 3 times postpartum as a prophylactic measure and up to 5 times if the VD was abnormal. Seven dairies chose nonantimicrobial intrauterine infusions as the first treatment option, but only if fever was not present ($n = 5$) or whenever fever and fetid odor were not present ($n = 2$). Moreover, dairy 17 infused with chlorhexidine as the

4th treatment choice if VD remained abnormal after systemic antimicrobial treatment. Dairy 21 used iodine intrauterine infusions if abnormal VD was observed after 5 d of systemic antimicrobial treatment. This dairy considered that intrauterine infusions had the potential to damage the friable uterus in the early postpartum period; thus, all infusions were done after 8 DIM.

Researchers have evaluated prophylactic and treatment strategies for endometritis using nonantimicrobial intrauterine infusions with antiseptics (Nakao et al., 1988; Knutti et al., 2000; Lew and Kim, 2007), 50% dextrose (Machado et al., 2015), carvacrol (Pinedo et al., 2015), or enzymes (Drillich et al., 2005) as active ingredients; however, the benefits for reproductive efficiency were limited or nonexistent. Despite the lack of strong supporting scientific evidence, our study found that nonantimicrobial intrauterine treatments were widely adopted probably because they do not pose a risk for antimicrobial residues in milk or meat. However, it is generally recommended to limit nonantimicrobial intrauterine treatments to avoid iatrogenic mechanical trauma, irritation, and contamination of the uterus (Paisley et al., 1986; Gilbert, 2016). Although in our study the hygiene of intrauterine infusion was not scored, we observed that often it was limited and presented a risk for uterine contamination. Future educational programs should address the mode of action, efficacy, and possible side effects of nonantimicrobial intrauterine infusions for metritis treatment.

Other Nonantimicrobial Treatments

In addition to systemic antimicrobial therapy, acetylsalicylic acid oral pills were used in 15 dairies as part of the metritis treatment when cows had abnormal VD and fever ($n = 3$), abnormal VD regardless of fever ($n = 7$), fever ($n = 4$), or depressed attitude ($n = 1$). The acetylsalicylic acid dose used was 46.8 g (3 pills) for Holsteins and 31.2 g (2 pills) for Jersey cows. Three dairies used i.v. flunixin meglumine to treat cows showing signs of health disorder associated with metritis, but only if VD was fetid ($n = 1$) or if fever was above 39.4°C ($n = 2$). Flunixin meglumine was only used by i.v. route as per label recommendation. Drugs used as a supportive treatment for metritis included i.m. vitamin B ($n = 3$), oral calcium ($n = 2$), oral propylene glycol ($n = 2$), oral drench ($n = 1$), oral probiotics and Mg oxide ($n = 3$), i.m. vitamin B and oral calcium ($n = 1$), and oral drench with probiotics and Mg oxide ($n = 1$). In all dairies, propylene glycol and probiotics were bought as powder and packaged on-farm in biodegradable capsules for oral administration.

The use of nonsteroidal anti-inflammatory drugs (NSAID) has been studied as a supportive treatment

(Drillich et al., 2007) or as the first treatment option (Pohl et al., 2016) for metritis. Although NSAID did not seem to improve reproductive efficiency or milk production when used in combination with systemic antimicrobials (Drillich et al., 2007), they reduced the number of animals that required systemic antimicrobials when used as the first treatment choice (Pohl et al., 2016). However, the most important benefit of using NSAID could be to improve animal well-being during a painful and stressful disease (Laven et al., 2012). Our study found that 19 (42%) dairies used NSAID as a supportive treatment for metritis. In the United States, flunixin meglumine has a 36-h milk withhold and 4-d meat withdrawal period; this probably discourages fresh cow evaluators from its use. Currently, no FDA-approved drugs exist for pain management in adult dairy cattle, and all current use of drugs for this purpose occur extra-label.

CONCLUSIONS

In our study, the identification and treatment of sick animals was performed mainly by dairy employees. We observed a remarkable lack of consensus across dairies on signs of health disorder that resulted in a metritis diagnosis and subsequent treatment. Often antimicrobial treatments were administered after screening for a limited number of signs of health disorder; this practice most likely resulted in workers being unable to properly discriminate between cows that benefited from antimicrobials and those that did not. Future research efforts should focus on developing validated diagnostic criteria and screening tools to objectively identify cows that may benefit from antimicrobial therapy. In the meantime, the urgency to address judicious use of antimicrobials on dairies justifies using current knowledge to develop educational materials that explain what combination of signs of health disorder should be treated as well as what antimicrobial and nonantimicrobial drugs have proved efficacious in metritis treatment. Fresh cow evaluators should also be educated on correctly administering labeled antimicrobial treatment regimens (drug type, dosing, and length) as well as the implications of incorrect administration.

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