Efficacy of Extended Pirlimycin Therapy for Treatment of Experimentally Induced \textit{Streptococcus uberis} Intramammary Infections in Lactating Dairy Cattle*

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\section*{ABSTRACT}

\textit{Streptococcus uberis} is an important cause of mastitis in dairy cows throughout the world, particularly during the dry period, around the time of calving, and during early lactation. Strategies for controlling \textit{S. uberis} mastitis have not received adequate research attention and are therefore poorly defined and inadequate. Objectives of the present study were to evaluate the efficacy of extended therapy regimens with pirlimycin for treatment of experimentally induced \textit{S. uberis} intramammary infections in lactating dairy cows during early lactation and to evaluate the usefulness of the \textit{S. uberis} experimental infection model for evaluating antimicrobial efficacy in dairy cows. The efficacy of extended pirlimycin intramammary therapy regimens was investigated in 103 mammary glands of 68 dairy cows that became infected following experimental challenge with \textit{S. uberis} during early lactation. Cows infected with \textit{S. uberis} in one or both experimentally challenged mammary glands were randomly allocated to three groups, representing three different treatment regimens with pirlimycin, including 2-day (n = 21 cows, 31 mammary quarters), 5-day (n = 21 cows, 32 quarters), and 8-day (n = 26 cows, 40 quarters). For all groups, pirlimycin was administered at a rate of 50 mg of pirlimycin hydrochloride via intramammary infusion. A cure was defined as an experimentally infected mammary gland.
that was treated with pirlimycin and was bacteriologically negative for the presence of *S. uberis* at 7, 14, 21, and 28 days after treatment. Experimental *S. uberis* intramammary infections were eliminated in 58.1% of the infected quarters treated with the pirlimycin 2-day regimen, 68.8% for the 5-day regimen, and 80.0% for the 8-day regimen. Significant differences (*P* < .05) in efficacy were observed between the 2-day and 8-day treatment regimens. The number of somatic cells in milk decreased significantly following therapy in quarters for which treatment was successful in eliminating *S. uberis*. However, there was no evidence to suggest that extended therapy with pirlimycin resulted in a greater reduction in somatic cell counts in milk than the 2-day treatment. The *S. uberis* experimental infection model was a rapid and effective means of evaluating antimicrobial efficacy during early lactation at a time when mammary glands are highly susceptible to *S. uberis* intramammary infection.

**INTRODUCTION**

Application of mastitis control methods, including teat disinfection, antibiotic therapy, and culling of chronically infected cows, has led to considerable progress in controlling mastitis caused by contagious pathogens such as *Streptococcus agalactiae* and *Staphylococcus aureus*. However, these mastitis control procedures are less effective against environmental mastitis pathogens. Several studies have demonstrated convincingly that as the prevalence of contagious mastitis pathogens was reduced, the proportion of intramammary infections (IMIs) by environmental pathogens increased.1-5 Therefore, environmental mastitis has become a major problem in many well-managed dairy farms throughout the world that have successfully controlled contagious mastitis pathogens. Environmental *Streptococcus* species involved in bovine mastitis include *Streptococcus uberis*, *Streptococcus dysgalactiae* subsp *dysgalactiae*, *Streptococcus equinus*, *Streptococcus equi*, and *Enterococcus* species. Among the environmental streptococci, *S. uberis* appears to be the most prevalent.6-8

*Streptococcus uberis* is an important cause of mastitis in dairy cows, particularly during the dry period, around the time of calving, and during early lactation, and this organism is not effectively controlled by current mastitis control practices. In a study of IMIs in a confined dairy herd, the number of new *S. uberis* IMIs increased markedly, especially during the early dry period and near calving.2 Antibiotic therapy at drying off reduced the rate of new infections during the early dry period but was not effective at the end of the dry period. Many *S. uberis* infections that originate during the dry period and near calving result in clinical and subclinical mastitis during early lactation. Control programs should focus on periods adjacent to the nonlactating period where opportunities exist to develop strategies to reduce the impact of *S. uberis* infections in the dairy herd.

Pirlimycin is a lincosaminide antibiotic that is active against many gram-positive mastitis pathogens.9,10 Pirlimycin functions by binding to the 50s ribosomal subunit of mRNA, inhibiting protein synthesis. In clinical studies, 50 mg of pirlimycin administered twice, with a 24-hour interval, into each affected mammary quarter was effective for treatment of mastitis caused by gram-positive pathogens in lactating dairy cattle.9,10 The length of time pirlimycin concentrations in milk remain above the minimum inhibitory concentration of the susceptible bacteria is key to efficacy of this compound. Theoretically, lengthening the duration of pirlimycin therapy should increase efficacy. In support of this concept, Gillespie et al11 demonstrated that the percentage of naturally occurring *S. uberis* IMIs eliminated following a
2-day pirlimycin therapy regimen was 50%. Following 5- and 8-day pirlimycin treatment regimens, 83% and 100% of S. uberis IMIs, respectively, were eliminated. However, the number of S. uberis IMIs in each treatment group in the study was relatively low. Objectives of the present study were to evaluate the efficacy of pirlimycin against experimentally induced S. uberis IMIs in lactating dairy cows during early lactation, to determine if extended therapy regimens would enhance the efficacy of pirlimycin, and to evaluate the usefulness of the S. uberis experimental infection model for evaluating antimicrobial efficacy in dairy cows.

**MATERIALS AND METHODS**

**Cattle**

Holstein dairy cows (n = 42) from The University of Tennessee Middle Tennessee Experiment Station, Spring Hill, TN and Jersey dairy cows (n = 26) from the Dairy Experiment Station, Lewisburg, TN were used in this study. All cows were in their second lactation. Two uninfected quarters of each cow were experimentally challenged with S. uberis during early lactation at 11 to 39 days after calving.

**Challenge Bacteria**

*Streptococcus uberis* strain UT888 was used in this study. This organism was isolated originally from a Jersey cow with chronic mastitis and identified as described previously. This strain of S. uberis causes mild clinical mastitis following experimental infection and has been studied extensively in the authors’ laboratory. The minimum inhibitory concentration of pirlimycin for S. uberis UT888 was less than 0.5 µg/ml using the Sensititre (Trek Diagnostic Systems) panel.

**Experimental Infections**

*Streptococcus uberis* UT888 was revived from storage at –80°C. After incubation, colonies were inoculated into Todd-Hewitt (Becton Dickinson) broth and incubated for 7 hours at 37°C. Following this incubation, the broth culture was diluted in sterile phosphate-buffered saline (PBS, 0.01M, pH 7.4) to provide approximately 1,000 colony-forming units/ml. Two mammary quarters of each cow were selected for bacterial challenge based on milk somatic cell counts (SCCs) being less than 250,000/ml 7 days before challenge and absence of S. uberis or other mastitis pathogens in quarter foremilk samples obtained 14 and 7 days before challenge.

Following the afternoon milking on the day of experimental challenge, 5 ml of inoculum containing S. uberis in sterile PBS were infused into two uninfected quarters of each cow. Before inoculation, teat ends were cleaned thoroughly with swabs containing 70% ethanol. The bacterial suspension was infused using sterile disposable syringes fitted with sterile disposable teat cannulas that were fully inserted through the streak canal. The infused inoculum was massaged upward into the gland cistern. Teats were immersed in a postmilking teat disinfectant when the above procedure was completed.

**Sample Collection**

Foremilk samples from each challenged mammary quarter were obtained for microbiologic evaluation immediately before challenge and daily for the first week during the challenge period. Foremilk samples from challenged mammary quarters that subsequently became infected were collected immediately before antibiotic treatment and 7, 14, 21, and 28 days after the last antibiotic treatment for microbiologic evaluation and for SCC determination.

All samples were collected immediately before a regular milking using standard procedures described by Hogan and colleagues. Before sample collection, the teats were cleaned.
thoroughly and dried with individual disposable paper towels. Teat ends were sanitized with swabs containing 70% isopropyl alcohol. Foremilk samples for determination of SCCs were collected after the strip cup evaluation and collection of the milk sample for microbiologic evaluation.

**Evaluations**

Milk samples for microbiologic evaluation were examined following procedures recommended by the National Mastitis Council and essentially as described by Oliver et al. Briefly, foremilk samples (10 µl) from each quarter were plated onto one quadrant of a trypticase soy agar plate supplemented with 5% defibrinated sheep blood (Becton Dickinson). Plates were incubated at 37°C, and bacterial growth was observed and recorded at 24-hour intervals for 3 days. Bacteria on primary culture media were identified tentatively according to colony morphologic features, hemolytic characteristics, Gram-stain reaction, and catalase test. Isolates identified presumptively as streptococci were initially evaluated for growth in 6.5% sodium chloride, hydrolysis of esculin, and CAMP reaction. Streptococcal organisms were identified at the species level using the API 20 Strep System (bioMerieux Vitek) upon first and last isolation of the organism from infected mammary quarters.

The number of somatic cells in foremilk was determined by the Dairy Herd Improvement Association Laboratory, Knoxville, TN for samples collected from each infected mammary quarter immediately before antibiotic treatment and at 7, 14, 21, and 28 days after the last treatment.

Qualified farm personnel determined a palpation/physical condition of udder and milk score for each challenged mammary gland when milk samples were collected. The following scoring system was used:

1: Normal mammary gland and normal milk
2: Normal mammary gland and slight alterations in milk (a few flakes)
3: Abnormal mammary gland (hot and/or swollen) and normal to slightly altered milk (a few flakes) or normal mammary gland and abnormal milk (clots, clumps, changes in milk color)
4: Abnormal mammary gland (hot and/or swollen) and abnormal milk (clots, clumps, changes in milk color)
5: Swollen mammary gland, abnormal milk and systemic signs (elevated rectal temperature, depression, dullness) or infection.

Mammary glands were considered to have clinical mastitis when *S. uberis* was isolated from foremilk samples twice and the udder and milk score was 3 or higher during the first week after challenge. Mammary glands were considered to have subclinical mastitis when *S. uberis* was isolated twice from foremilk samples and the udder and milk score was 2 or less during the first week after challenge. All infected mammary quarters were treated by 7 days after challenge. Some cows were treated earlier based on their response to bacterial challenge. Mammary glands of cows with an udder and milk score of 4 for 2 consecutive days were treated prior to 7 days after challenge.

**Treatments**

Challenged cows were randomly allocated to three treatment groups as follows: pirlimycin 2-day treatment (n = 21 cows, 31 mammary quarters), pirlimycin 5-day treatment (n = 21 cows, 32 mammary quarters), and pirlimycin 8-day treatment (n = 26 cows, 40 mammary quarters). Mammary glands that became infected following challenge were treated with 50 mg of pirlimycin hydrochloride (Pirsue Sterile Solution, Pfizer Animal Health) per 10-ml plastet administrated via intramammary infu-
Current recommendations in the United States call for two infusions of pirlimycin per infected mammary gland with a 24-hour interval (pirlimycin 2-day treatment group). Infected mammary glands of cows in the pirlimycin 5- and 8-day treatment groups were treated once daily for 5 or 8 consecutive days, respectively. Milk was discarded during the challenge period, during the antibiotic treatment period, for 36 hours after the last treatment in the pirlimycin 2-day treatment group, and for 8 days after last treatment in the 5- and 8-day treatment groups.

Analysis

A cure was defined as an experimentally infected mammary gland treated with pirlimycin that was bacteriologically negative for *S. uberis* at 7, 14, 21, and 28 days after treatment. The percentage of *S. uberis* IMIs eliminated in mammary glands receiving extended-therapy regimens (pirlimycin 5- or 8-day treatments) was compared with the percentage of *S. uberis* IMIs eliminated in mammary glands receiving the standard pirlimycin 2-day treatment. Additionally, the percentage of *S. uberis* IMIs eliminated by the pirlimycin 8-day extended-therapy regimen was compared with the percentage of IMIs eliminated for mammary quarters receiving the 5-day treatment. Comparisons of cure rates between treatment groups were made using chi-square testing (SAS Institute). A general mixed model (PROC MIXED, SAS Version 8.2) was used to analyze SCC data, and the logarithm of SCC over time was modeled as a repeated measure on time. A general mixed model (PROC MIXED) was also used to analyze mammary and milk score data as a repeated measure on time.

### RESULTS

The mammary glands (n = 103) of the 68 dairy cows that became infected following experimental challenge with *S. uberis* during early lactation were treated with pirlimycin. In the 2-day treatment group, 18 of 31 infections (58.1%) were eliminated. In the pirlimycin 5- and 8-day treatment groups, 22 of 32 infections (68.8%) and 32 of 40 infections (80%), respectively, were eliminated (Table 1). Significant (*P* < .05) differences in treatment efficacy were observed between the 2- and 8-day pirlimycin treatment groups. However, no significant differences in efficacy were detected between the 2- and 5-day treatment groups or between the 5- and the 8-day pirlimycin treatments.

![Table 1. Efficacy of Extended Pirlimycin Therapy Against *Streptococcus uberis* Experimental Intramammary Infections](image)

<table>
<thead>
<tr>
<th>Days Treated with Pirlimycin</th>
<th>Infections Eliminated/ Total Infections (%)</th>
<th>Infections Not Eliminated/ Total Infections (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>18/31 (58.1%)</td>
<td>13/31 (41.9%)</td>
</tr>
<tr>
<td>5</td>
<td>22/32 (68.8%)</td>
<td>10/32 (31.2%)</td>
</tr>
<tr>
<td>8</td>
<td>32/40 (80.0%)*</td>
<td>8/40 (20.0%)</td>
</tr>
</tbody>
</table>

*Significantly different from pirlimycin 2-day treatment (*P* = .045).

Efficacy of the three pirlimycin therapeutic regimens against clinical and subclinical *S. uberis* experimental IMIs in Holstein and Jersey cows is in Table 2. The proportion of mammary glands that became infected in Jersey cows (86.5%) was significantly (*P* < .05) greater than for Holsteins (69%) following challenge with *S. uberis* UT888. More than 93% of *S. uberis* experimental infections in Holstein cows and nearly 78% in Jersey cows resulted in clinical mastitis (Table 2). The majority (10 of 14) of subclinical infections observed were in Jerseys.

Efficacy of the 2-day pirlimycin treatment was significantly (*P* < .003) higher in Holstein
than in Jerseys. When pirlimycin 2-day and 5-day treatment data were combined, there was also a significant \((P < .05)\) breed difference, in that Jersey cows had fewer cures than did Holsteins. However, no differences in efficacy of the 8-day pirlimycin treatment regimen were observed between Holstein and Jersey cows.

All intramammary antibiotic infusions in Jerseys were performed 7 days after challenge. In contrast, 25 of 42 Holsteins were treated sooner based on their response to bacterial challenge. Of these Holstein cows, two were treated 3 days after challenge, eight were treated 4 days after challenge, 12 were treated 5 days after challenge, and three were treated 6 days after challenge. Because these cows were randomly distributed across three treatment regimens and treated at different times following bacterial challenge, it is difficult to draw meaningful conclusions on response to treatment based on how early cows became infected after challenge. However, it is clear that Holsteins developed clinical mastitis after bacterial challenge with \(S.\ uberis\) UT888 earlier than Jerseys did.

Somatic cell counts for each pirlimycin treatment group are shown by success or failure of cure in Table 3. Somatic cell counts decreased significantly \((P < .05)\) in mammary quarters for which pirlimycin treatment was successful in eliminating \(S.\ uberis\). A significant \((P < .05)\) reduction in SCCs was observed in milk samples 7 days after the final treatment in cases for which \(S.\ uberis\) was successfully eliminated, and this reduction persisted at all subsequent sampling times. Conversely, the number of somatic cells in milk did not change significantly in cases where treatment was unsuccessful at eliminating \(S.\ uberis\) except in milk from quarters treated 5 days. There was no evidence to suggest that extending pirlimycin therapy to either 5 or 8 days resulted in a greater reduction in SCCs than for the standard 2-day treatment.

Mammary and milk scores of clinically infected mammary glands following different pirlimycin treatment regimens are presented in Table 4. A significant \((P < .05)\) reduction in mammary and milk scores was observed 7 days after challenge.

### Table 2: Efficacy of Pirlimycin Therapeutic Regimens Against Clinical and Subclinical \(Streptococcus\ uberis\) Experimental Intramammary Infections

<table>
<thead>
<tr>
<th>Breed</th>
<th>Mastitis Type</th>
<th>Pirlimycin 2-day</th>
<th>Pirlimycin 5-day</th>
<th>Pirlimycin 8-day</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Cure</td>
<td>Fail</td>
<td>Cure</td>
</tr>
<tr>
<td>Jersey*</td>
<td>Clinical</td>
<td>3</td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>Subclinical</td>
<td>1</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td>4</td>
<td>10</td>
<td>8</td>
</tr>
<tr>
<td>Holstein†</td>
<td>Clinical</td>
<td>10</td>
<td>3</td>
<td>14</td>
</tr>
<tr>
<td></td>
<td>Subclinical</td>
<td>4</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td>14</td>
<td>3</td>
<td>14</td>
</tr>
<tr>
<td>Combined‡</td>
<td>Clinical</td>
<td>13</td>
<td>10</td>
<td>21</td>
</tr>
<tr>
<td></td>
<td>Subclinical</td>
<td>5</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td>18</td>
<td>13</td>
<td>22</td>
</tr>
</tbody>
</table>

*26 Jersey cows with 45 infected mammary quarters.
†42 Holstein cows with 58 infected mammary quarters.
‡68 total cows with 103 infected mammary quarters.
after the final treatment irrespective of the success or failure in eliminating *S. uberis* from the challenged quarters. A further numerical reduction was observed in mammary and milk scores as time after last treatment increased. Generally, milk and mammary scores were lower in cases for which *S. uberis* was successfully eliminated following treatment. However, few statistical differences were observed between the different pirlimycin treatment regimens or between cases within a treatment regimen for which *S. uberis* was successfully eliminated and those for which the organism was not eliminated.

**DISCUSSION**

Results of the present study support the concept that pirlimycin is an effective antibiotic for eliminating *S. uberis* IMIs and that extended pirlimycin therapy is significantly more effective at eliminating *S. uberis* IMIs than standard 2-day pirlimycin intramammary treatment. Although the standard 2-day pirlimycin intramammary treatment was effective, increasing the duration of pirlimycin therapy significantly increased treatment efficacy. This has been previously demonstrated for natural IMIs caused by *S. uberis*, other environmental *Streptococcus* species, and *S. aureus*.11,18

A recent study by Gillespie and coworkers11 demonstrated that 67% of IMIs caused by naturally occurring environmental *Streptococcus* spp were eliminated following the 2-day pirlimycin therapy regimen, compared with 85% with the 5-day regimen and 100% following 8 days of treatment. Significant differences in efficacy were detected in that earlier study between the untreated control group and the 2-, 5-, and 8-day pirlimycin treatment groups.11 Differences in efficacy between the 8- and the 2-day regimen also were significant. However, no differences were observed between the 2- and the 5-day treatment groups or between the 5- and the 8-day treatment groups in the present study. In that earlier study,11 41 of 61 infections (67%) attributed to environmental *Streptococcus* spp were due to *S. uberis*. Following treatment with pirlimycin, 50% (2 days), 83.3% (5 days), and 100% (8 days) of naturally occurring subclinical *S. uberis* IMIs were cured.11 Efficacy of pirlimycin against experimentally-induced *S. uberis* IMI was somewhat lower than that observed by Gillespie et al11 using naturally occurring *S. uberis* IMIs but followed a similar pattern. This could be due, in part, to the fact that the majority of *S. uberis* IMIs (86.4%) observed in the present study resulted in clinical mastitis.

### TABLE 3. Somatic Cell Counts in Milk Samples from Mammary Glands Experimentally Infected with *Streptococcus uberis* and Treated with Different Pirlimycin Regimens

<table>
<thead>
<tr>
<th>Pirlimycin Treatment Group</th>
<th>Status After Treatment</th>
<th>Somatic Cell Counts (log₁₀)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Day 0</td>
</tr>
<tr>
<td>2-day Cure</td>
<td></td>
<td>6.89a</td>
</tr>
<tr>
<td>2-day Fail</td>
<td></td>
<td>6.75a</td>
</tr>
<tr>
<td>5-day Cure</td>
<td></td>
<td>6.94a</td>
</tr>
<tr>
<td>5-day Fail</td>
<td></td>
<td>6.87a</td>
</tr>
<tr>
<td>8-day Cure</td>
<td></td>
<td>6.84a</td>
</tr>
<tr>
<td>8-day Fail</td>
<td></td>
<td>6.67a</td>
</tr>
</tbody>
</table>

Means within rows having different superscript letters are significantly different (*P* < .05). Means within columns having different superscript symbols are significantly different (*P* < .05).
A study by Deluyker and coworkers evaluated efficacy of pirlimycin for treatment of subclinical mastitis. In that study, mammary glands of cows received no treatment or pirlimycin for either 2 days or 8 days. A mammary quarter was considered not cured when the same bacterial species cultured before treatment was isolated in one of two posttreatment samples. Cure rates for *S. uberis* were 21% for the pirlimycin 2-day treatment and 75% for the 8-day treatment. These results are similar to the efficacy observed in the present study, which produced a cure rate of 80% for the 8-day treatment of *S. uberis* IMIs. However, efficacy of the 2-day treatment was considerably higher in the present study than that in the study reported by Deluyker and coworkers.

The *S. uberis* experimental model employed in the present study was quite useful for evaluating efficacy of pirlimycin and extended therapy approaches. Results using the *S. uberis* experimental IMI model agree reasonably well with the few studies that have evaluated efficacy of pirlimycin against naturally occurring *S. uberis* IMIs. The *S. uberis* experimental infection model was developed in early lactation dairy cows because this is a time when mammary glands of dairy cows are highly susceptible to new *S. uberis* infection. One significant advantage of the experimental IMI approach is the capability of rapidly determining if compounds and approaches are effective before proceeding to large-scale, expensive, field trial-based studies. Another significant advantage is the opportunity to generate a sufficient number of IMIs for determining statistical validity of treatment approaches against a target pathogen. Based on results of the present study, the strain of *S. uberis* used can infect a large proportion of experimentally challenged mammary glands without overwhelming cows and host defense mechanisms. The strain of *S. uberis* used caused mild clinical mastitis in the majority of mammary glands that became infected, and many *S. uberis* IMIs were eliminated following antibiotic therapy. Thus, the *S. uberis* experimental IMI model used in this study will be invaluable for rapid evaluation of new antimicrobials, and experimental antigens and vaccines.

**CONCLUSION**

Treatment of mammary quarters with pirlimycin for 2, 5, or 8 days eliminated 58.1%,

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**TABLE 4. Mammary and Milk Scores of Mammary Glands Experimentally Infected with *Streptococcus uberis* and Treated with Different Pirlimycin Regimens**

<table>
<thead>
<tr>
<th>Pirlimycin Treatment Group</th>
<th>Status After Treatment</th>
<th>Mammary and Milk Scores</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Day 0</td>
<td>Day 7</td>
</tr>
<tr>
<td>2-day Cure</td>
<td>3.69**</td>
<td>2.62*</td>
</tr>
<tr>
<td>2-day Fail</td>
<td>3.89*</td>
<td>2.89*</td>
</tr>
<tr>
<td>5-day Cure</td>
<td>3.95*</td>
<td>2.00↑</td>
</tr>
<tr>
<td>5-day Fail</td>
<td>3.71*</td>
<td>1.57↑</td>
</tr>
<tr>
<td>8-day Cure</td>
<td>3.61*</td>
<td>1.71↑</td>
</tr>
<tr>
<td>8-day Fail</td>
<td>4.00*</td>
<td>2.57↑</td>
</tr>
</tbody>
</table>

Means within rows having different superscript letters are significantly different (*P* < .05).

Means within columns having different superscript symbols are significantly different (*P* < .05).
68.8%, and 80% of experimental *S. uberis* infections, respectively. Significant differences (*P* < .05) in treatment efficacy were observed between the pirlimycin 2- and 8-day treatment groups. However, efficacy of the 2- versus the 5-day pirlimycin treatment regimen and the 5- versus the 8-day treatment regimen was similar. Results of this study indicate that pirlimycin therapy was effective for eliminating *S. uberis* experimental IMIs, and that pirlimycin 8-day treatment was significantly (*P* < .05) more effective than 2- or 5-day pirlimycin treatment regimens. Thus, it would appear increasing the duration of pirlimycin therapy increases treatment efficacy. This has been demonstrated for *S. uberis*, other environmental *Streptococcus* species, and *S. aureus*. The *S. uberis* experimental IMI model appears to be a rapid and effective means of evaluating antimicrobial efficacy during early lactation at a time when mammary glands are highly susceptible to *S. uberis* infection. Enhanced effectiveness of pirlimycin extended therapy must be weighed against several factors. Extra labor and treatment costs and additional loss of milk due to a longer treatment withholding time versus the potential benefits of increased milk production following elimination of the infection and better milk quality should be considered. Studies to evaluate economic benefits that producers might gain from pirlimycin extended antibiotic therapy of *S. uberis* and other pathogens that cause mastitis need to be conducted to fully evaluate costs and benefits associated with this type of therapy.

### REFERENCES

