

# A Randomized Blind Trial on Dry Cow Antibiotic Infusion in a Low Somatic Cell Count Herd

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## ABSTRACT

The objective of the study was to evaluate the effect of administration of antibiotics to cows at dry-off in a low SCC herd. Cows were infused at dry-off with an intramammary antibiotic on the left or the right side of the udder. Selection of the infused quarters was random, and all people evaluating the occurrence of mastitis were unaware of which half of the udder was infused. The quarters that were infused with an antibiotic showed a significantly lower incidence of clinical mastitis in the dry period. Quarters that were uninfused had 10 cases of clinical mastitis versus 1 case in quarters that were infused with antibiotics. The quarters that were infused showed a reduction of minor pathogens at calving. The uninfused quarters showed little evidence of spontaneous cure during the dry period.

Milk leaking was frequent during the drying off period. Milk leaking was also associated with the occurrence of clinical mastitis later in the dry period. Cows that leaked milk had a four times greater risk of clinical mastitis in the dry period. (**Key words:** mastitis, somatic cell counts, dry cow antibiotics, clinical trial)

## INTRODUCTION

In the battle against mastitis, the five-point plan that resulted from extensive field trials has proved to be very successful (2, 7) worldwide and has decreased subclinical mastitis caused by contagious pathogens. Modern well-managed dairy herds have low SCC and a low prevalence of quarters infected with major

pathogens such as *Staphylococcus aureus* and *Streptococcus agalactiae*.

An important component of the five-point plan is the use of antibiotics at drying off. In herds with a high prevalence of IMI, infusion of dry cow antibiotics can reduce prevalence (6). When hygiene and management practices are good, and, as a result, prevalence of IMI is limited to a small proportion of the quarters, the necessity of infusion of antibiotics at drying off is questionable. Dodd (3) raised this question in 1987 and concluded that data were insufficient to answer it.

Before recommendations are given for administration of dry cow therapy to all cows in all herds, including those with a low prevalence of subclinical mastitis as indicated by low bulk milk SCC, or for selective dry cow therapy in herds that meet certain criteria, data should be collected to support such advice.

The current study evaluated the use of dry cow antibiotics in a herd with a low bulk milk SCC to determine the effect of antibiotic infusion on prevention of clinical mastitis and dynamics of IMI in the dry period.

## MATERIALS AND METHODS

### The Herd

The dry cow trial was conducted at the institutional herd of the College of Veterinary Medicine in Utrecht, The Netherlands. The 50 Holstein-Friesians were housed in free stalls; rolling herd average was approximately 9543 kg of 4% FCM. The bulk milk SCC in 1990 was, on average, 140,000 cells/ml, and individual SCC were monitored to detect infected cows. All cows in the herd were sampled bimonthly to determine the bacteriological status of the quarters. The prevalence of major pathogens was, on average, <5%. Clinical mastitis was not a problem in the herd and was annually <10% of the cows per lactation. Hygienic milking standards were

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used; no postmilking teat dip had been used for the past 7 yr. Until 2 yr before the start of the trial, all quarters of all cows were infused at dry-off with an approved dry cow antibiotic. During the final 2 yr, no antibiotics were applied, and, consequently, clinical cases of mastitis occurred in the early dry period.

#### Dry-Off Procedures

From September 1988 to September 1990, 68 cows were enrolled in the trial. The following protocol was designed for the purpose of this trial. Two weeks before estimated dry-off, cows were moved from free stalls to stanchions. The ration was changed to a straw ration with 1 kg of concentrate in wk 1 and only hay or silage feeds in wk 2. Cows were milked only once a day for 3 consecutive d and then milked once a day on Mondays, Wednesdays, and Fridays. When production had dropped below 5 kg/d or when a maximum of 12 d had passed, cows were dried off. At dry-off (cessation of milking), two milk samples were collected aseptically from every quarter. For each cow, one-half of the udder (left or right) was randomly assigned for antibiotic dry cow infusion (Nafpenzal-N8®; Intervet International, Boxmeer, The Netherlands); the other half was not infused. A pilot study on 10 cows was performed to evaluate whether inhibitory concentrations of antibiotic crossed from infused to uninfused quarters. Five samples from each uninfused quarter were taken during the first 10 d of the dry period. Samples were evaluated with the Delvotest SP assay (Gist-Brocades, Delft, The Netherlands). None of these samples showed evidence that inhibitory concentrations of antibiotic crossed from infused to uninfused quarters. The herders who diagnosed clinical mastitis were unaware of antibiotic allocation. After the final milking, cows remained in the stanchions for an additional week and were observed for milk leakage. For the remainder of the dry period, the cows were moved to free stalls or pasture.

Cows were observed daily for occurrence of clinical mastitis defined as an observable abnormality on quarter or cow. When clinical mastitis was diagnosed, milk was sampled, and quarters were infused intramammarily with an antibiotic. After calving, duplicate samples were collected aseptically.

Not all cows could be observed during the complete period. Two cows aborted and were sold. One cow suffered an abomasal dislocation and was operated on in the clinic. Three cows were sold immediately after calving and were not milked, and 15 cows were used for other trials immediately after calving and were not available for sampling. Because randomization was on a within-cow basis, cows remained eligible for the study and were defined as being at risk as long as they could be observed.

#### Microbiological Procedures

Milk samples (.01 ml) were cultured aerobically on brilliant green phenol red agar medium (CM 263; Oxoid Ltd., Basingstoke, England) and aerobically on 6% bovine blood agar at 37°C either for 18 h or for 42 h when no growth was observed. For further identification of the streptococci, the CAMP reaction and 40% ox bile were used. Staphylococci were tested for presence of coagulase with a slide coagulase test (Bacto coagulase plasma EDTA; Difco Laboratory, Detroit, MI). Gram-negative microorganisms were differentiated using Kligler iron agar (CM33; Oxoid). For further determinations, lactose, urea, indol, ornithine, and gelatine agar were used; additionally, cytochrome oxidase activity also was tested on all Gram-negative, lactose-negative microorganisms. A quarter was considered to be infected when both samples yielded identical results. A quarter was considered to be uninfected (negative) when both samples were negative. Quarters with discordant samples were coded as "undecided". Results were compared assuming a Poisson distribution for clinical cases. Statistical significance was declared at the 5% level. Statistical analyses were performed using the program Statistix® (NH Analytical Software, St. Paul, MN).

#### RESULTS

Milk production in the 68 cows dropped rapidly during intermittent milking and restricted feeding. Approximately 60% of cows were dried off because they produced  $\leq 5$  kg/d of milk; the remaining 40% were dried off 12 d after change of management. Approximately 30% of the cows leaked milk during the period in the stanchion barn. The bacteriological status of the quarters at dry-off is shown in Table 1.

TABLE 1. Bacteriological status of quarters at cessation of milking.

Microorganism	Quarters			
	Infused		Uninfused	
	(no.)	(%)	(no.)	(%)
<i>Staphylococcus aureus</i>	3	2.2	5	3.7
<i>Streptococcus uberis</i>	3	2.2	2	1.5
<i>Streptococcus agalactiae</i>	1	.7	0	
<i>Staphylococcus</i> species	11	8.1	7	5.1
<i>Corynebacterium bovis</i>	50	36.8	57	41.9
Mixed minor pathogens	32	23.5	30	22.1
Undecided <sup>1</sup>	20	14.7	18	13.2
Negative	16	11.8	16	11.8
No sample	...	...	1	.7
Total	136		136	

<sup>1</sup>Combination of a negative and a minor pathogen.

At dry-off, 5.1% of the quarters were infected with major pathogens. Because no post-milking test disinfection was practiced, the prevalence of minor pathogens was high (65%). At the start of the trial, no significant difference existed in IMI pattern in infused and uninfused cows.

The average observed dry period in the cows was  $74 \pm 32$  d. During the 68 dry periods, 11 cases of clinical mastitis were observed (16% of the cows). Seven cases occurred within 2 wk after dry-off. Ten cases were in uninfused quarters, and 1 case was in

an infused quarter, indicating a 10-fold (95% confidence interval 3.1 to 27.8;  $P \leq .006$ ) increased risk of clinical mastitis in uninfused quarters. The bacteriology of the observed cases of clinical mastitis is shown in Table 2.

The dynamics of IMI during the dry period, as estimated by the difference in bacteriological results between dry-off and calving, is shown in Tables 3 and 4. Results for infused quarters are in Table 3 and for uninfused quarters in Table 4. For example, in the infused quarters, 3 quarters were infected with *S. aureus* at dry-off. One of these IMI was also

TABLE 2. Bacteriology of cases of clinical mastitis in the dry period.

Cow	Quarter code <sup>1</sup>	Infused	Days after dry-off	Bacteriological results		
				At dry-off	At clinical mastitis	At calving
1	RH	No	3	<i>Streptococcus agalactiae</i>	CNS <sup>2</sup>	Aborted
33	RH	No	4	No sample	CNS	No sample
18	LH	No	9	<i>Streptococcus uberis</i>	<i>Strep. uberis</i>	Negative
20	LF	No	4	<i>Corynebacterium bovis</i>	<i>Strep. uberis</i>	Negative
93	RH	No	1	<i>Staphylococcus aureus</i>	Negative	Mix minor
95	RF	Yes	124	<i>Staph. aureus</i>	<i>Staph. aureus</i>	<i>Staph. aureus</i>
35	LH	No	12	Undecided	<i>Strep. uberis</i>	<i>C. bovis</i>
119	LH	No	33	<i>C. bovis</i>	CNS	No sample
120	RH	No	35	Mix minor	CNS	No sample
18	RF	No	9	Mix minor	<i>Nocardia</i>	Undecided
94	LH	No	21	Mix minor	<i>Actinomyces pyogenes</i>	<i>A. pyogenes</i> (aborted)

<sup>1</sup>RH = Right hind, RF = right front, LH = left hind, LF = left front.

<sup>2</sup>CNS = Coagulase-negative staphylococci.

TABLE 3. Dynamics of IMI during the dry period in infused quarters.

At dry-off	At calving							Total
	SA	MP	CNS	CB	MM	U	N	
<i>Staphylococcus aureus</i> (SA)	1 <sup>1</sup>		1	1				3
Major pathogen (MP)				2		1		3
Coagulase-negative staphylococci (CNS)			1	4	2	2	2	11
<i>Corynebacterium bovis</i> (CB)		1	7	10	3	5	14	40
Mix minor (MM)		1	5	4	1	4	3	18
Undecided (U)				2	2	1	4	9
Negative (N)		1	1	1	1	2	4	10
Total	1	3	15	24	9	15	27	94

<sup>1</sup>Includes one treated quarter (clinical case).

present at calving, but 2 of these quarters cleared *Staph. aureus* and were infected with *Corynebacterium bovis* and coagulase-negative staphylococci, respectively.

In infused quarters, five out of six major pathogens and 29% of the minor pathogens were eliminated. Three new IMI occurred in the dry period in infused quarters. In uninfused quarters, three of four major pathogens were cured; two of the three cures were in quarters treated for clinical mastitis. Little change occurred in the prevalence of minor pathogens. Six new IMI with major pathogens occurred. When infused and uninfused quarters were compared, the proportion of minor pathogens eliminated was significantly reduced. The rate of new IMI in infused quarters was lower but not significant. These results are summarized in Table 5.

Cows that leaked milk during the period of intermittent milking had 4.0 times greater risk ( $P \leq .06$ ) of clinical mastitis during the dry period. These cows had also 6.1 ( $P \leq .03$ ) times greater risk of an IMI with a major pathogen during the dry period.

After calving, four cows had clinical mastitis, two in infused quarters and two in uninfused quarters.

## DISCUSSION

The results of this trial reaffirmed the high susceptibility of cows in the early dry period, even when the prevalence of IMI with major pathogens at dry-off was low. As described by Eberhart (4), the role of antibiotics at dry-off is twofold: 1) to reduce the number of prevalent IMI and 2) to prevent new IMI in the early dry

TABLE 4. Dynamics of IMI during the dry period in uninfused quarters.

At dry-off	At calving							Total
	SA	MP	CNS	CB	MM	U	N	
<i>Staphylococcus aureus</i> (SA)	1			1 <sup>1</sup>				2
Major pathogen (MP)					1		1 <sup>1</sup>	2
Coagulase-negative staphylococci (CNS)			1	3		2		6
<i>Corynebacterium bovis</i> (CB)	1	3	3	20	4	4	4 <sup>1</sup>	39
Mix minor (MM)		1 <sup>1</sup>	2	8	4	1 <sup>1</sup>	1	17
Undecided (U)			1	6 <sup>1</sup>	2	5	2	16
Negative (N)		1	1	5	1		4	12
Total	2	5	8	43	12	12	12	94

<sup>1</sup>Includes one treated quarter (clinical case); four clinical quarters were not sampled after calving and, therefore, were not included in this table.

TABLE 5. New IMI and spontaneous cure of IMI during in quarters during dry period.

	Quarters						P
	Infused			Uninfused			
	(no.)	(%)	(no.) <sup>1</sup>	(no.)	(%)	(no.) <sup>1</sup>	
New IMI							
Major pathogens	3	3	88	6	7	90	.5
Minor pathogens	3	30	10	7	60	12	.2
Spontaneous cure of IMI							
Major pathogen	5	83	6	3	75	4	.8
Minor pathogen	23	29	78	7	9	78	.001

<sup>1</sup>Number of quarters at risk for IMI or spontaneous cure of IMI.

period. In this low SCC herd, the prevalence of IMI with major pathogens at dry-off was low; thus, the apparent benefit for reducing the prevalence of existing IMI was low. However, the early dry period was a high risk period for new IMI. The data in this herd showed that 7 out of 10 clinical cases were caused by new IMI in an uninfused quarter that was previously uninfected by major pathogens. In contrast, no clinical cases occurred in the early dry period in infused quarters. The only clinical case in infused quarters occurred 3 d before calving in a cow with a long dry period (127 d).

In this trial, the incidence of clinical mastitis in the early dry period was high. This finding may be associated with the high incidence of milk leaking in the cows in the drying off period. Milk leaking was strongly associated with clinical mastitis and IMI with major pathogens in the dry period, as has been observed before (8).

Only 10 of 136 uninfused quarters (7%) encountered inflammation that might have been prevented by antibiotic infusion. This low percentage may have occurred either because of a uniform risk for all cows or because of a high risk for some cows and a low risk for others. Substantial evidence exists that the latter scenario is more realistic (1, 5, 9). The selection of appropriate cows to infuse at dry-off is therefore essential. Clinical cases and IMI with major pathogens are strongly related to observable risk factors (in this trial, milk leaking). This relationship implies that objective selection of high risk cows for antibiotic dry cow infusion may be possible, and other

cows with a low risk profile may remain uninfused. Great caution should be exercised, because proper risk indicators have not yet been determined. Milk leakage seemed to be a risk factor; previous clinical mastitis occurrence, high SCC, age, and teat lesions also are risk factors (1, 5, 9). Whether cows with risk factors should remain in the herd remains questionable. More emphasis on selective culling and breeding for mastitis resistance may improve long-term prospects.

In some herds in which selective dry cow therapy was practiced, risk of clinical mastitis did not increase (8); apparently, these farmers have developed highly predictive risk profiles for their cows. Further observational studies are necessary to identify this risk profile to allow more specific recommendations for antibiotic infusion at dry-off and to eliminate unnecessary use of antibiotics. Until such a risk profile is defined, infusion of all quarters of all cows with antibiotics at dry-off is the safest practice.

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