Invited review: Mastitis in dairy heifers: Nature of the disease, potential impact, prevention, and control

S. De Vliegher,^{*1} L. K. Fox,[†] S. Piepers,^{*} S. McDougall,[‡] and H. W. Barkema^{§*}

^{*}M-team and Mastitis and Milk Quality Research Unit, Department of Reproduction, Obstetrics and Herd Health, Faculty of Veterinary Medicine, Ghent University, Merelbeke 9820, Belgium

[†]College of Veterinary Medicine, Washington State University, Pullman 99164-6610

[‡]Animal Health Centre, Morrinsville 3340, New Zealand

[§]Department of Production Animal Health, Faculty of Veterinary Medicine, University of Calgary, Calgary, AB, Canada T2N 4N1

ABSTRACT

Heifer mastitis is a disease that potentially threatens production and udder health in the first and subsequent lactations. In general, coagulase-negative staphylococci (CNS) are the predominant cause of intramammary infection and subclinical mastitis in heifers around parturition, whereas *Staphylococcus aureus* and environmental pathogens cause a minority of the cases. Clinical heifer mastitis is typically caused by the major pathogens. The variation in proportions of causative pathogens between studies, herds, and countries is considerable. The magnitude of the effect of heifer mastitis on an individual animal is influenced by the form of mastitis (clinical versus subclinical), the virulence of the causative pathogen(s) (major versus minor pathogens), the time of onset of infection relative to calving, cure or persistence of the infection when milk production has started, and the host's immunity. Intramammary infection in early lactation caused by CNS does not generally have a negative effect on subsequent productivity. At the herd level, the impact will depend on the prevalence and incidence of the disease, the nature of the problem (clinical, subclinical, non-functional quarters), the causative pathogens involved (major versus minor pathogens), the ability of the animals to cope with the disease, and the response of the dairy manager to control the disease through management changes. Specific recommendations to prevent and control mastitis in late gestation in periparturient heifers are not part of the current National Mastitis Council mastitis and prevention program. Control and prevention is currently based on avoidance of inter-sucking among young stock, fly control, optimal nutrition, and implementation of hygiene control and comfort measures, especially around calving. More risk factors for subclinical and clinical heifer mastitis have

been identified (e.g., season, location of herd, stage of pregnancy) although they do not lend themselves to the development of specific intervention strategies designed to prevent the disease. Pathogen-specific risk factors and associated control measures need to be identified due to the pathogen-related variation in epidemiology and effect on future performance. Prepartum intramammary treatment with antibiotics has been proposed as a simple and effective way of controlling heifer mastitis but positive long-lasting effects on somatic cell count and milk yield do not always occur, ruling out universal recommendation of this practice. Moreover, use of antibiotics in this manner is off-label and results in an increased risk of antibiotic residues in milk. Prepartum treatment can be implemented only as a short-term measure to assist in the control of a significant heifer mastitis problem under supervision of the herd veterinarian. When CNS are the major cause of intramammary infection in heifers, productivity is not affected, making prepartum treatment redundant and even unwanted. In conclusion, heifer mastitis can affect the profitability of dairy farming because of a potential long-term negative effect on udder health and milk production and an associated culling risk, specifically when major pathogens are involved. Prevention and control is not easy but is possible through changes in young stock and heifer management. However, the pathogenesis and epidemiology of the disease remain largely unknown and more pathogen-specific risk factors should be identified to optimize current prevention programs.

Key words: heifer mastitis, impact, prevention, control

INTRODUCTION

Milk and dairy products are essential sources of food for the majority of the world population. To meet the growing global demand and to keep dairy farming profitable at the same time, average milk yield per cow, as well as average herd size, has increased in recent

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¹Corresponding author: Sarne.Devliegher@UGent.be

decades (Lucy, 2001). Higher milk yield has resulted from genetic selection as well as improved cow nutrition and management. The increase in average herd size has required an increase in the number of replacement heifers, prioritizing optimal dairy heifer rearing in modern intensive dairy systems. A heifer has returned little more than the investment cost after completion of the first lactation, provided it has remained healthy. One of the diseases threatening its health is mastitis.

When bacteria invade the mammary gland via the teat orifice an IMI can become established, which will often provoke an inflammatory response (mastitis), manifesting itself in either subclinical (in which visual symptoms are absent) or clinical mastitis (CM; in which local and/or systemic symptoms are visible). Mastitis, in general, is one of the most common and detrimental diseases cows can experience. Mastitis threatens the income of farmers as well as the image of the dairy sector because of animal welfare issues and issues related to milk quality and public health due to increased risk of residues in milk through (improper) use of antimicrobials and the emergence of resistant bacteria. Heifer mastitis may be defined as subclinical mastitis (detected through an elevated quarter or composite SCC), CM, or one or more nonfunctional quarter(s) in animals in the first lactation, particularly in the peripartum period. Heifer mastitis is a remarkable disease, given that these animals have never been milked and that the milking process is generally considered one of the principal risk factors for contagious mastitis in mature cows. Additionally, their teats have not been challenged by the milking vacuum.

Heifer mastitis was described many years ago (Schalm, 1942) but was only considered a significant problem decades later (Meaney, 1981; Oliver and Mitchell, 1983). The global scale of this disease has been documented in several publications from North America (e.g., Matthews et al., 1992; Oliver et al., 1992; Middleton et al., 2005), Europe (e.g., Myllys, 1995; Aarestrup and Jensen, 1997; Piepers et al., 2010), New Zealand (Pankey et al., 1996; Compton et al., 2007a; Parker et al., 2008), Japan (Seno and Azuma, 1983), and South America (da Costa et al., 1996).

Mastitis in heifers varies from that in cows in several ways. The incidence of CM in heifers is higher in the first few days postpartum than in cows (Barkema et al., 1998b; McDougall et al., 2007a; Figure 1). Additionally, the distribution of bacterial isolates from CM cases can vary by age, with heifers having a higher incidence of *Streptococcus uberis* and CNS and a lower incidence of *Staphylococcus aureus* infections compared with older animals (McDougall et al., 2007b; Figure 2). These differences are likely due to differences in management of heifers compared with older animals

Figure 1. Early lactation daily incidence rate of clinical mastitis for heifers (●) and cows (parity >1; ▽) from 30 New Zealand dairy herds (data derived from McDougall et al., 2007a).

and to physiological differences, including the fact that heifers are commencing lactation for the first time and are still growing. Age-specific differences in white cell differential counts and in subtypes within leukocyte populations have been demonstrated (Tanaka et al., 2008), illustrating one potential mechanism explaining differences among age groups in CM incidence. Importantly, these differences suggest that research needs to continue into heifer mastitis to aid in development of specific mastitis management practices for heifers.

Heifer mastitis is a costly disease. Typically, the costs of mastitis are ascribed to lost milk production; premature culling; additional labor, management, and veterinary needs; use of drugs and risk of residues; and production of nonsaleable milk (Huijps et al., 2009). Indeed, early lactation mastitis in heifers results in lost future milk yield (Coffey et al., 1986; Rupp and Boichard, 2000; De Vlieghe et al., 2005b). Additionally, heifer mastitis is coupled with an increased risk of premature culling (De Vlieghe et al., 2005a). Early lactation mastitis in heifers places these animals at greater risk for CM (Coffey et al., 1986; Rupp and Boichard, 2000), which would be associated with increased use of drug therapy, increase in discarded milk, and increased risk of residues appearing in the milk supply. Thus, reductions in heifer mastitis will logically lead to increased profitability to the dairy operator and a more wholesome milk supply.

The purpose of this review is to summarize the literature on heifer mastitis, focusing on the nature of the problem, causative pathogens, potential effects on future productive performance, risk factors, and non-antibiotic strategies to prevent and control the disease. Practical recommendations that could be added to the

Figure 2. Distribution of pathogens isolated from clinical mastitis cases from heifers ($n = 241$), 3- to 4- ($n = 182$), 5- ($n = 135$), 6- to 7- ($n = 261$), 8- ($n = 85$) and >8-yr-old cows ($n = 160$) from 28 New Zealand dairy herds (data derived from McDougall et al., 2007b).

National Mastitis Council (NMC) 10-point program (NMC, 2011) are included.

NATURE OF HEIFER MASTITIS AND CAUSATIVE AGENTS

Nature of Heifer Mastitis

Subclinical Heifer Mastitis. No consensus of the definition of IMI exists internationally (Andersen et al., 2010). Often, gland status is defined based on bacteriology (i.e., presence or absence of an IMI) or based on quarter-level or composite SCC. Differences in diagnostic techniques used and in cut points used to define “infection” likely contribute to the reported variation in prevalence and incidence of heifer mastitis (Sampimon et al., 2010).

Somatic cell count around calving is physiologically elevated, but no consensus exists on the length of the period for which SCC is increased, possibly because of the dynamics of IMI in the postpartum period (Dohoo, 1993; Barkema et al., 1999). As a result, almost all studies have focused on determining the presence of IMI around calving and very few have also determined SCC in quarter or composite samples. Studies using

DHI samples to measure the effect of subclinical mastitis in early lactation only had SCC data of composite samples available and IMI was not determined (e.g., De Vliegher et al., 2005b; Whist and Osteras, 2007). In the absence of bacteriology, the prevalence, incidence, and effect of species-specific IMI cannot be determined from many published studies. Longitudinal studies that determine both IMI and inflammation in quarter samples are needed. Additionally, the period and magnitude of the physiological elevation of SCC and possibly other markers of inflammation after calving should be determined in a study with a larger sample size than that of Barkema et al. (1999).

Prevalence of IMI and subclinical mastitis in udder quarters in heifers both pre- and postpartum varies widely between studies (Table 1). The prevalence of IMI ranges between 29 and 75% of quarters before parturition, whereas the immediate prevalence postpartum ranges from 12 to over 57% of quarters infected. A common denominator in all studies on subclinical mastitis is the high proportion of infections caused by CNS. Some studies have found that *Staph. aureus* was the most prevalent major pathogen, whereas other studies report environmental bacteria to be the more prevalent major pathogens (Table 1).

Table 1. Prevalence of intramammary infection in heifers before, at first calving, and in early lactation as reported in different studies¹

Stage and study	No. of herds (heifers)	No. of samples	Sample level	Infectious agent				
				Noninfected	CNS	CPS	Env	Other
Prior to first calving								
Oliver and Mitchell, 1983	1 (32)	252	Q	71.1	22.1	1.2	9.6	—
Trinidad et al., 1990	4 (97)	370	Q	25.4	52.9	14.9	2.7	0.8
Oliver et al., 1992	1 (115)	460	Q	39.3	52.8	1.7	4.3	1.7
Myllys, 1995	— ²	236	Q	61.0	28.8	4.7	4.6	0.8
Aarestrup and Jensen, 1997	20 (180)	554	Q	62.6	28.9	0.4	6.7	1.6
Fox et al., 1995	28 (1,583)	4,950	Q	64.0	21.8	2.8	7.7	3.5
Oliver et al., 1997	1 (82)	314	Q	34.4	55.1	3.2	5.7	8.3
Middleton et al., 2005	2 (183)	663	Q	53.4	37.3	3.9	3.9	1.5
At first calving								
Oliver and Mitchell, 1983	1 (32)	128	Q	68.8	18.8	0.8	12.5	0.8
Cook et al., 1992	— ²	525	C	43.0	43.0	6.0	—	8.0
Oliver et al., 1992	1 (41)	164	Q	55.4	39.0	0.6	4.9	—
Pankey et al., 1991	11 (382)	1,533	Q	81.7	11.4	0.7	4.8	1.7
Roberson et al., 1994a	18 (828)	828	C	45.0	39.0	8.0	13.0	—
Myllys, 1995	(160)	236	Q	71.5	18.5	4.6	3.9	1.5
Nickerson et al., 1995	5 (600)	600	C	58.4	27.9	8.0	4.2	1.4
Fox et al., 1995	28 (1,583)	4,950	Q	64.0	21.8	2.8	7.7	3.5
Pankey et al., 1996	11 (382)	458	Q	68.3	21.8	0.9	12.9	—
Parker et al., 2007a	5 (255)	252	Q	87.7	5.2	1.6	5.6	—
In early lactation								
Oliver and Mitchell, 1983	1 (32)	252	Q	87.3	7.5	0.4	4.8	0.4
Timms and Schultz, 1987	2 (51)	204	Q	78.5	18.6	0.0	0.0	—
Matthews et al., 1992	1 (36)	144	Q	81.2	15.3	3.5	—	—
Myllys, 1995	— ²	527	Q	71.5	18.6	4.5	3.8	1.5
Aarestrup and Jensen, 1997	2 (180)	713	Q	63.1	19.3	6.7	8.1	2.1
Oliver et al., 1997	1 (42)	172	Q	41.9	46.0	1.7	7.0	3.4
Piepers et al., 2010	20 (191)	762	Q	51.3	35.3	3.5	4.8	2.2

¹Percentage of mammary quarters (Q) or mammary glands, composite (C) that have a subclinical infection (CPS = coagulase-positive staphylococci; Env = environmental pathogens, non-*agalactiae* streptococci, and gram-negative rod-shaped organisms; and other pathogens) or are free of infection (noninfected).

²Information unknown.

Clinical Heifer Mastitis. The early lactation period of dairy heifers is characterized by a high incidence rate of CM, with more than 30% of cases in a lactation occurring in the first 2 wk of lactation (Barkema et al., 1998b; Nyman et al., 2007; Olde Riekerink et al., 2008). In general, the most common udder pathogens isolated from cases of CM in heifers are major pathogens such as *Staph. aureus*, *Streptococcus dysgalactiae*, *Streptococcus uberis*, and *Escherichia coli* (McDougall et al., 2007b; Persson Waller et al., 2009; Figure 2). Historically, CM in heifers was termed “summer mastitis syndrome” and the terms “summer mastitis” and “heifer mastitis” have been used synonymously (Seno and Azuma, 1983). Summer mastitis is typically seen in primigravid heifers but also in dry cows, and is caused by a combination of aerobic and anaerobic pathogens, including *Arcanobacterium pyogenes*, *Peptococcus indolicus*, and *Strep. dysgalactiae*, and is spread by the fly *Hydrotea irritans* (Nickerson et al., 1995). The incidence of summer mastitis is currently unclear due to a lack of recent studies being published on the subject. Still, *A. pyogenes* was reported to be an important cause of CM in heifers during the first week after calving in Sweden (Persson Waller et al., 2009).

Causative Bacteria

CNS. The CNS group consists of more than 45 different species and subspecies (www.bacterio.cict.fr/s/staphylococcus.html) of which approximately a dozen are commonly found in milk of dairy cows (Piessens et al., 2011; Supré et al., 2011). The epidemiology and relevance of this group as a cause of bovine mastitis is currently under debate (De Vlieghe et al., 2009). However, CNS have become the predominant bacteria found in milk samples from dairy cows and heifers in many areas around the world (e.g., Makovec and Ruegg, 2003; Pitkälä et al., 2004; Piepers et al., 2007). The description of the pathogenicity of CNS varies from being protective, over being indifferent for udder health, to being the cause of subclinical mastitis and (mild) CM (Nickerson and Boddie, 1994; De Vlieghe et al., 2003, 2004c; Taponen et al., 2007; Schukken et al., 2009). In heifers, they are the major cause of IMI and likely also subclinical mastitis around calving (Table 1).

Recently, it has been demonstrated that speciation of CNS on the basis of biochemical tests is not accurate for bovine CNS identification (Sampimon et al., 2009b). Hence, molecular identification has been pro-

posed as the gold standard (Zadoks and Watts, 2009). Many of the older papers describing CNS involved in heifer mastitis have used phenotypic identification and should be interpreted with care when looking at species distributions, species-specific effects, virulence traits, and antimicrobial resistance patterns. Ongoing studies are currently providing more robust data on prevalence, incidence, and risk factors for mastitis due to the different CNS species in both heifers and cows using several validated molecular tests (e.g., Supré et al., 2009; Piessens et al., 2010; Braem et al., 2011; Park et al., 2011). These studies have resulted in the detection of undescribed CNS species in milk and on teat apices of dairy cows (Supré et al., 2010; Taponen et al., 2011), and we expect many more to follow.

Staphylococcus aureus. Although prevalence of *Staph. aureus* IMI in heifers is generally lower compared with CNS, its importance should not be underestimated as this bacterium is one of the most difficult mastitis pathogens to control (Barkema et al., 2006). As well, newly calved heifers with *Staph. aureus* may represent an important infection source at milking for uninfected lactating herd mates (Roberson et al., 1994a) and provide a challenge to biosecurity systems.

The prevalence of subclinical *Staph. aureus* mastitis and IMI in heifers varies among studies and herds (Pankey et al., 1991; Roberson et al., 1996; Aarestrup and Jensen, 1997; Owens et al., 2001; Piepers et al., 2010) but is never as high as the prevalence of CNS IMI. Differences in management systems and factors such as the presence of flies capable of transmitting *Staph. aureus* may account for the observed variation in prevalence. *Staphylococcus aureus* can be a major cause of CM in heifers (Persson Waller et al., 2009).

Mycoplasma Species. *Mycoplasma* spp. can be considered an emerging mastitis pathogen (Fox et al., 2005; Barkema et al., 2009; Passchyn et al., 2011). *Mycoplasma* spp. are difficult pathogens to grow, and the sensitivity of detection of *Mycoplasma* spp. from mastitic milk samples is reduced when samples have been stored frozen (Biddle et al., 2004). Thus, it is likely that reported prevalence estimates of *Mycoplasma* mastitis are too low. Two recent reports indicate that this genus can cause CM in peripubertal calves: Roy et al. (2008) described a case of *Mycoplasma bovis* mastitis in a heifer that initially was presented to the veterinarian with a case of arthritis, and Fox et al. (2008) reported 3 cases of clinical *Mycoplasma bovis* mastitis on 2 adjacent dairy farms in young heifer calves. On-farm transmission through aerosols from animals with respiratory *Mycoplasma* infection can be a cause of *Mycoplasma* mastitis (Barkema et al., 2009). *Mycoplasma* causing mastitis in heifers can be a threat and can be

related to a *Mycoplasma* mastitis problem in the lactating herd.

Environmental Pathogens. Environmental pathogens can also cause significant mastitis problems in prepartum and recently calved heifers (Fox, 2009). *Coliforms* and non-*agalactiae* streptococci can cause the majority of subclinical mastitis cases after CNS and before *Staph. aureus* in some herds (e.g., Oliver and Mitchell, 1983; Pankey et al., 1991) (Table 1). *Streptococcus uberis* is the most common major pathogen of peripartum heifers managed in pasture-based systems, causing both subclinical and clinical mastitis (Compton et al., 2007a).

POTENTIAL CONSEQUENCES OF HEIFER MASTITIS

It remains a challenge to quantify the influence of each of the factors (e.g., causative pathogen, duration of infection before calving, persistence or cure of infection in early lactation, host immunity) involved in heifer mastitis on future performance of the heifers (Piepers et al., 2009a). Additionally, as discussed above, differences in definitions used among studies make comparisons difficult. Despite heifer mastitis being reported as a potential problem in the 1980s, relatively few studies have quantified the effect of heifer mastitis on udder health and milk production.

Subclinical Heifer Mastitis

Composite milk SCC records are often available from production testing programs and very useful to study subclinical mastitis (e.g., De Vliegher et al., 2001). However, as discussed above, inclusion of bacteriology in the study design would allow the pathogen-specific effect to be quantified. Time and expenses associated with such studies, however, limit the number of heifers that can be included, making culture-based studies rather uncommon. Still, a limited number of studies using either SCC data or culture results are available and help us to quantify the effect of subclinical heifer mastitis to some extent.

Effect on Future Udder Health. Heifers with an elevated SCC in early lactation maintain higher SCC throughout their first lactation (Coffey et al., 1986; De Vliegher et al., 2004a). Intramammary infections in early lactation caused by minor pathogens either have no effect on SCC for the remainder of the first lactation (Kirk et al., 1996; Compton et al., 2007a) or result in an SCC in first lactation between that of noninfected heifers and heifers infected by major pathogens at calving (Piepers et al., 2010). This finding suggests that CNS infections present in early lactation may persist and this

has been confirmed for a number of CNS species (Piesens et al., 2011; Supré et al., 2011). Conversely, the isolation of *Staph. aureus* and environmental bacteria in early lactating heifers substantially increases the risk of subclinical mastitis during first lactation (Compton et al., 2007a; Paradis et al., 2010; Piepers et al., 2010).

Effect on Future Milk Production. As mammary growth in heifers continues through lactation (Tucker, 1987), the presence of IMI before calving and during early lactation may disturb this process, resulting in suboptimal production during first lactation. Indeed, heifers with low first test-day SCC produce more milk during first lactation compared with heifers with elevated SCC in early lactation (Coffey et al., 1986; De VliegHER et al., 2005b). Intramammary infections due to CNS in heifers in early lactation had no negative effect on average milk production during early to mid lactation (Kirk et al., 1996). Later, Compton et al. (2007a) reported that even milk yield at first test-day and average daily milk yield over the entire lactation were higher in heifers with CNS IMI postpartum than in heifers with no pathogens isolated. More recently, a study specifically designed to estimate the pathogen-specific effect of IMI in early lactation heifers on future production substantiated the latter: CNS-infected heifers out-produced noninfected herd mates (Piepers et al., 2010). This finding was explained, to some extent, by the fact that heifers with CNS IMI in early lactation were less likely to develop CM during first lactation and were therefore protected from the associated milk losses compared with noninfected heifers. An alternate explanation is that heifers with a higher genetic potential for milk yield are more susceptible to IMI. Further research is needed to pinpoint the full explanation. As expected, heifers with IMI at calving caused by major pathogens produced substantially less milk over first lactation than noninfected heifers (Piepers et al., 2010). A recent study reported that mean test-day milk yield was not different between groups of heifers that were either culture-negative or culture-positive for *Staph. aureus* or CNS in the first month of lactation (Paradis et al., 2010). However, also in that study, CNS-infected heifers numerically out-produced the noninfected heifers (28.8 kg vs. 28.0 kg of milk/d). The authors concluded that not finding a significant difference might be the result of the small number of observations included in the study (Paradis et al., 2010).

Effect on Longevity. Heifers with an elevated SCC in early lactation are more likely to be culled (De VliegHER et al., 2005a), probably due to the association with high subsequent SCC and lower milk yield. Isolation of major pathogens within the first days after freshening also substantially increases the risk of removal from the herd during first lactation (Compton et al., 2007a).

Economic Cost. The average cost of subclinical heifer mastitis has only been calculated once. Accounting for the decreased milk production, the higher risk for subclinical and clinical mastitis during lactation, and the elevated culling hazard, the cost for a farm with 20 heifers calving in a year was estimated at €626 (US\$860, as calculated in October 2011), ranging between €85 (5th percentile) and €1,657 (95th percentile; Huijps et al., 2009). The large variation in costs between farms indicates that room for investment in improved heifer mastitis management is likely present. Pathogen-specific costs of subclinical heifer mastitis, which are expected to exist, have not yet been calculated.

Clinical Heifer Mastitis

Severe CM in heifers may result in increased risk of culling and death. Depending on study design, such events might be underreported, resulting in an underestimation of the effects of heifer mastitis and a bias toward reporting outcomes for heifers with moderate CM that are more likely to survive.

Effect on Future Udder Health. The occurrence of CM in early lactation was associated with elevated SCC at the first test-day and within 1 mo after calving but not later than that (Myllys and Rautala, 1995). This agrees with the finding that diagnosis of CM in one or more quarters within the first 2 wk of lactation is associated with an increased risk of heifer having a SCC >200,000 cells/mL at the next test-day (at least 14 d after the diagnosis of CM) but not at later test-days (Compton et al., 2007a). In both studies, heifers that were treated for CM and control heifers that were free of CM at the beginning of the study had equally low SCC during the remainder of the first lactation, indicating a good bacteriological cure.

Effect on Future Milk Production. Reported milk yield losses in heifers with CM around calving vary from less than 1% (Myllys and Rautala, 1995; Barnouin and Chassagne, 2001) to 5% (Oltenacu and Ekesbo, 1994) over the lactation. Heifers with CM in the first week of lactation produced substantially less than nonmastitic heifers, with the greatest losses occurring when heifers developed CM in wk 6 (Hagnestam et al., 2007). Compton et al. (2007a) did not, however, find an association between the presence of CM in the first 14 DIM and future milk production. *Streptococcus uberis* was the predominant major pathogen in the latter study. Milk production in heifers was not adversely affected beyond 1 wk after diagnosis (2.5 kg/d decrease) by CM caused by *Streptococcus* spp. occurring in early lactation (Gröhn et al., 2004). Clinical mastitis caused by CNS in early lactation resulted in a decrease in milk

yield of 3.2 kg/d in the week immediately following diagnosis, although this was not significant.

Effect on Longevity. Acute CM in the first weeks of lactation significantly increases the risk of culling (Beaudeau et al., 1995; Rajala-Schultz et al., 1999). Heifers treated for CM before calving or within the first 2 wk after calving are more likely to be culled because of mastitis reasons within 1 mo after treatment (Waage et al., 2000).

Economic Cost. Heifers experiencing a severe case of periparturient CM are at increased risk of being culled prematurely (Myllys and Rautala, 1995; Waage et al., 2000), which is associated with a significant cost (Stott and Kennedy, 1993). The exact economic cost of CM in heifers around calving has never, to our knowledge, been reported in the literature.

NONANTIBIOTIC STRATEGIES FOR PREVENTION AND CONTROL

Strategies to prevent and control mastitis in heifers should be based on risk or protective factors identified and tested through sound epidemiological research. Not all factors that have been identified as being associated with heifer mastitis can be implemented as prevention and control tools, either because they relate to animal-specific aspects that cannot be altered (e.g., trimester of gestation) or because they relate to factors that do not lend themselves to the development of specific intervention strategies (e.g., location of a herd, season). Still, knowledge that, for example, heifers in late gestation are more likely to get infected, should stimulate farmers to improve housing and comfort of this group of animals.

Housing, Hygiene, and Management

Group housing of preweaned calves and a high prevalence (>6% of all IMI) of coagulase-positive staphylococci (*Staph. aureus*) in the lactating herd did not translate into a high prevalence of mastitis due to these staphylococci at calving (Roberson et al., 1994a). This may indicate that infected udders of adult cows are not the reservoir of *Staph. aureus* for mastitis in heifers at first calving, although it conflicts with another study reporting that the presence of *Staph. aureus* in a herd increased the risk of *Staph. aureus* mastitis in the heifers (Bassel et al., 2003). It also conflicts with the fact that heifers raised in herds with a higher bulk milk SCC (BMSCC) were more likely to have subclinical mastitis caused by contagious pathogens in early lactation (Piepers et al., 2011). The incidence of CM in heifers is positively associated with that in cows when the 2 groups are co-managed in a pasture-based

systems (Parker et al., 2007b). Waage et al. (1998) reported the same finding: herds with a higher incidence of mastitis in cows or an elevated BMSCC also have higher incidence of heifer mastitis. Further studies using strain-typing will have to be conducted to elucidate whether or not primigravid heifers can act as *Staph. aureus* carriers, introducing this pathogen into the lactating herd, or whether heifers become infected after calving when being milked together with *Staph. aureus*-shedding lactating cows. We hypothesize that both are possible. Regular sampling of heifers at calving should help in detecting *Staph. aureus* shedders, which should be followed by appropriate action such as segregation, immediate antibiotic treatment, and follow-up of treatment results.

Poor hygiene of the calving area is, not surprisingly, associated with an increased prevalence of elevated SCC in heifers (De Vliegher et al., 2004b) and higher odds of being infected with environmental mastitis pathogens shortly after parturition (Piepers et al., 2011). Heifers with dirty udders also have a higher risk of mastitis (Compton et al., 2007b), and managing heifers in the same pasture areas as cows increases risk of CM as well (Parker et al., 2007b). Heifers with teats closer to the ground were more likely to have dirty teats and, as a potential consequence, had an increased risk of subclinical mastitis (Compton et al., 2007b). Having sawdust or shavings in the calving pen was related to poor udder health in heifers (Nyman et al., 2009). Moving heifers from the calving pen ≥ 2 d after calving, milking heifers at the calving site instead of in the parlor, and rinsing, cleaning, or disinfecting milking units before a heifer was milked also increased the odds of udder health problems in heifers (Nyman et al., 2009). In particular, the last management practice, instead of being a risk factor, will likely be the result of a response to udder health problems in heifers, and can therefore be seen as a cause-effect reversal.

Horn flies (*Haematobia irritans*) have been shown to transmit *Staph. aureus* to heifers (Owens et al., 1998; Roberson et al., 1998). Herds using some form of fly control had a lower percentage of heifers with mastitis than those without fly control (Nickerson et al., 1995), and heifers raised in herds with ineffective fly control were more likely to be infected with contagious mastitis pathogens in early lactation (Piepers et al., 2011). Although the major reservoir of *Staph. aureus* is the infected udder of lactating heifers and cows, this bacterium also colonizes teat skin, vagina, muzzle, and other body sites, as well as bedding, feedstuffs, air, and equipment (Boddie et al., 1987; Roberson et al., 1994b, 1998). Scabs on teats are also potential sources of *Staph. aureus* (Owens et al., 1998), and heifers with teat skin colonized by *Staph. aureus* were 3.3 times more likely to

have an IMI with the same bacterium at calving than were noncolonized heifers (Roberson et al., 1994b).

Probably the first study to report a managerial risk factor concluded that *Streptococcus agalactiae* might be transferred to the udders of calves by sucking pen mates fed infected milk (Schalm, 1942). The resulting IMI could persist until freshening. To our knowledge, this risk factor has never been reported for other pathogens and from an udder health point of view there is little risk of feeding mastitic or high SCC milk to calves when they are maintained in individual pens (Barto et al., 1982). In addition, heifers fed mastitic milk as calves suffered no more udder problems than did their mates that received other liquid feed (Kesler, 1981; Roberson et al., 1994a). Feeding high SCC or CM milk to calves should, however, not be promoted, because it is an important factor in within-herd spread of *Mycobacterium avium* ssp. *paratuberculosis* (Barkema et al., 2009).

Teat disinfection before calving was associated with a decreased risk of calving with IMI due to environmental pathogens (Bassel et al., 2003). It is also a management option when *Strep. uberis* is causing heifer mastitis because teat-end contamination with *Strep. uberis* was substantially lower in sprayed heifers compared with control heifers (Lopez-Benavides et al., 2009). Additionally, the prevalence of *Strep. uberis* IMI was significantly lower in the sprayed (3.5% of quarters) versus the control (7.4%) heifers in the first week after calving, and sprayed heifers tended to have a lower incidence of clinical *Strep. uberis* mastitis compared with control heifers. A beneficial effect of the use of a barrier teat dip before calving against environmental pathogens was not found (Edinger et al., 2000). Application of a teat sealer before calving reduces the prevalence of both postpartum subclinical mastitis and the incidence of pathogen-associated CM during the same period (Parker et al., 2007a, 2008; McDougall et al., 2008). It is believed that prevention of ingress of bacteria over the peripartum period is responsible for the observed efficacy of teat sealants.

Clinical heifer mastitis occurred more frequently in herds with a high milk production (>7,000 kg/yr), a low BMSCC, high treatment incidence, calculated optimal diet, and feeding ample dietary cereals (Myllys and Rautala, 1995). Another study reported similar findings: an increased risk of CM in heifers was seen with an increase in the incidence of CM in the herd, a decrease in the BMSCC, and an increase in the mean herd milk yield. Region and calving season were also significant variables (Waage et al., 1998).

Nutrition

In general, nutritional and dietary factors that have been linked to mastitis in the mature dairy cow can be

associated with mastitis in the first-lactation cow as well (Heinrichs et al., 2009). Heifers undergoing excessive body condition loss and those with elevated BHBA concentrations are at high risk of udder edema, which in turn is associated with increased risk of CM (Compton et al., 2007b). Thus, strategies to minimize loss of body condition and excessive mobilization of body tissue would appear to be a rational way of reducing the risk of heifer mastitis. Treatment with ionophores (antibiotics originally developed as coccidiostats for poultry, used as growth-enhancing feed additives for cattle, e.g., monensin) reduced the risk of CM in cows (McDougall et al., 2004; Duffield et al., 2008), whereas the use of ionophores in end-term heifers resulted in higher BCS at calving and reduced BHBA and NEFA concentrations, but not in a lower prevalence of subclinical mastitis at calving or CM incidence (McDougall et al., 2008). Feeding hay or silage, sugar-beet pulp, or corn silage before calving has been shown to increase the risk of mastitis (Waage et al., 1998; Nyman et al., 2009), although explanations for these findings are not obvious and possibly reflect certain management styles rather than actual associations between nutrition and mastitis.

Selenium and vitamin E enhance phagocytic activity and have been associated with a decreased CM risk (Weiss et al., 1990, 1997; Hogan et al., 1993; Barkema et al., 1998a). A large study, however, could not find any beneficial effect of treating cows and heifers parenterally before calving with vitamin E on the incidence of, among other diseases, CM (LeBlanc et al., 2002). Adverse results for udder health in nondeficient cows have even been reported (Bouwstra et al., 2010), indicating that usage should be well monitored and based on proven deficiencies, in heifers and cows. Moreover, differences between countries and regions (differences in soil, grain, silage, and so on) should be taken into account when advising on supplementation of vitamins, minerals, and trace elements. Selenium supplementation of heifers 1 mo before calving increased blood glutathione peroxidase activity, slightly reduced the prevalence of IMI, and lowered SCC at the time of calving in pastured first-lactation heifers, regardless of the selenium source (e.g., injectable barium selenate or Se yeast; Ceballos-Marquez et al., 2010). It did not, however, affect the odds of new IMI or new CM, nor did it influence SCC during the balance of the first month of lactation (Ceballos-Marquez et al., 2010). Supplementation of minerals and vitamins was associated with a higher viability of blood and milk polymorphonuclear neutrophils (key cells in the innate immune defense of the udder) around calving in heifers (Piepers et al., 2009b), although the relation with udder health still needs to be confirmed.

Copper has antioxidant functions and could reduce CM in heifers (Heinrichs et al., 2009). Zinc is implicated in maintaining the epithelial barriers to infection, but reports vary as to its role in udder health (Heinrichs et al., 2009). Vitamin A and β -carotene aid in maintaining the health of mucosal surfaces, and the latter may also have antioxidant properties. Vitamin and mineral requirements of dairy heifers are generally influenced by growth rate and body weight relative to mature size, although little specific data are available.

From a management standpoint, heifer rations should be supplemented where necessary, and a prefresh heifer diet is critical to ensure that first-lactation animals have adequate stores of minerals and vitamins in accordance with NRC guidelines (Heinrichs et al., 2009).

Vaccination

Successful immunization of heifers (and cows) against mastitis through vaccination could become a cornerstone in combating the disease. Still, vaccination needs to not only be efficient in reducing the risk of infection and in reducing clinical symptoms and shedding, but it should also be easily implementable in the daily routine and economically viable.

Vaccination of heifers was successful in reducing the incidence of *Staph. aureus* mastitis in one study (Giraud et al., 1997) but was not successful in another (Tenhagen et al., 2001). Recent data suggest that 2 doses of Lysigin (Boehringer Ingelheim Vetmedica Inc., St. Joseph, MO) during lactation did not reduce the incidence of new *Staph. aureus* or CNS mastitis cases (Middleton et al., 2009). A lack of vaccine-induced opsonizing antibodies in milk to facilitate phagocytosis and clearance of *Staph. aureus* from the udder was pinpointed as the reason. In contrast, heifers vaccinated with the same vaccine at 6 mo of age followed by a booster 2 wk later and subsequent vaccinations every 6 mo until calving resulted in a 45% reduction in both new *Staph. aureus* IMI during pregnancy and new *Staph. aureus* IMI at calving relative to control animals (Nickerson et al., 1999). In addition, vaccinates had a 30% reduction in new CNS IMI that became chronic and a 31% reduction in new CNS IMI at calving relative to controls, demonstrating that early vaccination followed by additional immunizations could be a control measure to combat staphylococcal mastitis in dairy heifers (Nickerson et al., 1999). Recently, a new vaccine containing an extracellular component from *Staph. aureus*, the so-called slime-associated antigenic complex, was introduced on the European market and elsewhere (Prenafeta et al., 2010). Recent data using this vaccine report higher cure rates and lower incidence of sub-

clinical and clinical mastitis due to CNS in vaccinated versus control heifers (Noguera et al., 2011).

Host Factors

Older heifers are more likely to have an elevated SCC in early lactation (De Vliegher et al., 2004b) and IMI with *Staph. aureus* and environmental pathogens (Bassel et al., 2003). This could be a reflection of, for example, a metabolic status (older heifers tend to be heavier, also affecting ease of calving) or merely the fact they have been at risk of being infected for a longer period.

The incidence of reproductive disorders such as retained placenta, endometritis, pyometra, dystocia, and twin births was positively associated with the incidence of CM during the periparturient period on Swedish dairy farms (Svensson et al., 2006). The authors hypothesize that the association between reproductive disorders and CM could be due to a common factor affecting both disease complexes.

Open teat ends (due to premature loss of the keratin plug as detected by clinical examination) before calving are a risk factor for heifer mastitis at calving as well. In a German study, teat canals of heifers did not open until 80 d before calving, whereas more than half of the teat canals were open at 60 d before calving (Krömker and Friedrich, 2009). In total, 77% of IMI present at calving were actually established before calving, and the incidence of CM during first lactation was influenced largely by the duration of infection before calving and the mastitis pathogen involved. Eighty-five percent of all CM cases during the first 100 DIM and 74% of all CM cases in the first lactation were found in quarters that had an open teat canal at 10 d before calving. Although these are very important findings, it is still not clear what proportion of heifer mastitis cases can be attributed to open teat canals before calving. We strongly suggest, therefore, that this should be included in studies on heifers. Additionally, there is a paucity of knowledge on the factors that determine whether and when teat canals open before calving.

Udder edema, teat edema, blood in the milk, and milk leakage at time of calving are significant risk factors for CM occurring during the first weeks after calving. Teat edema, blood in the milk, and milk leakage also increase the odds of clinical *Staph. aureus* mastitis (Waage et al., 1998, 2001). Precalving milking can reduce the risk of IMI and of CM, possible by reducing udder edema or physically removing bacteria from the teat canal (Bowers et al., 2006; Daniels et al., 2007).

Holstein-Friesians are at higher risk of mastitis than other breeds (Myllys and Rautala, 1995; Compton et

al., 2007b). The difference in susceptibility to mastitis between breeds could be the result of the difference in the prevalence of specific genes, although this should further be investigated. Differences in innate immunity among heifers may affect the incidence of heifer mastitis as it has been shown that heifers without IMI precalving had higher expression levels of β -defensins and molecule possessing ankyrin-repeat (a component of the sensory arm of the innate immune system) than heifers that did develop IMI (Compton et al., 2009).

Knowledge of the role of specific genes in the etiology of heifer mastitis is still limited. Recent work scrutinized polymorphisms in the *CXCR1* gene of heifers, encoding the homonymous receptor for IL-8 on neutrophils (J. Verbeke, S. Piepers, L. Peelman, M. Van Poucke, and S. De Vlieghe; Ghent University, Merelbeke, Belgium; unpublished data). Binding of IL-8 causes migration from blood to milk, activation, and prolonged survival of PMNL, a crucial process in the innate immune defense against invading mastitis pathogens. The *CXCR1* genotype was not associated with quarter milk or composite SCC during first lactation, but one of the polymorphisms was related to IMI status at calving. These results indicate that genetic selection could offer possibilities for prevention and control of heifer mastitis in a sustainable way.

Miscellaneous Risk Factors

Herd, season, trimester of pregnancy, and location are associated with the presence of heifer mastitis (Fox et al., 1995; Hallberg et al., 1995). Heifers are most susceptible for mastitis at the end of gestation, which is most likely associated with the rapid development of the udder. Fall appears to be the season in which most heifers start their lactation free of IMI (Fox et al., 1995; Hallberg et al., 1995; De Vlieghe et al., 2004b).

PREPARTUM ANTIMICROBIAL THERAPY

In general, prepartum treatment of heifers with lactating or dry cow products results in bacteriological cure of infected quarters (Oliver et al., 1997; Nickerson, 2009). However, lower SCC and higher milk yield over the first lactation, as reported by Sampimon et al. (2009a), are not always seen (Borm et al., 2006), indicating that potential herd-specific factors yet to be identified are playing a role. The studies that report a positive effect on milk yield or a decreased incidence of clinical mastitis had a high prevalence of major pathogen IMI (Kreiger et al., 2007; Bryan and Taylor, 2009; Sampimon et al., 2009a), whereas studies not finding an effect found a high prevalence of prepartum IMI with minor pathogens such as CNS (Borm et al.,

2006; Parker et al., 2008). Another important reason why prepartum treatment of heifers is successful in one herd and not in another is that treatment of subclinical mastitis is generally more effective in well-managed than in poorly managed herds (where cured cows are more likely to become re-infected; Barlow et al., 2009). Therefore, although the authors have personally experienced the value of prepartum antimicrobial treatment in herds with a heifer mastitis problem when major udder pathogens were involved, blanket prepartum treatment of heifers should never be a general recommendation, because it does not comply with the need for more prudent use of antimicrobials. Additionally, farmers and herd managers should be cautioned that treatment of bred heifers constitutes extra-label drug use and should be carried out under the supervision of the herd veterinarian and within the context of a valid veterinary-client-patient relationship (Nickerson, 2009).

From a practical standpoint, the administration of antibiotics by a parenteral route would be preferred over intramammary infusion with lactating or dry cow products. However, it has been questioned whether subcutaneous or intramuscular injection of drugs can cure IMI in bred heifers because insufficient concentrations of antibiotic might reach the mammary gland (Nickerson, 2009). A recent study indicates that penethamate hydroiodide injected intramuscularly in heifers before calving results in levels of penicillin G in udder tissue and mammary secretions substantially higher than the MIC₉₀ of pathogens associated with heifer mastitis (Passchyn et al., 2010). This confirms the fact that some antibiotics (notably penethamate and some macrolides) can reach the udder in sufficient concentrations to exceed the MIC of the bacteria involved in heifer mastitis (Ziv, 1980). Whether the findings from Passchyn et al. (2010) also have clinical relevance should be substantiated with data from clinical trials that study whether prepartum treatment with penethamate (or other injectable antibiotics) reduces the risk of heifer mastitis and whether udder health and milk yield benefit from this treatment in the long term. To our knowledge, only one peer-reviewed publication is available on systemic treatment of heifers before calving (Parker et al., 2008). Treatment on average 27 d before the planned start of the seasonal calving period with an injectable antibiotic (3 intramuscular injections of 5 g of tylosin antibiotic at 24-h intervals) neither increased cure of precalving infection nor reduced the risk of new IMI. Treatment of heifers at calving (not before) in a herd with a high prevalence of *Staph. aureus* with penethamate hydroiodide prevented IMI during the first week after calving and resulted in a significant increase in milk yield (Kreiger et al., 2007). Another study conducted in New Zealand (Bryan and Taylor, 2009) reported that

preventative treatment of heifers immediately following calving (not before) with 15 million IU of micronized procaine penicillin parenterally reduced the odds of having CM within the first week of lactation by over half, reduced the odds of having mastitis within the first 100 DIM by just under half, and increased the median days to CM.

AREAS OF FUTURE RESEARCH

Important progress has been made in the last decades in our knowledge of heifer mastitis. However, prevention and control of heifer mastitis is still difficult because the pathogenesis and epidemiology of the disease remain largely unknown. Therefore, the implementation of heifer-specific practices in udder health programs should be accompanied by research efforts to further complete and refine them. In the following, the most important research questions that should be examined are highlighted.

Although the heritability of CM and subclinical mastitis is relatively low (e.g., De Haas et al., 2002), it has been incorporated within the breeding objectives of several dairy industries around the world. A remaining question is whether differences exist among parities in the estimates of breeding value, potentially due to gene-environment interactions. As discussed above, heifers differ from multiparous cows in several ways. Thus, it is feasible that heritability of clinical and subclinical mastitis may differ among parities due to different mechanisms among the parities. Additionally, dairy bull selection programs have moved toward genomic selection (Hayes et al., 2009). However, knowledge of genes directly and indirectly coding for udder health, particularly CM, is limited. Large phenotypic databases that include pathogen identification of clinical and subclinical mastitis cases are needed to evaluate the association of genes and genetic markers with udder health. The genetic markers will probably differ between heifers and older cows and between different housing and management systems.

By definition, heifers are entering lactation for the first time. This first transition from a nonlactating to lactating animal may increase the risk of mastitis. For example, heifers have a higher incidence of udder edema (Greenhalgh and Gardner, 1958; Emery et al., 1969; Mitchell et al., 1976), which is a risk factor for clinical mastitis (Compton et al., 2007b). Additionally, around calving, concentrations of NEFA, BHBA, and other metabolites that are associated with udder health (Nyman et al., 2008) are different in first-calving heifers compared with older cows. Trying to understand differences in metabolic adaptation of heifers when

entering the milking herd compared with older cows should therefore be the focus of more research.

The prevalence of IMI late in gestation and at calving is high. However, it is not known when and how heifers get infected prepartum and what the source of the infections is (e.g., skin, older cows, milk, environment). This is particularly important when studying risk factors for pathogen-specific IMI. When studying the transmission of bacteria, in addition to determining the species, strains have to be distinguished using molecular techniques. Sampling of young stock should start at a young age to learn when they become infected and whether the same bacterial strains are able to persist until calving. Infection sources could, at the same time, be traced by sampling other parts of the body and the heifers' environment.

The significance of CNS isolation in both the udder and the teat canal is still a topic of debate. Matthews et al. (1990) found that a naturally occurring IMI with CNS had a considerable protective effect against intramammary challenge with *Staph. aureus* and suppressed colonization by other mastitis-causing pathogens (Matthews et al., 1991). Other studies regarding the protective effect of minor pathogens (CNS, *Corynebacterium* spp., and micrococci) against the development of infections with a major organism were not conclusive, however, as some showed a protective effect (Linde et al., 1980; Brooks and Barnum, 1984; Lam et al., 1997) and others did not (Doane et al., 1987; Hogan et al., 1988). Studying these microorganisms as one group rather than at the species level could partly explain the disagreement between studies. Additionally, it may very well be that significant differences exist between strains of the same species, as De Vliegher et al. (2004c) found in vitro for *Staphylococcus chromogenes*. The relation between CNS IMI and milk production should be investigated further, in both heifers and multiparous cows.

Significant regional and international differences exist in how heifers are reared and managed. In larger dairy farms, as often found in Australia, New Zealand, and some parts of the United States, heifers are removed from the milking herd (farm/barn) and managed as separate groups. This may lead to significant difference in nutrition, exposure to pathogens, and other disease processes. There is a need to understand these risk factors.

Within farming systems, heifers are generally expected to adapt to the environment of the older cows. For example, stall size (for housed cattle) may be a risk factor for mastitis, and stall sizes optimized for mature cattle may not be optimized for heifers. Similarly, milking machines optimized for multiparous cows in terms of shell length, liners, and vacuum may not be optimal for heifers with their shorter teat lengths.

PRACTICAL APPROACH TO PREVENTION AND CONTROL OF HEIFER MASTITIS

In contrast to multiparous cows, no mastitis prevention and control program has been designed or verified for heifers (NMC, 2011). An integrated strategy to prevent and control this disease should include goal setting, assessment of the current farm systems, application of appropriate farm-specific interventions, and monitoring of outcomes (McDougall et al., 2009).

We consider a herd to have a heifer mastitis problem if >15% of heifers have CM around calving or if >15% of all heifers have a first test-day SCC (measured between 10 and 35 DIM) >150,000 cells/mL (De VliegHER et al., 2001). Herds exceeding these thresholds should be investigated and prevention and control measures optimized. A herd-level surveillance program using culture of milk samples should be put in place.

Of course, target prevalence and incidence rates vary across farm systems, but farm-specific goals should be applied on every farm. Heifer mastitis is a multifactorial disease, meaning that all aspects related to this disease should be optimized. Control strategies are aimed at reducing the incidence of heifer mastitis. The specific set of control and treatment practices should be customized to each farm. If necessary, eliminating existing infections could be achieved using prepartum antibiotic treatment on a tactical basis.

Farm-specific interventions that should be in place on any farm are as follows (10-point program to prevent and control heifer mastitis):

1. Improve general udder health management at the farm level to decrease the pressure of infection with udder pathogens from older cows to heifers;
2. Control for cross-suckling in calves and young stock;
3. Implement an effective and efficient fly control system;
4. Keep young and primigravid heifers in a clean and hygienic environment and separate from multiparous animals—provide as much attention to this group of animals related to hygiene and cleanliness as is spent on lactating animals;
5. Avoid any nutritional deficiency—monitor vitamin E and selenium levels when any doubt exists, especially in relation to CM; zinc, copper, and vitamin A play a role as well and could be checked;
6. Minimize the risk of negative energy balance before and after calving through appropriate transition feeding systems;

7. Reduce the incidence of udder edema through optimized peripartum management;
8. Minimize stress around calving (e.g., by not moving heifers to the calving pen when already in labor) and minimize incidence of dystocia and peripartum disease;
9. Consider use of internal teat sealants prepartum where a high risk of environmental mastitis exists in the peripartum period;
10. Use prepartum antibiotic treatment in heifers under certain conditions only:
 - a. under the supervision of the herd veterinarian, within the context of a valid veterinary/client/patient relationship;
 - b. after quantification of the problem and identification of major pathogens (not CNS) as the cause through culturing;
 - c. choice of the antibiotics should be based on antimicrobial susceptibility testing;
 - d. testing for residues before every milk delivery;
 - e. upgrading of management at the same time—discontinue treatment as soon as new management strategies become effective.

CONCLUSIONS

Heifer mastitis threatens production and udder health in the first lactation typically when major pathogens are involved, and the animals may pose a risk to non-infected (lactating) herd mates if they have contagious mastitis. Prevention of mastitis in late gestation and periparturient heifers is currently based on optimizing hygiene, feeding and fly control, avoidance of cross-suckling in young stock, and improving animal comfort at parturition. Still, the pathogenesis of the disease remains largely unknown and more pathogen-specific risk factors should be identified to optimize current prevention programs. In general, CNS have been identified as the predominant cause of IMI and subclinical mastitis in heifers around parturition, whereas *Staph. aureus* and environmental pathogens cause a minority of the cases of IMI. Clinical heifer mastitis is typically caused by the major pathogens. The role of CNS in heifer mastitis is far from clear, and longitudinal studies that determine IMI status and measure inflammation parameters are needed. Prepartum antibiotic treatment can be implemented only as a short-term measure to assist in the control of a significant heifer mastitis problem under supervision of the herd veterinarian. Positive long-lasting effects on udder health and milk yield do not always occur, ruling out universal recommendation of this practice. When CNS are the major cause of IMI

around calving, productivity is not affected, making prepartum treatment unwarranted.

REFERENCES

- Aarestrup, F. M., and N. E. Jensen. 1997. Prevalence and duration of intramammary infection in Danish heifers during the prepartum period. *J. Dairy Sci.* 80:307–312.
- Andersen, S., I. R. Dohoo, R. Olde Riekerink, and H. Stryhn. 2010. Diagnosing intramammary infections: Evaluating expert opinions on the definition of intramammary infection using conjoint analysis. *J. Dairy Sci.* 93:2966–2975.
- Barkema, H. W., H. A. Deluyker, Y. H. Schukken, and T. J. G. M. Lam. 1999. Quarter-milk somatic cell count at calving and at the first six milkings after calving. *Prev. Vet. Med.* 38:1–9.
- Barkema, H. W., M. J. Green, A. J. Bradley, and R. N. Zadoks. 2009. Invited review: The role of contagious disease in udder health. *J. Dairy Sci.* 92:4717–4729.
- Barkema, H. W., Y. H. Schukken, T. J. G. M. Lam, M. L. Beiboer, G. Benedictus, and A. Brand. 1998a. Management practices associated with low, medium, and high somatic cell counts in bulk milk. *J. Dairy Sci.* 81:1917–1927.
- Barkema, H. W., Y. H. Schukken, T. J. G. M. Lam, M. L. Beiboer, H. Wilmink, G. Benedictus, and A. Brand. 1998b. Incidence of clinical mastitis in dairy herds grouped in three categories by bulk milk somatic cell counts. *J. Dairy Sci.* 81:411–419.
- Barkema, H. W., Y. H. Schukken, and R. N. Zadoks. 2006. Invited review: The role of cow, pathogen, and treatment regimen in the therapeutic success of bovine *Staphylococcus aureus* mastitis. *J. Dairy Sci.* 89:1877–1895.
- Barlow, J. W., L. J. White, R. N. Zadoks, and Y. H. Schukken. 2009. A mathematical model demonstrating indirect and overall effects of lactation therapy targeting subclinical mastitis in dairy herds. *Prev. Vet. Med.* 90:31–42.
- Barnouin, J., and M. Chassagne. 2001. Predictive variables for the occurrence of early clinical mastitis in primiparous Holstein cows under field conditions in France. *Can. Vet. J.* 42:47–53.
- Barto, P. B., L. J. Bush, and G. D. Adams. 1982. Feeding milk containing *Staphylococcus aureus* to calves. *J. Dairy Sci.* 65:271–274.
- Bassel, L., D. Kelton, A. Godkin, K. Leslie, and K. Lissemore. 2003. Risk factors for intramammary infection at first calving in Ontario dairy heifers. Pages 177–178 in *Proc. 36th Ann. Conf. Am. Assoc. Bovine Pract.*, Columbus, OH. Am. Assoc. Bovine Pract., Auburn, AL.
- Beaudeau, F., V. Ducrocq, C. Fourichon, and H. Seegers. 1995. Effect of disease on length of productive life of French Holstein dairy cows assessed by survival analysis. *J. Dairy Sci.* 78:103–117.
- Biddle, M. K., L. K. Fox, D. D. Hancock, C. T. Gaskins, and M. A. Evans. 2004. Effects of storage time and thawing methods on the recovery of *Mycoplasma* species in milk samples from cows with intramammary infections. *J. Dairy Sci.* 87:933–936.
- Boddie, R. L., S. C. Nickerson, W. E. Owens, and J. L. Watts. 1987. Udder microflora in non-lactating heifers. *Agric. Pract.* 8:22–25.
- Borm, A. A., L. K. Fox, K. E. Leslie, J. S. Hogan, S. M. Andrew, S. P. Oliver, Y. H. Schukken, D. D. Hancock, C. T. Gaskins, W. E. Owens, and C. Norman. 2006. Effects of prepartum intramammary antibiotic therapy on udder health, milk production, and reproductive performance in dairy heifers. *J. Dairy Sci.* 89:2090–2098.
- Bouwstra, R. J., M. Nielen, J. A. Stegeman, P. Dobbelaar, J. R. Newbold, E. H. J. M. Jansen, and T. van Werven. 2010. Vitamin E supplementation during the dry period in dairy cattle. Part I: Adverse effect on incidence of mastitis postpartum in a double-blind randomized field trial. *J. Dairy Sci.* 93:5684–5695.
- Bowers, S., S. Gandy, K. Graves, S. Eicher, and S. Willard. 2006. Effects of prepartum milking on postpartum reproduction, udder health and production performance in first-calf dairy heifers. *J. Dairy Res.* 73:257–263.
- Braem, G., S. De Vliegher, K. Supré, F. Haesebrouck, F. Leroy, and L. De Vuyst. 2011. (GTG)₅-PCR fingerprinting for the classification and identification of coagulase-negative *Staphylococcus* species from bovine milk and teat apices: A comparison of type strains and field isolates. *Vet. Microbiol.* 147:67–74.
- Brooks, B. W., and B. A. Barnum. 1984. The susceptibility of bovine udder quarters colonized with *Corynebacterium bovis* to experimental infection with *Staphylococcus aureus* or *Streptococcus agalactiae*. *Can. J. Comp. Med.* 48:146–150.
- Bryan, M., and K. Taylor. 2009. Periparturient use of parenteral micronised procaine penicillin to reduce the risk of clinical mastitis in heifers after calving. *Vet. Microbiol.* 134:143–149.
- Ceballos-Marquez, A., H. W. Barkema, H. Stryhn, J. J. Wichtel, J. Neumann, A. Mella, J. Kruze, M. S. Espindola, and F. Wittwer. 2010. The effect of selenium supplementation before calving on early-lactation udder health in pastured dairy heifers. *J. Dairy Sci.* 93:4602–4612.
- Coffey, E. M., W. E. Vinson, and R. E. Pearson. 1986. Somatic cell counts and infection rates for cows of varying somatic cell count in initial test of first lactation. *J. Dairy Sci.* 69:552–555.
- Compton, C. W., R. T. Cursons, C. M. Barnett, and S. McDougall. 2009. Expression of innate resistance factors in mammary secretion from periparturient dairy heifers and their association with subsequent infection status. *Vet. Immunol. Immunopathol.* 127:357–364.
- Compton, C. W. R., C. Heuer, K. I. Parker, and S. McDougall. 2007a. Epidemiology of mastitis in pasture-grazed peripartum dairy heifers and its effects on productivity. *J. Dairy Sci.* 90:4157–4170.
- Compton, C. W. R., C. Heuer, K. I. Parker, and S. McDougall. 2007b. Risk factors for peripartum mastitis in pasture-grazed dairy heifers. *J. Dairy Sci.* 90:4171–4180.
- Cook, W. F., E. A. Fiez, and L. K. Fox. 1992. Mastitis in first lactation southwest Idaho dairy cows. *J. Dairy Sci.* 75(Suppl. 1):158. (Abstr.)
- da Costa, E. O., P. A. Melville, and A. R. Ribeiro. 1996. Prevalence of intramammary infections in primigravid Brazilian dairy heifers. *Prev. Vet. Med.* 29:151–155.
- Daniels, K. J., S. S. Donkin, S. D. Eicher, E. A. Pajor, and M. M. Schutz. 2007. Prepartum milking of heifers influences future production and health. *J. Dairy Sci.* 90:2293–2301.
- De Haas, Y., H. W. Barkema, and R. F. Veerkamp. 2002. Genetic parameters of pathogen-specific incidence of clinical mastitis in dairy cows. *Anim. Sci.* 74:233–242.
- De Vliegher, S., H. W. Barkema, G. Opsomer, A. de Kruif, and L. Duchateau. 2005a. Association between somatic cell count in early lactation and culling of dairy heifers using Cox frailty models. *J. Dairy Sci.* 88:560–568.
- De Vliegher, S., H. W. Barkema, H. Stryhn, G. Opsomer, and A. de Kruif. 2004a. Impact in dairy heifers of early lactation somatic cell count on somatic cell counts during the first lactation. *J. Dairy Sci.* 87:3672–3682.
- De Vliegher, S., H. W. Barkema, H. Stryhn, G. Opsomer, and A. de Kruif. 2005b. Impact of early lactation somatic cell count in heifers on milk yield over the first lactation. *J. Dairy Sci.* 88:938–947.
- De Vliegher, S., H. Laevens, H. W. Barkema, I. Dohoo, H. Stryhn, G. Opsomer, and A. de Kruif. 2004b. Management practices and heifer characteristics associated with early lactation somatic cell counts of dairy heifers in Belgium. *J. Dairy Sci.* 87:937–947.
- De Vliegher, S., H. Laevens, L. A. Devriese, G. Opsomer, J. L. M. Leroy, H. W. Barkema, and A. de Kruif. 2003. Prepartum teat apex colonization with *Staphylococcus chromogenes* in dairy heifers is associated with low somatic cell counts in early lactation. *Vet. Microbiol.* 92:245–252.
- De Vliegher, S., H. Laevens, G. Opsomer, E. De Muëlenaere, and A. de Kruif. 2001. Somatic cell counts in dairy heifers during early lactation. *Vlaams Diergeneesk. Tijdschr.* 70:212–215.
- De Vliegher, S., G. Opsomer, A. Vanrolleghem, L. A. Devriese, O. C. Sampimon, J. Sol, H. W. Barkema, and F. Haesebrouck. 2004c. In vitro growth inhibition of major mastitis pathogens by *Staphylococcus chromogenes* originating from teat apices of dairy heifers. *Vet. Microbiol.* 101:215–221.
- De Vliegher, S., R. N. Zadoks, and H. W. Barkema. 2009. Heifer and CNS mastitis. *Vet. Microbiol.* 134:1–2.

- Doane, R. M., S. P. Oliver, R. D. Walker, and E. P. Shull. 1987. Experimental infection of lactating bovine mammary glands with *Streptococcus uberis* in quarters colonized by *Corynebacterium bovis*. *Am. J. Vet. Res.* 48:749–754.
- Dohoo, I. R. 1993. An evaluation of the validity of individual cow somatic cell counts from cows in early lactation. *Prev. Vet. Med.* 16:103–110.
- Duffield, T. F., A. R. Rabiee, and I. J. Lean. 2008. A meta-analysis of the impact of monensin in lactating dairy cattle. Part 3. Health and reproduction. *J. Dairy Sci.* 91:2328–2341.
- Edinger, D., B.-A. Tenhagen, P. Kalbe, G. Klünder, B. Baumgärtner, and W. Heuwieser. 2000. Effect of teat dipping with a germicide barrier teat dip in late gestation on intramammary infection and clinical mastitis during the first 5 d post-partum in primiparous cows. *J. Vet. Med. A* 47:463–468.
- Emery, R. S., H. D. Hafs, D. Armstrong, and W. W. Snyder. 1969. Prepartum grain feeding effects on milk production mammary edema and incidence of diseases. *J. Dairy Sci.* 52:345–351.
- Fox, L. K. 2009. Prevalence, incidence and risk factors of heifer mastitis. *Vet. Microbiol.* 134:82–88.
- Fox, L. K., S. T. Chester, J. W. Hallberg, S. C. Nickerson, J. W. Pankey, and L. D. Weaver. 1995. Survey of intramammary infections in dairy heifers at breeding age and first parturition. *J. Dairy Sci.* 78:1619–1628.
- Fox, L. K., J. H. Kirk, and A. Britten. 2005. *Mycoplasma* mastitis: A review of transmission and control. *J. Vet. Med. B Infect. Dis. Vet. Public Health* 52:153–160.
- Fox, L. K., F. J. Muller, M. L. Wedam, C. S. Schneider, and M. K. Biddle. 2008. Clinical *Mycoplasma bovis* mastitis in prepubertal heifers on 2 dairy herds. *Can. Vet. J.* 49:1110–1112.
- Giraud, J. A., A. Calzolari, H. Rampone, A. Rampone, A. T. Giraud, C. Bogni, A. Larriestra, and R. Nagel. 1997. Field trials of a vaccine against bovine mastitis. 1. Evaluation in heifers. *J. Dairy Sci.* 80:845–853.
- Greenhalgh, J. F. D., and K. E. Gardner. 1958. Effect of heavy concentrate feeding before calving upon lactation and mammary gland edema. *J. Dairy Sci.* 41:822–829.
- Gröhn, Y. T., D. J. Wilson, R. N. Gonzalez, J. A. Hertl, H. Schulte, G. Bennett, and Y. H. Schukken. 2004. Effect of pathogen-specific clinical mastitis on milk yield in dairy cows. *J. Dairy Sci.* 87:3358–3374.
- Hagnestam, C., U. Emanuelson, and B. Berglund. 2007. Yield losses associated with clinical mastitis occurring in different weeks of lactation. *J. Dairy Sci.* 90:2260–2270.
- Hallberg, J. W., K. J. Dame, S. T. Chester, and C. C. Miller. 1995. The visual appearance and somatic cell count of mammary secretions collected from primigravid heifers during gestation and early postpartum. *J. Dairy Sci.* 78:1629–1636.
- Hayes, B. J., P. J. Bowman, A. J. Chamberlain, and M. E. Goddard. 2009. Invited review: Genomic selection in dairy cattle: Progress and challenges. *J. Dairy Sci.* 92:433–443.
- Heinrichs, A. J., S. S. Costello, and C. M. Jones. 2009. Control of heifer mastitis by nutrition. *Vet. Microbiol.* 134:172–176.
- Hogan, J. S., K. L. Smith, D. A. Todhunter, and P. S. Schoenberger. 1988. Rate of environmental mastitis in quarters infected with *Corynebacterium bovis* and *Staphylococcus* species. *J. Dairy Sci.* 71:2520–2525.
- Hogan, J. S., W. P. Weiss, and K. L. Smith. 1993. Role of vitamin E and selenium in host defense against mastitis. *J. Dairy Sci.* 76:2795–2803.
- Huijps, K., S. De Vlieghe, T. Lam, and H. Hogeveen. 2009. Cost estimation of heifer mastitis in early lactation by stochastic modeling. *Vet. Microbiol.* 134:121–127.
- Kesler, E. M. 1981. Feeding mastitic milk to calves: Review. *J. Dairy Sci.* 64:719–723.
- Kirk, J. H., J. C. Wright, S. L. Berry, J. P. Reynolds, J. P. Maas, and A. Ahmadi. 1996. Relationship of milk culture status at calving with somatic cell counts and milk production of dairy heifers during early lactation on a Californian dairy. *Prev. Vet. Med.* 28:187–198.
- Kreiger, M., G. Friton, J. Hofer, K. Fuchs, and P. Winter. 2007. Effects of periparturient systemic treatment with penethamate hydriodide on udder health and milk yield of dairy heifers. *J. Dairy Res.* 74:392–398.
- Krömker, V., and J. Friedrich. 2009. Teat canal closure in non-lactating heifers and its association with udder health in the consecutive lactation. *Vet. Microbiol.* 134:100–105.
- Lam, T. J., Y. H. Schukken, J. H. van Vliet, F. J. Grommers, M. J. Tielen, and A. Brand. 1997. Effect of natural infection with minor pathogens on susceptibility to natural infection with major pathogens in the bovine mammary gland. *Am. J. Vet. Res.* 58:17–22.
- LeBlanc, S. J., T. F. Duffield, K. E. Leslie, K. G. Bateman, J. TenHag, J. S. Walton, and W. H. Johnson. 2002. The effect of prepartum injection of vitamin E on health in transition dairy cows. *J. Dairy Sci.* 85:1416–1426.
- Linde, C., O. Holmberg, and G. Astrom. 1980. The interference between coagulase-negative staphylococci and *Corynebacterium bovis* and the common udder pathogens in the lactating cow. *Nord. Vet. Med.* 32:552–558.
- Lopez-Benavides, M. G., J. H. Williamson, S. J. Lacy-Hulbert, and R. T. Cursons. 2009. Heifer teats sprayed in the dry period with an iodine teat sanitizer have reduced *Streptococcus uberis* teat-end contamination and less *Streptococcus uberis* intra-mammary infections at calving. *Vet. Microbiol.* 134:186–191.
- Lucy, M. C. 2001. Reproduction loss in high-producing dairy cattle: Where will it end? *J. Dairy Sci.* 84:1277–1293.
- Makovec, J. A., and P. L. Ruegg. 2003. Results of milk samples submitted for microbiological examination in Wisconsin from 1994 to 2001. *J. Dairy Sci.* 86:3466–3472.
- Matthews, K. R., R. J. Harmon, and B. E. Langlois. 1991. Effect of naturally occurring coagulase-negative staphylococci infections on new infections by mastitis pathogens in the bovine. *J. Dairy Sci.* 74:1855–1859.
- Matthews, K. R., R. J. Harmon, and B. E. Langlois. 1992. Prevalence of *Staphylococcus* species during the periparturient period in primiparous and multiparous cows. *J. Dairy Sci.* 75:1835–1839.
- Matthews, K. R., R. J. Harmon, and B. A. Smith. 1990. Protective effect of *Staphylococcus chromogenes* infection against *Staphylococcus aureus* infection in the lactating bovine mammary gland. *J. Dairy Sci.* 73:3457–3462.
- McDougall, S., K. E. Agnew, R. Cursons, X. X. Hou, and C. R. W. Compton. 2007a. Parenteral treatment of clinical mastitis with tylosin base or penethamate hydriodide in dairy cattle. *J. Dairy Sci.* 90:779–789.
- McDougall, S., D. G. Arthur, M. A. Bryan, J. J. Vermunt, and A. M. Weir. 2007b. Clinical and bacteriological response to treatment of clinical mastitis with one of three intramammary antibiotics. *N. Z. Vet. J.* 55:161–170.
- McDougall, S., K. I. Parker, C. Heuer, and C. W. R. Compton. 2009. A review of prevention and control of heifer mastitis via non-antibiotic strategies. *Vet. Microbiol.* 134:177–185.
- McDougall, S., K. I. Parker, A. M. Weir, and C. W. R. Compton. 2008. Effect of application of an external teat sealant and/or oral treatment with a monensin capsule pre-calving on the prevalence and incidence of subclinical and clinical mastitis in dairy heifers. *N. Z. Vet. J.* 56:120–129.
- McDougall, S., L. Young, and F. M. Aniss. 2004. Production and health of pasture-fed dairy cattle following oral treatment with the ionophore lasalocid. *J. Dairy Sci.* 87:2967–2976.
- Meaney, W. J. 1981. Mastitis levels in spring-calving dairy heifers. *Ir. Vet. J.* 35:205–209.
- Middleton, J. R., C. D. Luby, and D. S. Adams. 2009. Efficacy of vaccination against staphylococcal mastitis: A review and new data. *Vet. Microbiol.* 134:192–198.
- Middleton, J. R., L. L. Timms, R. Bader, J. Lakritz, C. D. Luby, and B. J. Steevens. 2005. Effect of prepartum intramammary treatment with pirlimycin hydrochloride on prevalence of early first-lactation mastitis in dairy heifers. *J. Am. Vet. Med. Assoc.* 227:1969–1974.
- Mitchell, R. G., R. E. Mather, W. H. Swallow, and H. A. Randy. 1976. Effects of a corticosteroid and diuretic agent on udder edema and milk-yield in dairy-cows. *J. Dairy Sci.* 59:109–112.

- Myllys, V. 1995. Staphylococci in heifer mastitis before and after parturition. *J. Dairy Res.* 62:51–60.
- Myllys, V., and H. Rautala. 1995. Characterization of clinical mastitis in primiparous heifers. *J. Dairy Sci.* 78:538–545.
- Nickerson, S. C. 2009. Control of heifer mastitis: Antimicrobial treatment—An overview. *Vet. Microbiol.* 134:128–135.
- Nickerson, S. C., and R. L. Boddie. 1994. Effect of naturally occurring coagulase-negative staphylococcal infections on experimental challenge with major mastitis pathogens. *J. Dairy Sci.* 77:2526–2536.
- Nickerson, S. C., W. E. Owens, and R. L. Boddie. 1995. Mastitis in dairy heifers: Initial studies on prevalence and control. *J. Dairy Sci.* 78:1607–1618.
- Nickerson, S. C., W. E. Owens, G. M. Tomita, and P. Widell. 1999. Vaccinating dairy heifers with a *Staphylococcus aureus* bacterin reduces mastitis at calving. *Large Anim. Pract.* 20:16–28.
- National Mastitis Council (NMC). 2011. Recommended mastitis control program. www.nmc-online.org/docs/NMCchecklistInt.pdf.
- Noguera, M., R. March, R. Guix, A. Prenafeta, and A. Foix. 2011. Evaluation of the efficacy of a new vaccine against bovine mastitis caused by CNS field trial results. Pages 187–188 in *Proc. NMC Annual Meeting*, Arlington, VA. Natl. Mastitis Council, Madison, WI.
- Nyman, A. K., T. Ekman, U. Emanuelson, A. H. Gustafsson, K. Holtenius, K. P. Waller, and C. H. Sandgren. 2007. Risk factors associated with the incidence of veterinary-treated clinical mastitis in Swedish dairy herds with a high milk yield and a low prevalence of subclinical mastitis. *Prev. Vet. Med.* 78:142–160.
- Nyman, A. K., U. Emanuelson, A. H. Gustafsson, and K. Persson Waller. 2009. Management practices associated with udder health of first-parity dairy cows in early lactation. *Prev. Vet. Med.* 88:138–149.
- Nyman, A. K., U. Emanuelson, K. Holtenius, K. L. Ingvarsen, and K. P. Waller. 2008. Metabolites and immune variables associated with somatic cell counts of primiparous dairy cows. *J. Dairy Sci.* 91:2996–3009.
- Olde Riekerink, R. G. M., H. W. Barkema, D. F. Kelton, and D. T. Scholl. 2008. Incidence rate of clinical mastitis on Canadian dairy farms. *J. Dairy Sci.* 91:1366–1377.
- Oliver, S. P., M. J. Lewis, B. E. Gillespie, and H. H. Dowlen. 1992. Influence of prepartum antibiotic therapy on intramammary infections in primigravid heifers during early lactation. *J. Dairy Sci.* 75:406–414.
- Oliver, S. P., M. J. Lewis, B. E. Gillespie, and H. H. Dowlen. 1997. Antibiotic residues and prevalence of mastitis pathogen isolation in heifers during early lactation following prepartum antibiotic therapy. *Zentralbl. Veterinarmed. B* 44:213–220.
- Oliver, S. P., and B. A. Mitchell. 1983. Intramammary infections in primigravid heifers near parturition. *J. Dairy Sci.* 66:1180–1183.
- Olteneacu, P. A., and I. Ekesbo. 1994. Epidemiological study of clinical mastitis in dairy cattle. *Vet. Res.* 25:208–212.
- Owens, W. E., S. C. Nickerson, R. L. Boddie, G. M. Tomita, and C. H. Ray. 2001. Prevalence of mastitis in dairy heifers and effectiveness of antibiotic therapy. *J. Dairy Sci.* 84:814–817.
- Owens, W. E., S. P. Oliver, B. E. Gillespie, C. H. Ray, and S. C. Nickerson. 1998. Role of horn flies (*Haematobia irritans*) in *Staphylococcus aureus* induced mastitis in dairy heifers. *Am. J. Vet. Res.* 59:1122–1124.
- Pankey, J. W., P. A. Drechsler, and E. E. Wildman. 1991. Mastitis prevalence in primigravid heifers at parturition. *J. Dairy Sci.* 74:1550–1552.
- Pankey, J. W., P. B. Pankey, R. M. Barker, J. H. Williamson, and M. W. Woolford. 1996. The prevalence of mastitis in primiparous heifers in eleven Waikato dairy herds. *N. Z. Vet. J.* 44:41–44.
- Paradis, M.-È., É. Bouchard, D. T. Scholl, F. Miglior, and J.-P. Roy. 2010. Effect of nonclinical *Staphylococcus aureus* or coagulase-negative staphylococci intramammary infection during the first month of lactation on somatic cell count and milk yield in heifers. *J. Dairy Sci.* 93:2989–2997.
- Park, J. Y., L. K. Fox, K. S. Seo, M. A. McGuire, Y. H. Park, F. R. Rurangirwa, W. M. Sisco, and G. A. Bohach. 2011. Comparison of phenotypic and genotypic methods for the species identification of coagulase-negative staphylococcal isolates from bovine intramammary infections. *Vet. Microbiol.* 147:142–148.
- Parker, K. I., C. W. Compton, F. M. Aniss, C. Heuer, and S. McDougall. 2008. Quarter-level analysis of subclinical and clinical mastitis in primiparous heifers following the use of a teat sealant or an injectable antibiotic, or both, precalving. *J. Dairy Sci.* 91:169–181.
- Parker, K. I., C. W. Compton, F. M. Aniss, A. Weir, C. Heuer, and S. McDougall. 2007a. Subclinical and clinical mastitis in heifers following the use of a teat sealant precalving. *J. Dairy Sci.* 90:207–218.
- Parker, K. I., C. W. Compton, F. M. Aniss, A. M. Weir, and S. McDougall. 2007b. Management of dairy heifers and its relationships with the incidence of clinical mastitis. *N. Z. Vet. J.* 55:208–216.
- Passchyn, P., S. Piepers, L. De Meulemeester, F. Boyen, F. Haesebrouck, and S. De Vliegher. 2011. Between-herd prevalence of *Mycoplasma bovis* in bulk milk in Flanders, Belgium. *Res. Vet. Sci.* doi:10.1016/j.rvsc.2011.03.016.
- Passchyn, P., S. Piepers, E. Schmitt, C. Guidarini, and S. De Vliegher. 2010. Concentration of penicillin G in mammary tissue and secretion of end-term dairy heifers following systemic prepartum administration of penethamate hydriodide. *J. Dairy Res.* 77:33–36.
- Persson Waller, K., B. Bengtsson, A. Lindberg, A. Nyman, and H. E. Unnerstad. 2009. Incidence of mastitis and bacterial findings at clinical mastitis in Swedish primiparous cows—Influence of breed and stage of lactation. *Vet. Microbiol.* 134:89–94.
- Piepers, S., L. De Meulemeester, A. de Kruif, G. Opsomer, H. W. Barkema, and S. De Vliegher. 2007. Prevalence and distribution of mastitis pathogens in subclinically infected dairy cows in Flanders, Belgium. *J. Dairy Res.* 74:478–483.
- Piepers, S., S. De Vliegher, A. de Kruif, G. Opsomer, and H. W. Barkema. 2009a. Impact of intramammary infections in dairy heifers on future udder health, milk production, and culling. *Vet. Microbiol.* 134:113–120.
- Piepers, S., G. Opsomer, H. W. Barkema, A. de Kruif, and S. De Vliegher. 2010. Heifers infected with coagulase-negative staphylococci in early lactation have fewer cases of clinical mastitis and higher milk production in their first lactation than non-infected heifers. *J. Dairy Sci.* 93:2014–2024.
- Piepers, S., G. Opsomer, E. Meyer, K. Demeyere, H. W. Barkema, A. de Kruif, and S. De Vliegher. 2009b. Heifer and quarter characteristics associated with periparturient blood and milk neutrophil apoptosis in healthy heifers and in heifers with subclinical mastitis. *J. Dairy Sci.* 92:4330–4339.
- Piepers, S., K. Peeters, G. Opsomer, H. W. Barkema, K. Frankena, and S. De Vliegher. 2011. Pathogen-specific risk factors at the herd, heifer and quarter level for intramammary infections in early lactating dairy heifers. *Prev. Vet. Med.* 99:91–101.
- Piessens, V., K. Supré, M. Heyndrickx, F. Haesebrouck, S. De Vliegher, and E. Van Coillie. 2010. Validation of amplified fragment length polymorphism genotyping for species identification of bovine associated coagulase-negative staphylococci. *J. Microbiol. Methods* 80:287–294.
- Piessens, V., E. Van Coillie, B. Verbist, K. Supré, G. Braem, A. Van Nuffel, L. De Vuyst, M. Heyndrickx, and S. De Vliegher. 2011. Distribution of coagulase-negative *Staphylococcus* species from milk and environment of dairy cows differs between herds. *J. Dairy Sci.* 94:2933–2944.
- Pitkälä, A., M. Haveri, S. Pyörälä, V. Myllys, and T. Honkanen-Buzalski. 2004. Bovine mastitis in Finland 2001—Prevalence, distribution of bacteria, and antimicrobial resistance. *J. Dairy Sci.* 87:2433–2441.
- Prenafeta, A., R. March, A. Foix, I. Casals, and L. Costa. 2010. Study of the humoral immunological response after vaccination with a *Staphylococcus aureus* biofilm-embedded bacterin in dairy cows: Possible role of the exopolysaccharide specific antibody production in the protection from *Staphylococcus aureus* induced mastitis. *Vet. Immunol. Immunopathol.* 134:208–217.
- Rajala-Schultz, P. J., Y. R. Gröhn, C. E. McCulloch, and C. L. Guard. 1999. Effects of clinical mastitis on milk yield in dairy cows. *J. Dairy Sci.* 82:1213–1220.

- Roberson, J. R., L. K. Fox, D. D. Hancock, J. M. Gay, and T. E. Besser. 1994a. Coagulase-positive *Staphylococcus* intramammary infections in primiparous dairy cows. *J. Dairy Sci.* 77:958–969.
- Roberson, J. R., L. K. Fox, D. D. Hancock, J. M. Gay, and T. E. Besser. 1994b. Ecology of *Staphylococcus aureus* isolated from various sites on dairy farms. *J. Dairy Sci.* 77:3354–3364.
- Roberson, J. R., L. K. Fox, D. D. Hancock, J. M. Gay, and T. E. Besser. 1996. Prevalence of coagulase-positive staphylococci, other than *Staphylococcus aureus*, in bovine mastitis. *Am. J. Vet. Res.* 57:54–58.
- Roberson, J. R., L. K. Fox, D. D. Hancock, J. M. Gay, and T. E. Besser. 1998. Sources of intramammary infections from *Staphylococcus aureus* in dairy heifers at first parturition. *J. Dairy Sci.* 81:687–693.
- Roy, J. P., D. Francoz, and O. Labrecque. 2008. Mastitis in a 7-week old calf caused by *Mycoplasma bovis*. *Vet. J.* 176:403–404.
- Rupp, R., and D. Boichard. 2000. Relationship of early first lactation somatic cell count with risk of subsequent first clinical mastitis. *Livest. Prod. Sci.* 62:169–180.
- Sampimon, O. C., S. De Vlieghe, H. W. Barkema, J. Sol, and T. J. G. M. Lam. 2009a. Effect of prepartum dry cow antibiotic treatment in dairy heifers on udder health and milk production. *J. Dairy Sci.* 92:4395–4403.
- Sampimon, O. C., B. H. van den Borne, I. Santman-Berends, H. W. Barkema, and T. J. G. M. Lam. 2010. Effect of coagulase-negative staphylococci on somatic cell count in Dutch dairy herds. *J. Dairy Res.* 77:318–324.
- Sampimon, O. C., R. N. Zadoks, S. De Vlieghe, K. Supré, F. Haesebrouck, H. W. Barkema, J. Sol, and T. J. G. M. Lam. 2009b. Performance of API Staph ID 32 and Staph-Zym for identification of coagulase-negative staphylococci isolated from bovine milk samples. *Vet. Microbiol.* 136:300–305.
- Schalm, O. W. 1942. *Streptococcus agalactiae* in the udder of heifers at parturition traced to sucking among calves. *Cornell Vet.* 32:39–60.
- Schukken, Y. H., R. N. Gonzales, L. L. Tikofsky, H. F. Schulte, C. Santisteban, F. L. Welcome, G. J. Bennet, M. J. Zurakowski, and R. N. Zadoks. 2009. CNS mastitis: Nothing to worry about? *Vet. Microbiol.* 134:9–14.
- Seno, N., and R. Azuma. 1983. A study on heifer mastitis in Japan and its causative microorganisms. *Natl. Inst. Anim. Health Q. (Tokyo)* 23:82–91.
- Stott, A. W., and J. O. Kennedy. 1993. The economics of culling dairy cows with clinical mastitis. *Vet. Rec.* 133:494–499.
- Supré, K., S. De Vlieghe, I. Cleenwerck, K. Engelbeen, S. Van Trappen, S. Piepers, O. C. Sampimon, R. N. Zadoks, P. De Vos, and F. Haesebrouck. 2010. *Staphylococcus devriesei* sp. nov., isolated from teat apices and milk of dairy cows. *Int. J. Syst. Evol. Microbiol.* 60:2739–2744.
- Supré, K., S. De Vlieghe, O. C. Sampimon, R. N. Zadoks, M. Vaneechoutte, M. Baele, E. De Graef, S. Piepers, and F. Haesebrouck. 2009. Technical note: Use of transfer RNA-intergenic spacer PCR combined with capillary electrophoresis to identify coagulase-negative *Staphylococcus* species originating from bovine milk and teat apices. *J. Dairy Sci.* 92:3204–3210.
- Supré, K., F. Haesebrouck, R. N. Zadoks, M. Vaneechoutte, S. Piepers, and S. De Vlieghe. 2011. Some CNS species are affecting udder health more than others. *J. Dairy Sci.* 94:2329–2340.
- Svensson, C., A.-K. Nyman, K. Persson-Waller, and U. Emanuelson. 2006. Effects of housing, management, and health of dairy heifers on first-lactation udder health in southwest Sweden. *J. Dairy Sci.* 89:1990–1999.
- Tanaka, S., K. Miyazawa, A. Kuwano, K. Watanabe, S. Ohwada, H. Aso, S. Nishida, and T. Yamaguchi. 2008. Age-related changes in leukocytes and T cell subsets in peripheral blood of Japanese Black cattle. *Anim. Sci. J.* 79:368–374.
- Taponen, S., J. Koort, J. Björkroth, H. Saloniemi, and S. Pyörälä. 2007. Bovine intramammary infections caused by coagulase-negative staphylococci may persist throughout lactation according to amplified fragment length polymorphism-based analysis. *J. Dairy Sci.* 90:3301–3307.
- Taponen, S., K. Supré, V. Piessens, E. Van Coillie, S. De Vlieghe, and J. M. K. Koort. 2011. *Staphylococcus agnetis* sp. nov., a coagulase-variable species from bovine subclinical and mild clinical mastitis. *Int. J. Syst. Evol. Microbiol.* 63:61–65. doi:10.1099/ijs.0.028365-0.
- Tenhagen, B. A., D. Edinger, B. Baumgartner, P. Kalbe, G. Klunder, and W. Heuwieser. 2001. Efficacy of a herd-specific vaccine against *Staphylococcus aureus* to prevent post-partum mastitis in dairy heifers. *J. Vet. Med. A Physiol. Pathol. Clin. Med.* 48:601–607.
- Timms, L. L., and L. H. Schultz. 1987. Dynamics and significance of coagulase-negative staphylococcal intramammary infections. *J. Dairy Sci.* 70:2648–2657.
- Trinidad, P., S. C. Nickerson, and T. K. Alley. 1990. Prevalence of intramammary infection and teat canal colonization in unbred and primigravid dairy heifers. *J. Dairy Sci.* 73:107–114.
- Tucker, H. A. 1987. Quantitative estimates of mammary growth during various physiological states: A review. *J. Dairy Sci.* 70:1958–1966.
- Waage, S., S. A. Ødegaard, A. Lund, S. Brattgjerd, and T. Rothe. 2001. Case-control study of risk factors for clinical mastitis in post-partum dairy heifers. *J. Dairy Sci.* 84:392–399.
- Waage, S., H. R. Skei, J. Rise, T. Rogdo, S. Sviland, and S. A. Ødegaard. 2000. Outcome of clinical mastitis in dairy heifers assessed by re-examination of cases one month after treatment. *J. Dairy Sci.* 83:70–76.
- Waage, S., S. Sviland, and S. A. Ødegaard. 1998. Identification of risk factors for clinical mastitis in dairy heifers. *J. Dairy Sci.* 81:1275–1284.
- Weiss, W. P., J. S. Hogan, K. L. Smith, and K. H. Hoblet. 1990. Relationships among selenium, vitamin E, and mammary gland health in commercial dairy herds. *J. Dairy Sci.* 73:381–390.
- Weiss, W. P., J. S. Hogan, D. A. Todhunter, and K. L. Smith. 1997. Effect of vitamin E supplementation in diets with a low concentration of selenium on mammary gland health of dairy cows. *J. Dairy Sci.* 80:1728–1737.
- Whist, A. C., and O. Osteras. 2007. Associations between somatic cell counts at calving or prior to drying-off and clinical mastitis in the remaining or subsequent lactation. *J. Dairy Res.* 74:66–73.
- Zadoks, R. N., and J. L. Watts. 2009. Species identification of coagulase-negative staphylococci: Genotyping is superior to phenotyping. *Vet. Microbiol.* 134:20–28.
- Ziv, G. 1980. Practical pharmacokinetic aspects of mastitis therapy—1: Parenteral treatment. *Vet. Med. Small Anim. Clin.* 75:277–290.