Udder Health in the Periparturient Period

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ABSTRACT

The periparturient period is associated with rapid differentiation of secretory parenchyma, intense mammary growth, copious synthesis and secretion, and marked accumulation of colostrum and milk. Udder health during this time is an important factor associated with the production of maximum quantities of high quality milk. Intramammary infections that occur during the dry period can adversely affect udder health, resulting in decreased milk production, altered milk composition, and impaired mammary function. Bovine mammary glands are markedly susceptible to new infections during the periparturient period, especially prior to parturition. Many infections that occur at this time are associated with clinical mastitis during early lactation. Methods of controlling mastitis in the dry period have focused primarily on the use of antibiotics. However, antibiotic therapy at drying off does not appear to prevent new infections in the periparturient period. This is most likely due to lack of persistence of antibiotics. Furthermore, antibiotics used currently are less effective against environmental pathogens, in particular coliform bacteria, which can cause a high proportion of intramammary infections during the periparturient period. Methods of controlling bovine mastitis during the periparturient period is an important area that requires additional research. Procedures need to be developed that are effective against a variety of bacteria, including environmental mastitis pathogens, if additional control is to be achieved.

Received August 31, 1987.
Accepted November 12, 1987.

INTRODUCTION

The dry or nonlactating period of the dairy cow is a dynamic time when mammary glands undergo transition both from and to a state of active milk synthesis. The early dry period is associated with an abrupt cessation of milk removal, engorgement of cisternal spaces, ducts, and alveoli with milk constituents, marked changes in mammary secretion composition, and regression of secretory tissue (15, 19, 120, 150, 155, 156). Near parturition, mammary glands again undergo marked transition characterized by rapid differentiation of secretory tissue, intense growth, copious synthesis and secretion of proteins, fat, and carbohydrates, and accumulation of colostrum (16, 107, 115, 149, 155, 156).

Clinical and experimental data clearly support the concept that bovine mammary glands are highly susceptible to new intramammary infection (IMI) during transitions of the gland from lactation to involution and from involution to colostrogenesis (40, 114, 151, 152). Increased susceptibility to new IMI may be associated with physiological transitions of the mammary gland either from or to a state of active milk synthesis. In the context of this symposium, this review examines the importance of the dry period with respect to IMI with particular reference to IMI that occur during the periparturient period and effects of IMI on mammary function during early lactation.

DISCUSSION

A customary procedure implemented by dairy producers is the complete cessation of lactation in dairy cows during the 7th to 8th mo of pregnancy. Previous studies indicated that the duration of the nonlactating period was related critically to mammary development and secretory activity during the ensuing lactation (27, 159). Dairy cows with 10 to 40-d dry periods produced less milk in the following lactation than cows with a dry period of 40 to
Moreover, cows milked continuously throughout pregnancy produced 33% less milk during the subsequent lactation compared with their twins with a 2-mo dry period (159).

Benefits derived from a dry period involve more than improvements in the cow's nutritional status for the forthcoming lactation. The majority of mammary tissue growth and development in ruminants occurs during involution (5, 29, 160). Total population of secretory cells and biosynthetic activity of such cells play a decisive role in determining milk yield. Previous studies (1, 102, 157, 158) have shown that adequate proliferation and differentiation of mammary secretory epithelium during the nonlactating period were essential for optimal synthetic and secretory function in the ensuing lactation of both cows and goats. In heifers, mammary development during the first gestation followed a continuous exponential form of growth (159). More recently, histological, cytological, and biochemical evidence showed that lobulo-alveolar development in cows increased substantially during the last 2 wk of pregnancy (155). Effects of involution on subsequent milk yield appear to be related to regeneration or reactivation of secretory epithelium before the next lactation begins.

Functional Morphology During Transitions of the Mammary Gland

Two distinct types of tissue are associated with the mammary gland. Parenchymal tissue consists of secretory elements arranged into an extensive lobulo-alveolar system. The supporting tissue or stroma includes connective tissue, adipose tissue, and skin of the mammary gland (164). The microscopic structure of fully developed lactating mammary epithelia consists of a single layer of secretory cells resting on a basal network of myoepithelial cells and enclosed by a basal lamina (133). The shape of mammary secretory cells is governed by the amount of lacteal secretion stored in the alveolar lumen; cells are columnar in empty luminal areas but cuboidal when the lumen is full of secretion. Regardless of shape, lactating mammary epithelia are characterized as being well-polarized with microvilli extending from the apical surface into the alveolar lumen, extensive convolution of the basal plasma membrane, basally located nuclei, and a large cytoplasmic to nuclear ratio (133). Cytoplasmic areas are occupied by a complex of organelles needed for the synthesis and secretion of milk. Abundant parallel cisternae of rough endoplasmic reticulum (RER) occupy the basal and paranuclear cytoplasm while the smooth-surfaced endoplasmic reticulum cisternae of the Golgi apparatus occupies the supranuclear region (133). For a more detailed description of the fine structure of lactating mammary epithelium and the relationship between cellular organelles, milk component biosynthesis, and milk secretion [see (22, 29, 64, 103, 133, 153)].

Emphasis on mammary gland involution and regrowth has not been extensive. To date, the majority of information available concerning morphological changes occurring during mammary gland involution and lactogenesis has been generated in laboratory species (48, 65, 66, 67, 72, 94, 135, 136). The rate and extent to which milk-producing tissues regress following milk cessation and redevelop during lactogenesis vary greatly with species (80). A recent study (155) showed that the bovine mammary gland involutes gradually over a 2-wk period. In contrast to what was observed in the fully involuted rat mammary gland (135, 136), sloughing of epithelial cells into alveolar lumina was not apparent in caprine (158), ovine (80), or bovine mammary glands (73, 155). Instead, alveoli exhibited small lumina filled with electron dense proteinaceous material and undifferentiated epithelial cells (155). Following the 1st wk of involution in ruminants, secretory activity of mammary epithelium decreased as evidenced by a reduction in alveolar luminal area with a concomitant increase in stromal area (73, 155). Luminal spaces decreased when secretion no longer displaced the alveolar area. Once milk synthesis ceased and mammary fluid was resorbed, stromal areas expanded proportionately to compensate for reduced alveolar luminal area. Cytological analysis of mammary epithelium revealed an increase in prevalence of nonactive cells with a concurrent decrease in fully active cells through the first 2 wk of involution (155). Bovine epithelial cells (Figure 1) do not regress to the same extent observed in rat mammary glands and appear to maintain some synthetic and secretory activity throughout the nonlactating period (73, 155).
Although the actual timing and sequence of events leading to lactogenesis differ among species, the morphogenesis of secretory capability progresses gradually as parturition approaches (5, 22, 29, 46, 48, 155). Cowie (29) observed limited changes in the structure of primigravid goat mammary glands during the first half of pregnancy, but a period of advanced alveolar growth occurred between 60 and 120 d of gestation. Histological and cytological evidence showed that lobulo-alveolar growth increased rapidly in cows between d 110 and 140 of gestation (160). The immediate periparturient period in rats was
associated with intense mammary growth and rapid differentiation of secretory parenchyma (22). Prepartum cow (102, 155) and goat (157) mammary tissue exhibited characteristics indicative of copious milk synthesis and secretion as total area of stroma decreased with a synchronous increase in luminal and epithelial areas. Cytological examination of bovine and caprine mammary tissue also indicated gradual differentiation of secretory epithelium during the last few weeks of gestation with an increased cytoplasmic to nuclear ratio, a higher degree of cellular polarity, and more apically located secretory vesicles (Figure 1). As parturition approached, fully active cells became more numerous, whereas numbers of nonactive cells decreased (155, 157). During the last week of gestation, percentages of cell area occupied by nuclei, unoccupied cytoplasm, fat, and stasis vacuoles decreased significantly while percentages of RER, Golgi, mitochondria, and secretory vesicles increased significantly in comparison with cells from the fully involuted gland (155) (Figure 1).

During lactogenesis, dramatic changes in mammary secretion composition and volume accompany cytological and enzymatic differentiation of alveolar cells (46, 61, 75, 82, 153, 155, 157). In prelactating mammary glands, "leaky" tight junctions allow passive diffusion of components from blood to milk and vice versa (82). However, at parturition, tight junctions become less permeable and inhibit paracellular movement of serum proteins and ions into milk. Instead, most transport is via the transcellular pathway (82). In a recent study (153), biochemical changes in bovine mammary secretions were correlated with structural differentiation of mammary epithelial cells during lactogenesis. Decreased tight junction permeability and increased synthetic ability of secretory epithelia were observed during the last 2 wk of gestation. Increased concentrations of fat, citrate, and α-lactalbumin were accompanied by decreased concentrations of somatic cells, serum albumin, and lactoferrin. Changes in mammary structure coincided with alterations in secretion composition. Cell structure gradually assumed the morphology of lactating mammary glands with increased epithelium, lumen, and fully active secretory cells, and decreased amounts of stroma and nonactive secretory cells (155). Thus, the functional transition of the bovine mammary gland from involution to lactation probably occurs during the last 2 wk of the nonlactating period.

Colchicine has been used extensively to examine mechanisms that regulate milk synthesis and mammary gland development. The mode of action of colchicine appears to be disruption of intracellular microtubular integrity necessary for mitosis (84) and exocytosis (106). Intramammary infusion of colchicine into heifers and goats prior to parturition altered mammary secretion composition and decreased milk production in the early portion of the subsequent lactation (1, 102, 157, 158). Histological and cytological evidence indicated that prepartum colchicine treatment suppressed irreversibly differentiation of bovine and caprine mammary tissue (102, 157). Thus, factors that interfere with mechanisms associated with cellular differentiation, such as bacterial infections during the dry period, may have a pronounced effect on mammary function.

Intramammary Infections During the Dry Period

The importance of the dry period in the control of bovine mastitis has been recognized for almost 40 yr. A classic study by Neave et al. (99) demonstrated that mammary glands were markedly susceptible to new IMI during the early dry period. The rate of new infection during the first 21 d of the dry period was 6.25 times higher than the rate observed during the previous lactation (99). However, the rate of new infection for the remainder of the dry period was extremely low. When the entire dry period was considered, the rate of infection was 1.64/wk compared with 1.12/wk during the previous lactation. Many infections that occurred during the dry period caused clinical mastitis in the subsequent lactation. As a result of this study (99), the early dry period was identified as an extremely important time for the control of bovine mastitis.

Since the early work by Neave et al. (99), procedures were developed to control infections during the dry period. Most dairy advisors recommend that all quarters of all cows be given by intramammary infusion, antibiotics approved for use in nonlactating cows following the last milking of lactation. The
objectives of dry cow therapy are twofold: a) eliminate infections present during late lactation, and b) prevent new infections during the early dry period when mammary glands are highly susceptible to new IMI (13, 37, 95, 98, 131, 145). In spite of widespread use of antibiotic dry cow therapy, cows continue to calve with IMI and clinical mastitis is observed during the early postpartum period (36, 40, 45, 71, 152). This implies that: 1) antibiotic dry cow therapy is not effective in eliminating infections present during late lactation, 2) dry cow therapy is not effective in preventing new IMI during the early dry period, or 3) new infections occur at some point after the early dry period.

Experimental evidence suggests that dry cow therapy is effective in controlling IMI due to *Streptococcus agalactiae* and somewhat effective against *Staphylococcus aureus* (13, 34, 39, 95, 96, 98, 132, 143, 166). However, dry cow therapy appears to be less effective against streptococci other than *Strep. agalactiae* and ineffective against coliform bacteria (35, 40, 71, 140, 146, 151, 152, 163, 166).

Differences in effectiveness of dry cow antibiotic therapy to prevent new IMI are most likely related to several factors. *Strep. agalactiae* and *Staph. aureus*, commonly referred to as contagious mastitis pathogens, are thought to be transmitted primarily during the milking process, and transmission can be controlled by hygiene and antibiotic therapy (13, 95, 97, 145). The sources of these two organisms are infected mammary glands, colonized teat ducts, and teat lesions (13, 37, 146). Extramammary sources of contagious mastitis pathogens have been identified but appear to be relatively unimportant in the pathogenesis of infection (13). Thus, exposure of mammary glands to contagious pathogens during the dry period is most likely reduced in the absence of regular milking and therapy at drying off tends to control these pathogens effectively.

In contrast, streptococci other than *Strep. agalactiae*, which includes primarily *Strep. dysgalactiae*, *Strep. uberis*, *Strep. faecalis*, other species of fecal streptococci, and coliform bacteria, are ubiquitous in the cows' environment. Consequently, mammary glands are exposed continuously to environmental mastitis pathogens throughout the dry period, especially in herds in total confinement housing. Antibiotics currently formulated for use in dry cows were developed to control IMI caused by *Strep. agalactiae* and *Staph. aureus*, which at one time caused the majority of clinical and subclinical mastitis in dairy herds (13, 34, 98, 131). Thus, it is not surprising that current dry cow antibiotic formulations are ineffective against coliform mastitis pathogens.

It is unfortunate, perhaps, that so much research attention has focused on studies of antibiotic therapy during the dry period. As Eberhart (37) pointed out, the early successes with antibiotics most likely discouraged efforts to develop alternative or additional means of protection during the dry period. Furthermore, reports on the extent of new IMI during the dry period and when new infections occur are limited and were derived from trials evaluating the efficacy of antibiotic dry cow therapy. Many of these studies were conducted in herds with a high prevalence of *Strep. agalactiae* and *Staph. aureus*. However, recent reports have shown that mastitis caused by environmental pathogens can be a significant problem in herds that have eradicated *Strep. agalactiae* and reduced the prevalence of *Staph. aureus* (36, 37, 40, 113, 114, 121, 151, 152). This situation may be typical of many herds in which mastitis control procedures such as postmilking teat disinfection and antibiotic therapy during the dry period have been effective in controlling contagious mastitis pathogens. Consequently, widespread optimism that present methods of mastitis control would eliminate mastitis as a problem to dairy producers has been replaced with the realization that bovine mastitis is a complex and perplexing disease.

**Intramammary Infections in Primigravid Heifers**

Few studies have been reported on the occurrence of IMI in primigravid heifers in the periparturient period in the US. Previous investigations (13, 112, 152) have shown that the incidence of IMI is likely to increase with increasing age of animals under comparable conditions. It has been assumed, however, that the occurrence of IMI in heifers at first parturition is relatively low. It would appear that this assumption was based on the premise that contagious pathogens are transmitted primarily during the milking process. Because heifers have not been exposed to the milking process,
mammary glands of heifers at first parturition should theoretically be uninfected, at least by contagious mastitis pathogens. Thus, the importance of contagious and environmental mastitis pathogens in the etiology of heifer mastitis has not been well-documented.

A recent study by Oliver (111) was conducted to determine the frequency of mastitis pathogen isolation and incidence of IMI in 75 first lactation heifers during the periparturient period. This investigation was conducted in a herd that was Strep. agalactiae-negative and had a low prevalence of Staph. aureus. The frequency of mastitis pathogen isolation in heifers during the periparturient period is shown in Table 1. A total of 1497 quarter samples of mammary secretion were collected. Samples from one quarter of one heifer were not collected on 3 occasions because of an Actinomyces pyogenes (formerly referred to as Corynebacterium pyogenes) infection, which caused the quarter to be nonfunctional. The frequency of mastitis pathogen isolation was highest prior to parturition (22% of samples) and at parturition (28.1% of samples) and decreased markedly during early lactation (10.3% of samples).

Coagulase-negative staphylococci accounted for 55.7% of mastitis organisms isolated (Table 2). The frequency of coagulase-negative staphylococci isolation was high at all sampling times in the periparturient period. Environmental mastitis pathogens (coliforms and streptococci other than Strep. agalactiae) accounted for 35.7% of isolates. The frequency of C. bovis isolation was extremely low prior to and at parturition, but increased during early lactation. Coagulase-positive staphylococci accounted for only 2.9% of mastitis pathogens isolated.

The number of quarters with IMI and types of mastitis pathogens causing IMI are in Table 3. A quarter was considered infected if the same pathogen was isolated in two of three consecutive samples obtained during specific time periods. Time periods were: 1) parturition including samples collected 14 and 7 d prior to expected parturition and at parturition, and 2) early lactation including samples collected at parturition and 7 and 14 d postparturition. Fifty-nine of 300 quarters (19.7%) were infected at parturition. Forty-seven of 300 quarters (15.7%) were infected during early lactation. Twenty-two of these IMI persisted from parturition while 25 were new infections that occurred after parturition. Coliforms and streptococci other than Strep. agalactiae caused 40.4% of all IMI observed during early lactation and about 86% of major pathogen infections. The number of quarters infected with coagulase-negative staphylococci decreased markedly during early lactation, and only 38.1% of
TABLE 2. Frequency of mastitis pathogen isolation expressed as a percentage of all isolates from primigravid heifer mammary glands during the periparturient period (n = 75 heifers).

<table>
<thead>
<tr>
<th>Bacteria</th>
<th>-14&lt;sup&gt;1&lt;/sup&gt;</th>
<th>-7&lt;sup&gt;1&lt;/sup&gt;</th>
<th>0&lt;sup&gt;2&lt;/sup&gt;</th>
<th>7&lt;sup&gt;2&lt;/sup&gt;</th>
<th>14&lt;sup&gt;2&lt;/sup&gt;</th>
<th>Total&lt;sup&gt;3&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(% of Isolates)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Streptococci</td>
<td>13.6</td>
<td>14.3</td>
<td>26.2</td>
<td>32.1</td>
<td>12.9</td>
<td>20.4</td>
</tr>
<tr>
<td>Coliforms</td>
<td>10.6</td>
<td>14.3</td>
<td>15.5</td>
<td>19.6</td>
<td>19.4</td>
<td>15.3</td>
</tr>
<tr>
<td>Coagulase-positive staphylococci</td>
<td>4.5</td>
<td>1.3</td>
<td>2.4</td>
<td>3.6</td>
<td>3.2</td>
<td>2.9</td>
</tr>
<tr>
<td>Coagulase-negative staphylococci</td>
<td>66.7</td>
<td>64.9</td>
<td>51.2</td>
<td>37.5</td>
<td>54.8</td>
<td>55.7</td>
</tr>
<tr>
<td>Corynebacterium bovis</td>
<td>0</td>
<td>2.6</td>
<td>3.6</td>
<td>7.1</td>
<td>9.7</td>
<td>3.8</td>
</tr>
<tr>
<td>Other</td>
<td>4.5</td>
<td>2.6</td>
<td>1.2</td>
<td>0</td>
<td>0</td>
<td>1.9</td>
</tr>
</tbody>
</table>

<sup>1</sup> 300 quarters.  
<sup>2</sup> 299 quarters.  
<sup>3</sup> 1497 quarter samples.

Coagulase-negative staphylococcal IMI detected at parturition persisted into early lactation. Forty-eight of 75 heifers (64%) were infected in at least one quarter with any organism and 26 heifers (34.7%) were infected in at least one quarter with major mastitis pathogens.

All gram-negative bacteria were lactose-fermenting, and hence, were considered coliforms. The majority of coliforms identified were *Escherichia coli* (Table 4). A heterogeneous group of streptococcal species were isolated from heifer mammary glands (Table 4). Of the eight streptococcal IMI observed at parturition, four were identified presumptively as *Strep. uberis* [CAMP-negative, esculin-positive, inulin-positive] and four as *Strep. dysgalactiae* (CAMP-negative, esculin-negative, inulin-negative). During early lactation, 10 streptococcal IMI were observed and were due to *Strep. uberis* (n = 3), *Strep. dysgalactiae* (n = 4), and possibly *Strep. faecalis* (n = 3), (CAMP-negative, esculin-positive, inulin-negative).

Environmental mastitis pathogens caused the majority of major pathogen IMI in primigravid heifers at parturition and during early lactation. This was consistent with other bacteriological studies conducted simultaneously in this

TABLE 3. Intramammary infections in primigravid heifers during the periparturient period.<sup>1</sup>

<table>
<thead>
<tr>
<th>Intramammary infections</th>
<th>Parturition</th>
<th>Early lactation</th>
<th>Persisted from parturition</th>
<th>New during early lactation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Streptococci</td>
<td>8</td>
<td>10</td>
<td>3</td>
<td>7</td>
</tr>
<tr>
<td>Coliforms</td>
<td>5</td>
<td>7</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>Coagulase-positive staphylococci</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Coagulase-negative staphylococci</td>
<td>42</td>
<td>23</td>
<td>16</td>
<td>7</td>
</tr>
<tr>
<td><em>Corynebacterium bovis</em></td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Mixed</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Other</td>
<td>3</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>59</td>
<td>47</td>
<td>22</td>
<td>25</td>
</tr>
<tr>
<td>Uninfected</td>
<td>241</td>
<td>253</td>
<td>...</td>
<td>...</td>
</tr>
</tbody>
</table>

<sup>1</sup> n = 75 heifers, 300 quarters.
TABLE 4. Identification of coliform and streptococcal mastitis pathogens infecting primigravid heifer mammary glands during the periparturient period.

<table>
<thead>
<tr>
<th>Identification</th>
<th>Parturition</th>
<th>Early lactation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Coliforms</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Escherichia coli</em></td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td><em>Klebsiella pneumoniae</em></td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Not determined ³</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td><strong>Streptococci</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CAMP-negative, esculin-positive, inulin-positive</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>CAMP-negative, esculin-positive, inulin-negative</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>CAMP-negative, esculin-negative, inulin-negative</td>
<td>4</td>
<td>4</td>
</tr>
</tbody>
</table>

¹ n = 75 heifers, 300 quarters.
² Identified by Analytical Profile Index 20E Enterobacteriaceae diagnostic system (Analytab Products, Plainview, NY).
³ All gram-negative bacteria not identified to species level were lactose-positive.

Coagulase-negative staphylococci cause a high proportion of IMI in primigravid heifers during the periparturient period (8, 85, 111, 118). Coagulase-negative staphylococci are commonly referred to as minor mastitis pathogens and once were thought to be primarily *Staph. epidermidis*. However, recent studies have shown that coagulase-negative staphylococci are a heterogeneous group of bacteria consisting of several species (60, 85). Matthews (85) found that almost 50% of streak canal
swabs of 144 quarters of 36 primiparous cows obtained prior to parturition and 35.4% of quarter samples of mammary secretion collected at parturition were positive for staphylococci. *Staphylococcus hyicus* was isolated most frequently in samples of mammary secretion followed by *Staph. aureus*, *Staph. simulans*, *Staph. epidermidis*, *Staph. bovinus*, and *Staph. xylosus*. Similar results were reported by Boddie et al. (8) in 10 yearling Jersey heifers that were sampled bimonthly for 1 yr.

Several reports have been published on summer mastitis (14, 41, 42, 50, 109, 123, 165). Summer mastitis occurs in pregnant and nonpregnant heifers and nonlactating cows frequently in the summer months but also in dry cows in the winter. The disease is characterized by sudden onset, with serious anorexia, depression, wasting, and exhaustion, and generally results in an acute suppurative mastitis where the secretion is thick and creamy with a characteristic foul smell (165). Summer mastitis occurs primarily in the British Isles and Northwest Europe (Holland, Denmark, and North Germany). However, a recent study in Japan (142) indicated that heifer mastitis occurred frequently in the summer and appeared to be similar to the summer mastitis observed in many northern European countries (109, 165).

The prevalence of summer mastitis appears to vary by geographic location and year. A recent survey by O'Rourke et al. (123) indicated that summer mastitis was particularly prevalent in England and Wales in 1981. The survey showed that in a normal year approximately 40% of dairy herds in England and Wales have one or more cases of summer mastitis, and that of the animals at risk, the prevalence was higher in pregnant heifers than in dry cows and lowest in nonpregnant heifers. Egan (41) reported that 78% of herds surveyed in the Irish Republic had at least one case of summer mastitis. The percent of dry cows (8.6%) and pregnant heifers (7.1%) with summer mastitis was significantly higher than virgin heifers (2%).

Summer mastitis was once thought to be caused primarily by *A. pyogenes*. However, subsequent studies demonstrated that a combination of organisms is a characteristic feature of this disease (14, 42, 142, 165). *Peptococcus indolicus*, *A. pyogenes*, *Strep. dysgalactiae*, *Strep. uberis*, *Strep. agalactiae*, *Strep. faecalis*, *Staph. aureus*, and others have been isolated in pure or mixed culture from mammary glands experiencing summer mastitis. The most prevalent organisms appear to be *A. pyogenes*, *P. indolicus*, and *Strep. dysgalactiae*.

**Intramammary Infections in Multiparous Cows**

Since the early report by Neave et al. (99), few studies have been conducted on the incidence of new IMI during the dry period in the absence of antibiotic dry cow therapy. Thus, much of the information on the time when new infections occur during the dry period is based on one study conducted in the late 1940's in a herd of Milking Shorthorns that produced 4 to 5 kg of milk at the time of drying off under conditions very different from current systems of dairying.

Recently, studies were conducted to determine the incidence of new IMI during the dry period and types of pathogens causing IMI in a herd that was *Strep. agalactiae*-negative and had a low prevalence of *Staph. aureus* (112, 113, 114). Cows (n = 160) were producing 12 to 20 kg of milk at drying off and no quarters were infused with antibiotics following the last milking of lactation. Quarters of cows were sampled repeatedly during late lactation, early involution, prior to parturition, at parturition, and during early lactation, and all cows were in total confinement housing for the duration of the study.

The number of quarters infected with major mastitis pathogens (all organisms except *C. boui* and coagulase-negative staphylococci) increased threefold from late lactation (4.4% of quarters) to early involution (13.0% of quarters). At parturition, 15.8% of quarters were infected, which was 3.6 times higher than the number of quarters infected at drying off. During early lactation, a marked decrease in the number of quarters with IMI (10.2%) was observed. However, the number of quarters with major pathogen IMI during early lactation was still 2.3 times higher than the number of quarters infected at drying off (114).

Most major pathogen IMI were caused by streptococci other than *Strep. agalactiae*, primarily esculin-positive and CAMP-negative,
and coliforms, Forty-one of 83 major pathogen IMI detected during early involution persisted throughout the dry period and were present at parturition. About 60% of streptococci other than Strep. agalactiae and 50% of coliform IMI persisted. Of the 101 IMI detected at parturition, 63 were due to streptococci other than Strep. agalactiae and 26 were due to coliforms. During early lactation, 43 IMI by streptococci other than Strep. agalactiae were observed. Thirty of these IMI persisted from parturition and 13 were new infections that occurred after parturition. Eleven coliform IMI were detected during early lactation and only 3 of 26 coliform IMI at parturition persisted into early lactation, whereas 8 new coliform IMI occurred after parturition (112, 114).

Several IMI persisted for varying periods. Samples of mammary secretion from many quarters contained large numbers of bacteria over some portion of the dry period. However, on many occasions bacteria were not isolated in samples collected during the periparturient period. About 50% of major pathogen IMI persisted from early involution to parturition. A similar trend was observed from parturition to early lactation. These data suggest that a high rate of spontaneous elimination occurred during the dry period and agree with previous studies that indicated that about one-half of new major pathogen infections established during the early dry period do not persist into the next lactation (36, 99). Additional research is needed to determine if transient infections during the dry period affect mammary function and subsequent dairy cow performance.

These data show, at least with respect to environmental mastitis pathogens, that rates of new IMI are elevated during early involution, which agrees with previous reports (36, 99, 121, 144, 152, 163). However, these data demonstrated also that mammary glands are highly susceptible to new IMI during the periparturient period, which is in marked contrast with the early report by Neave et al. (99). Differences in results of the study by Oliver (114) and those by Neave et al. (99) are probably related to several factors such as milk yield at drying off, methods of milk cessation, and management factors such as type of housing, bedding materials, etc. However, one very important factor that has received little research attention is related to the prevalence of organisms causing IMI in dairy herds. Strep. agalactiae and Staph. aureus were the predominant pathogens associated with IMI in the study by Neave et al. (99). Exposure of mammary glands to contagious pathogens is concentrated at the beginning of the dry period and most likely decreases as the dry period progresses (37, 38). However, exposure to environmental pathogens, which were the predominate major pathogens isolated in the study by Oliver (114), is likely to continue throughout the dry period. Eberhart (37, 38) found that numbers of streptococci and Gram-negative bacteria recovered from teat ends increased significantly at parturition, which also coincides with the time that mammary glands are highly susceptible to new IMI. Consequently, changes in bacterial populations on the teat end during involution relate significantly to the epidemiology of bovine mastitis during physiological transitions of the mammary gland.

Eberhart and Buckalew (40) indicated that clinical mastitis remained a serious problem in a dairy herd with a low prevalence of IMI due to Strep. agalactiae and Staph. aureus despite good control of subclinical mastitis by postmilking teat disinfection and antibiotic therapy of infected quarters at the end of lactation. They found that 13.1% of 794 quarters that were uninfected at drying off and not treated with antibiotics were newly infected at parturition. Interestingly, 25.3% of 79 quarters infected at drying off and treated with antibiotics were infected at parturition. Streptococci other than Strep. agalactiae and coliforms, primarily Klebsiella pneumoniae, caused the majority of IMI in this study, and many cases of clinical mastitis were observed during early lactation.

Smith et al. (151, 152) have reported extensive data on environmental pathogens and IMI during the dry period. The majority of cows (83%) in their studies were infused with antibiotics following the last milking of lactation and all cows were housed in total confinement. They demonstrated that the rate of new coliform IMI was highest during the first and last quarters of the dry period. Rate of new coliform infection was influenced by parity; cows in their second and third dry period were more susceptible than cows in their first dry period which agrees with other reports (112). Rate of new coliform infection was also
affected by season during which dry periods occurred; rates of new coliform IMI were highest in spring and summer. A heterogeneous group of coliform bacteria were associated with IMI during the first half of the dry period. However, the majority of coliform IMI that occurred during the last half of the dry period that persisted into lactation were due to *Escherichia coli*.

Rates of streptococcal (streptococci other than *Strep. agalactiae*) IMI were similar to rates of new coliform infection throughout the dry period (152). Effects of parity and season were not significant. However, antibiotic therapy at drying off reduced streptococcal infection rate and most likely influenced results. Other studies have shown that older cows appear to be more susceptible to new IMI by streptococci (112, 163). Rate of streptococcal IMI in cows that were not treated with antibiotics at drying off was 6 to 7 times higher during the first 25% of the dry period when compared with rate in treated cows. These data suggest that dry cow therapy is effective in preventing new IMI by streptococci other than *Strep. agalactiae* during the early dry period but ineffective in preventing new infections during the periparturient period.

Experimental infection studies with environmental mastitis pathogens during the nonlactating period also have shown that bovine mammary glands are markedly susceptible to new IMI during early involution and near parturition. McDonald and Anderson (89) indicated that mammary glands inoculated with *Strep. uberis* on the day of drying off were resistant to experimental infection. However, at 7 d after drying off, 12% of inoculated quarters became infected, at 14 d, 50%; and at 21 d, 80% of quarters. All quarters (n = 18) inoculated during the last 50% of the dry period became infected. A similar study was conducted using *E. coli* (88). During the first 50% of the dry period, 32% of 34 inoculated mammary glands became infected. However, all experimental infections with *E. coli* at this time were eliminated by the cow without therapy, and no signs of mastitis were observed. However, during the last month of the dry period, 88% of 42 inoculated mammary glands became infected. Twenty-three IMI were eliminated by the cow without therapy, but infection in 14 quarters persisted through parturition, resulting in peracute toxic mastitis. Hill et al. (70) also showed that experimental *E. coli* infection of mammary glands of newly calved cows produced a very severe from of mastitis characterized by pyrexia, anorexia, and diarrhea.

One common characteristic of studies reported by Eberhart and Buckalew (40), Smith et al. (152), and Oliver (114) was that they were conducted in herds with a low prevalence of *Strep. agalactiae* and *Staph. aureus*. In spite of the control of contagious mastitis pathogens, mastitis continued to be a problem in these herds, and several IMI that were associated with clinical mastitis during early lactation originated at some point during the dry period. The pattern of infection observed in these studies may be typical of many herds in which mastitis control procedures such as postmilking teat disinfection and antibiotic therapy at drying off have been effective in controlling contagious mastitis pathogens. In support of this contention, Oliver and Mitchell (119) found that an average of 25.8% of cows and 10.3% of quarters were positive for major mastitis pathogens in 17 *Strep. agalactiae*-negative herds (n = 1521 cows) monitored annually from 1976 to 1981. There was little between-year variation. The predominant mastitis pathogens isolated were streptococci other than *Strep. agalactiae* (44.9%), *Staph. aureus* (34.6%), and coliforms (8.6%). Thus, environmental mastitis pathogens accounted for >50% of bacteria isolated, and all of these herds were utilizing postmilking teat disinfection, and antibiotic dry cow therapy. Other studies (44, 45, 71) revealed that environmental mastitis pathogens caused a high proportion of clinical mastitis during lactation, especially during the early postpartum period.

Few reports have been published describing the occurrence of minor mastitis pathogen (coagulase-negative staphylococci and *C. bosis*) IMI during the dry period. This is surprising, considering that minor mastitis pathogens may constitute the majority of IMI in dairy herds during lactation (58, 60). Oliver (114) found that in the absence of antibiotic therapy at drying off, the number of quarters infected with minor pathogens decreased from late lactation to early involution and was lowest during the periparturient period. About 30% of minor pathogen IMI persisted from early involution to parturition. Conversely, the
number of quarters infected with major mastitis pathogens was lowest during late lactation, increased during the early dry period, and was highest at parturition. Thus, in this herd, there appeared to be an inverse relationship between major pathogen and minor pathogen IMI during the dry period.

The decrease in minor pathogen IMI during the dry period was associated primarily with a marked reduction in the prevalence of C. bosis. Forty-eight of 638 quarters were infected with C. bosis during late lactation, but only one C. bosis IMI was detected at parturition. During early lactation, number of C. bosis IMI increased markedly (114). Harmon et al. (58) reported that the rate of spontaneous elimination of C. bosis in quarters of cows not infused with antibiotics at drying off was approximately 50% and that antibiotic therapy at drying off eliminated 94 to 100% of C. bosis IMI, depending on the antibiotic used. Bramley (10) showed also that antibiotic dry cow therapy was effective in eliminating C. bosis IMI.

In the absence of antibiotic therapy at drying off, the number of quarters infected with coagulase-negative staphylococci increased markedly from drying off to parturition, then decreased during early lactation (114). Antibiotic therapy at drying off appears to be effective in reducing the prevalence of coagulase-negative staphylococci (58). A recent study by Matthews (85) showed that numerous species of coagulase-negative staphylococci were isolated from bovine mammary glands at drying off and during the periparturient period. The predominant staphylococcal species isolated were Staph. hyicus, Staph. bominis, and Staph. epidermidis.

The importance of minor mastitis pathogen IMI that occur during the dry period is unknown. During lactation, numbers of somatic cells in milk from quarters infected with C. bosis (18, 47) and coagulase-negative staphylococci (60) are elevated slightly in comparison with uninfected quarters but are significantly lower when compared with quarters infected by major pathogens. Thus, minor mastitis pathogen IMI during the dry period could impair mammary function and affect subsequent lactational performance. However, many minor pathogen IMI may be confined to the streak canal area and are eliminated after animals are exposed to the milking process. Oliver (114) indicated that a high proportion of coagulase-negative staphylococcal IMI detected at parturition did not persist into early lactation. Additional research is needed to determine effects of dry period minor pathogen infections on mammary function.

Some reports have suggested that minor pathogens may play an important role in the prevention of IMI by major pathogens. Lactating quarters infected with C. bosis or coagulase-negative staphylococci (7, 10, 12, 18, 74, 134) appeared to be more resistant to new IMI by major pathogens than uninfected quarters. Quarters infected with C. bosis were more resistant to induced Strep. dysgalactiae and Staph. aureus IMI than uninfected quarters (10, 17, 81, 129) but were not resistant to Strep. agalactiae (17, 129) and Strep. uberis (33, 122) experimental infection. Harmon and Langlois (60) indicated that 16.7% of quarters shedding Staph. hyicus became infected after inoculation with Staph. aureus, compared to 86.7% of uninfected quarters, which were inoculated similarly. All of these studies were conducted in lactating cows. Additional studies using non-lactating cows need to be undertaken to determine if minor pathogens are important in the prevention of major pathogen IMI during the dry period.

Pathogenesis of Mastitis

Intramammary infections occur when microorganisms gain entrance to the gland via the teat canal, colonize the duct system and alveoli, and cause an inflammatory response. The heightened susceptibility of the bovine mammary gland to mastitis during early involution (28) and perhaps colostrogenesis, may be related to the ease by which pathogens penetrate the teat canal. Temporary increases in intramammary pressure following cessation of milking and accumulation of colostrum just prior to parturition may cause shortening and dilation of the streak canal (110). Changes in the microscopic anatomy of the bovine teat canal revealed considerable dilation of the teat canal lumen after 1 wk dry (25). It was suggested that such dilation may facilitate the mobility of bacteria through the teat canal and into the teat cistern (25, 87, 161).

Tissues lining the teat and gland cistern were the first affected from by-products of bacterial
growth and metabolism (51, 52). Several recent cytological studies have investigated the defense mechanisms of bovine teat end tissues (25, 101, 104, 105). Morphometric analysis demonstrated a progressive increase in numbers of infiltrating leukocytes from the distal teat cistern to Fürstenburg's rosette (104). Plasma cells and lymphocytes were the most prevalent cell types penetrating the basal epithelium in the distal region of Fürstenberg's rosette. It was suggested that locally produced antibody in response to antigenic stimuli of the teat canal may act by inhibiting bacterial attachment to epithelial surfaces or neutralizing bacterial toxins (105). Elevated numbers of polymorphonuclear neutrophils (PMN) migrating into the distal teat end epithelium and in cisternal milk of Staph. aureus-infected quarters were implicated also in suppressing bacterial growth and inhibiting upward progression of bacteria toward delicate milk producing tissues (105). Cells infiltrating the epithelial lining and subepithelial stroma of Fürstenburg's rosette were more numerous in lactating cows compared to cows during the first 21 d of involution. Reduced numbers of infiltrating cells may contribute to enhanced susceptibility to mastitis during this time (104, 105).

Organisms that penetrate the teat end barrier and colonize the teat canal may serve as reservoirs for infecting secretory tissue. Mastitis pathogens spread initially to large ducts and alveolar areas in the lower part of the quarter and eventually become established in other areas of the gland (4). The rate at which infection spreads through the quarter is probably related to the organism's ability to multiply along epithelial surfaces of the teat end and the upward passage of bacteria through secretion via retrograde pressure caused by cow movement (4, 51, 63, 162). The ability of organisms to adhere and multiply increased from the teat cistern toward the gland cistern and large ducts (56). Staphylococcus aureus and Strep. agalactiae colonized better on ductal epithelium than other mastitis pathogens such as Strep. faecalis, E. coli, or C. bovis. Bacterial adherence to mammary epithelium may be an important aspect of pathogenesis, especially during lactation when quarters are flushed out periodically. Adherence probably plays a less important role in the establishment of mastitis caused by coliforms and streptococci other than Strep. agalactiae (3, 139) during the early dry and periparturient periods when the flushing action of the milking process ceases and IMI with these organisms are greatest (114).

Varying degrees of inflammation are associated with all types of mastitis (53, 76, 139). However, severity of the infection and pathological changes of mammary tissue are dependent on competence of natural defense mechanisms (30, 79), stage of lactation (11, 68, 69), and nature of the invading organism (2, 3, 47, 139).

The internal environment of the gland is often favorable to survival and multiplication of invading pathogenic bacteria. This is particularly true during the periparturient period when mammary secretions have low concentrations of antibacterial components (phagocytes and lactoferrin), but high concentrations of casein, lactose, and citrate, which can be utilized by invading bacteria for colonization and growth (6, 16, 61, 107, 153). Also, phagocytosis and intracellular bacteriolysis by PMN can be inhibited by the indiscriminate ingestion of fat and casein in mammary secretion (124, 137, 138).

In the early stages of infection in both lactating and involuted glands, mastitis-causing organisms release toxins and other by-products of metabolism that perpetuate an inflammatory reaction (53, 68, 76, 69). Agents that increase vascular permeability during the early stages of inflammation include histamine, serotonin, prostaglandins, and leukotrienes (57). Breakdown products of ruptured epithelium, bacteria, and leukocytes serve as chemotactic agents, which augment emigration of blood PMN into affected areas (76, 139). In infected glands, leukocyte numbers can increase to counts as high as millions per milliliter, but only after microbial populations have increased, causing tissue irritation and damage (4, 125, 139). Secretion composition of mastitic quarters changes considerably as a direct result of increased capillary permeability and passage of serum constituents from blood into milk (78, 100).

During lactation, increased immunoglobulin, ion (sodium and chloride), and trace mineral concentrations accompany the influx of leukocytes with concomitant decreases in concentrations of lactose, total protein, SNF, total
solids, Ca, P, and K (78, 100). As PMN migrate through connective tissues and across mammary epithelium into milk, the fluid portion of blood flows freely into affected tissue areas and may produce swelling or edema (92, 139). Serum factors may supplement antimicrobial proteins in secretion to dilute the irritant and neutralize any existing bacterial toxins while PMN reduce bacterial numbers via phagocytosis (30, 77). Plasma fibrinogen also escapes into milk and is converted to fibrin strands in the inflamed area (139). Fibrin entangles leukocytes, sloughed epithelial cells, bacteria, and other debris to form clots within milk spaces that can occlude ducts draining lobulo-alveolar tissue. Formation of clots leads to reduced secretory potential, milk stasis, and involution of the lobule drained by the obstructed duct (62, 139). The ability of PMN to eliminate the irritant influences the magnitude and duration of the inflammatory response. If bacterial multiplication is prevented, the inflammatory reaction subsides and clots are flushed out during milking (139). The gland returns to normal production within several days either by redeveloping secretory potential or by compensatory hypertrophy of remaining healthy tissue (62). Alternatively, if bacteria predominate, fibrin clots remain, leading to prolonged milk stasis and involution of infected areas until the next freshening. Depending on the severity of infection, secretory cells are destroyed and alveolar structures replaced by scar tissue (4, 139).

Morphological Aspects of Mastitis in the Periparturient Gland

Histopathological responses of lactating tissue to mastitis are well-documented in laboratory animals (2, 3, 21, 154) and to a lesser extent in dairy cattle (53, 54, 70). However, relatively little information is available describing response of mammary glands to bacterial infection during the periparturient period when parenchymal tissues are developing synthetic and secretory potential for the ensuing lactation.

Mastitis during the periparturient and early lactating periods is often due to staphylococcal or coliform infection. Boddie et al. (8) investigated the incidence of IMI and prevalence of udder microflora in dairy heifers from 11 mo of age, through freshening, and into lactation. They found that teat skin flora, teat duct colonization, and bacterial isolates from secretions were mostly staphylococcal species. Colonization of the teat skin with coagulase-negative staphylococci and Staph. aureus at an early age was shown to persist for 1 yr. Oliver and Mitchell (118) also found these organisms to predominate in foremilk samples prior to and at parturition in primigravid heifers. Histological examination demonstrated a chronic inflammatory response of both teat end and parenchymal tissues to staphylococcal colonization (8). It was suggested that marked leukocyte infiltration during the periparturient period may be detrimental to developing mammary parenchymal tissue (8).

Sordillo and Nickerson (155) described morphological changes occurring in the bovine mammary gland during involution and the interaction of IMI with involution and lactogenesis. As observed in the immature gland of heifers (8), infection status of quarters influenced greatly the mean number of leukocytes infiltrating into mammary parenchymal tissues of multiparous cows (Figure 2). During the last 2 wk of gestation, approximately 25% of quarters contained Staph. aureus, 7% coagulase-negative staphylococci, 5% C. bovis, 5% Nocardia, and 58% were bacteriologically negative. Compared with uninfected quarters, numbers of macrophages and PMN within the epithelial lining, alveolar lumen, and stroma of infected quarters were high during the last week of gestation. Presence of bacteria within the gland apparently evoked an inflammatory response that resulted in amplified migration of leukocytes from blood to milk in numbers that exceeded those associated normally with involution (Figure 2). Morphometric analysis of infected mammary tissue during lactogenesis demonstrated depressed synthetic and secretory activity as indicated by lower percentages of lumen, RER, and secretory vesicles but higher percentages of stroma and nonactive epithelium than in uninfected quarters (155).

Changes in secretion composition with respect to mastitis were examined from drying off through early lactation (153). Compared with uninfected quarters, infected quarters had higher SCC, especially during colostrogenesis and early lactation. Differences in numbers of
Figure 2. Infected bovine mammary tissue obtained 2 wk prior to parturition illustrating the possible sequence of events leading to epithelial cell damage during leukocyte migration into luminal spaces. A) Numerous leukocytes (L) containing lysosomal granules (LY) infiltrate the subepithelial stroma area (S). ×4187. B and C) Polymorphonuclear leukocytes (P), lymphocytes (LM), and macrophages (MC) containing internalized residual bodies (RB) penetrate between the basal plasma membrane of mammary epithelium (E) and the underlying basal lamina (arrows); F, fat; N, nucleus; S, stroma. ×4187 and ×4816. D) Leukocyte (L) observed proximal to epithelial cells (E), which are detached from the underlying basal lamina (arrows) and adjacent epithelial cells (arrow heads) S, stroma. ×4187. E) Leukocytes (L) penetrating through degenerate cell cytoplasm (D); Lu, lumen; S, stroma. ×4816. F) Damaged epithelium with a pyknotic nucleus (N), loss of the apical plasma membrane, and release of cytoplasmic components into the alveolar lumen (Lu); S, stroma. ×3600.
macrophages were not detected between quarters. However, uninfected quarters had higher percentages of lymphocytes but lower percentages of PMN than did infected quarters. In addition, infected quarters had lower percentages of fat and higher pH in secretions during early lactation compared with those of uninfected quarters. It was suggested that normal mammary function during lactogenesis was impaired due to damage of PMN infiltration or action of bacterial toxins on delicate secretory tissues (153, 155).

In support of this hypothesis, a significant negative relationship was shown to exist between SCC and milk production (91). During experimentally induced Staph. aureus mastitis, migration of PMN through secretory epithelium resulted in extensive morphologic damage (59). Capuco et al. (20) assessed damage to mammary tissue of lactating cows by normal PMN function also. They found increased N-acetyl-β-D-glucosaminidase released by mammary tissue and cytologic damage of epithelium in response to PMN function.

Heald (62) reported decreased milk production in cows experimentally infected with Staph. aureus, which later returned to near normal. He suggested that damaged alveoli redeveloped secretory potential or that compensatory hypertrophy of healthy tissues occurred. However, dairy cattle with IMI during the nonlactating period have been known to freshen with nonfunctional quarters (126) or produce less milk during the subsequent lactation (144). The presence of bacteria within the gland during the nonlactating period appears to have a deleterious effect on development of synthetic and secretory capability of mammary tissue. Limited data available suggest that infections during the periparturient period interfere irreversibly with normal mammary secretory cell differentiation necessary for optimal milk production.

Environmental pathogens, especially E. coli, have been implicated as major causes of mastitis during the early nonlactating and immediate prepartum period (40, 114, 152). Clinical E. coli mastitis is rare in nonlactating glands but is most severe during the first few weeks of lactation (35). Experimental IMI with E. coli during the nonlactating period resulted in spontaneous recovery if inoculated early in the dry period (88). Conversely, infections persisted and cows freshened with severe clinical mastitis when inoculated during the last 30 d of the dry period (88). Bramley (11) found that quarters infected with E. coli 2 d prior to calving produced clinical signs.

Disparities in establishment and severity of E. coli mastitis with respect to stage of lactation have been explained by rate of inflammatory changes in the gland during the initial stages of bacterial multiplication. A rapid and intense inflammatory response in lactating tissue occurred following infusion of endotoxin and, in most cases, bacteria were eliminated rapidly (55, 68). When the disease persisted, inflammation was observed primarily within the lower portions of the gland with extensive desquamation of epithelium lining the teat and gland cistern (51, 55) but only minor changes associated with secretory tissue (69). In contrast, quarters infected with E. coli during the immediate postpartum period had minimal PMN influx (53), which probably allowed unrestricted growth of the organism. Ultrastructural examination of secretory tissue demonstrated numerous bacteria within alveolar cells and in necrotic alveoli. There was extensive loss of epithelium lining the lactiferous sinus with exudation of interstitial fluids into the lumen.

Hyperacute E. coli mastitis in the postpartum period may be due to delayed diapedesis of PMN and a slow inflammatory response within the gland (5, 68). Frost and Brooker (52) examined the effects of endotoxin in the nonlactating mammary gland. They suggested that the susceptibility of ductular epithelium to endotoxins declined throughout lactation and was lowest in the dry period. Because the inflammatory response to endotoxin was mild, they concluded that the refractory nature of nonlactating tissue was due to profound changes in mammary physiology during involution. Although conjecture, severity of coliform mastitis during the periparturient period may be a result of two factors: 1) delayed PMN recruitment to the gland or 2) increased sensitivity of alveolar and ductular epithelium to endotoxin during the functional transition from involution to lactation. Ad-
dITIONAL research is needed to determine effects of IMI on mammary tissue development during the periparturient period.

Prevention of Intramammary Infections During the Periparturient Period

Many cows calve with IMI, and many infections present at parturition result in clinical mastitis during early lactation (32, 36, 40, 45, 71, 130, 152). Erb et al. (43) indicated that the incidence rate for mastitis per 100 cows at risk was approximately four times higher during the first 15 d after parturition than any subsequent 15-d period during lactation. The occurrence of clinical mastitis before peak milk yield altered the lactation curve and decreased peak yield and lactation length (83). Smith et al. (144) showed that the presence of IMI, either throughout the dry period or originating in the dry period, reduced milk yield after parturition. Relative to yield of equivalent uninfected quarters, the reduction was about 35%. Quarters infected during late lactation but uninfected at parturition produced about 11% less milk. Thus, IMI that occur during the dry and periparturient periods can cause marked economic losses and represent a significant problem to dairy producers.

Antibiotic therapy at drying off plays an important role in the control of bovine mastitis during the dry period and has been reviewed (13, 95, 96, 97, 131, 132). Dry cow therapy is particularly effective against streptococci and to a lesser extent against Staph. aureus (95, 128, 131, 166). However, Smith et al. (152) demonstrated that antibiotic therapy at drying off reduced the rate of new environmental streptococcal infection during the early dry period only and that the rate of new coliform IMI was not affected at all. Similar findings have been reported by Eberhart and Buckalew (40), Schultze (140), and Ward and Shultz (163). Thus, two significant limitations of present antibiotic formulations used for dry cow therapy are: 1) ineffectiveness against coliform bacteria, which can cause a high proportion of IMI during the early dry period and the periparturient period (40, 114, 152), and 2) ineffectiveness in preventing new IMI during the periparturient period when mammary glands are highly susceptible to new infection (37, 40, 114, 117, 121).

As Eberhart (37) pointed out, dry cow antibiotic preparations are formulated primarily to maintain persistent activity during the early dry period and most likely provide little protection during the periparturient period. Recently, Boyd et al. (9) and Oliver and Maki (116), using the Bacillus stearothermophilus disc assay to detect antibiotic residues, demonstrated that dry cow antibiotics persisted for 14 to 28 d after infusion, but some persisted for shorter periods. Thus, based upon present methods of formulation, it would appear that antibiotic preparations currently available for use in dry cows will not control IMI that occur during the periparturient period.

Recognizing limitations of current methods of mastitis control during the dry period, some investigators have attempted to control partum IMI by infusion of antibiotics near parturition. Pankey et al. (127) evaluated four dry cow treatment regimens: 1) infusion of a high persistency product at drying off and low persistency product 1 to 3 d prepartum, 2) infusion of a high persistency product at drying off, 3) infusion of a low persistency product 1 to 3 d prepartum, and 4) no infusion at drying off or near parturition. Infusion of antibiotics at drying off and near parturition appeared to be no more efficacious than infusion at drying off only. However, prepartum antibiotic administration eliminated >90% of new Strep. uberis IMI, but numbers of Strep. uberis IMI in the respective treatment groups were generally low.

Philpot (132) conducted a similar study except that cows were treated with antibiotics at parturition. Spontaneous cure rates in untreated quarters were 27% for staphylococci and 70% for streptococci. Reductions in number of quarters infected at parturition following therapy at drying off were 48% for staphylococci and 60% for streptococci. Cure rates following a single treatment at parturition were 20% for staphylococci and 60% for streptococci. Treatment at drying off reduced clinical mastitis from 25 to 11 cases during the first wk of lactation while treatment at parturition only reduced the number of clinical cases of mastitis from 25 to 17. Treatment at both drying off and calving reduced the incidence of clinical mastitis from 25 to 8.

Fox et al. (49) infused cows with antibiotics at drying off and following the first and second
milking after parturition. Percentage of cows with major mastitis pathogens at 24 to 40 d after parturition was similar for treated cows (30.3%) and untreated controls (28.5%). Bacteria causing IMI in this study were not mentioned. No differences in milk production between the two groups were detected. They (49) concluded that intramammary treatment of cows with antibiotics at parturition did not improve udder health.

On the basis of the few reports available, intramammary infusion of antibiotics near parturition may be worthwhile in herds experiencing an environmental mastitis problem. Previous reports have shown that mammary glands are highly susceptible to new streptococcal IMI during the periparturient period (37, 40, 114, 152), and several antibiotics appear to be effective in eliminating streptococcal infections (13, 34, 95, 96, 131). However, potential problems with antibiotic residues in milk need to be considered.

Recent studies have attempted to control new IMI during the dry period by application of germicidal teat dips to teats of dairy cows during the early dry period and 7 to 14 d prior to parturition. Matthews (85) indicated that the number of new IMI at parturition in quarters dipped with a latex teat dip with germicide was similar to undipped controls and suggested that there was no benefit to prepartum teat dipping. McArthur et al. (86) showed that there was no advantage in dipping teats of cows in a latex teat dip for the first and last 7 d of the dry period. Schultze (141) concluded, from a study where cows teats were dipped twice daily with an iodophor teat dip for at least 7 d before parturition, that there were no advantages to prepartum teat dipping with respect to incidence of new IMI at parturition, new infections that persisted for longer than 14 d after calving, or new infections that required antibiotic therapy. Schultze (141) suggested that prepartum teat dipping was not effective in the prevention of new IMI, because exposure of teats to bacteria emanating from the environment does not occur at a single point in time, but continuously, and that germicidal activity of teat dips decreases markedly shortly after application.

Perhaps the most encouraging data on the prevention of mastitis during the periparturient period are reports that have suggested a role of trace minerals and vitamins in resistance to mastitis. Smith et al. (147, 148) and Conrad and Smith (26) showed that supplementation of dairy cattle diets deficient in vitamin E and selenium improved udder health as evidenced by a reduction in quarters infected at parturition, a reduction in the duration of IMI, a reduction in the incidence of clinical mastitis, and lower average lactation SCC. Vitamin A and \( \beta \)-carotene also may be related to mastitis resistance during the early dry period and near parturition (23, 24, 31). However, a recent report by Oldham et al. (108) showed that supplementation of vitamin A or \( \beta \)-carotene during the last 2 wk of lactation, throughout the dry period, and for the first 6 wk of lactation did not reduce the incidence of new IMI or decrease number of somatic cells in milk during the trial period. Additional studies on the relationship between trace mineral and vitamin nutrition and resistance to mastitis are warranted. Such studies may lead to relatively simple procedures that will be effective in the control of mastitis during the dry period that could be incorporated easily into routine dry cow management practices.

**CONCLUSIONS**

The nonlactating period of the dairy cow poses several unique problems with respect to mastitis control. Susceptibility to mastitis is elevated during the early dry period and prior to parturition. Methods of prevention that may be effective during early involution may not be effective throughout the entire dry period. Furthermore, the mammary gland regresses during early involution. However, during the late dry period, several biochemical and ultrastructural changes occur as the mammary gland is differentiating and preparing for the impending lactation. Methods of mastitis control during the peripartum period that interfere with these processes could have a detrimental impact on subsequent lactational performance. Further studies are needed to elucidate procedures that are effective not only during early involution but also near parturition. Procedures need to be effective against a variety of mastitis pathogens, particularly environmental bacteria, if additional mastitis control is to be achieved.
ACKNOWLEDGMENTS

The authors express their appreciation to Gena Gritzner for clerical assistance.

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