Coliform mastitis in sows: A review

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Summary

Coliform mastitis (CM) represents an economically very important disease complex in sows that also affects the health, welfare, and performance of the piglets. Most research has concentrated on the husbandry-influenced occurrence of CM. The pathogenesis of CM suggests a prominent role for *Escherichia coli* and its endotoxins, although other *Enterobacteriaceae* species have been isolated from affected animals. Most studies on CM were conducted between 1970 and 1990. It is time for a closer look at this disease, particularly with respect to the economic damage it causes and the lack of recent literature. Treatment and use of body temperature as a single indicator for diagnosis of CM must be regarded critically. A combination of appropriate criteria should be applied to achieve a proper diagnosis and to minimize use of antibiotics. Additional approaches, for instance, incorporating knowledge concerning virulence factors of *E coli*, are promising tools for future prevention.

Keywords: swine, mastitis, dysgalactia, sow, endotoxins

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Resumen - Mastitis coliforme en hembras: Una revisión

La mastitis coliforme (CM por sus siglas en inglés) representa un complejo infeccioso económicamente muy importante en hembras afectando también la salud, el bienestar, y el desempeño de los lechones. La mayor parte de la investigación se ha concentrado en la ocurrencia de la CM influenciada por el manejo. La patogénesis de la CM sugiere un papel importante de la *Escherichia coli* y sus endotoxinas, aunque otras especies de *Enterobacteriaceae* se han aislado de animales afectados. La mayor parte de los estudios sobre la CM se realizaron entre 1970 y 1990. Es tiempo de revisar más de cerca esta enfermedad, particularmente con respecto al daño económico que causa y la falta de literatura reciente. El tratamiento y la utilización de la temperatura corporal como un indicador único para diagnosticar la CM deben tomarse con reserva. Enfoques adicionales, como por ejemplo, el conocimiento relacionado a los factores de virulencia de la *E coli*, son herramientas prometedoras para el futuro.

Résumé - Mammite à coliformes chez les truies: Une revue

Les mammites à coliformes (CM) représentent une pathologie économiquement très importante chez les truies et affectent également la santé, le bien-être, et les performances des porcelets. La majorité de la recherche a porté sur l'influence des pratiques de régie sur la fréquence des CM. La pathogénie de la CM suggère un rôle prépondérant pour *Escherichia coli* et l'endotoxine, bien que d'autres espèces d'*Enterobacteriaceae* aient été isolées d'animaux malades. La plupart des études sur CM ont été réalisées entre 1979 et 1990. Il est approprié de réexaminer cette maladie, particulièrement en ce qui a trait aux pertes économiques entraînées et au manque de publications récentes. Un regard critique doit être jeté sur le traitement et l'utilisation de la température corporelle comme seul indicateur pour le diagnostic de CM. Une combinaison de critères appropriés devraient être appliqués afin d'arriver à un diagnostic approprié et minimiser l'utilisation des antibiotiques. Des approches supplémentaires, par exemple, l'incorporation des connaissances sur les facteurs de virulence de *E coli*, sont des outils prometteurs pour une prévention future.

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Postparturient disorders represent an economically important disease complex in sows world-wide,[1] incurring losses due to reduced productivity and high mortality rates. These disorders are commonly categorized under the terms mastitis-metritis-agalactia (MMA) complex,[2] postpartum dysgalactia syndrome (PPDS or PDS),[3] and periparturient hypogalactia syndrome.[4] Miscellaneous other names, such as agalactia complex,[5] lactation failure,[6] agalactia toxemica,[7] or agalactia postpartum syndrome,[8] reflect the numerous etiologies involved in the pathophysiology of this disease that varies in its clinical presentation. All these terms summarize the characteristic syndrome of greatly reduced milk production within 12 to 48 hours postpartum, leading rapidly to piglet starvation. However, the name MMA complex is misleading, as metritis is found only occasionally in affected animals,[9,10] and instead of total agalactia, sows continue to produce milk at a reduced level. Still, MMA is the commonly used term in European countries, while PPDS or PDS have become widely accepted in English-speaking areas.[3,10]

Of the variety of conditions related to puerperal disorders in sows, mastitis is one of the central clinical signs, as shown by several studies.[9,11,12] Bacteria most commonly isolated from affected sows are coliforms, including the genera *Escherichia*, *Citrobacter*, *Enterobacter,* and *Klebsiella.*[11-15] The predominant role of these organisms in mastitis of sows has been demonstrated by several infection experiments.[11,16,17] Hence, to avoid the confusing terminology and to point out the parallels to coliform

mastitis in cows, the term coliform mastitis (CM) was suggested for peripartal mastitis in sows.[18] This review will concentrate on CM as an essential part of the puerperal disease complex and as a major cause of dysgalactia in sows. Most investigations into CM were carried out between 1970 and 1990, and the scarcity of recent studies is reflected in the reference list of this review.

As shown in Sweden, udder problems are the reason for culling up to 13% of sows,[19] but the main adverse economic effect of CM is high pre-weaning piglet mortality.[20] The piglets are totally reliant on the sow for access to colostrum and milk, and growth rate depends both on milk yield and composition.[21] By lying on their mammary glands, affected sows refuse piglets access to the teats. As a result of dysgalactia in combination with pain in the mammary gland, the sow fails to meet the needs of the piglets. Mortality and growth retardation in piglets are the result.[5,7] The first 3 days after birth are the most critical period for survival of piglets. As glycogen stores are very low in newborn piglets and glyconeogenesis is insufficient, hypoglycemia may be induced by the rapid decrease in glycogen in piglets with insufficient milk intake.[22] Inadequate colostrum intake results in deaths primarily due to starvation and hypothermia, but also because of inadequate transfer of maternal immunoglobulins to the piglet. Due to its energy and immunoglobulin content, a sufficient intake of colostrum is essential for healthy development of piglets. Inadequate colostrum intake is often followed by severe health problems, for instance, diarrhea, poor growth, and inanition.[23] Thus, CM creates animal welfare issues both for the sow and her piglets.

Even though infection is not transmitted through animal-animal contact, CM may become nearly epidemic in affected herds, with up to 80% of sows affected.[24] In other herds, it may be limited to a few animals and may be only sporadic. The incidence of CM at farm level is reported to vary from 0.5% to 60%[25] in Scandinavia and from 1.1% and 37.2%[26] in Illinois, but average incidence at herd level is approximately 13%.[8,26-30] Herds managed using totally different hygiene practices and standards may be affected;[10,13] CM even occurs on excellently managed farms with optimized disinfection practices.[15,31]

Pathological findings

In recent years, several attempts have been made to classify the wide variety of clinical syndromes affecting the sow's mammary gland diagnosed in the peripartal period, but no classification has become widely accepted. For example, classifications have been based on the number of affected glands, including uniglandular or multiglandular mastitis, or, with regard to duration and state of inflammation, mastitis has been subdivided into acute and chronic mastitis.[10] Systemic signs of disease, such as fever and anorexia, are widespread, often associated with constipation and depression.[32] The infected glands show typical signs of inflammation, such as severe edema and skin congestion. There may be acute induration of the mammary region, although edema without signs of acute mastitis can be found, especially in primiparous sows.[2,33] Caudal glands are reported to be more affected than cranial ones,[34] but in contrast, a more recent study detected no differences with regard to anatomic location.[15] Other pathological findings may include fever, constipation, vulvovaginal discharge, skin discoloration, and anorexia. Hematological findings comprise leucopenia or leucocytosis, a decrease in packed cell volume and hemoglobin concentration, and an increase in serum phosphorus concentration, while concentrations of serum calcium, magnesium, and glucose may decrease.[35]

A histological study by Swarbrick[36] revealed an accumulation of secretion in mammary glands of affected sows. These findings, and the fact that early initiation of lactation (up to 24 hours before parturition) might result in engorgement of the mammary gland, suggest that early lactation is a predisposing cause of CM.[37,38] Initiation of lactation is induced by a decline in plasma progesterone level,[39] which may appear earlier in sows with CM.[38] In contrast, a delayed decline in plasma progesterone level was reported by Liptrap[40] as a causative factor for development of clinical CM.

In piglets, reduction of milk intake causes various clinical signs. The greater tendency of the sow to lie in lateral recumbency, combined with the weakness of malnourished piglets, results in an increased incidence of crushing.[41] Total piglet mortality up to the age of 1 week in the litters of CM-affected sows varies from 5.0%[42] to 38.6%.[26]

In a study with 46 sows, the mammary secretion of sows that subsequently developed CM within 12 to 24 hours after farrowing contained significantly higher concentrations of lactose and significantly lower concentrations of protein and Na^+ compared to milk from unaffected sows, while the concentration of fat and K^+ was similar.[38] From these results, the authors of this study suggested an analysis of colostrum to identify sows predisposed to CM, to indicate affected glands, and to monitor recovery, but as this was not put into practice, there is a lack of further evidence for this theory.

Coliform mastitis is often followed by temporary or permanent infertility[43] caused by direct bacterial and inflammatory effects on the genital tract that prevent conception. A direct effect on the onset of the estrus cycle may not be important for development of later infertility.[44]

Diagnosis

Diagnosis of CM in commercial herds is based mainly on clinical signs. Hypogalactia within the first 3 days postpartum suggests CM.[1] Piglets make vigorous nursing efforts. Both the decrease in nursing intervals and the increase in piglets' activity derive from absent or reduced milk ejection.[1] The piglets' strenuous nursing efforts may cause traumatized teats. After exhaustion of their energy reserves, piglets often retreat to the warmest parts of the farrowing crate and decrease their attempts to nurse.[3] In sows, mammary glands may appear normal or pathologically altered, eg, swollen, firm, and warm to the touch. In addition, skin color may be changed.

After studying the relationship between elevated temperature and CM, Hermansson et al[8] proposed using postfarrowing rectal temperature to determine whether CM was likely to become a serious problem. This study,[8] comparing 71 sows affected with mastitis to 71 healthy sows, showed a significantly higher mean body temperature for the affected sows. The first trial to evaluate sow rectal temperature as a predictor of CM and to determine the specific time when the sow's temperature should be taken was conducted by Furniss.[20] This study suggested that a rectal temperature of 39.4°C occurring 12 to 18 hours after farrowing is an appropriate threshold at which to give preventive treatment. Today, the most common practice used to detect an

animal's risk of CM is to measure the rectal temperature postpartum. Besides abnormal temperature, criteria for the diagnosis of CM must include the combination of clinical mammary gland changes, diminished milk production, and reduced appetite.[45] The range of critical temperature values varies between 39.3°C and 40.5°C,[10] but physiological hyperthermia is often observed in postparturient sows, leading to misinterpretations.[3,15]

Body temperature is a nonspecific parameter indicating alterations of the physiological state of warm-blooded animals. Plasma concentrations of acute phase proteins such as α1-acid-glycoprotein and haptoglobin, which are components of the immune system, increase in stressful situations and can be used as indicators of acute CM.[46] Plasma concentrations of cortisol and 15-ketodihydroxy-PGF2α have also been suggested as inflammation indicators.[47] All of these parameters can vary substantially at the time of parturition,[48,49] and as collecting blood samples is much more laborious than measuring body temperature, use of such nonspecific indicators to diagnose CM is not feasible under field conditions.

Another attempt to diagnose puerperal diseases in sows at a very early stage was made by Petersen,[50] who suggested the combination of several urine parameters to diagnose bacteriuria. In a further study, it has been shown that analysis of urinary concentrations of minerals, especially potassium, in urine samples collected from sows in the morning and afternoon during mid-lactation provide an acceptable estimation of milk production.[51]

Baer and Bilki[35] investigated the use of ultrasonography for differentiating sows that had suffered recurrent CM from healthy animals. It was shown that with a linear array technique and a frequency of 8.5 MHz, affected mammary glands provide hyperechogenic images. Furthermore, this study supports the theory that abdominal glands are more prone to pathological changes than pectoral glands. The use of ultrasonography as a precautionary measure has not been integrated into herd management due to impractical handling and additional costs.

Rapid mastitis tests as applied to cows are not commercially available for sows. Diagnosis via cell count is not common and data on thresholds are rare. For instance, a threshold of 5×10^6 cells per mL was proposed by Bertschinger and Bühlmann,[52] while Persson et al[53] suggested 10×10^6 cells per mL. All parameters used to detect CM are summarized in Table 1.

Factors influencing clinical CM

The etiology of CM seems to be inconsistent and challenging. Indeed, the occurrence of the disease is multifactorial. The anatomy of the sow's mammary gland is different from that of the cow. Two complete gland systems end in two teat orifices per teat, without muscular sphincters.[3] The gland cisterns are not well-defined. During the last part of each gestation, mammogenesis recurs, which implies that new glandular tissue is produced. This results in a great ability of the sow to restore mammary health from one lactation to the next, although chronic lesions of the teat canal are usually irreversible.[57,58]

Coliform bacteria are ubiquitous, and, therefore, influence the factors that determine the development of infection in the single animal. Factors contributing to clinically apparent CM include the strongly related main issues of nutrition, housing microclimate, management in general, and aspects of hygiene in particular. The factors thus far associated with an increase in CM prevalence are summarized in Table 2.

Information about the influence of parity number on occurrence of CM is contradictory.[34,35,59] The normal length of gestation in sows varies between 113 and 117 days, and CM often occurs in sows with a gestation of > 116 days.[14] All factors contributing to prolonged duration of the birth process increase the prevalence of CM,[34,50,59] as does the concurrent occurrence of urinary tract infections.[43] Nutrition clearly impacts fertility at various points in the life of the sow. Several factors, such as imbalanced diet, lack of fiber, excessive feeding, and mycotoxins (ie, in moldy feed), must be taken into account.[32,62] Obstipation due to diet and inadequate water intake creates further risk of CM, probably by increasing the endogenous transfer of bacteria and endotoxins to the mammary gland.[10,63] The influence of nutrition on the hypothalamo-hypophysial-gonadal axis was evaluated in a review by Cosgrove and Foxcroft,[64] who emphasized the importance of appropriate nutritional management to support the endocrine system and its influence on lactogenesis.

Seasonal influences are largely eliminated by the circumstances of modern production.[65] However, high ambient temperatures may cause stress responses in sows, with a negative effect on reproductive performance. During lactation, high ambient temperature (> 27°C) may reduce voluntary food intake and enhance lactational weight loss.[44,66] This results in a contradiction for swine management in intensive piggeries: the ideal temperature for the sow to exploit her full lactation potential (< 24°C) is not the ideal temperature for her piglets (> 30°C).[57] The significance of these influences has been considered in management practices by providing heat lamps and other heating devices in the creep area.

Table 1: Reported parameters altered in sows with coliform mastitis (CM)

Parameter	CM sows	Literature cited
Body temperature	> 39.3°C	Hoy[54]
	> 39.5°C	Furniss[20]
	> 40.0°C	Kiss and Bilkei[55]
Milk production	Hypogalactia, dysgalactia, agalactia	Kiss and Bilkei[55]
Appetite	Diminished; moderate or total anorexia	Kiss and Bilkei[55]
Cell count	> 10^7/mL	Waldmann and Wendt[10]
Milk pH	> 6.7	Waldmann and Wendt[10]
Urine parameters	Bacteriuria and proteinuria	Petersen[50]
Interleukines	Increased IL-1ß, IL-6, IL8, and TNFα	Zhu et al[56]

Table 2: Non-infectious factors increasing the occurrence of coliform mastitis in sows

Factor	Literature cited
At individual level	
Sows of higher parity (> 4)	Baer and Bilkei[35]
Sows of lower parity (1,2)	Bostedt et al,[34] Hoy,[54] Krieter and Presuhn[27]
Long gestation (> 116 days)	Awad Masalmeh et al[14]
Long duration of birth (> 3 hours)	Bostedt et al[34]
Obstetric intervention	Bostedt et al[34]
Large litter size (> 11)	Bostedt et al[34]
Urinary tract infections	Berner,[59] Petersen[50]
Obstipation	Bostedt et al[34]
Genetic disposition	Awad Masalmeh et al[14]
At herd level	
Increasing herd size	Bäckström et al[26]
Smaller herd size	Ringarp[7]
Change of housing	Waldmann and Wendt[10]
New herds of gilts	Waldmann and Wendt[10]
Seasonal influences	Awad Masalmeh et al[14]
Lack of crude fiber in the ration	Plonait and Bickhart[60]
Rapid changes in nutrition	Plonait and Bickhart[60]
Single housing, lack of exercise	Hoy,[61] Ringarp[7]

Late introduction into the farrowing pen, ie, after the 110th day of gestation, is associated with an increase in CM prevalence.[32] Furthermore, a tendency towards a lower prevalence of CM with increasing herd size was observed.[7] In contrast to this, Bäckström et al[26] found a higher prevalence of CM with increasing herd size.

Bacteria and endotoxins causing CM

The causative agents of CM and their role in pathogenesis have been discussed controversially, as many different bacterial species have been isolated from the milk of clinically diseased animals,[14,68] including mainly coliform bacteria (*Escherichia coli* and other lactose-splitting bacteria), but also *Streptococci*, *Staphylococci*, *Pseudomonas* species, and *Corynebacterium* species. One problem regarding the presence of different bacterial species in the milk of affected animals is the use of inadequate methods for identification.

Three main routes of infection for CM are proposed: the gut and uterus (endogenous) and the mammary gland (exogenous). The infectious dose for colonization of the mammary gland is extremely low at < 100 organisms.[49,51] Causative bacteria are located free in the milk or in phagocytic cells in the ductular and alveolar lumina and are often isolated from regional lymph nodes.[11,69,70] In a study comparing the bacterial flora of the uterus, the cecum, the ileum, and the mammary gland in order to identify a likely source of endotoxin absorption, the prevalence of only gram-negative bacteria in the mammary glands and in the ileum of CM-affected sows was remarkable.[71] The lack of gram-negative bacterial culture growth in uterine samples supports the theory that uterine involvement in CM is of minor importance, as has been suggested.[69,72,73]

The hypothesis of a galactogenous route of infection via the teat duct is supported by experiments carried out by Bertschinger et al[16] and Bertschinger et al,[74] who found a lower prevalence of CM when the mammary gland was protected against fecal contamination. Due to repeated sampling, the time of infection could be determined in this experimental setting. More than 50% of mammary glands were infected before parturition, but no new infections appeared before the 108th day of gestation.[16] New infections were limited to the first 2 days after farrowing. This was explained by the established teat preference of the piglets and suckling at regular intervals of three-quarters of an hour.[16]

All isolated gram-negative bacteria are common in the sow's environment, depending on a combination of circumstances. For instance, the use of wood shavings as bedding material leads to an increased occurrence of pathogenic *Klebsiella pneumoniae,*[75] that might end in more infections of the mammary glands of the sows due to a high contamination rate in the material. The origin of bacteria in the environment may be related to the excretion of urine and feces by the sows. In this context, it is notable that infections of the urinary tract are strongly related to puerperal diseases, even though urinary infections are not apparent clinically.[76] The most common organism associated with bacteriuria and vulval discharge was found to be *E coli*.[77]

The mammary gland as a source of gram-negative bacteria was first described by Elmore et al[78] and Jones.[79] The predominant role of coliform bacteria in pathogenesis was clearly shown by Wegmann et al;[12] both *E coli* and *K pneumoniae* were isolated from 79% of 131 mammary complexes of CM-affected sows. In a study with 663 sows suffering recurrent CM, bacterial culture of mammary glands showing gross pathological changes revealed the presence of mainly *E coli* and *Klebsiella* species, but also *Clostridium* species, *Actinobaculum suis*, *Pseudomonas aeruginosa*, *Proteus* species, gram-positive streptococci (especially *Enterococci* and *Streptococcus faecalis*), staphylococci (*Staphylococcus albus*, *Staphylococcus epidermis*, *Staphylococcus aureus*), and *Erysipelothrix rhusiopathiae*.[35]

The prominent role of *E coli* in mastitis has been emphasized in several studies.[11,12,69,70] Bacteriological examinations of milk and udder biopsies and necropsy material from sows with CM have indicated that *E coli* is the causative pathogen for agalactia in the majority of cases.[80,81] Typically, peripartum mastitis caused by *E coli* is acute,[26] but postparturient mastitis

has also been described in sows lacking signs of clinical CM.[81] *Escherichia coli* or *K pneumoniae* mastitis experimentally induced in sows provokes clinical and hematological changes comparable to natural infections.[70,82] The extensive interplay between pathogen and host can cause different clinical syndromes. While some sows develop clinical signs of CM after inoculation of the mammary glands with *E coli*, others remain unaffected.[83] A large study of 39 pairs of full siblings (Swedish Landrace × Swedish Yorkshire) over six parities demonstrated that less than half of the mammary glands with CM (diagnosed by milk bacteriology and cytology) showed clinically detectable mastitis.[84]

Nevertheless, the involvement of defined *E coli* strains and the occurrence of certain virulence determinants such as shigatoxins remain ambiguous with regard to the development of clinical appearance.[80] A wide variety of *E coli* serotypes have been substantiated in mastitic sows' milk in previous studies.[14,69] Bostedt et al [34] found a high percentage of antibiotic-resistant *E coli* in cervical swabs from sows with CM: the isolated strains were 100% sensitive only to gentamicin. Sensitivity to all other tested antibiotics was < 100%.

The findings of Pedersen Mörner et al[80] support the theory of a galactogenous route of infection. Serological homogeneity was found in *E coli* isolates from the same teats at different times during a lactation, while heterogeneity was encountered for different teats in the same sampling. On the basis of current knowledge, this may be interpreted as mastitis in sows being caused by several *E coli* strains harboring virulence factors which are as yet unknown. Indeed, recent genome-sequencing studies of various *E coli* strains have determined a core genome of only 30% harbored by all these strains, making this possibility a challenging concept.[85]

Lipopolysaccharide (LPS) endotoxins, present in all gram-negative bacteria, play a major role in the etiology of CM.[78] Like bacteria, endotoxins enter via the uterus, gut, and mammary gland. The systemic clinical signs elicited by endotoxin release are complex, as various endogenous mediators are involved in pathogenesis. The relevance of *E coli* endotoxins initiating complex reactions in the animal organism has been proven previously.[86,87] The administration of coliform endotoxins via intravenous, intramammary, intrauterine, or subcutaneous application causes clinical and blood chemical changes similar to those in natural CM cases.[73,78,88] For instance, subnormal serum concentrations of Ca^{++}, Zn^{++}, and iron are a clear indication of endotoxin exposure,[89] as is a rise in serum cortisol levels.[90] Furthermore, secretion of colostrum and milk depends on the complex and well-balanced interaction of a series of different hormones. These complex balances can be easily disturbed when LPS suppresses the release of prolactin by the anterior pituitary, increasing cortisol concentrations and decreasing circulating thyroid hormone.[91] Production and secretion of milk are affected adversely by these changes.

Immune response and innate immunity

To a large extent, the outbreak of disease is determined by the interaction between the invading microorganism and the host's immune system. Clinical signs of CM are most often seen in the first 24 hours after parturition, indicating a strong connection to the postpartum period. In an experimental setting, Magnusson et al[86] found that the time of inoculation of bacteria into the mammary gland influenced the development of disease: clinical signs were seen in sows infected 48 hours, but not 96 hours, before parturition. Furthermore, the number of circulating polymorphonuclear neutrophils was higher in sows that were more prone to develop disease. Whether this fact can be related to the presence of other microorganisms was not defined, but all sows had been diagnosed as healthy at the beginning of the infection trial.[86] Possibly, an exaggerated response to bacterial infections, causing tissue injury, aggravates clinical signs.[86] Moreover, lysozyme, an enzyme that non-specifically stimulates the phagocytic activity of leucocytes and the level of immunoglobulins, was present in high concentrations in sows from herds of low CM prevalence.[92] After experimental inoculation of *E coli* (0.5 mL of bacterial suspension per teat, 10^5 colony forming units per mL), Österlundh et al[49] showed no significant differences in functional capacities of granulocytes in sows affected and non-affected by CM.

After inoculation of 12 sows with *E coli* by the intramammary route (0.5 mL of bacterial suspension per teat, 10^5 colony forming units per mL), Zhu et al[93] detected an increase in proinflammatory cytokines. The mammary glands appeared capable of producing IL-1ß, IL-6, IL-8, and TNF-α, and the authors concluded that local cytokine mRNA expression differs between mammary glands of sows that do or do not develop clinical signs of mastitis. Especially TNF-α is considered to be a useful indicator to monitor the severity and course of CM.[56,94,95] Löving and Magnusson[96] showed a significantly higher density of $CD4^+$ and $CD8^+$ cells in animals developing clinical mastitis compared to those without clinical disease, supporting the theory that massive inflammatory reactions are triggered by endotoxins. In addition, in the study by Löving and Magnusson,[96] sows developing clinical disease had a lower density of MHC class II^+ cells. This down-regulation may be related to the adverse effects of LPS. Therefore, the authors postulated that the outcome of mammary infection was related to sensitivity to LPS rather than to an ineffective immune response.[96]

Furthermore, the immune response is modified both by cortisol and estrogen affecting resistance to infection,[97] and both hormones vary considerably in their concentrations at the time of parturition. Resistance to infection in swine is also influenced by sex hormones.[48,98] However, in another study by Magnusson et al,[86] a difference in concentration of these hormones could not be identified in sows with and without CM, suggesting that development of mastitis in sows before parturition is not modulated by cortisol and estrogen.

Treatment

After diagnosis of CM, antibiotic treatment must be started as soon as possible to reduce the negative effects on both the sow and the piglets. Antibiotics are often administered immediately after diagnosis to shorten the time period of undernutrition for the piglets, but antimicrobial susceptibility is not tested. Therefore, the use of broad-spectrum antimicrobials administered parenterally, for example amoxicillin,[99] tylosin,[10] or potentiated sulphonamides,[10] is indicated. Antibiotics must reach effective levels in the mammary gland; consequently, pharmacokinetics have to be considered. Another antibiotic showing a concentration in colostrum and milk explicitly above its minimum inhibitory concentration is enrofloxacin.[100] In several studies, its use as a highly efficient antibiotic given orally at

2.5 mg per kg body weight twice a day is recommended.[32,101,102] In a study[9] on the therapeutic performance of the cephalosporin cefquinom, this antibiotic, injected intramuscularly at 2 mg per kg body weight every 24 hours for 3 days was more efficient than the control drug, amoxicillin.

In order to reduce inflammatory reactions, therapy with non-steroidal anti-inflammatory drugs (NSAIDs), especially meloxicam at 0.4 mg per kg body weight per sow in a single injection, has become popular in recent years.[13,103] The advantages of this treatment are better recovery rates and reduced piglet weight losses.[103] Use of flunixin meglumine combined with enrofloxacin achieved no advantages compared to use of enrofloxacin alone.[104] Occasionally, oxytocin (10 IU), injected five times at 2- to 3-hour intervals, can initiate milk production.[10] However, as routine use of oxytocin is associated with poorer herd performance,[105] overuse should be avoided.

The effect of prostaglandin F2α (PGF2α) injection is controversial. In some herds, the risk for periparturient disorders was minimized,[35] while in others, no effect could be proven.[106,107] As prostaglandin F2α has its main impact on uterine debris postpartum, administration in cases of CM is not indicated. As proposed by Kirkwood,[108] in the absence of vulval discharge, PGF2α does not improve sow and litter performance. An alternative attempt to treat CM with bee venom was proposed by Choi and Kang.[109] Animals treated with apitherapy showed significantly shorter periods of abnormal milk secretion (clots, blood traces, or discoloration) compared to animals receiving antibiotic treatment with penicillin G at 400,000 IU per animal.

Besides treatment of sows, all economically reasonable efforts to save the piglets should be attempted. To save the litter, piglets may be cross-fostered or fed milk replacer.[3]

From the very first recognition of CM as a problem in sows, there have been various efforts to reduce prevalence of CM by a considerable number of measures. Nutrition management is proposed as a useful tool to minimize the risk of CM.[110] High-fiber diets in late gestation have been used to decrease the occurrence of early lactation problems, but it is unclear whether fiber addition or resultant protein dilution in the feed ration is the cause of a lower prevalence of CM.[3] Feed reduction before parturition is a widespread practice and might reduce not only obstipation, but also the amount of feces produced. Consequently, the exposure of the teats to contamination is reduced, and CM risk decreases as well.[3] On the day before and after farrowing, provision of ad libitum drinking water is recommended.[10] Supplementation with lactulose as a prebiotic in periparturient sows results in better sow and piglet performance.[63] Other measures to avoid obstipation are feeding of linseed and other laxatives and adequate exercise for the sow.[63,111] Good hygiene practice with all-in, all-out management, adequate temperatures in the farrowing houses, and introduction of sows to clean farrowing houses 10 to 14 days prior to farrowing are management factors that should be taken into account.[112] Manual interventions, eg, manual obstetrics in the peripartal period, should be reduced to a minimum. Nevertheless, neither this nor other management practices are able to totally prevent CM. Identification and reduction of risk factors, combined with excellent hygiene management, are the only ways to cope with a herd problem in the long term.[54]

Nonspecific paramunity inducers, like an immunostimulator containing inactivated *Parapovirus ovis* (Bayer AG, Leverkusen, Germany), were proved to have positive effects on sows affected by CM.[109] However, after natural infection, mammary glands did not develop resistance to subsequent infections.[52] Therefore, the effect of vaccines against *E coli* with regard to CM can be doubted. Furthermore, there must be strict adherence to subcutaneous injection of the vaccine, as the same dose administered via intramuscular or intravenous injection may cause severe endotoxemia.[18,47] While vaccines against infections with enterotoxigenic *E coli* in piglets are commercially available and show positive effects,[113] the current knowledge about pathogen-host-interactions in CM is still too limited to develop useful prevention tools.

Conclusion and future approaches

Commercial sow lines from pig breeding companies are continuously being improved in their reproductive capabilities, with large litters and high-milk-producing potential, and pigs are therefore exposed to a physiologically extreme situation during and soon after birth. Although severe forms of CM are rare, piglet mortality and failure to gain weight contribute to the outstanding economic relevance of this disease complex. The demands for sufficient growth rate of suckling piglets and greater litter size puts pressure on the lactating sow. The transition from gestation to lactation is of paramount importance to sufficient milk yield and prevalence of CM during that period. High piglet mortality, poor growth of suckling piglets, and poor average weaning weights can be prevented only when CM is approached in a holistic way.

The current method to deal with postparturient disorders includes immediate antibiotic treatment of sows if body temperature is above a defined threshold. This threshold is defined rather subjectively and the use of it might be regarded critically, since increases and decreases in body temperature may be physiological. To minimize the administration of antibiotics, it is therefore essential to diagnose CM and PPDS not only by temperature increase, but also by a combination of appropriate criteria. A threshold of 39.5°C in the time frame 12 to 24 hours postpartum is recommended to avoid confusion of fever with physiological hyperthermia.[15]

Prevention is the best way to cope with CM in a population, but is difficult to accomplish, as the etiology of CM is extremely variable. At the current state of knowledge, the reason for only some sows developing clinical signs of infection after contact with ubiquitous bacteria remains unknown. The immune response and the development of clinical signs seem to depend on the immunological reactivity of the sow. Hence, one may hypothesize that developing clinical CM is largely dependant on the individual resistance of the sow. Immune competence, including resistance to infections, is genetically determined.[114,115] The heritability for CM resistance is approximately 10%.[116,117] As shown by Heringstad et al[118,119] for mastitis resistance in dairy cattle, it is possible to achieve a sustainable selection response for disease traits of low heritability. Thus, the analyzed heritabilities for CM resistance indicate the opportunity to use this trait for selection.[116,117] In pig production, genetic disease resistance, particularly resistance against certain *E coli*, is applied as a breeding tool in the United States, Canada, Denmark, and Switzerland. Since infectious organisms evolve resistance against drugs used to control them, as shown for

pathogens that cause CM,[120] and since the costs of treatment and veterinary care are increasing faster than the value of animals, breeding for enhanced disease resistance offers a number of advantages over other control measures. Additionally, on the basis of the current knowledge of *E coli* strains involved in CM, no common virulence factor has been identified. To discover this genetic component in the involved *E coli* strains and other bacterial species is an immense challenge for further research, as are the scientific questions relating to CM in general.

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