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Whereas the management of acute mastitis seems clear, there is little scientific evidence to support management of chronic mastitis/breast pain. This article reviews bacteriological findings, their possible meanings, and their use in clinical settings. Clinical experience, newer and more accurate microbiological techniques, and the growing knowledge about our metagenome have many insights to offer.

Keywords: mastitis, chronic breast pain, lactational mastalgia, antibiotics, probiotics

Chronic mastitis is also known as chronic breast pain, deep breast pain, or chronic breast inflammation. However, there is no clear definition of any of these terms. Generally, in lactation literature, chronic mastitis refers to a lasting breast pain with no evidence of acute inflammation, such as erythema, warmth, or induration. The pain is described in various ways, often as deep, shooting pain, or burning sensation in one or both breasts that may happen during or between feeds. It may, or may not, be associated with nipple pain or nipple wounds (Betzold, 2007; Eglash, Plane, & Mundt, 2006; Witt, Mason, Burgess, Flocke, & Zyzanski, 2014). For simplicity, in this article, we will refer to this group of symptoms as lactational mastalgia (the suffix-itis in mastitis implies inflammation or infection; mastalgia is the medical term for breast pain). The broad spectrum of symptoms makes it likely that lactational mastalgia is not one single entity but a group of diverse conditions with diverse etiologies and with varying clinical manifestations.

Mastalgia is also found in nonlactating women, the pain described as "drawing," "burning," "achy," and "sore" (Smith, Pruthi, & Fitzpatrick, 2004). Therefore, the cause of mastalgia cannot be always ascribed to breastfeeding difficulties, which makes the etiology of the pain even more difficult to establish.

Management of Lactational Mastalgia

The most frequent cause of lactational mastalgia in breastfeeding women seems to be milk stasis or inadequate draining of the breast (Betzold, 2007; World Health Organization [WHO], 2000). This may be because of latch difficulties of diverse origins such as anatomical problems of mother's nipple and/or breast and anatomical or functional difficulties in the baby's latch/

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sucking ability. Other factors resulting in poor draining include rapid weaning, oversupply, blocked ducts, missed feedings, external mechanical pressure on the breast, or incorrect hand/pump draining technique. Mastalgia may relate to the relative diameter of the milk ducts: the wider the ducts, the more severe the pain, as has been seen in ultrasound studies (Walker, 2010).

Several studies and clinical observations make us suspect other etiologies of lactational mastalgia, which may be a cause on their own or may be contributing to the milk stasis. These may include referred pain caused by nipple trauma secondary to an inadequate latch (Amir et al., 2013; Ellis, 1993; Hopkinson, 1992), musculoskeletal (pectoral/cervical thoracic muscle contraction secondary to strain, fear of painful latch, or unergonomic breastfeeding positions; Kernerman & Park, 2014; Thorley, 2005), or emotional in origin as also occurring in nonbreastfeeding women (Colegrave, Holcombe, & Salmon, 2001).

This pain requires thorough evaluation, a close observation and follow-up, and emotional support by a board-certified lactation consultant. Regardless of the presumed etiology, the basic treatment is consistent: effective milk drainage, breastfeeding support, and comfort measures for the mother (Betzold, 2007). While maintaining these three key interventions, the clinician can then address the etiological issues suspected (Table 1). A detailed history, evaluation of both mother and baby, and observation of a feed are necessary to unravel the cause/causes of lactational mastalgia in each dyad.

Breast Pain, Candida and Bacteria: The Microbiological Debate

For many years, the main hypothesis was that lactational mastalgia is caused by *Candida albicans*, although recent studies on this issue show conflicting results. In a systematic review of seven studies of women with deep

Table 1. Management of Lactational Mastalgia^a

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Basic management: Maintain while working on the etiological issues.

- 1. Frequent, regular, and efficient drainage of the breast (baby, hand, or pump)
- Aim for 8–12 adequate feeds/expressions per 24 hours. Permit 3–4-hour stretch of sleep once per 24 hours.
- 2. Support and encouragement
- 3. Comfort measures (warmth, massage, analgesia)

Suspected Etiology	Action to Take as IBCLC	Referral
Inadequate draining of breast	Correct latch/position.	
	Correct infant anatomical/ functional difficulties.	Refer to MD, CST, OT or other specialist you consider the infant to need
	Correct milk expression technique.	
Referred pain from nipple trauma	Correct cause of nipple trauma.	
Muscular/skeletal problems	Correct unergonomic breastfeeding positions.	If not enough, Refer mother to physical therapist
Thoracic constriction-like symptoms	Pectoral muscle stretches	If not enough, Refer mother to physical therapist
Infectious origin	Milk culture	If positive, refer to MD for antibiotic/antifungal treatment.
Vasospasm	Comfort measures, correct latch.	If not enough, refer to MD for nifedipine.
Emotional issues	Support, counseling, Omega 3, sunlight, exercise	If not enough, refer to mental health specialist.
Mastodynia (hormonal related mastalgia)	Inform woman. Support	
Multifactorial	Take all actions needed.	
	Can try alternative ideas (acupuncture, probiotics, homeopathy, etc.)	
You are unsure		Refer to another IBCLC.
Medical issues (costochondritis, necrotizing fasciitis, breast cancer, etc.)		Refer to MD with your suspicions.

Note. $MD = medical \ doctor; \ CST = craneosacral \ therapist; \ OT = occupational \ therapist.$

^aBetzold, 2007; Kendall-Tackett, 2007; Kernerman & Park, 2014; Strong & Mele, 2013; Thorley, 2005.

breast pain, Betzold (2012) concluded that evidence points to an infectious origin, either by *C. albicans* or *Staphylococcus aureus*.

latest studies, which use more modern techniques, find no trace of C. *albicans* in human milk (Hale, Bateman, Finkelman, & Berens, 2009; Jiménez et al., 2015).
Clearly, further research is required to ascertain if C. *albicans* can be responsible for some cases of lactational mastalgia.

candidiasis (Amir et al., 2013; Eglash et al., 2006). The

A few small studies have demonstrated that the milk cultures among women with lactational mastalgia are more likely to reveal bacterial pathogens than Delgado et al. (2009) propose that disruption in the normal bacterial flora balance in breast milk could lead to coagulase-negative staphylococci (CNS; mainly *Staphylococcus epidermidis*) overgrowth, and this overgrowth would be the cause of lactational mastalgia. This theory, however, has not been confirmed by other studies.

In a prospective, descriptive case control study, Witt, Mason, et al. (2014) detected a significant elevation of S. aureus in the subjects group (breastfeeding mothers with chronic mastalgia) as compared to the control group (asymptomatic breastfeeding mothers). Both the cases and the controls had similar levels of CNS. The authors point out that, in the case group, the higher the count of S. aureus in a mother, the lower her CNS and vice versa. "This inverse relationship between S. aureus and CNS growth," the authors conclude, "does not support a pathogenic role for coagulase-negative staphylococci." The results do support, however, a pathogenic role of S. aureus in chronic mastalgia, as other studies have (Eglash et al., 2006; Kvist, Larsson, Hall-Lord, Steen, & Schalén, 2008). Therefore, the current hypothesis is that S. epidermidis may be normal, health-promoting flora in the mammary microbiota. In his 2003 paper, Heikkilä and Saris (2003) observed that commensal milk bacteria (mainly S. epidermidis, Streptococcus salivarius, and Streptococcus mitis according to his study) have the capacity to suppress or diminish S. aureus growth. He also affirms that lactobacilli have an antimicrobial role, although only 10% of milk isolates had these bacteria. Therefore, CNS are the most abundant antimicrobials in breast milk.

More recently, Altuntas (2015) isolated, characterized, and evaluated the antimicrobial effect of *S. epidermidis* strains from different human milk samples. He observed that *S. epidermidis* has much activity against *E. coli* and Listeria *monocytogenes*. He also observed that all strains of *S. epidermidis* are active against *S. aureus*. Finally, he observed that, although probiotic microorganisms have antimicrobial activity, they were scarce in the human milk samples he studied.

Therefore, according to current available information, the most frequent cause of infectious lactational mastalgia seems to be *S. aureus*. There is doubt about *C. albicans* being a cause of lactational mastalgia, and it seems that CNS may play a protecting role and not a pathological one.

Based on these findings, several questions arise for the clinician. Should the milk of women with lactational mastalgia be cultured? If so, when? How should the results be interpreted? And what treatment should be implemented?

When to Culture Milk Samples

There are no current evidence-based guidelines to answer this question. The information available from cited authors (Betzold, 2012; Eglash et al., 2006; Witt, Burgess, Hawn, & Zyzanski, 2014; Witt, Mason, et al., 2014) suggests that cultures should be taken from women with lactational mastalgia who do not respond to conservative treatment (good lactation management and support, comfort measures).

How to Interpret Culture Results

We also have no evidence-based guidelines as to how to interpret milk culture results from women with lactational mastalgia. Existing guidelines are used by milk banks to screen for contamination of donated milk. An option for clinicians assisting mothers with lactational mastalgia is to use one of these guidelines as a baseline in interpreting culture results. For example, the National Institute for Health and Care Excellence clinical guideline CG93 Donor milk banks: Service operation revised in 2014 (National Institute for Health and Care Excellence, 2010) states that pooled donated milk is considered contaminated if the colony forming unit (CFU) counts are above 100,000 CFU/ml of total microorganisms, 10,000 CFU/ml of Enterobacteriaceae, or 10,000 CFU/ml of S. aureus. In Witt, Burgess, et al.'s (2014) study, all cases with S. aureus and pain had more than 10,000 CFU/ml. However, one mother in the control group had a higher count of S. aureus and was asymptomatic. Other studies confirm that many healthy breastfeeding women have potentially pathogenic bacteria in their breast milk and remain asymptomatic (Hunt et al., 2011; Kvist et al., 2008).

How to Treat When Infectious Lactational Mastalgia is Suspected

It seems logical, while we await for further evidence on this issue, to act on microbiological results according to women's clinical symptoms and evolution, with a close follow-up to help detect those in need of antibiotics. In these cases, oral antibiotics matched to breast milk culture may significantly decrease pain and is not associated with increased complications (Kvist et al., 2008; Witt, Burgess, et al., 2014).

Probiotics for Lactational Mastalgia

The global market for probiotics has risen vertiginously over the last decade (Transparency Market Research, 2015). In some European countries, the market for probiotics for breastfeeding women is now on the rise. The proposed use for these products is treatment of breast pain and prevention of mastitis, as can be seen in product web pages (see product web page in reference list). However, when reviewing the use of probiotics for the treatment of lactational mastalgia, we find no clear evidence in the only published study (Arroyo et al., 2010). In this article, 352 women with "breast inflammation and pain during breastfeeding" (termed subacute/subclinical mastitis by the authors) were studied. The women were divided into three groups: two for probiotic and one for antibiotic. At the end of the 21-day intervention, the women in the probiotic groups had less pain. However, the study is not blind and the clinical design of the study is unclear. There is no control in the study for other factors that might have affected the results, such as breastfeeding support received by the mothers during those 21 days. Also, some of the mothers in the antibiotic group were not receiving adequate antibiotics for S. aureus. Finally, the authors disclose that some of the funds for this study came from noncode compliant industries as part of the FUN C FOOD group (Consolider Fun C Food, 2010), so it is not clearly an independent study.

At this time, there is not enough evidence to support the use of probiotics in the management of mastitis or breast pain. More studies are required. As we have discussed, levels of lactobacilli do not seem to be naturally high in breast milk. In a very recent study, a Spanish group confirmed, with a very sensitive technique, a low presence of lactobacilli and bifidobacteria in a group of 20 women (Jiménez et al., 2015). The implications of artificially rising these levels by giving oral probiotics have to be carefully considered.

Conclusion: The Need to Learn More

Our main difficulty arises from our lack of knowledge about normal human milk microbiota. In a fascinating study, Hunt et al. (2011) characterized the diversity and temporal stability of bacterial communities in human milk. Her group used a newer technique (based on pyrosequencing of the 16S ribosomal RNA gene) than had previously been used. They studied milk samples collected at three time points over a 4-week interval from 16 asymptomatic breastfeeding women. They found a much greater diversity of bacteria than what had been previously reported.

They write that, as in other studies, the most frequent phylotypes are *Streptococcus* and *Staphylococcus*, and they also find *Serratia* and *Propionibacterium*. They state that "conversely, whereas previous work has identified Lactobacillus and Bifidobacteria as common, but minor members (2%–3% relative abundance) of milk microbiota, very few sequences from these phylotypes were observed in our samples" (p. 2). These conflicting findings may be because of genetic, cultural, or environmental differences in the women that were studied.

If we take a look at Figure 1, where Hunt's main results are shown, we can observe the great diversity and intrapersonal and interpersonal variability of the 15 main bacterial genre of these 16 mothers. Similar results can be seen in the Jimenez et al. (2015) study, to an even greater extent because these authors do a metagenomic study and find not only bacterial DNA but also the genomes of archaea, virus, fungi, and protozoa.

Hunt et al. (2011) reflect on the origin of the bacteria, because a great part of the Streptococcus and other genre such as Rothia are abundant in infant saliva. We know that when a child breastfeeds, there is a retrograde flow of saliva into the breast (Ramsay, Kent, Owens, & Hartmann, 2004). How does frequent milk removal change mother's microbiota? Why are some microbes pathogenic for some mothers but not for others? Does the child's microbiota regulate the mother's and in what way? What do the changes we observe in each mother's microbiota mean? Is the mother protecting the child or vice versa? Why do some mothers have a changing microbiota, whereas others have a stable one? Would we see the same variability or stability in their babies' saliva microbiota? Are we looking at a response to the environment or to changes in mother or baby's immunological state? These questions raise fascinating speculation.

Following these studies, Sam Ma and his group of bioinformaticists and medical ecologists (Sam Ma et al., 2014) used Hunt et al.'s (2011) information and studied, for the first time, the bacterial interactions within human milk using network analysis to visualize multivariate relationships. They describe two disconnected subnetworks, with diverse cooperation and inhibition relationships. It is a complex article but the conclusions are clear: the dynamic balance of human milk depends on the interaction of its different components, and of this system with the mother as a whole: her genetic, immunological, physiological, and demographic characteristics and the interaction with her infant's microbiome. We have much still to discover.

Citing Ward, Hosid, Ioshikhes, and Altosaar (2013, p. 10), "Perhaps, it is the diversity and/or sequences of DNA within the milk metagenome that is beneficial to infants, as opposed to any one specific bacterial genus or species."



Figure 1. The community composition of the 15 most abundant bacterial genera in each of the 3 samples for each woman.

Image reproduced from "Characterization of the Diversity and Temporal Stability of Bacterial Communities in Human Milk," by K. M. Hunt, J. A. Foster, L. J. Forney, U. M. Schütte, D. L. Beck, Z. Abdo, . . . M. A. McGuire, 2011, PLoS One, 6(6), e21313. Copyright by Creative Commons Attribution License. Reprinted with permission.

The sciences that study human milk and human lactation are very young. We have before us an incredibly complex biological design that should be observed and studied to the best of our abilities. It has achieved the survival of our species for thousands of years. Manipulation of the human milk microbiota (by the excessive use of antibiotics or the indiscriminate use of probiotics) based on premature or non–evidence-based conclusions should be considered very carefully.

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Over the past six years, she has coordinated 43 breastfeeding courses in which the educational team (four IBCLCs, including herself, two nurses, a pediatrician, and a midwife) has trained more than 3,000 doctors, midwives, and nurses from public hospitals in the Madrid area. They are a referent in breastfeeding training in Spain. Their page: http://www.centroraices.com/

She is part of a workgroup on ankyloglossia that is currently immersed in

a clinical study to determine the effectiveness of frenotomy versus conservative treatment on posterior tongue-tie.

She is also currently gathering data on the efficacy of oral Lactobacillus in women with chronic breast pain.

She coauthored (with Dr. Concha de Alba, IBCLC, MD) the chapter on breastfeeding in the book Pediatría Extrahospitalaria. Fundamentos Clínicos para Atención Primaria (Outpatient Pediatrics. Clinical Foundations for Primary Care), by M. T. Muñoz Calvo, M. I. Hidalgo Vicario, and J. Clemente Pollán, 2008, Madrid, Spain: Ergon.

She has published a book, Amar con los Brazos Abiertos, Ed Marova, 2013. It has two parts: The first is to make the science behind breastfeeding easy for parents to grasp, and the second is to address everyday parenting emotional issues that parents can turn from barriers into assets for their family growth.

She has published breastfeeding articles in several popular mothering magazines in the last five years and has had several appearances in public national television on breastfeeding basics.

She organizes the yearly Hot Topics in Breastfeeding Conference at the prestigious College of Doctors in Madrid. Each year, we invite one single speaker to lecture us on the areas of her expertise for two consecutive days. Carmela does the live translation for the speakers.

Carmela is married and has five children.