

Academy of Breastfeeding Medicine Annotated Bibliography MASTITIS

Lisa H. Amir, February 2014

This annotated bibliography is limited to:

- clinical mastitis in postpartum women (sub-clinical mastitis is not included)
- English language articles
- mostly articles published since 1995 which provide the best evidence.

Databases searched: PubMed (limits human, English) and the Cochrane library; from 2008 to February 2014.
Terms: mastitis, breast abscess.

BIBLIOGRAPHY BY TOPIC

PREVALENCE OF MASTITIS

Primarily population-based studies conducted since 1995

Reference by First Author, Country	Summary of Pertinent Findings	Evidence Level*
Kinlay, Australia ¹	Cohort study of women Lower Hunter region of New South Wales followed for 6 months postpartum. Definition: Painful, red area on one or both breasts and either a temperature greater or equal to 38 C, or one of the constitutional symptoms of fever (body aches, headaches and chills), or a diagnosis of mastitis from a medical practitioner Women with mastitis: 219/1075 = 20% .	II-2
Foxman, USA ²	Cohort study of breastfeeding women from Michigan and Nebraska (not population-based) followed for the first 3 months postpartum. Definition: Self-report of mastitis diagnosed by a health care provider. Women with mastitis: 90/946 = 9.5% .	II-2
Binns, Australia ^{3**}	Cohort of women recruited in 2 maternity hospitals in Perth, 1992-93. Telephone interview at 2, 6, 10,	II-2

	14, 18 and 24 wks or until stopped bf. Women with mastitis: 39/556 = 7.0% .	
Thomson, Australia ^{4**}	Population-based cohort study in the Australian Capital Territory, 1997. Questionnaires at 4 days, 8, 16 and 24 weeks. Definition: not defined. Women with mastitis: 255/1295 = 19.7% .	II-2
Waldenstrom, Sweden ^{5**}	Cohort of women recruited antenatally for a study about length of hospital stay recruited from all antenatal clinics in Sweden during 3 wk evenly spread over 1 y in 1999 to 2000, followed for 8 weeks. Definition: took antibiotics for mastitis. Women with mastitis: 91/2709 = 3.4%	II-2
Brown, Australia ^{6**}	Statewide postal survey of women in Victoria giving birth in a specified fortnight in 2000; 6 months postpartum. Definition: not defined. Women with mastitis: 292/1616 = 18.1%	II-2
Amir, Australia ⁷	Cohort study of women in Melbourne interviewed at 6 months postpartum. Definition: at least 2 breast symptoms (pain, redness, lump) and 1 systemic symptom (fever, flu-like illness) Women with mastitis: 206/1193 = 17% . Timing of mastitis: 53% episodes in the first 4 weeks; 71% in the first 8 weeks.	II-2
Scott, Scotland ⁻⁸	Cohort study of women in Glasgow in 2005-05. Telephone interviews at weeks 3, 8, 18 and 26. Definition:red, tender, hot, swollen area of the breast with fever, constitutional symptoms of fever or diagnosis from a medical practitioner. Women with mastitis 74/420 = 18% .	II-2
Tang, China ⁹	Cohort study of women in Jiangyou, Sichuan Province in 2010. Telephone interviews at 1, 3 and 6 months. Definition:red, tender, hot, swollen area of the breast with fever, constitutional symptoms of fever or diagnosis from a medical practitioner. Women with mastitis 42/670 = 6% .	II-2

**includes unpublished data provided by authors

PATHOPHYSIOLOGY

Reference by First Author, Country	Summary of Pertinent Findings	Evidence Level
Buesher, USA ¹⁰	Milk samples from 8 women with mastitis. Sixteen different milk components/activities were compared in mastitis and normal mature milk; only 4 were statistically increased during acute mastitis. Unexpectedly, there was no difference in Na:K ratio and lactoferrin levels in mastitis and normal samples.	III
Fetherston, Australia ¹¹	14 women with 22 episodes of mastitis. 24 hour lactose excretion in urine was significantly higher during mastitis than at other times, indicating increased permeability of the paracellular pathway. Levels	III

	of lactose in maternal blood also increased during mastitis, but were not significantly different to that of asymptomatic women. Single sample measurements of blood lactose cannot be recommended as a reliable measure of lactose excretion.	
Fetherston, Australia ¹²	26 women; 14 with mastitis. Found an increased breast permeability, reduced milk synthesis, and increased concentrations of sIgA and lactoferrin with increasing severity of breast and systemic symptoms. Level of lactoferrin in milk appears quite variable, suggesting it may not be a reliable marker for mastitis. Higher than normal levels of Na and CL in “healthy breasts” may be a normal response to lower concentration of lactose; challenges the assumption that a raised Na indicates subclinical mastitis.	III
Fetherston, Australia ¹³	14 women with 22 episodes of mastitis. Level of C-reactive protein (CRP) in blood was significantly increased during mastitis (p<0.001) and increased according to both the severity of breast and systemic symptoms. CRP was higher in milk from both symptomatic and asymptomatic breasts of women with mastitis compared to women without mastitis. The reason for high CRP in unaffected breast is unknown. Therefore CRP in milk is not useful in distinguishing between infective and noninfective forms of mastitis.	III
Mizuno, Japan ¹⁴	17 women with mastitis. Milk from breast with mastitis contained larger milk fat globules and higher levels of IL-6 than milk from healthy breast.	III
Hunt, USA ¹⁵	14 women with mastitis. Milk from breast with mastitis contained increased levels of free fatty acids, and IL-8, and higher somatic cell count, than milk from healthy breast.	III
Bjelakovic, Serbia ¹⁶	60 women recruited at day 1 and 2 ml colostrum collected (day 1 or 2); 7 developed mastitis. The enzyme alkaline phosphatase (ALP) was higher in milk from the symptomatic breast compared to the asymptomatic breast and to milk from women who did not develop mastitis. Authors say this could be a useful biomarker for risk of mastitis.	III

MICROBIOLOGY

Reference by First Author, Country	Summary of Pertinent Findings	Evidence Level
Thomsen, Denmark ¹⁷	165 women with infectious mastitis (leukocyte count >10 ⁶ /m, bacteria > 10 ³ /ml). <i>S. aureus</i> 43% (n=71). Other bacteria: CNS (n=41), beta-hemolytic strep (n=12), <i>Strep faecalis</i> (n=10), <i>E. coli</i> (n=11), other isolates (n=20).	II-2

Matheson, Norway ¹⁸	43 women with mastitis. <i>S. aureus</i> 40% milk samples. Other bacteria beta-hemolytic streptococcus, pneumococcus, CNS (CNS isolated from 18/43 unaffected breasts). 70% of <i>S. aureus</i> were resistant to phenoxymethylpenicillin. Conclusion: penicillinase-resistant penicillins should be used in women with no improvement after 2 days of conservative treatment and to those with excessive symptoms at the beginning.	II-2
Amir, Australia ¹⁹	99 women with mastitis. <i>S. aureus</i> isolated from 46% milk samples (n=45).	II-2
Fetherston, Australia ¹³	14 women with 22 episodes of mastitis. Only two of the 13 episodes of mastitis tested with milk cultures were positive for pathogenic bacteria: <i>S. aureus</i> . Other organisms: <i>Streptococci viridans</i> and CNS.	II-2
Osterman, Sweden ²⁰	41 samples from women with mastitis attending a breastfeeding clinic or on the postnatal ward. <i>S. aureus</i> 32% (n=13). Other bacteria isolated: Group B haemolytic strep (n=5), Group G haemolytic strep (n=1), CNS (n=20), non-beta haemolytic strep (n=9), coryneform bacteria (n=7), normal skin flora (n=1).	II-2
Amir, Australia ²¹	13 samples from women with mastitis attending an Emergency Dept. <i>S. aureus</i> 46% (n=6). Other bacteria isolated: Group B strep (n=1), Group D strep (n=1).	II-2
Bertrand, Canada ²²	222 women with mastitis. <i>S. aureus</i> 44% (n=98). Other bacteria: Beta-hemolytic strep 3% (n=7).	II-2
Reddy, USA ²³	Single-centre report of a relative increase in methicillin resistance among 48 cases of Staphylococcus aureus-associated postpartum mastitis during 1998-2005. Of 21 cases with methicillin resistance, 17 (81%) occurred in 2005.	III
Saiman, USA ²⁴	8 postpartum women with skin and soft-tissue infections caused by CA-MRSA at a mean time of 23 days (range, 4-73 days) after delivery. Infections included 4 cases of mastitis (3 of which progressed to breast abscess), a postoperative wound infection, cellulitis, and pustulosis.	III
Sax, Switzerland ²⁵	During a two-month period in 2000, Panton-Valentine leukocidin (PVL)-producing CA-MRSA was detected in five neonates in neonatal unit. The mother of the index case showed signs of mastitis and wound infection and consequently tested positive for CA-MRSA.	III
Kvist, Norway ²⁶	192 women with mastitis: <i>S. aureus</i> 45% (n=87); CNS 83% (n=160); GBS 21% (n=41). 466 breast milk donors: <i>S. aureus</i> 31% (n=145); CNS 90% (n=419); GBS 10% (n=47)..	II-2
Delgado, Spain ²⁷	20 women with mastitis: milk samples analysed by standard and molecular microbiology. <i>S. aureus</i> and <i>S. epidermidis</i> were the main organisms identified. The authors suggested that <i>S. epidermidis</i> "could be	III

	a widely underrated cause of lactational mastitis” (p. 6).	
Delgado, Spain ²⁸	30 women with mastitis (?includes the 20 women from 2008 study); 12 healthy women (milk collected for Jimenez et al. 2008 ²⁹ <i>S. epidermidis</i> was the main species identified in the milk of women with mastitis (<i>S. aureus</i> identified in 8 women). <i>S. epidermidis</i> in mastitis milk was higher in the biofilm indicator (ica) and percent of strains resistant to mupirocin, erythromycin, clindamycin and oxacillin than milk from healthy women.	III

CNS = coagulase-negative staphylococci (most commonly as *S. epidermidis*), regarded as normal skin flora, but can be problematic for preterm infants.

CA-MRSA = community acquired methicillin resistant *S. aureus*.

GBS = Group B streptococci.

CAUSES OF MASTITIS

Cohort or case-studies that have used multivariate analysis to examine factors associated with mastitis.

Reference by First Author, Country	Summary of Pertinent Findings	Evidence Level
Kinlay, Australia ³⁰	Cohort study of 1075 women followed for 6 months postpartum. Variables assoc with mastitis (significant using logistic regression): blocked ducts, cracked nipples, started consecutive feeds with same breast, used creams on nipples, past history of mastitis, higher education level.	II-2
Foxman, USA ²	Cohort study of 946 breastfeeding women from Michigan and Nebraska followed for 3 months postpartum. Variables strongly assoc with mastitis (significant using logistic regression): history of mastitis with a previous child, cracks and nipple sores in the same week as mastitis, using an antifungal nipple cream (presumably for nipple thrush) in the same 3-week interval as mastitis and (for women with no mastitis history) using manual breast pump.	II-2
Amir, Australia ¹⁹	Case-control study; 100 women with mastitis attending two maternity hospitals in Melbourne and 99 breastfeeding controls in community. Variables assoc with mastitis (significant using logistic regression): infant nasal carrier of <i>S. aureus</i> , cracked nipple, difficulty breastfeeding, tight bra.	II-2
Amir, Australia ⁷	Cohort study of 1193 women in Melbourne interviewed at 6 months postpartum. Variables strongly assoc with mastitis (significant using logistic regression): private health insurance, cracked nipple, nipple pain lasting more than 4 weeks.	II-2

MANAGEMENT – NON-PHARMACOLOGICAL

Reference by First Author, Country	Research Question, Study Design, Summary of Pertinent Findings	Evidence Level
Kvist, Sweden ³¹	Does acupuncture treatment hasten recovery from inflammatory processes in the lactating breast? RCT. 205 mothers with 210 cases of inflammatory symptoms of the breast, randomly assigned to one of three treatment groups, two of which included acupuncture among the care interventions and one without acupuncture. No difference in outcomes.	I
Jimenez ³² , Spain	20 women with “clinical symptoms of staphylococcal mastitis” (8 had <i>S. aureus</i>); 14 with fissures, following failed treatment with antibiotics for 2-4 weeks. 10 women received probiotic (2 strains of <i>Lactobacillus</i>). After 14 days, no signs of mastitis in women who received probiotic, whereas clinical signs persisted in control group. (Comment: Clinical details not provided).	I.
Arroyo ³³ , Spain	352 women with mastitis randomised to receive two strains of <i>Lactobacillus</i> or antibiotics; volunteers and investigators blinded. On day 21, bacterial counts and breast pain were lower in <i>Lactobacilli</i> groups compared to antibiotic group. (Comment: Trial was registered at ClinicalTrials.gov NCT00716183, which describes 3 <i>Lactobacillus</i> groups; non-randomised allocation, open label. Clinical assessment at days 0, 7, 14 and 21. Women were given antibiotics by clinics, and included inappropriate antibiotics.)	I

MANAGEMENT – PHARMACOLOGICAL

Reference by First Author, Country	Summary of Pertinent Findings	Evidence Level
Jahanfar ³⁴ , Canada	Cochrane review: "This review aims to examine the effectiveness of antibiotic therapies in relieving symptoms for breastfeeding women with mastitis with or without laboratory investigation. Two trials met the inclusion criteria. One small trial (n = 25) compared amoxicillin with cephradine and found no significant difference between the two antibiotics in terms of symptom relief and abscess formation. Another, older study compared breast emptying alone as 'supportive therapy' versus antibiotic therapy plus supportive therapy, and no therapy. The findings of the latter study suggested faster clearance of	I

	symptoms for women using antibiotics, although the study design was problematic. AUTHORS' CONCLUSIONS: There is insufficient evidence to confirm or refute the effectiveness of antibiotic therapy for the treatment of lactational mastitis. There is an urgent need to conduct high-quality, double-blinded RCTs to determine whether antibiotics should be used in this common postpartum condition."	
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WOMEN'S EXPERIENCES OF MASTITIS

Recent studies have described women's experiences with mastitis³⁵⁻³⁸ Common themes: breast pain, total body illness, disruption to life, perception of decreased milk supply, concerns about ability to continue breastfeeding, feelings of depression/anxiety, adjusting to motherhood, need for practical and emotional support.

PREVENTION OF MASTITIS

Reference by First Author, Country	Research Question, Study Design, Summary of Pertinent Findings	Evidence Level
Peters, Germany ³⁹	Does hand disinfectant by the bedside reduce mastitis during hospital stay? Historic controls. Mastitis results: Experimental group: 8/1230 women: 0.65%; Control group 32/1095 women: 2.9%; (p<0.01).	II-1
Jonsson, Finland ⁴⁰	Does antenatal / postnatal breast massage prevent mastitis? Concurrent controls.*	II-1
Waldenstrom, Sweden ⁴¹	Is birth centre care beneficial for breastfeeding? Does it increase duration and reduce complications (including mastitis)? RCT.*	I
Evans, Australia ⁴²	Does prolonged feeding on one breast per feed reduce breastfeeding complications, including mastitis? Historic controls.*	II-1
Gunn, Australia ⁴³	Does an early visit to a general practitioner reduce problems (including mastitis) compared to the standard six-week postnatal visit? RCT.*	I
Livingstone, Canada ⁴⁴	Are oral or topical antibiotics more effective in the treatment of <i>S. aureus</i> -colonised cracked nipples than standard care? RCT of 4 groups. Mastitis results: Oral antibiotics: 1/19, 5%; Other groups: 16/65, 25% (Fisher exact 0.1) Sample underpowered.	I
Amir, Australia ⁴⁵	Do systemic antibiotics reduce the number of episodes of mastitis in women with <i>S. aureus</i> -colonised cracked nipples? RCT. Recruitment ceased after 12 months due to lack of numbers.	I
Svensson, Sweden ⁴⁶	Does a specially treated cereal induce anti-secretory factor (AF) in human milk and protect against	I

	mastitis? RCT. Mastitis results: Specific cereal: 1/12; No cereal: 6/17. Also significantly higher levels of AF in experimental group (p<0.0001).	
de Oliveira, Brazil ⁴⁷	Does a breastfeeding technique intervention increase exclusive bf and reduce breast problems? RCT*	I

*No difference in proportion of women with mastitis in experimental and control groups.

BREAST ABSCESS: INCIDENCE

Reference by First Author, Country	Summary of Pertinent Findings	Evidence Level
Amir, Australia ⁴⁸	Cohort study of 1193 women in Melbourne interviewed at 6 months postpartum: 5 women developed an abscess; 0.4% of postpartum women (95%CI 0.14, 0.98), 2.9% of women treated with antibiotics for mastitis (95%CI 1.0, 6.7).	II-2
Kvist, Sweden ⁴⁹	1,454,068 singleton deliveries during 1987-2000. During the year following delivery 1401 women had surgery because of a breast abscess. Rate of abscess: 0.1% of postpartum women. Needle aspiration not reported, but author has said surgical treatment is standard care (personal communication).	II-2
	Since the last review in 2008, many case studies and case series reporting breast abscesses caused by MRSA have been published (first author, country): Al Benwan, Kuwait ⁵⁰ : 83 women with abscess, 13 MRSA: 16%. Alsubaie, Saudi Arabia ⁵¹ : 13 infants; 1 mother with MRSA abscess Berens, USA ⁵² : 33 women with breast abscesses, 21 MRSA: 64% Branch-Elliman, USA ⁵³ : 54 women with abscess, 30 MRSA: 56% Chen, Taiwan ⁵⁴ : 85 women with abscess, 52 MRSA: 61% Chick, USA ⁵⁵ : case study Chuwa, Singapore ⁵⁶ : 15 women with MRSA breast abscess Dabbas, UK ⁵⁷ : 62 women with breast abscess, 3 MRSA: 0.5% Hagiya, Japan ⁵⁸ : case study Lee, Taiwan ⁵⁹ : case study Manoharan, India ⁶⁰ : 20 women with MRSA breast abscess Montalto, Australia ⁶¹ : case study	III

	<p>Newnham, Jamaica⁶²: 44 women with breast abscess, 1 MRSA: 2%</p> <p>Perez, Spain⁶³: case study</p> <p>Sanchini, Italy⁶⁴: 4 women with MRSA mastitis</p> <p>Stafford, USA⁶⁵: 27 women with breast abscess, 16 MRSA: 67%</p> <p>Wilson-Clay, USA⁶⁶: case study</p>	
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BREAST ABSCESS: MANAGEMENT

Reference by First Author, Country	Summary of Pertinent Findings	Evidence Level
Dixon, UK ⁶⁷	Case series of 6 lactating women with breast abscess drained by aspiration using a 19-gauge needle, three times per week until no more pus was aspirated. The number of aspirations ranged from three to five. This appears to be the first paper to recommend aspiration, although in 1946 Florey et al suggested aspiration of small breast abscesses and instillation of penicillin (BMJ1946; ii:846-8).	III
Schwarz, Nepal ⁶⁸	Case series of 33 breast abscesses (30 women: 25 lactating, 2 pregnant). They concluded that aspiration should be standard care and that breastfeeding could continue with antibiotic treatment.	III
Ulitzsich, Sweden ⁶⁹	Case series of 43 women with breast abscesses drained by aspiration guided by ultrasound; treatment was successful in all but one woman.	III
Christensen, Denmark ⁷⁰	Ultrasound-guided drainage of breast abscesses: 151 patients (89 puerperal). Median number of follow-ups in Ultrasound Dept was 4 (range 1-10), median number of aspirations 1 (range 1-6) for puerperal patients.	III
Irusen ⁷¹	Cochrane protocol: Treatments for breast abscesses in breastfeeding women.	-

In conclusion:

- definition of mastitis is not universal
- prevalence: between 3 and 20% of women, most population-based estimates are around 15-20%
- *S. aureus* isolated in about 50% milk samples of women with mastitis
- increasing reports of mastitis and abscesses caused by MRSA; still uncommon in most settings, but ranges from less than 1% in the UK to around 60% in areas of the USA and Taiwan (N.b. calculated as % of women with abscess with microbiology collected, not % of *S. aureus*).

- causation: damaged nipples, nipple pain, factors leading to stasis
- only two small studies of pharmacological treatment of mastitis have been conducted; studies are needed to determine when to use antibiotics and best duration of treatment.
- penicillinase-resistant penicillins should be used in women with no improvement after 1 day of conservative treatment and to those with excessive symptoms at the beginning
- although many trials have attempted to prevent mastitis, only a dietary cereal and hand disinfectant have shown any benefit and need to be tested further
- breast abscess occurs in about 3% of women with mastitis and can usually be treated by needle aspiration.

***US Preventive Services Task Force Ranking of Evidence from Scientific Studies**

- I Evidence obtained from at least one properly randomized controlled trial.
- II-1 Evidence obtained from well-designed controlled trials without randomization.
- II-2 Evidence obtained from well-designed cohort or case-control analytic studies, preferably from more than one center or research group.
- II-3 Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments (such as the results of the introduction of penicillin treatment in the 1940s) could be regarded as this type of evidence.
- III Opinions of respected authorities, based on clinical experience, descriptive studies and case reports; or reports of expert committees.