# Candidiasis (Thrush)

When a mother has persistently sore nipples, candidiasis (also referred to as candidosis) may be present. The yeast *Candida albicans* (also called *Monilia* or thrush) is the likely cause when this infection occurs orally. *Candida* thrives in the warm, moist areas of the infant's mouth and on the mother's nipples. The infant's mouth can become infected during vaginal birth and can then infect the mother's breast and nipple during breastfeeding. Candidiasis should be suspected if the mother has been breastfeeding without discomfort and then rapidly develops extremely sore nipples, burning or itching, and burning, shooting, or stabbing nipple pain that radiates to the chest wall (Barrett et al., 2013a).

Although *Candida* is naturally occurring yeast that lives in the mucous membranes of the gastrointestinal and genitourinary tract and on the skin, the use of antibiotics promotes its overgrowth (candidiasis); consequently, infants and women who have received antibiotic therapy are more susceptible to candidiasis (Chetwynd et al., 2002). Mothers with vaginal candidiasis and nipple trauma are also predisposed to candidiasis of the breast.

In assessing for candidiasis, inspect the woman's breasts for inflammation of the nipples and areola. The inflammation is usually a striking deep pink, sometimes with tiny blisters (see Color Plate 12). The mother will complain of severe tenderness and discomfort, especially during and immediately after feedings. The baby may have a diaper rash, with raised, red, sore-looking pustules or red, scalded-looking buttocks. Also examine the child's mouth carefully for white patches surrounded by diffuse redness. The absence of symptoms in the child's mouth, however, does not rule out thrush because the infant may be asymptomatic. Conversely, thrush symptoms in the baby (fussiness, refusing breast) can go unnoticed or be attributed to something else. Whenever any woman has recurrent yeast infections, her sexual partner should be considered a potential reservoir of infection. Pacifiers and bottle nipples are another source of recurrent thrush infection; they may harbor persistent oral *Candida* colonization and should be replaced or boiled after each exposure in the infant's mouth.

Candidiasis is a "family" disease; it spreads quickly among family members, especially with intimate contact involving warm, moist areas of the body, as is the case with breastfeeding and with sexual contact. Candidiasis that develops during breastfeeding can persist and recur unless all areas of possible infection in the baby, mother, and her sex partner are treated promptly and aggressively. The infant's mouth and anal area, as well as the mother's breasts (nipples and areola) and vagina, are prime sites for *Candida* infection; all should be treated simultaneously if warranted.

## Diagnosis

Historically, candidiasis was most often diagnosed based on history, physical examination of the baby, and, to a lesser degree, physical examination of the mother (Brent, 2001). In Brent's survey of 312 members of the Academy for Breastfeeding Medicine, use of laboratory tests and cultures was reported to be infrequent (i.e., only 7% of providers used such methods), supposedly because cultures of the fungus would take days to grow and were difficult to differentiate from normal skin colonization.

To offset the well-recognized lack of evidence regarding accurate diagnosis of candidosis, Morrill and colleagues (2003, 2004, 2005) conducted research on detection of *Candida* on the

nipple and areolar skin and in breastmilk, diagnosis of mammary candidosis, and risk factors for candidosis. First, a new culture technique for detecting *Candida* in breastmilk was developed by Morrill et al. (2003) because the natural inhibition of *Candida* growth by lactoferrin in the milk samples can result in false-negative cultures. By adding iron to the breastmilk, the ability to detect *Candida* growth was increased two- to threefold, which markedly reduced the likelihood of false-negative culture results. Morrill and team (2004) also evaluated the sensitivity, specificity, and positive predictive value of signs (shiny or flaky skin of nipple/areola) and symptoms (burning pain of nipple/areola, sore but not burning nipples, stabbing breast pain, and nonstabbing breast pain) of mammary candidosis reported by lactating women at 2 and 9 weeks postpartum, based on laboratory confirmation of the presence of *Candida* on the nipple/areola or in breastmilk at 2 weeks postpartum. The positive predictive value for colonization was highest when three or more signs and symptoms occurred simultaneously or when flaky or shiny skin of the nipple/areola was reported together or in combination with breast pain.

Finally, in a prospective study of 100 lactating and 40 nonpregnant, nonlactating women (controls), the team of researchers led by Morrill (2005) sought to document risk factors for *Candida* colonization and the relationship between *Candida* colonization and breastfeeding at 9 weeks postpartum. None of the nonpregnant control subjects tested positive for *Candida*, somewhat contradictory to the assumption that *Candida* is normally present in many people. Risk factors for colonization of the mother were bottle use in the first 2 weeks postpartum and pregnancy duration of longer than 40 weeks. Risk factors for the infant were bottle use in the first 2 weeks postpartum and presence of siblings. Among women who tested positive at 2 weeks, 43% were still breastfeeding at 9 weeks postpartum compared with 69% who did not test positive ($P < 0.05$). The authors concluded that use of signs and symptoms could be helpful to clinicians in determining the need for cultures and for immediate treatment while awaiting culture results. Their risk factor research suggested that avoidance of bottle use in the early postpartum period may reduce the risk of mammary candidosis. Furthermore, such preventive practice may help to decrease early termination of breastfeeding due to infection and pain.

## Alternative Views of Candidiasis

In 2008, while speaking at the International Lactation Consultant Association conference, Thomas Hale questioned the presumption that sore and inflamed nipples with pain radiating into the axilla were due to infection with *Candida albicans* because most studies had not actually found culturable *Candida* present in breastmilk. Hale et al. (2009) followed up this query with a rigorous prospective study to determine if *Candida albicans* was present in the milk of women suffering from symptoms of severe nipple and deep breast pain. Women symptomatic of candidiasis (sore, inflamed, or traumatized nipples or intense stabbing or burning pain) were compared with women without symptoms. The skin of the nipple and areola was washed with detergent and thoroughly rinsed. Milk samples were analyzed for (1 –> 3)-beta-D-glucan and grown on *Candida* growth medium. Findings indicated no significant difference in (1 –> 3)-beta-D-glucan levels between the control and symptomatic group. Furthermore, no *Candida* species were culturable either before or after the addition of iron to stimulate growth, with the exception of one patient. Thus, Hale's study supported that *Candida albicans* was not present in milk ducts and therefore may not be associated with this painful syndrome.

Other researchers using similar approaches have since found similar results. For example, Jiménez et al. (2017) examined the milk of women with symptoms consistent with candidiasis. The 529 women used manual expression to collect milk for microbiological analysis, and nipple swabs and nipple biopsy samples were also collected. Results showed that *Candida albicans*

was not isolated from the milk samples. However, the results strongly supported that coagulase negative staphylococci and streptococci (mainly from the mitis and salivarius groups) were predominant in the cases. The researchers recommended that the term *mammary candidiasis* or *nipple thrush* should be avoided when referring to the condition and replaced by *subacute mastitis*.

Another view of this common breast infection is that coinfection with *S. aureus* and *C. albicans* or other *Candida* species in the lactating nipple and breast may lead to inflammation and pain. A large, prospective study ($n$ = 360 nulliparous women) conducted by Amir and colleagues (2013) in Australia investigated *Candida* species and *S. aureus* and the development of "nipple and breast thrush." The women in the study were followed from 36 weeks' gestation (baseline) to 8 weeks postpartum, completing seven data collections (including the baseline). The main outcome was a case definition of nipple and breast thrush based on the presence of a combination of burning nipple pain and breast pain by 4 weeks postpartum. Microbial (via culture) and molecular (via polymerase chain reaction) samples were obtained from maternal nasal/nipple/breastmilk/vagina and baby nasal/oral sites for analysis for *Candida* and *S. aureus*. Self-report data were collected for previous *S. aureus* and *Candida* infections, breastfeeding problems, and health problems.

According to the researchers, women with the case definition of thrush were more likely to have *Candida* species in their nipple/breastmilk/baby oral samples (54%) compared with other women (36%, $p$ = 0.014). *S. aureus* was also common in nipple/breastmilk/baby samples of women with (82%) and without (79%, $p$ = 0.597) these symptoms. Univariate and multivariate time-to-event analysis examined predictors of thrush up to and including the time of data collection; the presence of *Candida* and nipple damage significantly and independently predicted thrush, but the presence of *S. aureus* did not. In summary, this prospective cohort study provided evidence that *Candida* plays a role in nipple and breast pain in lactating women but that burning nipple pain is common, and alternative differential diagnoses should be considered when *Candida* infection is diagnosed. The authors called for future randomized clinical trials to investigate treatment or clearance of *Candida* infection.

Finally, a systematic review of nonrandomized trials and a meta-analysis by Betzold (2012) aimed to explore the etiology of deep breast pain and to identify possible explanations for the controversies surrounding this disorder. Seven studies, including one unmatched case control and six cohorts, that used microbial analysis of the milk were included (including Hale et al., 2009, and Thomassen et al., 1998). In lactating women reporting deep breast pain, evidence consistent with infection was routinely found. Women with deep breast pain were more likely to test positive for *Candida*, but they also had high risk of testing positive for *S. aureus*. Betzold concluded that women with deep breast pain should have cultures done, and management options should include treating immediately while awaiting results or waiting until results are available to guide treatment.

## Treatment

Despite the availability of antifungal medications, few clinical trials have investigated their effectiveness in treating candidiasis of the lactating dyad. Clinical trials with healthy versus immunocompromised infants are even more rare.

Thomassen et al. (1998) reported that treatment for mothers with mammary candidosis symptoms with 50 mg of fluconazole (Diflucan) was ineffective. Chetwynd et al. (2002) suggested that higher dosing (100 mg) of fluconazole for a longer duration (several weeks) might be necessary for treatment. A small ($n$ = 34) randomized study in two U.S. military clinics

compared nystatin (Mycostatin) and fluconazole oral suspensions for treatment of oral candidiasis in otherwise healthy infants (Groins et al., 2002). Clinical cures with nystatin were achieved in 6 of 19 patients (32%) and with fluconazole in 15 of 15 patients (100%). Microbiologic cures with nystatin at 10 days were observed in 1 of 18 infants (5.6%) and with fluconazole at 7 days in 11 of 15 infants (73%), with 10 of these 11 cures (91%) being apparent by day 3. Breastfeeding mothers of the infants, regardless of the study group, were prescribed nystatin cream for application to their nipples twice daily for the duration of the infant's treatment. However, the authors did not report on the outcomes for mothers in this study.

Generally, treatment of candidiasis for the infant includes placing an antifungal medication (e.g., nystatin suspension or micronazole [Monistat] oral gel) in the infant's mouth with a medicine dropper after feedings and swabbing it over the mucosa, gums, and tongue. The mother applies an antifungal topical cream or lotion to her nipples and breast before and after each feeding and to the infant's entire diaper area if any redness is visible. The mother may also have vaginal yeast infection and, if indicated, should simultaneously use an antifungal intravaginal preparation. Clotrimazole (Lotrimin) is an over-the-counter drug in the United States that is available as a vaginal suppository or as a cream but is not sold as a gel. These treatment recommendations are largely consistent with the ABM's guidance on *Candida* infection in the mother and infant (Berens et al., 2016).

Other recommendations that can be made to the mother on a case-by-case basis include the following:

- Air dry the nipples and, if possible, expose them directly to the sun for a few minutes twice a day.
- Throw away disposable breast pads as soon as they become wet.
- Dry the external genitalia with a hair dryer on a warm setting.
- Wear 100% cotton underpants and bras that can be washed in very hot water and/or bleach to kill spores.
- Avoid baths with other members of the family.
- Restrict consumption of alcohol, cheese, bread, wheat products, sugar, and honey.
- Take 1 tablet acidophilus daily (40 million to 1 billion viable units, found at health food stores) for 2 weeks beyond the disappearance of symptoms.
- Use condoms during coitus because cross-infection with a sexual partner is possible (Wilson-Clay & Hoover, 2008).

Nystatin is the most commonly used medication for candidiasis, although its effectiveness is poor according to some reports (Chetwynd et al., 2002; Groins et al., 2002), and occasionally it can cause gastrointestinal symptoms in the baby. Its use should be limited to never-treated cases of thrush. Nystatin oral suspension is painted on the baby's oral mucosa and tongue with a large cotton swab after every breastfeeding. In the case of frank thrush and persistent candidiasis, fluconazole is safe and effective and should be prescribed for both the mother and the infant. The amount of fluconazole that transfers through the mother's milk is not sufficient to treat the baby. One expert breastfeeding physician recommends that treatment of mother and infant be based on a holistic assessment of the case as well as the assumption that *Candida* is a problem of the host that causes overgrowth of the fungus (N. Powers, personal communication, 2007):

- If the mother has symptoms and the baby never had obvious oral thrush, the baby is not considered particularly susceptible, so do *not* treat the baby.
- If the baby has obvious thrush and the mother has symptoms, treat *both*.
- If the baby has obvious thrush and the mother has no symptoms, treat both or treat the baby, and have the mother call immediately if she develops symptoms.

Another treatment consists of painting ketoconazole (Nizoral) suspension on the breast twice a day for 5 days, followed by prolonged nystatin application. If the mother has allergies, the healthcare provider must be aware that Seldane (terfenadine) should *not* be taken in conjunction with the antifungal drugs ketoconazole or itraconazole (Sporanox) or the antibiotic erythromycin. Mixing these drugs can lead to a life-threatening interaction.

TABLE 10-4 lists recommended dosages for commonly used antifungal medications. Dr. Jack Newman's All Purpose Nipple Ointment (Newman & Pitman, 2000) is a combination nipple ointment of antifungal and cortisone agents.

| Drug Name | Preparations | Usual Dosage |
|---|---|---|
| Clotrimazole (Lotrimin, Mycelex) | Creams, solutions, vaginal cream, and vaginal tablets. | Skin cream: Apply twice daily.<br>Vaginal cream or tablet: 100 mg/day for 7 days or 200 mg/day for 3 days. |
| Fluconazole (Diflucan) | Oral. | Adult: 400 mg loading dose, then 100 mg twice daily for at least 2 weeks until pain-free for a week. Pediatric: Loading dose of 6–12 mg/kg; then 3–6 mg/kg. |
| Miconazole (Monistat) | Skin cream or lotion, vaginal cream, and vaginal suppositories. | Vaginal cream or suppository: 100 mg/day for 7 days.<br>Skin cream or lotion: Apply 3 to 4 times per day. |
| Nystatin (Mycostatin) | Suspensions, cream, powders, ointment, and vaginal suppositories; *Candida* resistance to nystatin is growing. Use only water miscible cream or gel products (avoid mineral paraffins contained in ointments) | Oral: Adult: 1.5–2.4 million into units/day divided into 3–4 doses. Infant: 400,000–800,000 units/day divided into 3–4 doses.<br>Topical: 1 million units applied twice a day. Duration of therapy: At least 2 days after symptoms disappear.<br>Vaginal: 1–2 million units/day. |
| Newman's All Purpose Nipple Ointment | Ointment mixed by a pharmacist. Clotrimazole can be left out if 10% dosage is not available. Use until pain-free. | Mupirocin (Bactroban) 2% ointment (15 gm); nystatin 100,000 unit/ml ointment (15 gm); clotrimazole 10% vaginal cream (15 gm); betamethasone 0.1% ointment (15 gm). |

After taking an antifungal medication, mothers need encouragement and follow-up; they may not get immediate relief from pain. In fact, after starting treatment, the pain may become worse before it begins to fade. If nystatin does not clear the fungal infection, other antifungal medications—such as miconazole (Monistat), clotrimazole (Lotrimin), naftifine (Naftin), or oxiconazole (Oxistat)—should be tried (Johnstone & Marcinak, 1990). For early cases, suggest that after feedings the mother try warm vinegar soaks (1 part vinegar, 4 parts water) followed by air drying and an antifungal preparation (La Leche League International, 2000).

Gentian violet, an old-fashioned antifungal drug, is rarely used for treatment of candidiasis, although the ABM's Protocol #26 (Persistent Pain with Breastfeeding) does list it with precautions (Berens et al., 2016). A well-known drawback of this remedy is that gentian violet stains anything with which it comes into contact, although blotting with alcohol and then a detergent solution helps to remove the dye. The more significant and dangerous side effect of gentian violet is irritation laryngotracheitis secondary to this agent and ulceration of the infant's oral mucous membrane exposure necessitating endotracheal tube placement (Utter, 1990). A case study (Baca et al., 2001) described a very serious case of obstructive feeding tube placement secondary to refusal of the infant to breastfeed. Given the availability of other antifungals with few side effects, the authors recommended extreme caution and consideration in prescribing gentian violet.

Another recommendation from Dr. Nancy Powers is to "treat" anything that comes into contact with the baby's mouth (pacifiers, nipples, teethers, or toys) or the mother's breasts (breast-pump parts, bras, breast pads) to destroy the heat-resistant spores. This treatment can be accomplished by soaking articles in a vinegar-and-water solution for 30 minutes, boiling the articles for 20 minutes, or sterilizing pump parts in microwaveable bags sold for pumps. Likewise, Dr. Christina Smillie, a pediatrician who treats only breastfeeding patients, views *Candida* as a normal flora that is everywhere and suggests that treatment of candidiasis should focus on restoring the skin to health so that the mother can resist infection.

It is not clear whether the expressed milk of a mother with candidiasis should be saved and frozen for later use. Freezing deactivates yeast but does not kill it. Generally, it is advisable to tell mothers with candidiasis who are pumping not to freeze their milk until they have completed a course of medication treatment and are symptom-free. In the situation where the mother has a large supply of stored milk, and both mother and infant are symptomatic, home pasteurization of the stored milk may be considered.

In one case of candidiasis infection of the breast (see Color Plate 12), the infant remained symptom-free for the entire 4-month period, whereas the mother had repeated episodes of candidiasis. Within 4 days after resolving the painful blistering and redness, she experienced a new flare-up. After four such episodes in 4 months, she obtained medication for both her infant and herself; after 5 days of treatments after *every* suckling episode, she was symptom-free and remained so (Johnstone & Marcinak, 1990).