A Pink Milk Bottle Mystery

The mother of a 5-week-old term infant brings the infant to the pediatrician’s office, along with a plastic milk bottle used to feed the baby. The bottle has splotches of red-pink material on the inside (Fig. 1). She wants to know what is happening to the milk in the bottle. The mother has been breastfeeding and has recently been transitioning to pumped breast milk in preparation for returning to work. For the past few days, she has noticed that the breast milk remaining in bottles that were left in a sink overnight after evening feedings turns bright pink by morning. The breast milk has been normal in color during pumping, in the pump tubing, and in bottles stored in the refrigerator before feedings.

The mother denies taking any medications, herbal supplements, or illicit drugs while breastfeeding. The pregnancy was complicated by multiple urinary tract infections, which were treated with nitrofurantoin and trimethoprim-sulfamethoxazole. She denies any signs or symptoms of mastitis.

The infant has been asymptomatic, feeding well, and is gaining weight. Birth was uncomplicated. The infant is afebrile and is well-nourished, well-hydrated, and in no distress. There are no lesions or abnormal findings on the oral mucosa. There is no lymphadenopathy. The remainder of the physical examination appears normal.

The pediatrician sent samples of pink exudate in the bottle as well as stored, expressed breast milk (which had not yet been fed to the infant) for culture. Both cultures yielded the same microbe.

What microbe is the most likely cause of this scenario? When the pediatrician calls to tell you this story and the culture results, what advice do you give? (See next page for discussion.)
Microbial answer to “A Pink Milk Bottle Mystery”

Specimens from the pink milk bottle and stored breast milk grew *Serratia marcescens*. The strain was susceptible to amikacin, cefepime, cefoxitin, ceftazidime, ceftriaxone, ciprofloxacin, gentamicin, imipenem, levofloxacin, tobramycin, and trimethoprim-sulfamethoxazole.

The pediatrician was hopeful the mother could continue to breastfeed. Is this reasonable? Should the mother, baby, or both be given antimicrobial therapy?

*Serratia marcescens*, the microbial culprit in this case, is widespread in the environment, especially in areas that remain moist. *S marcescens* is often the etiology behind pinkish slime or discoloration that is sometimes seen in showers, tubs, toilets, and even soap dishes [1–4]. The microbial metabolite responsible for red or pink color production is prodigiosin, which is a member of the prodiginine family of linear and cyclic tripyrrolic compounds [5].

*Serratia marcescens* commonly colonizes the respiratory and gastrointestinal tracts in infants [1, 6, 7] and the respiratory tracts in adults. In the early 1990s, *S marcescens* was thought to be nonpathogenic, but the microbe is now well recognized as a cause of infection, almost exclusively as a nosocomial pathogen. It is seen most commonly in intensive care settings, and at least 34 outbreaks have occurred in neonatal or pediatric intensive care units (ICUs) [8].

Contaminated expressed breast milk and various water supplies have been implicated as primary or secondary reservoirs of infection [6–10]. Contamination of an inhalation solution was the source of 1 neonatal ICU (NICU) outbreak of infection [2]. Recurrent outbreaks in the same NICU due to different clones of *S marcescens*, consistent with the ubiquitous environmental presence of this microbe, have been described [11].

Infections tend to occur mostly in compromised patients, but even in outbreak situations, the colonization rate is high compared with the infection rate [6, 12]. Common sites of invasive disease, when it occurs, include meningitis, pneumonia, bacteremia, urinary tract infection, soft tissue infection, and gastrointestinal disease. *Serratia marcescens* also causes central venous and urinary catheter-related infections, and it is a common contaminant of contact lens solutions and cause of contact lens-associated ocular infections [13]. *Serratia* is catalase-positive, and infection with this organism may be a sentinel event in patients with chronic granulomatous disease (CGD). In a study of 368 patients on a national registry of patients with CGD, *Serratia* was the most common cause of osteomyelitis [14].

“Red” pigment production by *S marcescens* during contamination of various foods in antiquity led to beliefs in miraculous appearances of blood and other superstitions. The microbial nature of such events was first recognized by Bartomoleo Bizio in 1819 when he correctly attributed a “strange reddening of polenta (cornmeal mush)” to a living organism [15]. Bizio named the substance *Serratia* after Italian physicist Serafino Serrati, who had developed a type of steamboat.

Before recognition of *S marcescens* as a potential pathogen, this pigment-producing property was considered to be a useful biomarker. In 1950, the US government, in an attempt to study wind currents in the event of biological warfare, aerosolized *S marcescens* over the Pacific Ocean and evaluated inland areas for red pigment to see where wind carried the organism [16]. Inoculation of the microbe also has to evaluate hand-to-hand transmission of bacteria and development of bacteremia after dental extraction.

When grown on solid agar, *S marcescens* colonies may appear to be white, gray, red, or pink [17]. Prodigiosin production is less common among clinical strains of *S marcescens* than among environmental strains (9% vs 61% in 1 study), and it varies among serotypes as well [18]. Prodigiosin production by *S marcescens* occurs
Prodigiosin and related compounds have various antimicrobial, antifungal, and/or antibacterial activities [5]. Prodigiosins also have cytotoxic and apoptotic effects against a wide range of human cancer cell types that are selective, sparing normal cells. T lymphocyte proliferation also can be inhibited by these compounds at concentrations below cytotoxic levels [20]. Serratia marcescens is the primary species used for bioproduction of prodigiosins [19]. Other Serratia species, actinomycetes (eg, Streptomyces coelicolor), and various marine bacteria such as Pseudoalteromonas species, Vibrio psychrophilus, and Habella chejuensis (a distant relative of pseudomonads) sometimes produce prodigiosin. Other bacterial species can produce closely related compounds [5, 19].

Serratia isolation from expressed breast milk has been described in several reports, and most have involved NICUs. In an outbreak in 2 NICUs that involved 17 infants with 2 deaths, the outbreak strain was isolated from expressed breast milk from a mother whose infant was known to be colonized. Breast pumps were shared on the units and disinfection practices were not adequate [10]. A similar outbreak involved 30 infants with no deaths. Rectal carriage among these infants was common and often prolonged [21].

Serratia has also been isolated from breast milk pumping units. In 1 such report, a mother presented to her obstetrician stating that her breast milk-pump tubing had turned bright pink. The expressed breast milk was being fed to her twin infants. The mother was well and had no signs of mastitis, but she was treated with antibiotics and subsequently stopped breastfeeding; the infants remained well [22]. One full-term neonate who developed S marcescens sepsis on day of life 17, after being fed expressed breast milk contaminated with the microbe, has been reported. The onset of this infection occurred 4 days after hospitalization for another illness [23].

Expressed breast milk seldom will be sterile. A recent study in Thailand demonstrated contamination of 44 of 51 (86%) samples of breast milk expressed using breast pumps [24]. In premature infants, contamination of expressed breast milk with >1000 gram-negative bacilli/mL is associated with feeding intolerance. Higher levels of contamination (>1 000 000/mL) were associated with sepsis among premature infants [25]. However, such high density of contamination is unlikely with refrigeration soon after pumping and use for feeding soon after warming.

Pigment production during infection is rarely evident. This likely is due to inhibition of production at temperatures normal for human hosts. In 1 case report, a term infant with birth asphyxia who developed nosocomial sepsis due to S marcescens was linked to a pink hypopyon. Culture of fluid from the anterior chamber of the eye grew Serratia [26].

Nosocomially acquired strains of S marcescens may be multiply drug-resistant. This species also commonly carries chromosomally encoded, inducible AmpC β-lactamases that may lead to development of resistance during therapy with broad-spectrum cephalosporins. This potential should be considered when selecting antimicrobial regimens for treatment of S marcescens infections [3, 27, 28]. Options include (1) concurrent use of aminoglycosides when penicillin or cephalosporin agents that exhibit in vitro susceptibility are administered, or (2) use of carbapenems, quinolones, or other agents that may be appropriate for the site of infection.

**Advice Given:** Based on the above knowledge of S. marcescens epidemiology and virulence, it was agreed that the mother could continue to breastfeed and to pump. No antibiotics were recommended for the mother or the baby, as the risk of developing disease from Serratia was believed to be extremely low, as well as less than the risks of adverse effects from any antimicrobial agent that might be prescribed. If the mother had had mastitis, it would have been appropriate to prescribe antimicrobial therapy for her and to continue breastfeeding.

The most likely explanation for this scenario is contamination of the pump from a water source or sink in the home, not the mother’s skin. The mother’s receipt of trimethoprim-sulfamethoxazole pirenally combined with the in vitro susceptibility of the Serratia strain in this case is consistent with, though does not prove, acquisition of the strain from an environmental source rather than the mother. No specific recommendations for decontamination measures of the breast pump or bottles beyond routine household washing was made, as it was unclear if any additional measures would be feasible, more effective or preventive of re-introduction of Serratia from the environment.

**Outcome:** The mother continued to pump and breast feed for two more weeks. The infant remained well throughout this time and continued to thrive months later.
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References