

Bench Research, Human Milk, and SARS-CoV-2

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In this issue of *Pediatrics*, Conzelmann et al¹ examined whether Holder pasteurization of human milk, that is, heating to 62.5°C for 30 minutes, can inactivate severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). In the laboratory, the authors “spiked” 5 individual women’s expressed milk samples with 5 different SARS-CoV-2 isolates, conducted Holder pasteurization (to 63°C), and then assessed tissue culture infectious dose 50 by infecting susceptible cells and monitoring the cytopathic effect. Holder pasteurization effectively inactivated SARS-CoV-2, and additionally, they noted a 40.9% to 92.8% viral titer decrease in human milk as compared with the control medium, confirming human milk’s unique antiviral properties.

This important study adds to the limited evidence that pasteurized donor human milk is safe,² but placing it within the clinical context is key.³ Providers and parents should not leap to any of several possible unfounded conclusions: (1) that the milk of a mother who has SARS-CoV-2 infection will be infected, (2) that her milk must be expressed to be fed to her infant, or (3) that her milk should be Holder pasteurized before feeding. Although much remains to be learned about human milk and SARS-CoV-2 infection, preliminary laboratory and clinical reports have led to professional guidance supporting the safety of breastfeeding if the mother infected with SARS-CoV-2 is well enough to care for her infant.⁴⁻⁷ When she is too ill to feed directly, or her preterm infant

cannot directly breastfeed, expressing her milk and feeding it to the infant is preferred.⁴⁻⁷ These recommendations appropriately acknowledge the extraordinary health benefits of human milk feeding.⁸⁻¹⁰

In fact, it is suggested in preliminary evidence from laboratory¹¹ and clinical studies^{12,13} that (1) SARS-CoV-2 is unlikely to infect human milk, and (2) any particles detected in human milk are likely not to be infectious. For SARS-CoV-2 to enter and infect cells, 2 processes have to occur. SARS-CoV-2 must bind to host cells via the angiotensin-converting enzyme 2 (ACE2) receptor and cell entry must be facilitated by host cell proteases TMPRSS2, CTSB, or CTSL. To investigate human milk susceptibility to SARS-CoV-2, Goad et al¹¹ examined whether human mammary gland luminal epithelial cells (in which milk is manufactured) express ACE2, TMPRSS2, and CTSB and/or CTSL. Just 5% of mammary gland cells expressed ACE2, and none of the cells coexpressed ACE2 with either TMPRSS2 or CTSB and/or CTSL, which would be the essential double unlocking needed for viral cell entry. The authors concluded that there is essentially no risk of vertical transmission of SARS-CoV-2 to the infant who is breastfeeding from an infected mother because the virus cannot enter the “milk-making machinery” of the breast.

Clinical confirmation of this laboratory-based hypothesis is challenging because, early in the pandemic, mother-infant dyads were separated at birth, with human milk feeding not permitted.

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However, recently, Chambers et al¹⁴ analyzed 64 human milk samples from 18 women infected with SARS-CoV-2, all but 1 of whom were ill, both before and after a positive test result. Only 1 sample of the 64 had detectable SARS-CoV-2 RNA by reverse transcription–polymerase chain reaction. This sample, as well as a subset of 26 samples from 9 of the women, was tested for ability to replicate by established culture methods, and all results were negative.¹⁴ This suggests, importantly, that particle detection does not equate to infectivity and supports the preliminary findings by Goad et al¹¹. In a comprehensive review, the World Health Organization reported that of 46 women with coronavirus disease 2019 (COVID-19) whose milk was tested, 43 test results were negative, and 3 had particles detected by reverse transcription–polymerase chain reaction; 1 of the 3 infants tested positive for SARS-CoV-2, but infant feeding practices were not reported.⁵ A recent case report of a preterm newborn (32 weeks, 1614 g) inadvertently fed SARS-CoV-2–positive human milk who did not become infected suggests that human milk is not infectious even for preterm infants.¹² In a retrospective cross-sectional study of 45 infants born to mothers positive for COVID-19, none of the 7 premature infants who were breastfed or fed pumped human milk developed symptoms of infection.¹³ To summarize, there is more to learn; however, the preliminary evidence reveals that human milk is not likely to be a source of SARS-CoV-2 infection for infants, term or preterm.

Finally, although Holder pasteurization is a best practice for assuring the safety of pasteurized donor human milk for preterm infants, it is not a benign intervention with respect to its impact on the immunologically competent proteins and other components of human milk¹⁵ and should not be undertaken

lightly as a faux preventive measure. In most studies, authors report that Holder pasteurization reduced secretory immunoglobulin A.¹⁵ This could jeopardize the protective effect of secretory immunoglobulin A directed against SARS-CoV-2 that has been detected in milk of mothers who have COVID-19.^{16,17}

CONCLUSIONS

With their illuminating laboratory research, Conzelmann et al¹ offer new insights about SARS-CoV-2 best appreciated within the clinical framework of our still sparse understanding of COVID-19 and human milk.

ABBREVIATIONS

ACE2: angiotensin-converting enzyme 2
 COVID-19: coronavirus disease 2019
 SARS-CoV-2: severe acute respiratory syndrome coronavirus 2

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