Research Overview: 
The Transmission of Cytomegalovirus to Preterm Infants via Breastmilk: Evidence and Issues

Breastmilk - with all of its bioactive, immunological, anti-inflammatory and nutritive components - is generally believed to be the most beneficial form of nourishment for human infants. However, breastmilk is also a mode of cytomegalovirus (CMV) transmission to infants. While term infants infected with CMV via breastmilk rarely exhibit any outward signs of illness, preterm infants infected with CMV can present with a variety of signs and symptoms, some quite serious. How to approach this clinical issue is both complex and controversial.

Women who have had CMV at some point in their lives are seropositive for CMV antibodies. During pregnancy and lactation, CMV may reactivate and be excreted in her milk and other mucosal surfaces. Infants receive CMV antibodies from their mothers during the third trimester of pregnancy such that at the time of birth, they have a form of passive immunity to the virus. Term infants are protected through breastmilk through what is thought to be a natural immunization process. CMV-infected term infants will shed the virus in urine and saliva, but are generally asymptomatic for the infection.

Researchers hypothesize that preterm infants miss the transmission of maternal antibodies to CMV. Thus, when preterm infants - who are by nature physically immature and vulnerable - acquire CMV postnatally via breastmilk, they are at greater risk than term infants of exhibiting symptoms of the disease.

The distinctions among asymptomatic infection, symptomatic infection and a CMV sepsis-like syndrome in preterm infants have evolved through clinical studies and case reports. Asymptomatic infection is the most common scenario in term and preterm infants: the infant sheds CMV in urine and saliva but otherwise shows no signs or symptoms of illness. In studies reporting symptomatic infections in preterm infants, infants present with a variety of laboratory and/or clinical conditions. Generally, they recover spontaneously without evidence of long-term consequences. Of greatest concern to researchers, health care providers and parents is a CMV sepsis-like syndrome evidenced by a very small percent of preterm infants. These cases can clinically be very challenging, however most resolve spontaneously.

Strategies to reduce or prevent CMV transmission to preterm infants have focused on breastmilk treatment such as pasteurization or freezing or simply withholding breastmilk until the infant is more mature. None of these options is ideal: each option prevents the preterm infant from receiving fresh mother’s milk during a time of critical growth and development. Theoretically, withholding milk may not protect against CMV exposure from other maternal secretions.

In addition, studies of human milk consistently demonstrate not all components survive heating and freezing intact. For example, live milk cells such as leukocytes and lymphocytes are significantly diminished or damaged by pasteurization and freezing. The emerging science of human milk illuminates promising new discoveries, e.g., live stem cells, antigen-specific T cells and highly-activated memory B lymphatic cells, which, as live cells, are vulnerable to temperature changes. In this context, the risks and benefits of freezing and pasteurizing breastmilk require additional scrutiny.

These articles present current research related to breastmilk-acquired CMV infection in preterm infants.
Through them, we will explore dominant themes in the literature and their implications for clinical practice. Article reprints are included for your review.


**References:**


Research Overview: The Transmission of Cytomegalovirus to Preterm Infants via Breastmilk: Evidence and Issues

Clinicians and researchers have studied CMV acquisition by preterm infants via breastmilk for more than 40 years. In this collection of materials, you will find summaries with commentary on three current research articles. These materials provide an overview of breastmilk-acquired CMV infection in preterm infants and discuss implications of common management strategies.

Key Points

• CMV is a common virus present in body tissues and sheds in body fluids: saliva, urine, genital secretions, blood, and breastmilk.

• However, if acquired early in pregnancy, initial CMV infection may result in congenital infection.

• Women who have had CMV are seropositive for CMV antibodies. During pregnancy and lactation, CMV can reactivate, causing asymptomatic infection in the mother with viral shedding in her breastmilk, cervical secretions and urine. The terms seropositive, CMV-seropositive, CMV-positive, CMV- IgG-positive are interchangeable in this context.

• Infants can acquire non-congenital CMV infection during the birth process or through breastfeeding if mothers are seropositive.

• Term infants rarely show indications of breastmilk-acquired CMV infection.

• Preterm infants who acquire CMV via breastmilk may become symptomatic of the disease. The most common signs and symptoms are neutropenia, thrombocytopenia, hepatitis, elevated liver enzymes and hepatosplenomegaly.

• A sepsis-like syndrome may occur in preterm infants with breastmilk-acquired CMV. These symptoms may include apnea, bradycardia, distended abdomens and gray pallor.

• Despite a wide range of clinical symptoms, preterm infants recover from breastmilk-acquired CMV spontaneously and without long-term sequelae.

• Pasteurization eliminates CMV in breastmilk and freezing reduces viral load. Both processes affect milk components so are not recommended for usual feeding practices.
Concluding Remarks

The survival very premature infants presents challenges in neonatal care that did not exist forty years ago. The majority of reports of acute and serious CMV illness are clinical cases of extremely low birth weight infants born before 28 weeks gestation. Kurath and colleagues point out it is often difficult to distinguish between complications related to prematurity and complications from CMV infection. The research evidence suggests the actual risk of severe, symptomatic CMV infection is very low, even in very immature, tiny infants. All three studies in this collection, along with many others, support this conclusion.

At the time postnatal CMV came of interest, techniques for milk pasteurization were well established; thus, they were logical interventions for study and practice in response to CMV in breastmilk. Since that time, human milk science has expanded exponentially. Science supports the greater potential benefits from fresh milk compared to frozen or pasteurized milk and that this competes with the previous desires to reduce CMV transmission with heat and cold treatment of milk. This new information, along with current clinical and outcome data on CMV infection in preterm infants, obligates a more comprehensive analysis of the risks and benefits of temperature treatments on human milk. As such, the intentional withholding of fresh breastmilk from preterm infants deserves further attention.

Shifting focus away from breastmilk related interventions, two of the three authors presented in these materials suggested more study of prophylactic immunoglobulin therapy. Not everyone will agree this is the right approach or even necessary. Undoubtedly, additional research is needed before clinicians and researchers come closer to a consensus on the issue of CMV transmission via breastmilk.

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