Imported food risk advice

Human T-lymphotropic virus in human milk and human milk products

Context of this risk advice

- Human milk means expressed milk collected from lactating women to be fed to infants that are not the biological infants of the women supplying the milk.
- Human milk products means products derived from human milk that have been specially formulated to meet the specific nutritional needs of infants such as fortifiers and formula.
- The level of risk for this hazard in human milk and human milk products was determined assuming that the most vulnerable category of infants (preterm infants in hospital neonatal intensive care units) would be receiving the products.

Nature of the hazard

Human T-lymphotropic virus (HTLV) belongs to the *Retroviridae* family of viruses. There are two dominant forms of HTLV: HTLV type 1 (HTLV-1) and HTLV type 2 (HTLV-2). HTLV is an enveloped virus with a RNA genome and icosahedral capsid. Retrovirus virions are sensitive to heat, detergent and formaldehyde (Fujii and Matsuoka 2013; Goff 2013; Mylonas et al. 2010). Like all viruses, HTLV can multiply in living host cells but cannot replicate in food (Codex 2012). HTLV can cause potentially life threatening illness with chronic sequelae.

Transmission

HTLV can be transmitted sexually, parenterally[1], via mother-to-infant transmission (predominately through human milk) or though contact with infected bodily fluids (Carneiro-Proietti et al. 2014; Lairmore et al. 2012). The rate of mother-to-infant transmission in breast-fed infants has been reported to be 7-22%, compared to 2.5% for bottle-fed infants. Higher rates of transmission have been associated with infants breast-fed for longer periods (Biggar et al. 2006; Hino 2011; Li et al. 2004).

HTLV has been detected in human milk. A study by Li et al. (2004) showed that HTLV-1 provirus[2] was present in the human milk of 73% of HTLV-1-seropositive mothers (n=101). HTLV seroprevalence in pregnant women and potential human milk donors ranges from 0.01-0.5% in non-endemic regions and from 0-5.8% in endemic regions (Cohen et al. 2010; Gessain and Cassar 2012; Taylor et al. 2005).

Disease severity

HTLV is a severe hazard as it causes potentially life threatening illness with chronic sequelae. In most cases HTLV is asymptomatic, with the infection remaining latent for the life of the host (Mylonas et al. 2010). After a prolonged latency period approximately 3-5% of HTLV-1 infected individuals develop adult T-cell leukemia/lymphoma (ATL)[3] or other inflammatory disorders such as HTLV-1-associated myelopathy/tropical spastic paraparesis (HAM/TSP)[4]. ATL is an aggressive disease with survival ranging from four months to greater than five years, while HAM/TSP is a progressive neurodegenerative disease. Individuals infected in childhood may be at a higher risk of developing ATL (Goncalves et al. 2010; Lairmore et al. 2012). HTLV-2 has not been aetiologically linked with any disease, although there is accumulating evidence showing a link with a HAM/TSP[4]-like syndrome (Murphy and Biswas 2010; Mylonas et al. 2010).

[1] Route does not involve the gastrointestinal tract, e.g. intravenous
[2] Form of the virus that is permanently integrated into the genome of the host cell
[3] Highly aggressive T-cell cancer of the blood and/or lymph nodes
[4] Chronic nervous system disorder that affects the spinal cord, with paralysis of lower limbs, ataxia and urinary incontinence

Infectivity

HTLV is moderately infectious, with transmission associated with human milk with higher proviral loads. Li et al. (2004) reported the median proviral load in human milk in mothers who transmitted HTLV-1 was 1300 copies/ml, while the load in non-transmitting mothers had a median of 180 copies/ml.

Risk mitigation

Controls are needed to minimise contamination of human milk with HTLV. Pasteurisation of the milk is a primary control, however donor screening to exclude HTLV seropositive individuals can reduce the viral load in the donor milk to be pasteurised. An early study by Yamato (1986) showed that heating HTLV-1 producing MT-2 cells at 56^{o}C for 30 min inactivated the virus. Holder pasteurisation (62.5^{o}C for 30 min) is the method of choice to eliminate HTLV contamination of banked human milk (Tully et al. 2001). International human milk banks, including those in Australia, routinely perform Holder pasteurisation on human milk and serologically screen donors for HTLV-1 and HTLV-2 to ensure the microbiological safety of donor human milk (Bharadva et al. 2014; Hartmann et al. 2007; HMBANA 2015; UKAMB 2003).

Evaluation of uncertainty

There is uncertainty around the infectivity of HTLV in human milk and the viral load required for transmission.

Pooling of human milk from multiple donors is common practice amongst many human milk banks and would dilute the viral load from a single donor, however some milk banks only pool milk from individual donors (Haiden and Ziegler 2016). The Australian Red Cross milk bank pasteurises human milk in single donor batches (Australian Red Cross 2018).

Risk characterisation

There is evidence that HTLV can be present in human milk and can be transmitted to infants via human milk. HTLV is moderately infectious, with higher proviral loads in human milk associated with transmission. There is a medium likelihood of exposure as although there is a low incidence of HTLV amongst potential donors, a high proportion of HTLV seropositive mothers shed the virus in their milk. HTLV causes severe disease which can be fatal. HTLV in imported human milk and human milk products presents a potential medium or high risk to public health and safety.

This risk advice was compiled in: August 2018, updated October 2019

References

Australian Red Cross (2018) Milk bank media release. Australian Red Cross Blood Service, Melbourne. https://www.donateblood.com.au/milk-bank-media. Accessed 2 July 2019

Bharadva K, Tiwari S, Mishra S, Mukhopadhyan K, Yadav B, Agarwal RK, Kumar V, Infant and Young Child Feeding Chapter, Indian Academy of Pediatrics (2014) Human milk banking guidelines. Indian Pediatrics 51:469–474

Biggar RJ, Ng J, Kim N, Hisada MLH, Cranston B, Hanchard B, Maloney EM (2006) Human leukocyte antigen conconrdance and the transmission risk via breast-feeding of human T cell lymphotropic virus type 1. The Journal of Infectious Diseases 193:277–282

Carneiro-Proietti A, Amaranto-Damasio MS, Leal-Horiguchi CF, Bastos R, Seabra-Freitas G, Borowiak DR, Ribeiro MA, Proietti FA, Ferreira A, Martins ML (2014) Mother-to-child transmission of human T-cell lymphotropic viruses-1/2: What we know, and what are the gaps in understanding and preventing this route of infection. Journal of the Pediatric Infectious Society 3:S24-S29

Codex (2012) Guidelines on the application of general principles of food hygiene to the control of viruses in food (CAC/GL 79-2012). Codex Alimentarius, Rome. http://www.fao.org/fao-who-codexalimentarius/codex-texts/guidelines/en/. Accessed 22 May 2018

Fujii M, Matsuoka M (2013) Human T-cell leukemia virus types 1 and 2. In: Knipe DM, Howley PM (eds) Fields virology, 6th edition, Ch 48. Lippincott Williams & Wilkins, Philadelphia, pp 1474–1501

Goff SP (2013) Retroviridae. In: Knipe DM, Howley PM (eds) Fields virology, 6th edition, Ch 47. Lippincott Williams & Wilkins, Philadelphia, pp 1424–1473

Goncalves DU, Proietti FA, Ribas J, Araujo MG, Pinheiro SR, Guedes AC, Carneiro-Proietti A (2010) Epidemiology, treatment, and prevention of human T-cell leukemia virus type 1-associated diseases. Clinical Microbiology Reviews 23:577–589

Haiden N, Ziegler EE (2016) Human Milk Banking. Annals of Nutrition & Metabolism 69:8–15

Hartmann BT, Pang WW, Keil AD, Hartmann PE, Simmer K (2007) Best practice guidelines for the operation of a donor human milk bank in an Australian NICU. Early Human Development 83:667–673

Hino S (2011) Establishment of the milk-borne transmission as a key factor for the peculiar endemicity of human T-lymphotropic virus type 1 (HTLV-1): The ATL prevention program Nagasaki. Proceedings of the Japan Academy, Series B 87:152–166

HMBANA (2015) Guidelines for the establishment and operation of a donor human milk bank. Human Milk Banking Association of North America, Fort Worth

Lairmore MD, Haines R, Anupam R (2012) Mechanisms of human T-lymphotropic virus type 1 transmission and disease. Current Opinion in Virology 2:474–481

Li H-C, Biggar RJ, Miley WJ, Maloney EM, Cranston B, Hanchard B, Hisada M (2004) Provirus load in breast milk and risk of mother-to-child transmission of human T lymphotropic virus type I. Journal of Infectious Diseases 190:1275–1278

Murphy EL, Biswas HH (2010) Human T-cell lymphotropic virus types I and II. In: Mandell GL, Bennett JE, Dolin R (eds) Mandell, Douglas, and Bennett's principles and practice of infectious diseases, 7th edition, Ch 168. Churchill Livingstone, Philadelphia, pp 2303–2322

Mylonas I, Brüning A, Kainer F, Friese K (2010) HTLV infection and its implication in gynaecology and obstetrics. Archives of Gynecology and Obstetrics 282:493–501

Tully DB, Jones F, Tully MR (2001) Donor milk: What's in it and what's not. Journal of Human Lactation 17:152–155

UKAMB (2003) Guidelines for the establishment and operation of human milk banks in the UK. United Kingdom Association for Milk Banking, London. https://www.rcpch.ac.uk/sites/default/files/asset_library/Research/Clinical%20Effectiveness/Endorsed%20guidelines/Milk%20Banks/donor%20guidelines%203rd%20ed%20FINAL.pdf. Accessed 8 February 2018

Yamato K, Taguchi H, Yoshimoto S, Fujishita M, Yamashita M, Ohtsuki Y, Hoshino H, Miyoshi I (1986) Inactivation of lymphocyte-transforming activity of human T-cell leukemia virus type I by heat. Japanese Journal of Cancer Research 77:13–15