Imported food risk advice

Toxoplasma gondii 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

Toxoplasma gondii is a protozoan parasite which can infect all mammalian and avian species (Guy 2014). Felids, including domestic cats, are the definitive hosts. Oocytes shed in cat faeces undergo sporulation and become infective. Once ingested, they release sporozoites, which differentiate into tachyzoites (cell invasive form) and later bradyzoites (which form tissue cysts) (FSANZ 2014; Montoya and Liesenfeld 2004; Remington et al. 2011). All forms of the parasite are infectious to humans (Remington et al. 2011; Saridewi et al. 2013).
At least 30–40% of Australians are seropositive to *T. gondii* (Mie et al. 2008).

Postnatally acquired *Toxoplasma* infection is usually asymptomatic, but can cause illness of moderate severity.

Transmission

T. gondii is typically spread through contact with oocytes in cat faeces or contaminated soil or water, or by consuming tissue cysts in undercooked meats (Leeper and Lutzkanin 2018; Montoya and Liesenfeld 2004; Tenter et al. 2000). Maternal infection acquired during pregnancy can be transmitted to the foetus, causing miscarriage or severe congenital abnormalities which might not become apparent until later in life (Guy 2014).

Tachyzoites have been found in the milk of several mammalian intermediate hosts, including sheep, goats, and cows, and can be transmitted in milk from mother to offspring in several host species (Tenter et al. 2000). Toxoplasmosis transmission to humans has occurred via ingestion of tachyzoites in raw goat milk (Riemann et al. 1975; Sacks 1982).

There is limited evidence for the presence of *T. gondii* in human milk. (Jiménez et al. 2015) detected *Toxoplasma* DNA in 35% of human milk samples obtained from ten healthy women without present or past evidence of infection and from ten women with symptoms of lactational mastitis. No assessment of infectivity was undertaken.

A small number of studies describe possible transmission of *T. gondii* by breastfeeding:

- (Bonametti et al. 1997) reported possible transmission via human milk following an outbreak of acute toxoplasmosis among 17 guests, including a breastfeeding mother, who ate raw mutton at a party. The infant was exclusively breastfed, and developed symptoms 21 days after its mother.
- (Almeida et al. 2006) described the case of a two-month-old, exclusively breastfed infant presumptively infected postnatally. However, transmission via other routes could not be excluded.
- (Capobiango et al. 2015) considered a possible case of transmission via breastfeeding, but concluded that both the mother and her 6 month old infant were as likely to have been infected by ingestion of contaminated drinking water.

Definitive proof of transmission by breastfeeding in humans is lacking (Capobiango et al. 2015; Montoya and Liesenfeld 2004). Tachyzoites are vulnerable to proteolytic enzymes and stomach acidity, so infection following

ingestion is uncommon. However, infants have a lower concentration of proteolytic enzymes in the digestive tract, and may be more susceptible than adults (Tenter et al. 2000).

Disease Severity

Toxoplasma infection in immunocompetent individuals is usually asymptomatic, but presents as a mild to moderate self-limiting flu or glandular fever-like illness in 10–20% of cases. Postnatal and early childhood infection with *T. gondii* can cause illness of mild-to-moderate severity, with infrequent long-term sequelae—particularly the development of retinochoroiditis[1] (Dubey et al. 2012; FSANZ 2014; Guy 2014).

There appear to be regional variations in the severity of disease and the likelihood of chronic sequelae, related to differences in distribution and virulence of the three main *T. gondii* genotypes (I, II and III). The majority of human cases have been attributed to genotype II, which may be an artefact of an overrepresentation of this genotype in animals in Europe and the United States where most human cases have been documented. Genotype I or atypical genotypes have been associated with severe ocular disease in otherwise healthy individuals (Boothroyd and Grigg 2002; FSANZ 2014; Sibley and Ajioka 2008). In certain regions highly virulent atypical genotypes have caused severe disease in immunocompromised or immunocompetent individuals (Carme et al. 2009; Dubey et al. 2012).

Infectivity

The infectious dose of *T. gondii* is unknown. (Guo et al. 2016) derived a human dose-response model for infection due to tissue cysts (bradyzoites) of *T. gondii* in infected meats, scaled to match with human epidemiological data, based on mice and rat infection studies. Their results predict a 5% probability of infection on ingestion of $7x10^3$ tissue cysts, and 50% probability of infection on ingestion of 10^5 cysts.

Risk mitigation

Controls are needed to minimise contamination of human milk with pathogens, including pasteurisation of the milk. T*. gondii* tissue cysts are susceptible to temperature extremes (freezing and heat).

(Dubey et al. 1990) evaluated the inactivation of *T. gondii* tissue cysts in pork over a range of temperatures (49–67°C), and concluded that infectivity was lost by heating at 61°C or higher for 3.6 minutes. (Saridewi et al. 2013) showed that *T. gondii* tachyzoites in goat milk were inactivated by heating at 63°C for 30 minutes. International human milk banks, including those in Australia, routinely perform Holder pasteurisation (62.5°C for 30 min) to ensure the microbiological safety of donor human milk (Bharadva et al. 2014; Hartmann et al. 2007; HMBANA 2015; UKAMB 2003). This is sufficient to inactivate the infectious forms of *T. gondii* that are potentially present in human milk: tissue cysts (bradyzoites) and tachyzoites.

T. gondii tissue cysts in meat are inactivated after freezing at -10°C for 3 days or -20°C for 2 days (El-Nawawi et al. 2008). It would be expected that frozen storage would similarly inactivate *T. gondii* tachyzoites if they were to be present in human milk. Pasteurised human milk and human milk products should be stored and transported frozen (Hartmann et al. 2007).

Pooling of human milk from multiple donors is common practice amongst many human milk banks and would dilute the parasitic 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).

Evaluation of uncertainty

There is uncertainty around the transmissibility of *T. gondii* through human milk and the number of infectious particles required for this potential method of transmission. If the number of infectious particles required to potentially cause infection via human milk is assumed to be similar to the *T. gondii* tissue cyst animal studies, very large quantities of the parasite would be required for illness. The estimate of the infectious dose of *T. gondii* tissue cysts (Guo et al. 2016) is solely derived from animal studies, none of which met all of the data selection eligibility criteria listed in the analysis. The extrapolation to the dose-response in humans contains several untested assumptions. There are no data on the number or infectivity of *T. gondii* tachyzoites present in human milk.

[1] Inflammation of the vascular coat and retina of the eye, potentially leading to blindness.

Risk characterisation

T. gondii tissue cysts are estimated to be of very low-to-low infectivity. Postnatal toxoplasmosis is usually a mild-to-moderate illness, with infrequent long-term sequelae.

There is medium likelihood of exposure to *T. gondii* through consumption of human milk, as there is limited evidence for the presence of infectious forms of *T. gondii* in human milk, and some evidence for transmission through breastfeeding.

In imported human milk and human milk products, *T. gondii* does not present a potential medium or high risk to public health and safety.

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