Imported food risk advice

Coxiella burnetii 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

Coxiella burnetii is an obligate intracellular coccobacillus (Marrie and Raoult 2010). The large-cell vegetative form of the bacterium undergoes sporogenic differentiation to produce a spore-like form (small-cell variant). The small-cell variant is stable in the environment and is resistant to osmotic stress, ultraviolet light, chemical disinfectants, heat and desiccation (Angelakis and Raoult 2010; Eldin et al. 2017; Scott and Williams 1990).

C. burnetii is a zoonotic infection in humans, causing Q fever—an acute, self-limiting febrile illness with the potential to become a chronic illness with ongoing and occasionally life threatening sequelae.

Transmission

The main animal reservoirs for *C. burnetii* are mammals, birds and arthropods (ticks), with sheep, goats and cattle the main source of human infection. Transmission to humans usually occurs via aerosols contaminated with infected animal faeces, urine, birth material or milk (Marrie and Raoult 2010).

It remains unclear if consumption of unpasteurised dairy products contaminated with *C. burnetii* is another route of transmission. Although it causes the immune system to develop antibodies, the evidence that it has led to clinical disease is inconclusive and/or contested—with exposure via inhalation a possible route of transmission (Angelakis and Raoult 2010; Boarbi et al. 2016; Bryan 1983; Cerf and Condron 2006; EFSA 2010; Signs et al. 2012). The (OIE 2018) concludes that there is no significant evidence demonstrating the transmission of Q fever to humans by ingestion.

There is some evidence that DNA and viable cells of *C. burnetii* have been detected in human breast milk:

- (Kumar et al. 1981) and (Prasad et al. 1986) identified viable *C. burnetii* in 3 of 97 and 3 of 153 human milk samples, respectively, in India, where the organism is endemic in cattle and other domestic animals.
- (Mediannikov et al. 2010) found *C. burnetii* DNA by PCR in 1 of 44 human milk samples in rural Senegal.
- (Boden et al. 2012) found *C. burnetii* DNA by PCR in 1 of 5 human milk/colostrum samples investigated during a Q fever outbreak in Germany.

However, none of these studies provide evidence that transmission to infants has occurred through ingestion in human milk.

(Richardus et al. 1985) describe 18 cases of infantile Q fever and attributes at least one case to likely infection by breastfeeding, but the conclusion is not supported by compelling evidence.

The European Centre for Disease Prevention and Control (ECDC) concludes that, while *C. burnetii* has been identified in human breast milk, no case of transmission to breastfed children has been validated. The ECDC does not recommend against infected mothers breastfeeding except in cases of chronic disease that requires long-term treatment of the mother (ECDC 2010).

Disease severity

Q fever is typically an acute, self-limiting febrile illness with severe headaches, muscle and joint pain, rash and cough, occasionally leading to pneumonia and hepatitis. Cardiac sequelae, usually endocarditis, are seen in around 2% of cases, usually limited to immunocompromised individuals or those with existing cardiac defects (Angelakis and Raoult 2010; Fournier et al. 2001). Symptomatic disease is uncommon in children under 15 years of age (Angelakis and Raoult 2010; Maltezou and Raoult 2002).

Women who are infected during pregnancy are at risk for miscarriage, stillbirth, pre-term delivery, or low infant birth weight (Carcopino et al. 2007; CDC 2019; Munster et al. 2012).

In a review of 18 cases of Q fever in infants in the Netherlands ranging in age from 5-35 months old, (Richardus et al. 1985) described serious illness including fever, convulsions and pneumonia, with evidence for liver complications and rashes in some cases. All 18 cases required hospitalisation, ranging in duration from 4–80 days. There have been no longitudinal studies on potential sequelae arising from early childhood infection.

Infectivity

C. burnetii is highly infectious via airborne exposure. Brooke and colleagues modelled data from the 2007–2009 Q fever outbreak in the Netherlands, a 1983 outbreak in Switzerland, and human challenge trials, and concluded that as few as 1–5 viable bacteria are highly likely to cause infection and illness (Brooke et al. 2013; Brooke et al. 2015).

Tamrakar et al. (2011) modelled the dose-response of mice inoculated intraperitoneally and found a 50% average lethal dose (LD_{50}) in the range 10^8–10^{10} organisms for C57BL/6J and C57BL/10ScN strains of mice and 2.3×10^3 organisms for immunodeficient mice.

It is unclear if either study is applicable to infection of infants by ingestion of human milk. The contested evidence for infection through raw milk consumption (EFSA 2010) and the conclusion of the OIE about the lack of evidence for infection following ingestion (OIE 2018) support the conclusion that *C. burnetii* is of very low infectivity by this route of transmission.

Risk mitigation

Current heat pasteurisation standards for milk—particularly heating at 63°C for 30 minutes, or at 72°C for 15 seconds—result from studies by Enright and colleagues on the heat inactivation of *C. burnetii* (Enright et al. 1957a, 1957b). Such heat treatment provides between 4.7 and 8 log reduction of the pathogen (Cerf and Condron 2006). (Zhang et al. 2016) have confirmed that thermal inactivation of *C. burnetii* in non-bovine milks is similar to that achieved in bovine milk. International human milk banks, including those in Australia, routinely perform Holder pasteurisation (62.5°C for 30 minutes) 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 any *C. burnetii* contamination potentially present in human milk.

Pooling of human milk from multiple donors is common practice amongst many human milk banks and would dilute the bacterial 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 remains uncertainty about the potential for transmission of *C. burnetii* by ingestion of human milk by infants. The possibility of infection through ingestion of viable *C. burnetii* in food or drink remains an area of contention, and there are no studies on the infectious dose via human milk as a route of transmission. There is a lack of data on any long term sequelae following infection during infancy.

Risk characterisation

Q fever in infants is a serious illness. However, *C. burnetii* is likely to be of very low infectivity by ingestion. Transmission to infants via human milk has not been clearly demonstrated, even though there is some evidence for the presence of viable *C. burnetii* in human milk samples. *C. burnetii* in imported human milk and human milk products does not present a potential medium or high risk to public health and safety.

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References

Angelakis E, Raoult D (2010) Q Fever. Veterinary Microbiology 140:297–309

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

Boarbi S, Fretin D, Mori M (2016) Coxiella burnetii, agent de la fièvre Q. Canadian Journal of Microbiology 62:102–122

Boden K, Brueckmann A, Wagner-Wiening C, Hermann B, Henning K, Junghanss T, Seidel T, Baier M, Straube E, Theegarten D (2012) Maternofetal consequences of Coxiella burnetii infection in pregnancy: A case series of two outbreaks. BMC Infectious Diseases 12:359

Brooke RJ, Kretzschmar MEE, Mutters NT, Teunis PF (2013) Human dose response relation for airborne exposure to Coxiella burnetii. BMC Infectious Diseases 13:488

Brooke RJ, Mutters NT, Péter O, Kretzschmar MEE, Teunis PFM (2015) Exposure to low doses of Coxiella burnetii caused high illness attack rates: Insights from combining human challenge and outbreak data. Epidemics 11:1–6

Bryan FL (1983) Epidemiology of milk-borne diseases. Journal of Food Protection 46:637–649

Carcopino X, Raoult D, Bretelle F, Boubli L, Stein A (2007) Managing Q fever during pregnancy: The benefits of long-term cotrimoxazole therapy. Clinical Infectious Diseases 45:548–555

CDC (2019) Q Fever. Centers for Disease Control and Prevention, Atlanta. https://www.cdc.gov/qfever/. Accessed 14 February 2019

Cerf O, Condron R (2006) Coxiella burnetii and milk pasteurization: An early application of the precautionary principle? Epidemiology and infection 134:946–951

ECDC (2010) Risk assessment on Q fever. Technical report. European Centre for Disease Prevention and Control, Stockholm

EFSA (2010) Scientific Opinion on Q fever. EFSA Journal 8:1595

Eldin C, Mélenotte C, Mediannikov O, Ghigo E, Million M, Edouard S, Mege J-L, Maurin M, Raoult D (2017) From Q fever to Coxiella burnetii infection: A paradigm change. Clinical Microbiology Reviews 30:115–190

Enright JB, Sadler WW, Thomas RC (1957a) Pasteurization of milk containing the organism of Q fever. American Journal of Public Health and the Nation's Health 47:695–700

Enright JB, Sadler WW, Thomas RC (1957b) Thermal inactivation of Coxiella burnetii and its relation to pasteurization of milk. Public Health Monograph 47:1–30

Fournier PE, Etienne J, Harle JR, Habib G, Raoult D (2001) Myocarditis, a rare but severe manifestation of Q fever: Report of 8 cases and review of the literature. Clinical Infectious Diseases 32:1440–1447

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

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

Kumar A, Yadav MP, Kakkar S (1981) Human milk as a source of Q-fever infection in breast-fed babies. The Indian Journal of Medical Research 73:510–512

Maltezou HC, Raoult D (2002) Q fever in children. The Lancet Infectious Diseases 2:686–691

Marrie TJ, Raoult D (2010) Coxiella burnetii (Q fever). In: Mandell GL, Bennett JE, Dolin R (eds) Mandell, Douglas, and Bennett's principles and practice of infectious disease, 7th edition, vol 2. Churchill Livingstone, Philadelphia, pp 2511–2519

Mediannikov O, Fenollar F, Socolovschi C, Diatta G, Bassene H, Molez J-F, Sokhna C, Trape J-F, Raoult D (2010) Coxiella burnetii in humans and ticks in rural Senegal. PLoS Neglected Tropical Diseases 4:e654

Munster JM, Steggerda LM, Leenders AC, Aarnoudse JG, Hak E (2012) Screening for Coxiella burnetii infection during pregnancy: Pros and cons according to the Wilson and Jungner criteria. Euro Surveillance 17:20061

OIE (2018) Manual of diagnostic tests and vaccines for terrestrial animals (mammals, birds and bees), Seventh edition. OIE, Paris

Prasad BN, Chandiramani NK, Wagle A (1986) Isolation of Coxiella burnetii from human sources. International Journal of Zoonoses 13:112–117

Richardus JH, Dumas AM, Huisman J, Schaap GJ (1985) Q fever in infancy: A review of 18 cases. Pediatric Infectious Disease 4:369–373

Scott GH, Williams JC (1990) Susceptibility of Coxiella burnetii to chemical disinfectants. Annals of the New York Academy of Sciences 590:291–296

Signs KA, Stobierski MG, Gandhi TN (2012) Q fever cluster among raw milk drinkers in Michigan, 2011. Clinical Infectious Diseases 55:1387–1389

Tamrakar SB, Haluska A, Haas CN, Bartrand TA (2011) Dose-response model of Coxiella burnetii (Q fever). Risk Analysis 31:120–128

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

Zhang C, Zhai Y, Wang P, Fleischman G, Stewart D (2016) Thermal Inactivation of Coxiella burnetii and Micrococcus luteus in Bovine and Non-bovine Milk Pasteurization. Journal of Food Protection 79:187–188