

Q&A 376.3

Yellow Fever Vaccine – is it safe whilst breastfeeding?

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Background

Yellow fever is an acute flavivirus infection spread by the bite of an infected mosquito. It has an incubation period of approximately three to six days but may be longer (1). Under the International Health Regulations, countries may require immunisation against yellow fever as a condition of entry and a valid International Certificate of Vaccination would be required as evidence.

Yellow fever vaccine is a live, attenuated preparation of the 17D strain of yellow fever virus grown in specific pathogen-free embryonated chick eggs.(2) A single dose correctly administered confers immunity in 95 to 100% of recipients within approximately 10 days of administration, with immunity persisting for at least ten years and possibly for life. (1, 3)

This Q&A examines the data on the potential risks to a breastfed infant whose mother has received yellow fever vaccine.

Answer

Breastfeeding

The evidence for a potential risk to breastfed infants is based on three recent cases. In the first, a Brazilian woman who was exclusively nursing her newborn received yellow fever vaccine on day 15 postpartum. Eight days later her infant developed fever, irritability and refused to nurse. One day later, the infant developed seizure-like activity. The infant was hospitalised and had periods of somnolence and irritability and required intravenous anticonvulsants to control seizures. Magnetic resonance imaging (MRI) was consistent with encephalitis. Yellow fever-specific immunoglobulin-M antibodies were detected in serum and cerebrospinal fluid (CSF). Laboratory examination of the infant's cerebrospinal fluid confirmed the presence of a viral strain identical to the vaccine. No breast milk or maternal serum was collected for testing. Following treatment the infant recovered completely. Follow-up of the infant at 6 months showed normal neurodevelopment and growth (4).

A mother had received a yellow fever vaccination when her breastfed infant was 10 days of age. Three days later, the infant and mother travelled to Venezuela for one week. At 5 weeks of age, the infant developed focal seizures on alternating sides, poor appetite, and vomiting following a 2-day history of fever and irritability. The infant's serum was positive for yellow fever and the CSF was positive for yellow fever antigen, but negative for yellow fever virus. The infant recovered fully after receiving treatment and had no apparent neurological deficit as a result. Although the infant had travelled to Venezuela where yellow fever is known to be endemic, he was not in an area known to be infected, and there were no known urban outbreaks at the time of his visit. The authors concluded that the adverse reactions were probably caused by yellow fever vaccine transmitted via breast milk to the infant, although they could not entirely rule out other causes (5).

A further probable case of yellow fever vaccine-associated neurologic disease was reported in a 38-day-old infant whose mother was vaccinated 24 days earlier with the Brazilian-manufactured yellow fever vaccine 17D. The infant was exclusively breastfed. Although it was not possible to determine if the breast milk was the mode of transmission, no other plausible cause was identified (6).

A review by the WHO Global Advisory Committee on Vaccine Safety (7) stated that further research is needed to quantify the potential risk of transmission of yellow fever vaccine virus from mothers to infants, including the possibility of transmission through breast milk. They also recommend that, in areas where yellow fever is endemic, or during outbreaks, the benefits of vaccinating nursing mothers are likely to far outweigh the risk of potential transmission of vaccine virus to infants. Further, nursing mothers who are considering travel to endemic areas should be counselled regarding the benefits and potential risks of vaccination. Vaccination is indicated for breastfeeding women where travel cannot be avoided or postponed (7).

A review published just before the above case reports recommended that yellow fever vaccine should be avoided in a breastfeeding mother due to the theoretical risk of transmitting yellow fever virus to the breastfed infant (8). The authors re-affirmed this position subsequently (9) after publication of the first case of yellow fever from breast milk (4).

Use in infants

Yellow fever vaccine has been associated with rare reports of encephalitis, now termed vaccine-associated neurological disease (YEL-AND). The World Health Organisation has stated that, since 1945, there have been at least 26 cases of proven or probable YEL-AND of which 16 occurred in infants aged less than 6 months (3).

As a precaution against possible encephalitis, infants less than 9 months of age are not generally immunised, although it may be advisable to immunise at 6 to 8 months of age during epidemics. Infants over 9 months of age should be vaccinated themselves if they will be traveling with their mother to a yellow-fever endemic area (1).

Viraemia and Immunogenicity

Following yellow fever vaccine administration, primary vaccine recipients often develop a low-level viraemia with the vaccine virus. The viraemia usually occurs within 3 to 7 days and persists for 1 to 3 days, declining as yellow fever vaccine immunoglobulin M antibodies are developed (10).

Studies have demonstrated that 80%–100% of vaccinated people develop neutralizing antibodies by 10 days after vaccination (10). Most studies indicate that >99% of vaccinated people developed yellow fever vaccine neutralizing antibodies by 28 days after vaccination (11)

Summary

- ◆ Studies indicate that >80% of vaccinated people developed yellow fever vaccine neutralizing antibodies by 10 days after vaccination and >99% by 28 days.
- ◆ Adverse effects, specifically encephalitis (yellow fever vaccine associated neurological disease) have been seen in three breastfed infants whose mothers received yellow fever vaccine.
- ◆ Mothers travelling to endemic areas with infants under 9 months of age should be strongly encouraged to adjust their itinerary to avoid the need for vaccination, or postpone their trip until they are no longer breastfeeding or their infant is over 9 months of age and can be vaccinated themselves..
- ◆ Until further data is available, mothers of infants under 9 months of age who require vaccination, should be recommended to abstain from breastfeeding (express and discard) for two to three weeks (12). Maintaining breast milk production for this length of time is unlikely to be possible in practice, therefore discontinuing breastfeeding may need to be considered.
- ◆ Infants over 9 months of age should be vaccinated themselves if they will be travelling with their mother to a yellow-fever endemic area. Exposure to yellow fever vaccine via breast milk would not increase the risk to an infant who also receives the vaccination.

Limitations

- Evidence relating to excretion of the yellow fever virus in breast milk is relatively poor and limited.
- The paucity of evidence is exacerbated when considering other confounding factors e.g. origin of recipients and destination of travel.
- The information relates to full term and healthy infants. If the infant is preterm, of low birth weight or has other concomitant pathology or medical problems, then specialist advice should be sought as this answer may not apply. Contact the UK Drugs in Lactation Advisory Service (UKDILAS) provided by the Trent and West Midlands Medicines Information Services (Tel: 0116 258 6491 or 0121 311 1974).

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Quality Assurance

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Search strategy

- Embase and Medline (Standard UKDILAS Search Patterns) [\[link\]](#)
- In-house UKDILAS database
- Medications and Mothers' Milk Online (Medilact): Yellow Fever Vaccine
- Drugs and Lactation Database (LactMed). Toxnet Toxicology Data Network, United States National Library of Medicine. Available from <http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?LACT> Yellow Fever Vaccine monograph
- Centres for Disease Control and Prevention. Available from <http://www.cdc.gov/> Yellow Fever Vaccine Recommendations
- National Travel Health Network & Centre (NaTHNaC), Hospital for Tropical Diseases, London. Available from www.nathnac.org
- Manufacturers (eMC) of Yellow Fever Vaccine (Staril[®])