

EDITORIAL
**BOTULISM, BOTULINUS TOXIN, BYHEART BABY FORMULA: LIFE-
 SAVING THORACIC DUCT LYMPH DRAINAGE?**

M.H. Witte, K.E. Carr, N. Barnett, M.D. Seckeler

Departments of Surgery (MHW,NB) and Pediatrics (Cardiology) (KEC,MDS), University of Arizona, Tucson, Arizona, USA

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In November 2025, a series of cases of botulism were reported following infant ingestion of ByHeart Baby Formula (1). These infants exhibited symptoms characteristic of botulism (poor tone, weak sucking/swallowing, ptosis, constipation, respiratory distress), and botulinus toxin was identified in samples of the formula (2,3). While serious illness developed and lawsuits against the company were filed, to date, fortunately no deaths have been reported (1,4). There have been multiple outbreaks of botulism related to infant formulas over the past 20 years (3). In addition to supportive care (IV hydration, mechanical ventilation), all recently affected infants were treated with the only approved therapy for children under 1 year old, Human Botulism Immune Globulin-Intravenous [(BIG-IV), licensed as BabyBIG] (3,4).

Over the past decades, botulinum toxin (Botox) injections have become popular for treatment of spasticity as well as cosmetic enhancement. While generally considered safe, there are increasing reports of iatrogenic botulism related to these therapies (5).

Experiments performed by Barnes and Trueta in 1941 (6) reported the exclusive transport of black tiger snake venom and

tetanus toxin (both relatively large molecules) via the lymphatics (and thoracic duct) after direct wound inoculation, whereas the much smaller cobra venom immediately entered the blood stream, findings expanded in our recent study of coral snake venom infected subcutaneously (7). Indeed, different botulinus neurotoxins of different molecular weight have recently been examined and as much as 10% of the dose instilled into the ligated duodenum was recovered from thoracic duct lymph (8). Further, studies of direct entry of viruses of larger size into regional lymphatics rather than blood (9) and thoracic duct lymph cultures contrasted to central blood cultures promptly became positive for an array of bacteria including clostridium species after experimental ligation of the common bile duct or caecum (10). Clearly, it would be valuable to pursue the insights provided by this sequence of previous studies.

In 1969, we proposed thoracic duct lymph drainage by cannulation, a procedure performed in hundreds of patients with hepatic cirrhosis, heart failure, and assorted other medical conditions, to relieve excess fluid accumulation in the peritoneal cavity and edema elsewhere (11). We also proposed its use after venomous bites by snakes (12) including studies of the lymphatic route of transport and pharmacokinetics of *Micrurus fulvius* (coral snake) venom in sheep depend-

ing on the molecular weight of the specific venom (7). To our knowledge this approach has not been used clinically.

Now, the opportunity to take advantage of the lymphatic absorption of botulinus toxin in sick infants and (adults who have been exposed acutely to the toxin) could be a reasonable and possibly lifesaving alternative approach. Surgical exposure of the thoracic duct in the neck, a relatively minor procedure but nonetheless invasive, can now be potentially avoided as endovascular catheterization of the thoracic duct has increasingly been employed (13,14). This minimally invasive, and possibly lifesaving procedure, could be performed promptly after ingestion of botulinum toxin and allow for external drainage to avoid the significant morbidities and mortality of the exposure.

REFERENCES

1. U.S. Food and Drug Administration. Outbreak Investigation of Infant Botulism: Infant Formula (November 2025). <https://www.fda.gov/food/outbreaks-foodborne-illness/outbreak-investigation-infant-botulism-infant-formula-november-2025>. Website accessed December 27, 2025.
2. U.S. Food and Drug Administration. ByHeart Updates Information Regarding Voluntary Recall of all Batches of ByHeart Whole Nutrition Infant Formula Cans and Packs Because of Possible Health Risk. <https://www.fda.gov/safety/recalls-market-withdrawals-safety-alerts/byheart-updates-information-regarding-voluntary-recall-all-batches-byheart-whole-nutrition-infant>. Website accessed December 27, 2025.
3. Dabritz, HA, CH Chung, JS Read, et al: Global occurrence of infant botulism: 2007-2021. *Pediatrics* 155 (2025), e2024068791. doi: 10.1542/peds.2024-068791.
4. NBC News. More families sue ByHeart as company confirms botulism spores were found in its infant formula. <https://www.nbcnews.com/health/kids-health/families-sue-infant-formula-maker-byheart-botulism-outbreak-rcna244989>. Website accessed December 27, 2025.
5. Abouelkheir, AR, ACD Silva, AMA Sayed et al: Iatrogenic botulism following botulinum toxin injection: A scoping review of clinical characteristics, risk factors, and dermal considerations. *Cutan. Ocul. Toxicol.* 44 (2025), 374-387. doi: 10.1080/15569527.2025.2547599.
6. Barnes, JM, J Trueta: Absorption of bacteria, toxins and snake venoms from the tissues: Importance of the lymphatic circulation. *Lancet* 237 (1941), 623-626. doi: 10.1016/S0140-6736(00)60977-7.
7. Paniagua, D, L Jimenez, C Romero, et al: Lymphatic route of transport and pharmacokinetics of micrurus fulvius (coral snake) venom in sheep. *Lymphology* 45 (2012), 144-153.
8. Fujinaga, Y, MR Popoff. Translocation and dissemination of botulinum neurotoxin from the intestinal tract. *Toxicon* 147 (2018), 13-18
9. Yoffey, JM, FC Courtice: *Lymphatics, Lymph and Lymphoid Tissue*. Academic Press, 1970, 399-402.
10. Cole, WR, R Petit, A Brown, et al: Lymphatic transport of bacteria in surgical infection. *Lymphology* 1 (1968), 52-57.
11. Dumont, AE, MH Witte: Clinical usefulness of thoracic duct cannulation. *Adv. Intern. Med.* 15 (1969), 51-71.
12. Paniagua, D, I Vergara, R Roman, et al: Antivenom effect on lymphatic absorption and pharmacokinetics of coral snake venom using a large animal model. *Clin. Toxicol.* 57 (2019), 727-734. doi: 10.1080/15563650.2018.1550199.
13. Kim, H, D Hyun, SW Shin, et al: Factors contributing to successful transvenous retrograde thoracic duct cannulation. *J. Vasc. Interv. Radiol.* 34 (2023), 205-211. doi: 10.1016/j.jvir.2022.10.037.
14. Gremen, E, E Mathieu, Y Teyssier, et al: Optimization of venous access for transvenous retrograde cannulation of the thoracic duct. *J. Vasc. Interv. Radiol.* 35 (2024), 790-79. doi: 10.1016/j.jvir.2023.08.045.

Marlys H. Witte, MD
Professor of Surgery, Neurosurgery, & Pediatrics
University of Arizona College of Medicine
Tucson, AZ USA
Phone: (520) 626-6118
E-mail: lymph@surgery.arizona.edu