

April 30, 2024

Mandy K. Cohen, M.D., M.P.H.  
Director  
Centers for Disease Control and Prevention  
U.S. Department of Health and Human Services  
1600 Clifton Road  
Atlanta, GA 30329

Robert M. Califf, M.D.  
Commissioner  
Food and Drug Administration  
U.S. Department of Health and Human Services  
10903 New Hampshire Avenue  
Silver Spring, MD 20993

*Submitted electronically*

Dear Director Cohen and Commissioner Califf:

Public Citizen, a consumer advocacy organization with more than 500,000 members and supporters nationwide, is writing to express concerns about some of the information provided by the Centers for Disease Control and Prevention (CDC) in its April 23, 2024, Health Alert Network Health Advisory on the clusters of adverse effects reported in people receiving what the agency characterized as “counterfeit or mishandled botulinum toxin injections.”<sup>1</sup>

In December 2023, Public Citizen petitioned the Food and Drug Administration (FDA) to strengthen the safety warnings regarding iatrogenic botulism in the labeling of all approved botulinum toxin drugs and remove misleading promotional claims from the labeling of onabotulinumtoxinA (Botox and Botox Cosmetic).<sup>2</sup>

The CDC health advisory rightfully asks clinicians to consider the likelihood of adverse effects from botulinum toxin injections (including those given for cosmetic purposes) and realize that symptoms of localized adverse effects from injection of botulinum toxin may overlap with initial botulism symptoms. However, these recommendations include some

---

<sup>1</sup> Centers for Disease Control and Prevention. Adverse effects linked to counterfeit or mishandled botulinum toxin injections. April 23, 2024. <https://emergency.cdc.gov/han/2024/han00507.asp>. Accessed April 26, 2024.

<sup>2</sup> Public Citizen. Petition to the FDA to strengthen safety warning for Botox and related drugs and remove misleading claims from Botox/Botox Cosmetic labeling. December 12, 2023. <https://www.citizen.org/article/petition-to-the-fda-to-strengthen-safety-warning-for-botox-and-related-drugs-and-remove-misleading-claims-from-botox-botox-cosmetic-labeling>. Accessed April 26, 2024.

information that contradicts the agency’s 2021 clinical guidelines for diagnosis and treatment of botulism.<sup>3</sup>

First, the CDC advisory seems to limit botulism symptoms to symmetric cranial nerve palsies, possibly followed by a descending symmetric flaccid paralysis. In contrast, the CDC clinical guidelines state that up to 15% of botulism patients in large case series have reported asymmetry or unilateral neurologic deficits and that certain thorough case studies describe botulism patients who had asymmetric neurologic deficits.<sup>4</sup> These guidelines also acknowledge diagnostic challenges caused by “variations in the spectrum of signs and symptoms of botulism [that] were highlighted in the delayed recognition of a large foodborne botulism outbreak, in which some patients initially received diagnoses of myasthenia gravis, stroke, or psychiatric disorders.” Furthermore, Public Citizen has found published case reports showing that patients with iatrogenic botulism may present with asymmetric muscle weakness or asymmetric ptosis, which are signs and symptoms of asymmetric cranial nerve involvement.<sup>5,6</sup>

Second, the CDC advisory states that six of the 22 symptomatic people in 11 states received the botulism antitoxin to treat suspected botulism, but none of the seven people who were tested had a laboratory-confirmed diagnosis of botulism demonstrating the existence of botulinum toxin in serum (presumably using either mouse bioassay [MBA] or mass spectrometry as mentioned in the advisory). However, the MBA test may not be sufficiently sensitive to detect low levels of the toxin. In fact, the most recent U.S. laboratory-confirmed iatrogenic botulism case cited in the CDC advisory — which has been published by researchers from the CDC and the Los Angeles County Department of Public Health — had a negative MBA test results for serum samples collected on the fifth day after the onset of symptoms and prior to the administration of the antitoxin.<sup>7</sup> Instead, the diagnosis of iatrogenic botulism was confirmed in this person using a highly sensitive test called the matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS) whose results were available 19 days after serum collection.

Third, the CDC advisory downplays the risks of low-dose injections of botulinum toxin drugs by indicating that “low doses of injected toxins are not likely to reach circulation or produce botulism with its life-threatening manifestations.” Public Citizen’s FDA petition presents strong evidence supporting an association between treatment with initial or repeated approved low doses of approved botulism toxin drugs, including those used for

---

<sup>3</sup> Rao AK, Sobel J, Chatham-Stephens K, et al. Clinical guidelines for diagnosis and treatment of botulism, 2021. *MMWR Recomm Rep*. 2021;70(2):1-30.

<sup>4</sup> *Ibid*.

<sup>5</sup> Baig MA, Nogar J. A case of asymmetric cranial nerve palsy due to iatrogenic botulism. *Asia Pac J Med Toxicol*. 2021;10(4):149-150.

<sup>6</sup> Hovseth K, Badillo R, Schaeffer S, et al. Atypical botulism presentation following botulinum toxin with phenol therapy. In: *North American Congress of Clinical Toxicology*. Washington, D.C.; 2011:561.

<sup>7</sup> Halai UA, Terashita D, Kim M, et al. Notes from the field: Intestinal colonization and possible iatrogenic botulism in mouse bioassay-negative serum specimens - Los Angeles County, California, November 2017. *MMWR Morb Mortal Wkly Rep*. 2018;67(43):1221-1222.

cosmetic purposes, and systemic iatrogenic botulism that may necessitate timely administration of botulinum antitoxin.

For these reasons, Public Citizen urges the CDC to revise its advisory to encourage clinicians to err on the side of suspecting iatrogenic botulism in all patients experiencing adverse effects consistent with the effects of the distant spread of the toxin, including asymmetric neurological deficits, within hours to weeks after receiving botulinum toxin injections.

Public Citizen also asks the agency to promptly follow its guidelines that recommend the administration of botulinum antitoxin, the only specific therapy for botulism, as quickly as possible to all people with signs or symptoms that are suggestive of botulism instead of waiting until affected persons develop signs and symptoms of neurologic weakness.

Published reports show that dramatic clinical improvements have occurred when the antitoxin is administered even after the 10th<sup>8</sup> or 12th<sup>9</sup> day following the initial development of systemic symptoms.

As their investigations continue, the CDC and the FDA should fully consider the possibility that at least some of the cases may be related to recommended doses of approved and properly administered botulinum toxin drugs.

The recent clusters of people reporting adverse effects related to botulinum toxin injections underscore the urgent public health importance of strengthening the safety warnings of botulinum toxin drugs. The FDA should promptly grant Public Citizen's petition.

Thank you for considering our comments on this important public health issue.

Sincerely,



Azza AbuDagga, M.H.A., Ph.D.  
Health Services Researcher  
Public Citizen's Health Research Group  
1600 20<sup>th</sup> Street, N.W.  
Washington, DC 20009

---

<sup>8</sup> Mohammed EA, Salah Eldin HM. Highlights of serious distant effects after local injection of botulinum toxin therapy: a report of pediatric case. *Int J Case Rep Images*. 2020;11(June 2):101127Z01EM2020.

<sup>9</sup> Oner OG, Gudek HC, Cetin OE, Demir S. Iatrogenic botulism: a case treated with botulinum antitoxin. *Clin Neuropharmacol*. 2023;46(2):82-84.