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Maine Health Alert Network (HAN) System

PUBLIC HEALTH ADVISORY

To: All Health Care

From: Dr. Isaac Benowitz, State Epidemiologist

Subject: **U.S. CDC: Adverse Effects Linked to Counterfeit or Mishandled Botulinum Toxin Injections**

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Please take a moment to review this information on adverse effects linked to counterfeit or mishandled botulism toxin injections in the U.S.

U.S. CDC is reporting an increase of adverse effects associated with botulism toxin injections between the dates of November 4, 2023, to March 31, 2024. Most reported cases received botulinum toxin injections for cosmetic purposes. Currently, states reporting cases include California, Colorado, Florida, Illinois, Kentucky, Nebraska, New Jersey, New York City, Tennessee, Texas, and Washington.

Botulism is immediately reportable to the Maine CDC upon recognition or strong suspicion of disease. To contact Maine CDC, please call the 24/7 disease reporting number at 800-821-5821.

Do not delay reporting a suspected case. There is no stockpile of antitoxin at the state level. The Maine CDC will need to contact the U.S. CDC clinical botulism service for consultation, laboratory testing instructions, and antitoxin release. If public health clinical consultation supports botulism, treatment should begin as soon as antitoxin is available. It is not necessary to wait for laboratory confirmation to begin treatment, however, laboratory specimens should be obtained prior to the administration of antitoxin.

U.S. CDC: Adverse Effects Linked to Counterfeit or Mishandled Botulinum Toxin Injections

Summary
The U.S. Centers for Disease Control and Prevention (U.S. CDC) is issuing this Health Alert Network (HAN) Health Advisory to alert clinicians about risks of counterfeit or mishandled botulinum toxin injections. U.S. CDC, the U.S. Food and Drug Administration (FDA), and state and local partners are investigating clusters of 22 people in 11 U.S. states reporting adverse effects after receiving injections with counterfeit botulinum toxin or injections

administered by unlicensed or untrained individuals or in non-healthcare settings, such as homes or spas. Eleven patients were hospitalized, and none have died. When botulinum toxin diffuses around the injection site, it can result in adverse effects. Botulism is the disease caused by botulinum toxin circulating in the blood and producing effects remotely from the injection site. There may be symptom overlap between the presentation of localized adverse effects from injection of botulinum toxin, especially in the head and neck, and the early symptoms of botulism. Information about the botulinum toxin injection (e.g., dose) can help distinguish between botulism and localized adverse effects but is challenging to obtain for counterfeit products. Clinicians should consider the possibility of adverse effects from botulinum toxin injections in patients presenting with localized paralysis. Clinicians should immediately contact Maine CDC at 1-800-821-5821 if they suspect botulism.

Background

Botulism is a rare and sometimes fatal illness caused by botulinum toxin. Initial botulism symptoms may include double or blurred vision, drooping eyelids, slurred speech, difficulty swallowing, and difficulty breathing. These symptoms may be followed by a descending, symmetric muscle weakness that progresses over hours to days. Administration of botulism antitoxin can neutralize toxin circulating in the blood; therefore, treating botulism patients with botulism antitoxin early in the course of disease can prevent the progression of paralysis and consequent complications. Administration of antitoxin is not indicated for local effects of low-dose injections of botulinum toxin preparations, because the low doses of injected toxin are not likely to reach circulation or produce botulism with its life-threatening manifestations.

Some localized paralytic effects, resulting from diffusion of the toxin around the injection site, are expected from botulinum toxin administration. Most individuals with localized symptoms (e.g., dysphagia after injection to the neck) following low-dose cosmetic or therapeutic injections using FDA-approved products will not require treatment with botulism antitoxin. Iatrogenic botulism can occur after cosmetic or therapeutic injections of botulinum toxin when the toxin circulates in the blood and produces effects remotely from the injection site. Iatrogenic botulism is rare; the most recent laboratory-confirmed domestic case occurred in 2017.

As of April 18, 2024, 22 people with adverse effects have been reported in California, Colorado, Florida, Illinois, Kentucky, Nebraska, New Jersey, New York City, Tennessee, Texas, and Washington. Symptom onset dates ranged from November 4, 2023, to March 31, 2024. All symptomatic people were females aged 25 to 59 years. All reported receiving botulinum toxin injections by unlicensed or untrained individuals or in non-healthcare settings, including homes or spas. Most (20, 91%) reported receiving botulinum toxin injections for cosmetic purposes.

Among all 22 people, symptoms began a median of 3 days after exposure (range 0 to 20 days) and included symptoms near the injection site (e.g., blurred vision and ptosis after facial injection), dry mouth, slurred speech, shortness of breath, fatigue, and generalized weakness. Of 20 people with information available, 11 (55%) symptomatic people were hospitalized. Six of the 22 symptomatic people received botulism antitoxin to treat suspected botulism. Seven symptomatic people underwent botulinum toxin testing to determine if they had circulating botulinum toxin, which would support a diagnosis of botulism; results were negative for six symptomatic people and are pending for one symptomatic person. Negative results do not rule out botulism as levels of toxin in serum may have fallen below the limit of detection of laboratory tests. None of the 22 symptomatic people met the case definition for botulism, and none have died.

These adverse events have been linked to improper procurement and administration of botulinum toxin. Botulinum toxin should be administered only by licensed providers, using only recommended doses of FDA-approved botulinum toxin, preferably in a licensed or accredited healthcare setting. Providers should be trained in the proper administration of botulinum toxin, practicing in accordance with state and local requirements.

More information about the counterfeit products may be found on FDA's website.

Recommendations for Clinicians

Diagnosis, consultation, and treatment

- Consider the possibility of adverse effects from botulinum toxin injections, including those given for cosmetic reasons, in patients presenting with localized paralysis near the injection site.
    - Ask patients about history of botulinum toxin injections, including the dose.

- Be aware of symptom overlap between the presentation of localized adverse effects from injection of botulinum toxin and the early symptoms of botulism. To help distinguish early botulism symptoms from localized adverse effects:
    - Assess for symmetry of cranial nerve palsies; symmetric cranial nerve palsies are expected with botulism.
    - Assess for progression of cranial nerve palsies, possibly followed by a descending symmetric flaccid paralysis. These should raise suspicion for botulism.
- **If botulism is suspected, call your Maine CDC at 1-800-821-5821 immediately** for consultation. Health departments and health care providers can contact the CDC clinical botulism service 24/7 at 770488-7100.
- If public health clinical consultation supports botulism, request antitoxin and begin treatment as soon as it is available. **Do not wait for laboratory confirmation to begin treatment**.

Clinician reporting

- A suspected case of botulism is a clinical and public health emergency. Suspected botulism cases should be reported immediately to Maine CDC at 1-800-821-5821.
- Report adverse events related to the use of any medications, including suspected counterfeit medications, to FDA's MedWatch Safety Information and Adverse Event Reporting Program.

Counseling patients

- Counsel patients who report using or being interested in using botulinum toxin about potential adverse effects.
- Advise patients to receive injections only from licensed providers who are trained in proper administration of FDA-approved botulinum toxin products, preferably in a licensed or accredited healthcare setting.

Recommendations for Laboratories

- Diagnostic testing for suspected botulism may be done through the U.S. CDC National Botulism Laboratory or state public health laboratories.
- Laboratory confirmation of botulism is done by demonstrating the presence of botulinum toxin in serum through either mouse bioassay or mass spectrometry.
- Testing varies by state. Contact the U.S. CDC clinical botulism service (available 24/7 at 770-4887100) or Maine CDC for further guidance on submitting clinical specimens for testing.

Recommendations for the Public

- Get injections only from licensed and trained professionals in licensed or accredited healthcare settings.
- If you are concerned that you or someone you know might have symptoms of botulism, including trouble swallowing or breathing, see your doctor or go **immediately** to the emergency room. **Do not wait.**
- Report suspected counterfeit botulinum toxin products to FDA at 800-551-3989 or through FDA's form for reporting suspected criminal activity.
- Report harmful reactions related to the use of any medications, including suspected counterfeit medications, to FDA's MedWatch Safety Information and Adverse Event Reporting Program.

For More Information

- U.S. CDC: Harmful Reactions Linked to Counterfeit "Botox" or Mishandled Botulinum Toxin Injections
- FDA: Counterfeit Version of Botox Found in Multiple States
- Information for Health Professionals on Botulism | U.S.CDC
- About Botulism | U.S. CDC
- Preventing Botulism | U.S. CDC
- Injection Safety | U.S. CDC

References

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2. Rao AK, Sobel J, Chatham-Stephens K, Luquez C. Clinical Guidelines for Diagnosis and Treatment of Botulism, 2021. *MMWR Recomm Rep*. 2021;70(No. RR-2):1–30. doi:10.15585/mmwr.rr7002a1
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