Iatrogenic Botulism 101

A GUIDE FOR DOCTORS, NURSES,
& OTHER HEALTHCARE PROVIDERS

by Megan McCue

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ABOUT THE AUTHOR

Megan McCue, CCC-SLP, is a medical speech-language pathologist and writer. After developing iatrogenic botulism from 12 units of Xeomin (once!), she became passionate about educating the public and fellow medical professionals about adverse effects following botulinum toxin injections.

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OTHER BOOKS BY THE AUTHOR:

Me Tox Pretty (2024)
Notox (2025)

DEDICATION

To all the iatrogenic botulism victims who will come after me:
May you **never** have to fight the battle to be believed by medical providers while also suffering from one of the most horrific illnesses known to mankind.

And to Jane and Dennis:
Two very wise mentors who have patiently and graciously helped me untangle the complexities of this little toxin.

INTRODUCTION

In July of 2024, when I developed iatrogenic botulism in the days and weeks after receiving 12 units of Xeomin for the first time, I spent months desperately seeking medical care and answers about what was happening in my brain and body.

With every ER visit (and there were many), I was met with furrowed brows and exasperated sighs. No doctor knew what was wrong with me, and one by one they told me my symptoms had nothing to do with my recent botulinum toxin injections. My blood tests, cranial nerve exams, EKGs, and x-rays were all normal; my blood pressure and oxygen sats were perfect.

My symptoms (sudden onsets of near-daily anxiety, head pressure, neck muscle weakness, fatigue, brain fog, extreme dry mouth, difficulty swallowing solid food, severe insomnia, and significant hair loss within the days and weeks after my injections) were brand new, alarming, and

disabling to me, but they weren't exactly life-threatening per se. I'm sure the hospital staff (after seeing me show up at the ER for the fifth time in a month) assumed I was yet another frantic, anxious hypochondriac who was exaggerating her symptoms.

I had no way of proving that the terrifying botulism symptoms I was experiencing were *real*, as all of them were subjective symptoms that could not be measured by modern technology. Months passed without any answers from the medical community, and I was left unable to work, care for my children, or participate in life as I knew it.

Nearly three months after my injections, the brain fog and fatigue I had been experiencing began to clear up, and I became determined to figure out what had happened to me and why no doctors had been able to help me.

When I finally read through the Xeomin and Botox clinical trials, as well as pertinent medical literature related to botulinum toxin injections and their adverse effects, I realized that the symptoms I had been suffering from were not, in fact, unique.

They were all documented adverse effects of botulinum toxin injections that can occur when the toxin spreads systemically.

I continued digging online, and to my surprise, found tens of thousands of people gathered in online support groups who were also desperately seeking answers about the alarming and disabling symptoms they were experiencing after their recent Botox injections. I also found news articles detailing lawsuits that had been filed against Allergan, the makers of Botox, by people who had developed botulism in the days and weeks after their injections. Most of these victims were living with long-term complications from botulism, and some had even died in the weeks after their injections.

When I realized that there were many other iatrogenic botulism sufferers around the world who had all endured the same inadequate medical care I had, I felt an immediate call to figure out why accessible and accurate information about this 35-year-old illness was extremely hard to find, for patients and medical professionals alike.

I spent months voraciously reading through stories of iatrogenic botulism sufferers, the history and pathophysiology of botulinum toxin, and botulinum toxin manufacturers' clinical trial data.

I became determined to learn as much as I could about this little toxin, and I also began writing about the information I was uncovering.

Since publishing my first two books, *Me Tox Pretty* and *Notox*, I have personally heard from women and men around the world who have been struggling with botulism symptoms for *years* following these injections. The victims I hear from all have different ages, races, socioeconomic backgrounds, health statuses, and reasons for receiving Botox, and yet, they almost always have the following three things in common:

- They were not believed by their injecting doctors/nurses or primary care doctors when they reported botulism symptoms in the hours, days, and weeks after receiving their injections

- They were told that botulism from Botox injections is not possible, especially with “small” doses
- They were sent home on anxiety medications without diagnoses or antitoxin from emergency rooms

This book is the result of the research I have combed through to date, and my hope is that it will provide you with a concise yet thorough introduction to a disease that remains gravely understudied and misunderstood by healthcare providers and researchers alike.

I am not, nor do I claim to be, an expert on botulism. I am, however, a passionate medical professional who lived through iatrogenic botulism, and who has a deep reverence for truth, transparency, and medical informed consent.

I hope that the evidence I present in this book challenges any preconceived ideas you may have about the safety and risks of botulinum toxin injections, whether you’re a seasoned injector, an ER physician, or a consumer of these products.

My hope is that by writing this book and presenting medical professionals with up-to-date research, clinical trial data, and relevant case studies, I can help spark a long overdue conversation in the medical field about the very real risks of a drug whose safety we often take for granted.

1. WHAT IS IATROGENIC BOTULISM?

THIS CHAPTER INCLUDES:

- BOTULISM AND BOTULINUM TOXIN
- MECHANISM OF ACTION
- BOTULISM AS A SPECTRUM DISEASE
- IATROGENIC BOTULISM
- CURRENT INCIDENCE RATES OF IATROGENIC BOTULISM

IATROGENIC BOTULISM

Botulism that occurs following botulinum toxin injections

BOTULISM AND BOTULINUM TOXIN

During the 1800s, a mysterious foodborne illness was killing people within days of their last meal. Doctors at the time were perplexed, because these poisoned patients were presenting with atypical and bizarre neurological symptoms, including blurry vision, dizziness, dry mouth, difficulty swallowing, muscle weakness, and labored breathing. After their symptoms slowly worsened over days or weeks, more than 70% of these victims died suddenly of respiratory failure or cardiac arrest. Decades passed, while doctors and researchers remained clueless about the disease's cause and pathophysiology.

When an early outbreak of the illness was traced back to blood sausages in Germany, researchers gave the disease the name "botulism," after the Latin word for sausages, "botulus."

In 1895, the toxin responsible for this illness was finally discovered and isolated by Belgian scientist Emile Pierre van Ermengem: Botulinum toxin (abbreviated hereafter as "BoNT"), a neurotoxic protein that is produced by the bacterium *Clostridium botulinum*.

Once the toxin had been isolated, militaries around the world began experimenting with it as a biological war agent due to its astonishing lethality. Just one gram of the toxin, if aerosolized, is enough to kill over 1 million people, making it the most lethal toxin on Earth. The U.S. military spent decades studying the toxin and its effects, and they were the first to develop an antitoxin (which remains the only therapy available for botulism), as well as a BoNT vaccine for soldiers.

In the mid-1940s, British scientist Arnold Burgen and his colleagues discovered *why* this toxin was so deadly. Their research revealed that BoNT, once in the bloodstream, is taken up into the nervous system, where it blocks the release of various neurotransmitters, most notably acetylcholine.

MECHANISM OF ACTION

BoNT acts on the SNARE complex found within presynaptic neurons, where it prevents exocytosis of neurotransmitters by cleaving the SNAP-25 protein (a protein that facilitates the release of transport vesicles containing neurotransmitters). This action on the SNARE complex causes permanent and irreversible damage to nerve terminals, however new nerve terminals can (but do not always) regenerate around the permanently damaged ones in the ensuing months and years after poisoning.

Once in the body, the toxin can spread one of three ways, according to Fung et al.:

- Hematogenously (through the bloodstream)
- By diffusing through adjacent muscle tissue
- Through a process called retrograde axonal transport, when the toxin spreads backwards along nerve cells from the site of injection

What is a unit?
A BoNT unit is not a converted measurement representing milligrams or micrograms. It is a measurement of *lethality* of the toxin. The term "unit" is short for "mouse unit," and one of these units is the amount of injected toxin that caused half of a batch of test mice to die from botulism within a 3-day window. In toxicology, this amount is called the "LD50," or lethal dose, 50%. Each unit of BoNT contains millions of molecules, all of which can spread and attach to nerve synapses anywhere in the body once they have entered the bloodstream.

In the early 21st century, scientists discovered that BoNT was capable of blocking much more than the release of acetylcholine. In 2012, Akaike et al. noted that BoNT, once in the central nervous system (entering through the brainstem and/or retrograde axonal transport), is also capable of preventing the transmission of many other neurotransmitters, including glutamate, noradrenaline, dopamine, ATP, GABA, and glycine. These neurotransmitters are responsible for the following functions in the CNS:

- **Glutamate**: involved in learning and making new memories; regulates sleep/wake cycles; serves as an energy source for brain cells; necessary for making GABA
- **Noradrenaline**: increases alertness, arousal, and attention
- **Dopamine**: regulates movement, memory, sleep/wake cycle, mood, and learning, among other functions
- **ATP**: source of metabolic energy for all living cells
- **GABA**: reduces stress, relieves anxiety, helps us sleep
- **Glycine**: supports sleep quality and cognitive function

Research in the past 30 years has also revealed BoNT's ability to disrupt sensory neuron neurotransmitters/modulators, including substance-P and CGRP, both of which play a role in pain perception, leading to the current use of BoNT injections for pain relief. Chapter 2 will discuss the

potential symptoms that can occur once BoNT has spread into the PNS and CNS in more depth.

BOTULISM AS A SPECTRUM DISEASE

Early documented case studies of foodborne botulism proved to doctors at the time that the illness could present with varying symptoms and severities, making diagnosis challenging. Even amongst families who ate the same toxin-tainted dinner, botulism symptoms could be radically different.

While some patients experienced severe and rapid descending paralysis resulting in death within days of consuming the toxin, others would experience only transient blurry vision, nausea, and difficulty swallowing that eventually subsided in a few months.

Dr. Ray Wilbur, who served as the dean of Stanford University's Medical School from 1911-1916, documented dozens of botulism cases, and noted the following:

“The gradual onset of (botulism) symptoms and their marked variability are the most striking features.”

“In the patients seen by me there was a wide variation in the severity of the disease, some having only transient disturbance of vision or swallowing, others such complaints as: jaws seemed very tired, apparent inability to chew food, tongue seemed hard to move, sleepy all the time, could not walk fast, throat filled up with mucus all the time, tried to attend classes, legs and arms were almost powerless, hard work climbing stairs, throat felt as if there was a shelf in it beyond which food could not pass but it did not hurt…throughout you must be constantly reminded that the **symptoms may be extremely acute and followed by an early death** or they may be gradually unfolded in their entirety **or only one or two**

characteristic evidences may appear."

As will become evident in Chapter 2, symptoms that Dr. Wilbur and other 20th century physicians noted in foodborne botulism patients over 100 years ago are nearly identical to those often observed in iatrogenic botulism patients today. (The book *Recognizing Botulism* by J.A. Talkington highlights 120 case studies of foodborne botulism from the years 1902-1931.) The relevance of botulism being a **disease that occurs on a spectrum** will become apparent in Chapter 2, where potential signs and symptoms of botulism will be discussed in detail.

THE HISTORY OF IATROGENIC BOTULISM

The term "iatrogenic botulism" first appeared in the medical literature in the early 2000s. It is the term for botulism that occurs after BoNT injections.

There are currently seven known serotypes of BoNT: A, B, C, D, E, F, and G. Types A, B, E, F, and G are all capable of causing disease in humans; type A is the one currently used commercially, and various formulations of it are sold under the following brand names in the U.S.:

- Botox (onabotulinumtoxinA)
- Dysport (abobotulinumtoxinA)
- Xeomin (incobotulinumtoxinA)
- Jeuveau (prabotulinumtoxinA)
- Daxxify (daxibotulinumtoxinA)
- Letybo (letibotulinumtoxinA)

Botox was the first brand to be FDA-approved in the United States in 1989. It was originally used to treat muscle spasticity due to its paralytic action on the neuromuscular junction. Early conditions treated by Botox included strabismus (“lazy eye”), blepharospasm, and cervical dystonia.

In Botox’s 1996 product safety information insert, the following symptoms were reported in

clinical trial patients for cervical dystonia **(bolded symptoms are those that have been documented in foodborne botulism cases):**

> "The most frequently reported adverse reactions were **dysphagia** (19%), upper respiratory infection (12%), **neck pain** (11%), and **headache** (11%). Other events reported in 2-10% of patients in any one study in decreasing order of incidence include: increased cough, **flu syndrome, back pain**, rhinitis, **dizziness**, hypertonia, soreness at injection site, **asthenia (weakness)**, **oral dryness, speech disorder**, **fever**, **nausea**, and **drowsiness**. Stiffness, numbness, **diplopia**, **ptosis**, and **dyspnea** have been reported rarely (author's note: the word "rarely" was omitted from the product insert sometime in the early 2000s).

> Dysphagia and symptomatic general weakness may be attributable to an extension of the pharmacology of BOTOX® resulting from the spread of the toxin outside the injected muscles. The most common severe adverse event associated with the use of BOTOX® injection in patients with cervical dystonia is dysphagia with about 20% of these cases also reporting dyspnea."

Clearly, in the early 1990s, a certain percentage of patients who received Botox for cervical dystonia were developing symptoms of toxin spread (Botox's phrase for "iatrogenic botulism") in the days and weeks after injections; however, early product inserts never mentioned the word "botulism."

(The current Botox package insert now has four pages dedicated to a complete botulism warning, and on page 49 states the following: "In some cases, the effect of botulinum toxin may affect

areas of the body away from the injection site and cause symptoms of a serious condition called botulism.")

By the year 2000, 646 cases of serious adverse events (serious AEs are either life-threatening or disabling), and 17 deaths had been reported to FDA Adverse Events Reporting System (FAERS) following BoNT injections.

A 2006 meta-analysis by Hazell et al. that examined pharmacovigilance reporting systems like FAERS concluded that **only 2-10% of actual adverse effects experienced in the real world are ever reported to the FDA**. Thus, we can assume that *at least* 6,460 serious AEs and 170 deaths after BoNT injections occurred in the first 10 years that the product was on the market.

The first documented case study of iatrogenic botulism available in the medical literature occurred in 2003 in Spain. It involved a 6-year-old girl with cerebral palsy who was receiving BoNT injections for muscle spasms. She began showing signs of botulism (difficulty swallowing, muscle weakness, fatigue) after a round

of injections, but her doctor did not recognize these symptoms as botulism and reinjected her six months later. She developed severe botulism in the days following her last injection requiring ICU admittance and passed away in the weeks afterwards.

Her tragic story highlights how important it is for injecting doctors to feel confident in recognizing and responding to **any** symptoms of botulism that may arise in patients, even if they are mild and only last a few months. This is particularly important for doctors who inject pediatric populations, as all BoNT product inserts state that **children who are receiving BoNT for limb spasticity are the population that is most at risk of iatrogenic botulism.**

In 2007, the European Medicines Agency (the European equivalent of the FDA), after receiving numerous reports of people experiencing serious adverse effects and deaths after BoNT injections, required manufacturers to add a "toxin spread warning" to their product inserts to warn doctors and patients about the potential the drugs

had to cause botulism symptoms. Allergan (the makers of Botox) complied, but **chose to not add this new toxin spread warning to their American product inserts** until two years later when the FDA made it mandatory.

In 2008, a Public Citizen petition to the FDA requested that BoNT products include stricter warnings about the potential these drugs have to induce botulism symptoms. Part of the petition stated,

> "Unlike drug regulatory agencies in Europe, the FDA has not issued any warnings to patients or doctors about the dangers of using the toxin, which is commonly used in therapeutic and cosmetic procedures. Botox and Myobloc are intended to block nerve impulses to certain muscles, causing them to relax. However, in some cases, the toxin has spread to other parts of the body with serious consequences, such as paralysis of respiratory

muscles and difficulty swallowing (dysphagia), the latter possibly leading to food or liquids entering the respiratory tract and lungs, causing aspiration pneumonia."

In 2009, the FDA required the Black Box Warning to be added to all BoNT product inserts. It currently states the following:

WARNING: DISTANT SPREAD OF TOXIN EFFECT See full prescribing information for complete boxed warning. The effects of BOTOX and all botulinum toxin products may spread from the area of injection to produce symptoms consistent with botulinum toxin effects. These symptoms have been reported hours to weeks after injection. Swallowing and breathing difficulties can be life

> **threatening and there have been reports of death. The risk of symptoms is probably greatest in children treated for spasticity but symptoms can also occur in adults, particularly in those patients who have an underlying condition that would predispose them to these symptoms.**

Awareness about iatrogenic botulism grew throughout the 2000s, and reports of serious AEs and deaths following BoNT injections began to multiply rapidly after the Black Box Warning went into effect.

Several lawsuits were won against Allergan in 2010, 2011, and 2015 after consumers developed severe, life-altering botulism symptoms from their cosmetic and therapeutic BoNT injections.

One of these plaintiffs, Douglas Ray Jr., had received Botox injections for a hand tremor from a neurologist named Dr. Anna Hristova.

Dr. Hristova, after witnessing the severe nervous system complications Douglas suffered in the days and weeks following his injections, began conducting research on iatrogenic botulism patients.

Her work was groundbreaking, as she was the first (and, to date, the only) researcher to publish articles that followed iatrogenic botulism patients for multiple years.

Her articles provided in-depth descriptions of the wide variety of debilitating peripheral *and* central nervous system symptoms that were plaguing iatrogenic botulism patients she corresponded with. Her work will be referenced heavily throughout this book, as it remains the most thorough and insightful research published to date on iatrogenic botulism patients.

Since then, peer-reviewed case studies documenting iatrogenic botulism cases from doctors around the world have continued to grow, and Chapter 4 will highlight important details from 18 different case studies.

A second Public Citizen petition was submitted to the FDA on December 12, 2023, calling for more transparency on the Black Box Warning on BoNT products. Part of the petition states:

> "There is postmarketing evidence that both cosmetic and therapeutic (BoNT) products — even when used at recommended doses, either during initial or subsequent (repeated) treatment — are associated with systemic iatrogenic botulism or related symptoms, which may require prompt administration of botulinum antitoxin to avoid disease progression and possible serious outcomes, including temporary paralysis, hospitalization, and even death. This risk is neither adequately clear nor emphasized in the current labeling of these products. Instead, it is masked with the euphemism of

"distant spread of toxin effect"
beyond injection sites."

As of the publishing date of this book (April 2025), the FDA has not yet responded to this petition.

CURRENT INCIDECE RATES OF IATROGENIC BOTULISM

Determining the current incidence rates for iatrogenic botulism is complex, as manufacturers are not required to do research to obtain these numbers.

Using data from botulinum toxin package inserts and large meta-analyses, we can piece together rough estimates of the incidence rates of iatrogenic botulism. These numbers vary greatly depending on the injection site and number of units injected.

As discussed earlier, botulism symptoms will look different for everyone who is affected, depending on which nerves the toxin attacks once in the body, as well as how many units of toxin have

spread. Even patients with mild presentations of the disease should be considered cases of iatrogenic botulism, because their symptoms indicate that the toxin has spread unintentionally, making these patients at risk for more serious botulism symptoms if BoNT use is continued.

When looking at clinical trial data, I include patients who develop *any* signs or symptoms of botulism after BoNT injections as experiencing iatrogenic botulism.

According to data from various BoNT package inserts (Botox, Dysport, Xeomin, etc.), botulism symptoms occurred at rates of 1-20% or more in clinical trial patients who received BoNT for therapeutic purposes. Some of these symptoms may have resolved quickly, while others may have lasted for months or years. Again, Allergan and other manufacturers of BoNT are **not required to do research on how long patients suffer from adverse effects from their drugs**.

A 2025 pharmacovigilance study in France by Carpentier et al. estimated that incidence rates of serious neurological adverse effects following

BoNT injections for neurological purposes (e.g. muscle spasticity) were 25-413 per 100,000 injection sessions (or, occurring at rates of .02-.4%).

Compared to therapeutic doses, the risk of iatrogenic botulism from cosmetic doses is likely smaller, however the current rate is unknown. Accurate data is difficult to obtain for a number of reasons, including lack of funding for these studies and the persistent problem of underreporting.

In 2024 alone, over 2,520 serious adverse events (serious AEs must be life-threatening, disabling, or result in death) and 777 deaths were reported to the FDA following BoNT injections (clearly, more awareness about iatrogenic botulism is growing, as this number represents nearly 35% of the total deaths reported in over 30 years.)

Since 1990, over 15,200 serious AEs and 2,270 deaths have been reported to the FDA after BoNT injections. Keeping the reality of underreporting in mind, we can extrapolate those numbers and infer that in the past 35 years, 150,000-300,000 people have been seriously

injured by BoNT injections *just in the United States*. Serious AEs following as little as 5 units of BoNT have been reported to the FDA. The most common causes of death following BoNT injections are cardiac arrest, respiratory failure, and aspiration pneumonia.

Because many injecting clinicians are unaware of potential adverse effects following BoNT injections, they may be less likely to monitor their patients for these symptoms and to report them to the appropriate surveillance systems if they occur.

A University College of London survey of iatrogenic botulism sufferers reported that 92% of participants had not been informed of the Yellow Card Reporting Scheme (the pharmacovigilance reporting system in the UK) by their doctors. The researchers concluded that, “The lack of awareness of MHRA reporting structures is of particular concern. Coupled with the lack of regulation within the UK's cosmetic injectables sector, this presents a significant public health challenge. Finally, we call for further research and policy initiatives to raise

awareness of patients' experiences and rights in this burgeoning industry."

Because accurate data on iatrogenic botulism is underreported and muddled (does 3 months of dizziness/headaches post BoNT-injections count as iatrogenic botulism? Or are researchers only counting the patients who present with severe botulism, including flaccid paralysis and difficulty breathing?) and extremely hard to find, it is likely that even our best estimates of iatrogenic botulism incidence rates are gravely inaccurate.

WHAT ABOUT "COUNTERFEIT" BOTOX?

In recent years, there have been a handful of incidences where the use of "counterfeit" Botox by unlicensed providers has landed patients in the hospital with botulism. Counterfeit Botox is botulinum toxin, however it is research-grade, and thus is much more potent than pharmaceutical grade toxin (more units per vial). Although these cases are the ones that get the most airtime and publicity, the vast majority of iatrogenic botulism

cases reported to the FDA occur after the use of legitimate Botox and other BoNT brands administered by licensed and trained injectors.

Chapter 1 summary:

- Botulism is a horrific nervous system disease that claimed many lives over the past centuries
- Botulism symptoms can range from mild and transient, to severe and life-threatening
- Botulinum toxin injections can cause botulism symptoms (known as "iatrogenic botulism") when the toxin unintentionally spreads from the injection site; all BoNT package inserts report botulism symptoms as occurring in 1-5% or more of patients post-BoNT injections
- All BoNT products come with a "Black Box Warning", alerting physicians and consumers that these products can cause botulism and result in death
- Current incidence rates of iatrogenic botulism are difficult to obtain; recent data estimates that botulism symptoms can occur at rates of anywhere from .02-5% of more with each injection, depending on the injection site and unit amount

2. SIGNS AND SYMPTOMS

THIS CHAPTER INCLUDES:

- FOODBORNE VS. IATROGENIC BOTULISM SYMPTOMS
- IMPORTANT CONSIDERATIONS
- PNS SYMPTOMS OF BOTULISM
- CNS SYMPTOMS OF BOTULISM
- OTHER SYMPTOMS OF BOTULISM

Signs and symptoms of botulism can vary greatly depending on which nerves the toxin attacks once it has entered the bloodstream. This chapter will cover the wide range of botulism symptoms in detail.

FOODBORNE VS. IATROGENIC BOTULISM SYMPTOMS

According to the CDC, the most common symptoms of **foodborne botulism** include:

- Descending flaccid paralysis
- Dysphagia
- Blurry/double vision
- Slurred speech
- Hoarse voice (dysphonia)
- Gastrointestinal symptoms (nausea, diarrhea, constipation, etc.)
- Dry mouth
- Shortness of breath

Iatrogenic botulism shares many similarities with foodborne botulism but can also present with unique symptoms that are not typically present in foodborne cases.

As you are reading through iatrogenic botulism symptoms, it's important to remember that, as we learned in Chapter 1, these symptoms and their severity can vary greatly from patient to patient.

For example, while some patients with iatrogenic botulism will suffer from complete paralysis of the pharyngeal muscles, leading to aspiration and the need for NPO feeding, others may experience only transient feelings of "globus" (when food feels stuck in the esophagus) or occasional choking and/or coughing with boluses.

One of the largest studies conducted on iatrogenic botulism patients to date was published in 2018 by Lily Bai et al. The most common symptoms in their review of 86 iatrogenic botulism cases were (in order of most frequent to least frequent):

- Fatigue (86%)
- Blurry vision (83%)
- Dizziness (79%)
- Eyelid ptosis (72%)
- Dysphagia (70%)
- Dysarthria (slurred speech) (43%)
- Anxiety (42%)
- Insomnia (38%)
- Headache (21%)
- Constipation (17%)

Note that shortness of breath and descending flaccid paralysis, while common in foodborne patients, are not necessarily frequently reported symptoms in iatrogenic botulism patients (although they may be present in more severe cases).

This is likely because most iatrogenic botulism cases (as many as 75% in Bai et al.'s study) present as "**mild botulism**," which is a term that was coined to define iatrogenic botulism cases that are not immediately life-threatening. Bai et al. categorized "moderate botulism" as those cases that

included mild botulism symptoms as well as the need for NPO feeding, while “severe botulism” cases were those that required mechanical ventilation.

Another important symptom that distinguishes many iatrogenic from foodborne botulism cases is the presence of anxiety. While not commonly documented in foodborne cases, anxiety and/or panic attacks have been documented as a frequently experienced symptom in iatrogenic botulism patients.

Botox’s product insert lists anxiety as a “frequently reported adverse effect” in clinical trials patients (occurring in 3% or more of patients) following injections for hyperhidrosis (excessive sweating). Additionally, in a survey conducted at University College London in 2023, 85% of participants reported experiencing new onsets of anxiety (with 46% reporting new onsets of panic attacks) post-BoNT injections.

Why anxiety?

As of March 2025, there have been over 1,100 reports of new onsets of anxiety and/or panic attacks submitted to the FAERS database following BoNT injections.

This could be due to disruption of the parasympathetic nervous system, or even due to CNS neurotransmitter disruption. More research is needed to understand why anxiety is often present in iatrogenic botulism cases. Unfortunately, the presence of anxiety in iatrogenic botulism can lead to patients not being taken seriously when they are reporting their botulism symptoms and consequently being dismissed by medical providers.

IMPORTANT CONSIDERATIONS

As you are reading through the potential symptoms of iatrogenic botulism, it is important to keep a few things in mind:

- Most patients who develop iatrogenic botulism will begin to experience symptoms within hours or days of their injections, however some symptoms can take up to 4-6 weeks to develop

- Fatigue, anxiety, and headaches/head pressure were three of the most common early symptoms of iatrogenic botulism in Dr. Hristova's research
- The manufacturers of BoNT injections are not required to report on the anticipated duration of botulism symptoms resulting from their products. Thus, it is impossible to predict how long each of these symptoms will last. Prognosis of iatrogenic botulism will be discussed in the next chapter.

PERIPHERAL NERVOUS SYSTEM (PNS) SYMPTOMS OF BOTULISM

BoNT's effects on the peripheral nervous system (PNS) are what typically come to mind when one thinks of botulism. The PNS is made up of the autonomic nervous system (ANS) and the somatic nervous system (SNS), both of which contain motor and sensory neurons. The toxin can disrupt motor and/or sensory neurons anywhere in the body, but it has an affinity for attacking cranial nerves.

The table below includes iatrogenic botulism symptoms that can occur in the PNS, compiled from the following sources:

- the clinical trials for all botulinum toxin brands
- Dr. Hristova's research on iatrogenic botulism patients
- Post-marketing reports from the FDA FAERS database

The table includes a list of symptoms, the possible nerves affected with each symptom (if known), and the incidence rates of each symptom. Incidence rates were acquired from botulinum toxin clinical trial data across all brands of BoNT, and will be different for each injection site. Please refer to the package inserts listed in the References section for more information.

Symptom	**Possible nerves involved**	**Common (1-10% or more of patients across all BoNT brands)**	**Less common (.1-1% of patients)**	**Incidence Rate Unknown**
Dizziness		x		
Vision impairments (blurry vision, double vision, mistiness, floaters, over/under accommodation, eye pulling sensations)	CN III & IV	x		
Eyelid ptosis	CN III	x		
Dry eyes	CN V, VII	x		

Dry mouth	CN VII, X, para-sympathetic nervous system (PSNS)	x		
Muscle weakness	Somatic nervous system (SNS)	x		
Fatigue*		x		
Anxiety*	CN X, PSNS, possibly CNS	x		
Dysphagia (difficulty swallowing)	CN VII, IX, X, and/or XII	x		
Dyspnea** (difficulty breathing)	Phrenic nerve, CN X	x		
Dysarthria	CN X, XI	x		

Dysphonia (hoarseness)	CN X	x		
Constipation	CN X	x		
Diarrhea		x		
Nausea/ vomiting		x		
Headaches/ migraines		x		
Insomnia*	CN X, PSNS		x	
Lack of appetite*	CN X, PSNS		x	
UTIs / urinary retention	CN VII, X PSNS	x		
Paresthesia or numbness	SNS			x
“Buzzing” feeling in the nerves	SNS			x

Muscle spasms, Muscle pain	SNS	x		
Facial paresis	CN VII			x
Ear disorders (including tinnitus, ear congestion, hypoacusis)	CN VII, VIII		x	
Cardiac events, including heart arrhythmias, hyper-tension, POTS, chest pressure, and cardiac arrest	CN X, PSNS		x	

** starred symptoms are those that may be attributed to central nervous system disruption. More research is needed to determine what is causing these symptoms and whether they are occurring due to PNS or CNS disruption.*

*** the shortness of breath and/or difficulty breathing that occurs in botulism* ***does not typically*** *result in lowered oxygen saturation, unless there is full paralysis of the diaphragm. Foodborne botulism case studies demonstrated that patients could experience respiratory failure within minutes of normal O2 sats. Research on iatrogenic botulism patients conducted by Li et al. in 2018 reported that "Although some subjects had dyspnea, their blood gas analysis results were within the normal range, even in the most severe stage."*

CENTRAL NERVOUS SYSTEM (CNS) SYMPTOMS OF BOTULISM

As discussed in Chapter 1, BoNT can block the following neurotransmitters if it spreads into the CNS: acetylcholine, glutamate, glycine, GABA, dopamine, and noradrenaline. Ernest Dickson reported that autopsies conducted on botulism victims' in the early 1900s found toxin present in their brains. Furthermore, recent research conducted by Li et al. in 2018 on iatrogenic

botulism patients revealed abnormal MRI findings when compared with control groups, including decreased functioning within the cerebellum and parahippocampal gyrus.

If the toxin reaches the CNS, patients may present with the following symptoms:

Symptom	**Possible Neuro-transmitter (s) involved**	**Common (1-10% or more of patients across all BoNT brands)**	**Less common (.1-1% of clinical trial patients)**	**Incidence Unknown**
Fatigue	Glutamate	x		
Brain fog	Glutamate glycine			x
Difficulty concentrating	Glutamate glycine			x
Slow processing speed	Glutamate glycine			x

Word finding difficulties	Glutamate glycine			x
Short-term memory loss	Glutamate glycine			x
Anxiety / Panic attacks	GABA/ dopamine	x		
Depression, hopelessness, mood swings, and suicidal ideation	Dopamine		x	
Phonophobia Photophobia				x
Seizures		x		

OTHER DOCUMENTED SYMPTOMS OF IATROGENIC BOTULISM

The following symptoms have been reported in the days/weeks following BoNT injections:

Symptom	**Common (1-10% or more of patients across all BoNT brands)**	**Less common (.1-1% of clinical trial patients)**	**Incidence Unknown**
Alopecia (hair loss)			x
Maladrosis (loss of eyebrows/ eyelashes)			x
Hormonal changes and menstruation changes in women	x		
MCAS / food sensitivities			x
Pruritus / urticaria	x		

Back, neck, and/or jaw pain	x		
Blood in the urine	x		

**PLEASE NOTE: I have done my best to include most documented symptoms of iatrogenic botulism, however this is likely not a complete list. Due to the mechanism of action, BoNT is capable of causing a wide range of symptoms depending on which nerves it attacks in the body. Additionally, many individuals will develop autoimmune-type conditions after being poisoned, which can include new onsets of urticaria, histamine intolerances, and MCAS.*

Chapter 2 summary:

- Symptoms of iatrogenic botulism can vary greatly, depending on which nerves the toxin attacks once it has entered the peripheral and/or central nervous systems
- Patients will likely present with at least 3-5 symptoms of botulism
- Botulism symptoms can come and go over the course of weeks/months
- Botulism can affect the peripheral nervous system, including both motor AND sensory neurons, as well as the central nervous system
- The shortness of breath/ breathing difficulties that occur with botulism typically do **not** cause lowered oxygen saturations, but patients may present with labored breathing and the temporary "arrest" of breaths.

3. DIAGNOSIS, TREATMENT, AND PROGNOSIS

THIS CHAPTER INCLUDES:

- THE CHALLENGES OF DIAGNOSING IATROGENIC BOTULISM
- DIFFERENTIAL DIAGNOSIS
- TREATMENT
- DRUGS/PROCEDURES TO AVOID WHEN BOTULISM IS SUSPECTED
- PROGNOSIS OF IATROGENIC BOTULISM

THE CHALLENGES OF DIAGNOSING IATROGENIC BOTULISM

As we learned in Chapter 1, botulism is a spectrum disease that can present with radically different symptoms and different severities across patients. The CDC states the following about botulism:

> "The diagnostic challenges resulting from the variations in the spectrum of signs and symptoms of botulism 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**... botulism was most commonly misdiagnosed as myasthenia gravis and Guillain-Barré syndrome."

The wide variation of symptoms seen in botulism patients is likely due to a number of different factors, including:

- Amount of toxin that spreads into the nervous system (e.g. a smaller amount of units in the bloodstream may cause a milder illness. Each unit contains millions of molecules of BoNT, all of which are capable of attacking nerve synapses)
- Which nerves the toxin attacks (e.g. oculomotor nerve vs. vagus nerve disruption will present with different symptoms)
- Overall health and age of a person prior to poisoning may result in different clinical presentations

When iatrogenic botulism patients come to hospitals or to their doctor's offices, they will typically have subjective complaints that are not able to be confirmed via objective testing.

The only objective test for botulism is the bioassay mouse test conducted by the CDC; this test

is only considered valid within the first 2-3 days post-poisoning (typically well before individuals begin experiencing disabling symptoms), and has a **high rate of producing false negatives**. The CDC reports,

> "The critical initial treatment and management decisions for patients with suspected botulism **must be made based on clinical findings.** Botulinum antitoxin, the only specific therapy for botulism, should be administered **as quickly as possible**. Laboratory confirmation can take several days and delaying administration of antitoxin to a patient with a high or medium likelihood of botulism while awaiting laboratory results can worsen the patient's outcome."

Additionally, Dr. Hristova noted the following about diagnosing iatrogenic botulism:

> "...in the case of BoNT/A, we do not have readily available laboratory, imaging or other study abnormalities to establish a relationship between an adverse event and the toxin. Autopsies of people and animals who died from botulism did not display specific changes to identify the toxin as cause of death...at present, the main and often the only tools to establish diagnosis are the symptoms proximity to the toxin injection and the clinical picture which bares [sic] great similarity across the patient's population."

Due to these challenges, as well as the time-sensitive nature of botulism, it is imperative that medical professionals are well versed in the nuances of the disease and its unique cluster of potential symptoms in order to make a diagnosis quickly and obtain potentially life-saving antitoxin for patients.

DIFFERENTIAL DIAGNOSIS

The following list includes conditions that have some overlapping symptoms with botulism, and thus should be ruled out when botulism is suspected:

- Lambert-Eaton myasthenic syndrome
- Myasthenia Gravis
- Stroke
- Guillain-Barré syndrome
- Meningitis
- Lyme disease

In 2021, the CDC reported that from 1980-2016, 83% of physicians misdiagnosed botulism, with the most common alternate (incorrect) diagnoses being Guillain-Barré syndrome and myasthenia gravis. Other misdiagnoses often given to botulism patients include psychiatric conditions and stroke.

When iatrogenic botulism is suspected, the <u>most important question</u> to ask patients is, "Have you received Botox (or botulinum toxin) injections in the past month?"

This is a screening question that hospitals may want to incorporate into their protocols when assessing *any* patients who present with **new and worsening onsets** of dizziness, fatigue, muscle weakness, blurry vision, stroke symptoms, and/or heart attack symptoms. A sample ER protocol for assessing potential iatrogenic botulism patients can be found on page 129.

What makes botulism unique from other, similar conditions is that almost all botulism patients will present with **normal laboratory and testing findings**. Vital signs, blood work, EKGs, X-rays, and MRIs are typically **normal** in botulism patients, with a few exceptions (e.g. if a patient is having a heart attack due to toxin spread, they will have an abnormal EKG).

Botulism patients often feel and insist that something is very wrong with them, and will likely

present to the emergency department anxiously, with subjective complaints of 3-5 or more symptoms, including difficulty swallowing, muscular weakness, dizziness, hypertension, blurry vision, dry mouth, insomnia, etc. Please see the previous chapter for a thorough list of reported iatrogenic botulism symptoms.

For reference, the CDC's diagnostic criteria for foodborne botulism includes the following:

- Afebrile (<100.4°F [<38°C])
- Acute onset of at least one of the following symptoms:
    - Blurred vision
    - Double vision
    - Difficulty speaking, including slurred speech
    - Any change in sound of voice, including hoarseness
    - Dysphagia (difficulty swallowing), pooling of secretions, or drooling
    - Thick tongue

- At least one of the following signs:
    - Ptosis
    - Extraocular palsy or fatigability
    - Facial paresis
    - Fixed pupils
    - Descending paralysis, beginning with cranial nerves

TREATMENT

The only available therapy for any type of botulism (foodborne, iatrogenic, wound, etc.) is **botulinum antitoxin**, which is administered at the discretion of the CDC in coordination with state health departments. Botulinum antitoxin **cannot** undo damage that has already been inflicted on the nervous system by the toxin. Rather, it neutralizes any toxin remaining in the bloodstream to prevent further damage. **Rapid administration of antitoxin is imperative to avoid a worsening of botulism symptoms that could become life-threatening.**

Obtaining Antitoxin
Doctors can call their state health department, or the CDC's 24/7 phone line to report suspected botulism cases at **770-488-7100**. Physicians can consult with the CDC and learn how to obtain antitoxin. It is imperative that patients with suspected cases of botulism receive antitoxin as soon as possible, as botulism can progress quickly, leading to life-threatening symptoms.

For unknown reasons, it has proven to be extremely difficult to secure this medication from the CDC for iatrogenic botulism patients. This could be because many iatrogenic botulism patients present with normal laboratory findings and mild botulism (i.e. botulism that is not resulting in paralysis or respiratory failure, and thus does not appear to be immediately life-threatening).

Every effort should be made to obtain antitoxin for patients who are presenting with symptoms of botulism in the days/weeks after BoNT injections, regardless of the severity of their

symptoms, as even cases that present as mild initially can be unpredictable and worsen within hours or days. Additionally, untreated botulism can be a horrific and disabling disease with symptoms that last for many months, if not years, leading to a radically lower quality of life and health status for affected patients. The lack of rapid and proper treatment for botulism can add unnecessary strain to our already overburdened healthcare system.

RELEVANT REFERRALS AND TESTING

Botulism patients, once past the acute stage of the disease (first 3-6 months), may benefit from referrals to specialists, including neurologists (for muscle testing, ruling out other neurological disorders, etc.), ophthalmologists (for vision disturbances) physical therapists (for assistance with limb strengthening exercises), and/or speech-language pathologists (for swallowing/speaking difficulties). Unfortunately, due to the mechanism of action, impairments resulting from botulism do not always respond to therapy exercises in the same way that many other neurological diseases might;

however, every patient is unique and would benefit from an individualized treatment plan.

POTENTIAL THERAPIES

Unfortunately, the most likely scenario in the U.S. is that patients who present with mild or moderate botulism will not end up receiving antitoxin from the CDC. I have read through thousands of stories of iatrogenic botulism sufferers and have only heard of a lucky handful who received antitoxin. This means that most iatrogenic botulism patients will be left alone to heal on their own for many months or years.

Because botulinum toxin's action on nerve terminals is irreversible, potential therapies for botulism are extremely limited.

In the past 10 years, scientists have begun to study potential therapies for botulism beyond antitoxin.

In 2017, Bremer et al. supplemented BoNT-poisoned mice with IV copper and found that their lives were extended. However, the researchers noted many limitations with the study, as well as

the fact that copper could only be trialed on humans if it was used in tandem with antitoxin, due to ethical concerns.

Another study by Elgendy et al. looked at oral supplementation of copper and zinc in rats that had been injected with BoNT in the masseter muscle. The researchers found that the rat group that was given the human equivalent of 2 mg of oral copper for one week after the BoNT injections showed reduced masseter muscle atrophy (indicating potentially reduced BoNT activity), while the group given zinc supplementation showed increased masseter muscle atrophy. They did not study whether oral copper prevented the toxin from spreading to other parts of the body and/or prevented botulism symptoms. The researchers concluded, "It is crucial to establish the reliability and effectiveness of zinc and copper alongside BTX-A treatment, and to develop clear guidelines for their safe and optimal use, while also considering potential risks. It is necessary to keep in mind that these investigations are in their early stages and were carried out on rats. More investigations

including clinical trials are necessary to establish the optimal dosages of zinc or copper supplementation to maximize benefits while ensuring safety and minimizing side effects."

While the use of oral copper may prove to be beneficial in the early stages of botulism poisoning, more research is needed to determine safety and efficacy in humans.

Dr. Hristova suggested a few potential therapies in her research (please note: none of these have been formally studied, and they were suggestions based on limited research. See her article titled “Impaired Neuronal Communication Syndrome” in the References for more information):

- Activated charcoal
- 400 MG of Echinacea daily
- Coffee enemas
- Toosendanin
- Pyridostigmine
- Reserpine
- Celery juice consumption

- Potassium-rich foods

Iatrogenic botulism sufferers I have spoken to have found the following therapies helpful in improving symptoms:

- Hyperbaric oxygen treatment (should **not** be attempted in the first two years post-poisoning)
- Ashwagandha (nervous system support)
- GABA supplementation (anxiety relief)

Botulism patients should be encouraged to eat a well-rounded, whole foods diet (focused on clean protein, healthy fats, and avoidance of heavily processed and high sugar foods), stay as hydrated as possible, and get plenty of sleep while their body is in the healing process. The use of small amounts of benzodiazepines may be necessary for patients who are in the early months of botulism, as insomnia and anxiety can initially be extreme and debilitating. Patients should be informed of the habit-forming risks that come with taking

benzodiazepines, as long-term use of these drugs would not be recommended.

I believe the following foods, activities, and lifestyle factors helped me heal from my (very) mild botulism relatively quickly (within 6-12 months):

- Whole, organic food (I ate mostly meat, bone broth, eggs, whole fat dairy, rice, vegetables, some fruits; I avoided all processed foods and added sugar)
- Staying hydrated with water and electrolytes
- Getting good quality sleep
- Meditation and relaxation podcasts/audio
- Limiting stress as much as possible
- Avoiding toxic and/or fragranced personal care/cleaning products
- Joining a Botox injury support group (there are many online with tens of thousands of members) for community and advice
- Affirmations
- Support from family and friends while I was disabled and unable to work or care for my children

DRUGS/PROCEDURES TO AVOID IF IATROGENIC BOTULISM IS SUSPECTED

Even though there are no current treatments for botulism besides botulinum antitoxin, clinicians should provide patients with this important list of "**Things to Avoid**" while they are healing from the disease. This section includes a list of drugs, supplements, and procedures that botulism patients may want to avoid, as they are advised against on BoNT product inserts and in Dr. Hristova's research. Providers can access a printable PDF version of this guide here: https://www.meganmccue.com/post/botulism-don-ts

1. Procedures/therapies to **avoid** while patients are still presenting with botulism symptoms:

    - **Massage** - full body massages and/or massaging the area where injected can result in further spread of toxin

- **Chiropractic adjustments** - anything that "adjusts" the body and can potentially affect the nervous system
- **Acupuncture** - iatrogenic botulism sufferers I've spoken with have reported a worsening of symptoms after acupuncture treatments
- Anything that can **vibrate/disturb** the body, especially areas where toxin was injected (Dr. Hristova found that vibrating tools [such as massage tools and microneedling procedures] caused a worsening of symptoms in her patients
- **"Detox"** supplements, including liver cleanses, chlorella supplements, etc. were advised against in Dr. Hristova's research
- Patients should be advised to be **extremely wary** of alternative medicine practitioners who claim to be able to "treat" botulism. Not because alternative medicine isn't helpful sometimes, but because botulism is a unique illness that does not respond well to

(and may even be worsened by) many traditional or alternative therapies

2. Vitamins/supplements to **avoid** in the early months of the disease:

    - **Magnesium** (this is technically a type of muscle relaxer, and muscle relaxants are advised against on Botox's package insert)
    - **Synthetic B Vitamins** and **Zinc** (in the first 6 months) - these have caused a worsening of symptoms for iatrogenic botulism patients. BoNT is a zinc-dependent endoprotease.
    - **Melatonin** (this is a glutamate inhibitor, and should be avoided if the patient is presenting with low glutamate symptoms including brain fog and slow processing speed - see previous chapter)
    - **DHEA** (glutamate inhibitor, see "Melatonin")

3. Pharmaceuticals to **avoid and/or use with caution** while patients are still presenting with botulism symptoms**:**

- **Anticholinergic drugs** (Benadryl, Zyrtec, Hydroxyzine, Tylenol PM, Thorazine, Unisom etc.) – these are advised against in all BoNT product inserts, due to their ability to exacerbate the anticholinergic effects of botulism
- **Aminoglycoside antibiotics**, including: gentamicin, streptomycin, amikacin, tobramycin, and neomycin - advised against in BoNT product inserts
- **Doxycycline** - this antibiotic has also caused a worsening of symptoms in iatrogenic botulism patients I've interviewed
- **Blood pressure medications** should be used with caution, as botulism can cause hyper- or hypo- tension
- **Selective serotonin reuptake inhibitors (SSRIs)** - Dr. Hristova found

that SSRIs caused a worsening of symptoms in her iatrogenic botulism patients. If patients were on an SSRI prior to their poisoning, it will be important to use your clinical expertise and judgment to determine the right medication and dosage for your patient and their unique health situation.

- **Antipsychotics** (including Risperdal, Zyprexa, Seroquel, etc.), see SSRIs
- **All muscle relaxants** - advised against on all BoNT product inserts
- **All Benzodiazepines** (Per Dr. Hristova, these were OK in small amounts in the early months of the disease to help patients with panic attacks and insomnia, clinicians should use their best judgement when prescribing these medications.)
- **Exservan, Rilutek, Riluzole, Tiglutik** (these are all glutamate inhibitors, see Melatonin)
- **Epinephrine, Novocain,** and **Lidocaine** have caused a worsening of symptoms for

botulism patients. Patients should keep this in mind if they need to undergo dental treatments

- **Vaccinations** - Dr. Hristova noted a worsening of symptoms in patients after receiving vaccines, such as Tdap and flu shots, and recommended avoiding vaccines for at least a year after poisoning
- **Steroids** (Prednisone, etc.) either worsened the condition of or did nothing for Dr. Hristova's iatrogenic botulism patients

A full list of pharmaceutical drugs that may interact with BoNT can be found here: https://www.drugs.com/drug-interactions/onabotulinumtoxina,botox-index.html

4. Foods to **avoid**/ Histamine reactions:

After living through iatrogenic botulism myself and interviewing other iatrogenic botulism survivors, the following three foods/drugs seem to worsen botulism symptoms almost unanimously:

- Added sugar
- Caffeine
- Alcohol and other recreational drugs

Dr. Hristova noted that about 62% of the patients she followed suffered from new onsets of food, medication, and personal product intolerances (known as histamine reactions or MCAS). These can be alleviated with a **low histamine diet**, avoidance of commercialized personal care/cleaning products (especially those with fragrances), and the use of Claritin and/or Allegra (avoid anticholinergic medications if possible). Patients should pay special attention to any foods/medications/personal care products that bring on histamine reactions and avoid those in the early months. They may benefit from a referral to a holistic practitioner who can provide healing protocols for any underlying gut issues related to MCAS.

BOTULISM AND NUTRIENT DEFICIENCIES

Clinicians would be wise to conduct regular blood work for patients to ensure vitamins and mineral levels remain within normal limits, especially for patients who are consuming an altered diet due to food intolerances and/or swallowing difficulties. Iatrogenic botulism sufferers I've interviewed reported that botulism can cause new onsets of vitamin and mineral deficiencies (particularly iron/ferritin, folate, Vitamin B12, and Vitamin D), as well as thyroid problems (either hyper- or hypo-), in the months post-poisoning. Be aware that patients who are experiencing MCAS may not be able to tolerate synthetic vitamins or IV vitamin infusions.

PROGNOSIS OF IATROGENIC BOTULISM

Unfortunately, trying to predict an iatrogenic botulism patient's prognosis can be as complex as the disease itself.

There is a common misconception among many injectors and medical professionals that adverse effects from BoNT injections "wear off" in

3-6 months when the body regrows new nerve synapses, and thus systemic symptoms of botulism will do the same. While this may be the case when the toxin spreads into adjacent muscle tissue and stays at the neuromuscular junction, it is **not** the typical outcome when the toxin spreads systemically throughout the body (either through the bloodstream or through retrograde axonal transport).

Many iatrogenic botulism patients, just like foodborne botulism patients, can take many months or years to fully recover; unfortunately, in severe cases, some will be left with permanent damage or new health conditions triggered by the illness.

Dr. Hristova reported a "waxing and waning" of symptoms, as well as "relapses" of symptoms, that occurred almost universally in the iatrogenic botulism patients she corresponded with. Scientists do not currently understand why botulism symptoms can come and go, as well as why some symptoms can persist for years. More research surrounding the long-term outcomes of

foodborne and iatrogenic botulism patients is desperately needed.

Based on long-term research conducted on foodborne botulism patients, we can infer that prognosis is most likely to be impacted by the following (in order of importance):

- The severity of the disease symptoms
- Whether or not the patient received antitoxin in the early hours or days after poisoning
- Which nerves the toxin attacked
- Age/overall health of the patient prior to poisoning

The only data available on long-term outcomes for foodborne botulism victims comes from two different studies:

- Jonathan Mann et al (1981)
- Sam Gottlieb et al (2007)

In Mann et al.'s study, researchers followed 21 patients for two years after their botulism poisoning. The following list includes the rates of symptoms that persisted in patients in the "moderate botulism" group at 24 months post-poisoning:

Generalized weakness: 58%
Shortness of breath: 44%
Exercise intolerance: 33%
Blurry vision: 25%
Constipation: 20%
Dry eyes: 20%
Difficulty speaking: 18%
Dry mouth: 17%
Limb weakness: 11%
Double vision: 0%
Difficulty swallowing: 0%

Additionally, the following percentages reflect the amount of patients in the "severe botulism" group who were still suffering from the noted symptoms at 24 months post-poisoning:

Exercise intolerance: 87%
Generalized weakness: 83%
Shortness of breath: 83%
Dry mouth: 83%
Dry eyes: 66%
Limb weakness: 43%
Difficulty swallowing: 42%
Constipation: 40%
Difficulty speaking: 33%
Blurry vision: 16%
Double vision: 0%

In Gottlieb et al.'s study, researchers interviewed 211 patients who had suffered from foodborne botulism. At the time of the interview, the patients were anywhere from 6 months to 6 years out from their poisoning. Overall, 68% of respondents reported having worse health at the time of the interview than before their poisoning, with 49% of those patients rating their current health as "fair" or "poor," (compared with 25% of control subjects). The following symptoms were

more likely to be experienced by botulism survivors than by the control group:

- Fatigue (50% vs 30% in control group)
- Weakness (45% vs 25% in control group)
- Dizziness (25% vs 15% in control group)
- Dry mouth (15% vs 9% in control group)
- Difficulty lifting things (18% vs 10% in control group)

The symptoms that these patients had initially experienced upon poisoning, but that had remediated over time included:

- Blurry vision
- Double vision
- Difficulty swallowing
- Difficulty speaking
- Limb weakness
- Constipation

Dr. Hristova corresponded with 16 iatrogenic botulism patients for over four years and

found that while most patients made improvements year-to-year, **nearly 80% had not returned to their pre-injection health status** within that timeframe.

The following symptoms typically indicate a more moderate/severe botulism poisoning, and thus patients who experience them **may** be at a high risk of a longer healing period (if I've learned anything from my research, it's that botulism has no "definitive" rules):

- Severe cardiac issues, including severe arrhythmias, chest pain/pressure, and heart attacks
- Persistent respiratory difficulties and/or the need for mechanical ventilation
- Pins and needles feelings in the limbs
- Severe muscle weakness in the limbs
- Need for NPO feeding

Chapter 3 summary:

- Diagnosis of botulism can be difficult. The most important details to note are whether a patient is presenting with a cluster of 3-5 (or more) botulism symptoms, as well as the timeline from injections until onset of symptoms
- Clinicians should make every effort to get antitoxin from the CDC for patients who have iatrogenic botulism symptoms in the days/weeks after injections
- Due to the CDC's current practices (not giving out antitoxin unless paralysis and/or respiratory failure are occurring), obtaining antitoxin may not be possible
- Clinicians and patients should pay special attention to the list of **Things to Avoid**, to hopefully avoid a worsening of botulism symptoms
- Prognosis of iatrogenic botulism patients will vary, and symptoms can last for many months or years. Prognosis is likely correlated with severity of the disease and whether antitoxin was given

4. SELECTED CASE STUDIES

THIS CHAPTER INCLUDES:

- 18 IATROGENIC BOTULISM CASE STUDIES FROM THE MEDICAL LITERATURE, FROM 2003-2025
- MY PERSONAL EXPERIENCE WITH IATROGENIC BOTULISM

CASE STUDIES FROM THE LITERATURE

This chapter includes 18 published case studies of iatrogenic botulism, as well as details from my own personal experience with iatrogenic botulism.

Each reported case study includes the following information: authors' information, patient demographics (sex/age), time until onset of symptoms, reason for receiving BoNT, number of units and brand received (when available), as well as lab/testing findings, treatments (whether antitoxin was given), and outcomes. All of these case studies are free and easily accessible on PubMed.

As you are reading through these case studies that span more than 20 years and include patients aged 6-90 from countries around the world, pay close attention to the wide variety of symptoms, as well as the outcomes for patients who received antitoxin, compared with those who didn't.

1. Iatrogenic Botulism: A Complication to be Taken into Account in the Treatment of Child Spasticity (2003, Spain). Authors: B. Beseler-Soto, M. Sánchez-Palomares, L. Santos-Serrano, L. Landa-Rivera, F. Sanantonio-Valdearcos, J.M. Paricio-Talayero.

Patient Sex/Age:
F/6
Reason for receiving BoNT:
limb spasticity
Number of units:
600 U of Dysport (equivalent to 200 U of Botox)
Time until onset of symptoms:
1 week after injections
Symptoms:
high fever, progressive fatigue, refusal to eat, dysphagia, constipation, eyelid ptosis, dry mouth, facial paresis, limb weakness
Lab findings:
Normal bloodwork, X-ray found aspiration pneumonia

Treatment:

Antitoxin **not** given; NG tube placed for NPO feeding

Outcome:

Pt's condition worsened over the course of the week, pt put on ventilator. Six weeks after ICU admission, pt expired.

2. Rapidly Progressive Muscle Paralysis and Acute Respiratory Failure Following Endoscopic Botulinum Toxin Injection. (6/2016, U.S.). Authors: Geoffrey You, Ahmed Khan, Julia Shor, Gary P. Forester.

Patient Sex/Age:

F/90

Reason for receiving BoNT:

Esophageal spasms

Number of units:

80 U of Botox

Time until onset of symptoms:

Hours after injections

Symptoms:

Limb weakness, progressive paralysis of limbs

Lab findings:

Normal bloodwork; neurological exam normal except for upper limb weakness

Treatment:

Antitoxin **given** at hospital; mechanical ventilation required

Outcome:

Pt acquired UTI in hospital; Pt expired after 4 months in ICU

3. **Severe nervous system complications after botulinum type A therapy: three case reports with reviews of FDA-reported nervous system adverse effects (8/2012, U.S.).** Authors: Anna Hristova, Lenore Joseph, Swati Sathe, James Wade.

Patient Sex/Age:

F/55

Reason for receiving BoNT:

Hand tremor

Number of units:

300 U of Botox

Time until onset of symptoms:

3 days after injections

Symptoms:

full body rash, tachycardia, fatigue, severe headache, nausea, neck stiffness, memory loss, weakness

Lab/testing findings:

Normal bloodwork; normal vital signs, MRI showed multiple white matter lesions with predominantly frontal lobe distribution

Treatment:

Antitoxin **not** given

Outcome:

Pt developed worsening of neurological symptoms, resulting in ataxia; 6 months after injections, pt could not work due to frontal lobe deficits and ataxia

Patient Sex/Age:

F/59

Reason for receiving BoNT:

Blepharospasm

Number of units:

50 U of Botox

Time until onset of symptoms:

8 days after injections

Symptoms:

Fever of 103 F, severe fatigue, disorientation, headache, blurry vision, nausea, apraxia, dysarthria, tremors, generalized weakness, severe gait ataxia, urinary incontinence

Lab/testing findings:

Normal bloodwork; positive ANA titer test

Treatment:

Antitoxin **not** given

Outcome:

Within 2 months, urinary incontinence and gait ataxia resolved; other symptoms persisted

Patient Sex/Age:

M/64

Reason for receiving BoNT:

Hand tremor

Number of units:

235 U of Botox

Time until onset of symptoms:

1 day after injections

Symptoms:

-fever of 102 F, full body rash, lethargy, disorientation, gait ataxia, urinary incontinence

Lab/testing findings:

Normal bloodwork; MRI found multiple lesions in the right cerebellar peduncle and brainstem; positive ANA titer test

Treatment:

Antitoxin **not** given

Outcome:

6 months after injections pt was given an infusion of monoclonal antibodies, his symptoms returned and progressed rapidly, resulting in a bedridden/vegetative state; pt expired 5 years later

4. **Delayed Antitoxin Treatment of Two Adult Patients with Botulism After Cosmetic Injection of Botulinum Type A Toxin (7/2016, Hong Kong).** Authors: Kit-Ling Fan, Yan-Li Wang, Gary Chu, and Ling-Pong Leung.

   Patient Sex/Age:
   F/30
   Reason for receiving BoNT:
   Calves
   Number of units:
   500 U of Botox
   Time until onset of symptoms:
   6 days after injections
   Symptoms:
   Dysphagia, dysarthria, eyelid ptosis, blurry vision, bilateral upper and lower limb weakness
   Lab/testing findings:
   Normal vital signs; normal blood tests
   Treatment:
   Antitoxin **given** at ER, 9 days after injections
   Outcome:
   Clinical improvement noted at hospital with blurry

vision and choking. On discharge, pt was ambulatory with normal oral feeding.

Patient Sex/Age:
F/30
Reason for receiving BoNT:
Cosmetic (face) and Calves
Number of units:
400 U of Botox
Time until onset of symptoms:
7 days after injections
Symptoms:
Dysphagia, dysarthria, dyspnea, eyelid ptosis, blurry vision, bilateral upper and lower limb weakness
Lab/testing findings:
Normal vital signs; normal blood tests
Treatment:
Antitoxin **given** at ER, 7 days after injections
Outcome:
Upon discharge, speech and swallowing were normal, and limb weakness had remediated. Mild ptosis remained.

5. **Impaired Neuronal Communication Syndrome as a Novel Neurological Side Effect to Botulinum Toxin Type A Therapy with 16 Case Reports (2016, U.S.).** Author: Anna Hristova.

Patient Sex/Age:

F/34

Reason for receiving BoNT:

Cosmetic

Number of units:

27 U of Botox

Time until onset of symptoms:

1 hour after injections

Symptoms:

Profound fatigue, Autonomic nervous system symptoms (not specified), CNS symptoms (not specified)

Lab/testing findings:

Normal vital signs; normal blood tests

Treatment:

Antitoxin **not** given

Outcome:

Recovered fully in 4 months

Patient Sex/Age:

F/32

Reason for receiving BoNT:

Cosmetic

Number of units:

25 U of Botox

Time until onset of symptoms:

2-3 days after injections

Symptoms:

Involuntary muscle twitches, insomnia, vision distortion, CNS, psychiatric and autonomic nervous system symptoms (not specified), trophic changes

Lab/testing findings:

Normal vital signs; elevated ANA titers

Treatment:

Antitoxin **not** given

Outcome:

At 4 years out, pt had not yet regained full recovery of prior health status

Patient Sex/Age:

F/43

Reason for receiving BoNT:

Cosmetic

Number of units:

16 U of Botox

Time until onset of symptoms:

Minutes after injections

Symptoms:

Numbness in head, nausea, vomiting, breathing difficulties, dysphagia, unspecific CNS/ANS symptoms

Lab/testing findings:

Normal vital signs; normal blood work

Treatment:

Antitoxin **not** given

Outcome:

At 4 years out, pt had not yet regained full recovery of prior health status

6. **From Beauty to Botulism: A Case Report Highlighting the Rare Risk of Botox (2/2024, U.S.)** Authors: Jordan Richardson, Shannon Viviano.

Patient Sex/Age:

F/47

Reason for receiving BoNT:

Cosmetic

Number of units:

50 U of Dysport (equivalent to 16 U of Botox)

Time until onset of symptoms:

8 days after injections

Symptoms:

Blurry vision, dysphonia, shortness of breath, weakness, dysphagia

Lab/testing findings:

Normal vital signs; normal blood work

Treatment:

Antitoxin **given** within hours of arriving at ER

Outcome:

At 1 month out, pt was completely symptom-free

7. Iatrogenic botulism (2/2024, Norway).

Authors: Guri Hagberg, Emilie Ranheim Skytøen, Ingvild Nakstad, Kristin O' Sullivan, Jeanette Koht, Tone Kristin Bjordal Johansen, Siri L. Feruglio, Sten Frøyshov.

Patient Sex/Age:

F/40's

Reason for receiving BoNT:

Therapeutic (migraines)

Number of units:

Not specified, typically 155-195 U of Botox

Time until onset of symptoms:

15 days after injections

Symptoms:

Paralysis of pharynx, neck muscle weakness, constipation, dry mouth, headache, fatigue, eye ptosis, blurry vision

Lab/testing findings:

Normal vital signs; normal blood work; normal neurological exam

Treatment:

Antitoxin **not** given**;** NG tube placed for NPO feeding

Outcome:

At 3 months out, pt still relied on NG tube for feeding

8. Iatrogenic Botulism After Cosmetic Use of Botulinum Toxin-A: A Case Series (1/2025, Iran). Authors**:** Mohammad Asadi, Shahin Shadnia, Babak Mostafazadeh, Peyman Erfan Talab Evini, Faraz Zandieh, Mitra Rahimi.

Patient Sex/Age:

F/41

Reason for receiving BoNT:

Therapeutic (hyperhidrosis)

Number of units:

Not specified, typically 50-100 U of Botox

Time until onset of symptoms:

1 day after injections

Symptoms:

Dysphagia, dysphonia, dizziness dry mouth, muscle

weakness in limbs

Lab/testing findings:

Normal vital signs; normal blood work

Treatment:

Antitoxin **given** at 3 weeks post-injection date

Outcome:

While in hospital, pt regained muscle strength, and swallowing and dry mouth improved

Patient Sex/Age:

F/26

Reason for receiving BoNT:

Cosmetic (glabellar and lateral canthal lines)

Number of units:

Not specified, typically 40 U of Botox

Time until onset of symptoms:

1 day after injections

Symptoms:

Upper limb muscle weakness, blurry vision, eyelid ptosis, dizziness, difficulty swallowing solids

Lab/testing findings:

Normal vital signs; normal blood work

Treatment:

Antitoxin **given** 1 week post-injection date

Outcome:

While in hospital, pt regained muscle strength, and swallowing, dizziness, and blurry vision improved

Patient Sex/Age:

F/38

Reason for receiving BoNT:

Cosmetic (glabellar and lateral canthal lines)

Number of units:

Not specified, typically 30-40 U of Botox

Time until onset of symptoms:

5 days after injections

Symptoms:

Blurry vision, eyelid ptosis

Lab/testing findings:

Normal vital signs; normal blood work

Treatment:

Received 60 mg oral pyridostigmine every 6 hours for 10 days; Antitoxin **given** 2 weeks post-injection date

Outcome:
Discharged home symptom-free

9. Iatrogenic botulism after botulinum toxin type A: Five cases (5/2024, Turkey). Authors: Özlem Totuk, Ebru Kaya, Esra Nur Sancar, Sena Ayşe Emre, Serkan Demi

Patient Sex/Age:
F/29
Reason for receiving BoNT:
Therapeutic (hyperhidrosis) and Cosmetic (glabellar and lateral canthal lines)
Number of units:
600 U of Dysport, equivalent to 200 U of Botox
Time until onset of symptoms:
3 days after injections
Symptoms:
Eyelid ptosis, cough, dysphagia, dysphonia, muscle weakness in limbs and neck, constipation
Lab/testing findings:
Normal vital signs; normal blood work

Treatment:

Received oral pyridostigmine with no improvement of symptoms; Antitoxin **given** 2 weeks post-injection date

Outcome:

At 6-week follow up, pt was symptom-free

Patient Sex/Age:

F/36

Reason for receiving BoNT:

Therapeutic (hyperhidrosis)

Number of units:

200 U of Botox

Time until onset of symptoms:

1 day after injections

Symptoms:

Dyspnea, tachypnea, muscle weakness in limbs

Lab/testing findings:

Normal vital signs; normal blood work

Treatment:

Antitoxin **given** upon arriving at ER

Outcome:

Symptoms resolved within 24 hours post-antitoxin administration

Patient Sex/Age:

F/44

Reason for receiving BoNT:

Cosmetic (glabellar lines, platysmal bands) and Therapeutic (hyperhidrosis)

Number of units:

300 U of Botox

Time until onset of symptoms:

5 days after injections

Symptoms:

Dysphagia, dyspnea, eyelid ptosis, muscle weakness in limbs

Lab/testing findings:

Normal vital signs; normal blood work

Treatment:

Antitoxin **given** 5 days post-injections

Outcome:

Pt discharged home symptom-free after 10 days in hospital

10. My own person experience with iatrogenic botulism (7/2024)

Patient Sex/Age:

F/34

Reason for receiving BoNT:

Cosmetic (lateral canthal lines)

Number of units:

12 U of Xeomin

Time until onset of symptoms:

Hours after injections

Symptoms:

Dizziness, brain fog, nausea, head pressure, new onset of anxiety attacks every few days, neck muscle weakness, 50% hair loss in first 3 months, insomnia, dry mouth, difficulty swallowing solids ("globus" sensation), ear congestion, shortness of breath for a few days

Lab/testing findings:

Normal vital signs; normal blood work; normal EKGs

Treatment:

Antitoxin **not** given

Outcome:

Most of my symptoms lasted 3-4 months each (many of them had different onset dates and seemed to come in "waves"); At 9 months post-injections, I consider myself about 95% back to normal; mild ear congestion remains

Chapter 4 summary:

- Case studies from the medical literature report a wide range of iatrogenic botulism symptoms, treatments, and outcomes for patients
- Almost every patient who received antitoxin had preferable outcomes, with most of them experiencing complete symptom relief within days/weeks of receiving antitoxin
- **Patients who do not receive antitoxin are at a high risk of a prolonged disease course**

5. PREVENTION AND SAFETY

THIS CHAPTER INCLUDES...

- GUIDELINES FOR PROVIDING INFORMED CONSENT WHEN USING BOTULINUM TOXIN INJECTIONS
- POPULATIONS WHO SHOULD NOT RECEIVE BONT INJECTIONS
- CONCLUSION

PREVENTION AND INFORMED CONSENT

The best prevention method for iatrogenic botulism is simple: **avoiding BoNT injections.**

While the general consensus in the medical field is that the therapeutic and cosmetic use of BoNT is always safe, I hope this book has proven beyond any doubt that these drugs come with the very real risk of developing mild, moderate, or severe botulism symptoms. Many patients, once informed of this potential risk, may opt to receive alternative drugs/procedures for their medical conditions, including migraines, muscle spasms, overactive bladder, hypersalivation, etc.

It is the opinion of this author that the use of BoNT for cosmetic and/or elective purposes is **never** warranted, given how unpredictable the toxin can be, how difficult antitoxin is to obtain, and how long-lasting and disabling botulism symptoms can be. After living through iatrogenic botulism and speaking with fellow sufferers, I personally would never recommend the use of BoNT. Obviously, the decision to use BoNT lies

with the patient, and the risk-benefit analysis for receiving injections should be weighed in full.

It is imperative that **every patient** who receives BoNT injections is given a paper copy of the full medication safety guide that is included in each BoNT product's package insert.

When applicable, patients should be shown clinical trial data - including adverse effects reported and their frequency - related to their specific use of BoNT (e.g. migraines, hyperhidrosis, limb spasticity, etc.). This will ensure that patients are appropriately educated about the risks of developing iatrogenic botulism, and that you are receiving their **full informed consent** to continue with the use of BoNT. This practice will also help patients understand which symptoms to immediately report to their injectors should they develop them in the days/week after injections. Injecting doctors should never assume that a patient won't develop adverse effects following BoNT, simply because they have had successful treatments in the past.

Dr. Hristova noted the following:

"Our data demonstrate that a generalized spread of the toxin can occur even after years of uneventful toxin therapy. Patient #7 had 30 successful treatments over a decade before the adverse events occurred. **Prior uneventful injections cannot be a predictor for toxin safety**, because in our experience, generalized spread can occur at any time and with any injection. 44% of the patients develop a reaction after their first-time injection. From those who had more than one injection, 50% had an adverse event to prior injections **which remained unrecognized and lead to devastating effects with next injections.**"

Because many patients do not realize they are experiencing botulism symptoms when they begin to have adverse effects, it is imperative that clinicians regularly monitor every patient receiving BoNT injections. **At every appointment**, patients should be asked if they have experienced any signs/symptoms of botulism since their last set of injections. These symptoms can include (but are not limited to):

- Dizziness / headaches / head pressure
- Dry eyes / vision changes
- Dry mouth
- Voice changes
- Swallowing difficulties
- New onset of anxiety/panic attacks
- Muscle weakness
- Back/neck pain
- New onset of cardiac symptoms, including heart arrhythmias, POTS, high blood pressure, etc.

Dr. Hristova set forth the following considerations for physicians for safer BoNT use:

- Inform yourself, your colleagues and your patients about the existence of iatrogenic botulism and its consequences
- Advise patients who develop **any** reaction to BoNT that it is likely not safe to continue use of the drug
- Consider that the benefits of injecting BoNT for cosmetic reasons likely do not outweigh the risks of developing iatrogenic botulism
- Report **all** adverse effects experienced by patients (even mild ones) to the FDA or its equivalents in other countries (Medwatch link here: https://www.fda.gov/safety/medwatch-fda-safety-information-and-adverse-event-reporting-program)

- Publish case studies of iatrogenic botulism in peer reviewed literature to increase awareness of the condition

Again, it is important to understand that patients presenting with **any** botulism symptoms, even just one or two transient symptoms, are at a higher risk of developing more moderate to severe botulism symptoms if they continue use of BoNT products.

Botox's own product insert warns against the continued use of BoNT products in patients who have previously developed <u>any</u> side effects, no matter how mild they are.

POPULATIONS WHO SHOULD <u>NEVER</u> RECEIVE BONT INJECTIONS

The Botox Medication Guide states that the following populations should not receive BoNT injections:

- Anyone who is allergic to any of the ingredients in BOTOX or BOTOX Cosmetic.
- Anyone who has had an allergic reaction to any other botulinum toxin product
- Anyone who has a skin infection at the planned injection site
- Anyone who is being treated for urinary incontinence or has a urinary tract infection (UTI).

Additionally, the Botox Medication Guide states that doctors should be asking patients if they have any of the following medical conditions or medications **prior** to administering BoNT products (likely because BoNT use would **not** be recommended in these populations):

- Any disease that affects muscles and nerves (such as ALS, myasthenia gravis or Lambert-Eaton syndrome).

- Any allergies to any botulinum toxin product.
- Any side effects from any botulinum toxin product in the past
- Any breathing problems, such as asthma or emphysema.
- Any swallowing problems
- Any bleeding problems
- Any plans to have surgery
- Any weakness of forehead muscles, such as trouble raising eyebrows or drooping eyelids
- Any symptoms of a urinary tract infection (UTI) and/or being treated for urinary incontinence
- Any problems emptying the bladder and/or being treated for urinary incontinence
- Anyone who is pregnant or plans to become pregnant
- Anyone who is breastfeeding or plan to breastfeed

- Anyone who has received any other botulinum toxin product in the last four months
- Anyone who has recently received an antibiotic by injection
- Anyone who takes muscle relaxants
- Anyone who takes an allergy or cold medicine
- Anyone who takes a sleep medicine
- Anyone who takes anti-platelets (aspirin-like products) or anti-coagulants (blood thinners)

These patients may be at a high risk of experiencing botulism symptoms and complications post-injections due to the interactions between BoNT and their medical conditions and/or medications.

CONCLUSION

Iatrogenic botulism is an under-researched, misunderstood, and often misdiagnosed disease. It can present with a wide variety of symptoms that

range in severity from mild to life-threatening. Death by botulism can happen quickly, and mild botulism cases can turn life-threatening within hours; thus it is imperative that individuals with botulism are identified and given antitoxin treatment.

It is likely that the occurrence of iatrogenic botulism is much higher than what is currently being reported to the FDA, due to the acknowledged problem of underreporting of adverse effects, as well as the fact that many doctors and patients are uninformed about botulism symptoms that can result from BoNT use.

It is imperative that healthcare practitioners, including doctors, nurses, therapists, and other providers who have regular interactions with patients receiving BoNT injections, are aware of symptoms of iatrogenic botulism and are monitoring patients for any signs/symptoms of this disease

The purpose of this book was to provide readers with a concise introduction to iatrogenic botulism and encourage clinicians to formulate a

definitive plan for diagnosing and treating patients who may present with botulism symptoms after their BoNT injections.

I believe as healthcare providers, it is our duty to ensure every patient receives **full informed consent** when receiving any new drugs and/or medical procedures. I hope that you agree, and that this book has inspired you to spread awareness in your community about iatrogenic botulism.

SAMPLE ER PROTOCOL FOR IDENTIFYING/TREATING IATROGENIC BOTULISM

If a patient presents to the emergency room with a **sudden and new** onset of at least 2 of the following:

- Dizziness
- Blurry Vision
- Muscle weakness
- Difficulty swallowing
- Anxiety
- Cardiac complaints (elevated BP, chest pain/pressure)
- Shortness of breath complaints (patients may have **normal** O2 sats)

ASK:
Have you received Botox (or another botulinum toxin product) in the past month?

If the answer is **no**: continue normal evaluation
If the answer is **yes**: conduct blood work and testing as usual, and call your state health department, or the CDC's 24/7 phone line to speak with an infectious disease expert:

770-488-7100

Remember:

Even mild cases of botulism can progress quickly to severe, life-threatening emergencies. Every patient presenting with botulism symptoms after BoNT injections can benefit from antitoxin!

RESOURCES:

1. The CDC's Clinical Guidelines for Diagnosis and Treatment of Botulism, 2021
https://www.cdc.gov/mmwr/volumes/70/rr/rr7002a1.htm

2. IatrogenicBotulism.com
https://www.iatrogenicbotulism.com
A website for patients and clinicians that provides education, resources, and support for those suffering from iatrogenic botulism and their care providers.

3. Botox and Dysport – Iatrogenic Botulism documentary
https://www.youtube.com/watch?v=5ZNDfT6AOd0&t=1035s

REFERENCES:

Akaike N, Shin MC, Wakita M, Torii Y, Harakawa T, Ginnaga A, Kato K, Kaji R, Kozaki S. Transsynaptic inhibition of spinal transmission by A2 botulinum toxin. J Physiol. 2013 Feb 15;591(4):1031-43. doi: 10.1113/jphysiol.2012.242131. Epub 2012 Oct 29. PMID: 23109108; PMCID: PMC3591713.

Bai L, Peng X, Liu Y, Sun Y, Wang X, Wang X, Lin G, Zhang P, Wan K, Qiu Z. Clinical analysis of 86 botulism cases caused by cosmetic injection of botulinum toxin (BoNT). Medicine (Baltimore). 2018 Aug;97(34):e10659. doi: 10.1097/MD.0000000000010659. PMID: 30142749; PMCID: PMC6112997.

Beseler-Soto B, Sánchez-Palomares M, Santos-Serrano L, Landa-Rivera L, Sanantonio-Valdearcos F, Paricio-Talayero JM. Botulismo yatrógeno: una complicación a tener en cuenta en el tratamiento de la espasticidad en la infancia [Iatrogenic botulism: a complication to be taken into account in the treatment of child spasticity]. Rev Neurol. 2003 Sep 1-15;37(5):444-6. Spanish. PMID: 14533094.

Botox product insert:
https://www.rxabbvie.com/pdf/botox_pi.pdf

Bremer, Paul, Sabine Pellett, James P. Carolan, William H. Tepp, Lisa M. Eubanks, Karen N. Allen, Eric A. Johnson, Kim D. Janda. Metal Ions Effectively Ablate

the Action of Botulinum Neurotoxin A. *Journal of the American Chemical Society*, 2017; D
OI: 10.1021/jacs.7b01084

Carpentier VT, Weiss N, Salem JE, Joussain C, Levy J, Mariani LL, Montastruc F, Mahé J, Lebrun-Vignes B, Bensmail D, Denys P, Genêt F, Bihan K. Real-life prognosis of neurological complications of botulinum toxin: A nationwide pharmacovigilance study of adverse drug reactions reported in France between 1994 and 2020. Ann Phys Rehabil Med. 2025 Mar 12;68(3):101924. doi: 10.1016/j.rehab.2024.101924. Epub ahead of print. PMID: 40081132.

CDC MMWR. Clinical Guidelines for Diagnosis and Treatment of Botulism, 2021. Recommendations and Reports, Vol. 70, No. 2. May 7, 2021. https://www.cdc.gov/mmwr/volumes/70/rr/pdfs/rr7002a1-H.pdf

Dickson, Ernest Charles. *Botulism: A Clinical and Experimental Study*. 1918.

Dysport product insert: https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/125274s125lbl.pdf

Elgendy, Yasmin Saad et al. “Effect of zinc or copper supplementation on the efficacy and sustainability of botulinum toxin A "Botox" injection in masseter muscle of albino rats.” *Journal of stomatology, oral and maxillofacial surgery* (2024): 102156 .

Erbguth FJ. From poison to remedy: the chequered history of botulinum toxin. J Neural Transm (Vienna). 2008;115(4):559-65. doi: 10.1007/s00702-007-0728-2. Epub 2007 Apr 26. PMID: 17458494.

Fung HT, Chan KM, Lam SKT. A review on iatrogenic botulism. *Hong Kong Journal of Emergency Medicine*. 2020;27(6):356-367. doi:10.1177/1024907920934901

Gottlieb SL, Kretsinger K, Tarkhashvili N, Chakvetadze N, Chokheli M, Chubinidze M, Michael Hoekstra R, Jhorjholiani E, Mirtskhulava M, Moistsrapishvili M, Sikharulidze M, Zardiashvili T, Imnadze P, Sobel J. Long-term outcomes of 217 botulism cases in the Republic of Georgia. Clin Infect Dis. 2007 Jul 15;45(2):174-80. doi: 10.1086/518890. Epub 2007 Jun 5. PMID: 17578775.

Hazell, L., Shakir, S.A. Under-Reporting of Adverse Drug Reactions. *Drug-Safety* 29, 385–396 (2006). https://doi.org/10.2165/00002018-200629050-00003

Hristova, AH. Lenore, J. Swati, S., Wade, J. Severe Nervous System Complications After Botulinum Type A Therapy: Three Case Reports With Reviews of FDA-Reported Nervous System Adverse Effects, PM&R, Volume 4, Issue 8, 2012, Pages 613-623, ISSN 1934-1482,

Hristova, AH. Impaired Neuronal Communication Syndrome (INCS) as Novel Neurological Side Effect to Botulinum Toxin Type A Therapy with 16 Case Reports. J Bacteriol Mycol. 2016; 3(4): 1035.

Li GF, Ban S, Wang M, Zhang J, Lu H, Shi YH, He XW, Wu YL, Peng P, Liu YS, Zhuang MT, Zhao R, Shen XL, Li Q, Liu JR, Du X. Brain functional changes in patients with botulism after illegal cosmetic injections of botulinum toxin: A resting-state fMRI study. PLoS One. 2018 Nov 28;13(11):e0207448. doi: 10.1371/journal.pone.0207448. PMID: 30485326; PMCID: PMC6261580.

Mann JM, Martin S, Hoffman R, Marrazzo S. Patient recovery from type A botulism: morbidity assessment following a large outbreak. Am J Public Health. 1981 Mar;71(3):266-9. doi: 10.2105/ajph.71.3.266. PMID: 7468858; PMCID: PMC1619789.

Public Citizen Petition. *Stricter Warnings Needed for Botox, Myobloc Injections*. January 24, 2008. https://www.citizen.org/news/stricter-warnings-needed-for-botox-myobloc-injections/

Public Citizen Petition. *Background Information on Public Citizen's Petition to the FDA Regarding Botox and Related Drugs and Pertinent Postmarketing Evidence*. December 12, 2023. https://www.citizen.org/article/background-information-on-public-citizens-petition-to-the-fda-regarding-botox-and-related-drugs-and-pertinent-postmarketing-evidence/.

T. Wang, S. Martin, A. Papadopulos, C. B. Harper, T. A. Mavlyutov, D. Niranjan, N. R. Glass, J. J. Cooper-White, J.-B. Sibarita, D. Choquet, B. Davletov, F. A. Meunier.

Control of Autophagosome Axonal Retrograde Flux by Presynaptic Activity Unveiled Using Botulinum Neurotoxin Type A. *Journal of Neuroscience*, 2015; 35 (15): 6179 DOI: 10.1523/JNEUROSCI.3757-14.2015

Talkington, J.A. *Recognizing Botulism*. 1st Ed. 2025.

Wilbur, R.L., Ophuls, W. "Botulism: A Report of Food-Poisoning Apparently Due to Eating of Canned String Beans, with Pathological Report of a Fatal Case." Archives of Internal Medicine, vol. 14, no.4, 1914 pp. 589-604

Xeomin product insert: https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/125360s073lbl.pdf

Yiannakopoulou E. Serious and long-term adverse events associated with the therapeutic and cosmetic use of botulinum toxin. Pharmacology 2015;95(1- 2):65-9. DOI: 10.1159/000370245

Zargaran D, Zargaran A, Sousi S, Knight D, Cook H, Woollard A, Davies J, Weyrich T, Mosahebi A. Quantitative and qualitative analysis of individual experiences post botulinum toxin injection - United Kingdom Survey. Skin Health Dis. 2023 Jul 3;3(5):e265. doi: 10.1002/ski2.265. PMID: 37799369; PMCID: PMC10549845.