Narrative Review

The Evolution of Botulinum Toxin: A Historical Journey to its Modern Role in Paediatric Urology

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Abstract

Background: Botulinum neurotoxin has evolved from a feared cause of food-borne paralysis into a versatile therapeutic agent. In paediatric urology, onabotulinumtoxinA has become an important minimally invasive option for neurogenic detrusor overactivity and selected refractory lower urinary tract dysfunctions. **Objective**: This narrative review aims to trace the major historical and scientific milestones in the development of botulinum toxin, describe its mechanism of action and evolution as a urological therapy, and critically summarise current paediatric urological applications, injection techniques, limitations, adverse events, and emerging technologies. **Methods**: A narrative literature search was performed using PubMed/MEDLINE and reference lists of relevant reviews and landmark articles, with emphasis on the history of botulinum toxin, mechanism of action, detrusor-sphincter dyssynergia, neurogenic detrusor overactivity, paediatric neurogenic bladder, injection techniques, safety, treatment failure, neutralising antibodies, and novel delivery systems. Historical primary reports, pivotal clinical studies, paediatric trials, systematic reviews, and recent relevant publications available through August 2026 were prioritised. **Results**: The historical progression from Kerner's early clinical observations and van Ermengem's microbiological isolation to Scott's therapeutic use and subsequent urological applications is closely linked to advances in neurophysiology and drug delivery. Paediatric evidence supports meaningful improvements in continence and urodynamic parameters in appropriately selected patients; however, repeated procedures, urinary tract infection, transient retention, incomplete response in poorly compliant or fibrotic bladders, possible immunogenic failure, cost, and anaesthesia burden remain clinically relevant limitations. **Conclusion**: Emerging longer-acting formulations and non-invasive delivery systems are promising but remain investigational for paediatric urology.

Keywords: Botulinum neurotoxin; History of medicine; Neurogenic bladder; Overactive bladder; Paediatric urology

Introduction

Botulinum toxin is a powerful neurotoxin produced by Clostridium botulinum that inhibits acetylcholine release at cholinergic nerve terminals, resulting in reversible neuromuscular blockade. Originally recognised as the cause of a potentially fatal form of food poisoning, it has progressively become an established therapeutic agent in several medical specialties, including paediatric urology.

The objective of this narrative review is to provide a coherent historical-to-clinical account of botulinum toxin, from the first descriptions of botulism to its modern therapeutic use, with particular emphasis on paediatric urology. We specifically examine the milestones that enabled clinical translation, the evidence supporting intravesical treatment in children, the evolution of injection techniques, the principal causes of treatment failure and adverse events, and emerging strategies intended to extend efficacy or reduce procedural burden

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Methods

This article was prepared as a narrative review. Literature was identified through PubMed/MEDLINE and by screening the reference lists of relevant historical reviews, clinical studies, guidelines, and systematic reviews. Search concepts included combinations of “botulinum toxin”, “botulism”, “history”, “mechanism of action”, “paediatric urology”, “neurogenic bladder”, “neurogenic detrusor overactivity”, “detrusor-sphincter dyssynergia”, “overactive bladder”, “intradetrusor”, “suburothelial”, “submucosal”, “treatment failure”, “neutralising antibodies”, “urinary tract infection”, “urinary retention”, “anaesthesia”, and “delivery”.

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Priority was given to landmark historical publications, pivotal urological reports, paediatric cohorts and trials, systematic reviews, and recent studies relevant to safety and innovation. The search was updated through August 2026. Because the purpose was historical and narrative rather than a systematic assessment of comparative effectiveness, no formal meta-analysis or risk-of-bias synthesis was undertaken.

Historical Evolution: From Food-borne Poison to Purified Neurotoxin

Food-borne botulism—a severe and potentially fatal disease caused by the neurotoxin produced by Clostridium botulinum—has likely coexisted with human civilisation since its inception. One of the earliest documented historical accounts dates back to the Byzantine era, when Emperor Leo VI the Wise (866–912 AD) recognized the association between blood sausage consumption and food-borne illness, subsequently issuing an edict "prohibiting the preparation and consumption of blood sausage made from pig stomachs."[1]

Centuries later, outbreaks during the Napoleonic Wars (1795–1813) further highlighted the impact of poor hygiene and poverty on food safety.[2] A particularly severe outbreak occurred in 1793 in the village of Wildbad (Württemberg), resulting in 13 cases and 6 fatalities. In 1817, J.G. Steinbuch, a health officer from Herrenberg, submitted case reports detailing seven patients poisoned by a single meal composed of liver sausage and peas.[3] Around the same time, Christian Andreas Justinus Kerner (1786–1862), a 29-year-old medical officer, romantic poet, and occultist, reported a fatal case of food poisoning.[4] Kerner published the first monograph on "sausage poisoning" in 1820, summarising the case histories of 76 patients and providing an exhaustive clinical description of what is now recognised as botulism.[5] The diagnostic precision of his symptom description remains remarkable today (Figure 1).



Figure 1: Justinus Andreas Christian Kerner (1786–1862), physician, poet, and medical writer. Painting by Ottavio D'Albuzzi.

In 1822, Kerner published his research findings and hypotheses regarding this "sausage poison" in a second monograph. This work included a clinical evaluation and summary of 155 suspected botulism cases, supplemented by post-mortem examinations. In his landmark study (Das Fettgift oder die Fettsäure und ihre Wirkungen auf den thierischen Organismus), Kerner detailed 27 animal experiments on cats, rabbits, and birds, alongside 24 descriptions of accidental human poisoning from liver and blood sausages. His visionary perspective is encapsulated in the statement: "The idea of 'fatty acid' as a therapeutic agent belongs to the realm of hypothesis and may be confirmed or refuted by future observations."[6]

The culmination of 19th-century scientific progress occurred in 1895, following a botulism outbreak after a funeral in the Belgian village of Ellezelles. On 14 December 1895, 34 musicians gathered at the café Le Rustic after the funeral of Antoine Creteur (aged 87) to consume beer, sausages, and ham (Figure 2).



Figure 2: The famous Le Rustic café. Currently serving as a museum, this historic site witnessed the infamous outbreak event.

Following the meal, 10 musicians became critically ill, and three subsequently died. Portions of the implicated ham, a second ham from the same pig, and organs from the deceased victims were sent to Émile van Ermengem in Ghent for investigation. Between 1895 and 1896, Van Ermengem successfully isolated Clostridium botulinum from a piece of the ham that had poisoned the members of the Fanfare Royale.[7]

The United States was similarly affected by the pathogen. In 1919, contaminated canned ripe olives caused a deadly outbreak of botulism across three states, resulting in 19 deaths: 7 in Ohio, 5 in Montana, and 7 in Michigan. This single outbreak accounted for nearly half of all historical fatalities attributed to commercially canned food in California.[8]

Pure botulinum toxin type A was first isolated as a stable acid precipitate in the 1920(s) by Hermann Sommer and colleagues at the Hooper Foundation, University of California, San Francisco. However, given that the deployment of toxic gases during World War I had paved the way for chemical warfare, the military potential of such a potent toxin as a biological weapon quickly attracted armed forces' attention.

Chemist Stanley P. Lovell (1890–1976) was recruited into the OSS by Colonel William Donovan, subsequently heading a covert group of scientists tasked with developing sabotage strategies. In an

attempt to utilize botulinum toxin as a lethal weapon against Japanese officers, Lovell prepared small gelatin capsules containing a fatal dose of the toxin. These were intended to be slipped into food and beverages by trained Chinese operatives. However, upon delivering the capsules to China, the US Navy tested them on donkeys—animals uniquely resilient to botulism—which survived the trial, ultimately leading to the abandonment of the project.[9]

Concurrently, the identification of other toxin serotypes advanced globally. In 1922, Bengston isolated Type C in the USA, while Seddon independently identified the same serotype in Australia. Type D was subsequently characterised in the USA by Meyer and Gunnison in 1928. This was followed by Bier's identification of Type E in Ukraine in 1936. Decades later, Type F and G toxins were identified in Scandinavia by Møller and Scheibel in 1960, and further characterised in Argentina by Giménez and Ciccarelli in 1970.

Edward Schantz first cultured *Clostridium botulinum* and isolated the toxin in 1944. By 1949, Burgen and colleagues demonstrated that botulinum toxin blocks neuromuscular transmission by inhibiting acetylcholine release.[10] Concentration and crystallization techniques developed at Fort Detrick between 1946 and 1947 by Carl Lamanna and James Duff provided the technical foundation for the clinical-grade product. Following the disbandment of the Army Chemical Corps, Schantz continued toxin manufacturing at the Food Research Institute in Wisconsin. Inspired by Schantz's work, Daniel Drachman (1932–2022), Professor of Neuroimmunology at Johns Hopkins University, utilised the neurotoxin to study embryonic hindlimb development in chicks. Years before its clinical introduction, Drachman demonstrated that administering botulinum toxin to chick fetuses successfully mimicked human arthrogryposis multiplex congenita.[11,12]

Development of Botulinum Toxin as a Therapeutic Agent

The transformative evolution of botulinum toxin from a potent biological threat into a breakthrough therapeutic agent is largely credited to the collaboration between ophthalmologist Alan B. Scott and Edward Schantz, who initially approached the toxin with distinct objectives.

Alan B. Scott (1932–2021), a Californian ophthalmologist at the Smith-Kettlewell Eye Research Institute, initiated research in the early 1970s seeking a neurotoxin that could weaken oculomotor muscles via a simple, cost-effective injection (Figure 3). His ultimate goal was to establish a minimally invasive alternative to conventional strabismus surgery under general anaesthesia in infants. In 1979, Schantz manufactured a standardised batch of botulinum toxin type A, designated as "batch 79-11," which consisted of two 200-mg crystalline doses approved by the FDA for human investigational use. Schantz became the primary supplier for Scott, initiating a historic partnership.

In 1978, Scott successfully injected the toxin into the extraocular muscles of a patient who had developed strabismus following retinal detachment surgery, effectively correcting the ocular deviation. Subsequent landmark publications in 1980 and 1981 documented positive outcomes in both non-human primates and adult patients with horizontal strabismus.[13] Consequently, the FDA granted approval for the clinical use of botulinum toxin type A (BTX-A) for strabismus in 1979, followed by approval for blepharospasm—a focal dystonia—in 1989. The drug, originally commercialized as Oculinum, was acquired by a multinational pharmaceutical company in 1991 and rebranded as Botox®. Since its introduction, the primary clinical application of botulinum toxin across medical specialties has centered on managing muscle hypercontractility.

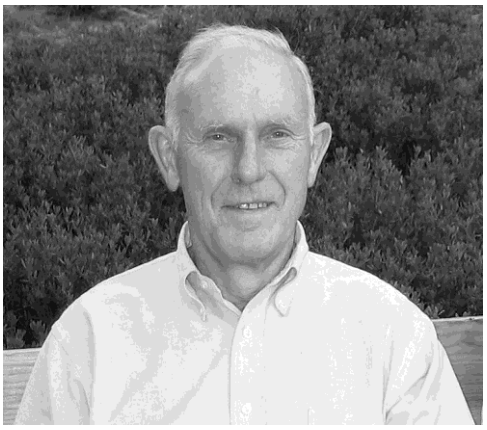


Figure 3: Alan B. Scott (1932–2021), Ophthalmologist. Widely regarded as the father of botulinum toxin therapy

Mechanism of Action

The active moiety of botulinum toxin is a 150-kDa neuroparalytic protein. Synthesised as an inactive single-chain polypeptide, it undergoes proteolytic cleavage to form a 100-kDa heavy chain and a 50-kDa light chain linked by a disulfide bond. The heavy chain mediates highly specific binding to surface receptors on cholinergic neurons, facilitating endocytosis and the subsequent translocation of the light chain into the cytosol. Once internalised, the light chain acts as a zinc-dependent endopeptidase, cleaving specific target proteins required for exocytosis and thereby preventing acetylcholine release at peripheral motor nerve terminals.

These target proteins belong to the soluble N-ethylmaleimide-sensitive factor attachment protein receptor (SNARE) complex. Specifically, the toxin cleaves synaptosomal-associated protein 25 (SNAP-25), synaptobrevin (VAMP), and syntaxin. By disrupting this macromolecular assembly, botulinum toxin prevents synaptic vesicle fusion with the presynaptic membrane, effectively blocking neurotransmitter release and inducing the desired localised muscle paralysis.[14]

Translation to Urology and Paediatric Urology

Today, botulinum toxin is utilised across a wide range of medical fields, including neurology, dermatology, and gastroenterology, with its clinical indications continuously expanding. In paediatric urology, the introduction of botulinum toxin represents a significant milestone in the management of neurogenic detrusor overactivity (NDO), a condition frequently encountered in children with spina

bifida and other neurogenic disorders.

OnabotulinumtoxinA, a specific formulation of the neurotoxin, has been shown to significantly reduce intravesical pressure and increase bladder capacity, thereby preventing upper urinary tract damage and improving the quality of life of affected children. This application highlights the therapeutic versatility and expanding potential of botulinum toxin in contemporary clinical practice.[9]

Clinical Development in Paediatric Urology

The first published urological application of botulinum toxin was reported by Dykstra *et al*., in 1988 for the treatment of detrusor-sphincter dyssynergia (DSD). Their study evaluated 11 men with spinal cord injuries and DSD; the authors conceptualised the treatment as a chemical, reversible sphincterotomy, utilising onabotulinumtoxinA (batch 79-11-48) provided by Dr. Alan Scott.[15] Subsequently, Schurch and co-workers were the first to treat NDO with intravesical onabotulinumtoxinA, establishing the foundational technique for its current urological application.[16]

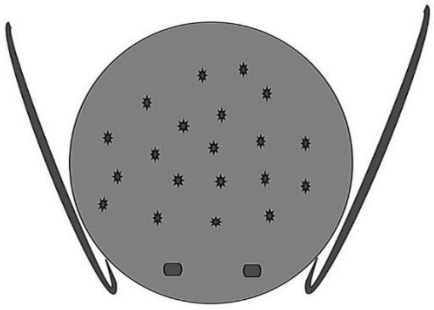


Figure 4: Multipoint injection scheme. The protocol involves 20–25 injection sites, each receiving 10 IU of BTX-A, while strictly sparing the trigonal area.

Result

The results of this pioneering 21-patient study were presented at the 1999 joint meeting of the International Continence Society (ICS), the International Urogynecological Association (IUGA), and the International Children's Continence Society (ICCS) in Denver, Colorado, and published in full in 2000. Six weeks post-injection, 17 out of 19 evaluable patients achieved complete continence, showing significant improvements in urodynamic parameters compared to baseline. Subsequently, Schulte-Baukloh *et al*., (2002) published the first paediatric study, demonstrating the efficacy of botulinum-A toxin in 17 children with neurogenic bladder due to myelomeningocele. The treatment led to significant urodynamic improvements 2 to 4 weeks post-injection, including a 112% increase in reflex volume and a 32.6% reduction in maximal detrusor pressure, offering a viable alternative to surgery (Fig. 4).[17] A study conducted by our group in children and adolescents with spina bifida treated with 200 units (U) of onabotulinumtoxinA similarly demonstrated substantial improvements in neurogenic bladder management. Our data revealed a mean 66.45% increase in leak point volume (LPV) and a 118.57% increase in specific capacity at 20 cm H2O (SC20); in line with clinical expectations, successive repeat injections were required to maintain efficacy.[18]

A landmark Phase 3 clinical trial evaluating the efficacy and safety of three distinct doses (50 U, 100 U, and 200 U) of onabotulinumtoxinA for paediatric neurogenic detrusor overactivity (NDO) refractory to anticholinergic therapy confirmed the benefit of intravesical administration in children. Specifically, the 200 U dose demonstrated a significant reduction in maximum detrusor pressure (MDP), an increase in maximum cystometric capacity (MCC), and a notable decrease in involuntary detrusor contractions (IDC).[19] Furthermore, a recent systematic review confirmed that onabotulinumtoxinA injections are clinically and urodynamically effective, and generally safe treatment for paediatric NDO. Conversely, fibrotic, non-contractile bladders characterised by poor compliance, a severely restricted baseline bladder capacity, or an open bladder neck were identified as key predictors of a poor therapeutic response.[20]

These collective milestones culminated in the regulatory approval of botulinum toxin for various urological indications, particularly in the paediatric population:

August 24, 2011: The FDA approves Botox for the treatment of specific forms of urinary incontinence.

January 18, 2013: The FDA approves Botox to treat neurogenic detrusor overactivity in adults.

February 10, 2021: The FDA approves Botox for paediatric detrusor overactivity associated with an underlying neurological condition.

Considerable clinical experience has also accumulated regarding the use of onabotulinumtoxin A for paediatric idiopathic overactive bladder (OAB). Although this indication remains off-label in children, it is heavily supported by encouraging literature. Contemporary guidelines suggest that clinicians should offer sacral neuromodulation (SNM), percutaneous tibial nerve stimulation (PTNS), or intravesical botulinum toxin injections to patients with refractory OAB who exhibit an inadequate response or intolerable side effects to pharmacological and behavioural therapies, with a recommended dose of 100 U of intravesical onabotulinumtoxinA.[21]

Injection Techniques for Intravesical Treatment

Botulinum toxin is primarily administered into the bladder via two distinct techniques: intra-detrusor injection and submucosal injection. The procedure can be performed under general anaesthesia, under local anaesthesia via the intravesical instillation of 20 mL of 0.5% lidocaine 10–15 minutes prior to the injection in compliant individuals, or even without any anaesthesia in selected patients.[22]

OnabotulinumtoxinA is delivered endoscopically using a 25G flexible or rigid needle across 20 to 30 evenly spaced sites on the bladder wall, aiming to cover the majority of the visible bladder field. The intradetrusor technique involves injecting the toxin directly into the detrusor muscle. This method is the most widely established and extensively studied approach for

Table 1: Major historical and clinical milestones in the evolution of botulinum toxin.

Date/period	Milestone	Relevance / supporting reference
1817–1822	Justinus Kerner described "sausage poisoning," characterised the clinical syndrome, and anticipated therapeutic use.	Foundation of clinical botulism and therapeutic concept.[1]
1895–1897	Émile van Ermengem isolated the causative anaerobic bacillus after the Ellezelles outbreak.	Microbiological identification of C. botulinum.[7]
1920s	Hermann Sommer and colleagues obtained stable purified type A toxin preparations.	Early purification enabling later experimental work.[1]
1949	Burgen, Dickens, and Zatman demonstrated blockade of neuromuscular transmission.	Mechanistic basis for chemodenervation.[10]
1970s–1980	Alan B. Scott developed therapeutic extraocular injection; landmark clinical publication followed.	Transition from toxin to therapeutic agent.[13]
1988	Dykstra *et al*., treated detrusor-sphincter dyssynergia.	First published urological application.[15]
1999–2000	Schurch *et al*., treated neurogenic detrusor overactivity.	Established intradetrusor urological use.[16]
2002	Schulte-Baukloh *et al*. reported treatment in children with myelomeningocele.	First paediatric neurogenic bladder study.[17]
2011	US FDA approved onabotulinumtoxinA for urinary incontinence associated with neurologic detrusor overactivity in adults.	Regulatory milestone.
2021	US FDA approval extended to paediatric detrusor overactivity associated with a neurologic condition.	Paediatric regulatorymilestone.[19]
2025	Mucosal-lifting suburothelial injection technique reported in children.	Technique refinement intended to improve placement and reduce extravesical leakage.[25]

both OAB and NDO. By targeting the detrusor, the toxin effectively dampens involuntary contractions, thereby expanding bladder capacity and reducing urinary incontinence episodes. While highly effective, this approach may carry a marginally higher risk of transient urinary retention compared to the submucosal pathway. Furthermore, as shown by Mehnert *et al.,* despite the assistance of bladder wall ultrasonography, there is a risk that some injections may penetrate the extravesical space, reducing treatment effectiveness[23] (Figure 5).



Figure.5: Intradetrusor injection of onabotulinumtoxinA. The needle is inserted perpendicularly into the bladder wall to a depth of 2–4 mm. The depth may be adjusted based on ultrasonically determined bladder wall thickness.

Conversely, the submucosal injection technique delivers Botox just below the mucosal layer; the needle is inserted tangentially, producing a visible mucosal bulge that confirms correct placement.

This approach targets the sensory nerve endings involved in sensing bladder fullness, thereby reducing urgency and frequency in overactive bladder (OAB) patients. A recent advancement within this specific technique (personal technique) utilises a rigid needle to lift the bladder wall during administration, ensuring a safer, more targeted sub-urothelial injection that avoids extravesical leakage [24,25] (Figure 6).

Overall, bladder Botox injections have significantly improved outcomes for children with anticholinergic-resistant NDO by enhancing compliance, reducing detrusor pressure, and increasing bladder capacity, ultimately offering a less invasive alternative that often delays or eliminates the need for enterocystoplasty. In this regard, long-term studies—including paediatric cohorts—confirm that repeated injections administered every 6 to 12 months remain safe and do not induce adverse histological changes, confirming long-term safety profiles comparable to adult populations.[20]

Indeed, enterocystoplasty appears necessary only in a subset of non-responders, specifically patients presenting with fibrotic, non-contractile bladders characterised by poor compliance, or children with a severely restricted baseline bladder capacity.

Table 2: Concise comparison of intradetrusor and submucosal/suburothelial injection techniques.

Feature	Intradetrusor injection	Submucosal/suburothelial injection
Target plane	Detrusor muscle	Immediately beneath urothelium/mucosa
Needle orientation	Usually perpendicular	Tangential or shallow; mucosal bulge confirms placement
Evidence base	Most established; widely studied in NDO and OAB	Smaller comparative evidence base; promising alternative
Potential advantages	Direct detrusor chemodenervation; standardised clinical experience	Visible confirmation of deposition; may reduce deep/extravesical injection
Potential limitations	Depth may vary with bladder-wall thickness; possible extravesical penetration; transient retention can occur	Technique dependent; comparative superiority has not been established
Representative references	[23]	[24,25]

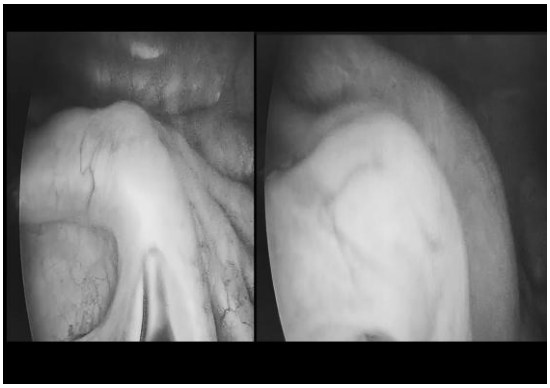


Figure 6: Submucosal injection of onabotulinumtoxinA using the mucosal lifting technique. After advancing the rigid needle 5–6 mm, the cystoscope and needle are lifted together to deliver the drug into the sub-urothelial space. Visible mucosal bulging confirms correct placement.

Nevertheless, some concerns have recently been raised regarding the clinical and logistical burden of requiring such regular, repeated therapy every 9 to 12 months.

To address these challenges, an expert consensus panel from South America recognised that the use of onabotulinumtoxinA for neurogenic bladder in paediatric patients holds a well-defined position in the treatment algorithm.[26] When patients become refractory to first-line medications, more selective second-line therapies such as beta-3 agonists and botulinum toxin-A offer robust alternatives that can delay the need for reconstructive cystoplasty, improve urinary incontinence scores, and maintain safe intravesical pressures. Ultimately, these advanced interventions successfully mitigate the morbidity associated with major reconstructive surgery, significantly enhancing both the quality of life and social integration of paediatric patients.

Treatment Limitations, Adverse Events, and Causes of Failure

Despite its clinical value, intravesical botulinum toxin should not be presented as uniformly successful or burden-free. Treatment failure may reflect advanced structural bladder disease rather than inadequate toxin activity. Fibrotic or poorly compliant bladders, very small baseline capacity, an open bladder neck, and an acontractile reservoir have repeatedly been associated with reduced response; in severely low-compliance bladders, repeated injections after an ineffective first treatment may offer limited benefit.[20,28,29] Urinary tract infection (UTI) is among the most frequent adverse events. A recent paediatric meta-analysis reported UTIs in approximately 13.6% of treated patients, while a long-term repeat-treatment study found UTI to be the most common treatment-emergent event across treatment cycles.[30,31] Transient urinary retention or increased post-void residual urine may occur, particularly in spontaneously voiding patients, and families should be counselled about the possible need for clean intermittent catheterization (CIC). Secondary loss of efficacy also deserves consideration. Neutralizing antibodies to botulinum neurotoxin A have been documented in paediatric patients receiving repeated detrusor injections and may account for otherwise unexplained treatment failure, although contemporary repeat-treatment trials have reported no neutralizing antibodies and suggest that clinically significant immunogenicity is uncommon.[31,32] The temporary duration of effect means that many children require repeated cystoscopic procedures. General anaesthesia remains common in younger or less cooperative children, creating cumulative logistical, economic, and anaesthetic burdens for patients, families, and health systems. Awake or local-anaesthetic approaches can reduce this burden in selected cooperative patients.[22,28] Cost-effectiveness is therefore influenced not only by drug acquisition but also by operating-room use, anaesthesia, follow-up, and the frequency of reinjection. These limitations reinforce the importance of careful patient selection and of recognising when reconstructive surgery remains necessary to protect the upper urinary tract.

Emerging Trends and Innovations

While the clinical application of botulinum neurotoxin (BoNT) in paediatric urology is still expanding, substantial interest surrounds the future of this novel therapeutic strategy.[27] Current innovations are primarily shaped by two key developments: the introduction of longer-lasting formulations and the refinement of delivery techniques designed to minimise invasiveness.

In particular, a novel formulation, daxibotulinumtoxinA (DAXI), has shown prolonged activity in the SAKURA clinical development program and was approved by the US Food and Drug Administration (FDA) in 2022 for cosmetic treatment of

glabellar lines. DAXI contains a highly purified 150-kDa core neurotoxin stabilised with a proprietary excipient peptide (RTP004) rather than human serum albumin.[33] Importantly, the evidence cited here is derived predominantly from aesthetic medicine. DAXI has not been established for paediatric urological use; its intravesical efficacy, dose, safety, immunogenicity, and duration of action in children remain investigational and should not be extrapolated from cosmetic studies.

As research progresses, modifications to natural neurotoxins and the development of engineered chimeric toxins—such as BoNT/BMY-WW—may offer enhanced efficacy and a reduced side-effect profile, potentially mitigating clinical challenges such as transient urinary retention or waning therapeutic responses over time. These advancements underscore a global commitment to expanding and refining BoNT therapy across multiple medical disciplines. [34,35]

Concurrently, innovative delivery platforms are being investigated to reduce procedural invasiveness. One notable approach involves utilising bioresorbable polymer films to achieve sustained intravesical BoNT release for up to 28 days, a method already successfully validated in a porcine model. If translated effectively to human clinical practice, this technology would enable intravesical BoNT therapy without requiring cystoscopy or general anaesthesia.

Additionally, alternative translational approaches have explored using dimethyl sulfoxide (DMSO) as a solvent for intravesical BoNT instillation. Although DMSO does not fully preserve the native tertiary structure of the BoNT protein and poses specific challenges regarding systemic absorption and clinician occupational exposure, it has demonstrated a unique capacity to enhance the metallo-proteolytic activity of the toxin during lipid membrane interactions. This investigative method could pave the way for a completely non-invasive treatment option, offering a promising alternative for patients with refractory bladder dysfunction and expanding the therapeutic landscape of BoNT.[36]

Conclusion

The historical trajectory of botulinum toxin represents a remarkable journey, transforming a lethal biological poison into a versatile therapeutic remedy of paramount interest across almost all medical fields, including paediatric urology and neurogenic bladder management. Its clinical implementation has successfully revolutionised the quality of life for thousands of young patients worldwide. Ongoing collaborative research among academic institutions, pharmaceutical entities, and healthcare providers continues to explore novel clinical indications for existing serotypes while engineering long-lasting molecular variants. These efforts aim to deepen our understanding of the toxin's precise macromolecular structure and intracellular dynamics. Ultimately, these ongoing technological breakthroughs are poised to optimise treatment efficacy, prolong the duration of effect, minimise adverse events, and broaden the therapeutic options available to patients.

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