Botulinum Toxin for LUTS
Past, Present and Future

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Introduction: Botulinum neurotoxins (BoNTs) are well known for their ability to potently and selectively disrupt and modulate neurotransmission. BoNT is currently undergoing regulatory evaluation for urological disorders across the world.

Personal Journey: I want to acknowledge the pioneers in the field who made my experience possible. Dennis Dykstra was the first pioneer to report urologic application of BoNT in 1988. He is a physiatrist with exceptional creativity. Brigitte Schurch first reported high-quality studies of BoNT application in the urethra and bladder in 2000 and Rick Schmidt first reported experiments with BoNT in the prostate in 1998. I want to also acknowledge the work of my friends Professor H. Kumon and Dr. T. Yokoyama in Okayama who have pioneered research into BoNT in Japan.

I began using botulinum toxin for lower urinary tract symptoms (LUTS) in 1998, frustrated with the lack of alternative therapies for refractory overactive bladder and detrusor-sphincter dyssynergia. My first patients were women with multiple sclerosis and significant detrusor-sphincter dyssynergia who could not void. A neurologist friend informed me of the BoNT-A preparation. I injected one side of my forehead and found onset of action in approximately three days. The result was fascinating: while frowning, my left brow felt completely normal, yet my forehead muscles did not move. My first few sphincter injection patients were successful and able to void without catheters or high residual urine volume. This compelled me to investigate BoNT in the research laboratory, resulting in this 10-year journey from the bedside to bench top and back with the botulinum toxin.

Several key observations I noted with BoNT include: 1. An approximate 90% decrease in need for bladder augmentation. This can fundamentally change how we treat neurogenic bladder. Detrusor compliance and vesicoureteral reflux improved in over 50% of patients. 2. Submucosal and trigone injection had similar efficacy with low rate of retention. No case of clinical vesicoureteral reflux has been noted with trigone injection technique. 3. Duration of efficacy increased with second and further BoNT injections that may result in improved health economics benefits. 4. Duration of effect for prostate injection is often 12 months with symptom improvement. 5. BoNT has allowed me to help my patients with difficult LUTS symptoms for over ten years. An outline of my presentation will reflect where we have been, current status and looking into my crystal ball on new developments in toxin research in urology:

Past: I will touch on what urology has contributed to the science of toxin research

- Leaders and friends
- Discover long-term smooth muscle and prostate effect
- Contribution on sensory nerve activity and pain relief

Present: I will highlight the current international trials for these three topics

- Neurogenic detrusor overactivity
- Idiopathic detrusor overactivity
- Prostate

Future: New possibilities with BoNT research

- Pain and inflammation and urine nerve growth factor biomarker
- Liposome liquid BoNT bladder instillation
- Health economics of BoNT versus neuromodulation and augmentation

Conclusion: In my personal experience over the past 10 years BoNT is promising for a variety of LUTS. International, multicenter, randomized trials for bladder and prostate indications are currently ongoing seeking regulatory approval.