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A consumer's guide to Botox



In 2001, when Health Canada approved botulinum toxin type A for the treatment of frown lines, Botox® suddenly became a household name. While you may know that the drug is great for smoothing out those wrinkles between your eyes, you may not know that it has been licensed in Canada since 1990 as a safe and effective treatment for a number of disorders caused by overactive muscles. A surge in research and clinical studies has confirmed the emergence of new cosmetic and therapeutic areas in which the drug might show benefit—some you may already suspect, but some you may never have imagined.

This website is developed by SkinCareGuide.ca to provide you with accurate information about approved indications for and emerging uses of botulinum toxin type A. SkinCareGuide.ca is founded by a prestigious group of international dermatologists with extensive knowledge and achievements in clinical, academic and business aspects of dermatology. It is created to serve as a source for reliable and in-depth information on skin care, dermatology, and cosmetic surgery. All information on this website is based on published clinical papers and is reviewed by independent physicians to ensure that it is accurate and up to date.

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## > Background

Botox<sup>®</sup>, manufactured by Allergan Inc., belongs to a class of drugs called botulinum toxins, which derive from the bacterium *Clostridium botulinum*. Strange as it sounds, this is actually a very similar source of many common medicines, such as penicillin and other antibiotics, which derive from mould. Although there are seven different types of botulinum toxin (A, B, C1, D, E, F, and G), most of the research conducted to date has focused on type A—called BTX-A, manufactured as Botox<sup>®</sup>. The bacterium produces a protein that blocks the release of acetylcholine, which normally transmits messages from the nerves to the muscles to make them contract and move. Once transmission has been blocked, muscles relax, providing relief to patients with overactive muscles, reducing spasms and pain. The effect is completely reversible and generally lasts for a few months in most clinical uses.

## > Approved Indications

### *Frown Lines*

The "Botox<sup>®</sup> buzz" began with the discovery that the toxin somehow inhibited the ability to frown when injected between the eyebrows; now, Botox<sup>®</sup> has been used for cosmetic purposes for over 10 years and is the only BTX approved for cosmetic use in North America. Two large clinical trials of 405 patients demonstrated that Botox<sup>®</sup> safely and effectively diminished frown lines (glabellar rhytides) for up to 4 months without any serious adverse effects (Carruthers 2002; Carruthers 2003). Over 80% of study participants reported an improvement in their frown lines a week after injection; after 30 days, patients rated their glabellar lines much improved or non-existent. Improvements were still reported up to 4 months later.

### *Crossed Eyes*

Years before the discovery of its benefits in cosmetics, Botox<sup>®</sup> was first used successfully to treat a human medical condition—strabismus—in 1980 (Scott 1980). Strabismus is a disorder in which eyes are misaligned or crossed due to weakened eye muscles. Botox<sup>®</sup> injections into the overactive muscles help rebalance the strength and realign the eyes for about 3 months, as demonstrated by numerous studies (Carruthers 1985; Flanders 1987; Petitto 1991; Lennerstrand 1998). Even in infants and children, Botox<sup>®</sup> is safe and has been used instead of or in addition to surgical correction. (Biglan 1989; Magoon 1989; Scott 1990). There were no serious complications reported in any of the studies. The Food and Drug Administration approval for adults came in 1989, with Health Canada approval following shortly after, in 1990.

### *Eye and Facial Spasms*

The term blepharospasm can be applied to any abnormal uncontrolled muscle contraction around the eyes, from blinking or eyelid tics to twitches and the inability to keep the eyes open for significant periods of time. Long-term studies have shown that up to 90% of patients with

blepharospasm obtain almost complete relief lasting 3 to 4 months after Botox® injections (Carruthers 1985; Carruthers 1987; Scott 1985; Tsoy 1985; Dutton 1986; Dutton 1994; Pongvarin 1997).

Hemifacial spasm is a disorder characterized by frequent involuntary contractions of the muscles on one side of the face. Hemifacial spasm is treated primarily with Botox® injections, with up to 95% of people with involuntary facial spasms and tics reporting improvement after treatment (Wang 1998). There is evidence that repeated injections over a longer period of time may increase the benefit (Jankovic 1993).

### *Wry Neck*

Botox® has been used since 1985 in the treatment of cervical dystonia (also known as spasmodic torticollis or wry neck), which is characterized by neck muscles contracting involuntarily, causing abnormal movements of the head and neck that may be sustained or jerky. Spasms in the muscles or pinched nerves in the neck can result in considerable pain and discomfort. Botox® injections directly into the affected neck muscles are the primary and most effective form of treatment for cervical dystonia, reducing the amount of uncontrollable movement and relieving the associated pain in about 70% of patients (Jankovic 1990; Velickovic 2001).

### *Foot Deformity (with Juvenile Cerebral Palsy)*

Injections of Botox® are used in children with equinus foot, a deformity associated with cerebral palsy, which generally causes stiff, spastic muscles. In severe cases, children may be unable to walk or control their movements. Studies have shown that Botox® relaxes the spastic muscles and improves balance, ability to walk, and foot deformity (Koman 1993; Calderon-Gonzalez 1994; Koman 1994) and may help avoid orthopedic surgery (Metaxiotis 2002). Injected directly into the muscle, the drug stops overly active muscles from tensing and reduces muscle stiffness, allowing the muscles to be stretched and encouraging normal growth. Injections are required every 3 to 6 months or when the effects of the toxin wear off. Adverse effects are mild to moderate and include muscle weakness. In a large study of 114 children, no serious, severe, or irreversible adverse effects were experienced, and the majority of the side effects were mild (Koman 2000).

### *Spasticity*

In November 2001, Health Canada approved Botox® injections to reduce spasticity that can occur after a stroke, when muscles no longer respond to signals from the central nervous system telling them to relax, and they remain contracted instead. Examples of post-stroke spasticity include a clenched fist, flexed wrist, bent elbow, or arm pressed against the chest. Botox® relaxes the affected muscles, reducing spasticity and helping patients function more normally, with improvements in hygiene, dressing, and pain. The safety and efficacy of the injections in the

treatment of wrist and finger spasticity after stroke were examined in a large study of 126 patients. Botox® was better than placebo (non-drug injections) in improving wrist and finger muscle tone and reducing disability in daily life for at least 3 months following one treatment. Side effects were mild and included pain at the injection site, headache, dizziness, and muscle weakness (Brashear 2002).

### *Hyperhidrosis*

Hyperhidrosis is a chronic disorder of excessive sweating that can affect any body part, including the underarms, the palms, the soles of the feet, and the face. By blocking the release of acetylcholine, which activates the sweat glands, Botox® injections can relieve excessive sweating, a life-altering procedure for those suffering from the embarrassing ailment, and were approved for use under the arm in September 2001. Previous treatments for excessive underarm perspiration—which is known as axillary hyperhidrosis—were often ineffective and short-acting, or were associated with significant risks. Studies have shown that 80 to 95% of patients respond to one treatment session (Naumann 2001; Lowe 2003; Naumann 2003). Along with a decrease in perspiration, injections can improve quality of life (Campanati 2003) and decrease body odour (Heckmann 2003) for up to 7 months (Naumann 2003). A long-term study has shown that side effects are minimal, and repeated injections over 16 months are safe and efficacious, with 50% or greater reduction in sweating seen in 96% of patients after the first treatment (Naumann 2003).

## > Emerging Uses

### *Expanding Cosmetic Applications*

Although Botox® has been officially approved only for use in the treatment of frown lines, many physicians have used it for a number of other cosmetic areas for years. It has been found effective in smoothing out horizontal lines in the forehead, crow's feet, mouth frown, dimpled chins, and lines on the neck (Carruthers A 2001). Botox® is now being used in more artistic manners, to lift the brow and shape eyebrows (Huang 2000; Carruthers A 2001; Fagien 2001), widen the eyes to produce a more rounded look (Carruthers J 2001; Flynn 2001), shape the jaw and sides of the face (Park 2003), and to balance asymmetrical features (due to injury or surgery). In addition, studies have found that the addition of Botox® to traditional cosmetic surgery or other procedures (such as laser resurfacing) enhances the result (Fagien 2001).

### *Back Pain*

Preliminary studies have suggested that, in patients who do not find relief from traditional pain medication, Botox® injections are safe and provide local relief of low back pain without systemic side effects (unlike central nervous system side effects seen with other more traditional pain treatments). In a small randomized trial of 31 adults with low back pain lasting longer than 6 months, 73% of participants who received injections reported significant pain relief

after 3 weeks (Foster 2001). More studies—especially larger, randomized trials—are necessary to further evaluate the use of Botox®. Although there was initially concern that large doses repeatedly injected into the spinal muscles could lead to muscle weakness, this occurrence has not been noted in any studies (Difazio 2002; Wheeler 1998).

### *Migraine and Tension Headaches*

Studies in the treatment of migraine have shown a decrease in the incidence and severity of headaches for a period of 3 to 4 months after injection of Botox®, along with a reduction in the use of pain killers (Barrientos 2002; Mauskop 2002). Some people respond well after only a single treatment session, while others improve after repeated injections (Binder 2000; Silberstein 2000; Mathew 2002). Some physicians believe that Botox® may even change or halt the course of headaches (Mathew 2002).

The efficacy of Botox® in the treatment of chronic tension headaches is under debate. Some studies suggest positive benefits (Relja 1998; Schulte-Mattler 1999; Smuts 1999; Freund 2000), while others have shown no effect on pain intensity (Zwart 1994; Göbel 1999). A recent study analyzed the results of 271 patients with chronic daily headaches, tension headaches, or migraines, and found that Botox® injections decreased the frequency of all headaches by more than 50% (Blumenfeld 2003). Overall, 85.6% of study participants claimed their symptoms improved. Temporary eyelid or eyebrow drooping was each reported by three people; other side effects were minimal.

## > Side Effects and Safety

As with any medication, potential side effects of Botox® do exist and vary according to injection site, dose, frequency of injections, and the amount of physician expertise. Most side effects—such as pain, tenderness, or bruising at the injection site—are temporary and occur within a few days after treatment. The most common side effects of injections around the eyes and in the face include temporary bruising, eyelid drooping (ptosis), dry eyes, and double vision (diplopia) (Hsiung 2002; Tan 2002), and facial droop can occur with injections into the cheek. It is generally agreed that in the hands of experienced physicians, these side effects are considered rare.

The most common side effects in patients receiving Botox® for cervical dystonia are difficulty swallowing (dysphagia), upper respiratory infection, neck pain, and headache. Potential complications when using Botox® in the face and neck occur when too much toxin is injected or when the right amount is injected into the wrong muscle. Inaccurate injections in the forehead or around the eyes can cause drooping lids; too much injected in the neck can cause muscle weakness and difficulty swallowing. In general, when used at recommended doses by skilled physicians, Botox® is safe and is not known to cause any long-term side effects.

What long-term clinical data exist show a medication with a good record of safety. In a study of 65 patients who received repeated injections for 10 years, side effects were all temporary and

mild and decreased after repeated injections (Defazio 2002). Examination of the eye muscles after Botox® has shown that repeated injections do not cause irreversible muscle atrophy (wasting) or any other degenerative changes (Borodic 1992), and muscle function after injection reverts to normal (de Paiva 1999). A large study of 235 patients who received Botox® injections for cervical dystonia, hemifacial spasm, and blepharospasm showed a 75% benefit from treatment for up to 10 years. Although side effects occurred in 27% of study participants at any one time, only 1.3% stopped receiving injections because of intolerable adverse effects (Hsiung 2002).

What does this tell you? Botox® injections have not been shown to permanently change your muscles or cause any long-term problems. The side effects of Botox® injections are usually exactly what the therapy is supposed to cause: muscle weakness. It's crucial to inject into the right muscle with the appropriate dose. Finding an experienced physician is of utmost importance, as many complications are the result of misplaced injections or too-large doses.

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