The use of botulinum toxin in the dental office for the treatment of dentally related conditions including parafunctional clenching, extracapsular myogenic temporomandibular disorder (TMD), trismus, and the associated headaches is a new option for symptom relief in patients in whom conventional treatments are not effective. Used appropriately and with a fully informed patient who understands that no treatment is guaranteed, botulinum toxin injections represent a different treatment protocol for patients who visit their dentists seeking relief from these conditions.

To understand the effects of botulinum toxins on extracapsular myogenic disease in the masticatory system, the non-diseased state should be recognized. In the non-diseased state, the masticatory system functions to preserve all the tissues in the entire system. In the non-diseased, semi-relaxed state, the teeth remain separated by the freeway space. This space is maintained by a balance in force between the opening and closing muscles of the jaw. The jaw-closing muscles are not truly relaxed to prevent gravity from allowing the mandible to drop and the mouth to gape open. As the teeth make contact, there is a reduction in contractile force by the mandibular elevators, particularly the temporalis, medial pterygoid, and masseter muscles, in order to reduce sustained force between opposing teeth. The jaw-opening muscles, particularly the lateral pterygoid muscles, are activated just before teeth-to-teeth contact. These muscles act like an air brake to limit the force of the teeth in opposing jaws from biting too hard into each other. As the bite opens, the lateral pterygoid relaxes. Tooth-to-tooth contact initiates a swallowing reflex to remove the bolus from between the teeth and to eliminate the reason for mastication. These basic functions prolong the life of the periodontium and the health of the entire system.

Certain conditions can cause an increase in sympathetic muscle tone. These conditions include stress, hormones, diet, drugs, trauma, and certain neuromuscular diseases. The increased tone affects the trigeminal centre in the brain, which stimulates the masticatory closing muscles causing masticatory muscle dystonia recognized as masticatory muscle hypertonicity and parafunction.
This is most evident in the anterior aspect of the temporalis muscles. Dystonia in the masticatory system is a disorder characterized by involuntary sustained muscle contractions resulting in repetitive movements or abnormal postures. It is also recognized as parafunctional clenching.

If the temporalis muscles do not relax when the teeth come together, the lateral pterygoid in an attempt to separate the teeth remains contracted and is unable to relax. The lateral pterygoid muscles are unable to open the mandible because of the superior strength and tenacity of the temporalis. As lactic acid accumulates in the muscles, they start to cramp. Lateral pterygoid muscular pain symptoms are usually secondary to temporalis hypertonicity. When the temporalis is able to relax, symptoms from the lateral pterygoid in spasm usually disappear without any other specific treatment to the lateral pterygoid.

The pathological conditions attributed to masticatory muscle hypertonicity and parafunction are shown in Table 1. Patients who are not susceptible to muscle hypertonicity and parafunction maintain freeway space. These patients are less likely to exhibit any of the conditions listed in Table 1 that are associated with hypertonicity and parafunction. This is why patients with malocclusion and missing teeth are often symptomless as these factors are not synonymous with muscle pain and other conditions listed.

Many of the symptoms, especially pain, may be transient. Accurate scientific observations combined with astute clinical observation of masticatory physiology and pathology using noninvasive objective electronic measurement may be useful for identifying the precursors to extracapsular muscle disorders and susceptibility characteristics of patients. Parafunction can be measured using electromyography, electrosonography, and electokinetic tracings analysed properly in retrospective studies. These diagnostic tools also demonstrate what effect a specific treatment may have on this disorder.

Traditionally, dentistry has attempted to treat and prevent this transient disease with methods that are expensive, risky, irreversible, and not evidence-based. These include analgesics, splints, moist heat, exercises, transcutaneous electrical nerve stimulation, muscle relaxants, low-dose tricyclic antidepressants, local anaesthetics, alpha adrenergic receptor antagonists, occlusal adjustments, full mouth rehabilitation, orthodontics, orthognathic surgery, or a combination of these treatments.8

Ideal dental procedures and restorations will not have any affect on sympathetically innervated muscle hypertonicity. An ideal intraoral device or splint made with the greatest of intentions will not work if the patient has poor compliance, which includes the majority of patients when it comes to wearing orthotics or most other intraoral devices.8 Many dentists are not comfortable with prescribing medication that has severe, unwarranted side effects. Major occlusal adjustments are risky, expensive, and have no guarantee of success.8–11

Table 1. Pathological conditions attributed to masticatory muscle hypertonicity and parafunction

<table>
<thead>
<tr>
<th>Condition</th>
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<tbody>
<tr>
<td>- Abfraction</td>
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<tr>
<td>- Alveolar bone loss</td>
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<tr>
<td>- Cervical pain</td>
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<tr>
<td>- Cervical erosion</td>
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<tr>
<td>- Chipped anterior teeth</td>
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<tr>
<td>- Delayed healing to periodontium after trauma</td>
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<tr>
<td>- Difficulty chewing</td>
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<tr>
<td>- Dysphagia (difficulty swallowing)</td>
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<tr>
<td>- Facial and pericranial muscle pain (nonspecific)</td>
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<tr>
<td>- Flared upper anterior teeth</td>
</tr>
<tr>
<td>- Fractured cusps and restorations</td>
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<tr>
<td>- Gingival recession</td>
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<tr>
<td>- Limited mouth opening</td>
</tr>
<tr>
<td>- Locked upper buccal cusps</td>
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<tr>
<td>- Loss of molars</td>
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<tr>
<td>- Masseteric hypertrophy</td>
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<tr>
<td>- Open interproximal contacts</td>
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<tr>
<td>- Painful teeth</td>
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<tr>
<td>- Scalloping of lateral border of tongue</td>
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<tr>
<td>- Tender, sensitive teeth</td>
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<tr>
<td>- Thermal sensitivity (hot and cold)</td>
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<tr>
<td>- Tinnitus (ringing in the ears)</td>
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<tr>
<td>- Tooth mobility</td>
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<tr>
<td>- Wear facets gums</td>
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Botulinum Toxin

The profession obviously has a need for a conservative reversible noninvasive treatment that is quick, easy, relatively inexpensive, long acting, and effective. A longer acting, more reliable method of obtaining masticatory muscle relaxation can be achieved by injecting measured doses of botulinum toxin (BTX) into specific sites in the major muscles of mastication.12–14 These doses are sufficient to shut down the efferent response from spindle cells within the muscles that are implicated in initiating and potentiating the sympathetic dystonic cycle. The effect of BTX is to act as a governor on sympathetically driven trigeminal innervation to the masticatory muscles. The obvious treatment goal is to reduce spasm but not to interfere with normal function.15 A reduction in dystonia and pain with optimization of function is easily achievable with a site-specific and dose-specific BTX injection protocol.16

BTX, a natural protein, is one of the most potent biological substances known. The toxin inhibits the release of acetylcholine (ACH), a neurotransmitter responsible
for the activation of muscle contraction and glandular secretion. Administration of the toxin results in a reduction of tone in the injected muscle. Some nerve terminals are not affected by the toxin, allowing the injected dystonic muscle to contract, but with less force. This weakness allows for improved posture and function of the hypertonic muscle. The degree of weakening depends on the dose, and the duration of weakness is further dependent on the serotype of BTX employed.

The seven distinct serotypes, A, B, C, D, E, F and G, differ in their potency, duration of action, and cellular target sites. BTX-A is marketed worldwide under the name Botox® (Allergan Inc, Irvine, CA, USA), and in Europe as Dysport® (Speywood Pharmaceuticals Ltd, Maidenhead, UK). Botox® has been approved by the US Food and Drug Administration (FDA) for the treatment of strabismus, blepharospasm, local spasms including hemifacial spasm, cosmetically for the facial glabellar lines, and more recently for the treatment of cervical dystonia and axillary hyperhidrosis. BTX-B has been approved by the FDA for the treatment of cervical dystonia, and will be marketed under the name Myobloc® in the United States and Neurobloc® in Europe (Solstice Neurosciences Inc, South San Francisco, CA, USA).

**Structure**

BTX is synthesized as a large single-chain peptide. Activation requires a two-step modification in the tertiary structure of the protein. This process converts the single-chain neurotoxin to a di-chain neurotoxin comprising a 100,000-Da heavy chain (HC) linked by a disulfide bond to a 50,000-Da light chain (LC). BTX acts at the neuromuscular junction where it exerts its effect by inhibiting the release of ACH from the presynaptic nerve terminal.

ACH is contained in vesicles, and several proteins (vesicle-associated membrane protein [VAMP], synaptosome-associated protein 25 kDa [SNAP-25], and syntaxin) are required to release these vesicles through the axon terminal membrane. BTX binds to the presynaptic terminal via the HC. The toxin is then internalized and the HC and LC are separated. The LC from BTX-A cleaves SNAP-25, the LCs from serotypes B and F cleave VAMP, and that from serotype C cleaves syntaxin.

This disrupts ACH release and subsequent neuromuscular transmission, resulting in weakness of the injected muscle.

**Potency**

The potency of BTX is expressed as mouse units, with 1 mouse unit equivalent to the median lethal dose (LD 50) for mice. Botox® is dispensed in small vials containing 100 U, while a vial of Dysport® contains 500 U. The relative potency of Botox® units to Dysport® units is approximately 1:4.

The lethal dose of Botox® in humans is not known, although it has been estimated to be about 3,000 U. The usual maximum total recommended dose at an injection session in the dental office is about 80–100 U. This means that the injector will have to inject 30 vials before a potentially lethal outcome. There is such a huge disproportion between the clinical dose and the lethal dose that a fatal overdose is almost impossible.

**Preparation**

The toxin is produced by the Gram-negative anaerobic bacterium Clostridium botulinum. It is harvested from a culture medium after fermentation of a toxin-producing strain of C. botulinum, which lyses and liberates the toxin into the culture. The toxin is then extracted, precipitated, purified, and finally crystallized with ammonium sulfate. In this form, BTX-A should be stored in a refrigerator but not frozen. BTX-A should be diluted with preservative-free saline and the preparation used within 4 hours of reconstitution. Conditions for stability of the toxin in solution include pH 4.2–6.8 and temperature less than 20°C. The large molecule is very fragile and is inactivated easily in solution by shaking.

**Dentofacial applications of BTX injections**

Patient education and counselling are essential components of a comprehensive therapeutic approach to all patients with masticatory parafunctional conditions. Dentists and physicians administering BTX must have a good understanding of both the anatomy of affected muscles and the resultant movement disorder. BTX can be used as sole therapy or as an adjunct to oral medications. Oral disclusion devices may also play a role as a supplement to BTX. The ideal of BTX treatment is to achieve a balance between weakness sufficient to reduce spasm but insufficient to interfere with function. The dental applications of BTX injections are shown in Table 2.

**Treatment protocols**

The treatment techniques involve the use of a 100-U vial of BTX diluted with 4 mL of unpreserved sterile saline. With this dilution, each 0.1 mL contains 2.5 U of BTX-A. The BTX is aspirated into and injected using a 1-mL tuberculin syringe and a 0.30-gauge half-inch needle.

The applications of BTX evolved serendipitously from the original ophthalmic indications. Blepharospasm patients (unable to open eyes) who had BTX injected around their eyes reported that their forehead lines disappeared. Patients injected for their brow lines reported that their headaches disappeared. Other patients injected for brow lines and crow’s feet reported that the pain...
Table 2. Dentofacial applications of botulinum toxin injections

- Extracapsular myogenic pain caused by masticatory muscle hypertonicity
- Secondary dental pain
- Trismus
- Adaptation to rapid change in vertical dimension associated with oral prostheses
- Elimination of bruxism
- Masseter hypertrophy
- Increased success with immediate loaded implants
- Gummy smiles (injecting levator anguli oris alaeque nasi)
- Limit muscle forces during orthodontic treatments
- Limit clenching after periodontal treatments
- Limit muscle hypertonicity after orthopaedic and orthognathic surgery; postoperative muscle pull on the periosteum is responsible for pain
- Sialorrhoea associated with stroke or Parkinson’s disease
- After trauma to oral tissues

associated with migraines and extracapsular myogenic temporomandibular joint caused by masticatory muscle hypertonicity improved or disappeared. The treatment protocol for masticatory muscle hypertonicity became more predictable with injections into the masseter and temporalis muscles.

The current treatment protocol ranges from one injection of 7.5 U bilaterally into the anterior vertical fibres of each temporalis muscle. In more severe cases, additional injections of 2.5 U are given into the middle and posterior third of the temporalis muscles. Treatment begins with lower doses because it is always possible to titrate up to a higher dose if necessary. The masseteric component of pain is treated with 5 U injected into the belly of the masseter below an imaginary line joining the tragus of the ear and the corner of the mouth. Pain relief from the tendon of temporalis is achieved with multiple injections of 2.5 U equidistantly spaced in the temple area outside the orbital rim of the eyes.

The side effects of botulinum toxin injections are site and dose related. Any injections given within 1 cm above the eyelid and outside the midpupillary line will cause eyelid ptosis. Additionally, any injections given below the eye and inside the midpupillary line may cause diplopia (double vision). When injecting above the tragus-labial commissure line, the zygomaticus muscles are weakened and the corner of the mouth will droop. The rules governing cosmetic injections should be followed while treating all masticatory muscle hypertonicity-related disorders to avoid cosmetic side effects, for example eyelid ptosis or a droopy corner of the mouth. For this reason, the dentist should be familiar with the cosmetic treatment protocols. The sites and doses for BTX therapy are shown in the Figure.

Contraindications
No absolute contraindications to the use of BTX-A are known. Relative contraindications for clinical application of BTX are pregnancy and lactation, neuromuscular disease (e.g. myasthenia gravis, Eaton-Lambert syndrome), motor neuron disease, and concurrent use of aminoglycosides.

Conclusion
The use of BTX in dentistry offers the dentist another extremely effective tool to add to the armamentarium for treating conditions that derive from masticatory and other pericranial muscular conditions. Most dentists are familiar with the oral anatomy and are comfortable injecting into the oral musculature. The treatment protocols and injection techniques require essential, yet minimal training for the general dentist. BTX in dentistry will offer the general dentist who is not an expert in gnathology and occlusion a safe, effective treatment for controlling the symptoms of masticatory muscle hypertonicity.

References
8. Gobel H. Botulinum toxin A is effective is cases of oromandibular dysfunction even if previous bite splint therapy has proved unsuccessful. Cephalalgia 2001;21:514–5.
Figure. Review of sites and doses for botulinum toxin therapy.