Eighty-six injections in 49 patients with adult onset spasmodic torticollis were evaluated for efficacy with respect to single point per muscle versus multiple point per muscle injection techniques. Parameters of the syndrome assessed were pain, posture deformity, range of cervical motion, disfigurement, cervical muscle hypertrophy, activity limitation, and degree of involuntary movement. The multiple point per muscle injection strategy appeared superior to the single injection per muscle technique with respect to pain ($p < 0.002$, chi-square), posture deformity ($p < 0.001$), range of motion ($p < 0.001$), and improvement in activity endurance ($p < 0.001$). No significant differences were noted with respect to cervical muscle hypertrophy or degree of involuntary movements, although the injections were considered beneficial in both groups to these syndrome components.

Botulinum A toxin injections have proven to be useful in managing adult onset spasmodic torticollis.$^1$–$^5$ Although prior clinical studies have shown drug efficacy, considerable variability in response rates exists in the literature.$^1$–$^{10}$ For instance, in one study “no objective improve-
ments” were noted yet substantial subjective improvements$^4$ were noted. Other studies reported objective improvement in over 80%.$^1$ Although some variability in response may result from the fluctuating course of the disease, other factors relating to administration techniques or biologic activity consistency within the lyophilized toxin preparations are possible. Initially, injection sites and techniques were empirically determined based on muscle palpation and inspection for dystonic muscular contractions. Recently, several refinements proposed for the technique have included (1) subclassification of the syndrome with injection standardization,$^5$ (2) electromyographic direction for needle placement,$^9$ and (3) dose limitations over the sternomastoid muscle to limit complications.$^{11}$

The purpose of this paper is to report the clinical response rates using single point per muscle versus multiple point per muscle injection strategies.

**METHODS AND MATERIALS**

Botulinum A toxin was obtained from Oculinum Incorporated. The clinically useful preparation of the toxin is derived entirely from the 1979-Schantz source. The toxin is stabilized during lyophilization using human serum albumin and reconstituted within 1 hour prior to use with nonpreservative normal saline. The concentra-
tion of reconstituted toxin ranged from 10 IU/0.1 mL to 5 IU/0.1 mL.

Patients inducted into the study were diagnosed as having adult onset spasmodic torticollis by 2 clinicians and demonstrated signs and symptoms for at least 1 year. Each patient had been treated with at least 2 types of neuroleptic medications prior to receiving the toxin and had obtained no benefit from conventional drug treatment. Informed consent was obtained before induction into the study with approval from the internal review board at the Massachusetts Eye and Ear Infirmary.

Injections were done with a 25-gauge needle and tuberculin syringe. The muscles were chosen for injection based on obvious hypertrophy, involuntary contractions, perceived increase in resting tone, location of pain, or an impression that excess contraction of that muscle was producing abnormal posture. Muscles usually targeted for an injection were the sternocleidomastoid, splenius capitis, splenius cervicis, levator scapulae, trapezius, and scalene group. Each patient was randomized into a single point per muscle group (SPMG) and multiple point per muscle group (MPMG). The administered dose ranged from 100 to 250 IU based on previous clinical reports.1-10

In patients receiving a single injection per muscle, a single injection was placed in the middle of the muscle belly or the position perceived to have an increased tone or involuntary contraction. The selection and number of muscles injected in each patient depended on direct inspection for increased tone, involuntary contractions, or hypertrophy. In each group, no muscle targeted for injection received more than 100 IU. The number of punctures used in the single point group ranged from 1 to 7 per treatment session depending on the number of cervicle muscles involved. In the multiple point group, injections were given over at least 4 points per muscle and the number of injections in the cervical region ranged from 4 to 28 punctures per session.

Patients in each group were followed in 3 weeks and 3 months. Objective assessments reported in this study were generally made at 3 weeks, whereas subjective assessments made by the patient were evaluated after 3 months. Evaluations with respect to pain relief were made during patient interviews.

To be considered a favorable result, the patient needed to feel that there was at least a 50% improvement of preinjection pain. Posture deformity was assessed by evaluation of head position for degree of rotation or head tilt, extension or flexion with the patient seated, and asymmetry in shoulder elevation. Active and passive rotations of the cervical spine were evaluated by the clinician.

FIGURE 1. (A) Example of single point injection per muscle strategy over the sternocleidomastoid muscle. (B) Example of single point per muscle injection strategy over posterior cervical muscles.
The treatment's influence on daily or routine activities, such as driving and maintaining gainful employment, was assessed during repeated interviews. Objective evaluation of the treatment on cervical muscle hypertrophy was made by the clinician examiner's inspection of the sternocleidomastoid muscle because this muscle is most superficial and accessible. Improvement was defined as decrease in sternomastoid tone, palpable size, or visual prominence after the injection as noted by the patient or clinician observer.

RESULTS
Forty-two injection sessions in 21 patients were given using the single point per muscle injection strategy (SPMG). Forty-four injection sessions given to 28 patients were evaluated with the multiple injections point per muscle technique (MPMG). The average total dose of botulinum A toxin administered in the single point per muscle group was 161 IU (range, 80–250). The multiple point injection group received an average injection of 151 IU (range, 80–275). There was no statistical significance in total dose comparing each group using Wilcoxon analysis. The single point injection group received an average of 2.0 injections per patient whereas the multiple point group received 1.8 injections per patient. Only 1 muscle was injected in the multiple point group during 4 sessions whereas the single point group contained 6 sessions in which only 1 muscle was injected.

The most common component of this syndrome was posture deformity, which was present in all patients in both groups. Decrease in range of head motion was also present in almost all patients in the study (39/42-93% SPMG, 44/44-100% MPMG). Some impairment in daily routine activities, such as driving or reading, was present in most patients in each group (39/42 SPMG-93%, 38/44 MPMG-86%). Some form of cervical muscle hypertrophy was also found to be present in most patients (39/42 SPMG-93%, 44/44 MPMG-100%). Pain was also present in most patients (31/42 SPMG-74%, 31/44 MPMG-71%) Tremor or substantial involuntary movement was less common (17/42 SPMG-40%, 17/44 MPMG-39%).

Patients responding to this therapy generally noted maximum improvement 3 weeks after injection with diminishing benefit over a 3-month period. Decreased pain was noted in both groups. However, the MPMG group responded at a significantly higher rate (Table 1, 87%-MPMG, 48%-SPMG). The rate of response with respect to other common components of the syndrome (posture deformity, limitation of range of head motion, impaired activity) were also significantly higher in the multiple point per muscle strategy group (Table 1). The reduction of muscle hypertrophy was substantial in each group (69%-

Botulinum Toxin for Spasmodic Torticollis

**FIGURE 2.** (A) Example of multiple injection points per muscle strategy over sternocleidomastoid muscle. (B) Example of multiple injection points per muscle strategy over posterior cervical muscles.
### TABLE 1. Response rates to botulinum toxin for spasmodic torticollis comparing single and multiple point injection strategies.

<table>
<thead>
<tr>
<th></th>
<th>Single point response</th>
<th>Multiple point response</th>
<th>Chi-square (response)</th>
<th>Mean dose of favorable response</th>
<th>Mean dose of no response</th>
<th>Wilcoxon test (dose)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain</td>
<td>15/31 = 48%</td>
<td>27/31 = 87%</td>
<td>p &lt; 0.002</td>
<td>165.7 IU</td>
<td>147 IU</td>
<td>NS</td>
</tr>
<tr>
<td>Posture deformity</td>
<td>13/42 = 31%</td>
<td>33/44 = 75%</td>
<td>p &lt; 0.001</td>
<td>162.7</td>
<td>148.3</td>
<td>NS</td>
</tr>
<tr>
<td>Range of motion</td>
<td>15/39 = 38%</td>
<td>33/44 = 75%</td>
<td>p &lt; 0.001</td>
<td>156.4</td>
<td>144.3</td>
<td>NS</td>
</tr>
<tr>
<td>Activity</td>
<td>13/39 = 33%</td>
<td>29/38 = 76%</td>
<td>p &lt; 0.001</td>
<td>187.9</td>
<td>145.6</td>
<td>p = 0.04</td>
</tr>
<tr>
<td>Hypertrophy</td>
<td>27/39 = 69%</td>
<td>34/44 = 77%</td>
<td>NS</td>
<td>161.4</td>
<td>154.6</td>
<td>NS</td>
</tr>
<tr>
<td>Tremor</td>
<td>4/17 = 24%</td>
<td>9/17 = 53%</td>
<td>NS</td>
<td>163.5</td>
<td>149.5</td>
<td>NS</td>
</tr>
<tr>
<td>Mean dose</td>
<td>161</td>
<td>151</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

IU, international unit of botulin toxin activity; NS, not statistically significant.

SPMG, 77%-MPMG); there were no significant response differences between groups with respect to muscle hypertrophy. Botulinum A toxin was least effective in the treatment of involuntary movements (24%-SPMG, 53%-MPMG); there were also no significant differences between the rates of response for this component of the syndrome.

To evaluate the importance of total dose to outcome relative to various syndrome components, the dose given to patients responding favorably was compared with the dose given with no response (Table 1). With respect to pain, posture deformity, cervical range of motion, sternocleidomastoid hypertrophy, and tremor, there were no significant differences in total dose when comparing patients receiving a favorable result to those with no response. Patients who experienced increased activity tolerance had, however, received significantly greater botulinum toxin total dose.

### DISCUSSION

The first involuntary movement disorder effectively treated with botulinum toxin was blepharospasm. Injection points were chosen to give the greatest weakening effect on the orbicularis muscle. The multiple point injection strategy used for the treatment of blepharospasm was empirically derived based on efficacy.2 Attempts at using fewer injection points were associated with less satisfactory results.13,14 Not only were injection sites important for degree of clinical effect, but also in limiting spread to contiguous muscles such as the levator palpabrae superioris, extracocular muscles, or Horner's muscle projecting into the lacrimal sac.

Complications arising from contiguous spread are ptosis (levator muscle), diplopia (extraocular muscles), and epiphora (Horner's muscle). Injecting the upper lid close to the lash line and at extreme medial and lateral points maximizes the distance between the upper orbicularis injection points and muscular portion of the levator muscle, hence limits spread to the levator muscle. Likewise, injections placed laterally in the lower lid avoiding the medial portions of the lid prevent diplopia and epiphora resulting from toxin spread into the inferior oblique muscle and Horner's muscle.15 As both drug efficacy and complication rate appear to be dependent on administration technique for involuntary blepharospasm, administration technique may have similar implications for other indications.

Early in the clinical study, methods of administering the toxin involved using smaller doses of botulinum toxin injected over only several points along 1 or several cervical muscles with hypertrophy or obvious involuntary contractions or pain.1–5 Few references were made to the exact administration technique. Interestingly, earlier reports with smaller intervals of follow-up indicated lower response rates than rates reported after several years of active experience. This observation suggests that technical experience is important to clinical results. Standardization of administration techniques with emphasis on efficacy and complications will probably be useful in achieving consistent beneficial results while minimizing complications.

Subclassification of the adult onset spasmodic torticollis syndrome into 4 categories based on posture deformity and head position5 can help determine which cervical muscle sets should be injected. Additionally, dysphagia, the major complication of cervical botulinum toxin injection, has been associated with larger doses of the toxin given into the sternomastoid muscle.11 Limiting the dose given to this muscle to less than 100 IU was associated with a decrease in this complication based on prospective data.11

Although these observations of clinical data
begin to provide some guidelines for injection strategy, the optimal number and location of injections to give to each cervical muscle remain undetermined. Although there has been the perception that multiple point injections per muscle is more effective than single point injection per muscle for spasmodic torticollis, there are no clinical data to substantiate this impression. The analysis of spasmodic torticollis syndrome components in this study suggests that better results are achieved with respect to pain, posture deformity, range of motion, and activity tolerance in the multiple point injection group. But efficacy was apparent in the single point injection group with respect to all components of the syndrome.

These findings paralleled the results obtained by comparing multiple injections to motor point injections for the treatment of involuntary blepharospasm. When an electrically determined motor point was outlined in patients with blepharospasm and only the motor point injected, the clinical results appeared worse than multiple injections without motor point direction, although some benefit was derived. The innervation zone of orbicularis muscle, that is, the distribution of neuromuscular junctions, appears to be diffuse based on limited sampling of human orbicularis oculi muscle specimens.

The distribution of neuromuscular junction has not been evaluated for cervical muscles to the best of the authors’ knowledge. Wolf and Coers have generally found innervation zones in long muscles with parallel fiber arrangement close to the mid position, a situation that may apply to the sternomastoid muscle.

One potential explanation for the greater effect in the multiple injection group is that multiple injections were necessary to bring the injected botulinum toxin into a more uniform contact with the innervation of the dystonic muscles being treated. It appears that a given quantity of botulinum toxin produces denervation over a defined distance from the injection site, and single point injections over larger muscles may not create as great or as uniform a denervation effect as multiple point injections.

On the basis of these and previous results, the efficacy and safety of botulinum toxin denervation therapy may be improved by the availability of a more detailed description of neuromuscular junction distribution within affected muscles.

REFERENCES