

did not have a peripheral tremor. We considered the diagnosis to be palatopharyngeal myoclonus/tremor and posited a direct relationship to metoclopramide. The drug was stopped and her symptoms subsided over approximately 8 hours.

Palatopharyngeal myoclonus is typically a slow form of tremor at 1 to 4 Hz. It can involve the pharynx, larynx, diaphragm, and extend to involve even eye muscles. The rhythmic movement can occur both during phonation and at rest. Voice tremor and clicking or popping sounds can be associated with the movement. The disorder is usually secondary to an interruption in the central tegmental tract from brainstem infarct or from idiopathic degeneration. Treatment may include serotonin precursors, carbamazepine, and clonazepam, but in general the condition is resistant to treatment.

Previously described adverse reactions to metoclopramide include several conditions associated with more typical neuroleptic agents: acute dystonias, parkinsonian symptoms, including perioral, jaw, and extremity rest tremors, akathisia, tardive dyskinesia in several clinical forms, and neuroleptic malignant syndrome.^{1,2} The risk of developing metoclopramide-induced movement disorders has been found to increase with age, female sex, and some coexistent illnesses.^{1,3} Diabetes mellitus appears to confer additional risk for extrapyramidal symptoms.⁴ There is a 2:1 risk ratio for tardive dyskinesia in diabetics compared to nondiabetics.⁵ Diabetics who have been treated with metoclopramide also have a significantly greater severity of tardive dyskinesia than nondiabetics who have been treated with metoclopramide.⁵ We alert colleagues to our observation because we have not found other reports of metoclopramide-induced palatopharyngeal myoclonus/tremor, and because the patient responded fully and promptly to metoclopramide cessation.

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When It Comes to Botulinum Toxin, Children and Adults Are Not the Same: Multimuscle Option for Children With Cerebral Palsy

Taking a look at pharmacotherapy for children, a “reverse lifeboat philosophy” seems to apply,¹ that is, children come last. All too often adequate information on the appropriate use of indicated substances for children is lacking. A prime example is botulinum toxin (BoNT), used for treating spasticity in cerebral palsy (CP).

Having undergone nine double-blind, placebo-controlled, and randomized trials and documented within a total of 460 publications (PubMed search for clinical trials on “botulinum” and “children,” January 2006), BoNT is now well established as a valuable option for the effective and safe treatment of children with CP. Yet to date, only one of the available BoNT preparations has been registered for CP, only in a limited number of countries, only for focal indications, and only in low doses. Such restrictions have led to the recommendation to treat a maximum of four muscles at a time.² The clinician has two options: either to follow the registered use and treat the child below his or her clinical needs, or to respect the clinical needs but practice off-label use.

This unsatisfactory situation has partially arisen because dose calculations are based on scientific studies conducted on adults, where focal dystonia is much more commonly treated with BoNT than spasticity is. For the treatment of dystonias, dose conversion factors between different BoNT preparations are in use. However, the validity of such calculations is controversial and such calculations may lead to using inappropriate dosing regimens. For the off-label use in CP, any such conversion factors will lead to dangerous miscalculations.

We present data from our comprehensive Duisburg–Munich Botulinum Toxin (DuMBo) database (n = 454 patients; 1,721 treatment sessions) to support our claim that more muscles can be safely treated in a multimuscle approach in patients who are comparably young and have far less body mass than adults.

We started in the early 1990s with the licensed dosage of 4 U BoNT per kilogram body weight (preparation Botox, indication spastic equinus in CP). Over the years, to better meet the clinical needs of children with CP, we gradually increased the number of treated muscles and the total dosage per treatment session while the dosing regimes per site and muscle remained stable.

The clinical necessity and justification for this multimuscle approach were derived from the clinical movement pattern of children with CP, substantiated by gait analysis.³ As verified by these observations, many of the common gait patterns in CP can only be adequately treated if several muscles are addressed simultaneously in one treatment session. This assumption is supported by the pioneer work of Molenaers and colleagues,⁴ who showed that such an approach will significantly delay and reduce the frequency of orthopedic surgical procedures, which can be considered one of the most relevant indicators for successful treatment.

In the period from 2000 to 2005, 165 patients with bilateral spastic CP (bodyweight less than 33 kg) received a total of 495 treatment sessions with a mean dosage of 16.6 U per kg body weight BoNT per session (preparation Botox, mean dosage per

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TABLE 1. Overview

Number of treated muscles per session	n ≤ 4	5 < n ≤ 8	9 < n ≤ 12	12 < n < 19	Cumulative
Mean dosage per kg body weight per session (units of Botox)	9.9	15.8	20.3	23.9	16.6
Number of sessions	80	239	158	18	495
Number of sessions with adverse events	4	21	15	4	44
Percentage of sessions with adverse events	5.0%	8.8%	9.5%	22.2%	8.8%
Severity of adverse events					
Mild	0%	4.2%	5.7%	11.1%	4.2%
Moderate	5.0%	3.0%	0.6%	11.1%	3.2%
Severe	0%	0%	0.6% ^a	0%	0.2%
Not assessed	0%	0.8%	2.5%	0%	1.2%
Discontinuation due to adverse events	0	0	0	0	0

^aMultilevel treatment in a 4.5-year-old boy, GMFCS IV (Gross Motor Function Classification System) with a total dosage of 18 U/kg body weight. For 3 weeks, the patient lost his ability to stand, yet no systemic, drug-related adverse event was observed. The adverse event was considered to be a treatment-related focal weakness.

muscle: 36.6 U; mean total dosage per session: 282.2 U). In 83.8% of these patients, we injected more than 4 muscles, with a mean of 8.5 treated muscles (mean dosages per kg body weight: 17.9 U; range: 5.1–32.3 U; mean dosage per muscle: 35.6 U; mean total dosage per session: 303.0 U). The data are summarized in Table 1.

We did not observe any cases of adverse events that would have required discontinuation of BoNT therapy. The total rate of adverse events seen here was 8.8%. This is well below the 28% reported by Jankovic and Schwartz⁵ for the treatment of cervical dystonia in adult patients (58 of 205 patients). Thus, over a 5-year observational period, BoNT (preparation Botox) proved safe and effective in our multimuscle treatment regimen.⁶ These clinical observations are supported by experiments in a mouse model showing that BoNT (preparation Botox) has a migration profile with a particularly broad safety margin.⁷

In conclusion, as far as pharmacotherapy with BoNT is concerned, some of the needs of children with CP can be met: we can safely treat more muscles and give more substance.

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Adverse Reaction after Tetrathiomolybdate Treatment for Wilson's Disease: A Case Report

Patient 1 is a 36-year-old man who was diagnosed with Wilson's Disease (WD) at the age of 20, when he began suffering from personality changes with depressive and recurrent obsessive thoughts together with speech and walking difficulties. At this time, WD diagnosis was based on standard copper metabolism parameters (ceruloplasmin was 7 mg/dL and 24-hr urinary copper excretion was 247 µg/24 hr) and the presence of Kayser–Fleischer rings. After 16 years of anticopper therapy (penicillamine and zinc sulphate), there has been no significant improvement. At 36 years of age, his gait and speech disorders worsened and occasional choreoathetotic movement of the left arm became apparent. When the patient came under our observation, neurological examination revealed a posture slightly stooped with gait characterized by short stride, shuffling and en bloc turning; moderate extrapyramidal hypertonia of the four limbs associated with moderate diffuse bradykinesia and postural tremor at the left arm; moderate dysarthria and drooling. He scored 17 on our previously described score for WD patients,¹ ranging from 30 (no impairment) to 0 (the greatest degree of inability). Brain magnetic resonance imaging scan did not reveal any signal change in the brain parenchyma, and no Kayser–Fleischer rings were apparent on slit-lamp examination. Laboratory data are given in Table 1; serum ceruloplasmin level 0.02 g/L. Liver biopsy showed septal fibrosis and, in

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