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Meige Syndrome: What's in a Name?

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Abstract

Frequently, blepharospasm is associated with involuntary movements of the platysma, lower face and masticatory muscles. Similarly, masticatory dystonia may occur in isolation or in combination with dystonia of other cranial and cervical muscles. The non-possessive and possessive forms of Meige and Brueghel syndromes have been variably and imprecisely ascribed to various anatomical variations of craniocervical dystonia. Herein, the origin of eponymic terms as applied to craniocervical dystonia is reviewed as support for proposed elimination of these eponyms from clinical usage. Although the term "segmental craniocervical dystonia" more accurately captures the combination of blepharospasm and dystonia of other head and neck muscles, delineation of craniocervical subphenotypes is essential for etiological/genetic and treatment studies. To conclude, the clinical features, epidemiology, pathophysiology and therapeutic management of segmental craniocervical dystonia are examined with a particular focus on "blepharospasm-plus" subphenotypes.

1. Introduction

The terms "Meige's syndrome" and "Meige syndrome" are often used by neurologists and other clinicians to describe the combination of blepharospasm and involuntary movements of the lower facial and/or masticatory (jaw) muscles. Application of "Meige's syndrome" and other eponyms to the various forms of dystonia is problematic for a multitude of reasons. First of all, Meige, a physician, did not suffer from the syndrome that bears his name. Along this line, the possessive form of eponyms has been discouraged by the Council of Science Editors [1] and the father of Online Mendelian Inheritance in Man®, the late Dr. Victor McKusick [2]. Second, Meige was not the first person to describe the combination of blepharospasm and dystonia of other cranial muscles [3]. Lastly, "Meige's" or "Meige syndrome" could be confused with Meigs syndrome which is defined as the triad of a benign ovarian tumor, ascites and hydrothorax [4].

2. Historical Perspective

Dr. Horatio Wood, a Philadelphia neurologist, first drew attention to blepharospasm and other cranial dystonias in 1887 [3]. Wood briefly mentioned facial and oromandibular dystonia in his textbook on disorders of the nervous system [3]. He stated, "The contraction is tonic, causing a complete closure of the eye, and consequent blindness. This is accompanied by

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innumerable bizarre grimaces, due to the efforts of the antagonistic muscles to overcome the force which is closing the lids." Clearly, his second sentence was incorrect.

In 1910, Henri Meige, a French neurologist, described approximately ten patients with involuntary closure of the eyelids [5]. Blepharospasm was associated with involuntary contractions of the jaw muscles in only one of these patients. Over 60 years later, an American neurologist, George Paulson, reported three patients with blepharospasm and oromandibular dystonia and emphasized the probability of a common pathophysiological basis [6].

In 1976, David Marsden, an English neurologist based in London, called attention to a work of art, *De Gaper*, by Pieter Brueg(h)el the Elder, a Flemish Northern Renaissance painter, in an article on blepharospasm and oromandibular dystonia [7]. Brueg(h)el the Elder was not a physician and his painting of a yawning subject has nothing to do with dystonia. Pieter Brueghel the Elder dropped the 'h' from his name in 1559, one year after painting the *De Gaper* [8]. Brueghel the Younger was also a painter, further confounding historically exact usage of this eponym [8].

Careful inspection of the relevant medical literature over the past 30 years indicates that "Brueghel" and "Meige" syndromes remain poorly delineated. One author, Dr. Gordon Gilbert, suggested that the essential sign of "Brueghel syndrome" is "a widely and dystonically opened jaw [9]." In reality, however, jaw-opening dystonia may occur in the setting of segmental, multifocal or generalized dystonia and may be associated with blepharospasm [10–12]; application of "Brueughel syndrome" to these cases would be unnecessarily complicated and confusing. Marsden, in the title of his 1976 article on the subject, actually defined blepharospasm-oromandibular dystonia syndrome as "Brueghel's syndrome" and he did, in fact, use the possessive eponym [7].

The eponymic terms "Meige's syndrome" and "Meige syndrome" are used much more frequently than the 4 variations of "Brueghel syndrome." PubMed (www.ncbi.nlm.nih.gov) search (April 18, 2009) with the terms "Brueghel's syndrome," "Bruegel's syndrome," "Brueghel syndrome," and "Bruegel syndrome" generated 9, 0, 5, and 0 hits, respectively. In contrast, PubMed search with the terms "Meige syndrome" and "Meige's syndrome" generated 263 and 95 hits, respectively. For comparison, "cranio-cervical dystonia," "craniocervical dystonia" and "cranial dystonia" produced 6, 29 and 77 hits, respectively. Even in recent years, application of the eponymic terms remains highly variable. "Meige syndrome" and "Meige's syndrome" have been ascribed to both primary and secondary dystonias and diverse craniocervical anatomical patterns. For instance, Zesiewicz and colleagues reported substantial improvement in "Meige's syndrome" with levetiracetam treatment although their patient also exhibited cervical dystonia [13]. For an even more divergent example, a 15-year-old boy with "Meige syndrome" was described as showing "a stiff face, labial incompetence, prominent mental creases and dimples with a lot of involuntary blinking and involuntary movements of the lower face [14]." Kraft and Lang [15] defined "Meige's syndrome" as blepharospasm associated with dystonic movements of other muscle groups in the face, neck or limbs. Clearly, the time has come to terminate usage of poorly-defined eponymic terms for dystonia of the craniocervical region.

3. Anatomically-Based Classification of Dystonia by Distribution

In 1984, an *Ad Hoc* Committee of the Dystonia Medical Research Foundation developed a widely-accepted definition of dystonia and classification of dystonic movements [16]. Dystonia was defined as a motor syndrome characterized by sustained muscle contractions, usually producing twisting and repetitive movements or abnormal postures. It was noted that dystonia is often precipitated by action and almost all dystonic movements share a directional

quality that is typically sustained, sometimes for only an instant. The *Ad Hoc* committee classified dystonia by age at onset, etiology and distribution [16].

Classification by distribution includes the following categories: focal dystonia, segmental dystonia, generalized dystonia, multifocal dystonia and hemidystonia [16]. The term "focal dystonia" indicates involvement of a single body part. Common names such as blepharospasm, spasmodic dysphonia, writer's cramp and spasmodic torticollis are often assigned to the focal dystonias. The term "segmental dystonia" denotes involvement of two or more contiguous regions of the body. The segmental dystonias are subdivided into regional categories: cranial, axial, brachial and crural [16]. Within this classification scheme, segmental "cranial" dystonia indicates involvement of any combination of musculature in the head and neck region. In reality, however, the neck and mandible are not parts of the cranium [17]. Therefore, the combination of blepharospasm, masticatory dystonia and cervical dystonia, for example, is more precisely classified as segmental "craniocervical" dystonia rather than segmental "cranial" dystonia [18]. Alternative terms such as "facio-cervical" are less precise since the masticatory muscles neither arise nor attach to the face. In fact, most facial muscles attach to the cranium and/or mandible. The term "segmental craniocervical" encompasses all muscle groups in this body segment with "cranio" serving as the rostral component of this segment and cervical forming the caudal portion.

The diagnosis and anatomical classification of dystonia remains a clinical exercise profoundly influenced by experience and training. Regional involvement may be subtle, intermittent and task-specific [19]. Moreover, the origins and insertions of many muscles are located in different anatomical regions of the body (e.g., levator scapulae, digastric, platysma, semispinalis capitis and longissimus capitis). Accordingly, clear demarcation of "focal" from "segmental" dystonia may be difficult in many patients. For instance, cervical dystonia patients with retrocollis often exhibit mild, electromyographically-demonstrable involvement of the upper thoracic paraspinous musculature.

There are several reasons why use of the term "**segmental craniocervical dystonia**" may be more accurate than "segmental cranial dystonia" in most patients with "blepharospasm-plus" subphenotypes. First, involuntary contractions of the platysma muscle can be seen in an important percentage of patients with blepharospasm. In these subjects, mild contractions of the platysma muscles may be time-locked with those of the orbicularis oculi muscles. The platysma is innervated by the facial nerve, the same nerve which innervates the orbicularis oculi muscles in the eyelids [17]. The platysma is a broad, thin, superficial muscle that extends from the upper chest, shoulder and clavicle upwards to the chin, mandible and lower face [17]. Second, the pharyngeal musculature, which can be affected in subjects with blepharospasm, encompasses both the cranial and cervical regions [17,20]. Similarly, several muscles involved in jaw-opening originate in the cervical region [17,21]. Based on these considerations, "segmental craniocervical dystonia" is an anatomically more precise term that envelops virtually all past clinical utilization of the terms "Meige syndrome" and "Breughel syndrome."

The anatomical complexity of the craniocervical region also confounds employment of currently-available rating scales for dystonia [22–24]. The widely-used Burke-Fahn-Marsden (BFM) rating scale includes the following regions: eyes, mouth, speech and swallow, neck, right arm, left arm, trunk, right leg and left leg. For each region, severity ratings range from 0 (none) to 4 (severe dystonia). In addition, provoking factors are rated from 0 to 4 for each region. Scores for the eyes, mouth and neck are multiplied by 0.5 whereas the score for speech and swallow is multiplied by 1.0. Clearly, the BFM does not allow for unambiguous differentiation of masticatory, lingual and pharyngeal dysfunction. Lingual involvement, for

instance, is infrequent in primary blepharospasm-plus dystonia [11,25]. On the other hand, upper facial dystonia may occur without involvement of the orbicularis oculi muscles [26].

The Unified Dystonia Rating Scale (UDRS) was "designed to include a more detailed assessment of individual body areas, including separate ratings for proximal and distal limbs, and elimination of the subjective patient rating for speech and swallowing" included in the BFM rating scale [23]. Eyes and upper face, lower face, jaw and tongue, and larynx are among the 14 body areas included in the UDRS. The Global Dystonia Severity Rating Scale (GDS) is a simplified version of the UDRS and includes the same body areas. The GDS rates the maximal dystonia for each body area, but, unlike the UDRS, does not include a separate duration factor. The Jankovic Rating Scale (JRS) was designed to access the frequency and severity of blepharospasm and/or oromandibular dystonia [24]. For illustration, JRS severity category 3B is defined as "moderate movements or spasms of mouth, jaw, or tongue, interfering with speech, voice, chewing, or swallowing, causing moderate drooling; moderately disabling." In patients with complex segmental craniocervical dystonia, the UDRS, GRS and JRS are unmistakenly compromised by many of the same problems as the BFM. In addition, none of these scales provide due consideration to dyspnea and involvement of respiratory muscles, including the diaphragm, which may be affected in some patients with dystonia [27–29]. Complaints of dyspnea, often with breathing arrests, are not unusual in patients with craniocervical dystonia [28]. The BFM and UDRS are viable rating scales for DYT1 and other forms of generalized dystonia which predominantly affect the appendicular musculature but are less desirable for adult-onset primary dystonia which is concentrated in the craniocervical region. For these reasons, there is an evident need for improved methods of measuring the severity and anatomical distribution of craniocervical dystonia.

4. Clinical Features of Segmental Craniocervical Dystonia

Patients with blepharospasm may also manifest other types of craniocervical involvement including lower facial, masticatory, lingual, pharyngeal, laryngeal or cervical dystonia. With the passage of time, involvement of the lower facial and masticatory muscles becomes fairly common in patients with blepharospasm [30–32]. Involuntary lower facial and masticatory movements may include lip pursing, chewing, jaw thrusting, grimacing, jaw opening and jaw closing/clenching [15]. In some patients, the lower facial and jaw movements may be rhythmic or tremor-like. In addition, the involuntary lower facial and jaw movements seen in patients with blepharospasm may not result in sustained postures, and, as such, may not be compatible with the definition of dystonia. Instead, these involuntary movements are oftentimes described as dyskinesias, a poorly-defined term which encompasses several forms of involuntary movements (e.g., chorea, athetosis and myoclonus), each of which carries a more precise meaning.

Most of the time, dystonia in the craniocervical region begins focally. Over time, however, dystonia may spread to involve other muscles of the body. Most commonly, dystonia spreads to contiguous muscles. For example, when blepharospasm does spread, it typically spreads to the lower face and/or masticatory muscles [30–32]. Rarely, craniocervical dystonia may spread to more distant muscles in the arms and legs [30–32]. Although the probability of spread is highest within the first 3 years after dystonia onset, spread may occur a decade or more later [30,31]. In patients with blepharospasm, older age-of-onset, female gender and history of head trauma may increase the risk of spread [33]. Overall, patients with initial onset of dystonia in the eyelids (i.e., blepharospasm) have at least a 50% lifetime probability of spread [30–34].

Patients with craniocervical dystonia may report the presence of useful geste antagonistes or sensory tricks [35,36]. Touching the periorbital region and biting a toothpick are commonly employed tricks. Other tricks include touching the chin, lips or back of the head. Patients with

blepharospasm-plus subphenotypes many benefit from whistling, humming, singing, looking downwards or chewing gum.

Segmental craniocervical dystonia should be diagnosed and managed by a clinician with extensive experience in movement disorders. Occasionally, patients with segmental craniocervical dystonia are treated by general ophthalmologists and otorhinolaryngologists without adequate workups for secondary or neurodegenerative etiologies. For example, segmental craniocervical dystonia may be associated with one of the spinocerebellar ataxias [37] or a neurodegenerative disorder such as progressive supranuclear palsy [38]. Not infrequently, segmental craniocervical dystonia is caused by medications which block dopamine receptors in the brain such as antiemetics (e.g., metoclopramide) or antipsychotics (e.g., haloperidol) [39]. Oftentimes, a brain MRI scan and blood tests are ordered to exclude the possibility of a heredodegenerative or secondary cause such as Wilson disease [40] or an ischemic stroke [41], respectively. The etiological classification and differential diagnosis of craniocervical dystonia is presented in Table 1. Ordinarily, all diagnostic studies will prove to be normal and the affected subject will be diagnosed with primary dystonia.

The term “primary dystonia” does not preclude a distinct genetic etiology or genetic contributions. Blepharospasm and segmental craniocervical dystonia clearly have a hereditary component [25,34,42–47]. In particular, some studies have reported that over 10% of patients with blepharospasm and other forms of craniocervical dystonia have at least one first- or second-degree relative with dystonia [25,34,45–47]. Moreover, subjects with the classic DYT1 ΔGAG deletion may rarely present with craniocervical dystonia [48–50] and the majority of patients with mutations in *THAP1* (DYT6) exhibit some form of craniocervical dystonia [51].

Blepharospasm and segmental craniocervical dystonia are significantly more common in women with a male:female ratio of roughly 1:2 [25,30–34,42,49]. The average age of onset for blepharospasm is around 55 years whereas the average age of onset for jaw dystonia is only a couple of years earlier [25,30–34,46,49]. In comparison, cervical and focal hand/arm dystonia begin approximately one and two decades earlier, respectively [30–34,46]. Of note, these are only averages, and, occasionally, patients may have disease onset in their twenties or seventies. Patients with blepharospasm or blepharospasm-plus subphenotypes of craniocervical dystonia have a small (<10%) chance of spontaneous remission [52].

Prevalence estimates for blepharospasm and segmental dystonia vary widely [53,54]. True differences in prevalence can be ascribed to the effects of race and ethnicity. Diverse ascertainment methods, diagnostic criteria and sample sizes have contributed to false variability in crude prevalence estimates. Prevalence measures are especially problematic in the context of blepharospasm-plus subphenotypes. Record-linkage studies based on the review of charts from several medical specialities could generate unreliable estimates for segmental craniocervical dystonia as a consequence of treatment focus on particular anatomical regions (e.g., eyes, jaw, neck). In addition, all forms of segmental dystonia are lumped together in most published studies [53,54]. Crude prevalence estimates for blepharospasm range from 16 to 133 per million [55]. Overall prevalence for all anatomical patterns of segmental dystonia in eight European countries has been estimated at 32 per million [53].

5. Etiopathogenesis and Pathophysiology of Segmental Craniocervical Dystonia

Given that the anatomical distributions of DYT1, DYT3 and DYT6 dystonia often incorporate parts of the craniocervical musculature, molecular, cellular and systems studies of torsinA, TAF1 and THAP1, respectively, are pertinent to understanding the molecular and cellular biology of segmental craniocervical dystonia [48,51,56]. Gene expression profiles in rats and

functional neuroimaging in humans have provided evidence that DYT1 dystonia is a neurodevelopmental network disorder [57,58]. At the cellular level, torsinA appears to mediate interactions between the nuclear envelope and cytoskeleton [59]. As such, mutant torsinA could indirectly perturb movement of transcription factors and transcripts in and out of the nucleus, respectively. Transcriptional dysregulation may be a common underlying pathophysiological mechanism in many forms of primary dystonia given that TAF1 and THAP1 are transcription factors expressed in the central nervous system.

The sporadic occurrence of most primary focal dystonias and incomplete penetrance and variable expressivity of several hereditary dystonias indicates that environmental factors may play an important role in the pathophysiology of this movement disorder. Maladaptive sensorimotor plasticity to peripheral sensorimotor perturbations may be implicated in all focal dystonias [60]. For example, cases of blepharospasm often begin with symptoms of ocular irritation due to conditions such as dry eye or blepharitis [61]. These patients typically exhibit increased blink frequency (an adaptive response) prior to the development of full-blown blepharospasm (a maladaptive response). In similar fashion, most patients with primary oromandibular dystonia have experienced blunt facial trauma or dental procedures prior to the onset of their movement disorder [62] and, in some series, more than 20% of patients with cervical dystonia reported substantial prior cervical trauma [63]. Based on this clinical information, a reasonable case has been made that dystonia is a disorder of abnormal sensorimotor integration [64].

Relatively few hypothesis-driven pathophysiological studies have specifically focused on segmental craniocervical dystonia or included subjects with blepharospasm-plus phenotypes [65–67]. Nevertheless, investigations of blepharospasm, masticatory and cervical dystonia are clearly pertinent to our understanding of segmental craniocervical dystonia since the focal dystonias share genetic and physiological underpinnings. Physiological studies have demonstrated abnormal excitability of brainstem interneuronal pathways and sensorimotor areas of cerebral cortex in patients with focal dystonias of the craniocervical region [65–68]. Brainstem interneuronal pathways have been studied with the blink reflex and masseter inhibitory reflex. The recovery cycles of the R2 component of the blink reflex and the SP2 component of the masserter inhibitory reflex are enhanced in patients with craniocervical dystonia. Even subjects with isolated cervical dystonia show enhanced R2 recovery, indicating that abnormal interneuronal excitability extends beyond regions of clinical involvement. Dresel and colleagues [68] used silent event-related functional MRI to compare three experimental groups: isolated blepharospasm, blepharospasm plus oromandibular dystonia and controls. Both dystonia groups showed increased activation of somatosensory and caudal supplementary motor cortices during a whistling task. Cortical silent period shortening in blepharospasm and blepharospasm plus oromandibular dystonia experimental groups is consistent with hypoexcitability of cortical inhibitory neurons in cranial dystonia.

6. Treatment of Segmental Craniocervical Dystonia

Segmental craniocervical dystonia is commonly treated with injection of botulinum toxins. Successful treatment of dystonia with injection of botulinum toxins is both art and science. Results depend on accurate targeting of affected muscles with an appropriate amount of toxin. Electromyographic guidance is frequently used when injecting masticatory, laryngeal and cervical muscles [69–71]. Unfortunately, many patients with segmental craniocervical dystonia are forced to see two or more physicians for their botulinum toxin injections. For example, in the worse case scenario, a single patient may see an ophthalmologist for blepharospasm, an otorhinolaryngologist for spasmodic dysphonia and a neurologist for cervical dystonia. In patients with blepharospasm, attention to concomitant masticatory and lower facial involvement is often highly variable and dictated by the skill and experience of

the treating physician along with patient expectations. Injections of botulinum toxin into the perioral, masticatory and platysma musculature in patients with coexisting blepharospasm can provide significant subjective clinical benefit with a low risk for side effects [72–74].

Botulinum toxin type A is approved by the United States Food and Drug Administration (FDA) for the treatment of blepharospasm and cervical dystonia and botulinum toxin type B is FDA-approved for cervical dystonia. Injections into lower facial, masticatory, laryngeal and lingual musculature are off-label applications of botulinum toxin in the United States. In comparison with isolated blepharospasm, excellent subjective and objective improvement with injections of botulinum toxin is less common in blepharospasm-plus subphenotypes [75–78]. For instance, Van den Bergh and colleagues [75] reported dramatic improvement in patients with blepharospasm (79%) but only moderate improvement in patients with "Meige's syndrome (53%)." On average, patients with blepharospasm-plus subphenotypes may have more severe blepharospasm than individuals with isolated blepharospasm. In addition, blepharospasm may be accompanied by either jaw-opening or jaw-closing dystonia [11,35]. In comparison to jaw-closing dystonia, jaw-opening dystonia can be difficult to treat with injections of botulinum toxin [37,78].

An extensive list of oral medications has been used to treat segmental craniocervical dystonia; however, there are no multi-center, placebo-controlled, double-blind studies to reference in this regard. A single-center, double-blind crossover study showed no benefit of sodium valproate in "Meige syndrome [79]." Similarly, a single-center, randomized, placebo-controlled, crossover trial showed that super blue-green algae was not an effective treatment for patients with blepharospasm or "Meige syndrome [80]." Recent publications described the benefits of zolpidem and levetiracetam in isolated cases of "Meige syndrome [13,81,82]." Unfortunately, the magnitude of improvement typically obtained with commonly used drugs such as the anticholinergics (e.g., trihexyphenidyl and benztropine), benzodiazepines (e.g., clonazepam and lorazepam), baclofen, and tetrabenazine is often modest, at best [10,83]. Although side-effects are often problematic, anticholinergics have proven value in segmental craniocervical dystonia [84–87]. In many patients, low-dose clonazepam is also efficacious [88,89]. Moreover, the side effects associated with benzodiazepines are usually more tolerable than those due to anticholinergics. Many of the medications that have been used to treat blepharospasm and other craniocervical dystonias are listed in Table 1 [10,81,84,90–97].

In recent years, deep brain stimulation (DBS) has garnered increasing attention as a therapeutic choice in patients with intractable dystonia. Clearly, DBS is an important therapeutic option in patients with DYT1 generalized dystonia [98]. Currently available data suggests that DBS is also an effective treatment for many, but not all patients with segmental craniocervical dystonia [99–102]. Most commonly, the internal segment of the globus pallidus (GPi) has been targeted in patients with primary adult-onset segmental craniocervical dystonia [98]. Bilateral stimulation of the GPi may be required for control of axial symptoms [103]. Unlike the situation for Parkinson disease and essential tremor, the benefits associated with DBS for dystonia often develop gradually over several months [104]. Interestingly, long-term GPi DBS may correct those neural networks abnormalities responsible for the appearance of dystonia such that continued stimulation may ultimately prove unnecessary [105].

DBS is associated with a small risk of stroke, infection and the development of new neurological signs including but not limited to hemiparesis, visual field deficits, dysarthria and dysphagia. In some patients with dystonia, stimulation of the GPi can produce mild worsening of motor function in previously non-dystonic body regions [101]. Based on these considerations, DBS should be seriously considered in patients with segmental craniocervical dystonia only if other treatment options, administered by skilled and experienced neurologists, are ineffective.

7. Summary

The eponymic terms Meige syndrome and Brueghel syndrome are imprecise, have been used inconsistently for decades, and should be avoided in the classification of craniocervical dystonia. The term segmental craniocervical dystonia faithfully incorporates various blepharospasm-plus subphenotypes which appear to share common genetic and physiological underpinnings. Confident identification of genetic and environmental risk factors for segmental craniocervical dystonia may permit the developmental of better treatments which target pathways of cellular dysfunction within the central nervous system.

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References

1. JAMA and Archives Journals. AMA manual of style: a guide for authors and editors. Vol. 10. New York: Oxford University Press; 2007.
2. McKusick VA. On the naming of clinical disorders, with particular reference to eponyms. Medicine (Baltimore) 1998;77:1–2. [PubMed: 9465859]
3. Wood, HC. Nervous diseases and their diagnosis: a treatise upon the phenomena produced by diseases of the nervous system. Philadelphia: JB Lippincott; 1937. p. 1887
4. Lurie S. Meigs' syndrome: the history of the eponym. Eur J Obstet Gynecol Reprod Biol 2000;92:199–204. [PubMed: 10996681]
5. Meige H. Les convulsions de la face. Ue forme clinique de convulsion faciale bilaterale et mediane. Rev Neurol (Paris) 1910;21:437–43.
6. Paulson GW. Meige's syndrome. Dyskinesia of the eyelids and facial muscles. Geriatrics 1972;8:69–73. [PubMed: 5046545]
7. Marsden CD. Blepharospasm-oromandibular dystonia syndrome (Brueghel's syndrome). J Neurol Neurosurg Psychiatry 1976;39:1204–9. [PubMed: 1011031]
8. Roberts-Jones, P.; Roberts-Jones, F. Pieter Breugel. New York: Harry N. Adams; 2002.
9. Gilbert GJ. Brueghel syndrome: its distinction from Meige syndrome. Neurology 1996;46:1767–9. [PubMed: 8649591]
10. Jankovic J, Ford J. Blepharospasm and orofacial-cervical dystonia: clinical and pharmacological findings in 100 patients. Ann Neurol 1983;13:402–11. [PubMed: 6838174]
11. Blitzer A, Brin MF, Greene PE, Fahn S. Botulinum toxin injection for the treatment of oromandibular dystonia. Ann Otol Rhinol Laryngol 1989;98:93–7. [PubMed: 2916831]
12. Kalita J, Misra UK. Markedly severe dystonia in Japanese encephalitis. Mov Disord 2000;15:1168–72. [PubMed: 11104201]
13. Zesiewicz TA, Louis ED, Sullivan KL, Menkin M, Dunne PB, Hauser RA. Substantial improvement in a Meige's syndrome patient with levetiracetam treatment. Mov Disord 2004;19:1518–21. [PubMed: 15390069]
14. Sabesan T. Meige syndrome: a rare form of cranial dystonia that was treated successfully with botulinum toxin. Br J Oral Maxillofac Surg 2008;46:588–90. [PubMed: 18346825]
15. Kraft SP, Lang AE. Cranial dystonia, blepharospasm and hemifacial spasm: clinical features and treatment, including the use of botulinum toxin. CMAJ 1988;139:837–44. [PubMed: 3052771]
16. Fahn, S.; Marsden, CD.; Calne, DB. Classification and investigation of dystonia. London: Butterworths; 1987. p. 332-58.
17. Williams, PL.; Warwick, R. Gray's Anatomy. Vol. 36. Philadelphia: W.B. Saunders; 1980.
18. Csala B, Deuschl G. Craniocervical dystonia. Pragmatic general concept or nosologic entity? Nervenarzt 1994;65:75–94. [PubMed: 8164772]

19. Schramm A, Naumann M, Reiners K, Classen J. Task-specific craniocervical dystonia. Mov Disord 2008;23:1041–3. [PubMed: 18381644]
20. Cersósimo MG, Juri S, Suárez de Chandler S, Clerici R, Micheli FE. Swallowing disorders in patients with blepharospasm. Medicina (B Aires) 2005;65:117–20. [PubMed: 16075804]
21. Jankovic, Tinter R. Botulinum toxin type A in the management of oromandibular dystonia and bruxism. In: Brin, MF.; Hallett, M.; Jankovic, J., editors. Scientific and Therapeutic Aspects of Botulinum Toxin. Philadelphia: Lippincott Williams & Wilkins; 2002. p. 343-50.
22. Burke RE, Fahn S, Marsden CD, Bressman SB, Moskowitz C, Friedman J. Validity and reliability of a rating scale for the primary torsion dystonias. Neurology 1985;35:73–7. [PubMed: 3966004]
23. Comella CL, Leurgans S, Wuu J, Stebbins GT, Chmura T. Dystonia Study Group. Rating scales for dystonia: a multicenter assessment. Mov Disord 2003;18:303–12. [PubMed: 12621634]
24. Jankovic J, Orman J. Botulinum A toxin for cranial-cervical dystonia: a double-blind, placebo-controlled study. Neurology 1987;37:616–23. [PubMed: 3561773]
25. Grandas F, Elston J, Quinn N, Marsden CD. Blepharospasm: a review of 264 patients. J Neurol Neurosurg Psychiatry 1988;51:767–72. [PubMed: 3404184]
26. Hirota N, Hirota M, Mezaki T. Dystonic frowning without blepharospasm. Parkinsonism Relat Disord 2008;14:579–80. [PubMed: 18316230]
27. Braun N, Abd A, Baer J, Blitzer A, Stewart C, Brin M. Dyspnea in dystonia. A functional evaluation Chest 1995;107:1309–16.
28. Lagueny A, Burbaud P, Le Masson G, Bergouignan FX, Ferrer X, Julien J. Involvement of respiratory muscles in adult-onset dystonia: a clinical and electrophysiological study. Mov Disord 1995;10:708–13. [PubMed: 8749989]
29. LaBlance GR, Rutherford DR. Respiratory dynamics and speech intelligibility in speakers with generalized dystonia. J Commun Disord 1991;24:141–56. [PubMed: 2066472]
30. Weiss EM, Hershey T, Karimi M, Racette B, Tabbal SD, Mink JW, et al. Relative risk of spread of symptoms among the focal onset primary dystonias. Mov Disord 2006;21:1175–81. [PubMed: 16673404]
31. Abbruzzese G, Berardelli A, Girlanda P, Marchese R, Martino D, Morgante F, et al. Long-term assessment of the risk of spread in primary late-onset focal dystonia. J Neurol Neurosurg Psychiatry 2008;79:392–6. [PubMed: 17635969]
32. Svetel M, Pekmezović T, Jović J, Ivanović N, Dragasević N, Marić J, et al. Spread of primary dystonia in relation to initially affected region. J Neurol 2007;254:879–83. [PubMed: 17401742]
33. Defazio G, Berardelli A, Abbruzzese G, Coviello V, Carella F, De Berardinis MT, et al. Risk factors for spread of primary adult onset blepharospasm: a multicentre investigation of the Italian movement disorders study group. J Neurol Neurosurg Psychiatry 1999;67:613–9. [PubMed: 10519867]
34. Defazio G, Berardelli A, Hallett M. Do primary adult-onset focal dystonias share aetiological factors? Brain 2007;130:1183–93. [PubMed: 17242025]
35. Singer C, Papapetropoulos S. A comparison of jaw-closing and jaw-opening idiopathic oromandibular dystonia. Parkinsonism Relat Disord 2006;12:115–18. [PubMed: 16271495]
36. Lo SE, Gelb M, Frucht SJ. Geste antagonistes in idiopathic lower cranial dystonia. Mov Disord 2007;22:1012–17. [PubMed: 17575581]
37. Manto MU. The wide spectrum of spinocerebellar ataxias (SCAs). Cerebellum 2005;4:2–6. [PubMed: 15895552]
38. Barclay CL, Lang AE. Dystonia in progressive supranuclear palsy. J Neurol Neurosurg Psychiatry 1997;62:352–6. [PubMed: 9120447]
39. Ananth J, Edelmuth E, Dargan B. Meige's syndrome associated with neuroleptic treatment. Am J Psychiatry 1988;145:513–15. [PubMed: 2894781]
40. Machado A, Chien HF, Deguti MM, Cançado E, Azevedo RS, Scaff M, et al. Neurological manifestations in Wilson's disease: Report of 119 cases. Mov Disord 2006;21:2192–6. [PubMed: 17078070]
41. O'Rourke K, O'Riordan S, Gallagher J, Hutchinson M. Paroxysmal torticollis and blepharospasm following bilateral cerebellar infarction. J Neurol 2006;253:1644–5. [PubMed: 17219037]

42. Defazio G, Livrea P, Guanti G, Lepore V, Ferrari E. Genetic contribution to idiopathic adult-onset blepharospasm and cranial-cervical dystonia. Eur Neurol 1993;33:345–50. [PubMed: 8243508]
43. Nutt JG, Hammerstad JP. Blepharospasm and oromandibular dystonia (Meige's syndrome) in sisters. Ann Neurol 1981;9:189–91. [PubMed: 7235635]
44. Jankovic J, Nutt JG. Blepharospasm and cranial-cervical dystonia (Meige's syndrome): familial occurrence. Adv Neurol 1988;49:117–23. [PubMed: 3344632]
45. Chan J, Brin MF, Fahn S. Idiopathic cervical dystonia: clinical characteristics. Mov Disord 1991;6:119–26. [PubMed: 2057004]
46. Maniak S, Sieberer M, Hagenah J, Klein C, Vieregge P. Focal and segmental primary dystonia in north-western Germany--a clinico-genetic study. Acta Neurol Scand 2003;107:228–32. [PubMed: 12614318]
47. Defazio G, Martino D, Aniello MS, Masi G, Abbruzzese G, Lamberti S, et al. A family study on primary blepharospasm. J Neurol Neurosurg Psychiatry 2006;77:252–54. [PubMed: 16421132]
48. Bressman SB, Sabatti C, Raymond D, de Leon D, Klein C, Kramer PL, et al. The DYT1 phenotype and guidelines for diagnostic testing. Neurology 2000;54:1746–52. [PubMed: 10802779]
49. O'Riordan S, Raymond D, Lynch T, Saunders-Pullman R, Bressman SB, Daly L, et al. Age at onset as a factor in determining the phenotype of primary torsion dystonia. Neurology 2004;63:1423–6. [PubMed: 15505159]
50. Xiao J, Bastian RW, Perlmutter JS, Racette BA, Tabbal SD, Karimi M, et al. (2009) High-throughput mutational analysis of *TOR1A* in primary dystonia. BMC Med Genet 2009;10:24. [PubMed: 19284587]
51. Bressman SB, Raymond D, Fuchs T, Heiman GA, Ozelius LJ, Saunders-Pullman R. Mutations in THAP1 (DYT6) in early-onset dystonia: a genetic screening study. Lancet Neurol. 2009 Apr 1;[Epub ahead of print]
52. Castelbuono A, Miller NR. Spontaneous remission in patients with essential blepharospasm and Meige syndrome. Am J Ophthalmol 1998;126:432–5. [PubMed: 9744377]
53. Epidemiological Study of Dystonia in Europe (ESDE) Collaborative Group. A prevalence study of primary dystonia in eight European countries. J Neurol 2000;247:787–92. [PubMed: 11127535]
54. Defazio G, Abbruzzese G, Livrea P, Berardelli A. Epidemiology of primary dystonia. Lancet Neurol 2004;3:673–8. [PubMed: 15488460]
55. Defazio G, Livrea P. Epidemiology of primary blepharospasm. Mov Disord 2002;17:7–12. [PubMed: 11835433]
56. Makino S, Kaji R, Ando S, Tomizawa M, Yasuno K, Goto S, Matsumoto S, et al. Reduced neuron-specific expression of the TAF1 gene is associated with X-linked dystonia-parkinsonism. Am J Hum Genet 2007;80:393–406. [PubMed: 17273961]
57. Xiao J, Gong S, Zhao Y, LeDoux MS. Developmental expression of torsinA transcript and protein. Dev Brain Res 2004;152:47–60. [PubMed: 15283994]
58. Carbon M, Eidelberg D. Abnormal structure-function relationships in hereditary dystonia. Neuroscience. 2009 Jan 1;
59. Vander Heyden AB, Naismith TV, Snapp EL, Hodzic D, Hanson PI. LULL1 Retargets TorsinA to the Nuclear Envelope Revealing an Activity that Is Impaired by the DYT1 Dystonia Mutation. Mol Biol Cell. 2009 Apr 1;[Epub ahead of print]
60. Quartarone A, Morgante F, Sant'angelo A, Rizzo V, Bagnato S, Terranova C, et al. Abnormal plasticity of sensorimotor circuits extends beyond the affected body part in focal dystonia. J Neurol Neurosurg Psychiatry 2008;79:985–90. [PubMed: 17634214]
61. Martino D, Defazio G, Alessio G, Abbruzzese G, Girlanda P, Tinazzi M, et al. Relationship between eye symptoms and blepharospasm: a multicenter case-control study. Mov Disord 2005;20:1564–70. [PubMed: 16092106]
62. Sankhla C, Lai EC, Jankovic J. Peripherally induced oromandibular dystonia. J Neurol Neurosurg Psychiatry 1998;65:722–8. [PubMed: 9810945]
63. Duane DD. Cervical dystonia. Mov Disord 2002;17:222–3. [PubMed: 11835474]
64. Kanovský P. Dystonia: a disorder of motor programming or motor execution? Mov Disord 2002;17:1143–7. [PubMed: 12465050]

65. Berardelli A, Rothwell JC, Day BL, Marsden CD. Pathophysiology of blepharospasm and oromandibular dystonia. Brain 1985;108:593–608. [PubMed: 4041776]
66. Pauletti G, Berardelli A, Cruccu G, Agostino R, Manfredi M. Blink reflex and the masseter inhibitory reflex in patients with dystonia. Mov Disord 1993;8:495–500. [PubMed: 8232360]
67. Currà A, Romaniello A, Berardelli A, Cruccu G, Manfredi M. Shortened cortical silent period in facial muscles of patients with cranial dystonia. Neurology 2000;54:130–5. [PubMed: 10636138]
68. Dresel C, Haslinger B, Castrop F, Wohlschlaeger AM, Ceballos-Baumann AO. Silent event-related fMRI reveals deficient motor and enhanced somatosensory activation in orofacial dystonia. Brain 2006;129:36–46. [PubMed: 16280353]
69. Comella CL, Buchman AS, Tanner CM, Brown-Toms NC, Goetz CG. Botulinum toxin injection for spasmodic torticollis: increased magnitude of benefit with electromyographic assistance. Neurology 1992;42:878–82. [PubMed: 1565246]
70. Brans JW, de Boer IP, Aramideh M, Ongerboer de Visser BW, Speelman JD. Botulinum toxin in cervical dystonia: low dosage with electromyographic guidance. J Neurol 1995;242:529–34. [PubMed: 8530982]
71. Blitzer A, Brin MF, Stewart CF. Botulinum toxin management of spasmodic dysphonia (laryngeal dystonia): a 12-year experience in more than 900 patients. Laryngoscope 1998;108:1435–41. [PubMed: 9778279]
72. Blitzer A, Binder WJ, Aviv JE, Keen MS, Brin MF. The management of hyperfunctional facial lines with botulinum toxin. A collaborative study of 210 injection sites in 162 patients. Arch Otolaryngol Head Neck Surg 1997;123:389–92. [PubMed: 9109785]
73. Laskawi R, Rohrbach S, Rödel R. Surgical and nonsurgical treatment options in patients with movement disorders of the platysma. J Oral Maxillofac Surg 2002;60:157–62. [PubMed: 11815912]
74. Møller E, Werdelin LM, Bakke M, Dalager T, Prytz S, Regeur L. Treatment of perioral dystonia with botulinum toxin in 4 cases of Meige's syndrome. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2003;96:544–9. [PubMed: 14600688]
75. Van den Bergh P, Francart J, Mourin S, Kollmann P, Laterre EC. Five-year experience in the treatment of focal movement disorders with low-dose Dysport botulinum toxin. Muscle Nerve 1995;18:720–9. [PubMed: 7783762]
76. Mauriello JA Jr, Dhillon S, Leone T, Pakeman B, Mostafavi R, Yepez MC. Treatment selections of 239 patients with blepharospasm and Meige syndrome over 11 years. Br J Ophthalmol 1996;80:1073–6. [PubMed: 9059273]
77. Poungvarin N, Devahastin V, Viriyavejakul A. Treatment of various movement disorders with botulinum A toxin injection: an experience of 900 patients. J Med Assoc Thai 1995;78:281–8. [PubMed: 7561552]
78. Bhidayasiri R, Cardoso F, Truong DD. Botulinum toxin in blepharospasm and oromandibular dystonia: comparing different botulinum toxin preparations. Eur J Neurol 2006;(Suppl 1):21–9. [PubMed: 16417594]
79. Snoek JW, van Weerden TW, Teelken AW, van den Burg W, Lakke JP. Meige syndrome: double-blind crossover study of sodium valproate. J Neurol Neurosurg Psychiatry 1987;50:1522–5. [PubMed: 3121795]
80. Vitale S, Miller NR, Mejico LJ, Perry JD, Medura M, Freitag SK, et al. A randomized, placebo-controlled, crossover clinical trial of super blue-green algae in patients with essential blepharospasm or Meige syndrome. Am J Ophthalmol 2004;138:18–32. [PubMed: 15234278]
81. Yardimci N, Karatas M, Kilinc M, Benli S. Levetiracetam in Meige's syndrome. Acta Neurol Scand 2006;114:63–6. [PubMed: 16774630]
82. An JY, Kim JS, Kim YI, Lee KS. Successful treatment of the Meige syndrome with oral zolpidem monotherapy. Mov Disord 2008;23:1619–21. [PubMed: 18581473]
83. Jankovic J. Treatment of hyperkinetic movement disorders with tetrabenazine: a double-blind crossover study. Ann Neurol 1982;11:41–7. [PubMed: 6460467]
84. Tanner CM, Glantz RH, Klawans HL. Meige disease: acute and chronic cholinergic effects. Neurology 1982;32:783–5. [PubMed: 7201118]
85. Duvoisin RC. Meige syndrome: relief on high-dose anticholinergic therapy. Clin Neuropharmacol 1983;6:63–6. [PubMed: 6850651]

86. Nutt JG, Hammerstad JP, Carter JH, deGarmo P. Meige syndrome: treatment with trihexyphenidyl. Adv Neurol 1983;37:201–5. [PubMed: 6344588]
87. Klawans HL, Tanner CM. Cholinergic pharmacology of blepharospasm with oromandibular dystonia (Meige's syndrome). Adv Neurol 1988;49:443–50. [PubMed: 3278551]
88. Hípola D, Mateo D, Giménez-Roldán S. Meige's syndrome: acute and chronic responses to clonazepan and anticholinergics. Eur Neurol 1984;23(6):474–8. [PubMed: 6510447]
89. Ransmayr G, Kleedorfer B, Dierckx RA, Poewe W, Kemmler GW, Gerstenbrand F. Pharmacological study in Meige's syndrome with predominant blepharospasm. Clin Neuropharmacol 1988;11:68–76. [PubMed: 3280128]
90. Greene P. Baclofen in the treatment of dystonia [Review]. Clin Neuropharmacol 1992;15:276–88. [PubMed: 1516073]
91. Schneider SA, Mohire MD, Trender-Gerhard I, Asmus F, Sweeney M, Davis M, et al. Familial dopa-responsive cervical dystonia. Neurology 2006;66:599–601. [PubMed: 16505323]
92. Newman RP, LeWitt PA, Shults C, Bruno G, Foster NL, Chase TN, et al. Dystonia: treatment with bromocriptine. Clin Neuropharmacol 1985;8:328–33. [PubMed: 3907823]
93. Bhatia KP, Quinn NP, Marsden CD. Clinical features and natural history of axial predominant adult onset primary dystonia. J Neurol Neurosurg Psychiatry 1997;63:788–91. [PubMed: 9416818]
94. Evidente VG. Zolpidem improves dystonia in "Lubag" or X-linked dystonia-parkinsonism syndrome. Neurology 2002;58:662–3. [PubMed: 11865155]
95. Hanagasi HA, Bilgic B, Gurvit H, Emre M. Clozapine treatment in oromandibular dystonia. Clin Neuropharmacol 2004;27:84–6. [PubMed: 15252269]
96. Fasanella RM, Aghajanian GK. Treatment of benign essential blepharospasm with cyproheptadine. N Engl J Med 1990;322:778. [PubMed: 2308610]
97. Ohara S, Tsuyuzaki J, Hayashi R. Mexiletine in the treatment of blepharospasm: experience with the first three patients. Mov Disord 1999;14:173–5. [PubMed: 9918369]
98. Alterman RL, Tagliati M. Deep brain stimulation for torsion dystonia in children. Childs Nerv Syst 2007;23:1033–40. [PubMed: 17551738]
99. Foote KD, Sanchez JC, Okun MS. Staged deep brain stimulation for refractory craniofacial dystonia with blepharospasm: case report and physiology. Neurosurgery 2005;56:E415. [PubMed: 15670394]
100. Houser M, Waltz T. Meige syndrome and pallidal deep brain stimulation. Mov Disord 2005 Sep;20 (9):1203–5. [PubMed: 15954126]
101. Ostrem JL, Marks WJ Jr, Volz MM, Heath SL, Starr PA. Pallidal deep brain stimulation in patients with cranial-cervical dystonia (Meige syndrome). Mov Disord 2007;22:1885–91. [PubMed: 17618522]
102. Loher TJ, Capelle HH, Kaelin-Lang A, Weber S, Weigel R, Burgunder JM, et al. Deep brain stimulation for dystonia: outcome at long-term follow-up. J Neurol 2008;255:881–4. [PubMed: 18338193]
103. Blomstedt P, Tisch S, Hariz MI. Pallidal deep brain stimulation in the treatment of Meige syndrome. Acta Neurol Scand 2008;118:198–202. [PubMed: 18336624]
104. Bereznai B, Steude U, Seelos K, Bötzel K. Chronic high-frequency globus pallidus internus stimulation in different types of dystonia: a clinical, video, and MRI report of six patients presenting with segmental, cervical, and generalized dystonia. Mov Disord 2002;17:138–44. [PubMed: 11835451]
105. Hebb MO, Chiasson P, Lang AE, Brownstone RM, Mendez I. Sustained relief of dystonia following cessation of deep brain stimulation. Mov Disord 2007;22:1958–62. [PubMed: 17674409]

Table 1

Etiological Classification and Diagnosis of Craniocervical Dystonia

Primary craniocervical dystonia: syndromes in which dystonia is the sole phenotypic manifestation with the exception that tremor can be present as well
Secondary craniocervical dystonia: due to structural lesions and/or neural insults
vascular (e.g., ischemic stroke, hemorrhagic stroke, cerebral palsy)
infectious (e.g., human immunodeficiency virus, arboviruses)
toxins (e.g., manganese, carbon disulfide)
medications (e.g., neuroleptics, antiemetics, anticonvulsants)
autoimmune/inflammatory (e.g., multiple sclerosis, lupus erythematosus, Behcet disease)
metabolic (e.g., hypoxia, extra-pontine myelinolysis)
neoplasms (e.g., glioblastoma, metastatic tumor, meningioma)
Craniocervical dystonia-plus: disorders distinct from primary dystonia and heredodegenerative diseases with dystonia
dopa-responsive dystonia (DYT5)
myoclonus-dystonia syndrome (DYT11)
Heredodegenerative diseases with craniocervical dystonia: typically associated with pathological changes in brain tissue and may be hereditary (e.g., progressive supranuclear palsy, Parkinson disease, multiple system atrophy, corticobasal ganglionic degeneration, spinocerebellar ataxias, Huntington disease, Lubag [DYT3], rapid-onset dystonia parkinsonism [DYT12], Wilson disease, Lesch-Nyhan syndrome, pantothenate kinase-associated neurodegeneration, mitochondrial encephalopathies, Niemann-Pick type C, neuronal ceroid lipofuscinosis)
Psychogenic craniocervical dystonia: dystonia primarily due to psychological factors

Table 2

Oral Medications for Blepharospasm and Other Cranial Dystonias

Class	Names	Mechanism(s) of action	Most frequent side effects
Anticholinergic [84]	trihexyphenidyl benztropine	block acetylcholine receptors	dry mouth, constipation, blurred vision, mild memory impairment
Benzodiazepine [63]	clonazepam lorazepam diazepam	potentiate the effects of GABA on $GABA_A$ receptors	drowsiness, disequilibrium
$GABA_B$ receptor agonist [90]	baclofen	stimulates $GABA_B$ receptors	drowsiness, disequilibrium, weakness
Dopamine precursor [91]	levodopa	converted to dopamine	nausea
Dopamine receptor agonist [92]	bromocriptine	stimulates D_2 dopamine receptors, 5-HT_2 antagonist	nausea, lightheadness, drowsiness
Neuroleptic [93]	pimozide haloperidol	blocks dopamine receptors ($D_2 > D_3 > D_1$ & D_4)	tardive dyskinesias**
Monoamine depleter [93]	tetrabenazine	inhibits monoamine transporters in the brain	depression, drowsiness, Parkinsonism
Anticonvulsant [81]	levetiracetam	binds to the synaptic vesicle protein SV2A	irritability, headaches
Imidazopyridine [94]	zolpidem	binds to the benzodiazepine receptor 1	drowsiness, dizziness, headache
Atypical antipsychotic [95]	clozapine	blocks dopamine receptors ($D_4 \gg D_1$, D_2, D_3, & D_5), partial 5-HT_{1A} agonist, cholinergic and histaminergic antagonist	constipation, sedation, agranulocytosis
Serotonin receptor antagonist [96]	cyproheptadine	5-HT_2 antagonist, antihistaminic	drowsiness, nausea
Antiarrhythmic agent [97]	mexiletine	inhibits inward sodium currents	nausea, dizziness, tremor

* None of these medications are FDA approved treatments for blepharospasm

** Tardive dyskinesias may be a permanent side effect