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Cervical Dystonia

Pathophysiology and Treatment Options

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Abstract

Dystonia is a syndrome of sustained involuntary muscle contractions, frequently causing twisting and repetitive movements or abnormal posturing. Cervical dystonia (CD) is a form of dystonia that involves neck muscles. However, CD is not the only cause of neck rotation. Torticollis may be caused by orthopaedic, musculofibrotic, infectious and other neurological conditions that affect the anatomy of the neck, and structural causes.

It is estimated that there are between 60 000 and 90 000 patients with CD in the US. The majority of the patients present with a combination of neck rotation (rotatory torticollis or rotatocollis), flexion (anterocollis), extension (retrocollis), head tilt (laterocollis) or a lateral or sagittal shift. Neck posturing may be either tonic, clonic or tremulous, and may result in permanent and fixed contractures.

Sensory tricks ('geste antagonistique') often temporarily ameliorate dystonic movements and postures. Commonly used sensory tricks by patients with CD include touching the chin, back of the head or top of the head.

Patients with CD are classified according to aetiology into two groups: primary CD (idiopathic – may be genetic or sporadic) or secondary CD (symptom-

atic). Patients with primary CD have no evidence by history, physical examination or laboratory studies (except primary dystonia gene) of any secondary cause for the dystonic symptoms. CD is a part of either generalised or focal dystonic syndrome which may have a genetic basis, with an identifiable genetic association. Secondary or symptomatic CD may be caused by central or peripheral trauma, exposure to dopamine receptor antagonists (tardive), neurodegenerative disease, and other conditions associated with abnormal functioning of the basal ganglia. In the majority of patients with CD, the aetiology is not identifiable and the disorder is often classified as primary.

Unless the aetiological investigation reveals a specific therapeutic intervention, therapy for CD is symptomatic. It includes supportive therapy and counselling, physical therapy, pharmacotherapy, chemodenervation [botulinum toxin (BTX), phenol, alcohol], and central and peripheral surgical therapy. The most widely used and accepted therapy for CD is local intramuscular injections of BTX-type A. Currently, both BTX type A and type B are commercially available, and type F has undergone testing. Pharmacotherapy, including anticholinergics, dopaminergic depleting and blocking agents, and other muscle relaxants can be used alone or in combination with other therapeutic interventions. Surgery is usually reserved for patients with CD in whom other forms of treatment have failed.

Dystonia is defined as a syndrome of sustained involuntary muscle contractions, frequently causing twisting or repetitive movements or abnormal postures.[1]

Dystonia can involve any voluntary muscle. Because the movements and resulting postures are often unusual and the condition is rare, it is one of the most frequently misdiagnosed neurological conditions.[2] In most patients, torticollis is a form of dystonia involving the neck muscles; hence it has been called ‘cervical dystonia’ (CD).

1. Epidemiology

CD is the most common form of focal dystonia presenting to a physician, but the incidence and prevalence of CD are only poorly known. One study suggests an incidence of 1.2 per 100 000 person-years.[3] The prevalence of all focal dystonias has been estimated to be 300 per million, 9 times the prevalence of generalised dystonia.[4] There have been a few epidemiological studies of the prevalence of CD. An estimate of 22 250 patients with CD in the US (assuming a US population of 250 million) is based on a medical record review at the Mayo Clinic.[4] The prevalence of CD in this study was 8.9 in 100 000. Similarly, the prevalence of primary CD was 6.1 cases in 100 000 people in the north of England.[5] This is probably an underestimate by a factor of 2 to 4 because this number represents only patients with focal dystonia, and we know from our large database that in approximately 50% of patients, cervical dystonia is part of segmental or multifocal dystonia.[6,7] In addition, at the time of the Mayo study,[4] many affected individuals did not come to medical attention; now that we have effective therapy [botulinum toxin (BTX) type A (BTX-A)] and support groups are better organised, more patients are coming to medical attention. We suspect that there are between 60 000 and 90 000 patients with CD in the US. This includes the large number of individuals with dystonic cerebral palsy, many with neck involvement.

Epidemiological studies have shown a female predominance for idiopathic CD with the ratio of men to women of 1 : 1.4 to 2.2.[3-10] The difference at age of onset of CD by sex was observed by the Epidemiologic Study of Dystonia in Europe

(ESDE) Collaborative Group.[10] The mean age of onset was 39.2 years for men and 42.9 for women. Other studies showed the peak of incidence to be in the fifth decade, with equal distribution of age at onset for both men and women.[6-9]

2. Classification

In general, dystonia is classified by (i) clinical symptomatology (i.e. distribution of signs), (ii) age at onset (childhood/young *vs* adulthood), and (iii) aetiology. Classification may be important because it can provide clues about prognosis and also an approach to management. When classified by distribution, focal dystonia involves one small group of muscles in one body part; segmental disease involves a contiguous group of muscles; and generalised dystonia is widespread. Generalised dystonia usually has an early onset, and focal dystonia is usually adult onset.

Most patients with CD have an adult onset, and therefore the classification by aetiology is the most relevant. Patients with CD are classified according to aetiology in two groups: primary CD (idiopathic – may be genetic or sporadic) and secondary CD (symptomatic). For a patient to have primary CD, there should be no evidence by history, physical examination or laboratory studies (except dystonia genetic studies) of any secondary cause for the dystonic symptoms. Therefore, there must be a normal perinatal and early developmental history, no history of neurological illness or exposure to drugs known to cause acquired dystonia (e.g. phenothiazines). There also must be normal intellectual, pyramidal, cerebellar and sensory examinations, and diagnostic studies.[11] Patients who have abnormalities noted above are classified as having symptomatic or secondary CD. Clinical phenomenology is often a clue as to aetiology.

3. Clinical Characteristics

We use the term 'cervical dystonia' because spasmodic torticollis implies rotation only, and in addition to rotatory torticollis (rotatocollis), we see patients with neck flexion (anterocollis), extension (retrocollis), head tilt (laterocollis), or a lateral or sagittal shift.[12] 66 to 80% of patients with CD present with a combination of these movements.[6,7] However, the adjectives 'spasmodic' or 'spastic' are misleading since there is no evidence that CD is a spastic disorder or caused by dysfunction of the pyramidal tracts. Furthermore, the movements are not always spasmodic but may be sustained. Patients present with postural changes that may be either tonic and fixed, or intermittent, and either clonic or tremulous.[13] Symptoms may change in nature and directional preponderance over time.[6] By convention, the direction of the rotation is defined by the chin, so 'right-turning torticollis' means that the chin is turning to the right.

The course of CD varies from one individual to another, and the symptoms of a particular patient may vary throughout the course of their illness. Reviews of patients referred to movement disorder centres show that about 10 to 20% of patients go into remission, with recurrence in nearly all within a few months or years. Remissions are often not complete or prolonged.[14,15] However, these studies are biased because patients with mild torticollis that remitted would have no reason to present to a movement disorder centre for treatment and would, therefore, not be included in the reviews cited above. Many patients who present with focal CD report a progression in severity of symptoms during the first 5 years and then symptoms appear to stabilise.[15] However, as we have continued to treat individual patients for almost two decades, we have noticed that some have progression of dystonia symptoms, including to other body parts.

Many patients have signs of dystonia involving other body segments at the time of presentation. Oromandibular dystonia, blepharospasm, writer's cramp and axial dystonia can be found in approximately 20% of patients with CD.[6,7] In another study, extracervical spread was documented in one-third of 72 patients initially diagnosed with CD who were followed for a mean of 7.7 years.[15]

Sensory tricks often ameliorate dystonic movements and postures, and this manoeuvre can be effective in different parts of the body. These sensory tricks are also known as a 'geste antagonistique'.

Patients with CD often find that gently touching the chin, back of head or top of head will relieve symptoms. The use of sensory tricks to keep the head in the body midline position was reported by 88.9% of patients in one series.[16] The physiology of sensory tricks remains unknown. In a recent study, 13 of 25 patients with idiopathic CD had markedly reduced electromyographic (EMG) activity (50% or more) even during arm movement, but before the arm touched the skin, while performing a sensory trick.[17] Some patients have been reported to have reduced dystonia while thinking about a sensory trick.[18]

Other factors have been reported to ameliorate or aggravate CD. Stress or self-consciousness were reported by 80% of the patients as aggravating factors.[16] Walking, fatigue and carrying objects worsened CD in more than 70% of patients. More than 40% of patients reported improvement of CD in the supine position, by relaxation, sleep and lying on the side, but these same factors aggravated CD in 16 to 25% of patients.

Pain is a major source of disability in two-thirds to three-quarters of patients with CD.[6,7,19,20] A higher prevalence of pain in CD than in other types of focal dystonia has been attributed to the larger muscle masses involved, stronger forces within muscles, higher numbers of pain receptors, and involvement of underlying arthritic skeletal structures. Pain severity was related to the intensity of dystonia and muscle spasms in some studies,[6] but not to the duration of CD and severity of motor dysfunction in others.[19] Pain was commonly described as tiring, radiating, tugging, aching and exhausting.[19] It has been estimated that two-thirds of patients require analgesics at some point of their illness.[9]

4. Pathogenesis

4.1 Genetics

Incomplete penetrance and clinical heterogeneity are the rule in inherited dystonia. In families with dystonia, various members may have generalised, segmental or focal dystonia, suggesting that those with milder manifestations are related to those with more generalised dystonia, that is, have the same gene abnormality. This clinical observation has been confirmed by genetic studies where the gene defect is known.[21] It is essential to obtain a complete family history from every patient who presents with any form of dystonia. It is not uncommon to discover that a patient who presents with focal dystonia has a relative similarly affected (approximately 10%) or affected with subtle signs of dystonia in another body region.[7,9] Symptoms of dystonia affecting another segment of the body or essential tremor are found in 26 to 52% of relatives.[7-9]

Genetic subtypes of dystonia have been identified in which the only identifiable cause is the locus of a presumed gene abnormality; the biochemical or pathophysiological abnormalities that are manifestations of these genetic abnormalities are being sought (table I).

Childhood-onset dystonia is more common in the Ashkenazi Jewish population, and the *DYT1* gene mutation, initially thought to be different in the Jewish and non-Jewish population with a founder effect in the Jews,[61] was ultimately found to be the identical mutation in both ethnic groups, encoding a 332 amino acid protein, torsinA. This mutation, a GAG deletion with consequent loss of 1 glutamic acid residue near the C terminus of torsinA,[23] is responsible for the majority of idiopathic childhood-onset classical limb-onset dystonia, independent of ethnic background. In addition, most 'sporadic' occurrences of childhood-onset Ashkenazi Jewish dystonia are inherited and due to the same mutation of *DYT1* that underlies familial dystonia.[62] The torsinA protein has a distant homology to the heat shock superfamily of proteins; the deletion is in a putative adenosine triphosphate (ATP)-binding region, and presumably causes a loss of or change in function. In the central nervous system, torsinA is distributed widely in substantia nigra, neocortex, hippocampus and cerebellum,[63] and is found unexpectedly in Lewy bodies.[64] On a subcellular level, the precise localisation of torsinA is being actively explored.[63,65-67]

Table I. Dystonia: molecular classification (modified from Brin[22])

OMIM designation (OMIM no.)	Location	Classic/variant	Typical age at onset	Primary phenotype/comment	References
DYT1 (128100)	9q34	Classic	Child or adolescent; <28y	AD childhood and adolescent limb onset. Ashkenazi Jewish – most due to single mutation (GAG deletion) in DYT1.[a] Non-Jewish – some due to DYT1 mutation, or mutations at other locations, including chromosome 8 (*DYT6*)	23, 24
DYT2 (224500)	Unknown	Unknown		AR in Gypsies, presence as a distinct entity is disputed	25
DYT3 (314250)	Xq13.1	Variant	Adult	X–linked parkinsonism–dystonia (Lubag, Philippines)	26-32
DYT4 (128101)	Unknown	Variant	Adult	AD hereditary whispering dysphonia in Australian family	33, 34
DYT5 (128230)	14q22.1–22.2	Variant	Child or adolescent	Dopa–responsive dystonia (DRD). Due to mutation in GTP cyclohydrolase I gene. Sex influenced	35-38
DYT6 (602629)	8p21–q22	Classic	Child or adolescent	Mennonite/Amish families with mixed (cranial/cervical or limb onset) phenotype	39
DYT7 (602124)	18p	Classic	Adult	German, adult cervical, cranial or brachial–onset	40-42
DYT8 (118800)	2q33–q35	Variant	Child or adolescent	Paroxysmal dystonia; paroxysmal dystonic choreoathetosis. May be a channelopathy	43-45
DYT9 (601042)	1p	Variant	Child or adolescent	Paroxysmal choreoathetosis with episodic ataxia and spasticity (CSE = choreoathetosis/spasticity, episodic)	46
DYT10 (128200)	Unknown	Variant	Child or adolescent	Paroxysmal kinesigenic choreoathetosis (PKC); may be same as *DYT8*	47-50
DYT11 (159900)	11q23 7q21–q31	Variant	Child or adolescent	Myoclonic dystonia; hereditary alcohol–responsive myoclonus. Mutation in dopamine D_2 receptor in one family	51-54
DYT designation unassigned (128235)	19q13	Variant	Child or adolescent	Rapid–onset dystonia–parkinsonism (RDP)	55-58
LDYT (535000)	mtDNA	Variant	Child or adolescent	Leber's hereditary optic neuropathy	59, 60

a The torsinA protein is the gene product of the *DYT1* gene mutation on chromosome 9.

AD = autosomal dominant; **AR** = autosomal recessive; **OMIM** = Online Mendelian Inheritance in Man (http://www3.ncbi.nlm.nih.gov/Omim/).

Until the genes for all dystonic conditions are identified and it is possible to differentiate between each genetic subtype and the non-genetic phenocopies, the term 'primary' may be preferred when describing focal, segmental and generalised dystonia musculorum deformans as originally introduced by Oppenheim in 1911[68] and elaborated by Herz in 1944.[69-71]

4.2 Pathophysiology

Excessive co-contraction of agonist and antagonist muscles is one of the clinical hallmarks of dystonia and might be a consequence of impaired central reciprocal inhibition. Abnormal muscle activity, as registered by EMG, may show co-contraction of agonist and antagonist muscles and overflow activity to other muscles.[72] However, in one study of rotatory torticollis, muscle activity in sternocleidomastoid (SCM) muscle and splenius muscle (on the side responsible for rotation) was increased compared with the corresponding muscles on the other side.[73] Either with or without a sensory trick and the head in midline position, agonist muscle activity decreased and approached the antagonistic activity. This implies that the voluntary normalisation of head position was accompanied by a reduction in agonistic activity, rather than an overabundance of antagonistic activity in the patients studied.

Reciprocal inhibition, which is a normal neural mechanism for modulating movement, is reduced in patients with dystonia.[74] This reduction in neural inhibition, as reviewed by Hallett,[74] is seen in patients with generalised and also focal dystonia, including blepharospasm, writer's cramp and CD. Furthermore, patients with dystonia have reduced inhibition in asymptomatic limbs, suggesting that this abnormality is widespread in affected individuals.

Similarly, the blink reflex recovery time is a measure of central excitability and reflex inhibition. Patients with focal, segmental and generalised dystonia have a reduction in the blink reflex recovery time, consistent with reduced central inhibition.[74] As in the reciprocal inhibition studies cited in the previous paragraph, a shortened blink reflex recovery time can be seen in patients without clinical involvement of the eyelids.

Abnormalities of vibration activated Ia sensory afferents may provoke the postures of action dystonia;[75] this clinical effect was not observed in normal individuals. Dilute lidocaine, injected locally at a dose below that required to cause anaesthesia, preferentially blocks γ and Ia afferent fibres, and results in an amelioration of both action- and vibration-induced dystonia.[74] These studies support the importance of the afferent system in the clinical manifestations of dystonia.

Positron emission tomography (PET) and single photon emission computerised tomography studies have shown decreased binding of [^{18}F]-spiperone and [^{123}I]-epidepride to dopamine D_2 receptors in the putamen in patients with focal dystonia including CD. At the same time the binding of [^{123}I]-beta-CIT to the dopamine transporter on presynaptic dopaminergic nerve endings was normal.[76,77] This supports the hypothesis that abnormalities of the indirect striatothalamic pathway, associated with the D_2 receptor, might be important in the pathophysiology of dystonia. However, recent studies suggest that the currently accepted notion associating the D_2 receptor with the indirect pathway and the D_1 receptor with the direct pathway has been reappraised.[78]

Frontal lobe activity contralateral to head turn seems to be abnormal in patients with CD. Somatosensory evoked potentials of the median nerve showed increased amplitude of N22/P30 wave[79] contralateral to the head turn, which was not observed in healthy controls who had their neck rotated by 60 degrees; this work is supported by McEwen and Reilly[80] but not by Mazzini et al.[81] In a PET study, activity of the supplementary motor area and primary sensorimotor cortex was decreased contralateral to the head turn when a sensory trick facilitated bringing the head to the near-neutral position.[82] These findings of a decrease in motor output associated with a sensory trick are consistent with those of Buchman et al.[73] cited above, and those of Leis et al.[83]

Abnormalities of the amplitude and latency of motor evoked potentials and silent period elicited by transcranial magnetic stimulation have been observed in both SCM and trapezius muscles, both at rest and with facilitation (contraction).[84,85] However, it is not clear if this hyperexcitability of the motor system takes place at a cortical or subcortical level.

Trauma is an important factor in the pathogenesis of CD in some patients. Head/neck trauma has been reported in 5 to 21% of patients with CD.[6-8,20,86] The timing of onset of CD after the injury might be an important indicator for the severity of CD and its response to treatment. In the limited published case reports, acute-onset CD, usually within 4 weeks of an injury, has markedly reduced cervical mobility, prominent shoulder elevation, absence of involuntary movements, sensory tricks or activation manoeuvres, and poor response to treatment, including BTX.[87,88] However, Samii et al.[86] found more similarities than differences between patients whose symptoms began after trauma and those without a traumatic history. Trauma usually causes significant pain, which may lead to development of focal dystonia, through either a peripheral or central mechanism.[74] These observations do not refute the importance of trauma as a trigger for the onset of dystonia, but suggest that retrospectively classifying patients may be difficult. In our practice, we accept trauma as a trigger for dystonia when the onset of the dystonia is within 6 to 12 months of the identified trauma. In many patients, the peripheral injury which preceded the dystonia was acute, brief and well defined. In some of our patients, the injury was relatively mild or chronic or repetitive, as had been noted by Schott.[89] Furthermore, the dystonia typically occurs in the traumatised body part or region, and in many patients is associated with pain. Sometimes the dystonic posture evolves as the pain improves.

Autoimmune thyroid disease[9] and elevated titre of antinuclear antibodies[90] are commonly seen in patients with CD. A trial of intravenous methylprednisolone improved symptoms in only two of five patients with recent-onset CD.[91] One patient had primary CD and the other secondary CD caused by administration of Rho(D)-immune globulin. Improvement in CD or other signs of dystonia has not been demonstrated in a subsequent study by the same authors.[91]

Abnormalities of copper and manganese metabolism, including increased content of both metals in the lentiform nucleus,[92] decreased levels of Menkes protein and increased levels of ceruloplasmin and Wilson protein in the lentiform nucleus,[93] and decreased serum copper and ceruloplasmin levels, have been described in patients with CD.[94]

5. Evaluation

Once CD is either diagnosed or suspected, a neurologist with expertise in movement disorders should be consulted. The purpose of this consultation is to confirm the diagnosis and provide guidance in therapeutic interventions. In addition, some of the therapies use are specialised.

Patients presenting with symptoms of CD should have a comprehensive history taken and neurological examination performed. The family history should be carefully reviewed, in addition to careful attention to any factors suggesting secondary dystonia or pseudodystonia (table II). When we obtain a detailed family history, we describe the various clinical presentations of dystonia and search for a history of any movement disorder.

When evaluating the patient, we introduce the concept of the potential genetic basis of their symptoms. The availability of genetic counselling services is discussed. Although it is currently not usually possible to determine adult onset dystonia in a particular patient is genetic or a phonocopy, we expect to be able to make that distinction in the future. Adult-onset CD preceded by limb dystonia may be due to the *DYT1* mutation (torsin A), and

Table II. Classification of cervical postural deformity (modified from Weiner and Lang[95])

I. Dystonia: associated with abnormal involuntary excessive muscle contraction causing abnormal postures
II. Structural causes
A. Orthopaedic
1. Atlanto-axial dislocation
2. Cervical fracture
3. Degenerative disc
4. Osteomyelitis
5. Klippel-Feil syndrome
B. Musculo-fibrotic
1. Congenital torticollis associated with absence or fibrosis of cervical muscles (usually as a result of local trauma, haemorrhage)
2. Postradiation fibrosis
3. Acute stiff neck
C. Local infectious
1. Pharyngitis
2. Painful lymphadenopathy, adenitis
D. Other neurological
1. Vestibulo-ocular dysfunction (head tilt with 4th nerve paresis, or labyrinthine disease)
2. Posterior fossa tumour
3. Arnold Chiari syndrome
4. Bobble-head doll syndrome (with third ventricle cyst)
5. Nystagmus
6. Sandifer's syndrome
7. Spinal cord tumour/syrinx
8. Extraocular muscle palsies, strabismus
9. Head thrusts with oculomotor apraxia
10. Hemianopia
11. Spasmus nutans
12. Focal seizures

we recommend genetic testing in these such patients.

Most patients presenting with symptoms of a twisted neck have dystonia. However, it is important to evaluate for ‘pseudodystonia’ secondary to structural abnormalities (table II). Comprehensive lists of diagnostic tests to be performed when secondary or pseudodystonia is suspected are available;[11,96-98] findings on neurological examination suggestive of secondary dystonia should be followed up with appropriate diagnostic studies. All patients should receive screening biochemical studies (SMA-20, complete blood count, thyroid function) in addition to a ceruloplasmin. Although CD would be an uncommon presentation for Wilson’s disease, this condition is amenable to treatment. We obtain an MRI scan of the brain or cervical cord if there are any findings on history or examination suggestive of additional neurological compromise or symptomatic dystonia.

Patients with CD may have coexisting signs of limb or head tremor. These signs can make the differential diagnosis between dystonia and essential tremor difficult. Limb tremor in CD may represent subtle limb dystonia, and a careful assessment for associated involuntary movements, such as inappropriate posturing (dystonia) of the hand or limb when holding the arms outstretched in the supine, prone and wing posture, or when writing, will often assist in making the differential diagnosis. Essential limb tremor occurs with action (postural and/or kinetic) but not rest; the tremor is usually bilateral and not of sudden onset. Limb tremor can be caused or aggravated by many pharmacological agents and by endocrine disturbances.

Patients with CD and head tremor have more frequent associated neck pain and essential-like hand tremor than patients with CD without head tremor; in addition, they often have a positive family history of essential like head/hand tremor.[99] Head tremor is attributed to essential tremor when there is no preferential head posture. Clues that the tremor is a manifestation of a dystonic tremor are a head tilt, amelioration of the tremor when the head is rotated in one particular direction, aggravation of tremor when lying down and supporting the head against gravity, and presence of sensory tricks.

We videotape patients[100] to document their examination before initiating therapeutic interventions.

6. Treatment

6.1 General Considerations

The purpose of the neurological evaluation is to attempt to diagnose an underlying cause or contributing factors. If an underlying biochemical basis is identified, specific therapy can be instituted. However, for the majority of patients, intervention is supportive and symptomatic.

Various options are available for treating patients with CD and therapy must be individualised. The overall treatment plan usually depends on the age of the patient, previous exposure to medications, other concurrent medications or medical problems, and physician and patient bias. We choose a treatment strategy attempting to keep the potential for adverse events to a minimum. Very few systematic drug trials have been conducted in patients with CD; much of what we know about pharmacotherapy has resulted from empirical trials. In order to avoid potential harm when evaluating the therapeutic options, surgical therapies and drugs that have the potential to cause irreversible adverse effects (table III) should be reserved for patients who have failed to respond to more conservative medical therapies, including BTX.

Treatment of CD is challenging, and it is wise for the treating physician and associated staff to nurture a responsive relationship with the patient. In most situations, we counsel the patient that both the doctor and the patient ‘hold hands’ in proceeding through the treatment options. In all situations, the elements of informed consent (verbal or written) must be reviewed, following disclosure of the major risks of treatment or procedure being contemplated, an accurate assessment of the benefits that can be reasonably expected, and a discussion of alternative forms of treatment.[101]

Table III. Drugs potentially used to treat cervical dystonia that may cause tardive dystonia or worsen primary dystonia

Acetophenazine maleate
Amoxapine
Chlorpromazine
Fluphenazine
Haloperidol
Loxapine
Mesoridazine
Metaclopramide
Molindone
Perphenazine
Pimozide
Piperacetazine
Prochlorperazine
Promazine
Promethazine
Thiethylperazine
Thioridazine
Thiothixene
Trifluoperazine
Triflupromazine
Alimemazine (trimeprazine)

6.2 Supportive Interventions

Patients are encouraged to participate in support groups and international foundations that advance education and research on dystonia; this is via patient support materials on the world wide web (for listings, see www.wemove.org). The importance of this type of support cannot be underestimated. Reactive or primary depression may aggravate disability[102-109] and patients may benefit from supportive psychotherapy.

6.3 Pharmacotherapy

Specific pharmacotherapy directed at the underlying identified biochemical defect is available for only a limited number of symptomatic dystonias, most notably Wilson's disease. For tardive CD, caused by exposure to dopamine receptor antagonists, the best treatment is avoidance of offending drugs when possible, and providing the patient with a list of these drugs (table III). Although all patients with childhood-onset idiopathic dystonia are given a trial of levodopa to test for dopa-responsive dystonia (DRD), it would be unusual for DRD to first appear as focal adult-onset CD.

Pharmacotherapeutic agents in low doses, such as benzodiazepines, baclofen or anticholinergics[110] may be useful early in therapy. However, the higher doses of these agents that were used before the availability of BTX are unacceptable to most patients because they are complicated by adverse effects in most patients with CD. For instance, in our initial series of patients,[6] 39% of those with CD improved with anticholinergics [trihexyphenidyl, profenamine (ethopropazine)], but their benefits were often limited by the development of dose-limiting adverse effects (dry mouth, cognitive disturbance, drowsiness, blurred vision, glaucoma, urinary retention). A double-blind trial comparing trihexyphenidyl with BTX-A reported greater efficacy and fewer adverse effects with BTX.[111]

Tetrabenazine is a presynaptic catecholamine-depleting agent with some blocking activity, which is not commercially available in the US.[112] Its efficacy in treating primary and secondary dystonia, including CD, has been documented in both double-blind[113] and nonblind studies.[114,115] It has never been reported to cause tardive dystonia, although there are rare reports of acute dystonic reactions[116] and neuroleptic malignant syndrome.[117-119] Our clinical experience and the experience of others[115] has demonstrated that the addition of lithium may ameliorate the parkinsonian and depressive effects of tetrabenazine, while enhancing the beneficial treatment effect on dystonia. When used alone, lithium is not of major benefit in patients with dystonia.

Clozapine, beneficial for tardive dystonia, failed to show major improvement of CD when given at dosages of 100[120] and 300 mg/day.[121] However, in a nonblind study conducted at the National Institutes of Health (NIH),[122] four patients with generalised and 1 with segmental cranial dystonia received benefit but most experienced dose-related troublesome adverse effects.

When any medication is initiated, the initial dosage should be low and then gradually increased as tolerated and adjusted to identify the most effective dosage with a minimum of adverse effects ('regulation of dose'). If a drug is of no benefit at a dosage that causes adverse effects, it should be gradually tapered and discontinued. If a drug is documented as helpful, it can be continued at the regulated dose and the next intervention added when needed. When removing a drug from a treatment programme, the dose should be tapered and only rarely abruptly discontinued; in a rare instance, a drug may cause neuroleptic malignant syndrome (typically seen with antipsychotics), or drug allergy, in which case the offending drug should be abruptly discontinued. Treatment interventions should be monitored and adjusted according to the response benefits versus adverse effects. Patients thus build a portfolio of 'response to therapy' and this portfolio can be consulted frequently as each new strategy is considered. A drug treatment list may be kept accessible in each patient chart.

6.3.1 Botulinum Toxin Chemodenervation

Most focal dystonias, including CD, are now effectively treated with local injections of BTX-A. The first experimental chemodenervation with BTX was performed on monkeys;[123] the first treatment in humans was in 1980.[124] Safety and efficacy have been established in nonblind and double-blind clinical trials in many countries around the world.[125-135] Dose-dependent amplitude reduction of maximal voluntary EMG activity in SCM muscles has been observed in patients with CD treated with BTX-A (both US and UK commercial forms).[136] Improvement in quality-of-life parameters has also been documented with careful neuropsychiatric testing.[131] Published series report that 70 to 92% of treated patients experience relief in postural abnormality or painful contractions. Of the 133 individuals with CD participating in one survey, 29 (21%) have stopped BTX-A therapy.[137] Of those, 11 had received only one or two treatments. Two-thirds of the patients who continued BTX-A therapy reported that injections always helped, whereas one-quarter estimated that one set of injections did not help. The average duration of benefit is 12 to 14 weeks. Similar effectiveness of BTX-A treatment has been seen in other studies.[133] In our practice, we often evaluate patients referred as having a suboptimal response to therapy; these issues (such as minimal to mild improvement of involuntary neck posturing) are discussed in this section.

We have used the therapeutic modality described here since 1984 with excellent results in most patients. Improvements in quality-of-life measurements have been demonstrated.[133] Most patients with CD are candidates for treatment with BTX-A, and in most patients, BTX-A is the treatment of choice.

Selection of muscles for injection and choosing an effective dosage are the key to a successful result. Usually, the affected muscles can be identified by palpation and the injection is administered through a tuberculin-like syringe and needle. We use EMG guidance for most patients, in conjunction with the clinical evaluation. The electrode used is a hollow Teflon-coated monopolar needle which is connected to the EMG machine. The most powerful rotators of the neck are present in the postvertebral region and overlie each other. Our experience and that of others[138-140] is that targeting the toxin specifically into the offending muscles with EMG control may result in a more effective treatment session. Some evidence indicates that a lower dose may be used with EMG guidance.[141,142]

Physical therapy is recommended as an adjunct to BTX treatment. After treatment, there is less opposition from the dystonic musculature. The goal of physical therapy at this time is to facilitate the increased control of the patient over head movement and posture once the antagonists are weakened.

BTX-A is available in the US and many other countries from Allergan Pharmaceuticals as BOTOX®**1**. It is available in some countries in Europe from Ipsen (UK) as Dysport®**1**. Although the products show similar efficacy and adverse effect pro-

1 Use of a tradename is for identification purposes only and does not imply endorsement.

files, the unit potency of BOTOX® is approximately three times that of Dysport®.[143,144] The units for BTX-A used in clinical trials are different from the units used for the two commercially available type A preparations. From our current experience, 5000 to 15 000U (or more) of type B toxin may be required for patients with CD.[145,146] Therefore, it is crucial to know which product is being used when comparing treatments. Currently, the type A products (BOTOX®, Dysport®) have been approved by the ministries of health in many countries, including the US. The type A toxin is used therapeutically for many disorders other than CD, including focal dystonias of all types (blepharospasm, laryngeal dystonia, writer's cramp),[147,148] spasticity, tremor, tics, achalasia, and cosmetic reduction of wrinkles.[149-151] The American Academy of Neurology,[152] NIH,[153] and American Academy of Otolaryngology–Head and Neck Surgery[154] have issued statements that BTX-A therapy is well tolerated and appropriate for treating patients with CD.

Most adverse effects from either type A or type B toxin are self-limited and well tolerated (table IV). Immediate adverse effects include slight pain from the needle injection, local haematoma, pneumothorax or needle irritation of local nerves, including the occipital nerve and brachial plexus. Subacute adverse effects are related to an extension of the pharmacology of the toxin, i.e. excessive weakness in either injected or adjacent muscles. Neck weakness occurs when the patient has a strong response to the toxin. Dysphagia may be subclinical, present in 11% of the untreated CD population and 22% radiographically prior to treatment.[155] After BTX-A, an additional 33% developed new radiographically demonstrated dysphagic symptoms and 50% of patients developed new peristaltic abnormalities in the early studies.[127,156] This symptom is probably due to diffusion into regional pharyngeal muscles; most patients compensate by temporarily modifying the diet. In our practice, these complications can usually be avoided by reducing the dose on subsequent treatment. Less frequent adverse effects include symptoms of generalised weakness without objective signs of weakness, or a temporary sense of malaise or headache.

Some patients present for consultation with a history of a waning or lack of response to therapy. Reasons for lack of response include inappropriate muscle selection, inappropriate dose or immunoresistance.

Initially, when we began to use BTX-A, antibodies to BTX were rarely detected in patients exposed by food poisoning;[160] we therefore did not expect therapeutic use to induce an antibody response. However, using the original formulations of BTX-A, approximately 5% of patients developed antibodies to the toxin, rendering the toxin inactive.[134,161-165] A cumbersome *in vivo* mouse neutralisation assay (mouse lethality test) has been used for assay of presence of antibodies to BTX-A.[166] A similar but more sensitive test (mouse protection test) has been recently developed.[167] Enzyme-linked immunosorbent assay (ELISA) has been used for the detection of BTX antibody, but clinical correlation between the presence of such antibodies and a lack of response to BTX injections has not been established.[168-172] In one study using a sphere-linked immunodiagnostic assay,[173] antibodies were detected in more than 50% of all patients treated with BTX-A, including those who continued to respond to toxin treatment. This implies that patients may develop antibodies to regions of the toxin, or associated excipients, that may not be important to the biological effect.

Rather than send serum from patients for antibody assay, where the correlation with resistance to therapy is not 100%,[161] we perform the FTAT (frontalis type-A test) when clinical resistance is suspected. Approximately 15U BOTOX® or 50-60g Dysport® is injected into two sites of one side of the corrugator muscle. If the muscle does not move within 2 weeks, and the patient cannot furrow that side of the brow, they are not resistant to therapy; if the corrugator muscle moves properly, they are resistant. In the case of no resistance, the

Table IV. Common adverse effects associated with different types of botulinum toxins (BTX)

Agent (U)	No. of pts	Dysphagia (%)	Dry mouth (%)	Injection site pain (%)	Neck weakness (%)	Fatigue (%)
BTX type A						
Dysport® Poewe et al.[132]						
PBO	20	10	5	10	0	5
250	19	21	21	5	11	16
500	17	29	18	18	12	12
1000	18	39	33	28	56	17
BOTOX®[158,159]						
PBO	82	NR	NR	NR	NR	NR
236	88	19	<10%	<10%	NR	NR
BTX type B (Neurobloc®/Myobloc®)						
Lew et al.[157]						
PBO	30	0	3	10	0	0
2500	31	16	3	16	0	3
5000	31	10	10	19	0	3
10 000	30	27	33	17	0	7
Brashear et al.[145]						
PBO	36	3	3	8	NR	NR
5000	36	11	14	6	NR	NR
10 000	37	22	24	11	NR	NR
Brin et al.[146]						
PBO	38	5	3	8	NR	5
10 000	39	28	44	18	NR	8

NR = not reported; **PBO** = placebo.

patient may be treated on the opposing side to maintain expression symmetry.

Although the antibodies appear to cause no harm, they render the patient unresponsive to further treatments. In retrospective studies,[163,164] patients with antibodies had a shorter interval between injections, more 'boosters', a higher dose per 3-month interval, and a higher dose at the 'non-booster' injection. However, patients who did not develop antibodies, who received doses comparable to those who did develop antibodies, were not separately analysed. As well as high doses, Jankovic and Schwartz[161] also found that young age is a potential risk factor for the development of immunoresistance to the US-marketed BOTOX®. One of our patients who developed resistance and antibodies to US-marketed BOTOX® subsequently went to London, where he was found to be resistant to British-marketed Dysport®, and later to the Japanese experimental preparation of BTX-A. It has been reported that *in vivo* neutralising antibody titre may fall to zero,[174] at which point clinical response to BTX-A returns. However, this response is lost after repeat injections and concomitantly with the reemergence of neutralising antibodies.[162]

As a result of our experience with immunising patients to this important therapeutic agent, we warn clinicians against using booster injections and encourage patients to extend the interval between treatment as long as possible, certainly at least 3 months, and to use the lowest effective doses, keeping the dose below 300U (BOTOX®) per 3-month period. Some patients who developed BTX-A antibodies have benefited from injections of immunologically distinct preparations. The benefits of BTX-F appear to only last approximately 1 month;[175-180] these patients may ultimately become immune to BTX-F (personal communication, Mark Hallett). In a series of controlled clinical trials, BTX-B has been shown to be effective in patients with CD both with and without resistance to serotype A.[145,157,181-184]

Not all of the factors responsible for provoking antibody formation are known. No clinical data comparing different types of toxin and their immunogenic potential are available. Investigators have proposed that the specific activity, or the amount of active toxin per weight of protein in the preparation, may be an important factor in antibody development (table V). Some inactive toxin molecules may act as toxoid and contribute to development of neutralising antibodies.[185]

Dodel et al.[186] reported that the average dose of Dysport® used to treat patients with CD was 732U. Dysport® is packaged with 12.5 ng/500U, resulting in a protein exposure of 18ng. This protein exposure is higher than the threshold for increased neutralising antibody formation described by Goschel et al.[187] as 15ng or 600U.

Currently available BOTOX® (Lot 2024 and derivatives, released in November 1997) has a higher specific activity than the original batch (Lot 79-11) that was initiated in 1979 (Allergan, Dear Customer letter, November 1997). As reported in the Allergan product literature, there are 4.8ng of neurotoxin complex per 100U. The BOTOX® prepared from this new bulk toxin retained the same preclinical murine neuromuscular efficacy as the original but demonstrated lower immunogenic potential in rabbits.[188] The mean BOTOX® dose used to treat patients with CD reported in a German study was 187U.[186] This would have been 46.75ng protein with the original 79-11 lot, but would be 9.0ng with the current lot. This lowered neurotoxin complex protein exposure associated with an increased specific activity would be expected to further reduce the antigenic potential of BOTOX®.[188] Antibody formation had not been reported as of May 1999 in patients initiated on Lot 2024. The efficacy, duration of benefit and adverse effects were similar in both the 79-11 strain and 2024 strain.[189]

As noted in table V, BTX-B, studied under the trade name of Neurobloc®[1]/Myobloc®[1], has a specific activity of 100 U/ng of protein. The protein exposure, calculated for an average dose of 10 000U per treatment, would be equal to 100ng of protein.

An alternative strategy for patients who develop neutralising antibodies to BTX-A might be plasmapheresis or immunoadsorption on a protein A column (IA-PA). In a case report, plasmapheresis (1 treatment) and IA-PA (3 treatments) combined were used over a period of 15 months in a patient who had neutralising antibodies to BOTOX®. The patient maintained low titres of neutralising antibodies, and hence good therapeutic response to BOTOX®, during this period.[190] As previously mentioned, over time, the titre of neutralising antibodies might fall close to zero and patients might become responsive again to BTX-A. A recent study suggested that mycophenolate mofetil, a potent, reversible, noncompetitive inhibitor of purine biosynthesis of DNA currently used for prevention of solid organ transplant rejection, may prevent the recurrence of blocking antibodies. Duane et al.[191] used this agent as pretreatment in three patients with CD who had lost previous clinical responsiveness to BTX-A, had a positive FTAT, and had *in vivo* neutralising antibodies to BTX-A. Two of these patients had an excellent clinical benefit from re-treatment with the same type A toxin.

The use of BTX-A has been reported in humans since 1980,[124] and the safety of long term injections is established. Weakness or routine EMG changes in muscles distal to the site of injection have not been generally reported, although a recent study did report diminished size of type IIB fibres in muscles distant from the injection site in patients treated for CD.[192] In addition, there are detectable abnormalities on single fibre EMG and in some cardiovascular reflexes.[193-195] It is not known how long these abnormalities persist and they do not appear to have any clinical significance. Other uncommon reactions may occur.

There is a paucity of data regarding the use of BTX during pregnancy. One of nine patients treated with an unspecified dose during pregnancy

1 Use of a tradename is for identification purposes only and does not imply endorsement.

Table V. Botulinum toxins: dosage and protein exposure when used in patients with cervical dystonia[145,146,157]

	BOTOX®[186]	Dysport®[186]	Myobloc®/Neurobloc®
U/ng protein	25	42	100
ng protein exposure per treatment	8 ng/200U (150-300U)	17 ng/700U (500-1000U)	100 ng/10 000U (7500-25 000U)

gave birth prematurely. This was thought not to be related to the drug.[196] A recent survey reported on 16 women treated with BTX-A during pregnancy, primarily in the first trimester, with doses ranging from 1.25 to 300U. There were two miscarriages and 14 normal deliveries. None of the neonates showed any signs of BTX effect.[197] Nonetheless, until additional safety data are available, we recommend not treating patients who are pregnant or lactating with BTX.

A few patients with conditions affecting neuromuscular transmission have been treated successfully, including one patient with myasthenia gravis[198] and one patient of ours with Charcot-Marie-Tooth disease. However, we recommend proceeding with caution in treating such patients, particularly when large doses are required, such as in the treatment of CD. While the amount of toxin entering the systemic circulation after injection is thought to be minute, this must be balanced against the potential for complications and the severity of the hyperkinetic symptoms. One report has indicated the potential for systemic weakness following BTX-A injection in patients with amyotrophic lateral sclerosis.[199] In addition, there is one case report of a patient with blepharospasm in whom BTX-A injections unmasked subclinical Lambert-Eaton myasthenic syndrome,[200] and two patients with Machado-Joseph disease developed dysphagia after treatment with BTX-A.[201] Aminoglycosides interfere with neuromuscular transmission and may potentiate the effect of BTX-A therapy. We do not recommend treating a patient with BTX who is concurrently taking aminoglycosides.

Some patients who are resistant to BTX-A elect to receive phenol injections.[202] Phenol produces destruction of neural tissue and muscle atrophy.[203,204] A neuromotor points block in SCM and trapezius muscles with phenolglycerine injections was not effective in five patients with CD.[205] Massey[206] treated two patients with CD (one had lost clinical response to BTX-A) with 1% phenol injections. Both patients had minor tenderness and swelling at the site of the injections and a sustained clinical response. Ruiz and Bernardos[202] treated three patients with CD, initially with weekly and later with monthly injections of 10ml of 1% phenol solution. Only one patient had a sustained clinical benefit. In our personal experience, phenol injections provided minimal benefit to three patients with BTX-A-resistant CD. They were treated with 6% phenol (average dose 389.67 ± 120.71mg per visit). Minimal improvement in Toronto Western Spasmodic Torticollis Rating Scale severity scale (12.00 ± 7.8%) was observed. All our patients elected to discontinue the phenol injections because of the degree of pain experienced during the procedure and lack of significant improvement of their CD. Other patients resistant to BTX-A have elected treatment with a selective denervation procedure as described in section 6.4.

6.4 Surgery

6.4.1 Selective Peripheral Denervation

Selective peripheral denervation is a surgical technique that was popularised by Claude Bertrand[207,208] as a result of experience from former techniques and anatomic and electrophysiological studies. In an attempt to avoid the sequelae of bilateral cervical rhizotomy, following the lead of Cooper[209] in 1964, then Hassler and Dieckman,[210] Bertrand started to perform thalamotomy for the treatment of rotatory torticollis.[211,212] Subsequently, he combined thalamotomy with selective peripheral denervation after studying the cervical muscles through EMG and nerve blocks.[213-215] His early experience demonstrated that peripheral denervation alone could provide symptomatic relief from the abnormal movements in rotatory torticollis. Although championed by

Bertrand at Notre-Dame Hospital (Montreal, Canada) since 1978,[214,216] the procedure is also currently performed in other centres in the US and Europe.[217,218]

Standard Procedure

This surgical technique aims to abolish abnormal activity only in the muscles responsible for the abnormal posture of the head, by selectively denervating them peripherally, while preserving the innervation of the muscles that are not involved, so the patient is able to have a good range of movement of the head and neck after surgery. Choice of muscles for selective denervation prior to surgery is essential. The first step is to perform an examination to analyse the abnormal movements and/or posture exhibited by the patient; this includes direct observation and palpation of the nuchal muscles.

Once this clinical assessment has been performed, the choice of muscles is confirmed with multichannel EMG recording. As a standard procedure previously described,[208,219] four muscles are recorded at the same time. Both SCM and splenii muscles are recorded simultaneously, and then additional muscles are investigated as necessary. The recording is performed with the patient at rest and while performing voluntary movements of the head, such as rotation, inclination, extension and flexion. The EMG recording while the patient is not making any voluntary movements identifies which muscles are hyperactive during the involuntary movements, i.e. the ones responsible for the abnormal posture, and are the primary candidates for denervation. The recording during the performance of repetitive voluntary movements usually demonstrates which are the abnormally inhibited muscles that are not to be denervated because they are deemed essential for the recovery of a normal range of movements of head and neck after surgery, typically with the help of physiotherapy. In some patients, a temporary block of intramuscular 1% lidocaine without epinephrine, or bupivacaine, is useful to demonstrate the relative action of individual muscles.[219,220]

The following premises have been established as the best indications for this surgical treatment.[219,221]

- Previous conservative medical treatments, mainly BTX injections, no longer provide satisfactory relief, cause significant adverse effects or are becoming too difficult to pursue indefinitely.
- The clinical symptoms should be stable for at least 1 year, preferably evolving for more than 3 years. Before this period of relative stabilisation, CD may still change its pattern, i.e. other muscles may become active because the final pattern is still evolving. However, we have seen patients with a change in pattern of CD that occurs after more than 5 years of symptoms.
- The dystonic symptomatology should be restricted to or at least prevalent in the cervical region. Dystonic features elsewhere indicate a more generalised dystonia. In such patients, after surgery, a temporary flare-up of such other features as blepharospasm, oromandibular dystonia or tremor may be observed.
- Pure rotatory torticollis and its combination with mild inclination and/or extension are the forms of CD that show the best results.
- Previous surgical procedures, pre-existing fibrosis or severe arthrosis have been shown to favour poor postoperative results.

The description of this surgical technique has been previously published.[208,214,216,219,220] In a patients with typical rotatory torticollis to the right, the usual surgical procedure would be denervation of the left SCM muscle (through dissection of the ipsilateral spinal accessory nerve, sparing the branches that innervate the trapezius muscle) and right posterior ramisectomy (from C1 to C6). Unipolar stimulation is used as the surgeon exposes the posterior rami of the upper cervical nerves to identify the nerve divisions and their rootlets. Near-threshold stimulation is performed once the nerve branch is isolated before denervation. Intraoperative stimulation is also important to confirm that certain branches should be spared during the procedure. A limited muscle section and restoration of normal muscle attachments is imperative to recover the normal range of movements of the neck after surgery. The use of EMG and blocks and especially direct observation of the results of intraoperative stimulation have considerably increased the knowledge of the distribution and functions of the various branches of the cervical nerves.[219]

Patients are typically mobile within the first or second day after surgery and can be discharged on the fourth or fifth postoperative day. Specific physiotherapy starts on the third day after surgery and is recommended for the next 6 to 12 weeks (3 times a week) to re-educate the formerly inhibited antagonist muscles with the objective of restoring a normal or near normal range of movement of the neck.

Series of patients have been reported from Canada,[216,220] the US[217,218,222] and Europe,[223] with more than 800 patients having undergone selective peripheral denervation, typically with satisfactory results[224] and an acceptable adverse effect profile. In a retrospective review, we have reported a surgical cohort where the results were sustained and rated as excellent (no residual abnormal movements) or very good (very slight residual movements, not bothersome for the patient) in 88% of the patients.[219] Since the procedure is performed in a sitting position, monitoring is necessary to evaluate for possible air emboli, which may require the patient to return to the horizontal position temporarily. In patients with generalised dystonia with predominant CD, exacerbation of other features such as blepharospasm, oromandibular dystonia and tremor may be observed.

6.4.2 Other Neurosurgical Techniques

In addition to selective peripheral denervation, two other techniques have been used for the treatment of CD: bilateral cervical rhizotomy,[225,226] and microvascular lysis of the accessory nerve.[227,228]

Bilateral cervical rhizotomy was the surgical treatment most frequently used for CD until the 1970s, in spite of adverse effects such as weakness of the neck and frequent swallowing problems.[229-233] Currently, it has been established that the anterior divisions of C1 and C2 do not contribute at all to the innervation of the posterior cervical muscles. They innervate only the infrahyoid muscles of the throat responsible for swallowing.[219] Moreover, peripheral denervation of the posterior primary divisions of C3 to C6 is typically enough to achieve proper denervation of the posterior cervical group, and at the same time preserves the innervation of the antagonist muscles which are very important for recuperation of a normal range of movements after surgery.

Microvascular lysis of the accessory nerve roots is a restricted approach, possibly inspired by decompression of the facial nerve for facial tics, which nevertheless requires a laminectomy.[227,228,234,235] Results have been modest, and when there is benefit, results are usually delayed for many months.

Thalamotomy[236,237] has been abandoned by most practitioners because of the significant potential for serious adverse effects. Most patients with CD have required bilateral operations, which raise the risk of speech and swallowing complications.

Lesions of the pallidum were made by early stereotactic neurosurgeons including Gros,[238] Caracalos[239] and Cooper.[240] In the series reported, these patients are typically reviewed with thalamotomy patients. However, the pallidal ablation reports were encouraging, and in Cooper's report, the three patients had a substantial benefit.[240] Vitek et al.,[241] Iacono et al.[242] and others[243] have recently reported benefit from pallidotomy in patients with medically intractable dystonia.

Pallidal stimulation in the form of unilateral stimulation of globus pallidus contralateral to the involved SCM muscle in rotatory CD,[244] and bilateral stimulation of globus pallidus internus for more complex CD,[245] have been recently reported to be nondestructive and relatively effective and well tolerated procedures. However, further studies on safety and efficacy of the procedures are necessary.

6.5 Physical Therapy

Patients with mild symptoms may be managed with physical measures or pharmacotherapy. Physical measures include the simple 'geste antagonistique' (section 3), biofeedback, mechanical braces or physiotherapy. A common problem encountered when manipulation-based practitioners (physiotherapists, chiropractors) treat patients with CD is the assumption that the condition results from a spinal or orthopaedic abnormality. In most patients, it is not possible to physically overcome the brain's disordered central processing commands to displace the head position. Therefore, physiotherapists and chiropractors are advised not to use orthopaedic techniques or physical force, as this may result in further discomfort or injury to the patient. However, it is beneficial to assist the patient to use their own resources to improve head control via strengthening, enhanced flexibility, etc.

7. Conclusion

Although CD is the most common form of focal dystonia, the diagnosis and treatment of this disorder are often delayed. CD is not a life-threatening disorder, but it can cause significant morbidity. Familiarity with the clinical presentation and aetiology of primary and secondary CD will facilitate diagnosis and implementation of effective therapy. Recognition of inherited dystonic syndromes prompts a referral for genetic counselling and consideration for additional genetic assessment. Available medical and surgical therapy can markedly improve the patient's quality of life. Local injections of BTX (chemodenervation therapy) are considered primary therapy for most patients who require medical intervention. Pharmacotherapy (anticholinergics, muscle relaxants) is usually helpful in combination with chemodenervation therapy. Surgical treatment can be used in patients with pure rotatory torticollis or in those who do not respond (either primarily or secondarily) to previous treatment modalities. Recent advances in basic and clinical research will improve our understanding of pathogenesis of CD and facilitate its diagnosis and advanced management.

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