DYSTONIA - A REVIEW
Saravanan.S

Abstract: Dystonia is defined as the syndrome of sustained muscle contraction, frequently causing twisting, repetitive movements (or) abnormal postures. Dystonia can be classified depending upon the age of onset (or) on the both of anatomical distribution (or) according to the etiology. Dystonia are usually due to abnormal activity of various pathways in the extrapyramidal system and due to various changes in the structure and function of sensorimotor cortex. The various types of dystonias have specific clinical characteristics like age of onset, distribution of dystonia, progression and associated features. Secondary dystonias are common in our population when compared to western population. There are certain specific forms of focal dystonias which are commonly seen in our population. Diagnosis mostly depends on clinical characteristic of dystonia, though imaging studies may help to identify the etiologic causes for secondary dystonias. Identification of genetic loci is possible in genetically inherited dystonias. High dose anticholinergic drugs, dopa active drugs, baclofen and other medications are useful to the patient along with physical and occupational therapies. In specific circumstances, Botulinum toxin injection is very helpful in ameliorating symptoms. Few selected patients are benefitted by surgery.

Keywords: Dystonia

Introduction:
Dystonia is an extra pyramidal movement disorders, affecting significant proportion of the population. The discovery of genetically inherited dystonia and the genes responsible for them in the recent past has thrown more light into the patho-biology of these disorders. Dystonia are variably classified and the clinical features and the presentation of each one of these are specific and characteristic. Newer modes of investigations and treatment options for dystonia have encouraged the need for exact identification of the disease and efforts to improve their quality of life with appropriate treatment.

History:
In 1911, Oppenheim coined the word “dystonia” to indicate the disorder characterized by tonic muscle spasms. He called the syndrome by two different names - “Dystonia musculorum deformens” and “Dysbasia lordotica progressiva”. Presently this entity is termed “Idiopathic torsion dystonia” due to its characteristic and distinct nature and since this disorder is not a muscle based abnormality as implied by the word ‘musculorum’. Not all patients with this disorder progressed to deformities as suggested by the term ‘deformens’. The term “dysbasia lordotica progressiva” is no more in use, as a fairly large percentage of patients do not present with progressive lordosis (or) gait difficulties.

The genetic nature of the disease was recognized by Flatau and Sterling in 1911. Later, dystonia was recognized associated with other neurological diseases like Wilson disease and HIE. Zeman (1970) documented the first epidemiological study on the genetic patterns and described focal dystonia as “forme frustae” of generalized dystonias. Dystonia muscle research foundation was formed in 1976. Identification of the gene locus for Oppenheim dystonia and advances in the genetics has led to a better etiologic classification of dystonia.

Epidemiology:
Zeman and his colleague Dyken reported the first epidemiological study on Dystonia and emphasized an autosomal dominant pattern of Idiopathic torsion dystonia. They also documented the prevalence of idiopathic torsion dystonia in Minnesota as 3.4 per 1,00,000 population and the prevalence of focal dystonia as 30 per 1,00,000 population, and the prevalence of generalized dystonia among Jews as 7 per 1,00,000 population. In Japan, the prevalence of generalized dystonia is 3.4 per 1,00,000 persons and focal dystonia 10 per 1,00,000 persons. In England, the prevalence of generalized dystonia is 1.6 per 1,00,000 persons and focal dystonia 12 per 1,00,000 persons. Women develop focal dystonia at an earlier age when compared to men where as men develop cervical dystonia at an earlier age when compared to women. ITD is more common in Ashkenazi Jews when compared to other races.

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Definition:
The adhoc committee of the Dystonia Medical Research Foundation defined dystonia as the syndrome of sustained muscle contraction, frequently causing twisting, repetitive movements (or) abnormal postures. The twisting quality of the abnormal movement and postures, distinguishes dystonia from other extrapyramidal disorders such as chorea, rigidity, neuropathy, myotonia etc. Exception to this rule is twitching around joints, which does not allow torsion. Eg: Jaw dystonia - may be either Jaw opening or Jaw closing dystonia (or) rarely lateral Jaw dystonia without twitching of Jaws⁵.

Patho-Physiology of Dystonia:
The specific feature of dystonic movement is the presence of an involuntary, sustained, co-contraction of agonist and antagonist muscles. At times there may be contraction of adjoining muscle called overflow. Rhythmic contraction occurs on voluntary movements. This excessive, abnormal movement is presumed to be due to various patho-physiological changes occurring in extra pyramidal system and motor cortex. The excessive co-contraction of agonist and antagonist muscles is partly due to the loss of reciprocal inhibition at various levels in the central nervous system especially in the brainstem and spinal cord. There is evidence that sensory systems are abnormal in patient with dystonia as some of the manifestations are reduced by sensory tricks. There is abnormal somato-sensory, spatial discrimination, and temporal discrimination in dystonia. There is inefficient integration of inhibitory mainly proprioceptive afferent inputs in the cortex.⁶

Abnormal cortical motor and sensory excitability have been identified with trans-cranial magnetic stimulation studies. The phenomena of intra cortical inhibition (inhibition to second excitation after a primary excitation) is reduced in patients with dystonia due to decreased inhibition, there is a loss of ‘surround inhibition’ which favors excitation of adjacent areas responsible for the overflow of movements. Surround inhibition is essential for the production of precise, functional movements and it is believed that the excessive muscle contraction in dystonia is due to loss of this surround inhibition.⁷,⁸

Basal ganglia are the primary site of pathology in dystonia. Cortico-basal ganglia circuits pass through either direct pathways which precipitate movements or indirect pathways which inhibits movements. Inhibitory pathways are likely surround & there is decreased surround inhibition, finally causing excessive muscle contraction. This is mediated via reduced and irregular neuronal firing rates in the internal and external segments of globus pallidus with the reduced inhibition of thalamus with consequent over-activity of medial and prefrontal cortical areas and under activity of primary motor area during movements.⁵

There is abnormal motor cortex plasticity in patients with dystonia. The volume of putamen is increased about 10% in patients with primary dystonia. There were changes in the levels of nor epinephrine,
serotonin, & dopamine at various regions of the brain on postmortem biochemical analysis in patients with ITD. It is not clear if any of these alterations are related to patho-physiology of dystonia.

**Clinical Features of Dystonia:**

The core important clinical features of dystonic contraction are

1. Long duration of contraction (Myoclonus is short and brief).
2. Simultaneous contraction of agonist and antagonist muscles (co-contraction).
3. Twisting of the affected body parts.
4. Patterned movements with continual contraction of same muscle groups.

Dystonic movements are usually aggravated by voluntary movements called as action dystonia. Primary dystonia that usually begin with a specific action are called task specific dystonia. Later dystonia may occur even without that specific stimulus, but any other movement. The abnormal sustained contraction may then overflow and cause dystonic movements in other parts of the body. Dystonia are usually present continuously throughout the day, except dopa responsive dystonia, which are minimal in the early part of the day and worsens towards the end of the day. Most dystonic movement disappear during sleep. Dystonic movements may be reduced or corrected by sensory tricks (Geste antagoniste) (ie) touching the involved body part or adjacent body part reduces the muscle contraction. A finger placed over the chin reduce the torticollis or hand applied to the side of the face may reduce orolingual dystonia.

Pain is less common in dystonia except in cervical dystonia. Rhythmic tremors may be sometimes associated with dystonia. These dystonic movements are less regular than essential tremor. The severity of dystonia is sometimes increased markedly causing dystonic storm and status dystonicus, which may be fatal due to rhabdomyolysis, myoglobinuria & renal failure.

**Primary Dystonia:** The classical prototype of primary Dystonia is Oppenheim Dystonia (DYT-1 Dystonia) that is more commonly seen in Ashkenazi Jews. The inherited gene is on chromosome 9q34 (Table 2). This is autosomal dominant with a reduced penetrance of 30% - 40%. All cases of typical DYT – 1 Dystonia are caused by an in frame GAG deletion D GAG 302/303; D e in the DYT – 1 gene resulting in the loss of glutamic acid in the c-terminal region of encoded protein Tor-

<table>
<thead>
<tr>
<th>Gene</th>
<th>Locus</th>
<th>Features</th>
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<tbody>
<tr>
<td>DYT1</td>
<td>9q34</td>
<td>Early, limb-onset primary torsion dystonia; autosomal dominant with 30% penetrance; gene encodes torsin A; all mutations except 1 are GAG deletions</td>
</tr>
<tr>
<td>DYT2</td>
<td>None</td>
<td>Autosomal recessive in Gypsy populations;</td>
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<tr>
<td>DYT3</td>
<td>Xq13.1</td>
<td>X-linked (ie, Lubag) dystonia parkinsonism; almost all due to a founder Filipino mutation; young adult-onset, cranial (including larynx)</td>
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<td>DYT4</td>
<td>None</td>
<td>Whispering dysphonia in Australian family</td>
</tr>
<tr>
<td>DYT5</td>
<td>14q22.1</td>
<td>Childhood-onset dopa-responsive dystonia (DRD) and parkinsonism; autosomal dominant, sex influenced, reduced penetrance (higher in girls than in boys); gene encodes guanosine triphosphate cyclohydrolase I, with many different mutations</td>
</tr>
<tr>
<td>DYT6</td>
<td>8p</td>
<td>Adolescent and early-adult onset, mixed phenotype with limb, cervical, and cranial onset and limited and generalized spread;</td>
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<tr>
<td>DYT7</td>
<td>18p</td>
<td>Late-onset primary cervical dystonia in North German families; autosomal dominant with reduced penetrance</td>
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<tr>
<td>DYT8</td>
<td>2q33-35</td>
<td>Paroxysmal nonkinesiogenic dyskinesia or</td>
</tr>
<tr>
<td>DYT9</td>
<td>1p21</td>
<td>Episodic choreoathetosis/spasticity (CSE), episodic choreoathetosis with spasticity, autosomal dominant</td>
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<tr>
<td>DYT10</td>
<td>16p11.2</td>
<td>Paroxysmal kinesiogenic dyskinesia or choreoathetosis</td>
</tr>
<tr>
<td>DYT11</td>
<td>7q21</td>
<td>Myoclonus-dystonia, autosomal dominant, childhood-onset dystonia (especially limbs and neck) and myoclonus (especially neck,</td>
</tr>
<tr>
<td>DYT12</td>
<td>19q13</td>
<td>Rapid-onset dystonia parkinsonism</td>
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<tr>
<td>DYT13</td>
<td>1p36.13-35.32</td>
<td>Prominent craniocervical and upper-limb involvement and mild severity in a large Italian family</td>
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<tr>
<td>DYT14</td>
<td></td>
<td>Redefined as DYT5</td>
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<tr>
<td>DYT15</td>
<td>18p11</td>
<td>Myoclonus dystonia; autosomal dominant</td>
</tr>
<tr>
<td>DYT16</td>
<td>2q31</td>
<td>Progressive, generalized, early-onset dystonia with axial muscle involvement, oromandibular (sardonic smile), laryngeal dystonia,</td>
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<tr>
<td>DYT17</td>
<td>20p11.2</td>
<td>Primary focal torsion dystonia in a large Leb-</td>
</tr>
<tr>
<td>DYT18</td>
<td>1p35.3-31.3</td>
<td>Paroxysmal exertion-induced dystonia with hemolytic anemia; autosomal dominant</td>
</tr>
</tbody>
</table>

Note: Although the etiologies for these dystonic syndromes are attributed mainly to genetic causes and to no other secondary causes, only some of these conditions have dystonia as the sole clinical finding to fulfill the criteria for a diagnosis of primary torsion dystonia.

*Adapted from Bressman et al.(2000)*
tremors may be rarely present). Severity of disease varies considerably in the same family members. There is a reduced sequential learning of motor task in these patients. Pathologically no known consistent change is described. MRI studies of brain are normal. PET studies show increased lenticular activity and reduced thalamic metabolic activities consistent with increased direct striato-pallidal pathway. Primary dystonia present as sporadic, AD, AR (or) X linked recessive inheritance. 18 types of dystonia are thus distinguished by genetic studies.

Dystonic plus syndromes: (Neuro chemical disorders). Dystonia plus syndromes represent a group of syndrome that are associated with parkinsonism or myoclonus without known loss or degeneration of neuron. They are therefore considered neuro-chemical disorders rather than neurodegenerative disorders. These include

1. Dystonia with parkinsonism
2. Dopa responsive Dystonia (DRD)
3. Dopamine agonist responsive Dystonia
4. Rapid onset dystonia parkinsonism
5. Dystonic with myoclonus that responds to alcohol.

Dopa responsive Dystonia (DRD): Segawa in 1976 first described this syndrome of dystonia in children that shows diurnal variation. The common form of DRD is AD inheritance disease with different mutation of the gene for GTP cyclo-hydrolase 1 (GCH) located at 14q21.1. GTP cyclo-hydrolase1 enzyme mediates the first step in tetrahydrobiopterin (BH4) synthesis (Figure 1). Usually the disease starts in childhood, before 16 years of age as a dystonia of legs and a gait disorder. The disease affects girls more than boys. Symptoms are minimal in the morning and worsen towards the end of the day. There are associated Parkinson signs like bradykinesia and rigidity. Symptoms improve dramatically with low doses of L-Dopa. Not all patients with childhood- onset dystonia have the diurnal fluctuation pattern. No pathological neuro-degeneration is seen and imaging is mostly normal. Other forms of DRD are due to mutation of tyrosine hydroxylase gene on the chromosome 21. Other biotin deficient diseases include infantile or adult onset 6- pyruvoyl-tetra-hydropterin synthase deficiency (AR), Pterin-4a-carbinolamine dehydratase deficiency (AR), Dihydropyridine reductase deficiency (AR), or Sepiapterin reductase deficiency (AR). Many patients with onset of dystonia in childhood have features of parkinsonism, including rigidity, bradykinesia, flexed posture and loss of postural reflexes. This disorder usually, but not exclusively,
begins in childhood with a presentation of a peculiar gait, a tendency to walk on their toes. The disease begins in infancy, thereby resembling cerebral palsy. When the disorder begins in adulthood, it presents as a focal dystonia of arm, neck or cranium, or present as Parkinsonism, mimicking Parkinson disease. The patients respond remarkably well to low-dosage L Dopa. Cerebellar signs have also been seen, with response to L Dopa. DRD has to be differentiated from juvenile Parkinsons Disease, and childhood Idiopathic Primary Torsion Dystonia (Table 3).

**Myoclonic Dystonia:** This is an autosomal dominant disease. The gene is mapped to chromosome 7q 21, with a reported mutation in the epsilon sarcoglycan gene. These patients show alcohol responsive lightning like jerks which affect the upper part of the body sparing the legs. The onset may be during childhood, adolescence or adulthood with slow progression that often tends to plateau. The patho-biology is not known. Obsessive compulsive disorders and alcohol dependence are common in these individuals. Other psychiatric conditions like anxiety, phobia, and memory difficulties are described.

**Dystonia associated with heredo-degenerative disorders:** In these diseases, dystonia is associated with other neurological deficits and the dystonia manifests variably. These are classified as follows (Fahn, Bressmann & Marsden) (1998)\(^5\)

1. **X linked Recessive Disorder:**
   a. Lubag disease
   b. Deafness - dystonia syndrome
   c. Pelizaeus –Merzbacher disease
2. **X linked Dominant Disorder - Rett Syndrome**
3. **Autosomal Dominant Disorder**
   a. Juvenile Parkinsonism
   b. Huntington Disease
   c. Neuro-Ferritinopathy
   d. Machado-Joseph Disease
   e. Dentatorubro-pallidoluysian atrophy
   f. Other spinocerebellar / cerebellar degenerations
   g. Creutzfeldt Jacob Disease
4. **Autosomal Recessive Disorder**
   a. Wilsons Disease
   b. Neimann Pick Type C
   c. Batten Disease
   d. GMI Gangliosidosis
   e. GM2 Gangliosidosis
   f. Metachromatic Leuko Dystrophy
   g. Lesch Nyhan Syndrome
   h. Homocystinuria
   i. Glutaric Aciduria
   j. Triose Phosphate Isomerase
   k. Methyl Malonic aciduria
   l. Hartnup Syndrome
   m. Ataxia Telangiectasia
   n. Frederichs Ataxia
   o. Neuro-degeneration with brain Iron accumulation
   p. Neuro-acanthocytosis
   q. Neuronal intranuclear hyaline inclusion disease
   r. Hereditary Spastic Paraplegia with dystonia
   s. Sjögren Larsson syndrome
   t. Ataxia-amyotrophy-mental retardation-dystonia syndrome
5. **Probable Autosomal Recessive Disorder**
   a. Familial Basal Ganglia Calcification
   b. Progressive palilal degeneration
6. **Mitochondrial Disorders**
   a. Leigh disease
   b. Leber disease
   c. Other mitochondrial disorders
7. **Parkinsonism Syndrome associated disorder**
   a. Parkinson disease
   b. Progressive supranuclear plasy
   c. multi system atrophy
   d. Cortical Basal ganglia degeneration

**Other Disorders associated with Dystonia:**

- Tic disorders with dystonic TICS.
- Paroxysmal dyskinesias with dystonia
  - Paroxysmal kinesigenic dyskinesia
  - Paroxysmal nonkinesigenic dyskinesia
  - Paroxysmal exertional dyskinesia
  - Benign infantile paroxysmal dyskinesias
- Hypnogenic dystonia (occasionally associated with seizures)

**Pseudodystonia:** There are other neurologic syndromes in which sustained abnormal postures may be present, but that are not considered true dystonia,
hence are called pseudo-dystonia. These include

- Sandifer syndrome.
- Stiff-person-syndrome.
- Isaacs syndrome.
- Satoyoshi syndrome.
- Rotational atlanto-axial subluxation.
- Soft tissue nuchal mass.
- Bone disease.
- Ligamentous absence, laxity or damage
- Congenital muscular torticollis.
- Congenital postural torticollis.
- Juvenile rheumatoid arthritis.
- Ocular postural torticollis.
- Congenital Klippel-Feil syndrome.
- Posterior fossa tumour.
- Syringomyelia.
- Arnold-Chiari malformation.
- Troclear nerve palsy.
- Vestibular torticollis.
- Seizures manifesting as sustained twisting posture.
- Inflammatory myopathy.
- Torticollis from AV fistula at craniocervical junction.

Secondary dystonias: Secondary dystonias otherwise symptomatic dystonias which are due to underlying etiological causes. Secondary dystonias can occur due to

- Perinatal cerebral injury
  - Athetoid cerebral palsy.
  - Delayed onset dystonia.
  - Pachygyria.
- Encephalitis, infectious and post infectious
  - Reye syndrome.
  - Subacute sclerosing leukoencephalopathy.
  - CJD.
  - HIV infection
- Head trauma.
- Thalamotomy and thalamic lesions.
- Lenticular nucleus lesions.
- Primary antiphospholipid syndrome.
- Focal cerebral vascular injury.
- Arteriovenous malformations.
- Hypoxia.
- Brain tumour.
- Multiple sclerosis.
- Brainstem lesion, including pontine myelinolysis.
- Posterior fossa tumours.
- Cervical cord injury / lesion including syringomyelia.
- Lumbar canal stenosis.
- Peripheral injury.
- Electrical injury.
- Drug induced.
  - Levodopa
  - Dopamine D2 receptor blocking agents.
    - Acute dystonic reaction.
    - Tardive dystonia.
  - Ergotism.
  - Anticonvulsants.
- Toxins: Mn, CO, CS2, Cyanide, Methanol, Disulfiram, 3-nitropropionic acid, Wasp sting.
- Metabolic – Hypo-parathyroidism.
- Immune encephalopathy: Sjogrens syndrome, multiple myeloma, Rasmussen syndrome.
- Psychogenic

A major proportion of clinical investigations of dystonia deals with the question of the etiology of secondary dystonia. Of the well known secondary dystonia, Tardive Dyskinesia occurs due to long term antipsychotic drugs intake and acute dystonic reaction to drugs like metaclopramide. As already specified, idiopathic torsion dystonia usually starts before 30 years and usually starts as leg dystonia and later spreads. As is dominantly inherited, a positive family history may be available. Dopasensitive dystonias, also usually starts in legs or upper limbs and are usually associated with gait difficulties. Parkinson features are present in some. A good response to levodopa is characteristic. Secondary dystonias usually present with history of past neurological illness like head injury, birth hypoxia, encephalitis, drug intake etc. Presence of focal neurological signs like weakness of limbs, mental subnormality, exaggerated reflexes or extensor plantar is usually seen in secondary dystonia. Dystonia is present even at rest and dystonia limited to one side of the body as in hemidystonias are
usually secondary to insult to opposite hemisphere by vascular or traumatic causes. Imaging will show abnormalities. Thus the age of onset, site of involvement, progression of the disease and presence of other neurological signs will help in arriving at a diagnosis.

Across the spectrum in the American and European movement disorder clinics, primary genetically linked dystonias are reported more common than secondary dystonia. But in contrast, in our centre at Tirunelveli Medical College Hospital, we report more of secondary dystonia. Cerebral palsy, post-encephalitic dystonia, post head injury dystonia, dystonic reaction due to drugs, dystonia secondary due to vascular insult, hemidystonia occurring after a childhood MCA infarction, cervical cord lesions of various etiologies, metastatic brain calcifications are some of the secondary causes of dystonia that we have recorded. The other types of dystonia documented in our center at Tirunelveli Medical College Hospital are neurodegenerative disorders in whom dystonia is a common manifestation. Wilson disease due to lack of ceruloplasmin is one of the most common disease that present with dystonia, tremors and parkinson symptoms. Spino-cerebellar atrophy like SCA3, SCA2, SCA1, MSA, PSP, Ataxic telangiectasia, CJD, Huntington disease and genetically linked Parkinsonism are some of the neurodegenerative diseases documented at our center with dystonia as one of their manifestation. Another class of interesting dystonia, namely the task specific dystonia, wherein dystonia of abnormal posturing are associated with specific tasks like Writers cramp and Musician dystonia are documented commonly in our center. The interesting fact is that there are a significant group of our patients whose work involves continuous and prolonged fine use of fingers developing dystonia. Beedi workers who roll tobacco powder into the tobacco leaf to make beedie (traditional cigar in South India) develop dystonia after prolonged years of working, which we term as the “Beedi Workers Dystonia”. Workers in the Match Factory, who spread match sticks on a wooden frame before dipping them into the chemical, develop dystonia during spreading match sticks which we term as the “Match Workers Dystonia”. Flower merchants, who twine flowers into a garland develop dystonia after prolonged years of working which we term as the “Flower Workers Dystonia”. Rest to the hand from the specific task, or minimal changes in the style of work have yielded good results.

Treatment:
Medical treatment can be very specific for particular types of dystonia such as levo Dopa for dopa responsive dystonia and de-coppering therapy including chelators for dystonia secondary to Wilsons disease or broad spectrum for treating dystonia/hyperkinetic movements in primary and secondary dystonias. The dystonic storm or status dystonicus also requires prompt and specific treatment. The choice of anti dystonia medication should be related to the type of dystonia, severity of dystonic movements, age of the patient, concomitant drugs, medical conditions and potential risk of adverse effects. Only Botulinum Toxin in cervical dystonia and high dose tri-hexy-phenedyl in generalized and segmental dystonia have reached level A evidence of efficacy. The overall choice of therapy is often guided by personal experience with established regimen or of open label trials. Focal and segmental dystonia are more likely to be treated with local therapies (Botulinum Toxin injections and physiotherapy) whereas more severe and generalized dystonias are more likely to receive oral medications before any possibilities of surgery.

Physical and Supportive Therapy:
It is important to emphasis the role of patient education and supportive care, which are integral components of a comprehensive approach to patients with dystonia. Physical therapy and well fitted braces are designed primarily to improve posture and to prevent contracture, and braces may be used in some cases as a substitute for a sensory trick. Various hand devices have been developed in an attempt to help patients with writer’s cramp to use their hand more effectively and comfortably. Another technique using a repetitive task during regional anaesthesia of a weak arm in patients following
stroke, was also associated with improved hand functions. More recently tailored physiotherapy based on analysis of characteristic of dystonia has been proposed.\textsuperscript{17} This rehabilitation approach is designed as a relearning process. The first step is to use a relaxing technique until the patient can actively relax the muscles responsible for dystonic posture. The second step is to perform exercises to improve independence and precision of fingers and wrist movements. The muscles involved in the dystonic postures are trained by loops, curves, arabesques related to clinical form of writers cramp. Graphic exercises are made increasingly complex and fast. The aim of this rehabilitation is not to enable patients to write as they use to, but to help their dysgraphia evolve toward a more relaxed, more flexible and better controlled writing gesture.

Medical Treatment:

1. Dopaminergic therapy: The pharmacologic treatment of dystonia is based largely on empirical rationale rather than a scientific one, one exception is dopa responsive dystonia (DRD) in which the biochemical and genetic mechanism have been elucidated by molecular DNA and biochemical studies in patients and by studies of postmortem of brains. Many patients with DRD are initially misdiagnosed as having cerebral palsy. Some patients with DRD are not diagnosed until adulthood and family members of patients with typical DRD may present with adult onset Dopa responsive parkinsonism. So the therapeutic trial of L-Dopa should be considered in all patients with childhood onset of dystonia whether they have classic feature of DRD or not. Most patients with DRD improved dramatically even with small doses of L-Dopa but some might require doses of L-Dopa as high as 1000 mg /Day. In contrast to patients with juvenile PD, DRD patients usually do not develop L-Dopa induced fluctuations and dyskinesia.

If no improvement is noted after 3 months of therapy the diagnosis of DRD is probably in error and L-Dopa can be discontinued. Patients with L-Dopa also improve with dopamine agonist, anti-cholinergic drugs and carbamazepine.

2. Anti Cholinergic Therapy: High dose anti cholinergic medications such as trihexiphenedyl was introduced by Fahn in 1983\textsuperscript{18}, and confirmed by several groups. Treating patients with in the first 5 years of disease onset was statistically significantly more successful than delaying treatment in both children and adult. Thus starting treatment early is important. It is generally recommended to start with 5 mg a half tablet at bed time and adding a half tablet a week and slowly up-titrating upto 10 mg in 4 divided doses by the end of 4 weeks. Some patients require upto 60-140 mg / Day, but may experience dose related drowsiness, confusion, memory impairment that limit the dose. Children usually tolerate very high dosage whereas the adults do not.

3. Anti Dopaminergic Therapy: Tetrabenazine a vesicular monoamine transporter-II inhibitor (VMAT-II) has advantages over other antidopaminergic drugs in that it does not cause tardive dyskinesia although it may cause transient acute dystonic reaction.\textsuperscript{19} Risperidone D2 Dopamine receptor blocking drugs with the high affinity for 5-HT 2 receptor has been reported to be useful in 4 weeks trials. Clozapine a D4 Dopamine receptor blocker with relatively low affinity for D2 receptor and high affinity for 5HT2a receptor has been reported to ameliorate the symptoms of tardive dystonia.

4. Muscle Relaxants: High dosage oral baclofen appears to the next most effective agents for dystonia particularly in combination with high dosage anticholinergic treatment. Baclofen is a GABA-b auto receptor agonist that is used to treat spasticity, dosage range from 40-180 mg /Day. Benzodiazepines (Diazepam, lorazepam, clonazepam) may provide additional benefit for patients who response to anticholinergic drugs is unsatisfactory. Clonazepam might be particularly useful in myoclonic dystonia.\textsuperscript{20}

5. Intrathecal Baclofen: Narayan et al 1991 first sug-
gested the effectiveness of intrathecal baclofen. With in a few hours after institution of ITB infusion the pa
tients dystonia markedly improved. And this form of
therapy may be more effective when dystonia is asso-
ciated with spasticity or pain. ITB may have a role in
selected patients with dystonic storm and in selected
patients with pain and spasticity. ITB is the treatment
of choice for severe generalized secondary dystonia
after oral medication shown to ineffective. One poten-
tially serious complication of ITB is life threaten ing
intermittent catheter leakage which might not be de-
tectable by standard non invasive methods.  

6. Botulinum Toxin: The introduction of Botulinum
Toxin in clinical practice in late 1980’s revolutionized
treatment of dystonia. Most potent biological toxin
BTX has become a powerful therapeutic tool in the
treatment of neurologic , ophthalmic and other dis-
ease with abnormal excessive inappropriate muscle
contraction. In 1989, FDI approved this BTX-A as a
therapeutic agents in strabismus, blepharospasm
and other facial nerve disorder including hemifacial
spasm. In 2000 FDI approved BTX-A and BTX-B as
treatment for cervical dystonia. The therapeutic value
of BTX is ability to cause chemo denervation and to
produce local paralysis when injected in to a muscle.
BTX -A has been found to enter the neurons by bind-
ing to the synaptic vesicle protein SV-2 which act as
the BTX-A receptor. The neural membrane protein
synapto tagmin  I and II act as receptor for BTX-B and
BTX-G. The primary effect of BTX is to induce paraly-
sis of injected skeletal muscle especially the most
actively contracting muscle. BTX paralyses not only
the extrafusal fibers but also the intrafusal fibers thus
decreasing the activity of Ib afferent. This might ex-
plain the effect of BTX on reciprocal inhibition. BTX
corrects the abnormal reciprocal inhibiton by increas-
ing the 2nd phase possibly through the effects on mus-
cle afferents. BTX injections are usually considered
as a treatment of choice in segmental or generalized
dystonia.

Surgical Treatment:

1. Thalamotomy: Moderate to marked clinical benefit
in patients with generalized and focal dystonia has
been reported after thalamotomy together with a high
incidence of dysarthria/ dysphonia with bilateral les-
sions. Remarkable benefit has been noted in patients
with writers cramp and musicians dystonia.

2. Pallidotomy: Remarkable improvement has been
noted in unilateral and bilateral pallidotomy with some
loss of benefit over time.

4. Peripheral Surgery: Selective denervation proce-
dures are considered efficacious and safe in cervical
dystonia. The clinical improvement has been reported
to be approximately 70%

Deep Brain Stimulation:

1. Thalamic stimulation: VA and VP nuclei of thala-
mus can be targeted by DBS in patients with second-
ary dystonia, patients with dystonic tremor and in the
case of pallidal stimulation failure.

2. Pallidal stimulation: The GPi is presently consid-
ered the target of choice for DBS treatment in gener-
alized segmental dystonia and various clinical trials
provide evidence that bilateral GPi DBS is effective in
treating primary dystonia. The clinical improvement
has been reported to be 40-70% in generalized and
segmental dystonias.

3. Subthalamic stimulation: The subthalamic nuclei
has been reported more recently to be another effec-
tive target in improving generalized, segmental and
focal dystonias.

SUMMARY: Secondary dystonias are common in our population
when compared to western population. There are cer-
tain specific forms of focal dystonias which are com-
monly seen in our population. Diagnosis mostly de-
pends on clinical characteristic of the dystonia, though
imaging studies help to identify the etiologic causes for
secondary dystonias. Identification of genetic loci is pos-
sible in genetically inherited dystonias. High dose anti-
cholinergic drugs, dopa active drugs, baclofen and oth-
er medications are useful in these patients along with
physical and occupational therapies. Patients with seg-
mental or generalized dystonia of childhood onset ini-
tially started on L-DOPA upto 1000 mg/ day have
show significant responses. If ineffective after 3
months of initiation, a high dose anti cholinergic thera-
py eg. Trihexiphenidyl can be of use and could be ti-
trated to a highest tolerated level. Some patients in our
practice require Baclofen, BZD, Carbamazepine and
tetrabenazine in resistant variants. Botox therapy in-
jections may be helpful in controlling most disabling
symptoms of segmental and generalized dystonia and
are considered treatment of choice. In some patients
 treatment might be supplemented by other drugs or by
surgical peripheral denervation. DBS should be re-
served only for patients whose symptoms are con-
tinued to be disabling despite optimal medical therapy.
Finally it is important to emphasize that early identifi-
cation and correct diagnosis of appropriate types of
dystonia and treatment with appropriate drug dosages
and in selected patients surgical modalities may be
useful in ameliorating the symptoms of dystonia.

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