Movement Disorders
Part II

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CLASSIFICATION
OF
MOVEMENT DISORDERS

Classification of Movement Disorders

I. Hypokinesias

- Primary Parkinsonism (Parkinson Disease).
- Secondary Parkinsonism.
- Parkinsonism plus syndromes.

II. Hyperkinesias

- Chorea.
- Dystonias.
- Athetosis.
- Hemiballismus.
- Tics.
- Myoclonus.

Chorea

Chorea

- **Chorea refers to** involuntary, irregular, purposeless, nonrhythmical, abrupt, rapid, unsustained movements that flow from one body part to another.
- **When mild**, chorea can be difficult to differentiate from restlessness.
- **When chorea is proximal and of large amplitude**, it is called ballism.
- **Chorea is usually worsened by** anxiety and stress and subsides during sleep.
- **The majority of patients attempt to hide chorea** by integrating it into a purposeful activity (pseudopurposeful).
- **Chorea may be the expression of a wide range of disorders**, including metabolic, infectious, inflammatory, vascular, and neurodegenerative, as well as drug induced syndromes. (i.e. chorea is a symptom).
- **Whereas ballism** is most often encountered as hemiballism due to contralateral structural lesions of the subthalamic nucleus and/or its afferent or efferent projections.

Etiological Classification of Chorea

1 - Developmental and aging choreas

Physiological chorea of infancy	Senile chorea

2 - Infectious Causes

Sydenham's chorea	
Various other infections and postinfectious encephalitides, including Creutzfeldt-Jakob disease	

3 - Hereditary choreas

Huntington's disease	Benign hereditary chorea	Neuroacanthocytosis
Neurometabolic disorders: Wilson's disease, Lesch-Nyhan disease.		

4 - Drug-induced choreas

Antipsychotics (tardive dyskinesia)		Amphetamines	Tricyclic
Antiparkinsonian drugs	Contraceptives	Anticonvulsants	Anticholinergics

5 - Toxin-induced choreas

Alcohol intoxication and withdrawal		Anoxia	Carbon Monoxide
Mn	Hg	Thallium	Toluene

6. Metabolic causes

Hyperthyroidism	Hypoparathyroidism	Pregnancy (chorea gravidarum)
Hyper- and hyponatremia, hypomagnesemia, hypocalcemia		Nutritional—for example, beriberi, pellagra

Sydenham's

(Post-streptococcal , Rheumatic)

chorea

Sydenham's chorea (SC)

- **Sydenham chorea (SC)** is confined largely to prepubertal children (in girls more than boys) and almost never seen below the age of 5 years (typically 5-15 years).
- **It is the most common cause** of acute chorea in children worldwide.
- **SC is an autoimmune disorder** that may follow a group A beta-hemolytic streptococcal infection.
- **SC is a major criterion for the diagnosis** of acute rheumatic fever, and may be its first or only manifestation. One fifth of children with rheumatic fever will develop SC.
- **SC is now rare in developed countries,** following the introduction of wide spread antibiotic use. It is still found in developing countries.

Pathology of Sydenham's chorea

- **Most typically, Sydenham's chorea** is associated with infection and other sequelae of rheumatic fever.
- **Though the molecular etiology of SC is still uncertain,** it is clear that patients with SC have antibodies that bind antigens on the surface of basal ganglia neurons.
- **Consistent with this molecular specificity**, MRI and positron emission tomography (PET) scans may demonstrate changes limited to the basal ganglia.
- **Autopsy studies of patients with Sydenham's chorea** reveal edema, chromatolysis, and atrophy that affect primarily the striatum, but the cortex, thalamus, and other basal ganglial nuclei may be variably involved as well.

Clinical Picture of Sydenham's chorea

- **Sydenham's chorea (SC) presents** abruptly with neurological and psychological symptoms up to 6 months after a streptococcal pharyngitis.
- **SC is characterized by:**
  - **Chorea (which can include facial grimacing),**
  - **Hypotonia**
  - **Muscle weakness**
  - **Gait disturbance**
  - **Difficulty with writing and speaking.**
- **The chorea generally develops subacutely** and is usually bilateral, although 20–30% can have hemichorea.
- **It occurs at rest or with activity** but remits during sleep.
- **An important distinguishing clinical feature** is spooning of the fingers (hyperextension at the metacarpophalangeal joint upon extension of the arms).
- **The muscle weakness of SC presents** as an inability to do a continuous contraction, known as a "milkmaid's grip," in which patients relax and tighten their fists intermittently when asked to grip the examiner's fingers.

Clinical Picture of Sydenham's chorea

- **The chorea leads to disturbance of gait**, dropping of objects, and dysarthric speech.
- **Neuropsychiatric signs such as** emotional lability, dysfunction personality changes, obsessive-compulsive signs, anxiety, and attention deficit often precede the chorea.
- **These neuropsychiatric signs occur frequently**, and can lead to major dysfunction.
- **Physical examination typically consists of** four different motor tests: spooning, touchdown, milkmaid's grip, and darting tongue.
- **These four maneuvers typically expose** the characteristic movements of SC.
- **Exam should also search for other manifestations of acute rheumatic fever** including carditis, migratory polyarthritis, subcutaneous nodules, and erythema marginatum

Clinical Picture of Sydenham's chorea

1) **Spooning -** patient seated with arms fully extended forward from shoulders with pronated hands and fingers spread. Typical finding is symmetric hyperextension of the MCP joint (so the arms and hands look like spoons)
2) **Touchdown** - patient raises arms and hands up fully extended with palms facing one another. Typical finding is pronation of one or both hands and flexion of the elbows
3) **Milkmaid's grip** - patient grips examiner's index and middle fingers. Typical finding is partial release of grip and re-gripping, as if "milking the cow"
4) **Darting tongue** - patient sticks tongue out from mouth. Typical finding is tongue alternately withdrawing and protruding because patient cannot maintain the motor command.

- **Generally, there should be no sensory loss** on examination.
- **Gait is typically described as unsteady** due to the chorea in the muscles that enable movement.

Investigations for Sydenham's chorea

- **Diagnostic evaluation should be aimed at** diagnosing acute rheumatic fever.
- **Testing should be completed to look for** Group A streptococcal infection, along with cardiac evaluation.
  1. **Throat culture for Group A streptococcal infection.**
  2. **Serum testing for antistreptolysin O (ASOT)**
  3. **CRP, ESR**
  4. **Cardiac workup including ECG and echo**
  5. **Consider LP and/or neuroimaging if considering alternative diagnoses.**

N.B. ***Since SC may follow streptococcal infection by as much as 6-8 months***, *throat cultures, serum antibody titers (ASOT), and inflammatory markers (ESR and CRP) are often negative at the time symptoms develop*

Treatment of Sydenham's chorea

The condition is self limited within five to 16 weeks, but recurs in 20% of patients. It has a good prognosis for full recovery so treatment of chorea (while still treating the causative streptococcal infection) is not warranted in most cases.

I. Chronic antibiotic therapy to minimize recurrence and risk of heart disease.

- Length of therapy depending on risk of recurrence and severity of disease
- Long acting Penicillin is preferred agent (usually given IM every 21-28 days)

II. During the period of marked chorea

A. Symptomatic treatment of chorea

1) Antiepileptic medications (valproate or carbamazepine).
2) Dopamine-blocking agents (haloperidol)

B. Anti-inflammatory medications: Because of the autoimmune pathogenesis of SC, anti-inflammatory medications such as salicylates and corticosteroids can effectively reduce movement abnormalities.

III. In severe resistant cases: options ranging from prednisone to IVIG and plasmapheresis

Differential Diagnosis Of Choreic Movement

1. **Sydenham's chorea**
2. **Huntington's disease:** Autosomal dominant disorder. Prevalence of 4–8 per 100 000 people. Age of onset: 40 years (5% juvenile onset at 20 years). Choreic movements and hypotonia. Personality and mood changes, psychosis, and dementia are common. Rigidity, hypokinesia, and dystonia are common in juvenile onset cases. Relentlessly progressive with mean duration of 17 years.
3. **Neuroacanthocytosis:** A multisystem degenerative disorder. Variable mode of inheritance. Age of onset: approximately 30 years. Chorea as well as orofacial-lingual dystonia are prominent. Axonal neuropathy in 50% of cases. Presence of acanthocytes on peripheral blood smears. Relentlessly progressive (mean duration 15 years).
4. **Chorea gravidarum** or chorea occurring during pregnancy is an increasingly rare disorder. Affected patients usually have the previous episodes of chorea associated with the use of oral contraceptives or history of rheumatic fever

Dystonia

Dystonia

- **Dystonia is defined as** a movement disorder characterized by sustained or intermittent muscle contractions causing abnormal, often repetitive, movements, postures, or both.
- **Dystonic movements are caused by co-contraction of agonist and antagonist muscles that can manifest as:**
  - **Abnormal postures** that are typically mobile (not fixed) with or without twisting movements
  - **Slow writhing movements**
  - **Dystonic tremor**
- **Dystonia is classified along two axes:**
  1) **Clinical characteristics**, (including age at onset, body distribution, etc.)
  2) **Etiology.**

Classification of Dystonia

- **Classification of Dystonia by age at onset:**
  - **Infancy** (birth to 2 years)
  - **Childhood** (3–12 years)
  - **Adolescence** (13–20 years)
  - **Early adulthood** (21–40 years)
  - **Late adulthood** (>40 years)
- **Classification of Dystonia by body region affected (Body distribution):**
  1. **Focal dystonia.** Only one body region is affected. e.g. blepharospasm, oro-mandibular dystonia, cervical dystonia, and writer's cramp.
  2. **Segmental dystonia.** Two or more contiguous body regions are affected. e.g. cranial dystonia (blepharospasm with lower facial and jaw or tongue involvement).
  3. **Multifocal dystonia.** Two or more non-contiguous body regions are involved.
  4. **Generalized dystonia.** The trunk and at least two other sites are involved.
  5. **Hemidystonia.** More body regions restricted to one body side are involved. e.g. hemidystonia due to acquired brain lesions in the contralateral hemisphere.

❑Classification of Dystonia by Etiology:

I. **Inherited** (dystonias of proven genetic origin)
   1) **Autosomal dominant**; e.g. DYT1, DYT5b (dopa responsive dystonia), Huntington disease.
   2) **Autosomal recessive**; e.g. Wilson disease
   3) **X-linked**
   4) **Mitochondrial**

II. **Idiopathic** (unknown cause)
   1) **Sporadic**
   2) **Familial**

III. **Acquired** (dystonia due to a known specific cause)
   1) **Perinatal brain injury:** dystonic cerebral palsy
   2) **Infection**: viral encephalitis
   3) **Drug**: neuroleptics (dopamine receptor blocking drugs)
   4) **Toxic**: manganese, cobalt, carbon disulfide, cyanide
   5) **Vascular:** ischemia, hemorrhage, arteriovenous malformation
   6) **Neoplastic:** brain tumor, paraneoplastic encephalitis
   7) **Brain injury:** head trauma, brain surgery, electrical injury
   8) **Psychogenic** (functional)

N.B

- *The term "primary" is currently used as an etiological descriptor for genetic or idiopathic cases where dystonia is isolated and there is no consistent pathologic change*
- *Idiopathic forms may be reclassified as inherited, as new dystonia genes are recognized*

Inherited Dystonias

Type	Affected Chromosome Arm	Clinical Features	Mode of Inheritance
DYT1	9q34	Early onset, generalized; starts in a limb	AD
DYT2	Not known	Early onset, generalized or segmental	AR
DYT3	Xq13.1	Approximately 50% of patients with parkinsonism	X-linked
DYT4	Not known	Whispering dysphonia	AD
DYT5a	14q22.1-22.2	Onset in the first decade of life; starts distally in the leg and spreads to the proximal limb; diurnal fluctuation; dopa-responsive mutations in the guanosine triphosphate (GTP) cyclohydrolase I and tyrosine hydroxylase genes	AD
DYT5b	11p15.5	Dopa-responsive dystonia	AR
DYT6	8p21-22	Onset in adolescence; segmental	AD
DYT7	18p	Adult onset, focal (writer's cramp, torticollis, dysphonia, blepharospasm)	AD
DYT8	DYT82q33-25	Paroxysmal dystonia-choreoathetosis triggered by stress, fatigue, alcohol	AD
DYT9	1p21-13.8	Paroxysmal dystonia; paresthesias, diplopia; spastic paraplegia between attacks	AD
DYT10	Not known	Paroxysmal dystonia-choreoathetosis precipitated by sudden movements	AD
DYT11	11q23	Myoclonus and dystonia	AD
DYT12	19q	Rapid-onset dystonia and parkinsonism	Not known

Primary Dystonia

- **Primary dystonia (Primary torsion dystonia)** is defined as a syndrome in which dystonia is the only clinical sign, and there is no evidence of neuronal degeneration or an acquired cause by history or routine laboratory assessment.
- **Several genes** have been mapped for primary dystonia, e.g. DYT1, 2, 4, 6, 7, etc.

A. Late-onset focal and segmental Primary dystonia.

- The disease usually begins in mid-adulthood and usually starts with focal onset.
- Focal forms include:
  - **Cervical dystonia:** Variable involvement of cervical muscles results in an abnormal head, neck, and shoulder positions, most frequently involving horizontal turning (torticollis) and dystonic head tremor.
  - **Blepharospasm** is caused by dystonic contractions of the orbicularis oculi.
  - **Oromandibular dystonia** affects the jaw muscles, with prominent jaw opening or closing.
  - **Writer's cramp** is a task-specific dystonia, triggered by writing.

B. Early-onset generalized Primary dystonia :

- Dystonia beginning in childhood often progresses to generalized involvement, sometimes quite rapidly.

Dopa-responsive Dystonia

- **Dopa-responsive dystonia** typically begins in childhood or adolescence, most often with walking difficulties.
- **Symptoms worsen towards the evening** and improve in the morning after sleep (Diurnal variation).
- **Show a highly positive and sustained** response to levodopa.
- **Patients often experience a delay** between symptom onset and a correct diagnosis

Evaluation of Dystonia

- **The diagnosis of primary dystonia should be considered in** any patient with an abnormal posture and a family history of variable problems with cramps, spasms, and tremors.
- **Gather information about** age at onset, initial and subsequent areas of involvement, course and progression of disease, tremor or other movement disorders, possible birth injury, developmental milestones, and exposure to neuroleptic medications, as well as a family history of dystonia, parkinsonism, or other movement disorders.
- **Consanguinity**.
- **The ceruloplasmin level should be obtained in** all patients in whom onset of dystonia occurs before the age of 50 since Wilson's disease is highly treatable.
- **Other blood tests, including genetic tests**, depend on the clinical setting.
- **A brain MRI scan** is important in the evaluation of structural abnormalities.
- **Skull, neck, and spine evaluations** may be needed if there is evidence of a secondary myelopathy or scoliosis due to axial dystonia.

Treatment of Dystonia

1. **All patients with childhood-onset dystonia** deserve a trial of levodopa, for exclusion of dopa-responsive dystonia.
2. **Anticholinergics** such as trihexyphenidyl, benztropine, biperidin.

   In treating primary dystonia, high-dose anticholinergic therapy may be effective in ameliorating dystonia, particularly in younger patients. However, many patients are unable to tolerate such high doses because loss of memory, hallucinations, blurring of vision, and other anticholinergic side effects may occur.
3. **Muscle relaxants** such as baclofen, benzodiazepines, chlorzoxazone, cyclobenzeprine, etc.

   Many patients derive at least partial benefits, especially those with pain from uncontrolled muscle pulling.
4. **Intramuscular injections of botulinum toxins** are effective treatment for focal dystonia.
5. **Other medications**

   A wide variety of other drugs have been advocated for specific forms of dystonia. For example, carbamazepine and other anticonvulsants.
6. **Surgical Interventions**

   Multiple surgical interventions are available for the treatment of the dystonias. Typically these more invasive approaches are reserved for patients who fail more conservative therapies.

Wilson's Disease (Hepatolenticular degeneration)

- **Wilson disease** (WD) is an inherited disorder (autosomal ressive) of copper metabolism caused by pathological copper accumulation in many organs, particularly the liver and brain.
- **In Wilson's disease, ceruloplasmin levels** will usually be low, but urinary excretion of copper will be high.
- **Ceruloplasmin is a serum ferroxidase** responsible for 90% of copper transport. It is well known for its role in the pathogenesis of Wilson disease.

EPIDEMIOLOGY

- **WD occurs** in approximately 1 in 40,000 people.
- **Although the disorder may not become clinically evident** until the fourth or fifth decade of life, the initial presentation most often appears in the early 20s.

Clinical Presentation of Wilson's Disease

I. **Hepatic manifestations.**

Liver disease can be the first clinical manifestation (40–60%) of WD but may accompany other symptoms. A wide spectrum of hepatic presentation.

II. **Neurological manifestations**

different movement disorders. clinical forms are those with a predominance of tremor, dystonia, and parkinsonism, all of which are often associated with dysarthria, gait and posture disturbances, and dysphagia.

1) **Tremor**

A characteristic and frequent neurological symptom of WD is tremor, which is experienced by up to 55% neurological WD patients at diagnosis. It can be resting, postural or kinetic.

2) **Dystonia**

Dystonia is reported as the first WD symptom in 11–65% of patients. It can be focal, segmental, multisegmental, or even generalised. The most characteristic WD dystonic presentation is abnormal facial expression or risus sardonicus, which presents as a fixed smile due to dystonia of the risorius muscle.

3) **Parkinsonism**

Parkinsonism occurs in 19–62% of WD patients and usually presents as symmetric bradykinesia, rigidity, gait and posture disturbances.

IV. **Other neurological symptoms**, e.g. Ataxia occurs in 30% of WD patients, Chorea occurs rarely in patients with WD (6–16%).

IV. **Psychiatric manifestations.** can occur before, concurrent with or after the diagnosis of WD.

V. **Ophthalmological manifestations**. e.g. the Kayser-Fleischer ring

Wilson's Disease

Investigations

I. **All patients should be evaluated** by an ophthalmologist (slit-lamp examination) for the presence of the Kayser-Fleischer ring.

II. **Serum ceruloplasmin** is decreased.

III. **24-hour urinary copper excretion** is increased.

IV. **A liver biopsy** with measurement of hepatic parenchymal copper concentration is required if the clinical signs and noninvasive tests do not allow a final diagnosis or if there is suspicion of other or additional liver pathology.

V. **Brain MRI** may show the "face of the panda" sign in the midbrain.

Treatment

drugs that create negative copper body balance

I. **Chelators (d-penicillamine)** that increase urinary copper excretion.

II. **Zinc salts** that decrease copper absorption from the digestive tract.

Tics
Athetosis
Ballism
Myoclonus

Tics

- **Tics are defined as** simple or complex repetitive stereotyped movements that occur out of background of normal motor activity.
- **Types of tics:** Tics can be divided into abnormal movements (motor tics), abnormal sounds (vocal tics), and combinations of the two.
  1. **Simple motor tics**, such as frequent eye blinking, facial grimacing, head jerking, or shoulder shrugging.
  2. **Complex motor tics** include squatting, hopping, skipping, hand shaking.
  3. **Simple vocal tics** such as throat clearing, sniffing, grunting, snorting, hissing, barking, or other noises.
  4. **Complex vocal tics** include semantically meaningful utterances, including shouting of obscenities and profanities (coprolalia).
- **When** childhood-onset tics are multifocal, motor, and vocal, last longer than 1 year, and naturally wax and wane, the term **Gilles de la Tourette syndrome (GTS)** is applied.
- **Tics can be voluntarily** suppressed for seconds to minutes.
- **Tics respond to** dopamine-blocking drugs (neuroleptics).

Athetosis

- **Athetosis refers to** slow, writhing, continuous movements.
- **The speed of these involuntary movements** can sometimes be faster and blend with those of chorea, and the term choreoathetosis is used.
- **Athetosis most commonly occurs as a result of** injury to the basal ganglia in the neonatal period or during infancy.
- **When athetosis occurs in infants**, the movements are slow and twisting.
- **In adults, athetosis is usually** unaccompanied by posturing and its speed approaches that of chorea (choreoathetosis).

Ballism

- **Ballism refers to** very large amplitude choreic movements.
- **When involving proximal musculature,** these high amplitude motions of the limbs are demonstrated by flinging and flailing movements due to the speed of choreic movements.
- **Ballism is most frequently unilateral**, and this form is referred to as hemiballism**.**
- **This disorder is usually the result of a lesion** of the contralateral **subthalamic nucleus** or multiple small infarcts (lacunes) in the contralateral striatum.
- **In rare instances, ballism occurs bilaterally** (biballism) due to bilateral lacunes in the basal ganglia.
- **Like chorea, ballism sometimes** occurs as a result of overdosage of levodopa.

Myoclonus

- **Myoclonus is defined as** rapid, brief, jerky, or shock-like movements involving muscle or group of muscles.
- **Among all hyperkinetic movement disorders, Myoclonus** is considered to be the most rapid and brief.
- **When caused by sudden muscle contraction**, it is known as "positive myoclonus," **while a brief loss of muscular tone** results in "negative myoclonus" as in asterixis.
- **Myoclonus is classified in different ways** according to its physiology, anatomical site of origin, and etiology.
- **Myoclonus can be** focal, multifocal, segmental, or generalized, and can be one of the signs in a wide variety of nervous system disorders.
- **Myoclonus can arise from several levels in the nervous system**, ranging from the cerebral cortex to the peripheral nerves.

تمت بفضل الله

Thank you