Overview Of Movement Disorders

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Head of Ain Shams Movement Disorders Group
Chair of African Education Committee of Movement Disorder Society
Member of MDS Africa Executive Committee
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Fellow of University Colleague of London
Objectives

1. Identify definitions & clinical phenotypes of MDs.
2. Recognize common types of other MDs.
3. Identify the clinical picture of Parkinson’s disease.
4. Recognize tools of treatment of PD.
What are Movement Disorders?

**MOVEMENT DISORDERS**

**Hypokinetic MD**
- Parkinson's disease
- Atypical Parkinsonism
- Progressive Supranuclear Palsy
- Corticobasal degeneration
- Multiple System Atrophy
- Dementia with Lewy Body

**Hyperkinetic MD**
- Dystonia: sustained or intermittent muscle contractions causing abnormal-often repetitive-movements, postures, or both.
- Chorea: irregular rapid, low amplitude, brief movements of extremities & face
- Athetosis: involuntary writhing movements
- Hemiballism: large amplitude involuntary movement restricted to one side of the body; usually involves proximal upper limb
- Myoclonus: sudden brief jerk or shock-like movements
- Tremor: rhythmic oscillation of a body part due to alternating or synchronous contractions of opposing muscles
- Tics: sudden, brief, purposeless, stereotyped simple or complex movements or vocalizations, with urge
- Akathisia: inner restlessness; often associated with external signs of restless behavior

**Restless legs Syndrome:** an urge to move the legs, usually accompanied by uncomfortable and unpleasant sensations in the legs, begin or worsen during periods of rest or inactivity, partially or totally relieved by movement, worse in the evening.

**Characteristics of Hyperkinetic MDs**

<table>
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**RLS**
- An urge to move the legs, usually accompanied by uncomfortable and unpleasant sensations in the legs, begin or worsen during periods of rest or inactivity, partially or totally relieved by movement, worse in the evening.
Parallel Organization Of Motor & Non-motor Basal Ganglia Loops

Body movements: Motor loop
- Primary motor, premotor, supplementary motor cortex
- Motor, premotor, somatosensory cortex
- Cortical input

Eye movements: Oculomotor loop
- Frontal eye field, supplementary eye field
- Posterior parietal, prefrontal cortex
- Striatal input

Attention, planning: Prefrontal loop
- Dorsolateral prefrontal cortex
- Dorsolateral prefrontal cortex
- Pallidal input

Emotions, motivation: Limbic loop
- Anterior cingulate, orbital frontal cortex
- Amygdala, hippocampus, orbitofrontal, anterior cingulate, temporal cortex
- Thalamic input
Parkinson's Disease
(Hypokinetic Movement)

- Decreased output of SNc dopaminergic projections
  - Decrease excitation in direct pathway
  - Increase inhibition in indirect pathway
- Net effect: more inhibition of thalamus and therefore less excitatory input to motor cortex

![Diagram of neural pathways](image-url)
NEUROTRANSMITTERS

- Dopamine (-): substantia nigra to corpus striatum
- ACh (+): intrastriatal putamen –caudate circuit.
- GABA (-): from corpus striatum to globus pallidus and substantia nigra. Globus pallidus to thalamus.
- Norepinephrine, serotonin, enkephalin from basal ganglia to brain stem
- Glutamate from cerebral cortex to corpus striatum, from thalamus to cerebral cortex.
Parkinsonism is defined as *bradykinesia*, in combination with at least 1 of *rest tremor* or *rigidity*.

MDS Clinical Diagnostic Criteria for PD
Postuma et al 2015

- Parkinsonism – bradykinesia plus either rigidity or rest tremor1
- Clinically established PD:1
  - Absence of absolute exclusion criteria; at least 2 supportive criteria; no ‘red flag’

**Primary**

- Idiopathic Parkinson’s disease
- Atypical Parkinsonism
- Heredodegenerative Parkinsonism

**Secondary**

- Progressive Supranuclear Palsy
- Corticobasal degeneration
- Multiple System Atrophy
- Dementia with Lewy Body

**Supportive criteria**:1

- A clear and distinct positive response to dopaminergic therapy
- Corticobasal syndrome
- Documentation of normal tone at least at 1 visit
- A positive diagnostic test of either auditory loss or cardiac sympathetic denervation on sonography

**Absolute exclusion criteria**:1

- Comella sign
- Supranuclear gaze palsy
- Established diagnosis of PD
- Parkinsonism restricted to the lower limbs only for >3 years
- Treatment with an anticholinergic, or with dopamine-depletion agents
- Presence of tremor in infancy
- Sensory-cortical loss
- No evidence for dopaminergic deficiency on functional imaging
- Other Parkinsonism-inducing condition

**Red flags**:1

- Rapid deterioration of gait
- Absence of motor symptom progression over 5 years
- Early autonomic failure
- Respiratory dysfunction
- Early onset ataxia
- Early severe autonomic failure
- Early recurrent falls due to inattention
- Diagnospecific ataxia
- Absence of common motor features of disease during 19 years
- Pyramidal tract signs
- Bilateral symmetric presentation

**Vascular (e.g., white matter disease)**
- Drug-induced (e.g., neuroleptics)
- Metabolic (e.g., uremia)
- Infectious (e.g., HIV, syphilis, Whipple, Lyme, prion)
- Endocrine (e.g., hyperparathyroidism, hypothyroidism)
- Autoimmune (e.g., Hashimoto disease, collagen disease)
- Toxic (e.g., CO poisoning, manganese, MPTP)
- Paraneoplastic (e.g., CRMP5 antibody)
- Nutritional (e.g., vitamin B1, B12 deficiency)
- Normal pressure hydrocephalus
Parkinson’s Disease

- PD prevalence 1% of populations older than 65 years (Abbas et al., 2018)
- From 1990 to 2015, the number of PD patients doubled to over 6 million, and double again to over 12 million by 2040 (Dorsey et al., 2018)
- Aging populations, increasing longevity, decreasing smoking rates, and the by-products of industrialization
Parkinson’s Disease (PD)

- **Incidence:** increases dramatically with age, onset 50 - 60 years old.
- Overall incidence: 15 -25/100.000.
- 4-10% have onset before 40 years old.
  - *Young onset PD; onset before 40 or 50 years old.*
  - *Juvenile onset PD; onset before 20 years old.*
- PD is sporadic disease, rarely familial due to single gene mutations (Parkin, SNCA, LARRK).
- Susceptibility genetic loci: ↑↑ risk of PD (HLA DR, HLA DQ, SNCA, LRRK2, PARK 16), or risk (MAPT).
Genetic Diversity

**undiscovered genetic factors**

- A genetically confirmed PD kindred from the East African region (North Tanzania) due to a homozygous PRKN deletion (Dekker et al, 2020)
- In Nigeria, a few genetic studies have also been conducted and did not detect pathogenic mutations in PRKN (parkin), LRRK2, and ATXN3 (Okubadejo et al, 2008, 2018; Oluwole et al, 2020)
  - a PTRHD1 mutation was identified in a Xhosa family with Parkinsonism and intellectual disability (Kuipers et al, 2018)
  - LRRK2 in Arabic barber in Tunisia (40%), not present in Nigeria, Ghana, Tanzania, Zambia.
- Genetic studies in African populations have the potential to be of great benefit for PD research globally but have largely been unexplored.
Neuropathology of PD

Poewe, W. et al. (2017) Parkinson disease
Ubiquitin-dependent proteasomal proteolysis

System failure

Susceptibility
- Expression of UPS components
  - Age-related UPS activity
  - Oxidative dopamine metabolism

Toxic processes
- Oxidative stress
- Mitochondrial dysfunction
- Toxins

Gene mutations
- α-synuclein
- Parkin
- UCH L1
- LRRK2

Protein accumulation

Cell dysfunction

Lewy body formation

Cell death

Clinical Picture

• insidious onset, progressive course.
• Start unilateral then bilateral → Usually Asymmetric

Bradykinesia or akinesia:
Difficulty in initiation and slowness of voluntary movements.
Decreased facial expression → mask faced, infrequent blinking. Decreased adjustment of posture.

Rigidity: 2 types:
1. *Lead pipe*: present all throughout the movement.
2. *Cog wheel*: lead pipe interrupted by tremors.
• Proximal > distal, flexors and extensors.
• Affects muscles of limbs > neck, and trunk → flexed posture (gorilla like attitude).
PD Tremor

• Regular, rhythmic oscillatory involuntary movements.
• At rest, ± postural (reemergent tremor), distal > proximal.
  Affect mainly ULs, neck, jaw and LLs.
• Special characters: coarse, at rate of 4-8 c/s:
• Increased by stress, and emotions.
  Decreased by sleep and voluntary movements.
• Pill rolling: thumb & fingers are moving parallel & opposite to each
  [thumb (flexion & extension), fingers (abduction & adduction)].
Others

- **Gait:** shuffling, short steppage, and festinant gait (running to reach the center of gravity).
- **Loss of emotional and associated movements:** specially swinging of the arms during walking.
- **Loss of postural reflexes;** retropulsion and propulsion.
- Freezing phenomenon.
- The Myerson’s sign, or glabellar tap sign
- Monotonous speech, micrographia, striatal hands.
Non-motor symptoms of Parkinson’s disease: Patient burden

- Postural hypotension
- Sialorrhea
- Dribbling of saliva, dysphagia and choking, reflux, constipation
- REM sleep behavioral disorders, restless legs, insomnia
- Sensory disorders
- Autonomic dysfunction
- Gastrointestinal disorders
- Sleep disorders
- Orthostatic hypotension
- Pain, paraesthesia, olfactory disturbance
- Neuropsychiatric disorders e.g. psychosis, depression, anxiety and dementia
- Urologic disorders
Non-Motor Symptoms as Predictors of Quality of Life in Egyptian Patients With Parkinson’s Disease: A Cross-Sectional Study Using a Culturally Adapted 39-Item Parkinson’s Disease Questionnaire

Ali S. Shalash¹*, Eman Hamid¹, Hanan Hani Elrassas², Ahmed Safwat Bedair¹, Abdelrahman Ibrahim Abushouk³, Mohamed Khamis¹, Mostafa Hashim², Nahed Salah-Elzin Ahmed¹, Samia Ashour¹ and Mahmoud Elbalkimy¹

¹Department of Neurology, Faculty of Medicine, Ain Shams University, Cairo, Egypt, ²Faculty of Medicine, Okasha Institute of Psychiatry, Ain Shams University, Cairo, Egypt, ³Faculty of Medicine, Ain Shams University, Cairo, Egypt
The frequency and severity of individual non-motor symptoms in the enrolled Parkinson's disease patients. Shalash et al. Front Neurol 2018

Non-Motor Symptoms as Predictors of Quality of Life in Egyptian Patients With Parkinson’s Disease: A Cross-Sectional Study Using a Culturally Adapted 39-Item Parkinson’s Disease Questionnaire

OPEN ACCESS

Shalash et al Front Neurol 2018
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Postuma et al 2015

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- Clinically established PD:
  - Absence of absolute exclusion criteria; at least 2 supportive criteria; no ‘red flags’

**Absolute exclusion criteria**
- Cerebellar signs
- Supranuclear gaze palsies
- Established diagnosis of BVFTD
- Parkinsonism restricted to the lower limbs only for >3 years
- Treatment with an antidopaminergic, or with dopamine-depletion agents
- Absence of response to levodopa
- Sensory–cortical loss
- No evidence for dopaminergic deficiency on functional imaging
- Other parkinsonism-inducing condition

**Red flags**
- Rapid deterioration of gait
- Absence of motor symptom progression over 5 years
- Early bulbar dysfunction
- Respiratory dysfunction
- Early severe autonomic failure
- Early recurrent falls due to misbalance
- Disproportionate anterocollis
- Absence of common non-motor features of disease during >5 years
- Pyramidal tract sings
- Bilateral symmetric presentation

**Supportive criteria**
- A clear and dramatic positive response to dopaminergic therapy
- Levodopa-induced dyskinesia
- Documentation of resting tremor of a limb
- A positive diagnostic test of either olfactory loss or cardiac sympathetic denervation on scintigraphy

Specificity at least 90%
Clinical symptoms associated with PD progression

Poewe, W. et al. (2017) Parkinson disease
Differential Diagnosis of PD:

1. **Essential tremors**: AD, kinetic, and/or postural, absent at rest and increase with movement.

2. **Atypical Parkinsonian (Parkinsonism Plus) Syndromes**: include:
   - **Progressive supranuclear palsy (PSP)**: characterized by symmetrical akinetic rigid syndrome, early falling, supranuclear gaze palsy, dysarthria, dysphagia, and pyramidal dysfunction.
   - **Multiple system atrophy (MSA)**: characterized by variable presentations of parkinsonism, cerebellar and pyramidal signs, and autonomic dysfunction.
   - **Corticobasal degeneration (CBD)**: Asymmetrical rigidity & bradykinesia, dystonia, myoclonus, Progressive aphasia, progress to dementia, Cortical sensory loss.
   - **Dementia with Lewy bodies (DLB)**.
Differential Diagnosis of PD:

3) **Vascular parkinsonism:**

   Old age, risk factors of stroke, gradual or stepwise onset.

   Rigidity is predominant, pyramidal signs.

   Early and severe gait disturbance with falling.

   Mainly affecting lower limbs, so called lower body parkinsonism.

   Early cognitive impairment.

   Poor response to levodopa.

   Abnormal MRI brain; subcortical infarcts.

4) **Drugs and toxins (CO) induced parkinsonism.**

5) **Wilson's disease** (young onset).
TREATMENT OF PARKINSON’S DISEASE

• Medical
  • Dopaminergic agents
  • Anticholinergics
  • MAO-B inhibitors
  • Therapies of NMSs
  • Others
• Surgical
  • Ablative
  • Advanced therapies; DBS, Duodopa, apomorphine infusion.
  • Restorative
• Physical therapies
• Others: botulinum toxin, TMS
Pharmacological Treatment of PD

- Levodopa
- Dopamine Agonists
- Monoamine Oxidase-B Inhibitors
- Catechol-O-methyltransferase (COMT) inhibitors
- Others:
  - Anticholinergics
  - Amantadine
  - Clozapine
  - Istradeephyline; Adenosine A2A receptor antagonist
Treatment of Non-Motor Manifestations:

1. **Dementia**: rivastigmine, donepezil, memantine.
2. **Depression/ Anxiety**: antidepressants (SSRI, SNRI).
3. **Psychosis**: assess medication, clozapine (efficacious) or quetiapine, pimavanserin.
4. **Impulse control disorders**: reduce dopamine agonists, clozapine, and quetiapine, donepezil.
5. **Drooling**: anticholinergics, botulinum toxin.
6. **Postural hypotension**: increasing salt intake, changing position slowly, wearing elastic stockings and avoiding aggravating factors, midodrine, fludrocortisones.
7. **Constipation**: laxative, macrogol.
8. **Fatigue**: methylphenidate.
Applying Advanced Therapies, Egypt Experience

PD DBS insured in Egypt June 2021

Pre DBS

Post DBS
Availability of Therapies and Services for Parkinson’s Disease in Africa: A Continent-Wide Survey

MDJ, 2021

Eman Hamid, MD, PhD,¹ Biniyam A. Ayele, MD,² Daniel Gams Massi, MD,³ Samia Ben Sassi, MD,⁴ Houyam Tobar, MD,⁵ Emmanuel Epenge Djonga, MD,⁶ Sarah Misbah El-Sadig, MD,⁷ Wahiba AMER EL KHEDOUD, MD,⁸ Julien Razafirahafo, MSc,⁹ Ange Eric Kouame-Assouan, MD,¹⁰ Djibrilla Ben-Adji, MD,¹¹ Yilédoma Thierry Modeste Lengané, MD,¹² Abdu Kisekka Musubire, MD,¹³ Muhyadin Hassan Mohamed, MSc,¹⁴ Tiwonge Elisa Phiri, MBBS, FCN,¹⁵ Nsengiyumva Nestor, MD,¹⁶ Wael Abdulgader Alwahchi, MSc,¹⁷ Saara Ndinelago Neshuku, MBChB, FCN, MMed,¹⁸ Cassandra Ocampo, MD,¹⁹ Foksouna Sakadi, MD,²⁰ Moulid Ali Midal, MBBS,²¹ Gift Wilson Ngwende, MBChB, MMed, FCP,²² Juzor Hooker, MB, ChB, MMed, DCN, FCP,²³ Kigocha Okeng’o, MD, Med, MSc,²⁴ Augustina Charway-Felli, MD, PhD, FGCPs,²⁵ Mashari Atadzanov, PhD, FRCP,²⁶ Jonathan Carr, MBChB, PhD,²⁷ Njideka U. Okubadejo, MBChB, FMCP, FAAN,²⁸ and Ali Shalash, MD, PhD* ²⁹

• 28 countries (of 43 contacted countries).
• 51.9% of the 54 countries within Africa.
• 84.7% of the total continent population.
Availability of Levodopa in Africa

Levodopa preparation was

- Always available in 13 countries (46.4%),
- Mostly available in 13 countries (46.4%)
- Occasionally/ sometimes available in 2 countries
## Availability of Therapies and Services for Parkinson's Disease in Africa: A Continent-Wide Survey

<table>
<thead>
<tr>
<th>Therapy Type</th>
<th>ichte</th>
<th>intermittently available</th>
<th>not available</th>
<th>unknown</th>
</tr>
</thead>
<tbody>
<tr>
<td>PD support groups</td>
<td>25</td>
<td>7.1</td>
<td>57.2</td>
<td>10.7</td>
</tr>
<tr>
<td>Specialized PD Nurses</td>
<td>7.1</td>
<td>10.7</td>
<td>82.2</td>
<td>0</td>
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<tr>
<td>Specialized PD/MD clinic</td>
<td>25</td>
<td>7.1</td>
<td>67.9</td>
<td>0</td>
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<tr>
<td>Physiotherapy (general)</td>
<td></td>
<td></td>
<td>87.1</td>
<td>14.3</td>
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<tr>
<td>Drugs for overactive bladder</td>
<td>57.2</td>
<td>25</td>
<td>10.7</td>
<td>7.1</td>
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<tr>
<td>Laxatives</td>
<td></td>
<td></td>
<td>85.7</td>
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<tr>
<td>Cholinesterase Inhibitors</td>
<td>42.9</td>
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<td>42.8</td>
<td>14.3</td>
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<tr>
<td>Drugs for postural hypotension</td>
<td>25</td>
<td>32.1</td>
<td>42.9</td>
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<td>SSRI</td>
<td></td>
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<td>85.7</td>
<td>0</td>
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<td>TCA</td>
<td></td>
<td></td>
<td>89.3</td>
<td>0</td>
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<tr>
<td>Antipsychotics</td>
<td>50</td>
<td></td>
<td>39.3</td>
<td>10.7</td>
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<td>Ablative surgeries/ DBS</td>
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<td>Anticholinergic drugs</td>
<td>57.1</td>
<td></td>
<td>28.6</td>
<td>14.3</td>
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<tr>
<td>MAOB Inhibitors</td>
<td>7.4</td>
<td>28.3</td>
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<td>COMT Inhibitors</td>
<td>4.6</td>
<td>21.4</td>
<td>67.9</td>
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<tr>
<td>Ergot DA</td>
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<td></td>
<td>46.4</td>
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<tr>
<td>Levodopa preparations</td>
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Hamid...Shalash et al MDJ 2021
Mucuna pruriens in Parkinson disease
A double-blind, randomized, controlled, crossover study

ABSTRACT
Objective To investigate whether Mucuna pruriens (MP), a levodopa-containing leguminous plant growing in all tropical areas worldwide, may be used as an alternative source of levodopa for indigent individuals with Parkinson disease (PD) who cannot afford long-term therapy with marketed levodopa preparations.

Methods We investigated efficacy and safety of single-dose intake of MP powder from roasted seeds obtained without any pharmacologic processing. Eighteen patients with advanced PD received the following treatments, whose sequence was randomized: (1) dispersible levodopa at 3.5 mg/kg combined with the dopa-decarboxylase inhibitor benserazide (LD+DDCI: the reference treatment); (2) high-dose MP (MP-Hd; 17.5 mg/kg); (3) low-dose MP (MP-Ld; 12.5 mg/kg); (4) pharmaceutical preparation of LD without DDCI (LD−DDCI; 17.5 mg/kg); (5) MP plus benserazide (MP+DDCI; 3.5 mg/kg); (6) placebo. Efficacy outcomes were the change in motor response at 90 and 180 minutes and the duration of on state. Safety meas-

- Mucuna Pruriens is a leguminous plant whose seed contain Levodopa without Dopa-Decarboxylase Inhibitor
- Available in all tropical areas worldwide

MP-Ld showed similar motor response with fewer dyskinesias and AEs, while MP-Hd induced greater motor improvement at 90 and 180 minutes, longer ON duration, and fewer dyskinesias. MP-Hd induced less AEs than LD+DDCI and LD−DDCI.

In courtesy of Dr Roberto Cilia (in press)

Roberto Cilia et al. Neurology 2017;89:432-438
**Advocacy & Awareness**

- Increase awareness, patients’ supportive groups, increase education & training, fight discrimination, contacting stakeholders

**Prevention & Risk Reduction**

- An increased risk has been reported among those with exposure to pesticides.
- Amphetamine or methamphetamine, lack of physical activity, heavy metals, air pollution, traumatic brain injury, and industrial solvents, such as trichloroethylene (TCE)
- Avoid exposure to pesticides, protective tools, physical activities, caffeine.

**Diagnosis, Treatment, and Care**

- Strengthening Health and Social Systems and Building Capacity. Education & training, tele-education & telemedicine,
- Ensuring the Availability of Essential Drugs, Diagnostics, and Interdisciplinary Therapies.

**Caregiver Support**

- Provision of a timely diagnosis; effective communication and education about caregiver roles, medications, and adverse effects; and rehabilitation and palliative care strategies, including governmental entitlements and discussions of decision-making capacity. Social workers, patient support groups, and community-based support.

**Research**

- investigate cultural and population differences of variable risk factors, genetics, and phenomenology.

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*Schiess et al, JAMA Neurology 2022*
## Characteristics of Hyperkinetic MDs

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Observe MD During Examination

- Rhythmic vs. arrhythmic
- Sustained vs. nonsustained
- Paroxysmal vs. Nonparoxysmal
- Slow vs. fast
- Amplitude
- At rest vs. action
- Patterned vs. non-patterned
- Combination of varieties of movements
- Supressibility

- Observe any involuntary movements during history and their distribution; speech and vocalizations
"It is a movement disorder characterized by sustained or intermittent muscle contractions causing abnormal, often repetitive, movements, postures, or both”

- It’s typically patterned, twisting, and may be tremulous.

- It is often initiated or worsened by voluntary action and associated with overflow muscle activation.

- ± *Alleviating maneuvers* (sensory tricks or gestes antagonistes).

- ± *Task-specificity*: selective activation by specific tasks (e.g. writing, playing music).
Dystonia Classification

Clinical features
- Age at onset
- Body distribution
- Temporal pattern
- Co-existing MD

Aetiology
- Nervous system pathology
- Inherited, acquired or idiopathic

Focal
- (single region affected)

Segmental
- (≥ 2 connected regions affected)

Multifocal
- (≥ 2 unconnected regions affected)

Generalised
- (trunk and ≥ 2 other parts affected)

Hemidystonia
- (entire side of body affected)

MD, movement disorders.
Old Dystonia Classification

Recent Dystonia Classification

Clinical Aspects

- Age at Onset
  - Infancy
  - Childhood
  - Adolescence
  - Early Adulthood
  - Late Adulthood

- Body distribution
  - Focal
  - Segmental
  - Multifocal
  - Generalized
  - Hemidystonia

- Temporal Pattern
  - Course
    - Variability
  - Static
    - Persistent
  - Progressive
    - Action Specific
    - Diurnal
    - Paroxysmal

- Other movement disorder
  - Isolated
  - Combined

- Other manifestations

Etiology

- CNS pathology
  - Evidence of degeneration
  - Evidence of structural static lesions
  - No evidence of degeneration/structural

- Inherited of Acquired
  - Inherited
  - Acquired
  - Dominant
  - Perinatal
  - Recessive
  - Infection
  - X-linked
  - Toxic
  - Mitochondrial
  - Neoplastic
  - Vascular
  - Psychogenic
  - Brain injury
  - Toxic

- Idiopathic
  - Sporadic
  - Familial

Albanese et al MDJ 2013
Retrocollis (neck extension)
Anterocollis (neck flexion)
Laterocollis (head tilt)

Variation in neck muscle involvement leads to Torticollis (neck turning).

BOTOX® medical. Available at: https://hcp.botoxmedical.com/CervicalDystonia/Subtypes (Accessed May 2014).

Oromandibular Dystonia or Meige’s Syndrome
Affects the lower facial and jaw muscles causing involuntary opening, closing, or deviation of the jaw. The tongue may also be involved.

Cervical Dystonia or Spasmodic Torticollis
Affects the neck muscles leading to abnormal movements of the neck and head.

Spasmodic Dysphonia or Laryngeal Dystonia
Affects the vocal cords to have strangled, hoarse quality or a breathy, whispering voice.

Limb Dystonia
Involuntary movements, cramping and spasming of the legs or feet.

Limb Dystonia, Writer’s Cramp, Musician’s Dystonia
Involuntary movements, cramping and spasming of the hands or arms, which can be brought on by repetitive and task-specific movements.
Acquired Dystonia

1. CNS tumour, congenital malformation, or stroke, trauma.
2. Perinatal cerebral injury (cerebral palsy).
3. Viral encephalitis, subacute sclerosing panencephalitis, prion disease, tuberculosis.
5. Autoimmune: NMDA-R (frequent), GABA_A-R, DPPX, IgLON5.
6. Drug induced: levodopa, dopamine antagonists (e.g., neuroleptics, prochlorperazine, metoclopramide), SSRI, buspirone, cocaine, monoamine oxidase inhibitors, flecainide, calcium antagonists.
7. Toxins, e.g., CO, manganese, cyanide, methanol, disulfiram, carbodisulphide, and methanol.
8. Metabolic: hypoparathyroidism
9. Paraneoplastic syndromes
10. Functional
## INHERITED ISOLATED DYSTONIAS

<table>
<thead>
<tr>
<th>Gene (previous DYT symbol)</th>
<th>Inheritance</th>
<th>Age at onset</th>
<th>Prevalent site at onset</th>
<th>Distribution</th>
<th>Body parts involved</th>
<th>Additional signs</th>
</tr>
</thead>
<tbody>
<tr>
<td>TOR1A (DYT1)</td>
<td>Autosomal dominant</td>
<td>First to third decade</td>
<td>Lower limbs much more likely than upper limbs</td>
<td>Mostly generalized</td>
<td>• Lower limbs&lt;sup&gt;b&lt;/sup&gt; • Upper limbs • Trunk</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td><em>Clinical penetrance of only 30-40% The GAG deletion in TOR1A</em></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>THAP1 (DYT6)</td>
<td>Autosomal dominant (autosomal recessive in rare cases)</td>
<td>Second to third decade (ranging from first to seventh decade)</td>
<td>Neck and upper limbs Older-onset cervical or craniocervical dystonia with likely involvement of the larynx</td>
<td>Focal, segmental and generalized</td>
<td>• Neck&lt;sup&gt;b&lt;/sup&gt; • Upper limbs&lt;sup&gt;b&lt;/sup&gt; • Orofacial areas • Larynx • Lower limbs</td>
<td>None</td>
</tr>
<tr>
<td>GNAL (DYT25)</td>
<td>Autosomal dominant (autosomal recessive in rare cases)</td>
<td>Fourth decade (ranging from first to seventh decade)</td>
<td>Neck</td>
<td>Mostly focal or segmental and occasionally generalized</td>
<td>• Neck&lt;sup&gt;b&lt;/sup&gt; • Orofacial areas • Larynx • Upper limbs • Lower limbs</td>
<td>None</td>
</tr>
<tr>
<td>ANO3 (DYT24)</td>
<td>Autosomal dominant</td>
<td>Fourth to fifth decade (ranging from first to fifth decade)</td>
<td>Neck and larynx</td>
<td>Segmental</td>
<td>• Neck&lt;sup&gt;b&lt;/sup&gt; • Upper limbs • Orofacial areas • Larynx</td>
<td>None</td>
</tr>
</tbody>
</table>
# Combined Dystonia

<table>
<thead>
<tr>
<th>Genetic Syndrome</th>
<th>Allele</th>
<th>Type</th>
<th>Primary Clinical Presentation</th>
</tr>
</thead>
<tbody>
<tr>
<td>GCH1</td>
<td>DYT5a</td>
<td><strong>DYT-GCH1</strong></td>
<td>Dopa-responsive</td>
</tr>
<tr>
<td>TH</td>
<td>DYT5b</td>
<td><strong>DYT-TH</strong></td>
<td>Dopa-responsive</td>
</tr>
<tr>
<td>SPR</td>
<td>Not assigned</td>
<td><strong>DYT-SPR</strong></td>
<td>Dopa-responsive, cognitive impairment</td>
</tr>
<tr>
<td>TAF1&lt;sup&gt;1&lt;/sup&gt;</td>
<td>DYT3</td>
<td><strong>DYT-TAF1</strong></td>
<td>Neurodegeneration</td>
</tr>
<tr>
<td>PRKRA</td>
<td>DYT16</td>
<td>DYT-PRKRA</td>
<td>Dystonia w/mild parkinsonism</td>
</tr>
<tr>
<td>ATP1A3</td>
<td>DYT12</td>
<td><strong>DYT-ATP1A3</strong></td>
<td>Rapid-onset</td>
</tr>
<tr>
<td>SGCE</td>
<td>DYT11</td>
<td><strong>DYT-SGCE</strong></td>
<td>Psychiatric disease</td>
</tr>
<tr>
<td>PNKD&lt;sup&gt;2&lt;/sup&gt;</td>
<td>DYT8</td>
<td><strong>PxMD-PNKD</strong></td>
<td>Paroxysmal nonkinesigenic dyskinesia</td>
</tr>
<tr>
<td>PRRT2</td>
<td>DYT10</td>
<td><strong>PxMD-PRRT2</strong></td>
<td>Paroxysmal kinesigenic dyskinesia</td>
</tr>
<tr>
<td>SLC2A1</td>
<td>DYT18</td>
<td><strong>PxMD-SLC2A1</strong></td>
<td>Paroxysmal exertion-induced dyskinesia</td>
</tr>
<tr>
<td>ECHS1</td>
<td>Not assigned</td>
<td><strong>PxMD-ECHS1</strong></td>
<td>Paroxysmal exertion-induced dyskinesia</td>
</tr>
</tbody>
</table>
c.207C>G mutation in sepiapterin reductase causes autosomal dominant dopa-responsive dystonia

ABSTRACT

Objective: To elucidate the genetic cause of an Egyptian family with dopa-responsive dystonia (DRD), a childhood onset dystonia, responding therapeutically to levodopa, which is caused by mutations in various genes.

Methods: Rare variants in all coding exons of GCH1 sequencing was applied for 1 unaffected and 2 affected family members. The functional consequences of detected genetic variants were determined by high-performance liquid chromatography.

Results: A heterozygous rare nonsynonymous variant c.207C>G, p.Asp69Glu) was found in all affected family members. The enzyme activity of sepiapterin were above the standard of normal control. The functional biochemical consequences of the mutation in the tetrahydrobiopterin pathway, required for levodopa converted to dopa by the enzyme sepiapterin reductase (DHFR, rs7098272) was significantly stronger associated with the biochemical abnormality and the clinical disease state as opposed to 1 variant only.

Conclusions: The rare SPR mutation can cause autosomal dominant DRD with incomplete penetrance. The common DHFR variant might have synergistic effects on production of tetrahydrobiopterin and levodopa, thereby increasing penetrance. Neurogenet 2017;3:e197; doi: 10.1212/NXG.0000000000000197
# Paroxysmal Dyskinesias

<table>
<thead>
<tr>
<th></th>
<th>Paroxysmal kinesigenic choreoathetosis (PKD)</th>
<th>Paroxysmal Non kinesigenic choreoathetosis (PNKD)</th>
<th>Paroxysmal exercise-induced dystonia (PED)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Duration</strong></td>
<td>Very brief</td>
<td>0.5-1 hr</td>
<td>2 min – 2 hrs</td>
</tr>
<tr>
<td><strong>Triggering factors</strong></td>
<td>Sudden movements</td>
<td>Alcohol, coffee, tobacco, emotions, fatigue, hunger</td>
<td>Prolonged or sustained exercise</td>
</tr>
<tr>
<td><strong>Age of onset</strong></td>
<td>7-15 yrs</td>
<td>Infancy - childhood</td>
<td>2 – 30 yrs</td>
</tr>
<tr>
<td><strong>Treatment</strong></td>
<td>carbamazepine</td>
<td>Benzodiazepine</td>
<td>Gabapentin</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Anticonvulsants</td>
<td>L-dopa</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Acetazolamide</td>
<td></td>
</tr>
<tr>
<td><strong>Gene</strong></td>
<td>PRRT2 (Chr 16p11)</td>
<td>MR1 (Chr 2q35), KCNMA1 (10q22)</td>
<td>SLC2A1 (1p34.2)</td>
</tr>
</tbody>
</table>
Diagnostic Approach for Dystonia *(Balint et al, 2018)*

- **Clinical syndromic approach**
  - Information from medical history
  - Isolated versus combined
  - Body distribution
  - Temporal course

- **Define dystonia syndrome**

- **Diagnostic work up**
  - Routine work-up
    - MRI
    - Copper and ceruloplasmin levels
  - Specific investigations
    - Genetic testing
    - CSF analysis (analysis of pterins, dopamine and serotonin metabolites and serum and/or CSF glucose ratio)
    - Lysosomal enzyme assays
    - Long-chain fatty acids
    - Urine metabolic screen (amino acids)
    - Skin or tissue biopsy

- **Aetiological diagnosis**

- **Pseudodystonia** *(Imitators of Dystonia)*
Management of Dystonia

Pharmacological Therapies

- Anticholinergics
- Baclofen
- Clonazepam
- Dopamine-related medications

Botulinum Toxin Injection

Surgical Interventions

- DBS
- Ablative Surgeries
- Dorsal Rhizotomy

Table 1: Demographic and clinical data of patients with truncal dystonia underwent pallidal stimulation

<table>
<thead>
<tr>
<th>Patient</th>
<th>Gender</th>
<th>Age at surgery (years)</th>
<th>Age of disease onset (years)</th>
<th>Duration at surgery (years)</th>
<th>Clinical presentation</th>
<th>Pre-BFMDRS Total/trunk</th>
<th>Post-BFMDRS Total/trunk</th>
<th>Percentage of Improvement Total/Trunk</th>
<th>Dystonia Disability Scale-Preop</th>
<th>Dystonia Disability Scale-Post-op</th>
<th>Dystonia Disability Scale-Improvement</th>
<th>Current (Best) DBS setting</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient 1</td>
<td>female</td>
<td>46 (2017)</td>
<td>45</td>
<td>1</td>
<td>dystonia started at right shoulder and arm, followed by trunk (on action), and generalized gradually with severe truncal and oromandibular dystonia, cortical, lateral tilt, and twisting</td>
<td>57.5/16</td>
<td>3/2</td>
<td>94.78/87.5%</td>
<td>20</td>
<td>1</td>
<td>95%</td>
<td>(C+2) 3.8v/90us/130 hz</td>
</tr>
<tr>
<td>Patient 2</td>
<td>female</td>
<td>20 (2014)</td>
<td>10</td>
<td>10</td>
<td>dystonia started at right upper limb on action, that generalized gradually with severe truncal and oromandibular dystonia, oromandibular, lateral tilt, and twisting</td>
<td>66/16</td>
<td>5/1</td>
<td>92.2/89.75%</td>
<td>25</td>
<td>4</td>
<td>84%</td>
<td>(C+0) 2.7v/60us/130 hz</td>
</tr>
<tr>
<td>Patient 3</td>
<td>male</td>
<td>15 (2018)</td>
<td>25</td>
<td>12</td>
<td>dystonia started at left lower limb, mobile (tremulous) generalized, oromandibular, dystonia, oromandibular, lateral tilt, and twisting</td>
<td>84/16</td>
<td>16/2</td>
<td>80.95/87.5%</td>
<td>24</td>
<td>12</td>
<td>50%</td>
<td>(C+10) 3.8v/120us/130 hz</td>
</tr>
</tbody>
</table>
CHOREA

- Irregular rapid, low amplitude, brief movements of extremities & face.
- Semi purposeful or apparently purposeful.
- Severe cases → obvious movement of the hand, feet, face.
- ± Facial grimacing, eye brow movement and respiratory noises.
- Increase by stress and disappear during sleep.
- ± Athetosis (slower, distal, writhing and sinuous).
- Ballismus: high amplitude movement of a limb in a flinging or flailing motion, including the most proximal segments.
• Motor impersistence: difficulty sustaining ongoing movement e.g. inability to maintain forced eye closure, or protrude the tongue for long periods.

Special Signs

1. Tongue sign: patient cannot keep his tongue protruded outside mouth.
2. Boat hands or scaphoid hands
3. Pronator signs.
4. Dancing gait.
Causes of Choreic Syndromes

**GENETIC CHOREAS**

1. Huntington’s disease (AD).
2. Huntington’s disease-like 2 (AD).
3. Dentatorubropallidoluysian atrophy (DRPLA)
4. Neuroacanthocytosis
5. Ataxia telangiectasia
6. Benign hereditary chorea (AD)
7. Spinocerebellar ataxia (types 2, 3, or 17)
8. Paroxysmal kinesigenic choreoathetosis

**AQUIRED CHOREAS (non-genetic)**

1. Structural basal-ganglia lesions: stroke
2. Parainfectious & autoimmune disorders: Sydenham’s chorea, SLE.
3. Infectious chorea
4. Metabolic or toxic encephalopathies
5. Drug induced
6. Functional forms.
Huntington’s Disease

- AD causing choreic and mental changes.
- Caused by unstable trinucleotide CAG repeat expansion in chromosome 4p, HTT gene, which encodes a protein (Huntingtin) widely expressed in neuronal and other tissues.
- Age: 30 – 55 years around 40 years.
- < 20 years → juvenile HD (Westphal variant) 5 %.
- >60 years → elderly onset disease 25%.
- Gradual, progressive, 2/3 starts by motor symptom (chorea).

**Motor**
- Chorea
- Parkinsonism
- Dystonia
- Myoclonus
- Motor impersistence
- Gait disorder

**Psychiatric**
- Personality
- Affective; depression
- Obsessive compulsive
- Psychosis (rare)

**Cognitive**
- Executive dysfunction
- Dementia
Huntington Disease Phenocopies

Suspected HD cases

HD 99%

HD phenocopy cases

Undiagnosed 98%

Genetically diagnosed phenocopy cases

- SCA17
- Friedreich ChAc
- SCA8
- Prion
- C9orf72
- HDL2

Junctophilin 3 (JPH3) Expansion Mutations Causing Huntington Disease Like 2 (HDL2) are Common in South African Patients with African Ancestry and a Huntington Disease Phenotype

Amanda Krause, Claire Mitchell, Fahmida Essop, Susan Tager, James Temlett, Giovanni Stevanini, Christopher Ross, Dobrila Rudnicki, and Russell Margolis

In a sample of unrelated South African individuals referred for diagnostic HD testing, 62% (106/171) of white patients compared to only 36% (47/130) of black patients had an expansion in HTT. However, 15% (20/130) of black South African patients and no white patients (0/171) had an expansion in JPH3, confirming the diagnosis of Huntington disease like 2 (HDL2). Individuals with HDL2 share many clinical features with individuals with HD and are clinically indistinguishable in many cases, although the average age of onset and diagnosis in HDL2 is 5 years later than HD and individual clinical features may be more prominent. HDL2 mutations contribute significantly to the HD phenotype in South Africans with African ancestry. JPH3 haplotype studies in 31 families, mainly from South Africa and North America, provide evidence for a founder mutation and support a common African origin for all HDL2 patients. Molecular testing in individuals with an HD phenotype and African ancestry should include testing routinely for JPH3 mutations.
Workup of Chorea

1. Routine blood work, Thyroid studies, ESR, ANA, antiphospholipid antibodies, ASO titers...

2. Test for thyroid function, renal and liver function, electrolytes, erythrocyte sedimentation rate, antinuclear antibodies, anti double-stranded DNA antibodies, ↑↑ CPK, anticardiolipin antibodies, and lupus anticoagulant.

3. Test for acanthocytes in peripheral fresh blood film. perform three assays.

4. Perform brain MRI.

5. Genetic test: for Huntington disease. If the latter genetic test is negative, consider spinocerebellar ataxia type 17 and C9orf72 in white individuals, and Huntington disease-like syndrome type 2 in subjects with black African ancestry.
Treatment of Chorea

• Treat underlying acquired cause: autoimmune, WD.

• No protective treatment

• Symptomatic treatment of chorea:
  1. Dopamine receptor blockade
     • Typical neuroleptics—caution!
     • “Atypical” neuroleptics: tiapride, olanzapine, and risperidone
       Presynaptic dopamine depletion: Tetrabenazine
       25-100 mg/day, deutetrabenazine (HD), valbenazine (tardive dyskinesia)
  2. Glutamate antagonism: Amantadine
  3. GABA-ergic: Valproic acid.

• Treat associated symptoms: psychiatric, seizures
• Botulinum toxin, DBS for certain cases
**Tic Disorders**

**Definition:** Rapid, non-rhythmic, stereotyped involuntary movements usually affecting the face, head, or UL.

- More semi purposeful, which may be:
- Simple or complex, motor or vocal.
- Acute, subacute or chronic.
- Brief or sustained "dystonic tics."

**Motor tics:**
- *Simple motor tics:* blinking, head jerking, shrugging shoulder, grimacing.
- *Complex motor tics:* picking at the body or object, gestures, rubbing or manipulative movements.

**Vocal tics:** simple (noises, cough, sniffs) or complex (words, phrases).

- Waxing and waning, transient remissions.
- Persist during sleep (all stages)
## Causes of Tics

<table>
<thead>
<tr>
<th>Primary</th>
<th>Secondary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transient tic disorder (&lt; 1 year)</td>
<td>a) HD, choreo-acanthocytosis</td>
</tr>
<tr>
<td>Chronic motor tic disorder</td>
<td>b) Drugs;</td>
</tr>
<tr>
<td>Chronic vocal tic disorder</td>
<td></td>
</tr>
<tr>
<td>Tourette's syndrome</td>
<td>c) Encephalitis, CJD, PANDAS</td>
</tr>
<tr>
<td></td>
<td>d) PD, PSP.</td>
</tr>
<tr>
<td></td>
<td>e) Rett's syndrome.</td>
</tr>
<tr>
<td></td>
<td>f) Focal BG lesion.</td>
</tr>
</tbody>
</table>
Tourette's Syndrome
DSM-IV Diagnostic Criteria

- Both multiple **motor** and one or more **vocal** tics have been present at some time during the illness, although not necessarily concurrently.
- The tics occur many times a day (usually in bouts) nearly every day or intermittently throughout a period of more than 1 year, and during this period there was never a tic-free period of more than 3 consecutive months.
- The onset is before age 18 years.
- The disturbance is not due to the direct physiological effects of a substance (e.g., stimulants) or a general medical condition (e.g., Huntington’s disease or postviral encephalitis).
Treatment of Tic Disorders

1. Education; Patient, family, and school
2. Counseling for family and patient
3. Relaxation therapy
4. Supportive therapy
5. Habit Reversal Therapy
6. Pharmacological: $\alpha_2$ agonists (Clonidine), neuroleptics
7. Treatment of comorbidities.
Consensus Statement on the classification of tremors, the task force on tremor of the MDS

During voluntary contraction of muscle

Voluntarily maintaining position against gravity

Simple kinetic tremor
Intention tremor
Task-specific kinetic tremor
Position independent
Position dependent
Isometric tremor
Postural tremor
Kinetic tremor
Rest tremor
Consensus Statement on the classification of tremors, the task force on tremor of the MDS

(a) Axis 1: clinical features

- Historical features
  - Age at onset
  - Temporal onset and evolution
  - Past medical history
  - Family history
  - Alcohol and drug sensitivity

- Tremor characteristics
  - Body distribution
  - Activation conditions
  - Tremor frequency

- Associated signs
  - Signs of systemic illness
  - Neurologic signs
  - Soft signs

- Additional laboratory tests
  - Electrophysiological tests
  - Structural imaging
  - Receptor imaging
  - Serum and tissue biomarkers

(b) Axis 2: etiology

- Acquired
- Genetically defined
- Idiopathic

- Familial
- Sporadic
tremor syndromes

- action or rest tremor
  - ET and ET plus
    - isolated segmental action tremor
      - isolated rest tremor
    - enhanced physiologic tremor
  - focal tremors
    - voice, head, jaw, face, others
  - task and position specific tremors
    - writing, sports, musicians
  - orthostatic tremors
    - primary orthostatic
    - pseudo-orthostatic
either with prominent additional signs
  - dystonic tremors
    - parkinsonism associated tremors
    - indeterminate tremor
  - functional tremor
  - intention tremor
  - Holmes tremor
  - myorhythmia
  - symptomatic palatal tremor
  - others
Essential Tremor (ET):

- Sporadic or familial AD, insidious, and progressive.
- Bimodal onset; late adolescence and older adulthood.
- Mixture of kinetic and (> ) postural tremor, 4 -12 hz.
- Bilateral roughly symmetric or mild asymmetric.
- Start in UL (95%), head, face, voice....
- ± mild intentional component, ± mild gait ataxia.
- No other neurological deficits (except Froment's sign).
- Isolated focal or task specific (vs. dystonic).
1. Propranolol (up to 320 mg/day), and other B blockers.
2. Primidone (up to 250 mg three times daily).
3. Gabapentin (1200 to 3600 mg/day), and topiramate.
4. Mirtazapine, alprazolam, Phenobarbital, Clonazepam
5. Botulinum toxin for task-specific, severe isolated head, or dystonic tremors.
6. Wearing wrist weights while eating, drinking from a heavier mug, using a fat pen rather than a thin one, and using heavier utensils
7. Surgical: Vim thalamotomy or Vim DBS.
**Classification of Myoclonus:** The essential feature is the sudden, brief, and shock-like movement.

### Clinical Presentation

<table>
<thead>
<tr>
<th>Distribution</th>
<th>1. Focal</th>
<th>1. Segmental</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1. Multifocal</td>
<td>1. Generalized</td>
</tr>
</tbody>
</table>

**Relation to activity:**

<table>
<thead>
<tr>
<th>a) Spontaneous</th>
<th>a) Action</th>
<th>a) Reflex</th>
</tr>
</thead>
</table>

**Pattern**

<table>
<thead>
<tr>
<th>I. Rhythmic</th>
<th>I. Irregular</th>
</tr>
</thead>
<tbody>
<tr>
<td>I. Repetitive or oscillatory</td>
<td></td>
</tr>
</tbody>
</table>

**Etiology**

<table>
<thead>
<tr>
<th>1. physiological</th>
<th>1. Essential</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Epileptic</td>
<td>1. Symptomatic</td>
</tr>
<tr>
<td>1. Psychogenic</td>
<td></td>
</tr>
</tbody>
</table>

**Neurophysiologic origin**

<table>
<thead>
<tr>
<th>1) Cortical</th>
<th>1) Subcortical</th>
</tr>
</thead>
<tbody>
<tr>
<td>1) Spinal</td>
<td>1) Peripheral nerve or root</td>
</tr>
</tbody>
</table>

- **Positive Myoclonus:** muscle contractions.
- **Negative Myoclonus:** interruptions of tonic muscle activity = asterixis= flapping tremor.
- **Treatment:** piracetam, levetiracetam, valproic acid and clonazepam
### Causes of Myoclonus

**Generalised Myoclonus:**

a) **Essential myoclonus**: Non-progressive condition in which myoclonus is only or most important neurological symptom and sign.

b) **Progressive myoclonic encephalopathies (PME):**  
   - Myoclonus (with or without seizures) is part of a progressive encephalopathy.
   
   e.g., mitochondrial encephalomyopathy (esp. MERFF); Creutzfeldt–Jacob disease, Alzheimer’s disease; and **Metabolic myoclonus** (e.g. uraemia, hepatic failure,

a) **Static myoclonic encephalopathies**: obvious myoclonus occurs after some acute and now static cerebral insult, e.g. postanoxic action myoclonus (Lance–Adams syndrome).

b) **Myoclonic epilepsies**: epilepsy is the main problem, but myoclonus is present.

**Focal Myoclonus**: myoclonus is restricted to one small discrete part of the body. → Spinal myoclonus, Hemifacial spasm.
Wilson’s Disease

Onset: the ages of 5 and 35 years (mean 13 years)

Hepatic
18-84%
- Asymptomatic
- Acute hepatitis
- Chronic hepatitis
- Cirrhosis

Neurological
18-73%
AAO: 20-30 yrs
- Dysarthria, dystonia, tremor, parkinsonism, chorea, or myoclonus, ataxia

Psychiatric
10-100%
- Emotional lability, hypersexuality, impulse control disorders, psychosis, depression, or attempted suicide-
  Drop in scholastic grades or work performance

Deterioration in school performance
Behavioral Changes
Incoordination (handwriting deteriorates)
Resting and intention tremors
Dystonia
Dysarthria
Excessive salivation
Hunt-Neet Bars
Ophthalmoplegia

Hepatomegaly
Jaundice
Acute hepatitis
Fulminant hepatic failure
Portal hypertension: bleeding varices
Cirrhosis

Renal
Bone
Arthritis
Rickets

Central nervous system

Wilson’s Disease

Eye
Kayser-Fleischer rings
### TABLE 1. Clinical and MRI brain characteristics in patients with Wilson’s disease with and without dystonia

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Patients With WD: Total</th>
<th>WD With Dystonia</th>
<th>WD Without Dystonia</th>
<th>P²</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>22 (100)</td>
<td>14 (63.6)</td>
<td>8 (36.4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sex; Male/female</td>
<td>14/8</td>
<td>9/5</td>
<td>5/3</td>
<td>0.842</td>
<td>NS</td>
</tr>
<tr>
<td>No. with positive family history</td>
<td>13 (59.1)</td>
<td>8 (57.1)</td>
<td>5 (62.5)</td>
<td>0.548</td>
<td>NS</td>
</tr>
<tr>
<td>Duration of illness, y</td>
<td>7.4 ± 7.2 [0.5–30]</td>
<td>8.3 ± 8.03 [0.5–30]</td>
<td>8.1 ± 5.97 [0.5–16]</td>
<td>0.489</td>
<td>NS</td>
</tr>
<tr>
<td>Neurological presentation</td>
<td>9 (40.9)</td>
<td>5 (35.7)</td>
<td>4 (50)</td>
<td>0.239</td>
<td>NS</td>
</tr>
<tr>
<td>Parkinsonism</td>
<td>13 (59.1)</td>
<td>9 (40.9)</td>
<td>4 (50)</td>
<td>0.662</td>
<td>NS</td>
</tr>
<tr>
<td>KFR</td>
<td>17 (77.3)</td>
<td>12 (85.7)</td>
<td>5 (62.5)</td>
<td>0.309</td>
<td>NS</td>
</tr>
<tr>
<td>Dysarthria severity</td>
<td>1.727 ± 1.316</td>
<td>2.288 ± 1.204</td>
<td>0.750 ± 0.886</td>
<td>0.007</td>
<td>S</td>
</tr>
<tr>
<td>Walking impairment</td>
<td>1.409 ± 1.141</td>
<td>1.857 ± 1.187</td>
<td>0.625 ± 0.517</td>
<td>0.006</td>
<td>S</td>
</tr>
<tr>
<td>BFMDRS score</td>
<td>36.9 ± 29.94</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. with extensor truncal dystonia</td>
<td>11 (50)</td>
<td>11 (87.6)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Score</td>
<td>8.9 ± 3.73</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MRI brain abnormality</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bilateral lentiform lesions</td>
<td>19 (59.1)</td>
<td>12 (85.7)</td>
<td>7 (87.5)</td>
<td>0.709</td>
<td>NS</td>
</tr>
<tr>
<td>Bilateral lentiform and caudate lesions</td>
<td>15 (68.2)</td>
<td>10 (71.4)</td>
<td>5 (62.5)</td>
<td>0.510</td>
<td>NS</td>
</tr>
<tr>
<td>Bilateral GP lesions</td>
<td>10 (45.5)</td>
<td>7 (50)</td>
<td>3 (37.5)</td>
<td>0.454</td>
<td>NS</td>
</tr>
<tr>
<td>Brainstem lesions</td>
<td>6 (27.3)</td>
<td>5 (35.7)</td>
<td>1 (12.5)</td>
<td>0.255</td>
<td>NS</td>
</tr>
<tr>
<td>Bilateral thalamic lesions</td>
<td>5 (22.7)</td>
<td>3 (21.4)</td>
<td>2 (25)</td>
<td>0.820</td>
<td>NS</td>
</tr>
<tr>
<td>Treatment</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Compliant patients</td>
<td>9 (40.9)</td>
<td>5 (35.7)</td>
<td>4 (50)</td>
<td>0.618</td>
<td>NS</td>
</tr>
<tr>
<td>D-penicillamine, mg</td>
<td>403.41 ± 308.44; n = 16</td>
<td>330.36 ± 267.61; n = 10</td>
<td>531.25 ± 364.43; n = 6</td>
<td>0.148</td>
<td>NS</td>
</tr>
<tr>
<td>Zinc sulfate, mg</td>
<td>100 ± 76.38; n = 16</td>
<td>108.93 ± 88.04; n = 10</td>
<td>84.38 ± 51.65; n = 6</td>
<td>0.419</td>
<td>NS</td>
</tr>
</tbody>
</table>

WD gene, ATP7B
CHALLENGES

1. Awareness, early diagnosis, advocacy.
2. Lack of basic medications (unavailable and unaffordable)
3. Lack of different medications for motor, LD-induced complications, non-motor
4. Dealing with old medications
5. Shortage of Neurologists, Nurses, neurosurgeons,.....
6. Lack of training and education
7. Unavailability of functional surgeries and advanced therapies
8. Barriers of Telemedicine
9. Need for comprehensive care for PD patients
10. Limited resources for research
RECOMMENDATIONS

1. Early diagnosis: awareness, screening, access to healthcare
2. Contact stakeholders, provision of affordable drugs.
3. Promote training of neurologists, practitioners, and allied health professionals.
4. Improve knowledge of available tools.
5. Facilitate access for PD treatment.
6. Use of available and affordable alternatives.
8. PD supportive groups.
The International Parkinson and Movement Disorder Society (MDS)

• Task Force on Africa

• African Steering Committee ( Created in 2017)

• African MDS education committee 2019

• MDS Africa Section 2021
Delegates from the African Section can apply for a **FREE No-Fee Membership with MDS**

Membership Benefits

Learn more about all MDS member benefits at: [www.movementdisorders.org/benefits](http://www.movementdisorders.org/benefits)

- **Video Library**
  - Over 2,000 searchable videos

- **MDS Journals**
  - MDS peer-reviewed Journals

- **Moving Along**
  - Quarterly newsletter

- **Member Directory**
  - Online-only directory

- **Reduced Registration Fees**
  - Discounted rates for live courses and MDS Congresses

- **E-Learning**
  - Coffee Break CME, Journal CME, Fundamentals Course Series, Interactive Courses and more

- **Voting Rights**
  - Regular and Waived Dues Members are eligible to vote in MDS leadership elections

- **Rating Scales**
  - MDS-UPDRS & UDysRS Online Training Programs
MDS-AS African Multicenter Grand Rounds 5-part Series
Session 4 (Functional Movement Disorders): November 11, 2022 at 16:00 EET

IN-PERSON MDS-Africa School for Young Neurologists
Tunis, Tunisia | December 1-3, 2022

Registration is **FREE** for MDS Members. Non-members from the African region can apply for No-Fee Membership and register at no cost.
2020 MDS-AS Education

- 1 – In person MDS-AS Education Course
- 2 - MDS-AS Regional Online Courses
- 4 - Outreach Programs
- 1 – Developing World Education Programs (DWEP)
- 2 – MDS Supported/Endorsed Meetings
MDS-AS Online Regional Course

MDS Outreach Programs

“Does Your Program Need…”

- MDS Endorsement (use of MDS logo)?
- MDS Financial Support for your local Event?
- MDS Expert Recommendations / Honoraria Support?
- Technology Support through access to MDS Zoom Webinar Account?

Contact the MDS Secretariat to learn more at education@movementdisorders.org
Enkosi
Ngiyabonga
Amesege'hallo'
Zikomo Kwambiri
Siyabonga kakulu

Thank You

Asante sana
Ndatenda
Murakoze
N'itumezi
Masvita
Kea leboha
Zikomo

شكراً