Approach to Chorea
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Disclosures: None
Outline

• Chorea definition
• Pathophysiology
• Classification
• Approach to management
• Patient’s Videos
In 1894

William Osler wrote:

“In the whole range of medical terminology, there is no such “olla podrida*” as chorea which for centuries served as a nosological pot into which authors have cast indiscriminately”

*olla podrida: mixed stew
What is Chorea?

• **Definition**
  • The term chorea is derived from the Greek term for dance “choros”
  • Chorea consists of involuntary, continual, abrupt, rapid, brief, unsustained, irregular movements that flow randomly from one body part to another*
**Parakinesia;** Patients frequently camouflage some of the movements by incorporating them into semi purposeful activities

- **Motor impersistence;** The inability to maintain voluntary contraction
  - milkmaid grip
  - tongue protrusion

- **Pseudochoreoathetosis;** a movement disorder that is phenomenologically similar to chorea due to loss of proprioception\(^1\)

- **Athetosis;** is a slow, continuous, involuntary writhing movement that prevents maintenance of a stable posture
  - In contrast to chorea, in athetosis the same regions of the body are repeatedly involved \(^2\)

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1. Walker, Mov Disorders, Sept 2010
2. Jankovich et al., Parkinson's and movement disorders book
Classification of Chorea

Etiology
- Hereditary
- Non Hereditary (acquired)

Age of onset
- Young
- Adult
Classification of chorea
“Etiology”

• **Hereditary**
  - AD
    - Huntington’s disease
    - HDL 1, 2,
    - SCA 17
    - DRPLA
    - Neuroferritinopathy
  - AR
    - NBIA, Niemann pick type C
    - Ataxia ( FA, AT, AOA)
  - X-linked
    - Neuroacanthocytosis, Lesch-Nyhan, x-linked parkinsonism dystonia
  - Mitochondrial
    - Leig’s syndrome

• **Non Hereditary**
  - Drug induced
  - Vascular
  - Infectious
  - Immunological
  - Endocrine metabolic
  - Miscellaneous
When the family history is negative

A parent carrying a causative mutation may have died before the disease manifested

Partial penetrance can be seen

Phenotypic variation may result in a disease not recognized by the family members

Psychiatric features may have resulted in long-term care, that the neurological disease was not recognized

Non paternity

De novo mutation

Walker, Mov Disorders, Sept 2010
Classification of chorea
“Age of onset”

• **Adult onset**
  - Genetic
    • Huntington's dis
    • Huntington’s phenocopies
    • Benign hereditary chorea
    • Others
  - Acquired:
    • Stroke
    • Drugs
    • Metabolic
    • Infectious
    • Autoimmune

• **Young onset**
  - Genetic:
    • Benign hereditary chorea
  - Acquired:
    • Sydenham’s
    • Basal ganglia stroke\post op ischemic changes
    • psychogenic
Immunological chorea's

- Sydenham’s chorea
  - Chorea gravidarum
  - Contraceptive induced chorea
- Systemic lupus erythematosus
- Antiphospholipid Syndrome
- Para neoplastic
- Others
Sydenham’s Chorea

• The most common cause of acute chorea in children
• Major feature of acute rheumatic fever
• Complication of group A Beta hemolytic strep. Infection

You tube video
Sydenham’s Chorea

• Clinically
  • Age of onset: 8 years
  • Female > male
  • 4-8 weeks after infection
  • Hemichorea/ Generalized
  • OCD, ADHD
  • 60-80% have carditis

• How to diagnose?
  • Evidence of recent Strep infection
  • Cardiac involvement
  • Rule out alternative causes (SLE, APAS)
Management of Sydenham’s chorea

Chorea & behavior
“Off label use“

- Valproic acid
- Neuroleptic (risperidone)
- Steroids / IVIG

2ry prophylaxis with penicillin

Cardoso, Park insondis & mov disorder, Ch20, Pg. 207:2016
Notes:

• SC is the most common cause chorea in children
• 25% remain with persistent chorea
• Treatment requires
  • Antichoreic drugs
  • Strep prophylaxis
Huntington’s disease

- HD is a rare disorder
- Age of onset 30 -50 years
  - Juvenile < 20 years
  - Lateonset > 70 years
- 5:100,000
- CAG expansion in Ch4q
- Anticipation
- Clinically:
  - Cognitive & Behavioral disorders
  - Movement disorder

Sanitint and frank, PD & movement disorder, Ch 19, Pg 197
Penetrance Based on CAG repeat Length

<table>
<thead>
<tr>
<th>CAG repeat</th>
<th>Probability of disease development</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 40</td>
<td>Definite</td>
</tr>
<tr>
<td>36 – 39</td>
<td>High risk</td>
</tr>
<tr>
<td>27 – 35</td>
<td>Low– no risk</td>
</tr>
<tr>
<td>&lt; 26</td>
<td>normal repeat length</td>
</tr>
</tbody>
</table>

Santinti & Frank, PD & Mov Disorders Chapter 16, pg 198
Management of Huntington's disease

- No disease modifying therapy
- Gene silencing therapy
- Chorea
  - Tetrabenazine
  - Neuroleptics
- Behavioral problems
  - Neuroleptics and antidepressants
Therapeutic guidelines in HD
AAN -2012

**DOPAMINE-MODIFYING DRUGS**

<table>
<thead>
<tr>
<th>Moderate evidence</th>
<th>If HD chorea requires treatment, clinicians should prescribe tetrabenazine (TBZ) (up to 100 mg/day) (Level B). Clinicians should discuss possible adverse effects (AEs) with patients with HD and monitor for their occurrence.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>TBZ likely has very important antichoreic benefits. Clinicians should discuss possible AEs with patients with HD and monitor for their occurrence, particularly parkinsonism and depression/suicidality with TBZ.</td>
</tr>
<tr>
<td>Insufficient evidence</td>
<td>Data are insufficient to make recommendations regarding use of clozapine or other neuroleptics for HD chorea treatment (Level U).</td>
</tr>
</tbody>
</table>

**GLUTAMATERGIC-MODIFYING DRUGS**

<table>
<thead>
<tr>
<th>Moderate evidence</th>
<th>If HD chorea requires treatment, clinicians should prescribe amantadine (300–400 mg/day) or riluzole (200 mg/day) (Level B). Clinicians should discuss possible AEs with patients with HD and monitor for their occurrence, particularly elevated liver enzymes with riluzole.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Riluzole 200 mg/day likely has moderate antichoreic benefits (Level B).</td>
</tr>
<tr>
<td>Insufficient evidence</td>
<td>The degree of benefit for amantadine is unknown (Level U).</td>
</tr>
<tr>
<td>Moderate evidence</td>
<td>Whereas riluzole 200 mg/day likely decreases chorea, clinicians should not prescribe riluzole 100 mg/day for moderate short-term benefits (Level B negative) or for any long-term (3-year) HD antichoreic goals (Level B negative). Modest short-term benefits of riluzole 100 mg/day cannot be excluded.</td>
</tr>
</tbody>
</table>
**Tetrabenazine:**
It should be started at a low dose and increased slowly
Maximal dose is usually 75 mg /day
CYP2D6 genotyping is recommended if the dose more than 50mg/day to identify slow metabolizers

**Amantadine:**
Experts do not usually use it
The evidence is sparse

**Riluzole:**
Data available do not support it

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**Pharmacological Treatment of Chorea in Huntington’s Disease—Good Clinical Practice versus Evidence-based Guideline**

Ralf Reilmann, MD, PhD*

*Huntington Group, Department of Neurology, University Clinic Muenster, Westfälische Wilhelms University of Muenster, Muenster, Germany*

R.Reilmann, MovDisorders, Vol 29, No 8, 2013
Indications to treat chorea
interference with work activities, physical injury, loss of balance, social stigma, sleep disturbance

Yes

depression psychosis aggression non-comp.

No

APD
wait 6-12 months
evaluate response & benefit

optimise dose
switch APD

optimise dose
TBZ
wait 6-12 months
evaluate response & benefit

monotherapy APD and/or TBZ unsatisfactory

referral to HD specialist prior to any other intervention

Reilmann, MovDisorders, Vol 29, No 8, 2013
Dec 2017: Promising Huntington’s Therapy “IONIS-HTTRx”

The randomized, double-blind, placebo-controlled trial (NCT02519036) tested the safety and tolerability of several increasing doses of IONIS-HTTRx in Huntington’s disease patients. The drug was found to have an acceptable safety and tolerability profile. It also reduced the amounts of the mutant huntingtin protein (mHTT) that causes Huntington’s disease in the patients tested.

Initiating an open-label extension of the study for participants who completed the Phase 1/2a trial.
Drug induced Chorea

• Dopaminergic drugs

• Neuroleptics (tardive dyskinesia, withdrawal emergent syndrome)

• Stimulants
  • amphetamines, cocaine, oral contraceptives

• Toxins
  Alcohol intoxication and withdrawal, carbon monoxide, manganese, mercury, thallium
DIAGNOSTIC EVALUATION OF CHOREA

**History**
- Age at onset (childhood vs. adult choreas)
  - Childhood choreas:
    - Autoimmune
    - SC
    - SLE
    - Postvaccinal
    - Infectious
    - Genetic
    - BHC
    - AT, ATLD
    - AOA1,2
    - PKC, ICCA
    - Wilson disease
    - PKAN
  - Drug-induced
    - Static encephalopathy
    - Ataxic cerebral palsy
    - Bilirubin encephalopathy
    - Metabolic
    - Basal ganglia tumors
- Genetic choreas
- Family history
- Time course
- Drug exposure
- Distribution of chorea
- Focal or hemichorea
- Structural basal ganglia lesions
- Drug-induced chorea

**Neurological examination**
- Associated neurological findings
  - Metabolic/endocrine chorea
  - Structural basal ganglia lesions

**Laboratory tests**
- Blood chemistry
- Hematology (acanthocytosis)
- Antibody screen
  - CHAC
  - MLS
  - HDL2
  - PKAN
  - SCA2,3, 17
  - DRPLA
  - AT
  - AOA1,2
  - PKAN
  - Wilson disease
  - BHC

**Molecular genetic testing**
- Anti-streptococcal
- Anti-phospholipid
- Anti-nuclear
- ABGA (currently only available in research settings)

**Imaging**
- CT/MRI
- PET/SPECT

Jankovic et al, Parkinson dis & mov disorder, Ch20,
Thank you