Tardive Dyskinesia

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Learning Objectives

Accurately diagnose tardive dyskinesia based on diagnostic criteria and assessment tools.

Apply guideline-based treatment of tardive dyskinesia.
“Involuntary athetoid or choreiform movements lasting at least a few weeks, developing in association with the use of a neuroleptic medication for at least a few months, and persisting beyond 4-8 weeks”

Medication-induced movement disorder, caused by dopamine receptor blocking drugs, that starts after a few months of medication use (or less in an older patient) and persists at least one month after medication change or discontinuation.
Implications of *DSM-5* Definition of TD

**DELAYED IN ONSET**

**PERSISTENT** but **REVERSIBLE**

*or*

**PERSISTENT** and **IRREVERSIBLE**
Tardive Syndromes

Oro-bucco-lingual dyskinesia
- Classic oro-bucco-lingual dyskinesia
- Tardive dyskinesia

Tardive akathisia

Tardive dystonia

Tardive tics
- Tardive tourettism

Tardive tremor
- Tardive myoclonus
- Tardive parkinsonism

Classic (Tardive) Oro-Bucco-Lingual Dyskinesia

**INDUCED BY EXPOSURE TO DOPAMINE-BLOCKING DRUGS**

- Anatomical sites involved
- Stereotypical appearance
- “Late” appearance
- Persistence – *for a while*
- Persistence – *for good*
First-generation antipsychotics (FGAs)
- Prevalence of TD at 5 years: 32%
  at 15 years: 57%
  at 25 years: 68%
- Annual incidence of TD: 7.7%  

Second-generation antipsychotics (SGAs)
- Prevalence of TD at 5 years: 13%
- Annual incidence of TD: 2.9%  

Metoclopramide
- Approved for use up to 12 weeks
- Risk for TD <1%  

Mechanism of TD

TD: Risk Factors

- Dose of antipsychotic drug
- Length of exposure to antipsychotic drug
- Concomitant use of anticholinergics
- **AGE**
  - Female gender
  - African-American ancestry
  - Presence of mood disorder
  - Presence of dementia
  - Prior history of acute extrapyramidal syndrome

TD: Genetics

- **Pharmacokinetics**
  - CYP2D6, VMAT2, SOD2, HSPG2

- **Pharmacodynamics**
  - DRD2, DRD3, 5HTRA, 5HTRC

- **Examples:**
  - rs363224 polymorphism of the VMAT2 gene has been associated with TD
  - rs1799732 polymorphism of the DRD2 gene has been associated with TD in a study sample of European ancestry

Abnormal Involuntary Movement Scale (AIMS)

● Includes an examination procedure
● Developed by NIMH and in the public domain
● The exam can usually be done in 10 minutes or less

NIMH = National Institute of Mental Health.
ABNORMAL INVOLUNTARY MOVEMENT SCALE (AIMS)

NAME: ____________________________________________

DATE: ____________________________________________

Prescribing Practitioner: ______________________________

CODE: 0 = None
       1 = Minimal, may be extreme normal
       2 = Mild
       3 = Moderate
       4 = Severe

INSTRUCTIONS:
Complete Examination Procedure (attachment d.)
before making ratings

MOVEMENT RATINGS: Rate highest severity observed. Rate movements that occur upon activation one less than those observed spontaneously. Circle movement as well as code number that applies.

<table>
<thead>
<tr>
<th>Movement Type</th>
<th>Movements</th>
<th>Rating Example</th>
</tr>
</thead>
<tbody>
<tr>
<td>Facial and Oral Movements</td>
<td>Muscles of Facial Expression: e.g., movements of forehead, eyebrows</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td></td>
<td>periorbital area, cheeks, including frowning</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td></td>
<td>blinking, smiling, grimacing</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td></td>
<td>1. <strong>Lips and Perioral Area</strong>: e.g., puckering, pouting, smacking</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td></td>
<td>2. <strong>Jaw</strong>: e.g., biting, clenching, chewing, mouth opening, lateral</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td></td>
<td>movement</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td></td>
<td>3. <strong>Tongue</strong>: Rate only increases in movement both in and out of mouth.</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td></td>
<td>NOT inability to sustain movement. Darting in and out of mouth.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>4. <strong>Upper extremities (arms, wrists, hands, fingers)</strong>: Include</td>
<td></td>
</tr>
<tr>
<td></td>
<td>choreic movements (i.e., rapid, objectively purposeless, irregular,</td>
<td></td>
</tr>
<tr>
<td></td>
<td>spontaneous) athetoid movements (i.e., slow, irregular, complex, serotonin).</td>
<td></td>
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<tr>
<td></td>
<td>DO NOT INCLUDE TREMOR (i.e., repetitive, regular, rhythmic)</td>
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<tr>
<td></td>
<td>5. <strong>Lower extremities (legs, knees, ankles, toes)</strong>: e.g., lateral knee</td>
<td></td>
</tr>
<tr>
<td></td>
<td>movement, foot tapping, heel dropping, foot squirming, inversion and</td>
<td></td>
</tr>
<tr>
<td></td>
<td>eversion of foot.</td>
<td></td>
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<td></td>
<td>6. <strong>Trunk movements</strong>: Neck, shoulders, hips e.g., rocking, twisting,</td>
<td></td>
</tr>
<tr>
<td></td>
<td>squirming, pelvic gyrations</td>
<td></td>
</tr>
</tbody>
</table>

This scale is available in the public domain and has not been modified. Final 9/2000.
### AIMS (Continued)

| Global Judgments | 8. Severity of abnormal movements overall | 0 | 1 | 2 | 3 | 4 | 0 | 1 | 2 | 3 | 4 | 0 | 1 | 2 | 3 | 4 | 0 | 1 | 2 | 3 | 4 |
| 9. Incapacitation due to abnormal movements | 0 | 1 | 2 | 3 | 4 | 0 | 1 | 2 | 3 | 4 | 0 | 1 | 2 | 3 | 4 | 0 | 1 | 2 | 3 | 4 |
| 10. Patient’s awareness of abnormal movements. Rate only patient’s report | No awareness | 0 | | | | | | | | | | | | | | | | | | | | |
| Aware, no distress | 1 | | | | | | | | | | | | | | | | | | | | |
| Aware, mild distress | 2 | | | | | | | | | | | | | | | | | | | | |
| Aware, moderate distress | 3 | | | | | | | | | | | | | | | | | | | | |
| Aware, severe distress | 4 | | | | | | | | | | | | | | | | | | | | |
| 11. Current problems with teeth and/or dentures | No | Yes | No | Yes | No | Yes | No | Yes | No | Yes | No | Yes | No | Yes | No | Yes | No | Yes | No | Yes | No | Yes |
| 12. Are dentures usually worn? | No | Yes | No | Yes | No | Yes | No | Yes | No | Yes | No | Yes | No | Yes | No | Yes | No | Yes | No | Yes | No | Yes |
| 13. Edentia? | No | Yes | No | Yes | No | Yes | No | Yes | No | Yes | No | Yes | No | Yes | No | Yes | No | Yes | No | Yes | No | Yes |
| 14. Do movements disappear in sleep? | No | Yes | No | Yes | No | Yes | No | Yes | No | Yes | No | Yes | No | Yes | No | Yes | No | Yes | No | Yes | No | Yes |

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TD: Differential Diagnosis

- Huntington’s disease
- Wilson’s disease
- Neuroacanthocytosis
- Prion diseases
- Neurodegeneration with brain
- Sydenham chorea antiphospholipid antibody syndrome
- Systemic lupus erythematosus
- Anti-N-methyl-D-aspartate receptor
- Other autoimmune diseases

TD: Treatment

- Insufficient evidence for withdrawal of dopamine receptor blocking agents
- Insufficient evidence for switching from first generation antipsychotics to second generation antipsychotics

Mechanism of Action of VMAT2 Inhibitors

**TD: Treatment**

- Deutetrabenazine 24 mg BID max
- Valbenazine 40 - 80 mg QD

- Tetrabenazine 50 mg TID max (my choice)
  - Level C

- Clonazepam 0.5 - 4.5 mg QD  
  - Gingko biloba
  - Level B

- Amantadine 300 - 400 mg QD
  - Level C

- Diazepam – Propranolol – Melatonin – Levetiracetam – Piracetam  
  - Vitamin B6 – Vitamin E – BCAAs – Botulinum neurotoxin
  - Level U

- Pallidal deep brain stimulation
  - Level C

BCAAs = branched-chain amino acids.

The term TD may denote tardive syndromes in general or may denote only one of the tardive syndromes (the classic oro-bucco-lingual dyskinesia).

Exposure to dopamine receptor blocking agents (DRBAs) is usually at least 3 months; TD persists after discontinuation of the DBRAs, sometimes for only a while, sometimes forever.

The classic oro-bucco-lingual dyskinesia may include involvement of trunk and limbs (especially hands and feet).

The pathogenesis of TD is still viewed as the result of induction of dopamine receptor supersensitivity.

The advent of VMAT2 inhibitors has brought about a significant change for the better in the treatment of TD.
SMART Goals
Specific, Measurable, Attainable, Relevant, Timel

- Assess the signs and symptoms of TD in patients treated with antipsychotic medications
- Determine appropriate evidence-based treatment of TD
Don’t forget to fill out your evaluations to collect your credit.