Tardive Dyskinesia

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Characteristics: Involuntary movements, usually occurring after months or years of antipsychotic treatment. The most common symptoms are oro-buccal-lingual, such as chewing, lip smacking, and tongue protrusion. Occasionally causes movements of fingers or toes and rarely, in severe cases, may affect torso and gait.

Meds That Cause It: Antipsychotics, especially first-generation antipsychotics (3%–5% per year); the risk is smaller with second-generation antipsychotics. Among second-generation antipsychotics, risperidone confers the highest risk.

Mechanism: D2 blockade leading to dopamine receptor supersensitivity.

Diagnosis:

- Ask patients if they've ever been told they have TD or other movement disorders.
- Assess all patients who are on antipsychotics for TD by administering the Abnormal Involuntary Movement Scale (AIMS).
    - The AIMS has 12 items to be rated and can be completed in about 10 minutes. The patient should not have anything in their mouth (dentures, gum) and should be seated in a firm, armless chair. See our fact sheet reproducing the full AIMS and instructions on how to use it.

General Management:

- **Discontinuation**. Gradually discontinue the offending antipsychotic, if possible. If you abruptly discontinue a long-term antipsychotic, the TD symptoms can paradoxically worsen, because you are "uncovering" the hypersensitive dopamine receptors.
- **Switching**. If the patient's psychotic illness is too severe for discontinuation of the antipsychotic, you should gradually transition to a second-generation antipsychotic with low dopamine occupancy, such as quetiapine, clozapine or lurasidone.

First-Line Medications:

VMAT2 inhibitors (Vesicular monoamine transporter type 2 inhibitors) are clearly the most effective medications for reducing TD symptoms and should be the first line agents—and they take about 6 weeks to yield measurable improvement. All three VMAT2 inhibitors are likely equally effective, but Valbenazine is generally the first choice simply because it can be dosed once daily. Tetrabenzine has the advantage of being generic but the disadvantages of not having FDA approval for TD (though data shows it is effective) and of requiring three times daily dosing.

- **Valbenazine** (Ingrezza) 40 mg/day; increase to 80 mg/day after a week. FDA approved for TD.
- **Deutetrabenazine** (Austedo): Start 6 mg BID; ↑ _weekly by 6 mg/day increments to maximum dose of 48 mg/day (divide doses >12 mg/day BID); use QD dosing with ER formulation. FDA approved for TD.
- **Tetrabenazine** (Xenazine): Start 12.5 mg QD for one week, increase by 12.5 mg/day increments weekly to usual dose of 75–150 mg QD (divided doses >37.5 mg TID). FDA approved for Huntington's disease. Not FDA approved for TD but likely effective.

- **Side effects of VMAT2 inhibitors:**
    - Most common side effect: sedation, which generally improves over time.
    - Less common: akathia, tremor, depression, anxiety.
    - Both deutetrabenazine and tetrabenazine are contraindicated in patients with suicidal ideation or untreated/inadequately treated depression.

Second-Line Medications:

- **Benzodiazepines** (eg, clonazepam [Klonopin] or lorazepam [Ativan] 0.5–1 mg daily or BID). Can help with both dyskinesia and anxiety associated with TD.
- **Amantadine** (Symmetrel) 100–300 mg/day.
- **Gingko biloba extract** 240 mg/day.

Clinical Pearls:

- Risk factors for TD include first-generation antipsychotics more so than second-generation antipsychotics, higher-potency agents, duration of exposure, higher dose, elderly age, and Black ethnicity.
- Increasing the dose of the antipsychotic will improve symptoms temporarily but probably make them worse in the long run.

Fun Fact:

Antipsychotics aren't the only medications that may cause TD. Prolonged use of medications for nausea and reflux like metoclopramide (Reglan) and prochlorperazine (Compazine), which also block dopamine, have also been associated with TD.