

Rare Side Effects of Antipsychotics

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What are Antipsychotics?

- They are a class of drugs that can be used to treat a variety of conditions in psychiatry.
- Antipsychotics are separated into **2 categories**:
First-generation and Second-generation
- **First-generation antipsychotics**, also known as neuroleptics, are used to manage:
 - Acute psychosis of any cause
 - Acute agitation
 - Chronic psychotic disorders
 - Bipolar mania
- **Second-generation antipsychotics**, also known as atypical antipsychotics, are used to manage:
 - Chronic psychotic disorders
 - Bipolar mania / depression
 - Treatment resistant depression

Examples of Antipsychotics

First Generation Antipsychotics

Second Generation Antipsychotics

Fluphenazine

Trifluoperazine

Aripiprazole

Ziprasidone

Haloperidol

Chlorpromazine

Olanzapine

Lumateperone

Loxapine

Thioridazine

Paliperidone

Lurasidone

Pimozide

Perphenazine

Quetiapine

Asenapine

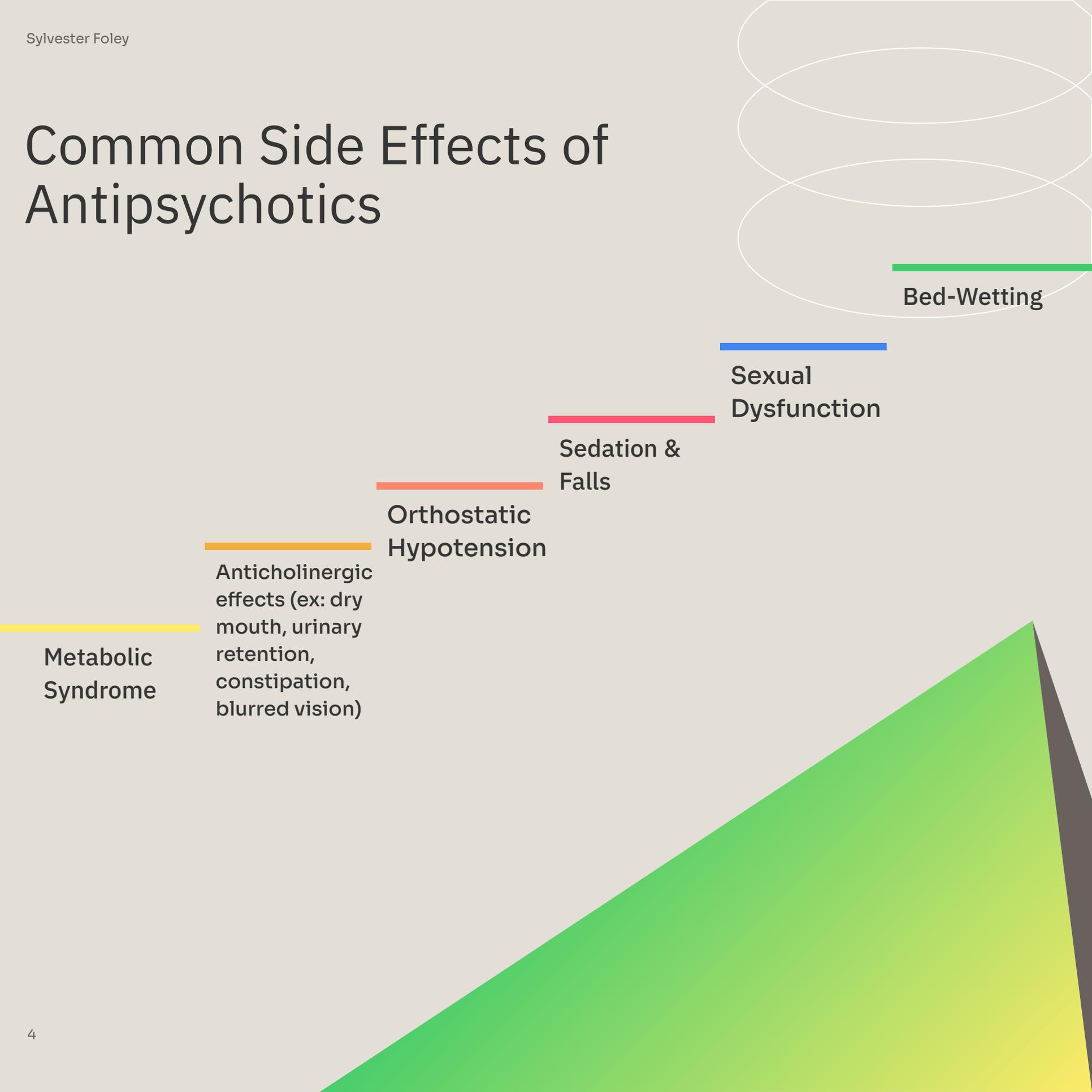
Thiothixene

Prochlorperazine

Risperidone

Clozapine

Common Side Effects of Antipsychotics



Rare Side Effects of Antipsychotics

At times, taking antipsychotics can lead to rare side effects. They can be very dangerous, impactful to one's quality of life, and some can even be irreversible.

Some of the most known rare side effects include:

- Tardive Dyskinesia
- Extrapiramidal Symptoms (Parkinsonism, Acute Dystonia, and Akathisia)
- Cardiovascular Events
- Agranulocytosis
- Seizures
- Neuroleptic Malignant Syndrome

Tardive Dyskinesia (TD)

- TD is a condition that is usually associated with **longer term use of first generation antipsychotics**. Usually after at least **6 months** of medication, but can show up as early as **1 month** in **elderly** patients.
- Symptoms consist of **random involuntary movements** such as: lip-smacking, tongue thrusting, jaw movements, facial grimacing, and arm or leg movements.
- To **screen** for these symptoms, psychiatrists ask patients to fill out a standardized assessment called **Abnormal Involuntary Movement Scale (AIMS)**.
 - This can help to determine changes of TD overtime

Extrapyramidal Symptoms (EPS)

- EPS is also a condition associated mostly with first-generation antipsychotics (FGAs), major examples include: haloperidol, fluphenazine, loxapine, pimozide, and thiothixene
- EPS is a **group of movement disorders** that includes **Parkinsonism, Acute Dystonia, and Akathisia**
- Patients on FGAs should be asked about restlessness, slow movements, shaking, and rigidity at baseline and weekly during dose increases.

Parkinsonism

- Slower body movements
- Body rigidity
- Tremors (usually on one side of the body)

Acute Dystonia

- Sudden, painful, muscle contractions
- Parts of the body that are usually affected are: eyes, head, neck, and diaphragm
- **IMPORTANT:** If diaphragm is affected, this can potentially lead to suffocation

Akathisia

- Feelings of restlessness, shaking or inability to stay still

Cardiovascular Events

- Both first- and second-generation antipsychotics can increase the risk for adverse cardiovascular events including: QT prolongation, myocarditis, and increased risk of death

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QT Prolongation

- QT prolongation means that the heart's **electrical system** takes **longer** than usual to recover between heartbeats
- Cases of sudden death that are seen from antipsychotic use are believed to be due to this cause

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Myocarditis

- Myocarditis is **inflammation** of the heart muscle
- **Clozapine** has been associated with potentially fatal cases of myocarditis. Most often in the first few weeks or months of treatment

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Increased Risk of Death

- antipsychotic medications are associated with an increased risk of **stroke, myocardial infarction**, and **death** when used to treat behavioral symptoms in older adults with dementia
- The mechanism for this association has not been fully figured out

Agranulocytosis

- This is a condition that results in very **low absolute neutrophil count (ANC)**. It is officially defined as an ANC count of **less than 100**
- **Neutrophils** are a type of white blood cell that helps our body to **fight infections**
- Agranulocytosis has been associated with use of first-generation antipsychotics, but is mainly associated with **clozapine** (a second-generation antipsychotic)
- Patients who take clozapine have to get their ANC checked **weekly** for the first 6 months on the medication, then **every other week** for an additional 6 months, then **monthly** after that.

Seizures

- There is an increased risk of seizures with use of first-generation antipsychotics, especially haloperidol and tri fluphenazine
- When it comes to second-generation antipsychotics, clozapine has the highest risk of seizures
- Patients who have underlying risk of seizures (ex: epilepsy) or are taking other medications that lower seizure threshold should be cautious when initiating antipsychotic medications

Neuroleptic Malignant Syndrome (NMS)

- This is a combination of symptoms that are mostly associated with first-generation antipsychotics. These symptoms include:
 - Fever
 - Muscle rigidity
 - Autonomic Instability (on/off high blood pressure, palpitations)
 - Tremors
 - Excessive sweating
 - mental status changes (ex: delirium)
- This condition can lead to death and is considered a **medical emergency**
- Treatment consists of **immediately stopping** the prescribed antipsychotic, providing **supportive care** (hydration, cooling, etc.), and using **dantrolene** (to reverse muscle rigidity if needed)

Key Takeaways

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Be Aware of Your Symptoms

The symptoms mentioned in this presentation are rare, but can occur in patients. It is important to **recognize symptoms** and let your Primary Care Provider & Psychiatrist know.

2

Track Progress if Symptoms Are Present

If these side effects do occur, it is important to consistently **track your symptom progress** with your psychiatrist with **standard screenings** such as: Abnormal Involuntary Movement Scale (AIMS) & The Barnes Akathisia Scale or Simpson Angus Scale

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Remember These Side Effects Are RARE

It is important to remember that these side effects are **rare**. Many patients can remain completely free from symptoms while on antipsychotics, and if symptoms do occur they are more likely to be more common ones.

Key Takeaways

References

- Jibson MD. First-generation antipsychotic medications: Pharmacology, administration, and comparative side effects. In: UpToDate, Connor RF (Ed), Wolters Kluwer. (Accessed on December 18, 2025.)
- Jibson MD. Second-generation and other antipsychotic medications: Pharmacology, administration, and side effects. In: UpToDate, Connor RF (Ed), Wolters Kluwer. (Accessed on December 18, 2025.)