

● NCLEX 2026 ● PSYCHOSOCIAL ● PHARM EMERGENCIES

Serotonin Syndrome *VS* Neuroleptic Malignant Syndrome *VS* Extrapyramidal Symptoms

Three high-yield psychiatric pharm emergencies that NCLEX writers love to confuse. Compare the trigger drugs, the timeline, the muscle/reflex signature, and the priority intervention — these are your differentiators.

SYSTEM · MENTAL HEALTH · PHARMACOLOGICAL THERAPIES · REDUCTION OF RISK POTENTIAL

PRIORITY · RECOGNITION · ACTION

SS · TOO MUCH SEROTONIN

Serotonin Syndrome

Excess 5-HT activity from serotonergic drug combos or overdose.

Onset · Hours (<24h)

NMS · TOO LITTLE DOPAMINE

Neuroleptic Malignant Syndrome

D2 dopamine blockade from antipsychotics → autonomic + thermal storm.

Onset · Days to 2 Weeks

EPS · DOPAMINE PATHWAY EFFECT

Extrapyramidal Symptoms

Nigrostriatal D2 blockade → 4 motor syndromes across a timeline.

Onset · Hours → Years

1 Definition & Overview

WHAT IT IS · WHY IT MATTERS

SEROTONIN SYNDROME

- Life-threatening reaction to **excess CNS serotonin**, usually from drug-drug interaction.
- Defined by the **Hunter Criteria**: mental status change + autonomic instability + neuromuscular hyperactivity.
- Why it matters: prevention is nursing-led — assess every new med added to a serotonergic regimen.

NMS

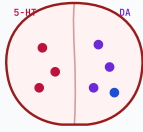
- Rare but lethal idiosyncratic reaction to **dopamine-blocking agents** (antipsychotics).
- Tetrad: **hyperthermia, lead-pipe rigidity, altered mental status, autonomic instability**.
- Mortality 5–20% if unrecognized — early ID and ICU-level supportive care are everything.

EPS

- Group of **4 movement disorders** from D2 blockade in the nigrostriatal pathway.
- Not directly life-threatening except **acute dystonia with laryngospasm**.
- Assessed with the **AIMS scale**; tardive dyskinesia is often irreversible — prevention > treatment.

2 Pathophysiology

MECHANISM · STEP BY STEP



The big idea: SS and NMS sit on opposite ends of the neurotransmitter seesaw — too much serotonin in one, too little dopamine in the other. EPS comes from the same dopamine blockade as NMS, just expressing as motor pathway dysfunction instead of an autonomic storm. Recognize which neurotransmitter system you're disturbing and the rest of the picture follows.

Serotonin Syndrome 5-HT EXCESS

- Two or more serotonergic agents combined **OR** overdose of one.
- Excess 5-HT floods **5-HT_{1A} & 5-HT_{2A}** receptors in brainstem & spinal cord.
- Hyperactivity of autonomic, neuromuscular, and cognitive pathways.
- **Triad:** mental status change · autonomic instability · neuromuscular hyperactivity (clonus, hyperreflexia).

NMS D₂ BLOCKADE

- Antipsychotic blocks **D₂ receptors** in hypothalamus, basal ganglia, & mesolimbic pathways.
- Hypothalamic dysregulation → **thermoregulation failure** (hyperthermia).
- Basal ganglia blockade → **lead-pipe rigidity** → muscle breakdown.
- Rhabdomyolysis → ↑CK, myoglobinuria → **acute kidney injury**.

EPS NIGROSTRIATAL D₂ BLOCK

- Antipsychotic blocks D₂ in the **nigrostriatal pathway**.
- Loss of dopamine's inhibition → unopposed cholinergic activity in striatum.
- 4 motor syndromes emerge along a **timeline:** dystonia → akathisia → parkinsonism → TD.
- Tardive dyskinesia: chronic blockade causes **D₂ receptor supersensitivity** (often irreversible).

3 Signs & Symptoms

RED FLAGS • HALLMARK FINDINGS

FEATURE	SEROTONIN SYNDROME	NMS	EPS
Onset	Rapid — minutes to <24 hrs after dose change	Slow — 1–3 days, up to 2 weeks	Varies: hrs (dystonia) → years (TD)
Mental status	Agitation, restlessness, hypomania, confusion	Stupor, mutism, coma (slower decline)	Usually intact
Temperature	Hyperthermia (often <40°C / 104°F)	SEVERE hyperthermia (>40°C / 104°F)	Normal
Muscle tone	Rigidity + clonus (esp. lower extremities)	Lead-pipe generalized rigidity	Spasms, tremor, OR involuntary movements (by type)
Reflexes	HYPERreflexia (hallmark!)	HYPO or normoreflexia	Normal
Pupils	Mydriasis (dilated)	Normal / variable	Normal
GI	Hyperactive bowel sounds, diarrhea, nausea	Decreased / ileus	Drooling (parkinsonism)
Autonomic signs	Tachycardia, HTN, diaphoresis, shivering, flushing	Tachycardia, BP fluctuations, profuse diaphoresis, pallor	Generally absent
Labs	Mildly ↑ CK, ↑ WBC	↑↑ CK (often >1000), ↑ WBC, ↑ LFTs, myoglobinuria	Usually normal

SS • THE TELL

- **Inducible clonus** at ankles + **hyperreflexia** = nearly diagnostic.
- 🔴 **Temperature >41.1°C / 106°F = medical emergency.**
- "Bobbing" eye movements (ocular clonus).

NMS • THE TELL

- **Lead-pipe rigidity** across ALL muscle groups (not just one limb).
- 🔴 **CK > 1,000 + cola-colored urine = rhabdo → call provider STAT.**
- Slower, sicker, hotter than SS.

EPS • THE TELL

- 🔴 **Acute dystonia of neck/throat → laryngospasm = airway emergency.**
- Pill-rolling tremor + mask-like face = pseudoparkinsonism.
- Lip-smacking, tongue protrusion = TD (often irreversible).

3a The Four EPS Syndromes

MEMORIZE BY TIMELINE OF ONSET

01

Acute Dystonia

HOURS → DAYS

Sudden sustained muscle spasms: **torticollis**, **oculogyric crisis**, **opisthotonus**, jaw clenching. 🚑 **Laryngospasm = airway emergency.**

Tx: benztropine OR diphenhydramine IM/IV STAT.

02

Akathisia

DAYS → WEEKS

Subjective motor **restlessness**, inability to sit still, pacing, foot tapping. Often misread as anxiety or worsening psychosis — don't ↑ the dose.

Tx: propranolol, benzos, lower antipsychotic dose.

03

Pseudoparkinsonism

WEEKS → MONTHS

Tremor (pill-rolling), **rigidity**, **bradykinesia**, mask-like facies, shuffling gait, drooling. Mimics Parkinson disease.

Tx: benztropine, trihexyphenidyl, amantadine.

04

Tardive Dyskinesia

MONTHS → YEARS

Involuntary lip smacking, tongue protrusion, chewing, facial grimacing, choreoathetoid limb movements. 🚑 **Often irreversible.**

Tx: Stop / switch antipsychotic; valbenazine or deutetrabenazine (VMAT2 inhibitors).

AIMS scale (Abnormal Involuntary Movement Scale) — performed q3–6 months on all clients on antipsychotics. Detects TD early, when intervention may still help.

4 Priority Nursing Interventions

ABCS • SAFETY • NCLEX PRIORITY

SEROTONIN SYNDROME

🚑 **STOP all serotonergic agents — this is the priority action.**

- **Airway:** assess gag, prepare for intubation if rigidity severe.
- **Breathing:** continuous SpO₂, supplemental O₂ PRN.
- **Circulation:** 2 large-bore IVs, IV crystalloids, continuous cardiac monitor.
- **Cool** aggressively if temp >38.5°C: ice packs, cooling blanket, evaporative cooling.
- Administer **benzodiazepines** for agitation, myoclonus, rigidity.
- Anticipate **cypheptadine** (5-HT antagonist) PO/NG — the antidote.
- Strict I&O, monitor renal function (rhabdo risk).
- Avoid antipyretics — fever is from muscle activity, not central.

NMS

🚑 **STOP the antipsychotic immediately — priority action.**

- **A/B:** airway protection, O₂; intubate if needed.
- **C:** aggressive IV fluids to prevent AKI from rhabdo.
- **Cool** aggressively — temps frequently >40°C.
- Administer **dantrolene** (muscle relaxant — direct on skeletal muscle).
- Administer **bromocriptine** or **amantadine** (dopamine agonists).
- Monitor **CK, BUN/Cr, urine output, urine color** — rhabdo → AKI.
- Transfer to **ICU**; expect a 7–14 day course.
- Do **not** resume same agent; if antipsychotic needed later, wait ≥2 wks, try low-potency atypical.

EPS

🚑 **Acute dystonia w/ laryngospasm = STAT: airway first, then benztropine 1–2 mg IM/IV or diphenhydramine 25–50 mg IM/IV.**

- Akathisia: rule out worsening psychosis — don't ↑ dose; consider **propranolol**.
- Pseudoparkinsonism: fall precautions, anticholinergic (**benztropine**).
- TD: assess with **AIMS q3–6 months**; if found, notify provider — may need med change.
- Anticholinergic teaching: dry mouth, urinary retention, constipation, blurred vision.
- Switch from typical (haloperidol) → atypical (risperidone, olanzapine) for lower EPS risk.
- Document baseline movement assessment before starting any antipsychotic.

The shared #1 priority for SS & NMS: stop the offending drug. For EPS with airway involvement (laryngospasm), airway management precedes everything else — including the antidote.

5 Pharmacology — Triggers & Treatments

CAUSE IT • TREAT IT

Drugs that CAUSE each syndrome

SS TRIGGERS

- SSRIs: fluoxetine, sertraline, paroxetine, citalopram
- SNRIs: venlafaxine, duloxetine
- ⚠️ MAOIs + any serotonergic = highest risk
- TCAs: amitriptyline, clomipramine
- Triptans: sumatriptan (migraines)
- Opioids: tramadol, meperidine, fentanyl
- linezolid, methylene blue, St. John's Wort, dextromethorphan, ondansetron
- Recreational: MDMA, cocaine, LSD

NMS TRIGGERS

- ⚠️ High-potency typicals (FGAs): haloperidol, fluphenazine — highest risk
- Typical: chlorpromazine, thioridazine
- Atypicals (lower but real risk): risperidone, olanzapine, clozapine, quetiapine
- Antiemetics with D2 blockade: metoclopramide, prochlorperazine, promethazine
- Abrupt withdrawal of Parkinson meds (levodopa) can also cause it
- Risk ↑ with: dose ↑, depot/long-acting injections, dehydration, hot environment, male, agitation

EPS TRIGGERS

- ⚠️ FGAs (typicals): highest EPS risk — esp. haloperidol, fluphenazine
- SGAs (atypicals): lower risk; risperidone at higher doses still causes EPS
- Clozapine & quetiapine: lowest EPS risk
- Non-psychiatric culprits: metoclopramide, prochlorperazine, promethazine
- Risk ↑ with: higher dose, longer duration, older adults (TD), female (TD), drug-naïve youth (dystonia)

Drugs that TREAT each syndrome

DRUG	CLASS / MECHANISM	USE & KEY NURSING NOTES
Cyproheptadine	5-HT _{2A} antagonist (antihistamine)	SS antidote. 12 mg PO/NG, then 2 mg q2h until response. SE: sedation, anticholinergic.
Dantrolene	Direct skeletal muscle relaxant (↓ Ca ²⁺ release)	NMS (also malignant hyperthermia). IV dosing. Monitor LFTs — hepatotoxic.
Bromocriptine	Dopamine agonist	NMS. Restores dopamine tone. SE: nausea, hypotension, psychosis worsening.
Benztropine	Anticholinergic	EPS — acute dystonia & pseudoparkinsonism. IM/IV for emergencies. Anticholinergic SEs: "can't see, can't pee, can't spit, can't sh*t."
Diphenhydramine	H1 antihistamine w/ anticholinergic activity	Acute dystonia. 25–50 mg IM/IV. Faster than benztropine — use when in doubt.
Propranolol	Beta-blocker (lipophilic, crosses BBB)	Akathisia. Hold for HR <60 or SBP <90. Avoid in asthma.
Valbenazine / Deutetrabenazine	VMAT2 inhibitors (deplete presynaptic dopamine)	Tardive dyskinesia. Monitor for QT prolongation, depression, sedation.
Benzodiazepines	GABA enhancers	Adjunct in SS (agitation, myoclonus) and NMS (rigidity, agitation).

6 NCLEX Test Traps

WHERE STUDENTS LOSE POINTS

⚠️ "Confusion + Fever + Rigidity" → Don't auto-pick SS

SS and NMS share these. The decider: **onset speed + reflexes**. Hours + hyperreflexia/clonus = SS. Days + lead-pipe rigidity + hyporeflexia = NMS. Look at the **drug** too — SSRI → SS; antipsychotic → NMS.

⚠️ Akathisia ≠ anxiety or worsening psychosis

A client just started on an antipsychotic who's "pacing and can't sit still" is the classic **akathisia** trap. **Wrong action:** ↑ the antipsychotic dose. **Right action:** recognize EPS, notify provider, expect propranolol or dose reduction.

⚠️ First action is always STOP the drug

For SS and NMS, the priority intervention on NCLEX is **discontinue the offending agent** — before antidotes, before cooling, before fluids (after airway/breathing in ABCs). The antidote is treatment *after* removal of cause.

⚠️ Acute dystonia of the neck = airway, NOT just give benztropine

Laryngospasm or opisthotonus involving the throat is an **airway emergency**. Position for airway patency first, call rapid response, THEN IM/IV diphenhydramine or benztropine. Don't pick "administer benztropine" if airway isn't yet secure.

⚠️ Don't use antipyretics in SS or NMS

Acetaminophen is **ineffective** — fever comes from muscle hyperactivity, not central thermoregulation. Treatment is **external cooling** + treating the muscle problem (benzos, dantrolene). NCLEX will offer "administer acetaminophen" as a distractor.

⚠️ CK + dark urine = NMS rhabdo, not "infection"

A client on haloperidol with elevated CK, tea-colored urine, and ↑ creatinine has rhabdomyolysis from NMS. NCLEX may distract with sepsis. Look at the medication list — antipsychotic + rigidity + ↑ CK = NMS.

⚠️ "Pill-rolling tremor" in a psych client → not Parkinson's

In someone on an antipsychotic, classic Parkinson features mean **pseudoparkinsonism (EPS)**. Treat with anticholinergic (benztropine), not levodopa. Levodopa would worsen psychosis.

⚠️ Tardive dyskinesia: lower the dose can make it WORSE first

D2 receptor supersensitivity means abruptly lowering or stopping the antipsychotic can **unmask** TD before it improves. Slow taper + switch to atypical or VMAT2 inhibitor. NCLEX answer is rarely "stop abruptly."

7 Patient & Family Education

PREVENTION • RECOGNITION • REPORTING

📖 For SS prevention

- ✓ Show the pharmacist your **complete med list** — including OTCs, herbals, migraine meds.
- ✓ Wait **2 weeks** (5 weeks for fluoxetine) between MAOI and SSRI.
- ✓ Avoid **St. John's Wort** while on SSRIs.
- ✓ Tell every provider you're on an SSRI/SNRI before any new prescription.
- ✓ Report: agitation, sweating, shivering, twitching, fever, diarrhea — even mild signs.

📖 For NMS prevention

- ✓ **Stay hydrated** on antipsychotics — esp. in summer or with exercise.
- ✓ Don't stop Parkinson meds suddenly.
- ✓ Report immediately: muscle stiffness, fever, sweating, fast heart rate, confusion.
- ✓ Tell ER staff **every** psych med you're on, including long-acting injectables.
- ✓ If you had NMS once, you're at higher risk again — flag in chart.

📖 For EPS

- ✓ Report: stiffness, drooling, tremor, restlessness, or jaw/neck spasms.
- ✓ Don't stop antipsychotic suddenly — can worsen movements & psychosis.
- ✓ Take with food to ↓ nausea; rise slowly (orthostasis).
- ✓ Sun protection — antipsychotics cause photosensitivity.
- ✓ Avoid alcohol — additive CNS depression.
- ✓ Keep follow-up for **AIMS** screening.

8

Memory Boosters & Mnemonics

LOCK IT IN

SHIVERS

SEROTONIN
SYNDROME

- S** Shivering
- H** Hyperreflexia / clonus
- I** Increased temperature
- V** Vital sign instability
- E** Encephalopathy (confusion)
- R** Restlessness / tremor
- S** Sweating

FEVER

NMS

- F** Fever (very high, >40°C)
- E** Encephalopathy (mental status ↓)
- V** Vital sign instability (autonomic)
- E** Elevated CK / enzymes
- R** Rigidity (lead-pipe)

ADAPT

EPS TIMELINE

- A** Acute dystonia (hours)
- D** Dopamine block — all 4 share this cause
- A** Akathisia (days)
- P** Pseudoparkinsonism (weeks)
- T** Tardive dyskinesia (months/years)



Pattern Recognition — Lock-in Phrases

SS = "SEROTONIN SPRINTS"

Fast onset, HYPER everything (reflexes, bowel sounds, tone), MYDRIASIS. Think: *serotonin sprints into the synapse*.

NMS = "DOPAMINE DROPS & DEAD"

Slow onset, lead-pipe rigidity, HIGH fever, HIGH CK. Think: *dopamine drops out, muscles freeze and break down*.

EPS = "EARLY → LATE MOTOR"

ADAPT timeline: dystonia first (hours) → TD last (years). Mental status preserved.

One-line differentiator: Hyperreflexia + clonus + fast onset = SS · Lead-pipe rigidity + sky-high CK + slow onset = NMS · Motor signs only + clear mind + tied to antipsychotic dose = EPS.