

Serotonin Syndrome

A plain-English guide for you and your family

WHAT IS HAPPENING

Your brain uses serotonin—a chemical messenger—to steady your mood, keep you alert, control your body temperature, and move your muscles smoothly. Normally serotonin rises a bit when you need to focus or feel good, then drops back to a calm level. Serotonin syndrome happens when two medicines (or a medicine plus a drug like MDMA) stack up and flood the brain with way too much serotonin all at once. The brain circuits that use serotonin get locked into overdrive. Your body tries to fight the flood: your heart races, your blood pressure shoots up, you sweat and shake, your muscles jerk and stiffen (especially your legs), your pupils grow wide, and you may feel confused, restless, or see things that aren't there. In severe cases your temperature spikes dangerously high, which can damage muscles, kidneys, and other organs. This is not random chaos—every symptom is your nervous system screaming because it cannot turn off the serotonin signal. The good news: if the medicines are stopped quickly and your body is cooled and calmed, most people recover fully. The danger is waiting too long or not recognizing the pattern, because high fever and rigid muscles can lead to organ failure within hours.

What you might feel

- Agitation or restlessness
- Fast heart rate (tachycardia)
- Dilated pupils (mydriasis)
- Muscle twitching or jerking (myoclonus)
- Rigid or stiff muscles (especially in the legs)
- Sweating more than usual (diaphoresis)
- Confusion or trouble thinking clearly
- High fever (hyperthermia)
- Shivering or tremor
- Diarrhea

Call the doctor right away if...

- High fever above 104°F (40°C)—this means the body is overheating dangerously and can damage organs.
- Seizures (sudden shaking you can't stop)—the brain is firing out of control.
- Very stiff muscles that won't bend (severe rigidity)—this can break down muscle tissue and poison the kidneys.
- Fast, confused thinking that gets worse quickly—sign the brain is overwhelmed.
- Low blood pressure or trouble staying awake—means the body is starting to shut down.

What the care team will do

- Stop all serotonin-raising medicines immediately and hold them until a doctor reviews the case.
- Check temperature every 15 minutes, and if it is 102.2°F (39°C) or higher, start aggressive cooling right away with ice packs to the groin and armpits, cold IV saline, and a cooling blanket.
- Give lorazepam (Ativan) 1 to 2 mg IV or diazepam (Valium) 5 to 10 mg IV, and repeat every 10 to 15 minutes until the patient is calm and muscles relax.
- Monitor heart rate, blood pressure, and oxygen levels continuously, and place the patient on a cardiac monitor.
- If the patient is confused, agitated, or having seizures, protect the airway and keep suction and intubation equipment at the bedside.
- Draw blood to check creatine kinase (CK, a marker of muscle breakdown), kidney function (creatinine and BUN), liver enzymes, and electrolytes, and send a urine sample to check for myoglobin.
- Start two large-bore IV lines and give normal saline at 200 to 300 mL per hour if the patient is sweating heavily, has a fever, or has signs of muscle breakdown.
- If agitation, fever, and muscle rigidity do not improve with benzodiazepines and cooling, prepare to give cyproheptadine (Periactin) 12 mg by mouth or feeding tube, then 2 mg every 2 hours, as ordered by the doctor.

Medicines you may be given — and why

Stop all serotonin-boosting drugs immediately

The body has too much serotonin (a brain messenger that controls mood, movement, and body heat) because of the medicines the person is taking. Stopping those drugs lets serotonin levels

fall back to safe levels. Most people start feeling better within 24 hours after the last dose leaves the body.

Aggressive cooling (ice packs, cooling blankets, cold IV fluids)

Serotonin syndrome causes dangerously high body temperature (hyperthermia) because too much serotonin makes muscles contract rapidly (like shivering on overdrive) and disrupts the hypothalamus (the brain's thermostat). Cooling from the outside and inside lowers core body temperature and prevents organ damage from the heat.

Lorazepam or diazepam

Lorazepam and diazepam boost GABA (the brain's main calming signal) in the brain and spinal cord. This calms the overactive nerves that are firing too fast because of excess serotonin, relaxes stiff muscles, lowers agitation, and helps control fever by reducing muscle activity.

Cyproheptadine

Cyproheptadine blocks serotonin from locking onto 5-HT_{2A} receptors (the serotonin docking sites that drive fever, muscle stiffness, confusion, and agitation when overstimulated). By blocking these receptors, it directly reverses the core problem in serotonin syndrome—too much serotonin activity.

AVOID antipsychotic drugs (e.g., haloperidol, olanzapine, chlorpromazine)

Antipsychotic drugs block dopamine receptors (the brain's movement and reward control system) and can also block receptors that help cool the body. In serotonin syndrome, giving an antipsychotic worsens muscle stiffness, raises body temperature even higher, and can trigger neuroleptic malignant syndrome (NMS)—a similar but distinct life-threatening reaction. They do NOT help serotonin syndrome and actively make it more dangerous.

Intubation, mechanical ventilation, and ICU-level supportive care

In severe serotonin syndrome, the person may become so confused or sedated (from benzodiazepines and cyproheptadine) that they cannot protect their airway, or muscles may be so rigid that breathing becomes too hard. Intubation (placing a breathing tube) and mechanical ventilation (a machine that breathes for the person) keep oxygen flowing to the brain and organs while the serotonin clears. ICU monitoring catches and treats complications like seizures, heart rhythm problems, kidney failure, and dangerously low blood pressure.

Where this information comes from

- Boyer & Shannon 2005, New England Journal of Medicine
- American College of Medical Toxicology (ACMT)

- Toxicology and Applied Pharmacology consensus reviews
- UpToDate clinical reference (Lexicomp drug interaction database)

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