

Serotonin syndrome

Introduction

Serotonin syndrome is a condition characterized by dangerously high levels of serotonin — a chemical produced by nerve cells — in your body.

Serotonin syndrome can occur when you take certain combinations of prescription medications that affect serotonin levels in your body. For example, serotonin syndrome can occur if you take selective serotonin reuptake inhibitors (SSRIs) or serotonin and norepinephrine reuptake inhibitors (SNRIs) for depression along with triptan medications to treat migraine. Serotonin syndrome can also occur if you take SSRIs with other drugs or supplements that affect serotonin levels, such as St. John's wort.

Signs and symptoms of serotonin syndrome range from restlessness and rapid heartbeat to muscle rigidity and seizures. These go away quickly with treatment, which may include discontinuing use of the medications causing the symptoms along with taking other drugs such as muscle relaxants and serotonin-production blocking agents. If not treated quickly, serotonin syndrome can become life-threatening.

Signs and symptoms

Signs and symptoms of serotonin syndrome typically occur within several hours of taking a new drug or taking a previously used drug at an increased dosage level, and may include:

- Extreme agitation or restlessness
- Confusion
- Hallucinations
- Loss of coordination
- Fast heartbeat
- Rapid changes in blood pressure
- Fever
- Heavy sweating
- Overactive reflexes
- Nausea, vomiting and diarrhoea
- Seizures
- Coma

Causes

Your nerve cells produce serotonin as a normal part of their functioning. Nerve cells in your brain and spinal cord (central nervous system) produce serotonin that helps regulate your attention, behaviour and body temperature. Other nerve cells in your body, primarily in your intestines, also produce

serotonin. In these other areas, serotonin plays a role in regulating your digestive process, blood flow and breathing.

When your body has too much serotonin, typically from taking too much medication that affects serotonin levels, the excess can cause serotonin syndrome.

Serotonin syndrome generally occurs when you take multiple drugs that affect serotonin levels in your body. In particular, taking an selective serotonin reuptake inhibitor (SSRI) along with triptans, a class of migraine medications, may cause the condition — potentially raising serotonin to dangerous levels.

However, serotonin syndrome can also occur when you start a single new drug that affects serotonin levels or when you take an increased dose of such a drug that you've previously used. Many drugs may lead to serotonin syndrome. These drugs include but aren't limited to:

- **SSRIs** such as citalopram (Celexa), fluoxetine (Prozac, Sarafem), fluvoxamine, paroxetine (Paxil) and sertraline (Zoloft)
- **Serotonin and norepinephrine reuptake inhibitors (SNRIs)** such as trazodone (Desyrel) and venlafaxine (Effexor)
- The **norepinephrine and dopamine reuptake inhibitor (NDRI)** bupropion (Wellbutrin, Zyban)
- **Monoamine oxidase inhibitors (MAOIs)** such as isocarboxazid (Marplan) and phenelzine (Nardil)
- **Pain medications** such as fentanyl (Sublimaze), meperidine (Demerol), pentazocine (Talwin) and tramadol (Ultram)
- **Anti-nausea medications** such as granisetron (Kytril), metoclopramide (Reglan) and ondansetron (Zofran)
- **Anti-migraine medications** such as almotriptan (Axert), naratriptan (Amerge), sumatriptan (Imitrex) and zolmitriptan (Zomig)
- **Over-the-counter cough and cold medications** containing dextromethorphan (Robitussin DM, Sudal DM)
- **Illegal drugs** such as Ecstasy, LSD and Syrian rue
- **Herbal supplements** such as St. John's wort and ginseng
- **Lithium** (Eskalith, Lithobid)

Screening and diagnosis

No single test can confirm a serotonin syndrome diagnosis. Your doctor will diagnose the condition by ruling out other possibilities.

Your doctor will likely start by asking about your medical history and any medications you're taking. Serotonin syndrome can mimic other conditions: for example, neuroleptic malignant syndrome — a condition that can occur following use of certain tranquilizer (neuroleptic) drugs — or an overdose of cocaine or an MAOI.

To rule out other conditions, your doctor may use tests that measure any other drugs you're using or abusing, check your hormone levels, and assess key body functions that may be affected by serotonin syndrome.

To be diagnosed with serotonin syndrome, you must be taking a drug that can affect your body's serotonin levels and be experiencing three of the following:

- Agitation
- Uncoordinated movements
- Heavy sweating not due to activity
- Diarrhoea
- Overactive reflexes
- Fever
- Mental status changes such as confusion
- Muscle spasms
- Shivering
- Tremor

Treatment

Serotonin syndrome is treated by stopping any medications you're taking that could be increasing your serotonin levels. Your doctor also may keep you in the hospital for observation for several hours. Serotonin syndrome often resolves within 24 hours of stopping any medication that increases serotonin and starting any necessary treatment.

More severe cases of serotonin syndrome may require additional medications and longer hospitalization. Depending on your symptoms, you may receive the following treatments:

- **Monitoring your vital signs**, such as heart rate, blood pressure and temperature, and treating those as needed.
- **Muscle relaxants.** Benzodiazepines, such as diazepam (Valium) or lorazepam (Ativan), can help control agitation, seizure-like movements and muscle stiffness.

- **Serotonin-production blocking agents.** If other treatments aren't working, the drug cyproheptadine can help by blocking serotonin production.
- **Drugs that control heart rate and blood pressure.** These could include esmolol (Brevibloc) or nitroprusside (Nitropress) to reduce an increased heart rate or high blood pressure, or phenylephrine (Neo-Synephrine) or epinephrine to increase blood pressure that's too low.

If your condition is severe, you may also need a breathing tube and machine and medications that keep your muscles still (paralyze them).

Prevention

If you're taking serotonin-related drugs, particularly more than one, such as a triptan, with either an SSRI or SNRI, you may be at increased risk of serotonin syndrome. Talk to your doctor about possible risks. Don't stop taking any such medications on your own. If your doctor prescribes a new medication, make sure he or she knows about all the other medications you're taking — especially if you receive prescriptions from more than one doctor.

If you and your doctor decide the benefits of combining certain serotonin-level-affecting drugs outweigh the risks, be alert to the possibility of serotonin syndrome. If you develop restlessness, hallucinations or any other signs or symptoms of serotonin syndrome, seek medical attention immediately.