CONDITION

Serotonin syndrome

Serotonin syndrome is a potentially serious reaction to medicines or drugs that raise serotonin activity.

WHAT IT IS
Excess serotonin activity affecting nerves, muscles, and temperature control

BODY SYSTEM
Nervous system, muscles, and body temperature control

MAIN SYMPTOMS
Agitation, sweating, tremor, overactive reflexes

WHAT CAUSES IT
Medicines, drug interactions, or overdose

HOW IT IS DIAGNOSED
Clinical examination; no single confirmatory test

MAIN TREATMENT
Stopping trigger medicines and supportive hospital care

CAN IT BE CURED?
Yes - usually resolves when trigger removed

IS IT AN EMERGENCY?
Yes - with fever, rigidity, seizures, or reduced consciousness

LONG-TERM OUTLOOK
Most recover fully; severe complications can cause lasting harm

Overview

Serotonin syndrome is a reaction caused by too much serotonin activity in the body. Serotonin is a chemical messenger involved in mood, digestion, sleep, temperature control, and muscle movement.

The condition most often develops after starting a serotonin-raising medicine, increasing its dose, taking too much, or combining substances that affect serotonin. It can also follow an interaction between a prescribed medicine and an over-the-counter product, supplement, or recreational drug.

Symptoms can range from mild shaking and sweating to severe muscle rigidity, very high body temperature, seizures, and loss of consciousness. Because the condition can worsen quickly, suspected serotonin syndrome needs prompt medical assessment.

It is an acute reaction, not a long-term psychiatric condition. Once the triggering substances are stopped and complications are treated, most people recover fully. Severe cases can damage muscles, kidneys, or other organs.

Symptoms

Symptoms usually begin within several hours of taking a new substance, increasing a dose, or combining interacting substances. A delayed start is possible, especially when a medicine remains in the body for a long time.

The symptoms tend to involve three areas: changes in thinking or behaviour, overactive muscles and reflexes, and disruption of automatic body functions such as sweating and temperature control.

Possible symptoms include:

Clonus is an especially important sign. It may appear as repeated ankle movements when the foot is flexed, rhythmic eye movements, or spontaneous muscle jerking. A healthcare professional checks for this during the examination.

Severe serotonin syndrome may cause marked muscle rigidity, rapidly rising temperature, seizures, an irregular heartbeat, or reduced consciousness. These are emergency symptoms.

Not everyone has every symptom. Mild medication side effects, panic attacks, infections, and several other conditions can cause some similar features, so symptoms alone cannot confirm the diagnosis.

- Restlessness, anxiety, agitation, or confusion
- Tremor, muscle twitching, or jerking movements
- Overactive reflexes
- Repeated, involuntary muscle contractions called clonus
- Sweating, flushed skin, or shivering
- Diarrhoea, nausea, or vomiting
- Fast heartbeat or changing blood pressure
- Dilated pupils
- Fever

Causes and risk factors

Serotonin syndrome can occur when one substance strongly increases serotonin activity. It is more often linked to an overdose or a combination of substances that affect serotonin in different ways.

Potential triggers include some:

This does not mean that everyone taking these substances is at high risk. Most people who use a serotonin-raising medicine as directed do not develop serotonin syndrome.

Risk rises when serotonergic substances are combined, when a dose is increased, or when too much is taken. Some combinations are particularly dangerous, including a monoamine oxidase inhibitor with another strongly serotonergic medicine.

A previous medicine may still be present after it has been stopped. The time needed before starting another treatment differs greatly between medicines. This is why a planned change between antidepressants like sertraline or fluoxetine may require a carefully managed gap or gradual transition.

Liver or kidney problems can sometimes slow the removal of medicines from the body. Medication errors, duplicate prescriptions, and using products obtained from different sources can also increase risk.

- Antidepressants, including SSRIs, SNRIs, and monoamine oxidase inhibitors
- Opioid pain medicines, particularly medicines with serotonergic effects
- Migraine medicines
- Cough and cold products containing dextromethorphan
- Antibiotics such as linezolid
- Medicines containing methylene blue
- Mood treatments such as lithium
- Herbal products, including St John's wort
- Recreational substances, including MDMA

Diagnosis

There is no blood test or scan that confirms serotonin syndrome. Diagnosis is based on recent substance use, the timing of symptoms, and a physical examination.

The clinician will need to know about all prescription medicines, non-prescription products,

supplements, recreational drugs, and any recent dose changes. Information about an accidental or intentional overdose is also important.

The examination may include checks of temperature, heart rate, blood pressure, pupils, muscle tone, reflexes, and clonus. The Hunter Serotonin Toxicity Criteria are one set of clinical rules used to support diagnosis, particularly when a serotonergic substance has been taken.

Blood and urine tests do not measure whether there is too much serotonin activity in the nervous system. Instead, they help look for complications such as muscle breakdown, kidney injury, or changes in body salts. An electrocardiogram, or ECG, may be used to check the heart's rhythm.

Clinicians also consider other causes of similar symptoms. These include severe infection, heat illness, stimulant intoxication, withdrawal states, and neuroleptic malignant syndrome, a rare reaction to certain antipsychotic medicines.

Treatment and management

Treatment begins by stopping the substances thought to be causing the reaction. In someone being assessed for symptoms, this is managed alongside urgent medical review. If you take a serotonin-related medicine but have no symptoms, do not stop it suddenly without advice, because some medicines can cause withdrawal effects.

Supportive care helps the body recover while the substances are cleared. Depending on severity, this may include monitoring, fluids through a vein, oxygen, and medicine to settle agitation and reduce excessive muscle activity.

Benzodiazepines like diazepam or lorazepam may be used in hospital for agitation, tremor, clonus, or seizures. In some cases, clinicians use cyproheptadine, a medicine that blocks some serotonin effects. Evidence for specific serotonin-blocking treatments is limited, so they do not replace careful monitoring and supportive care.

A high temperature in serotonin syndrome is caused mainly by intense muscle activity, not by a change in the brain's fever setting. Cooling measures and control of muscle activity are therefore important. Standard fever medicines do not correct the underlying cause.

Severe cases may require intensive care. Treatment can include deep sedation, breathing support, and medicines that temporarily stop muscle movement. This is different from using physical restraints, which can increase muscle activity and body temperature.

People are usually observed until their temperature, mental state, heart rate, blood pressure, reflexes, and muscle activity have returned to a safe range.

Complications

Most cases resolve without lasting harm when they are recognised and treated. Complications are more likely when body temperature is very high or severe muscle activity continues.

Possible complications include:

Severe complications can be life-threatening, but they are not the expected outcome for every person with the condition.

- Dehydration and abnormal levels of body salts
- Breakdown of muscle tissue, called rhabdomyolysis
- Kidney injury caused partly by muscle breakdown
- Seizures
- Abnormal blood clotting
- Irregular heart rhythms
- Breathing problems
- Damage to organs from extreme overheating

Prevention

Many cases can be prevented, although accidental reactions cannot always be predicted.

Keep an up-to-date list of prescription medicines, non-prescription products, herbal remedies, and recreational substances. Share the complete list whenever a medicine is started, stopped, or changed.

Check before combining an antidepressant with a cough medicine, pain medicine, supplement, or recreational substance. Products bought without a prescription can still affect serotonin.

Take medicines only as directed, and avoid using another person's prescription. If you miss a dose, follow the medicine's instructions rather than taking extra to compensate.

Do not shorten a required waiting period between medicines. Some substances, including certain antidepressants, can remain active after the last dose.

If you previously had serotonin syndrome, tell future prescribers and pharmacists. The same substance or combination may need to be avoided, but a previous episode does not automatically rule out every serotonin-related treatment.

Living with it and what to expect

Serotonin syndrome is generally a short-term reaction rather than an illness that continues for months or years. Many people begin improving within a day after the trigger is stopped, although recovery can take longer when long-acting substances are involved.

Severe illness may require several days of hospital care. Recovery can take longer if there has been kidney injury, muscle damage, a seizure, or another complication.

After recovery, a medication review can identify the likely trigger and whether an interaction occurred. The review may lead to a different medicine, a lower-risk combination, or closer monitoring during future changes. Do not restart a suspected trigger unless the clinician managing your medicines says it is appropriate.

Most people can return to their usual activities after symptoms and complications have resolved. Serotonin syndrome does not usually keep returning by itself. A new episode requires renewed exposure to a triggering substance or combination.

Some people feel anxious about taking medicines again. A pharmacist or prescribing clinician can explain which substance was most likely responsible and which alternatives may be reasonable.

When to get medical help

Call emergency services now if you or someone with you has:

Do not drive yourself if you are severely unwell. Bring medicine packets or a medication list if this can be done safely.

Seek urgent medical assessment if new tremor, sweating, diarrhoea, restlessness, muscle twitching, or overactive reflexes develop soon after a medicine change, overdose, or new combination of substances. Contact a local poison information service immediately after a suspected overdose, even if symptoms have not appeared.

A routine medication appointment is appropriate if you have no symptoms but are concerned about a possible interaction or want a review before starting an over-the-counter product. A pharmacist can also check combinations. Routine review is not a substitute for urgent care when symptoms are developing.

- A seizure, collapse, or loss of consciousness
- Difficulty breathing

- Severe confusion or rapidly worsening agitation
- Marked muscle rigidity or uncontrollable jerking
- A high or rapidly rising temperature
- A very fast or irregular heartbeat

Common questions

How quickly does serotonin syndrome start?

It usually starts within hours of a new medicine, dose increase, overdose, or interaction. The timing can be longer when a substance is absorbed slowly or remains active in the body.

Can one medicine cause serotonin syndrome?

Yes. It can follow an overdose of one serotonergic substance and, less often, use at a standard dose. Combinations of substances are a more common concern because they can raise serotonin activity through several pathways.

Will serotonin syndrome go away on its own?

Mild symptoms may improve after the trigger is removed, but it is not safe to judge severity at home. The condition can worsen quickly, and medical assessment may be needed to distinguish it from ordinary side effects or another illness.

Is serotonin syndrome the same as an antidepressant side effect?

No. Nausea, headache, sleep changes, and mild sweating can occur as individual side effects. Serotonin syndrome is a pattern of symptoms that often includes abnormal muscle findings such as clonus, marked tremor, or overactive reflexes. A clinician must assess the full pattern.

Can I take antidepressants after serotonin syndrome?

Sometimes. The answer depends on the substance involved, the severity of the reaction, and whether an interaction or overdose caused it. Any restart or switch should be planned by the clinician responsible for the medicine, with enough time for the previous substance to clear.

Is serotonin syndrome the same as neuroleptic malignant syndrome?

No. Both can cause fever, altered awareness, and muscle problems, but they are linked to different medicines and often develop differently. Neuroleptic malignant syndrome usually causes pronounced stiffness and may develop more slowly. Both require urgent medical care.

Sources



- MedlinePlus Medical Encyclopedia: Serotonin syndrome , US National Library of Medicine
- Boyer EW, Shannon M. The Serotonin Syndrome , New England Journal of Medicine , 2005;352:1112-1120
- Dunkley EJC, Isbister GK, Sibbritt D, Dawson AH, Whyte IM. The Hunter Serotonin Toxicity Criteria , QJM , 2003;96(9):635-642
- Foong AL, Grindrod KA, Patel T, Kellar J. Demystifying serotonin syndrome, or serotonin toxicity , Canadian Family Physician , 2018;64(10):720-727
- US Food and Drug Administration: FDA warns about several safety issues with opioid pain medicines and requires label changes , Drug Safety Communication, 2016