**Target Serotonin Syndrome**
*Definition: Toxicity caused by excessive serotonin levels that results from a drug overdose or interaction*

### Assess the patient
Symptoms start within hours to 1 day of increasing a dose or adding a drug.

<table>
<thead>
<tr>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nervousness</td>
<td>Hyperreflexia</td>
<td>Fever &gt;38.5°C/101.3°F</td>
</tr>
<tr>
<td>Insomnia</td>
<td>Sweating</td>
<td>Confusion/delirium</td>
</tr>
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<td>Nausea/diarrhea</td>
<td>Agitation/restlessness</td>
<td>Sustained clonus/rigidity</td>
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<td>Tremor</td>
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<td>Big pupils</td>
<td>Side-to-side eye movements</td>
<td>Death</td>
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</table>

### Assess all drugs
Most cases involve 2 drugs that increase serotonin in different ways – full list on back.

- **Prescription drugs**
- **OTC and natural drugs**
- **Illicit drugs**

### Rule out
Serotonin syndrome can look like other things; diagnosis requires an accurate drug history.

- Antidepressant Discontinuation
- Anticholinergic Toxicity
- Malignant Hyperthermia
- Neuroleptic Malignant Syndrome
- Meningitis/Encephalitis
- Drug Overdose
- Alcohol/Benzo Withdrawal

#### Similar-looking conditions

- Fever >38.5°C/101.3°F
- Confusion/delirium
- Sustained clonus/rigidity
- Rhabdomyolysis
- Death
- Severe Hyperreflexia
- Sweating
- Agitation/restlessness
- Inducible clonus
- Side-to-side eye movements
- Nervousness
- Insomnia
- Nausea/diarrhea
- Tremor
- Big pupils
- Fever >38.5°C/101.3°F
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- Big pupils

### If you suspect serotonin syndrome
Don’t wait, take action – it progresses rapidly.

- Stop the drug(s)
- Refer patient to hospital
- Try other drugs or restart low doses slowly

### Prevent serotonin syndrome
Stay alert – most cases can be prevented.

- Use lowest effective dose
- Check drug monographs for tapering and wash-out periods
- Reassess the need for a serotonin drug yearly
- Ask about illicit drug use
- Follow up 1-2 days after upping a dose or starting a new drug
- Teach patients to recognize serotonin syndrome
SEROTONIN SYNDROME

**Commonly listed but unlikely to cause serotonin syndrome**

Commonly listed but unlikely to cause serotonin syndrome

**Triptans** (e.g., sumatriptan)

- **Antidepressants:** amitriptyline, mirtazapine, trazodone

- **Antiemetics:** 5HT3 receptor antagonists (e.g., ondansetron), metoclopramide

- **Buspirone, lithium**

**Illicit drugs**

- Ecstasy (MDMA), amphetamine, cocaine

**Natural health products**

- St. John’s wort, L-tryptophan, diet pills

**Cough, cold and allergy**

- Tramadol, meperidine, methadone, fentanyl (unlikely with morphine, codeine, oxycodone, buprenorphine)

**Opioids and other pain medications**

- Metyrapone, hydrocortisone

**Selective and irreversible MAO-A/B**

- Selegiline (non-selective at higher doses)

- Rasagiline

**Selective and reversible MAO-A/B**

- Moclobemide

- Methylene blue (non-selective at higher doses)

**Selective and irreversible MAO-A**

- Methylene blue (non-selective at higher doses)

**Selective and reversible MAO-A**

- Methylene blue (non-selective at higher doses)

**Group A**

- Non-selective and irreversible

  - MAO-A and B
  - Isocarboxazid
  - Isoniazid
  - Phenelzine
  - Tranylcypromine

- Non-selective and reversible

  - MAO-A and B
  - Linezolid

**Group B**

- Antidepressants

  - Selective Serotonin Reuptake Inhibitors (SSRI): Paroxetine, fluvoxamine, sertraline, citalopram, escitalopram, fluoxetine
  - Serotonin Norepinephrine Inhibitors (SNRI): Venlafaxine, desvenlafaxine, duloxetine
  - Tricyclic Antidepressants: Clomipramine, imipramine

- Opioids and other pain medications

  - Tramadol, meperidine, methadone, fentanyl (unlikely with morphine, codeine, oxycodone, buprenorphine)

- Cough, cold and allergy

  - Dextromethorphan (“DM”), chlorpheniramine

- Natural health products

  - St. John’s wort, L-tryptophan, diet pills

- Illicit drugs

  - Ecstasy (MDMA), amphetamine, cocaine

**Avoid:**

- Group A with Group A or Group A with Group B

**Caution:**

- Two or more Group B drugs especially when one is used at a high dose

**Monitor:**

- If a patient uses a Group B drug and a second Group B drug is added, start low, increase the dose cautiously, and watch for symptoms for 24-48 hours after every change.

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- Non-selective and irreversible

  - MAO-A and B
  - Isocarboxazid
  - Isoniazid
  - Phenelzine
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