Target Serotonin Syndrome

def: 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>
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</thead>
<tbody>
<tr>
<td>Nervousness</td>
<td>Hyperreflexia</td>
<td>Fever &gt;38.5°C/101.3°F</td>
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<tr>
<td>Insomnia</td>
<td>Sweating</td>
<td>Confusion/delirium</td>
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<tr>
<td>Nausea/diarrhea</td>
<td>Agitation/restlessness</td>
<td>Sustained clonus/rigidity</td>
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<tr>
<td>Tremor</td>
<td>Inducible clonus</td>
<td>Rhabdomyolysis</td>
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<tr>
<td>Big pupils</td>
<td>Side-to-side eye movements</td>
<td>Death</td>
</tr>
</tbody>
</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  Remind all patients:

Non-toxic increases in serotonin can cause anxiety, restlessness and irritability for 1-2 weeks

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
Gardner DM. Serotonin Syndrome.  

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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 24-48h after every change

**Group A**

Non-selective and irreversible MAO A and B  
Isocarboxazid  
Isoniazid  
Phenelzine  
Tranylcypromine

Non-selective and reversible MAO A and B  
Linezolid

Selective and irreversible MAO B  
Selegiline (non-selective at higher doses)  
Rasagiline

Selective and reversible MAO A  
Moclobemide  
Methylene blue (non-selective at higher doses)

**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

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