

# SEROTONIN SYNDROME

ICU NEURO NUGGETS  
Dr Hayden Stephenson, 2021

= a potentially **life-threatening** toxic state, due to serotonin excess

A dose-dependent **drug reaction** (both medicinal and recreational) resulting in hyper-stimulation of serotonin receptors

Occurs from interaction of two- or more serotonin enhancing medications, or following large overdose of a single serotonergic drug. Onset can be insidious, or rapid within minutes to hours of exposure

Death usually due to hyperpyrexia-induced multi-organ failure

## CLINICAL FEATURES:

Rapid onset in presence of serotonergic agents:

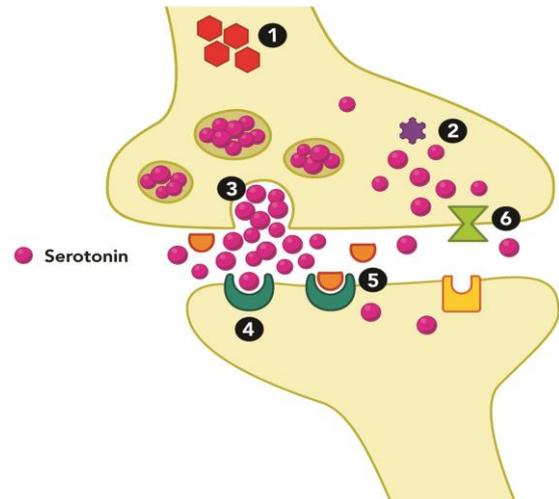
- **Altered mentation** (40%): agitation, confusion, delirium, hallucinations, coma, rarely seizures
- **Autonomic instability** (50%): sweating, tremor, tachycardia, flushing, diarrhoea, vomiting, hyperpyrexia
- **Neuromuscular excitation** (50%): tremor, teeth grinding, myoclonus, limb rigidity, hyper-reflexia

**Severe cases:** life-threatening pyrexia, rhabdomyolysis, raised creatine kinase, acute kidney injury, DIC, hyperkalaemia, multi-organ failure

## MANAGEMENT:

Most mild cases resolve spontaneously within 24 hours

- **STOP** all serotonergic agents (inc removing any transdermal patches, eg fentanyl)
- Maintain airway/breathing/circulation  
Ensure adequate hydration & urine output
- Perform 12-lead ECG, bloods (inc CK/coag), ABG
- Standard treatment is with **benzodiazepines**.  
Oral or IV **diazepam** (10-20mg) or **lorazepam** (1-2mg). IM **midazolam** (5-10mg)  
\*severe agitation may require high doses
- Agitation resistant to benzodiazepines may respond to **haloperidol** (5-10mg) or **ketamine** (1-1.5mg/kg IV or 5mg/kg IM)
- **Dexmedetomidine** inhibits serotonin release while also helping agitation/HTN/tachycardia



## RESPONSIBLE DRUGS:

1. Serotonin precursors: eg **tryptophan, L-dopa**
2. Serotonin breakdown inhibitors: eg **monoamine oxidase inhibitors, linezolid, methylene blue**
3. Serotonin release enhancers: eg **amphetamines, cocaine, ecstasy, opioids (oxycodone, buprenorphine), tramadol**
4. Serotonin receptor agonists: eg **LSD, triptans, mirtazapine, norpethidine** (metabolite of pethidine)
5. Serotonin receptor sensitivity enhancer: eg **lithium**
6. Serotonin re-uptake inhibitors: eg **SSRIs, SNRIs, TCAs (amitriptyline), trazodone, fentanyl, methadone, St John's wort, ondansetron**

- **Serotonin antagonists (5HT-2A): severe cases**  
**Cyproheptadine** 12mg PO or NG, followed by 4-8mg every 6 hours  
**Chlorpromazine** 12.5-25mg IV in severe cases followed by 25mg PO every 6 hours
- Mild-moderate hyperpyrexia:  
Fan, ice packs to groin/axilla, external cooling
- **Hyperpyrexia** management >38°C  
Measure core temperature  
RSI with paralysis (*avoid sux*) plus benzo infusion.  
Ice-baths, cold IV fluid, cold fluid lavage (gastric, bladder, peritoneal, chest), intravascular devices
- **Dantrolene** may benefit where there's muscular hyperactivity (*post synaptic muscle relaxant*)  
1mg/kg IV repeated up to max 10mg/kg
- Monitor for and manage **rhabdomyolysis** (IV fluid, renal replacement therapy) and **DIC** (clotting products) as necessary