

A **life-threatening condition** caused by **excessive serotonin activity** when exposed to serotonergic drugs (e.g. due to intentional overdose, therapeutic use, or drug interactions).

Serotonin modulates mood, cognition, sleep, temperature, platelets, GI motility, sexual behaviour.

## RISK FACTORS

- Using  $\geq 2$  serotonergic drugs
- Using  $\geq 1$  serotonergic drugs in combination with CYP450 inhibitors
- Switching serotonergic drugs without tapering
- MAO inhibitors** are associated with the most severe cases

## CONSULT PSYCHIATRY

to evaluate and manage concurrent mental health concerns, if appropriate.

## COMMONLY IMPLICATED DRUGS

**Serotonergic Agents:** *increase serotonergic activity*

- Antidepressants:** SSRIs, MAOIs, SNRIs, TCAs
- Stimulants:** amphetamines, cocaine, MDMA, methylphenidate
- Anti-emetics:** ondansetron, metoclopramide
- Opiates:** tramadol, fentanyl
- Herbals:** St. John's Wort, ginseng, tryptophan
- Other:** linezolid, triptans, dextromethorphan



**CYP450 Inhibitors:** *inhibit metabolism of serotonergic agents*

- E.g. antibiotics, antifungals, omeprazole, grapefruit juice

## CLINICAL FEATURES

Onset typically within 24h of consumption; occurs as a classic triad of:

### Autonomic Dysfunction:



Diaphoresis  
Tachycardia  
**Hypertension\*** / Labile BP  
Nausea, Vomiting, Diarrhea  
Mydriasis



### Neuromuscular Excitability:



Hyperreflexia  
**Muscle rigidity\***  
Myoclonus  
Clonus  
Horizontal ocular clonus



### Altered Mental Status:

Anxiety, Delirium  
Psychomotor agitation  
Lethargy  
**Altered LOC\***  
Shivering / Seizure



\* Occur more often in pediatric population vs adults

## DIAGNOSIS

Diagnosis is **CLINICAL** based on above features and serotonin exposure (*though may use "Hunter" criteria*)

## MANAGEMENT

- Immediate discontinuation of offending agent(s)
  - Symptoms should resolve within 24h of cessation
- Supportive care (oxygen, IV fluids, cooling)
- Investigate and manage complications:
  - Agitation, excessive muscle activity  $\rightarrow$  benzodiazepines
  - Autonomic instability  $\rightarrow$  antihypertensives
- Cyproheptadine may be considered for severe cases refractory to 1<sup>st</sup> line treatment such as benzodiazepines
- Consider ICU for severe cases



## PREVENTION

- Monitor **all** medications (prescriptions, OTC and herbal) and recreational drug use
- Avoid multiple serotonergic drugs
- Educate on signs and symptoms of toxicity and safe medication storage
- When prescribing – **start low, go slow**
- Do not misattribute irritability, agitation, or anxiety to patients' psychopathology
- Safety planning for patients with mental health concerns/history of suicidal ideation

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