



Serotonin Syndrome

Pediatric Emergency Medicine

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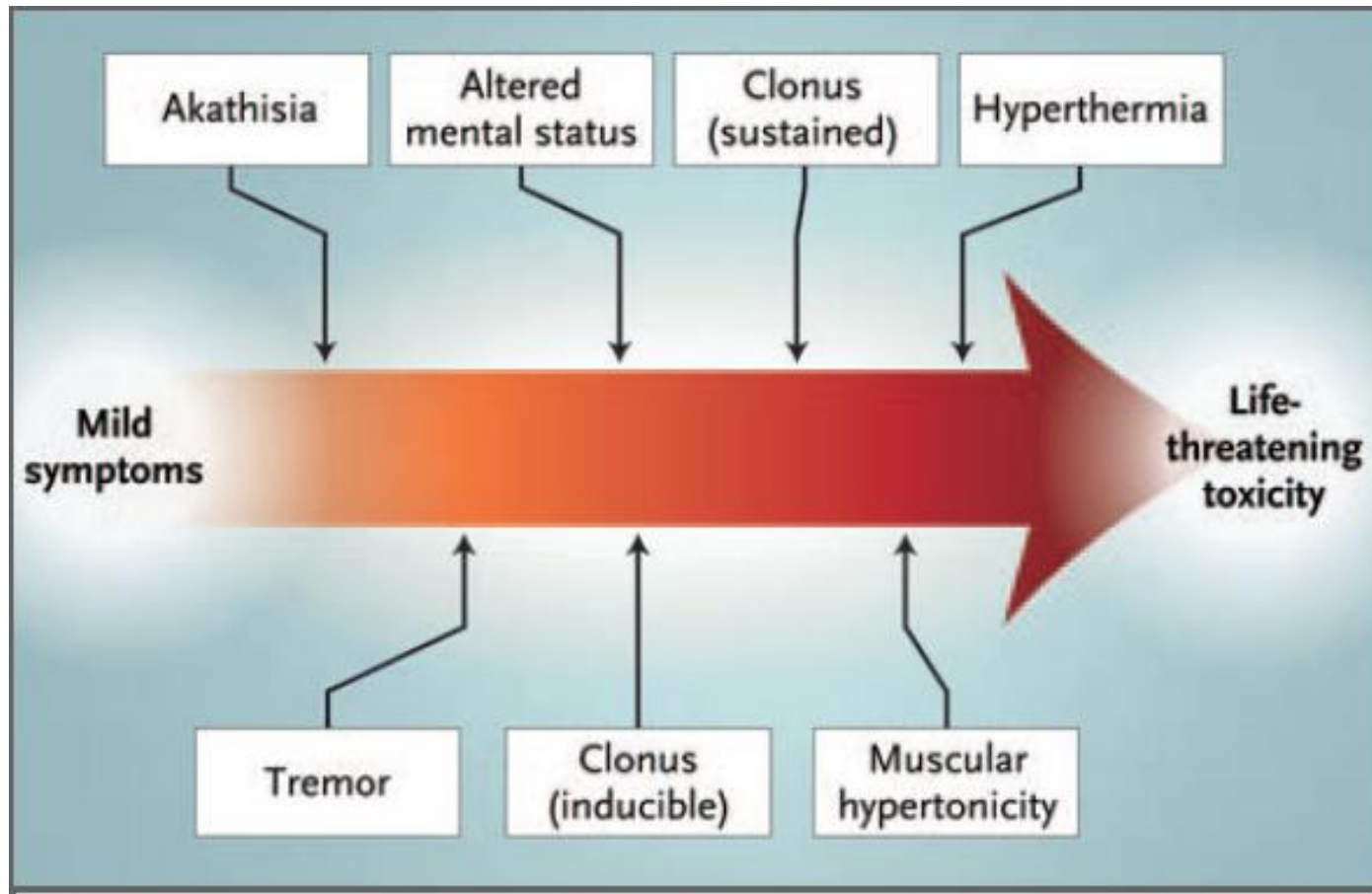
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Serotonin Syndrome

- Clinical triad of mental-status changes, autonomic hyperactivity, and neuromuscular abnormalities
- Classically associated with the simultaneous administration of two serotonergic agents, but it can occur after initiation of a single serotonergic drug, or increasing the dose of a serotonergic drug.
- Also described following intentional overdose

Spectrum of Clinical Findings



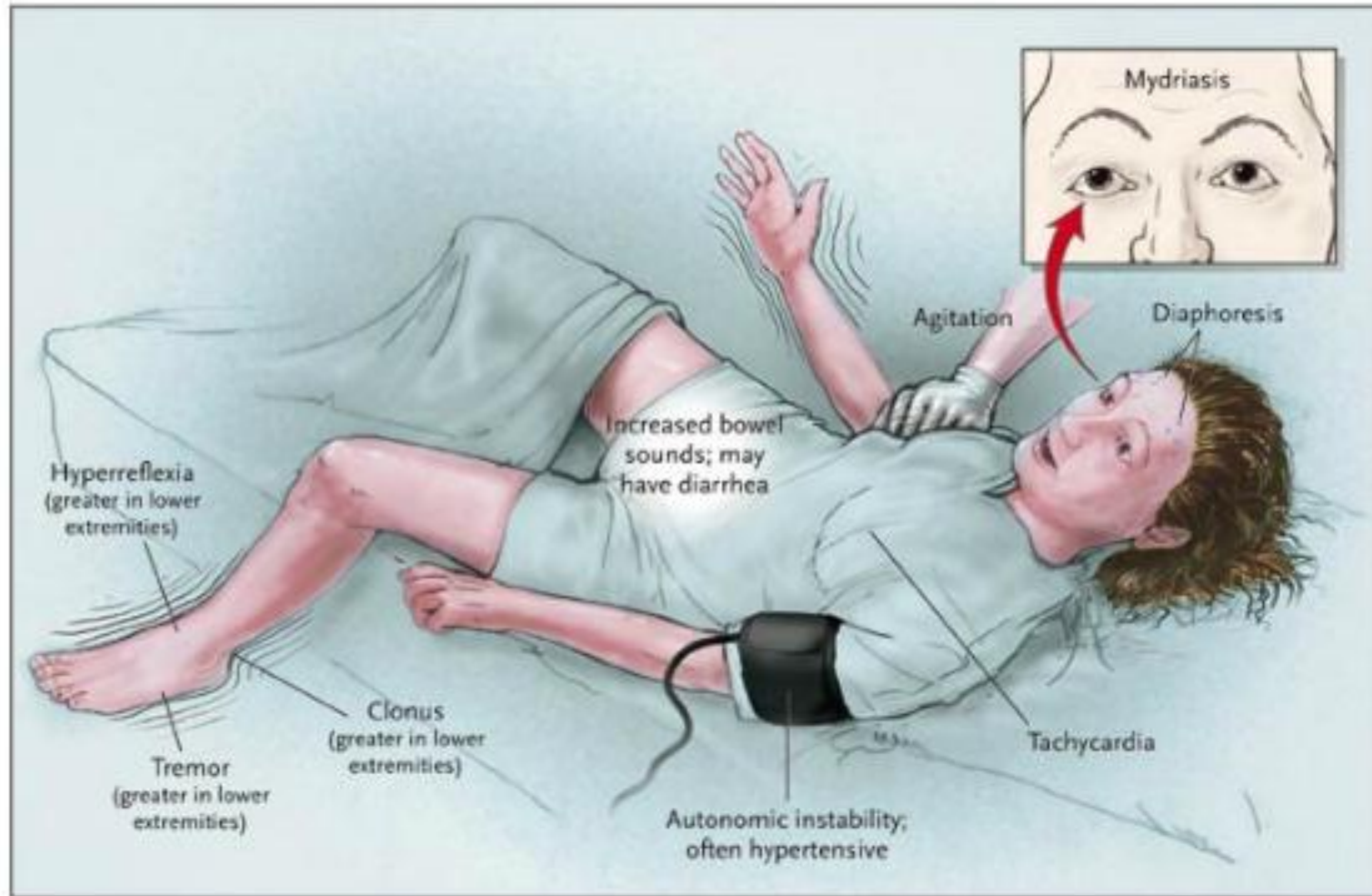
Pathophysiology

- Serotonergic neurons in the CNS
 - In the brainstem assists in the regulation of wakefulness, affect, food intake, thermoregulation, migraine, emesis, and sexual behavior.
 - Neurons in the lower pons and medulla participate in the regulation of motor tone.
- In the periphery, the serotonin system assists in the regulation of vascular tone and gastrointestinal motility.

Clinical Features

- Autonomic manifestations
 - Diaphoresis, Tachycardia, Hyperthermia, Hypertension, Vomiting, and Diarrhea
- Neuromuscular hyperactivity
 - Tremor, Rigidity, Myoclonus, Hyperreflexia, Bilateral Babinski

Neurological Manifestations



Associated Drugs

- SSRI's – Citalopram (Celexa), Sertraline (Zoloft), Fluoxetine (Prozac), Paroxetine (Paxil)
- Antidepressants: Trazodone, Bupropion (Wellbutrin), clomipramine, Venlafaxine (Effexor)
- MAOI's: Phenelzine
- Anticonvulsants: Valproate (Depakote)
- Analgesics: Fentanyl, Tramadol, Meperidine (Pethidine)
- Antiemetics: Ondansetron (Zofran), Metoclopramide (Reglan)
- Antimigraine: Sumatriptan
- Antibiotics: Linezolid, Ritonavir
- OTC: Dextromethorphan
- Abuse: LSD, MDMA (E)
- Supplements: St John's wort, Ginseng
- Other: Lithium

Citalopram

- Pharmacokinetics
 - Half-life elimination: Adults: Range: 24-48 hours; mean: 35 hours (doubled with hepatic impairment)
- Metabolism
 - Extensively hepatic, primarily via CYP3A4 and CYP2C19
- Poison Control Consult:
 - Overdose will impair hepatic clearance
 - Symptom manifestation can be expected up to 110 – 160 hours status post ingestion, with the most concerning QT prolongation occurring within 6 – 8 hours of ingestion

Management

- Discontinuation of all serotonergic agents
 - Often resolves within 24 hours of discontinuation, but drugs with long half-lives or active metabolites may cause symptoms to persist
 - Symptoms with MAOI's can persist for several days
 - SSRI's may contribute to Serotonin Syndrome up to several weeks after the drug has been discontinued
- Supportive care aimed at normalization of vital signs
 - Oxygen to maintain SpO₂ ≥94
 - Intravenous fluids for volume depletion, and hyperthermia
 - Continuous cardiac monitoring

Management

- Sedation with benzodiazepines
 - For controlling agitation as well as correcting mild increases in blood pressure and heart rate
- Administration of serotonin antagonists
 - In patients with severe symptoms, Cyproheptadine may be used
 - Pediatric dosing 0.25mg/kg/day divided q 6h
 - Dose titrated to maintain adequate sedation

References

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- Dunkley EJ, Isbister GK, Whyte IM et al -The Hunter Serotonin Toxicity Criteria: simple and accurate diagnostic decision rules for serotonin toxicity. QJM 2003;96:635-642
- [Uptodate.com/contents/SerotoninSyndrome](http://uptodate.com/contents/SerotoninSyndrome)