HYPERTHERMIC TOXIDROMES by Nick Mark MD

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OVERVIEW:

- Five toxidromes may present with overlapping features: ***hyperthermia***, ***rhabdomyolysis***, ***altered mental status/seizures***.
- Careful history & physical exam can help to differentiate, enabling prompt & correct treatment.
- These are clinical diagnoses (lab tests are not diagnostic)

GENERAL APPROACH TO TREATMENT:

- **Identify/Stop the causative medications**
- **Labs:** CK, U/A, BMP, LFTs, CBC, coags, BG, ECG (✓ QRS), VBG, toxicology testing (APAP, salicylates, etc to r/o co-ingestions)
- **ABCs:** intubation often necessary, ensure adequate MV
- **Cooling:** icepacks, cooling blankets, (antipyretics ineffective)
- **Agitation/Seizures:** BZDs (lorazepam)
- **IVF:** restore euvolemia, & prevent AKI from rhabdo
- **Blood Pressure control**: labetolol, dexmetomidine
- **GI decontamination:** depending timing of ingestion, & only with a secure airway
- Specific antidotes less important than general treatment
- **Poison center consultation** recommended

	SYMPATHOMIMETIC	ANTICHOLINERGIC	SEROTONIN SYNDROME	NEUROLEPTIC MALIGNANT	MALIGNANT HYPERTHERMIA
Mechanism	Excess release of monoamines (epi, NE, DA, 5HT) leadoing to overstimulation of adrenergic receptors.	Blockade of muscarinic Ach receptors impairs acetylcholine signaling in the CNS, on cardiac & smooth muscle, and on sweat glands.	Excessive release of 5H5, usually due to combination of 2 or more serotoninergic meds. Rarely it can occur with a single seratoninergic agent.	Ideosyncratic reaction to dopamine blockers (e.g. anti-psychotic) or due to abrupt cessation of dopamine agonists (e.g. Parkinson's Tx)	Rare ***pharmacogenetic*** disease caused by genetic susceptibility (AD mutations in ryanodine receptor) & triggered by inhaled anesthetics
Potential causes	**Illicits**: Methamphetamine, amphetamine, cocaine, MDMA,, "Designer": cathinones (bath salts), phenethylamines (NBOMe, Gravel), piperadines, tryptamines (DMT, "foxy-methoxy") **Rx Meds**: Methylphenidate, Theophylline *Toxicity may occur suddenly in body packers with ruptured pack.*	**Anti-histamines** (diphenhydramine) **sleep aids** (doxylamine), **TCAs**, **Parkinson's meds**, **Anti-spasmodics** (atropine, scopolamine), **skeletal muscle relaxants**, **Plants** (Jimson Weed, Nightshade) *Eye drops **can** cause systemic toxicity, esp in children/elderly*	**Antidepressants**: SSRIs, MAOIs, SNRI, nefazodone, trazadone **Stimulants**: cocaine, MDMA, methamphethamine, Triptans **Opioids**: fentanyl, tramadol, meperidine **Herbs** (St John's wort, nutmeg, ginseng) **Others** (lithium, valproate, ritonavir dextromethorphan, ***linezolid***, ondansetron, metoclopramide)	Most common with high potency **typical antipsychotics** (haloperidol,) but may also occur with **atypicals** (clozapine, olanzapine, risperidone, quetiapine) and other classes. **Anti-emetics** (metaclopramide, prochlorperazine, droperidol) **Withdrawal of chronic DA agonist** (levodopa/carbodopa, bromocriptine)	**Inhaled anesthesia agents** (all inhaled agents except NO) or **Depolarizing neuromuscular blockers** (**succinylcholine**) *Can occur after the first exposure to general anesthesia, however typically occurs after 3+ exposures to volatiles. Sux may be more likely to trigger MH on the 1st exposure*
Time from exposure	< 12 hrs	< 12 hrs	< 12 hrs	Usually 1-3 days after starting new med or after dose change	30 min to 24 hrs
Temp	↑ >38	↑ >38	↑ T >38	↑↑ T39-42	↑↑↑ Often T>42
Pupils	Normal	**DILATED** and **NON-REACTIVE**	**DILATED**	Normal	Normal
Muscle tone	normal	normal	May have **increased tone**, *particularly in lower extremities*	**RIGIDITY** present "lead pipe" RIGIDITY	**Extreme RIGIDITY** present "rigor mortis like" rigidity
Reflexes	normal	normal	**HYPERreflexia** of DTRs **CLONUS** present	**BRADYreflexia**	**HYPOreflexia**
Skin	sweaty	**RED, DRY, HOT**	sweaty	sweaty	sweaty
Urine	normal	**URINARY RETENTION**	normal	normal	normal
Bowel tones	normal	**ABSENT**	**HYPERACTIVE**	normal	normal
Other findings & diagnostic criteria	Extreme **HYPERTENSION**	May cause Lilliputian hallucinations Mneumonic: "Red as a beet, dry as a bone, hot as a hare, blind as bat, mad as a hatter"	Slow continuous horizontal eye movements (**OCULAR CLONUS**) Diagnosis is based on either **Hunter Criteria** (Se84% Sp97%) or presence of **Sternback criteria** (Se75 Sp96%)	Altered mental status can include **CATATONIA**, which may persist.	**HYPERCARBIA** may be first sign Rapid increase in core Temp (often 1°C increase / 10 minutes) & Muscle rigidity persists despite receiving NMB
Specific treatment	Laparotomy may be lifesaving for body packers with rupture. Use non-selective beta blockers (**labetolol**) to avoid "unopposed α stimulation. Theophylline is dialyzable	In severe cases consider slowly giving **Physostigmine** (risky as it can cause cholinergic toxicity; discuss risks/benefits with poison center) If wide QRS → bicarbonate	Consider **Cyproheptadine** as an adjunct in severe cases, however no evidence that **cyproheptadine** improves symptoms or outcomes	**Restart DA agonist if it was held** **DA agonists** (bromocriptine, amantadine) may also be useful In severe cases consider **dantrolene**	**Call for help & give Dantrolene** **Aggressive cooling, Match high MV needs** Education to patient about risk of recurrence (and testing for family)