HYPERTHERMIA SYNDROMES

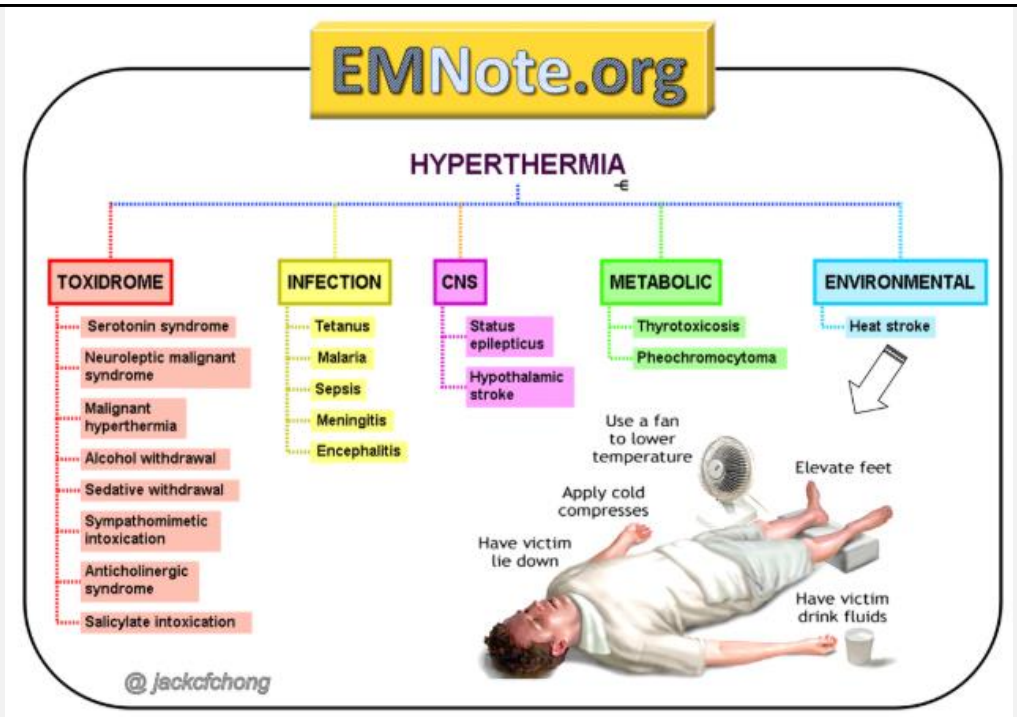
Andrew Bissonette

1

GOALS AND OBJECTIVES

- Expand fever differential
- Review select, high-yield tox disorders

2



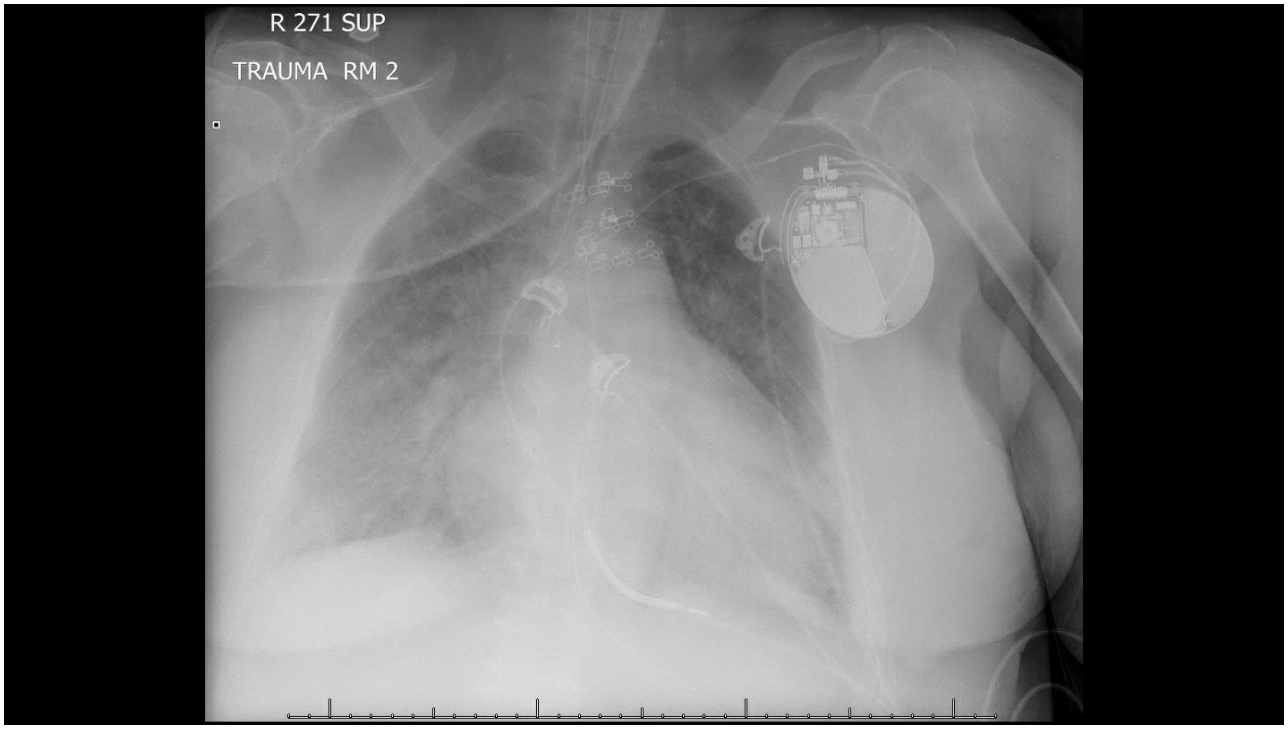
3

CASE #1

- 65 yo F with PMH of CKD stage 3, major depression on SSRI, and heart failure (EF 30%) s/p AICD who presents to the ED in respiratory extremis and is intubated
- Patient was coughing without fevers, chills, sweating
- Non-adherent to medications over past several days

- HR: 107 BP: 180/108 RR: 40 SpO_2: 74% Temp: 37.9° C

4



5

ED COURSE

- RSI intubation
- Treated with nitroglycerine drip up to 160 mcg/min
- Empiric antibiotics for pneumonia
- Central line: CVP = 20, $S_{CV}O_2$ = 37.2%
- Lactate 6.2 → 3.4

6

08/27/19 1306	40.3 °C (104.5 °F) !
08/27/19 1300	40.3 °C (104.5 °F) !
08/27/19 1249	40.3 °C (104.5 °F) !
08/27/19 1241	40.2 °C (104.4 °F) !
08/27/19 1230	40.2 °C (104.4 °F) !
08/27/19 1219	40 °C (104 °F) !
08/27/19 1206	39.9 °C (103.8 °F) !
08/27/19 1201	--
08/27/19 1200	39.8 °C (103.6 °F) !
08/27/19 1155	--
08/27/19 1145	39.5 °C (103.1 °F) !
08/27/19 1130	39.1 °C (102.4 °F) !
08/27/19 1116	38.8 °C (101.8 °F) !
08/27/19 1100	38.5 °C (101.3 °F) !
08/27/19 1052	38.5 °C (101.3 °F) !
08/27/19 1039	38.4 °C (101.1 °F) !

7

ED COURSE

- CVP = 12, $S_{CV}O_2$ = 67.3%
- Blood pressure drops
- Nitroglycerine 160 mcg/min → norepinephrine at 50 mcg/min
- Stress dose steroids, antibiotics broadened, Tylenol

- What else would you like to know or do?

8

Dantrolene given → temp resolves and pressors weaned

08/27/19 1851	--	36.4 °C (97.5 °F)
08/27/19 1746	--	38.9 °C (102 °F) !
08/27/19 1731	--	38.9 °C (102 °F) !
08/27/19 1725	--	38.9 °C (102 °F) !
08/27/19 1701	--	39 °C (102.2 °F) !
08/27/19 1646	--	38.9 °C (102 °F) !
08/27/19 1631	--	39.1 °C (102.4 °F) !
08/27/19 1616	--	39.2 °C (102.6 °F) !
08/27/19 1603	--	--
08/27/19 1601	--	39.3 °C (102.7 °F) !
08/27/19 1546	--	39.4 °C (102.9 °F) !
08/27/19 1516	--	39.5 °C (103.1 °F) !
08/27/19 1500	--	39.6 °C (103.3 °F) !
08/27/19 1446	--	39.6 °C (103.3 °F) !
08/27/19 1431	--	39.7 °C (103.5 °F) !
08/27/19 1416	--	39.8 °C (103.6 °F) !
08/27/19 1402	--	--
08/27/19 1400	--	39.9 °C (103.8 °F) !

9

Which finding is most commonly seen with malignant hyperthermia?

1) Rigidity
2) Rhabdomyolysis
3) Respiratory acidosis
4) Temperature > 40° C

10

Which finding is most commonly seen with malignant hyperthermia?

1) Rigidity
2) Rhabdomyolysis
3) Respiratory acidosis
4) Temperature > 40° C

11

EPIDEMIOLOGY

- Exposure to Succinylcholine or volatile anesthetic
- 1:100,000 administered anesthetics
- 50% of patients have had uneventful previous exposures
- 90% have negative family history
- 1-17% mortality rate
- 2:1 Male:Female

Anesth Analg. 2010;110(2):498
Anesth Analg. 2014 Dec;119(6):1359-66

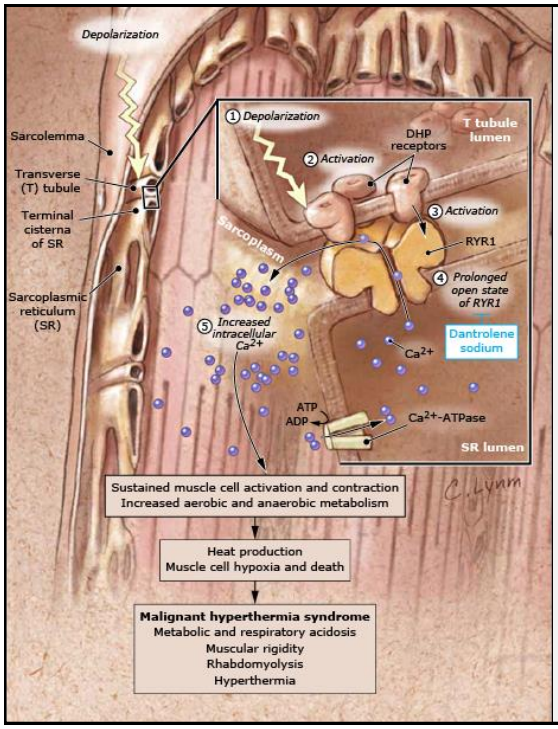
12

SIGNS/SYMPTOMS

- **Respiratory acidosis:** 99%
- **Rapidly rising temperature:** 50% (mean temp = 39.1)
  - Hyperthermia ≥ 10 minutes after triggering agent → look for alternative etiology
- **Generalized rigidity:** 40%
- **Metabolic acidosis:** 26%
- **DIC:** 7%
  - Cause of most deaths
- **Rhabdomyolysis**
- **Compartment syndrome**

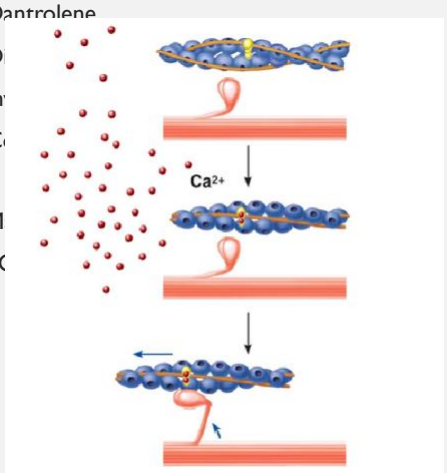
UpToDate.com, accessed 12/4/19
Anesth Analg. 2010;110(2):498

13



Management

- Dantrolene
- D
- In
- C
- M
- EC



UpToDate.com, accessed 12/4/19
Anesthesiology. 1994 Apr;80(4):771-9.

14

STUDIES

- ABG (pCO_2)
- BMP, K^+
- EKG
- CK, Urine myoglobin
- Coags and DIC panel

- WBC (leukocytosis 10,000-40,000 +/- left shift)

15

CASE #2

- 67 yo M with PMH of major depression on SSRI, metastatic breast cancer on chemo with chronic N/V on home ondansetron who presents with SOB
- T: 38.4 °C, HR 110, BP 92/65, RR 28, SpO2 82% RA
- CXR with RLL infiltrates
- Intubated for respiratory distress
- High dose fentanyl for pain/sedation
- Linezolid/cefepime, APAP, and sepsis resuscitation started
- T: 41.3 °C, HR 112, BP 122/86, RR 18, SpO2 99%
- Diffusely diaphoretic, shivering/tremulous, diarrhea

16

- Which diagnostic will you perform first?

1) Stool PCR
2) Lower Extremity Exam
3) C Diff Testing
4) Repeat Blood Cultures

17

- Which diagnostic will you perform first?

1) Stool PCR
2) Lower Extremity Exam
3) C Diff Testing
4) Repeat Blood Cultures

18

SEROTONIN SYNDROME

- No clear incidence
- Can occur with single drug, most common with ≥ 2
- Can occur long after SSRI discontinued ($T_{1/2}$ of fluoxetine = 1 week, meatbolite = 2.5 weeks)

Clin Toxicol (Phila). 2012;50(10):911.

19

Drugs involved and corresponding mechanisms implicate

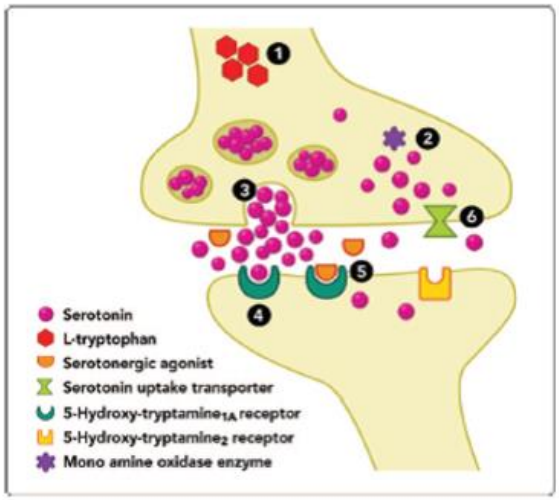


Fig. 1. Increase intrasynaptic serotonin levels: Mechanism

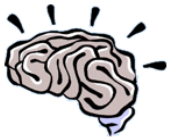
Anesthesiology 2011; 115:1291–8

- SSRIs, SNRIs, MAOIs, TCAs, Li^+
- Linezolid
- Most opioids, Tramadol
- Ondansetron
- Cocaine, Ecstasy
- Dextromethorphan, St. John's Wort

20

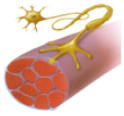
Serotonin syndrome

Rapid onset
Combination of 2+ serotonin agonists



Mental status changes
Agitation
Pressured speech

Autonomic instability
Tachycardia
Diarrhea
Shivering
Diaphoresis
Mydriasis



Neuromuscular abnormalitie
Clonus
Hyperreflexia (lower > upper)
Tremor
Seizure

Rx
Benzodiazepines
Hydration/Cooling
Cyproheptadine

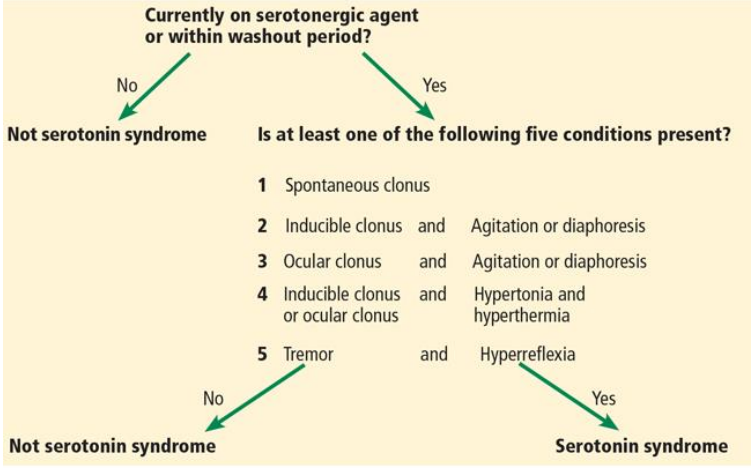
435 × 622

Rosh Review®

HARMFUL

- Hyperthermia
- Autonomic instability
- Rigidity (not lead pipe)
- Myoclonus (lower>upper)
- Fever
- Unconsciousness
- Loss of GI control (diarrhea)

21



HUNTER CRITERIA

SENSITIVITY: 84%
SPECIFICITY: 97%

QJM. 2003;96(9):635.

22

TREATMENT

- Discontinue serotonergic meds
- Supportive
  - Short-acting agents: esmolol, nitroprusside
- BENZOS
- CYPROHEPTADINE
  - 5-HT1A and 5-HT2A antagonist
  - Transient hypotension: typically responds to fluids
- T > 41 °C: sedation, intubation= +/- paralysis
  - Tylenol does not work
  - Cooling prn

23

STUDIES

- BMP, K^+
- EKG
- CK, Urine myoglobin
- Coags and DIC panel

- WBC (leukocytosis 10,000-40,000 +/- left shift)

24

CASE #3

- 69 yo M with PMH of Parkinson's disease on carbi/levo dopa who presents with abdominal pain, N/V
- T: 38.4 °C, HR 110, BP 92/65, RR 28, SpO2 96% RA
- CT A/P shows acute diverticulitis
- Improves and defervesced with CTX/metronidazole
- N/V improves with metoclopramide but still not tolerating PO
- Hospital day 2 → T: 39.3 °C, HR 115, BP 96/68, RR 26, SpO2 96% RA
- Diffusely diaphoretic, shivering/tremulous, lower extremities stiff

25

- What helps you differentiate serotonin syndrome from neuroleptic malignant syndrome?

1) Lower extremity reflexes
2) Degree of fever
3) Time course of symptoms
4) 1 + 3

26

- What helps you differentiate serotonin syndrome from neuroleptic malignant syndrome?

1) Lower extremity reflexes
2) Degree of fever
3) Time course of symptoms
4) 1 + 3

27

NEUROLEPTIC MALIGNANT SYNDROME

Epidemiology

- 0.02 to 3 percent among patients taking antipsychotic agents
- Male:Female 2:1

Mechanism

- Dopamine receptor blockade in the hypothalamus → dysautonomia
- Interference with nigrostriatal dopamine pathways → rigidity
- Skeletal muscle defect or toxic effect
- Disrupted sympathetic nervous system

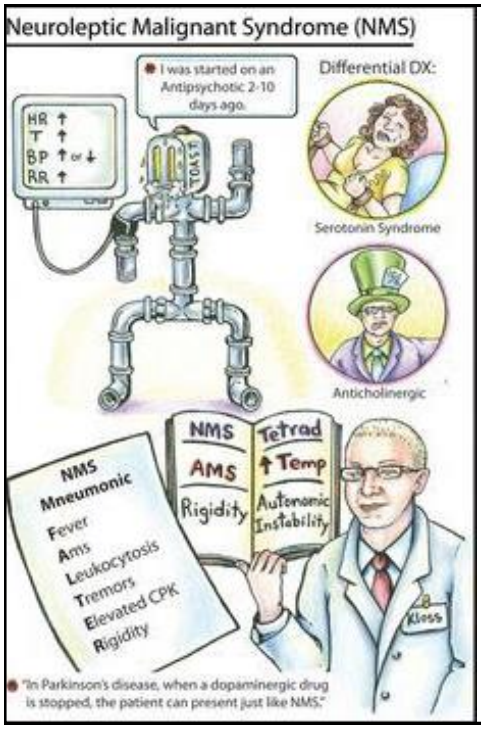
Am J Psychiatry. 1985;142(10):1137.

28

NOTABLE INCITING MEDICATIONS

- Neuroleptics
  - Typical
  - Atypical
- Li^+
- Metoclopramide, promethazine
- Withdrawal
  - Levodopa
  - Amantadine
  - Bromocriptine, cabergoline

29



FEVER

- Fever
- Encephalopathy
- Vitals unstable
- Elevated CPK
- Rigidity

30

NOTES ON THE TETRAD

- Typically evolves over 1-3 days
- Rigidity = "lead pipe"
- Mental status change
  - Often under-appreciated due to psychiatric co-morbidities
  - Agitated delirium
- Altered mentation → rigidity → hyperthermia → autonomic dysfunction

31

STUDIES

- BMP, K^+
- EKG
- CK, Urine myoglobin
- Coags and DIC panel

- WBC (leukocytosis 10,000-40,000 +/- left shift)

32

Condition	Serotonin syndrome	Anticholinergic "toxidrome"	NMS	Malignant hyperthermia
Medication History	Proserotonergic drug	Anticholinergic agent	Dopamine antagonist	Inhalational anesthesia
Onset	<12 hr	<12 hr	1–3 days	30 min to 24 hr
Vital Signs	Hypertension, tachycardia, tachypnea, Hyperthermia (>41.1°C)	Hypertension (mild), tachycardia, tachypnea, hyperthermia (typically < 38.8°C)	Hypertension, tachycardia, tachypnea, hyperthermia (>41.1°C)	Hypertension, tachycardia, tachypnea, hyperthermia (can be as high as (46.0°C)
Pupils	Mydriasis	Mydriasis	Normal	Normal
Mucosa	Sialorrhea	Dry	Sialorrhea	Normal
Skin	Diaphoresis	Erythema, hot and dry	Pallor, diaphoresis	Mottled, diaphoresis
Bowel Sounds	Hyperactive	Decreased or absent	Normal or decreased	Decreased
Neuromuscular Tone	Increased, predominantly in lower extremities	Normal	"Lead-pipe" rigidity present in all muscle groups	Rigor mortis–like rigidity
Reflexes	Hyperreflexia, clonus	Normal	Bradyreflexia	Hyporeflexia
Mental Status	Agitation, coma	Agitated delirium	Stupor, alert Mutism, coma	Agitation

33

TOX SEPSIS MIMICS BULLET POINTS

- Check axilla
- Check leg tone
- Check lower extremity reflexes
- Check bladder scan and bowel sounds
- Consider timing of symptoms
- Run the home and hospital med list (including withdrawn meds)

34

TOXICOLOGY

- 1-800-222-1222

35

QUESTIONS?

36