Malignant Hyperthermia:

What the ICU Needs to Know

Objectives

1. Compare the pathophysiology of malignant hyperthermia (MH) with presenting signs/symptoms in a critical care environment.

2. Identify critical, time based interventions that will stop progression of the MH crisis and reverse potential adverse effects to the patient.

Question #1

What is Malignant Hyperthermia?

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2. Triggered by inhaled anesthetics or succinylcholine
3. A potentially fatal disorder if not treated promptly
4. All of the above

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What is Malignant Hyperthermia (MH)?

- A rare but potentially fatal inherited disorder of skeletal muscle metabolism that leads to a hypermetabolic crisis
- MH only occurs in *susceptible individuals* following exposure to “triggering agents”
- Prompt recognition and treatment will reduce morbidity and mortality, but recognition can be challenging

Who is Affected?

- Any age, racial heritage, or gender
  - Most common in age < 18 and males
- MH is an inherited, autosomal dominant trait
  - Present in 1:3000 - 1:8,500 patients
  - MH incidence during anesthesia 1:100,000 surgeries
- Disorder of calcium metabolism in skeletal muscles
  - Incessant muscle activation / contraction occurs following exposure to a triggering agent

Question #2

Which of the following agents do NOT trigger an MH response?

1. Inhaled anesthetics: isoflurane, sevoflurane, desflurane
2. Succinylcholine
3. Propofol
4. None of the above

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Triggering Agents for an MH Crisis

Volatile Anesthetics

- Halothane
- Isoflurane
- Sevoflurane
- Desflurane
- Enflurane
- Methoxyflurane

Skeletal Muscle Relaxant

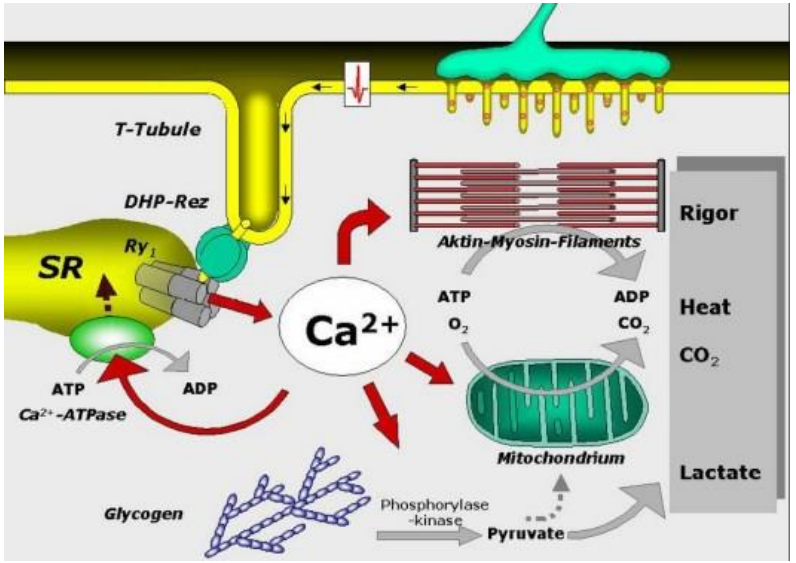
- Succinylcholine

Non-Triggering Agents (safe)

- Barbiturates
- Benzodiazepines
- Opioids
- Nitrous Oxide
- Etomidate
- Ketamine
- Propofol
- Local/regional anesthetics
- Nondepolarizing muscle relaxants (pancuronium)

Pathophysiology of MH

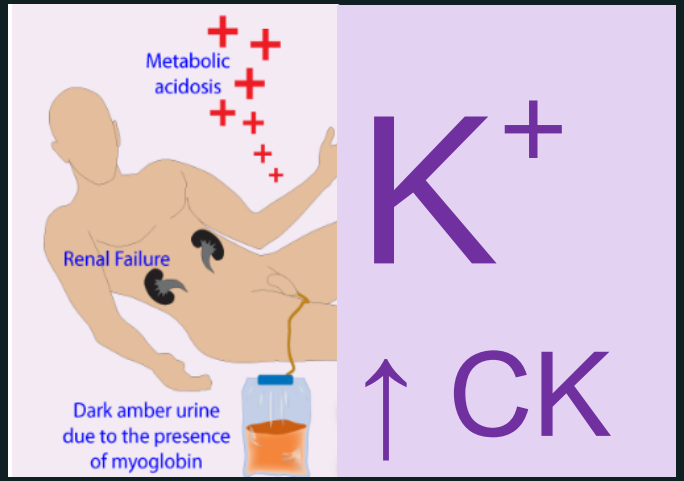
- A cellular disruption of calcium hemostasis in skeletal muscle
- Defective ryanodine receptors lead to prolonged release of Ca^{++} from the sarcoplasmic reticulum following a “trigger”
- Activation of *contractile filaments* persists with muscle rigidity
- Hypermetabolic state leads to:
  - Increased O2 consumption
  - Increased CO2 production
  - Lactic acidosis



http://circuit.perfusion.com/2016/12/perfusion-polices-101-malignant-hyperthermia/

Pathophysiology of Malignant Hyperthermia

- Exhaustion of cellular metabolism and loss of membrane integrity eventually leads to:
  - Hyperkalemia
  - Acidosis: respiratory and metabolic (lactate)
  - Creatine kinase release
  - Myoglobinuria



Question #3

Which of the following best describes the *initial presentation* of Malignant Hyperthermia?

1. Hypercapnia and severe hyperthermia are present in the majority of patients
2. Tachycardia and acidosis are present in the majority of patients
3. Mild and non-specific sinus tachycardia, muscle rigidity, and/or hypercarbia are often presenting signs
4. Life threatening arrhythmias often signal MH onset

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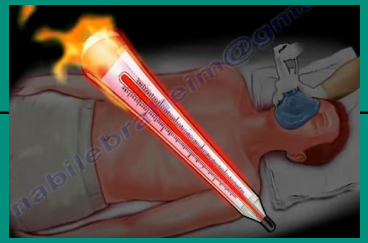
Clinical Presentation of MH

- Highly variable, non-specific responses:
  - aborted course with mild symptoms that resolves after brief exposure, often unrecognized
  - fulminant MH crisis with severe hypermetabolic reaction and life threatening complications
- Average of 3 exposures before a crisis
- *Do not ignore*: sinus tachycardia & increased $ETCO_2$

Riazi S, Kraeva N, Hopkins PM. *Can J Anesth* 2018. Pub online 29 March, 2018

Clinical Changes in MH



Anesthesia triggers a cascade of clinical events that begin with the skeletal muscles

Anesthetic Trigger

Contracture

Heat

Skeletal muscle affect by trigger

Hypermetabolism

Rhabdomyolosis

Hypoxia-Hypercapnia-Acidosis

Myoglobin↑

CK↑

K^+↑

Tachycardia

Renal failure

Cardiac arrhythmia

Cerebral damage

Prompt treatment with Dantrolene will stop this process

Clinical Indicators of MH

- EARLY
  - Masseter spasm (jaw/trunk)
  - Generalized rigidity (50-80%)
  - Tachycardia (>80%)
  - Hypercapnia / ↑$ETCO_2$
  - Hypoxia
  - Combined respiratory & metabolic acidosis
- LATE
  - Hyperthermia
  - Rhabdomyolysis
  - Acute renal failure
  - Cardiac dysrhythmias
  - Hypotension
  - Circulatory failure
  - DIC

Schneiderbanger D, et al. Therapeutics Clin Risk Management 2014;10:355-362.

Why The Diagnosis of MH is Challenging

- **Rising $ETCO_2$** is a highly reliable indicator *but is often masked by ventilatory adjustments to lower it*
- **Masseter muscle spasm** - rigidity of jaw, trunk, or generalized *is attributed to shivering or anesthesia recovery*
- **Dysrhythmias** – Sinus tachy, PVC's, bigeminy *mistaken for inadequate anesthesia/sedation, pain, fever, etc.*
- **Temperature increase –** occurs late, *rate of temperature rise* is most critical (up to *1-2° every 5 minutes)*

Time is of the essence . . .

Mortality occurs rapidly from cardiovascular collapse and dysrhythmias

If you suspect MH then act immediately – call for help !

Immediately obtain an MH cart from an OR or L&D unit

Supportive care until MH rescue medication Dantrolene is available

Question #4

Priorities in the *initial* management of Malignant Hyperthermia include:

1. Stop triggering agent, obtain MH cart, give dantrolene
2. Stop procedure, cool patient, initiate hydration
3. Hyperventilate, initiate cooling, initiate NG lavage
4. Initiate hydration, correct acidosis, initiate cooling

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Treatment of Acute MH Crisis

1 **During a procedure: alert provider to halt**

2 **Discontinue triggering agent, if present**

3 **Call for Help!** Bring MH and Crash Carts

4 Hyperventilate with 100% O_2 ≥ 10L/min

5 Dantrolene 2.5 mg/kg administer rapidly

6 Initiate Cooling internal / surface

7 Monitor $ETCO_2$ HR, Temp response

If unsure of diagnosis or have questions-
call the MH Hotline 1-800-644-9737 (1-800-MH HYPER)

Rescue Medication: Dantrolene versus Ryanodex

	Dantrolene (old) 	Ryanodex (new) 
Treatment dose is the same	**2.5 mg/kg**	**2.5 mg/kg**
Dosage per vial	20 mg	250 mg
Diluent: Sterile H_2O *preservative free*	60 mL/vial	5 mL/vial
Vials per cart	36	3
Mannitol concentration	3000 mg/vial	125 mg/vial
pH *(avoid extravasation)*	-9.5	-10.3

DOSAGE is the same - Ryanodex requires only 1 or 2 vials, with less diluent

MH Rescue Medication

- *What is it* - Rapid acting skeletal muscle relaxant
- *Weight Based Dosing the Same*
  - Crisis: 2.5 mg/kg (1 vial = 20 mg Dantrolene, 250mg Ryanodex)
  - Repeat q 5-10 min until symptoms subside (max 10 mg/kg)
- *Administration*:
  - Reconstitute each vial with *preservative free sterile water (no* D_5W/NS)
  - Agitate gently until a uniform color (longer preparation with Dantrolene)
  - Administer rapid IV push, clear line to ensure no residual
- *Redosing:*
  - Recurrence in 25% of patients; repeat 1 mg/kg IV q 6 hrs x 24 hrs

Ongoing Treatment Priorities

Supportive Care

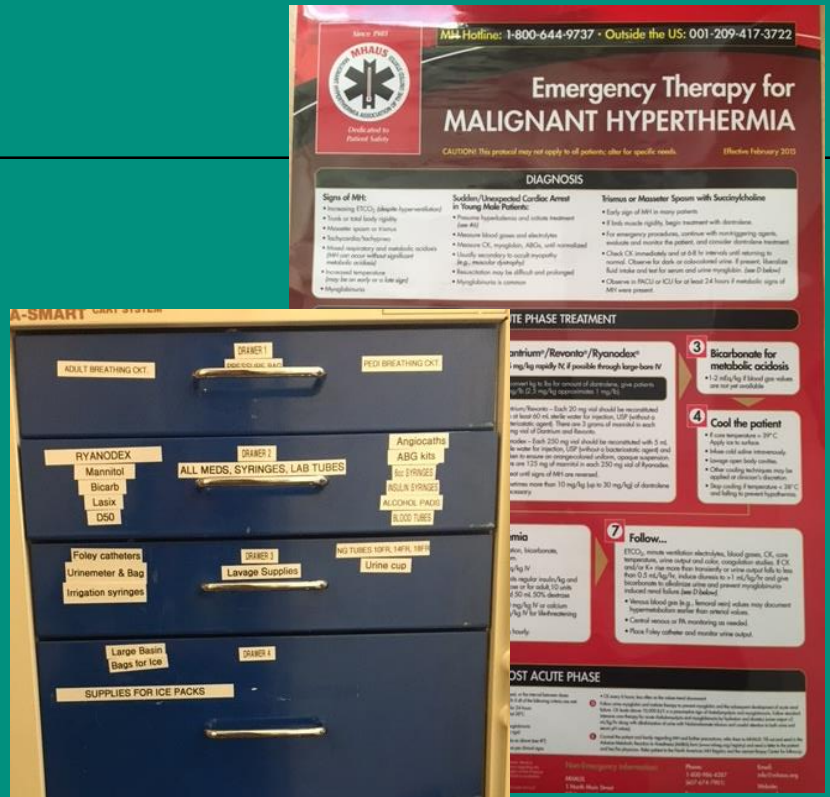
- Cool Patient
  - IV fluids, internal lavage
  - Surface cooling
  - Stop when temp 38.5^{o}C
- Maintain UO > 2 ml/kg/hr
- Correct K, ABG, CPK

Monitoring

- Lab Values:
  - ABG, K^{+}, CA^{++}, glucose
  - CPK
  - Coag panel
- Continuous ECG, BP, $ETCO_2$
- Compartment syndrome

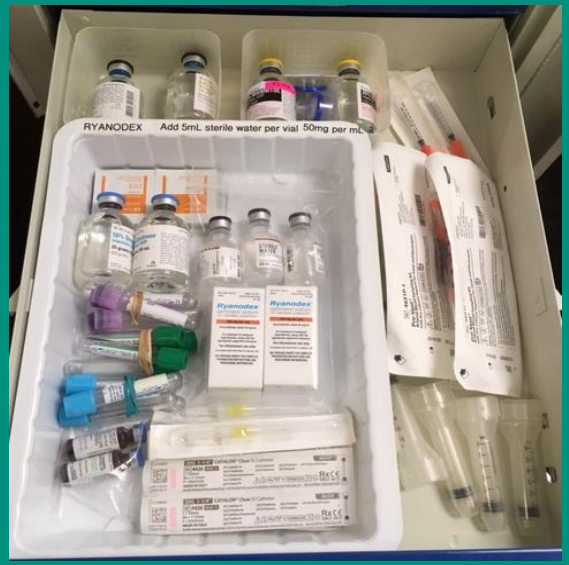
How To Be Prepared

- Watch for signs and symptoms
- Know where the MH Carts are
- Know what's in the MH cart
- Know how to access MHAUS
- Practice drills in your unit



MH Cart Recommendations: Meds

- Ryanodex (3) or Dantrolene (36)
- Sterile H_2O for injection
- Sodium bicarb – 8.4% 50-mL (5)
- D50 – 50 mL (2)
- CaCl – 10% 10-mL (2)
- Regular insulin 100-mL (1)
- Lidocaine or amiodarone
- Refrigerated NS (3-L) for IV cooling



Key Indicators of Patient Stability

- $ETCO_2$ is declining or normal
- Temperature is declining
- Generalized muscular rigidity is resolving, if present
- HR is stable or decreasing
- No ominous dysrhythmias

Responding to an MH Crisis

Recognize Signs and Symptoms (may be subtle or unclear)

Get Help! Bring MH and Crash Cart to area immediately

Begin supportive care
- discontinue trigger
- initiate cooling
- monitoring & tests

Administer Dantrolene or Ryanodex as soon as available

Summary

- Mortality from MH fell from 70% to 5% with the introduction of dantrolene, but has *risen to 14% since 2000*
- MH may appear at any time during anesthetic exposure and *up to 24 hours afterwards*
- Rapid recognition and management are essential to prevent morbidity and mortality
- Help and assistance are available 24/7 via the MH hotline

1-800-MH-HYPER

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