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.

Case Study

- 26 year old female admitted direct from surgery
- Exploratory laparotomy w/ repair of liver laceration s/p AA.
- In surgery for ~ 4 hours, anesthesia w/ inhaled isoflurane, propofol, and fentanyl.
- Intraop bleeding: 6 u RBCs, 6 u FFP, 4 u cryoprecipitate.
- Admission VS below; what is your assessment? What additional information is needed?

HR 116 (sinus w/PACs) RR 28 BP 88/60 T 36.3^{o}

Case Study

- She is intubated with the following ventilator settings:
  - 60% FiO_2 PEEP 5 Vt 550 (10/kg) RR 8
- Assessment findings:
  - SaO_2 97% $EtCO_2$ 42
- Current medications
  - Propofol 35 mcg/kg/min
  - Norepinephrine 0.25 mcg/kg/min

Case Study

- Lab assessment indicates the following:
  - Na 136 K 5.1 Cl 96 CO2 15
  - 7.32 / 48 / 120 / 17 / 95
  - HCT 28%

- What do these values indicate?

Case Study

- 20 minutes after admission you note the following:
- What is your assessment?
- What interventions are indicated?

HR 136 (sinus w/runs of VT) RR 24 BP 80/68 T 38.7^{o}

ETCO2 51%

Question #1

What is Malignant Hyperthermia?

1. A disorder of calcium metabolism
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 can lead to a hypermetabolic crisis
- Occurs only 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
- An inherited, autosomal dominant trait
  - Present in 1:3000 - 1:8,500 patients
  - Incidence from anesthesia estimated 1:100,000 surgeries
  - *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

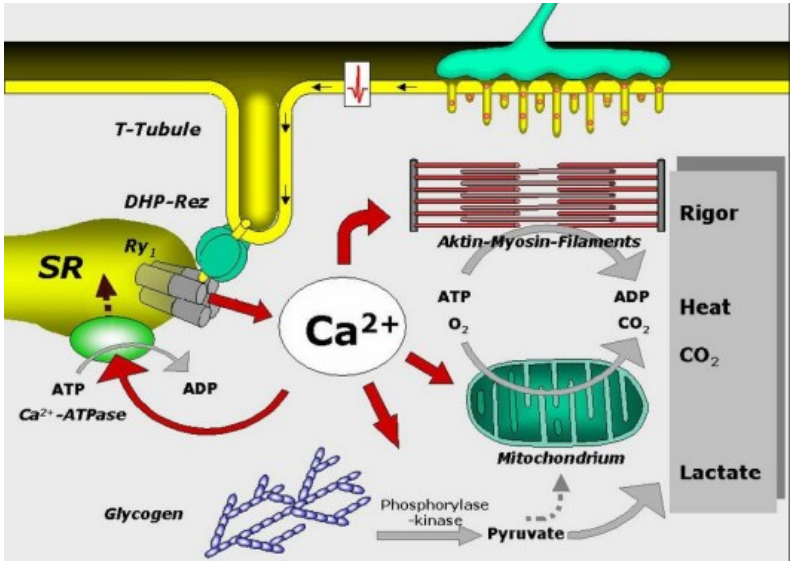
- Succinylcholine

Non-Triggering Agents (safe)

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

Pathophysiology of MH

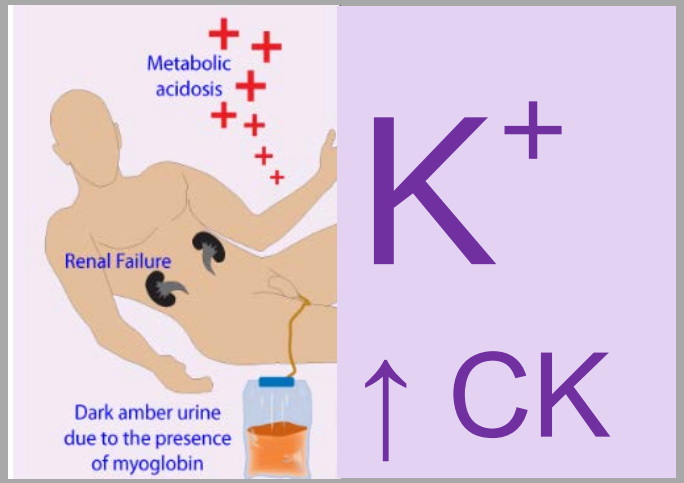
- Disruption of calcium hemostasis in skeletal muscle
- Defective ryanodine receptors lead to prolonged release of Ca^{++} from the sarcoplasmic reticulum following a “trigger”
- Activation of *contractile filaments*
- Incessant firing w/out relaxation
- Hypermetabolic state:
  - Increased O2 consumption
  - 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 describes the most *typical early presentation* of Malignant Hyperthermia?

1. Hypercapnia & severe hyperthermia
2. Tachycardia & metabolic acidosis
3. Mild and non-specific sinus tachycardia, muscle rigidity, and/or hypercarbia
4. Life threatening arrhythmias are often the first sign of an MH crisis

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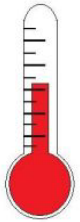
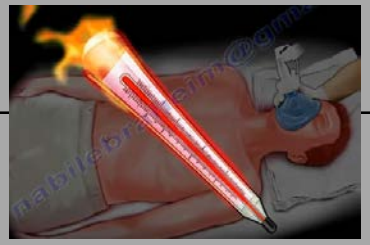
Clinical Presentation of MH



- Highly variable, non-specific responses:
  - Common: aborted course with mild symptoms that resolve after brief exposure, often unrecognized
  - Less often: fulminant MH crisis with severe hypermetabolic reaction and life threatening complications
- Average of 3 exposures before a crisis occurs
- *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^+↑

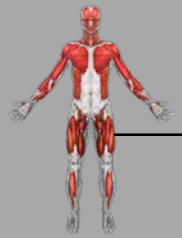
Tachycardia

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.

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 ED, OR, L&D

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 - Ryanodex®

- *What is it* - A rapid acting skeletal muscle relaxant
- *Weight Based Dosing is the Same as Dantrolene*
  - Initial Dose: 2.5 mg / kg (1 vial = 250mg)
  - Recurrent : 1 mg / kg q 4-6 hrs
    Do not exceed 10 mg / kg in 24 hrs

Once mixed, Ryanodex is stable for repeat administration for up to 6 hours

Dosage Charts

- Weight based dosing
  - 1st = Weight (kg)
  - 2nd = Wt x 2.5 = dose
  - 3rd = Total volume *(what to draw up)*
- Broselow colors for Pedi Doses
- Located on top of all MH carts

RYANODEX Dosing - add 5 mL Sterile Water to each 250 mg Vial = 50 mg/mL		
Patient Weight (kg)	Dose = 2.5mg/kg	TOTAL Volume (mL) of reconstituted Ryanodex
PEDIATRIC		
3.0	7.5	0.15
4.0	10.0	0.20
5.0	12.5	0.25
6.0	15.0	0.30
7.0	17.5	0.35
8.0	20.0	0.40

Ongoing Treatment Priorities

Supportive Care

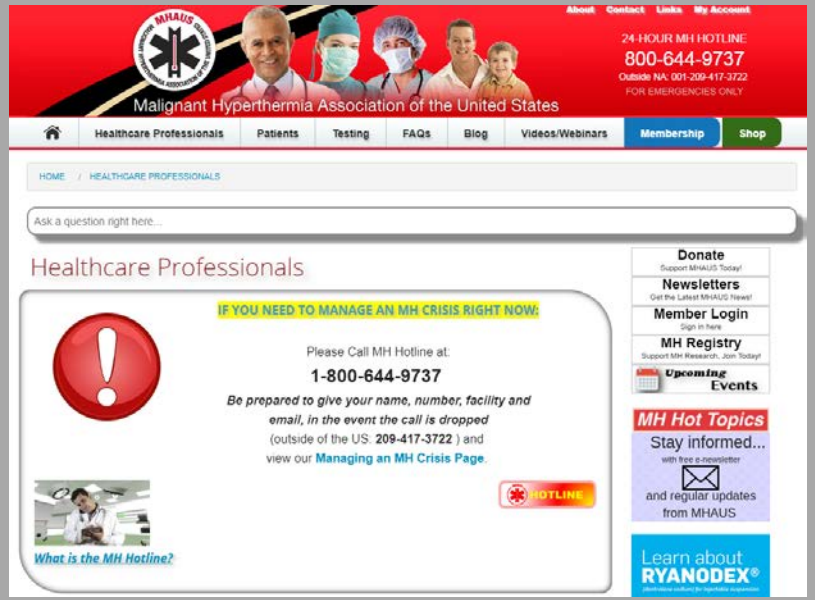
- Cool Patient
  - IV fluids, internal lavage
  - Surface cooling
  - Stop when temp 38.5°C
- Maintain UO > 2 ml/kg/hr
- Correct K, ABG, CPK

Monitoring

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

MHAUS Resources

- 24 / 7 / 365 Telephone support
- Available DURING a crisis
- Set regulatory standards

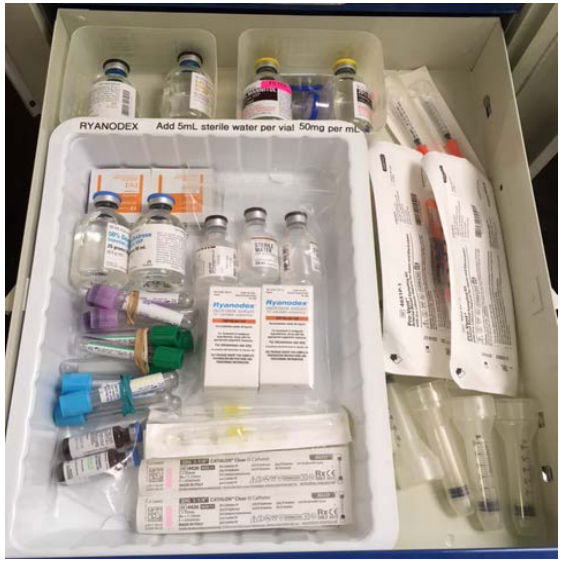


How To Be Prepared

- 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)



Key Indicators of Patient Stability

- $ETCO_2$ is declining or normal
- Temperature is declining
- Generalized muscular rigidity is resolving
- 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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