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.
What is Malignant Hyperthermia?

1. A disorder of cellular metabolism
2. Triggered by inhaled anesthetics or succinylcholine
3. A potentially fatal disorder if not treated promptly
4. All of the above
Question #1

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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

<table>
<thead>
<tr>
<th>Volatile Anesthetics</th>
<th>Non-Triggering Agents (safe)</th>
</tr>
</thead>
<tbody>
<tr>
<td>◦ Halothane</td>
<td>◦ Barbiturates</td>
</tr>
<tr>
<td>◦ Isoflurane</td>
<td>◦ Benzodiazepines</td>
</tr>
<tr>
<td>◦ Sevoflurane</td>
<td>◦ Opioids</td>
</tr>
<tr>
<td>◦ Desflurane</td>
<td>◦ Nitrous Oxide</td>
</tr>
<tr>
<td>◦ Enflurane</td>
<td>◦ Etomidate</td>
</tr>
<tr>
<td>◦ Methoxyflurane</td>
<td>◦ Ketamine</td>
</tr>
<tr>
<td>◦ Succinylcholine</td>
<td>◦ Propofol</td>
</tr>
</tbody>
</table>

**Skeletal Muscle Relaxant**

- 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

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$_2$

Clinical Changes in MH

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

Anesthetic Trigger

- Contracture
- Hypermetabolism
- Heat
- Hypoxia-Hypercapnia-Acidosis
- Rhabdomyolysis

- 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 / ↑ETCO₂
  – Hypoxia
  – Combined respiratory & metabolic acidosis

• LATE
  – Hyperthermia
  – Rhabdomyolysis
  – Acute renal failure
  – Cardiac dysrhythmias
  – Hypotension
  – Circulatory failure
  – DIC

Why The Diagnosis of MH is Challenging

• Rising \( \text{ETCO}_2 \) 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
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
Question #4

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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% \( O_2 \) \( \geq 10 \text{L/min} \)

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

<table>
<thead>
<tr>
<th></th>
<th>Dantrolene (old)</th>
<th>Ryanodex (new)</th>
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</thead>
<tbody>
<tr>
<td>Treatment dose</td>
<td>2.5 mg/kg</td>
<td>2.5 mg/kg</td>
</tr>
<tr>
<td>Dosage per vial</td>
<td>20 mg</td>
<td>250 mg</td>
</tr>
<tr>
<td>Diluent: Sterile H₂O</td>
<td>60 mL/vial</td>
<td>5 mL/vial</td>
</tr>
<tr>
<td></td>
<td>preservative free</td>
<td></td>
</tr>
<tr>
<td>Vials per cart</td>
<td>36</td>
<td>3</td>
</tr>
<tr>
<td>Mannitol concentration</td>
<td>3000 mg/vial</td>
<td>125 mg/vial</td>
</tr>
<tr>
<td>pH</td>
<td>-9.5</td>
<td>-10.3</td>
</tr>
</tbody>
</table>

**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_5 W/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°C
- Maintain UO > 2 ml/kg/hr
- Correct K, ABG, CPK

Monitoring
- Lab Values:
  - ABG, K⁺, CA++, glucose
  - CPK
  - Coag panel
- Continuous ECG, BP, ETCO₂
- 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 H₂O 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**
- **HR is stable or decreasing**
- **Temperature is declining**
- **Generalized muscular rigidity is resolving, if present**
- **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
References

- Malignant Hyperthermia Association of the US [www.mhaus.org](http://www.mhaus.org).