

## Malignant Hyperthermia Crisis Preparedness and Treatment *Position Statement*

*Malignant Hyperthermia Association of the United States  
 Emergency 24-Hour Hotline: (800) MH-HYPER (644-9737)*

### Introduction

Malignant hyperthermia (MH) is a rare, inherited skeletal muscle syndrome that presents as a hypermetabolic reaction triggered by exposure to volatile anesthetic gases or the depolarizing muscle relaxant, succinylcholine.<sup>1,2</sup> The incidence of MH is difficult to quantify. MH cases have been reported ranging from 1/5,000 – 1/100,000 anesthetics, which vary regionally and are highest in children and young adults.<sup>1,3-8</sup> Geographic variability of MH-susceptibility exists based on gene pool variation internationally.<sup>9</sup>

Early recognition of an impending MH crisis and prompt emergency response is critical for a patient’s survival.<sup>10</sup> Dantrolene is currently the only clinically accepted drug treatment for MH.<sup>1,2</sup> The availability of dantrolene and increased intraoperative monitoring have considerably reduced MH fatality.<sup>2,6,11-14</sup> An increase in the time interval between the first clinical signs of MH and the administration of dantrolene has been associated with increased complication rates.<sup>15-17</sup>

### AANA Position

#### *Availability of Dantrolene*

The AANA strongly recommends all anesthesia professionals delivering MH triggering agents such as potent volatile inhalation anesthetics or administering depolarizing muscle relaxants have the requisite drugs and supplies available as defined by the Malignant Hyperthermia Association of the United States (MHAUS). Dantrolene, along with other drugs and equipment necessary to treat an MH crisis, must be available at all facilities, including ambulatory surgical centers (ASCs) and offices, where MH triggering anesthetics or depolarizing muscle relaxants are administered or stocked.<sup>18</sup> Table 1 summarizes the known MH triggering agents. The standard of care is the same for large and small facilities and all facility types. Stocking dantrolene for the treatment of MH in an outpatient setting is cost-effective and promotes patient safety.<sup>2</sup>

**Table 1.** Known Triggers for MH-Susceptible Patients<sup>19</sup>

Inhaled General Anesthetics
<ul style="list-style-type: none"> <li>• Desflurane</li> <li>• Enflurane</li> <li>• Ether</li> <li>• Halothane</li> <li>• Isoflurane</li> <li>• Methoxyflurane</li> <li>• Sevoflurane</li> </ul>
Depolarizing Muscle Relaxant
<ul style="list-style-type: none"> <li>• Succinylcholine</li> </ul>

To treat an MH crisis, an initial dantrolene dose of 2.5 mg/kg is recommended.<sup>20</sup> Two formulations of dantrolene are currently available. A full complement of Dantrium®/ Revonto® is 36 vials and a full complement of Ryanodex® is three vials. If new dantrolene formulations become available, facilities should verify that the appropriate supply is stocked within the facility. MHAUS recommends that a full complement of dantrolene be available to administer at the anesthetizing location (e.g., operating room) within 10 minutes of the decision to treat for MH.<sup>20</sup> A facility must assess its size and proximity of anesthetizing locations when determining the appropriate number of MH carts/kits to stock. A patient experiencing an MH crisis must be stabilized prior to transport to a hospital.<sup>16,20</sup> Consideration needs to be given to obese patients, who may require a higher dose or total drug volume in order to be stabilized.

Approximately 55 percent of MH cases in the United States and Canada have included the administration of succinylcholine, either alone or in combination with volatile anesthetics.<sup>14,15,17</sup> MH risk may increase when succinylcholine is used in combination with volatile anesthetics.<sup>14</sup> MHAUS recommendations apply to all settings that stock MH triggering agents, even if only sedation services are provided and volatile anesthetics are not administered. Settings that stock succinylcholine, even if only for the purpose of emergency airway management, should have dantrolene available and a MH crisis protocol in place.<sup>18</sup>

## **Considerations for Policy Development**

Facilities establish policies and patient safety protocols to prevent and treat MH. Facility policies address the following considerations:

### *Governmental Regulations and Accreditation Standards*

Facilities must be aware of governmental regulations as well as standards and guidelines set by national organizations and accrediting organizations that relate to MH crisis emergency management.

### *Emergency Contact*

A policy appropriate for the facility type exists to treat and transport a patient in MH crisis. Contact information for emergency services and the MHAUS Emergency 24-hour Hotline – (800) MH-HYPER (644-9737) - should be clearly posted and available for all facility staff.

### *MH Emergency Drugs and Equipment*

If MH-triggering agents are used within the facility, even if only for emergency airway management, an MH cart/kit is available for emergency treatment of an MH crisis. The facility policy includes a process to inspect the MH cart/kit for expired drugs and equipment. Appendix 1 includes a detailed list of the contents of an MH cart/kit.

### *MH Screening*

MH susceptibility is inherited with an autosomal dominant inheritance pattern. Therefore, children and siblings of a patient with MH susceptibility usually have a 50 percent chance of inheriting a gene defect for MH and would be MH-susceptible. During the preanesthesia patient assessment and evaluation, an MH screening can aid in determining a patient's risk for MH.

When evaluating the patient, MHAUS recommends:<sup>21</sup>

- Review indicators of MH susceptibility, if known
- Assess level of suspicion for susceptibility to MH
- Review eligibility criteria for diagnostic testing
- Consult with MH expert, if necessary

Patients with muscular disorders should be evaluated by an anesthesia professional prior to surgery.<sup>22</sup> MH or MH-like events may occur in patients with underlying muscle diseases, such as muscular dystrophy and myotonia.<sup>22,23</sup>

Diagnostic testing options to evaluate MH susceptibility are not recommended as a screening tool for the general population.<sup>21</sup> Diagnostic tests are most useful when making treatment decisions for surgical patients where there is a high level of suspicion that the patient is susceptible to MH.<sup>21</sup> Patients known to be susceptible to MH may undergo anesthesia numerous times before an episode occurs.<sup>1</sup>

#### *Anesthetic Drug Selection and Anesthesia Machine Preparation*

If a patient is confirmed as MH-susceptible or has a family history of MH, proper anesthesia precautions must be taken.<sup>7,24</sup> MH-triggering volatile anesthetic agents and succinylcholine should be avoided. Pretreatment with dantrolene is not recommended.<sup>1,6,8</sup> The anesthesia plan of care focuses on the use of an anesthesia machine that has been prepared and flushed according to the manufacturer's recommendation.<sup>25,26</sup> Modern anesthesia workstations have variability in their components and effective flush times.<sup>27,28</sup> Additional considerations include use of an activated charcoal filter with the anesthesia machine and use of trigger-free drugs for induction, anesthesia maintenance, and emergent airway management.

Adding activated charcoal filters to the airway circuit will remove volatile anesthetic agents and is effective in keeping anesthetic agent concentration below 5 ppm for up to 12 hours with fresh gas flows of at least 3 L/min.<sup>25,28,29</sup> However, the anesthesia machine will still need to be flushed with high fresh gas flows ( $\geq 10$  L/min) for 90 seconds prior to placing the activated charcoal filters on the proximal end(s) of the inspiratory and expiratory limb(s) of the anesthetic circuit.<sup>25,29-31</sup>

Other alternatives include the use of a dedicated "vapor free" machine for MH-susceptible patients or, if appropriate to the institution, the use of an intensive care unit (ICU) ventilator that has never been exposed to volatile anesthetic agents.<sup>26</sup>

#### *MH Symptoms*

The initial symptoms of an MH episode are not specific and can range from mild to severe.<sup>6,32</sup> Clinical signs of MH are summarized in Table 2.

**Table 2.** Clinical Signs of MH<sup>5,6,8,10</sup>

Early Clinical Signs
<ul style="list-style-type: none"> <li>• Abrupt increase in ETCO<sub>2</sub></li> <li>• Cardiac arrhythmias</li> <li>• Generalized muscle rigidity</li> <li>• Hypoxia</li> <li>• Profuse sweating</li> <li>• Trismus / Masseter muscle rigidity (MMR)</li> <li>• Metabolic-respiratory acidosis</li> <li>• Mottling of the skin</li> <li>• Tachycardia</li> <li>• Tachypnea in spontaneously breathing patients</li> <li>• Unstable arterial pressure</li> </ul>
Late Clinical Signs
<ul style="list-style-type: none"> <li>• Acute renal failure</li> <li>• Circulatory failure</li> <li>• Dark colored urine due to myoglobinuria</li> <li>• Disseminated intravascular coagulation</li> <li>• Elevated blood creatine phosphokinase levels</li> <li>• Elevated blood myoglobin levels</li> <li>• Hyperkalemia</li> <li>• Hyperthermia (&gt; 38.8° C)*</li> <li>• Hypotension</li> <li>• Rhabdomyolysis</li> <li>• Severe cardiac arrhythmias and cardiac arrest</li> </ul>

\*A rapid temperature increase of >1° C in 15 minutes is more diagnostically relevant than peak temperature.<sup>6</sup>

*Trismus / Masseter Muscular Rigidity*

Trismus, or masseter muscular rigidity (MMR), which is characterized by difficulty in opening the jaw, is a rare but dangerous phenomenon. Mild and/or transient MMR is a normal response to succinylcholine and is not considered to be a significant prognostic sign of MH.<sup>33</sup>

If a patient has received succinylcholine and his/her jaw cannot be opened or the patient has peripheral muscle rigidity, the clinician should assume this is an MH event and immediately begin MH treatment (i.e., dantrolene administration).<sup>33,34</sup> Generalized rigidity may not be present, but when it is, it is typically associated with MH susceptibility.<sup>33</sup> The physiologic changes associated with the onset of MH, such as rise in ETCO<sub>2</sub>, may be delayed for up to 15 minutes after MMR, but will occur if triggering anesthetic agents are continued.<sup>33</sup> Anesthesia should be discontinued and an elective surgery should be postponed.<sup>33</sup> In an emergency, the anesthetic may continue with non-triggering anesthetic agents.<sup>33,34</sup>

Following MMR, patients should be admitted to an intensive care unit and monitored for signs of MH.<sup>34</sup> Rhabdomyolysis occurs in most patients who experience MMR.<sup>33</sup> Creatine kinase (CK) and urine myoglobin values should be monitored regularly.<sup>33-35</sup> CK levels peak 14-24 hours after an MMR episode.<sup>35</sup> Muscle biopsy for a definitive diagnosis may be considered.<sup>34</sup>

### *Core Temperature Monitoring*

Temperature elevation is an early sign of an impending MH crisis.<sup>11,17</sup> MHAUS recommends core temperature monitoring for all patients undergoing general anesthesia lasting more than 30 minutes.<sup>11,36</sup> Appropriate sites for continuous electronic core temperature monitoring include the esophagus, nasopharynx, bladder, and pulmonary artery.<sup>36</sup>

### *MH Crisis Treatment*

Numerous clinicians (e.g., surgeon/proceduralist, anesthesia professional, nursing staff) are required within a short time period when an MH crisis occurs for successful resuscitation. The use of a team leader, cognitive aids (e.g., the MHAUS manual), and staff dedicated to systematically read the protocol steps will support the clinical team with resources required to manage an MH crisis.<sup>5</sup>

Initial response during an MH crisis includes activation of the MH plan, discontinuation and elimination of potent inhalation anesthetics, increased ventilation rate with 100 percent oxygen, addition of an inline activated charcoal filters, treatment with intravenous dantrolene, active cooling by all available routes, and treatment of electrolyte and pH abnormalities.<sup>5,32,37</sup> Calcium-channel blockers should be avoided if dantrolene is used, because they may cause hyperkalemia.<sup>38</sup> When activated charcoal filters are used during an MH crisis, even though the volatile anesthetic agent is discontinued when MH is first suspected, activated charcoal filters may become saturated after one hour.<sup>31,37</sup> Therefore, the activated charcoal filters should be replaced after each hour of use.<sup>29,37</sup>

Obtain blood gas (venous or arterial) to determine degree of metabolic acidosis.<sup>37</sup> Consider administration of sodium bicarbonate, 1-2 mEq/kg dose, for base excess greater than -8 (maximum dose 50 mEq).<sup>37</sup> In an ASC or office-based facility, blood gas analysis may not be available. A single dose of sodium bicarbonate 1-2 mEq/kg may be considered for treatment of metabolic acidosis.<sup>39</sup> Clinical judgment, vigilance, and patient assessment are key factors in the treatment of an MH crisis.

### *Patient Transfer*

ASCs and office-based facilities have transfer agreements in place with a nearby hospital which has inpatient capabilities to care for a patient in an MH crisis.<sup>4,16,32</sup> The patient should be transferred out of an ASC or office when, according to the clinician's judgment, the patient is stable.<sup>16</sup> Hospitals have a procedure and policy for transfer of a stabilized MH patient to an ICU.

Signs of stability may include:<sup>16</sup>

- ETCO<sub>2</sub> declining or normal
- Heart rate stable or decreasing without dysrhythmia
- IV dantrolene has begun
- Temperature declining
- If present, generalized muscular rigidity resolving

Detailed communication regarding the transfer of care needs to occur between clinicians at the transferring and receiving facilities to support continuity of patient treatment and monitoring.<sup>4,16</sup> For a detailed MH patient transfer protocol, review the [Guide for the Transfer of Care of the Malignant Hyperthermia Patient from Ambulatory Surgery Centers to Receiving Hospital Facilities](#).<sup>16</sup>

#### *Post-Anesthesia Care Unit (PACU) and ICU*

In rare cases, an MH episode may occur in the immediate postoperative period.<sup>7,8,40</sup> In an MH-susceptible patient, if no signs of MH are noted one hour postoperatively after an MH safe anesthetic technique, it is unlikely that MH will occur.<sup>8,9,40</sup> The patient should be monitored in a phase I PACU for at least one hour and in a phase II/step down PACU for at least another hour.<sup>8,24,32,41,42</sup> MH-susceptible patients require close vital sign and temperature monitoring in the PACU and, if indicated based on the clinician's evaluation, may be kept longer for further observation.<sup>8,40,41</sup> Patients undergoing procedures in an ASC or office may be discharged home the same day.<sup>24,41</sup> Discharge instructions with clear guidance on signs, symptoms, and instruction on how to manage complications are important to provide to patients and their caregivers.<sup>40</sup>

After an MH crisis, the patient may need to be treated with dantrolene for at least 24-36 hours.<sup>3,43</sup> Patients should be monitored in the ICU for MH complications,<sup>43</sup> including:

- MH recrudescence, which can occur in up to 25 percent of patients within hours of the initial MH crisis<sup>5,9,24,43</sup>
- Disseminated intravascular coagulation<sup>9</sup>
- Myoglobinuric renal failure<sup>9</sup>

Although an MH crisis is typically seen in the operating room (OR) and rarely in the PACU, MH cases have also been documented in sedated patients in the ICU,<sup>44-46</sup> underscoring the importance of clinical vigilance, identification of the syndrome, and prompt treatment.

#### *MH Crisis Counseling*

If an MH crisis occurs, the event and immediate care steps should be discussed with the patient and family. Recommendation may be made to purchase and wear medical identification items or other identifiers.<sup>47</sup> The patient and family members may consider genetic counseling and be referred to MHAUS for further information and resources.<sup>6,32,48</sup>

#### *Quality Improvement*

As soon as possible, the team should debrief the MH event to review the response process and develop an action plan for any identified improvements. The team should engage in ongoing team competency training, integration of an emergency manual checklist, and a peer support process for staff emotional recovery, as needed.

### *Ongoing Competency*

Healthcare providers maintain familiarity with current MHAUS recommendations and guidelines. Conducting MH crisis team training, that includes the OR, PACU, and ICU teams, as a part of ongoing and annual competency education will prepare the clinical team to recognize, respond to, and treat an MH crisis.<sup>4</sup> Ongoing training may also include pharmacy, laboratory, and emergency medical services personnel to highlight their roles in MH-preparedness, promote continued awareness, and safeguard patient safety.

### **Conclusion**

Malignant hyperthermia is a rare, yet potentially fatal condition. Anesthesia professionals may be the first to recognize the onset of an MH crisis, but a coordinated team response is vital in the effective treatment and management of MH. Accessibility to an MH cart, stocked with dantrolene, is a requirement supported by MHAUS and the AANA for all facilities where MH-triggering agents are available. All facilities (e.g., hospital, ASCs, offices) can promote patient safety and MH awareness by establishing policies and protocols for clinical team competency training, mock drills, patient screening, anesthetic selection and anesthesia machine preparation, emergency response, MH treatment and management, patient transfer, patient and family counseling, and continued quality improvement.

## Appendix 1: Contents of an MH Cart/Kit

MHAUS recommends that the following drugs and equipment are available to treat an MH crisis.<sup>18</sup>

### *Drugs*

1. Dantrolene
  - a. Dantrium® / Revonto® – 36 vials should be available in each institution where MH can occur, each vial to be diluted at the time of use with 60 ml sterile water, USP (without a bacteriostatic agent). There are 3 grams of mannitol in each vial of 20 mg of dantrolene (0.15 g mannitol/ 1 mg dantrolene).
  - b. Ryanodex® – 3 vials should be available in each institution where MH can occur, each to be diluted at the time of use with 5 ml of sterile water for injection, USP (without a bacteriostatic agent). There are 0.125 grams of mannitol in each vial of 250 mg of Ryanodex® (0.0005 grams mannitol/1 mg dantrolene).
2. Sterile water for injection USP (without a bacteriostatic agent)
3. Sodium bicarbonate (8.4 percent) – 50 ml x 5
4. Dextrose 50 percent – 50 ml vials x 2
5. Calcium chloride (10 percent) – 10 ml vial x 2
6. Regular insulin – 100 units/ml x 1 (refrigerated)
7. Lidocaine\* for injection (2 percent) – 100 mg/5 ml or 100 mg/10 ml in preloaded syringes (3). Amiodarone is also acceptable. Advanced Cardiac Life Support protocols, as prescribed by the American Hospital Association, should be followed when treating all cardiac derangements caused by MH.
8. Refrigerated cold saline solution – A minimum of 3,000 ml for IV cooling

\* Lidocaine or procainamide should not be given if a wide-QRS complex arrhythmia is likely due to hyper-kalemia; this may result in asystole.

### *General Equipment*

1. Charcoal Filters - Two pairs of activated charcoal filters (Vapor-Clean™, Dynasthetics, Salt Lake City, UT). Attach activated charcoal filters to inspiratory and expiratory ports of the anesthesia machine to quickly reduce the concentration of gas (<5 ppm) from the anesthesia machine. In this situation, even though the anesthetic gas has been discontinued when MH was first suspected, the Vapor-Clean™ filter may become saturated after one hour; therefore, a replacement set of filters should be substituted after each hour of use.
2. Syringes – (60 ml x 5) to dilute dantrolene
3. Intravenous catheters – 16G, 18G, 20G, 2-inch; 22G, 1-inch; 24G, 3/4-inch (4 each) (for IV access and arterial line)
4. NG tubes – sizes appropriate for patient population
5. Toomey irrigation syringes – (60 ml x 2) with adapter for NG irrigation

### *Monitoring Equipment*

1. Esophageal or other core (e.g., nasopharyngeal, tympanic membrane, rectal, bladder, pulmonary artery catheter) temperature probes.
2. CVP kits (sizes appropriate for patient population). It is recommended that these be used in patients who are critically ill.
3. Transducer kits for arterial and central venous cannulation.

### *Nursing Supplies*

1. Large sterile Steri-Drape (for rapid drape of wound)
2. Urine meter x 1
3. Irrigation tray with piston (60cc irrigation) syringe
4. Large clear plastic bags for ice x 4
5. Small plastic bags for ice x 4
6. Bucket for ice
7. Test strips for urine hemoglobin

### *Laboratory Testing Supplies*

1. Syringes (3 ml) for blood gas analysis or ABG kits x 6 or point of care monitors; ISTAT with TB syringes (the point of care ISTAT device has replaced lab blood gas and electrolyte measurement).
2. Blood specimen tubes for CK, myoglobin, SMA 19 (LDH, electrolytes, thyroid studies), PT/PTT, fibrinogen, fibrin split products; and lactate, CBC, platelets. If no immediate laboratory analysis is available, samples should be kept on ice for later analysis. This may well prove useful on retrospective review and diagnosis. Blood cultures are very useful and should be included to rule out bacteremia.
3. Urine collection container for myoglobin level. Pigmenturia (e.g., brown or red urine and heme positive dipstick) indicates that renal protection is mandated, when the urine is centrifuged or allowed to settle, and the sample shows clear supernatant, i.e., the coloration is due to red cells in the sample.

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