

Malignant Hyperthermia Crisis

by **Connie Corrigan** CST, RN, CNOR, MS

FACTS ABOUT MALIGNANT HYPERTHERMIA

- Malignant hyperthermia (MH) is a rare complication of general surgery involving either halogenated, volatile anesthetic gases or depolarizing muscle relaxants as a triggering mechanism. This disease process has common symptoms including calcium build-up in the musculature, tachycardia, respiratory and metabolic acidosis, followed by hemodynamic failure.
- Currently only one medication, dantrolene sodium, is available for treatment of MH crisis. In addition to drug therapy, supportive measures taken by the entire perioperative team will help provide a positive outcome to a crisis situation.
- A MH crisis can be averted or the severity may be reduced if it is known that a patient has a susceptibility to the disease (through testing, family history, or previous crisis). Guidelines for preoperative evaluation of patients will be discussed.

MALIGNANT HYPERTHERMIA CRISIS

Malignant hyperthermia (MH) is a rare complication of general anesthesia involving a reaction to either volatile anesthetic gases (halothane, desflurane or isoflurane) or intravenous depolarizing muscle relaxants (succinylcholine).¹ This article will describe the perioperative team's role in identifying patients at risk for developing MH, the common signs and symptoms of a crisis situation, and treatment during a crisis as well as postoperative care.

LEARNING OBJECTIVES

- ▲ Review the necessary steps for a preoperative assessment for potential MH susceptibility
- ▲ Examine the causes of MH
- ▲ Assess the needs of your OR and its preparedness for a MH incident
- ▲ Evaluate the methods and materials necessary to successfully control a MH incident
- ▲ Identify the symptoms that indicate a MH incident

MALIGNANT HYPERTHERMIA PATHOPHYSIOLOGY

Skeletal muscle is composed of small myofibrils surrounded by transverse tubules (T-tubules) forming an intricate network between and through all the muscle fiber layers, allowing extracellular fluid to bathe the fibers.² In a normal muscular contraction, a calcium pump in the sarcoplasm will pump the calcium back into the tubules.² In MH, this pump fails, causing sustained muscle contraction.³ The increase in calcium levels causes myocin filaments to activate, leading to stiff, rigid muscles.⁴

As calcium is pumped back and forth from the sarcoplasm to the T-tubules, adenosine triphosphate (ATP) is used, which releases energy and produces heat (basal metabolic energy).⁵ A typical muscle cell only holds four-six seconds of ATP, and then becomes exhausted.⁶ In MH, when susceptible individuals are exposed to triggering agents, and the calcium pumps fail, the increased amount of calcium in the myofibrils causes sustained muscle rigidity, an increase in carbon dioxide production, hypoxia, and rhabdomyolysis. The patient's metabolic rate begins to rise with the sustained muscular contractions, leading to tachycardia, a high demand for oxygen, and eventually, a rise in temperature.⁴ The lactic acid and the increase in carbon dioxide will soon lead to a metabolic acidosis.⁷ As triglycerides are broken down for energy, free fatty acids alter the sodium channels, leading to hyponatremia.⁸ Rhabdomyolysis is the breakdown of muscle fibers resulting in the release of myoglobin into the bloodstream, which can cause kidney damage.¹⁵

PREOPERATIVE ASSESSMENT

While it is a rare disease, proper screening of all surgical patients will identify a predisposition toward MH. Because of the familial tendency of this disease, staff should question patients scheduled for general anesthesia regarding family members who became sick or died either during surgery or as a result of anesthesia. Even if the answer is "No," more specific questioning is warranted to identify anyone having an elevated temperature, or a difficult or extended recovery from anesthetics.³ It is important to note that some individuals will have the gene, but will fail to display symptoms until his or her second or third surgical procedure.⁹

Genetic testing can only identify 25-30 percent of MH-susceptible patients, due to more than 60 different mutations of the ryanodine receptor isoform 1 (RyR1), which is one of the genes controlling the calcium pumps in muscle cells.¹⁰ The RyR1 gene is very large and testing all the possible mutation sites is expensive, so current procedures often

involve only 17 of the most common mutations. The gold-standard for testing MH susceptibility is a muscle biopsy subjected to an *in vitro* caffeine-halothane-contraction test.⁴ Currently, only eight institutions in North America offer the biopsy procedure due to the need to have fresh muscle to perform the test, which must be completed within five hours of retrieval.¹¹ This presents difficulty for patients because of the need for many to travel great distances, and pay for a relatively expensive procedure – conservative estimates project at least \$6,000.¹¹

MH is most commonly found in patients between two- and 42-years old, and most commonly in men.¹ Chang and Scher believe incidence of MH to be one in 15,000 children and one in 50,000 adults.¹² Hommertzhim and Steinke, as well as McNeil, note that although the disease affects all racial groups equally, there is prevalence in individuals who also have other neuromuscular disorders, such as Duchenne muscular dystrophy or osteogenesis imperfecta.¹⁶ True inci-

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dence will vary depending on the concentration of affected families in a particular area. The Malignant Hyperthermia Association of the United States (MHAUS)¹¹ identifies several states with high incidence, including Wisconsin, Nebraska, West Virginia and Michigan.

MANAGEMENT OF INTRAOPERATIVE CRISES

When it is known or suspected that a patient is susceptible to MH, any potential triggering agents, including succinylcholine and halogenated inhalation anesthetics, are eliminated from the anesthetic regimen.³ Preoperative equipment and supplies should include a decontaminated anesthesia machine (as previous use of halogenated agents may linger in the unit), fresh soda-lime, a supply of dantrolene sodium on stand-by, and appropriate patient monitors (especially temperature and end-tidal carbon dioxide).¹²

However, if there is no suspicion of MH, and any of the triggering agents are used, attention to signs of MH crisis is important in order to start treatment immediately. All

Table 1. Dantrolene Mixing Time by Dose and Diluent Temperature

Dantrolene Dose	2.5 mg /kg		10 mg /kg	
	A Diluent	W Diluent	A Diluent	W Diluent
72-kg Adult				
*Time / seconds	94 seconds	59 seconds	94 seconds	59 seconds
Number of Vials	9 vials	9 vials	36 vials	36 vials
1 Mixer / minutes	14 minutes	9 minutes	56 minutes	35 minutes
3 Mixers / minutes	5 minutes	3 minutes	19 minutes	12 minutes

A = Ambient (22° C), W = Warmed Diluent Temperature (41° C)

*Comparative Study Results, Mean Times

Courtesy Anesthesia Patient Safety Foundation

health care workers caring for patients undergoing general anesthesia should understand the disease because the manifestations can occur rapidly. However, as Chang and Scher state, the onset of symptoms can take several minutes to several hours, and some reports indicate that the crisis began during the recovery phase in the post-anesthesia care unit (PACU).¹² Hommertzhaim and Steinke state that the crisis may begin up to 12 hours after the end of the surgery.¹

Masseter muscle rigidity, a jaw that is rigid longer than 90 seconds and is impossible to intubate or pass a laryngoscope through, can be one of the earliest signs of MH.¹² Other signs and symptoms that would indicate MH crisis include increased end-tidal carbon dioxide, tachycardia, tachypnea, cardiac dysrhythmias, cyanosis, increased temperature or unstable blood pressure.⁷ Hommertzhaim and Steinke believe that unexplained tachycardia can be one of the hallmarks of MH because it occurs in 96 percent of all

reported cases.¹ They also note that although cyanosis is present in 70 percent of patients, skin color first changes to bright red. Another sign of MH would be tightness of other muscle groups, and this can be noted by the surgeon, especially during abdominal surgery.⁹ Failure to identify signs of MH until the late stages

is detrimental to the patient's outcome.¹² These signs include prolonged bleeding, dark urine, oliguria, and myoglobinuria as well as an increase in creatinine kinase levels.

At the first indication of MH the triggering agent should be stopped. When possible, the surgical procedure is also halted.¹ In order to remove the triggering agent from contact with the patient, the breathing circuit is disconnected from the anesthesia machine, and the unit, soda lime, and patient's airway are flushed with 100 percent oxygen.¹ A MH crisis has similar activity to a cardiac arrest situation, and appropriate alarms are activated to bring additional personnel to the room. Instead of the traditional "crash cart," however, a malignant hyperthermia cart or box is used, which contains a large quantity of dantrolene sodium – the only known agent that is capable of treating MH.¹³ The crash cart must also include sterile water (without a bacteriostatic agent) to reconstitute the dantrolene, sodium bicarbonate, furosemide, dextrose, calcium chloride, regular insulin (refrigerated) and antiarrhythmics. If any potent, volatile agents are used, a full supply of dantrolene – 36 vials – should be available on site.¹⁶

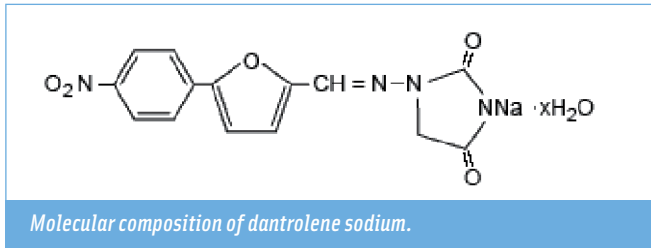
A supply of 36 vials should be stocked at any given time because during treatment of a MH episode, an initial dose of the drug at 2.5 mg/kg is recommended, with an upper limit of 10 mg/kg. If a patient of average weight (eg 70 kg – approximately 155 pounds) requires dantrolene sodium at the upper dosing limit, then at least 700 mg of the drug will be needed. In addition, a review of cases has shown that a "worst case" scenario with a very large patient (eg 100-110 kg – approximately 220-250 pounds) having an acute MH incident, as much as eight-10 mg/kg of dantrolene will be needed for treatment. Even higher doses may be required on rare occasions. Thirty-six vials of dantrolene sodium on site will allow for initial stabilization and treatment while more vials are being acquired to continue treatment as needed.¹⁶

A vial of dantrolene sodium contains 20mg of the drug, as well as 3000mg of mannitol and sodium hydroxide,



MPD Malignant Hyperthermia Cart with Refrigerator

which allows the powder to be reconstituted with 60cc of water.⁹ The use of water will speed the reconstitution of the powder, and MHAUS has indicated that warm water can be used to speed the process even further.¹¹ If the patient does not already have a central venous line placed, one should be inserted so that the dantrolene sodium can be administered quickly and blood can be drawn for analysis.^{9, 13}



One person is responsible for reconstituting several vials of medicine and passing those vials to another person for administration. The dose varies depending on the severity of the crisis. Reports note that an initial bolus of 2mg/kg is often increased to 10mg/kg or 20mg/kg until the signs of the crisis abate.⁹ Himmertzhaim and Steinke suggest that a well-stocked MH cart contain no less than 36 vials of dantrolene sodium, and two liters of water.¹

Because the patient has an increased carbon dioxide level, anesthesia providers should increase the ventilation rate to help provide more oxygen and remove the carbon dioxide.⁴ Heggie suggests treating the metabolic acidosis with bicarbonate as well as insulin and dextrose. While

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controlling the hyperkalemia often resolves any cardiac dysrhythmias, any remaining abnormalities should be treated with appropriate medicines; however, due to the nature of the disease, calcium-channel blockers are contraindicated. Although there is mannitol in the dantrolene sodium vial, additional diuretics, such as furosemide, may be given to increase urinary output and reduce the chance of renal failure.⁹

Although the crisis is named for the high temperatures generated by the extended muscle contractions, most experts agree that an increase in temperature is one of the last signs presented.⁴ Elster, et al, describe increases in temperature from one to two degrees Celsius every five minutes.⁸ As high temperatures can cause further injury and brain damage, it is important to reduce the patient's temperature as part of the crisis management. Himmertzhaim and Steinke recommend one designated person to control all of the hyperthermia measures. This person should decrease the room temperature and apply ice packs and cooling blankets (or even cool, wet blankets) to the patient's skin (where it does not interfere with the surgical procedure).¹ Anesthesia providers should use refrigerated saline intravenous solution and, if possible, a cold naso-gastric lavage. When the abdominal or thoracic cavities are exposed for the surgical procedure, cool irrigation solution is instilled in the cavities to help decrease core temperature.

POSTOPERATIVE CARE

Dantrolene sodium blocks the release of calcium from the sarcoplasmic reticulum, and when the calcium levels drop, the muscles finally begin to relax.¹³ Due to its nature as a muscle relaxant, dantrolene sodium is not without some side effects, such as generalized muscle weakness, phlebitis and respiratory failure.¹³ Some patients have also reported gastro-intestinal upset.

After any surgical repairs are completed, the patient is transferred to an intensive care unit for 24-48 hours, where further monitoring can be completed (including electrolytes, creatinine kinase, and urine myoglobin).⁹ Rebound crisis episodes are common, and continued treatment with intravenous dantrolene at 1mg/kg every six hours is recommended.⁹

CONCLUSION

MH recently became front-page news with the publication of a story regarding a Florida teenager who died during surgery from a crisis. Early details show that the staff did not act appropriately and may not have delivered enough of the drug in order to fight the disease.¹⁴ Before treatment with dantrolene sodium became common practice, mortality for MH was close to 70 percent. With appropriate treatment, the current mortality rate is less than 10 percent,¹ and some studies indicate mortality as low as five percent.⁵ Periodic review of signs and treatment for MH are essential to maintaining the low morbidity and mortality rates.

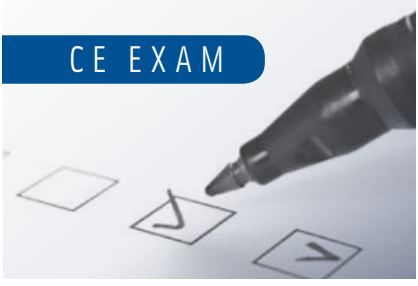
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Malignant Hyperthermia Crisis

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1. **The Malignant Hyperthermia Association of the United States (MHAUS) recognizes which of the following areas as having a high level of malignant hyperthermia susceptible individuals?**
 - a. Maine
 - b. California
 - c. West Virginia
 - d. Texas
2. **The most common initial sign of a malignant hyperthermia crisis is:**
 - a. Masseter muscle rigidity
 - b. Elevated temperature
 - c. Tachycardia
 - d. Hypertension
3. **Vials of dantrolene sodium are reconstituted with water because:**
 - a. malignant hyperthermia already causes an increase in sodium in the vascular spaces.
 - b. the vials also contain enough electrolytes to maintain an isotonic solution.
 - c. using sodium chloride would cause renal failure due to the increase in vascular volume.
 - d. the reconstitution should be a slow process and saline works too quickly.
4. **Which of the following medications should be included in a malignant hyperthermia cart?**
 - 1) furosemide
 - 2) diltiazem
 - 3) insulin
 - 4) sodium bicarbonate
 - a. 1 and 2
 - b. 1, 3 and 4
 - c. 1, 2, 3, and 4
 - d. 2, 3 and 4
5. **You are providing a tour of the operating room to some surgical technology students. One asks why the malignant hyperthermia cart is located in the PACU. You respond:**
 - a. "Patients have been known to have an MH crisis after the surgery is completed."
 - b. "This location helps us to distinguish between the regular crash cart and the malignant hyperthermia cart."
 - c. "It is normally stored in the pharmacy; there must be a patient with high potential for a crisis scheduled."
 - d. "The PACU area has a warmer ambient temperature and it prevents deterioration of the medication."
6. **Your next surgical patient is known to have a parent who demonstrated a high fever after surgery. Which statement indicates an appropriate set-up of the operating room for this patient?**
 - a. The temperature in the room is decreased to 65° Fahrenheit.
 - b. The anesthesia machine is prepared with fresh soda lime.
 - c. Anesthesia has succinylcholine prepared for rapid sequence intubation.
 - d. The malignant hyperthermia cart is stocked and placed in the PACU.
7. **The surgeon complains that the patient's abdominal muscles are "tight" and that the patient is getting too little anesthesia. The patient's skin is bright red and the end-tidal carbon dioxide level has risen sharply in the last few minutes. Anesthesia personnel should:**
 - a. Provide more inhalation agent to deepen the patient's anesthesia level.
 - b. Apply a bispectral monitor to determine if the patient is too light.

- c. Discontinue the inhalation anesthetic and call for the MH cart.
- d. Administer another dose of succinylcholine to cause the muscles to relax.

8. Patients suffering an MH crisis in the intraoperative setting should be monitored postoperatively for:

- 1) **respiratory difficulties**
- 2) **renal failure**
- 3) **cardiac arrhythmias**
- 4) **recurrence of MH**

- a. 1 and 2 only
- b. 3 and 4 only
- c. 1, 2, and 4
- d. 1, 2, 3, and 4

9. Your next patient states that his mother had an MH crisis during surgery. However, the patient had genetic testing which showed no mutations of the RyR1 gene. Which statement best describes his risk for developing a crisis.

- a. Low risk: genetic testing is the standard test for measuring MH susceptibility.
- b. High risk: family history is more important than genetic testing or contracture tests for determining susceptibility.
- c. High risk: muscle biopsy contracture tests are the best method of determining MH susceptibility.
- d. Low risk: transmission of the mutation is linked to paternal genes, not maternal.

10. Which of the following are considered "late" signs of a malignant hyperthermia crisis?

- 1) **unexplained tachycardia**
- 2) **oliguria**
- 3) **increased temperature**
- 4) **prolonged bleeding**

- a. 1, 2, and 3
- b. 2, 3, and 4
- c. 1, 3, and 4
- d. 1, 2, and 4

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Mark one box next to each number.
Only one correct or best answer can be selected for each question.