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# Malignant Hyperthermia

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## Introduction

The topic of Malignant hyperthermia (MH) will be presented in this poster. MH was chosen as the poster topic as this is an anesthetic crisis that can occur following the administration of triggering agents. It is of the upmost importance for the anesthesia providers, as well as support staff, to be able to recognize and respond to an MH crisis to optimize the patient's outcome.

Banek et al., (2013) stated that MH is a rare but potentially lethal genetic disease process that presents as muscle hypermetabolism upon exposure to certain anesthetic agents.

Butterworth et al., (2013) stated that MH impacts:
1:3000 - 1:15,000 pediatric patients
1:40,000 adult patients
The higher incidence in the pediatric population was seen in cases where both a volatile agent and succinylcholine were used.

Inhaled general/Volatile anesthetics/ Depolarizing muscle relaxants known to trigger MH:

| | |
|---|---|
| Desflurane | Sevoflurane |
| Isoflurane | Halothane |
| Enflurane | Ether |
| Methoxyflurane | Succinylcholine |

(Long & Ross, 2017).

Most reported cases have been in young males, very few have been reported in the geriatric population, and none have been reported in infants, but both sexes and all ages may be affected (Butterworth et al., 2013).

MH incidences greatly differ from country to country and even vary by geographical location within the same country. This illustrates that different gene pools can be impacted by this disease process. In the United States, the upper Midwest appears to have the greatest population of individuals that are susceptible to MH (Butterworth et al., 2013).

Inheritance patterns include:
Autosomal dominant
(Hines & Marschall, 2012).

Rosenberg et al., (2015) stated that specific point mutations have been found in the ryanodine receptor gene (*RYR1*) which is located on chromosome 19. Abnormalities have also been found on the dihydropyridine receptor.

## Pathophysiological Process

### Normal Physiology

To understand the pathophysiology of MH, one must first understand the normal physiology of muscle contraction.

In normal muscle physiology, an action potential causes membrane depolarization which releases calcium ($Ca^{2+}$) from the sarcoplasmic reticulum (SR). The $Ca^{2+}$ is thus inserted into the sarcoplasm via the ryanodine and dihydropyridine receptors. Both of these receptors are voltage-gated ion channels.

The $Ca^{2+}$ then interacts with the troponin-tropomyosin complex which creates the cross-bridge between actin and myosin and a muscle contraction occurs. At the completion of the muscle contraction, $Ca^{2+}$ is sequestered back into the sarcoplasmic reticulum and the another stimulus is needed to release $Ca^{2+}$ for a muscle contraction (Schneiderbanger et al., 2014).

### Underlying Pathophysiology

In MH, the mutated *RYR1* gene receptor threshold is decreased for $Ca^{2+}$ release. The *RYR1* receptors are also resistant to the negative feedback loop (increase $Ca^{2+}$ and magnesium) that would normally decrease the $Ca^{2+}$ conductance.

This equates to an overt release of $Ca^{2+}$, in response to lower levels of membrane depolarization. This causes an increased amount of $Ca^{2+}$ to be present in the sarcoplasm which causes continuous and prolonged muscle contractions when attached to the troponin-tropomyosin complex.

Adenosine triphosphate (ATP) is consumed in every step of intracellular $Ca^{2+}$ interactions. These steps include:
- Decoupling of $Ca^{2+}$ from troponin
- Removal of intracellular $Ca^{2+}$
- Returning ($Ca^{2+}$) to the SR and mitochondria
- Extrusion into the extracellular milieu (Hines & Marschall, 2012).

Oxygen and glycogen are thus used in massive quantities by the mitochondria as the body attempts to create more ATP in response to the highly increased metabolic demands. The metabolic byproducts of this process are carbon dioxide and lactate. In addition, the body produces massive amounts of heat as the ATP is used by muscles for contraction.

### Signs and Symptoms

Rosenberg et al., (2015) stated that some individuals have almost immediate reactions with exposure to triggers while others do not until well into the post-operative period.

The **early phase** presents as a masseter spasm, tachypnea (with spontaneous ventilation), tachycardia as well as an irregular heart heart, and a rapid exhaustion of soda lime as well as a warm soda lime container. The anesthesia provider will begin to see an increased minute ventilation, an increased end-tidal $CO_2$, and cardiac dysrhythmias, as well as peaked T waves. This is secondary to the patient having an increased $Pa_{CO2}$, a metabolic and respiratory acidosis, and hyperkalemia due to the release of potassium into the extracellular space (Hines & Marschall, 2012).

The **intermediate phase** presents with the continued irregular heart rate but the patient would also be cyanotic and warm to the touch. There will be dark blood in the surgical site as oxygen molecules would not be able to bind to hemoglobin molecules as the body is in an acidotic state as well as the decreased transit time of blood through the lungs, secondary to tachycardia. The anesthesia provider would thus observe an increasing core body temperature and a decreasing oxygen saturation. There would also be persistent cardiac dysrhythmias and peaked T waves secondary to hyperkalemia (Hines & Marschall, 2012).

The **late phase** presents with **a** generalized skeletal muscle rigidity secondary to an increased intracellular calcium and increased serum creatinine kinase level. There will be a prolonged bleeding time and cola colored urine, secondary to myoglobinuria associated with rhabdomyolysis. As the patient remains in a hyperkalemic state, the anesthesia provider will continue to notice cardiac dysrhythmias and peaked T waves but will begin to observe a widened QRS as well as ventricular arrhythmias (Hines & Marschall, 2012).

## Significance Of Pathophysiology

Long & Ross (2017) stated that if MH is not treated, the body's innate ability to maintain homeostasis is overwhelmed and this can lead to cardiovascular collapse and eventually death. Therefore, prompt recognition and intervention is necessary to prevent irreversible damage. Hirchey Dirksen et al., (2013) stated that the MH response leads to a variety of internal reactions secondary to the disruption of cell membranes such as an increase in serum potassium, phosphate, magnesium, and myoglobin in the extracellular fluid. Furthermore, the complications that can occur include permanent skeletal muscle damage, hyperthermia (core temperatures between 39°C & 41°C), renal failure (secondary to rhabdomyolysis), cardiac arrest, and possible death.

Some of the short and long term complications of MH are rhabdomyolysis with an accompanying compartment syndrome, disseminated intravascular coagulation (DIC), heart failure, pulmonary edema, cerebral edema with or without herniation, acute liver failure, shock secondary to a mixed metabolic and respiratory acidosis, bowel ischemia, other end multi organ failure, cardiac collapse, and eventually death (Epocrates: An Athenahealth Service, 2018).

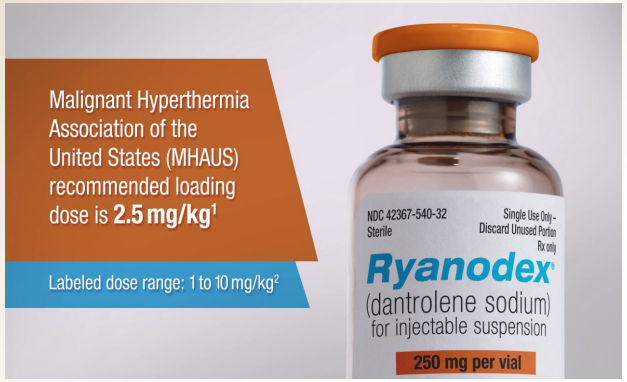


Figure 1: Ryanodex, concentrated dantrolene sodium for use in a MH crisis (Ryanodex, 2018).

## Implications for Nursing Care

Schneiderbanger et al., (2014) stated that the severity of a MH crisis depends on how quickly the disease process is suspected and how rapidly an appropriate treatment is initiated. Once MH has been recognized, it is imperative to discontinue the offending triggering agent. Anesthesia should immediately be converted to total intravenous anesthesia (TIVA) with the use of IV opioids, sedatives, and if the patient status necessitates it, a non depolarizing muscle relaxant. The vaporizer that was used for administration of the volatile anesthetic should be removed and the patient hyperventilated with 100% oxygen at maximum fresh gas flow while an activated charcoal filter is placed. There must also be an increase in the minute volume by 2x – 3x times the patient's baseline in an attempt to flush the volatile anesthetic from the patients system while also aiming to decrease the end-tidal $CO_2$ to within normal limits.

Hirchey Dirksen et al., (2013) states that the main medication that should be used in a MH crisis is dantrolene sodium at 2.5 mg/kg IV every 5-10 minutes based on actual body weight. Long & Ross (2017) state that this medication interferes with the release of $Ca^{2+}$ from the SR which results in a decrease in the $Ca^{2+}$ in the myoplasm. This is because dantrolene is a specific ryanodine receptor antagonist. It is recommended that 36 vials of dantrolene be stocked at any facility where the causative agents of MH are used to treat a patient in MH crisis as they will require a very large quantity of dantrolene.

Once a MH crisis has been confirmed, and the administration of dantrolene has begun, other supportive measures must be started. Hirchey Dirksen et al., (2013) states to administer sodium bicarbonate to correct the acid-base balance secondary to the mixed respiratory and metabolic acidosis.

## Implications Continued

The patient must also be cooled via administration of cold IV fluids, being packed with ice packs, having cold irrigation fluids instilled into open body cavities as well as having a cold lavage of the stomach, rectum, and bladder as well as the application of hypothermia blanket.

Diuretics, such as furosemide, must also be administered to reduce the incidence of fluid overload as well as the promotion of the excretion of potassium, sodium, and myoglobin.

Dantrolene, per 20 mg vial, also contains 3 g of mannitol, an osmotic diuretic which will help in this process.

To correct the marked hyperkalemia, glucose and insulin, as well as sodium bicarbonate, calcium chloride, or calcium gluconate can be administered.

The patient can also benefit from an antiarrhythmic to treat dysrhythmias that have not responded to the treatment of acidosis and hyperkalemia. The implementation of standard advanced cardiac life support (ACLS) measures is paramount with the exception of calcium channel blockers which can cause hyperkalemia and/or cardiac arrest in the presence of dantrolene.

## Differential Diagnosis

Malignant hyperthermia requires a high degree of suspicion when early signs and symptoms are present.

Unfortunately, the early signs and symptoms of MH are nonspecific and present as other hypermetabolic states would. The hypermetabolic states in question are:
Non-MH Rhabdomyolysis
Muscle disuse atrophy
Myotonia
Sepsis
Complications of laparoscopic surgery
Allergic reactions
Serotonin syndrome
Hyperthyroidism
Neuroleptic malignant syndrome
Baclofen with-drawl syndrome

## Differential Diagnosis Continued

Thyrotoxocosis
Pheochromocytoma
Metastatic carcinoid
Drug induced muscle injury
MDMA overdose
Use of designed drugs of new psychoactive substances
Alpha PVP or "Flakka"
Exertional heat stroke
Thermal dysregulation
Iatrogenic overheating
Meperidine/MAOI overdose
Cocaine intoxification
(Epocrates: An Athenahealth Service, 2018).

According to Rosenberg et al., (2015), patients with Central Core Disease, (CCD), Multi-minicore Disease (MmD), central nuclear myopathy, and King-Denborough syndrome are predisposed to episodes of MH.

## Clinical Resources

In the clinical setting, the anesthesia provider and support staff must be able to quickly address and treat MH. One of the primary resources that the healthcare provider has available is the Malignant Hyperthermia Association of the United States (MHAUS). This association can help facilities prepare for an MH emergency as well as manage a crisis in real time. They can be reached at:

**1-800-644-9737**

24 hours a day/7 days a week and providers are encouraged to call if MH is suspected (Malignant Hyperthermia Association of the United States, 2018).

Cain et al., (2014) stated that MH, a rare yet life-threatening event, can put clinicians at a disadvantage if they are unprepared to manage an MH crisis. The author of this article went on to indicate that a facilitated simulation of how to respond and treat MH in a safe environment can help clinical staff identify where improvement in gaps of knowledge and skills are needed. Two major points that came from the training exercise was the importance of role assignments, as well as the use of visual aids, when training for an MH crisis.

## Conclusions

Banek et al., (2013) stated that MH is a rare but potentially lethal genetic disease process that presents as muscle hypermetabolism upon exposure to certain anesthetic agents.

Rosenberg et al., (2015) stated that the main clinical features of MH are:
1) Unexplained elevation of expired carbon dioxide despite an increased minute ventilation
2) Muscle rigidity with an associated Rhabdomyolysis
3) Hyperthermia
4) Tachycardia
5) Acidosis [metabolic and respiratory]
6) Hyperkalemia

According to Hirchey Dirksen et al., (2013), the use of dantrolene sodium, in combination with early recognition, accurate diagnosis, and appropriate treatment, has decreased rates of mortality from 80% in the 1970s to approximately 5% as of 2007.

## References

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