Malignant Hyperthermia (MH)

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What is Malignant Hyperthermia?

MH is a biochemical chain reaction response, “triggered” in susceptible individuals by commonly used general anesthetics and the paralyzing agent Succinylcholine (neuromuscular blocker)

MH is a myopathy; that is, a pathologic change in muscle. There are scores of myopathies or muscle diseases, some with predictable dire consequences such as muscular dystrophy, while others are annoying and somewhat restrictive but compatible with a normal life.

Calcium levels in the cell “turn on” or “turn off” muscle contraction as well as energy production. We know that there are at least two regulatory proteins that are affected, the dihydropyridine receptor (DHPR) and the ryanodine receptor (RYR). Some studies indicate that there are other calcium regulatory proteins in muscle that when absent or deformed may also lead to the pathophysiologic changes of MH.

MH Simulation

Incidence- Under General Anesthesia

- The exact incidence of MH is unknown.
- Epidemiologic studies reveal that MH complicates one in about 100,000 surgeries in adults and one in about 30,000 surgical procedures in children.
- The incidence varies depending on the concentration of MH families in a given geographic area. High incidence areas in the United States include Wisconsin, Nebraska, West Virginia and Michigan. However, the prevalence of genetic change that predisposes to MH is much higher. About one in 2,000 patients harbor a genetic change that makes them susceptible to MH.

Who is susceptible to MH?

- MH is considered a dominantly inherited autosomal disorder, this means that children and siblings of a parent with MH susceptibility usually have a 50% chance of inheriting a gene defect for MH.
- All closely related members of a family in which MH has occurred must also be considered MH susceptible and managed accordingly, unless proven otherwise.
- Those who are susceptible may be completely unaware of this risk unless exposed to anesthetics leading to a life-threatening crisis.
- Not everyone who has the MH gene develops an MH episode upon each exposure to triggering anesthetics.
- MH related deaths have occurred even though patients have undergone multiple prior uneventful surgeries.

Some disorders associated with MH

- Muscular Dystrophy
- Heat Stroke
- Ptosis
- Strabismus
- Scoliosis
- Muscle cramps
- Intolerance to caffeine
- Hyperthyroidism
- Pheochromocytoma
- Neuroleptic malignant syndrome
- King Denbourgh syndrome
- Center Core disease

Over 80 genetic defects have been associated with MH.

What drugs trigger MH?

- Volatile gaseous inhalation anesthetics
  - Desflurane
  - Enflurane
  - Ether
  - Halothane
  - Isoflurane
  - Methoxyflurane
  - Sevoflurane
- Muscle Relaxant Succinylcholine

"Safe" Drugs

- Depressant drugs (barbiturates, tranquilizers)
- Non-Depolarizing Muscle Relaxants (NDMR)
- Antibiotics, Antihistamines, Antipyretics, Ketamine, Local Anesthetics, Nitrous oxide, Opioids, Porpanolol, and Propofol.

Causes of an MH episode

Although the cause of MH is not yet known with certainty in all inherited forms, research evidence points to a generalized derangement of the processes which regulate muscle contraction.

Causes of MH episodes

- The triggering agents induce increased concentrations of calcium in the muscle cells
- High calcium levels cause the muscles to contract and become rigid, leading to greatly increased metabolism. The process results in heat production (hyperthermia) and muscle cell breakdown.

General Signs of MH

Increased heart rate, greatly increased body metabolism, muscle rigidity and/or fever that may exceed 110˚F or 43.3˚C along with muscle breakdown, derangements of body chemicals and increased acid content in the blood.

Signs and symptoms of MH:

- Early signs
  - masseter muscle rigidity
  - unexplained increased in exhaled CO2
  - unexplained tachycardia
  - generalized muscle rigidity
- Late signs
  - dark, brown urine
  - bleeding/oozing from wound sites
  - dark blood in the operative field
  - temperature elevation

Biochemical changes

- Early
  - increased pCO2
  - acidosis (respiratory and metabolic)
  - hyperkalemia
  - hyper or hypo calcemia
  - hyperglycemia
- Late
  - elevated CK (peaks 12-24 hours after crisis)
  - myoglobinuria
  - increase in liver enzymes (unusual)
  - prolonged PT/PTT
  - decreased platelet count

Severe Complications

Cardiac arrest, brain damage, Internal bleeding or failure of other body systems. Thus, death, primarily due to a secondary cardiovascular collapse, can result.

Currently the most definitive diagnostic test for MH is a muscle biopsy

Treatment of MH

- Since 1979, the antidote drug dantrolene sodium was identified for the treatment of MH and contributed greatly to the dramatic decline of mortality. Dantrium® (dantrolene sodium for injection) is available in powdered form. It must be reconstituted by adding sterile water to it.
- Dose- Initial dose 2.5mg/kg, then 1 mg/kg every 5 minutes to total of 10 mg/kg.

Dantrolene (Proctor & Gamble) needs to be mixed with 60 ml of sterile water. Once diluted it should look like a light yellow color. Once the drug is mixed the concentration is .333 mg/ml. 60 ml = 20 mg

New Drug called Ryanodex (still is Dantrolene) different concentration. Reconstitute with 5 ml of water to create a 50 mg/ml solution

Many large countries, such as China do not have Dantrolene readily available. We hear of deaths or near misses from MH in countries such as the Philippines and Peru to name just a few, because Dantrolene is not available.

Case Study

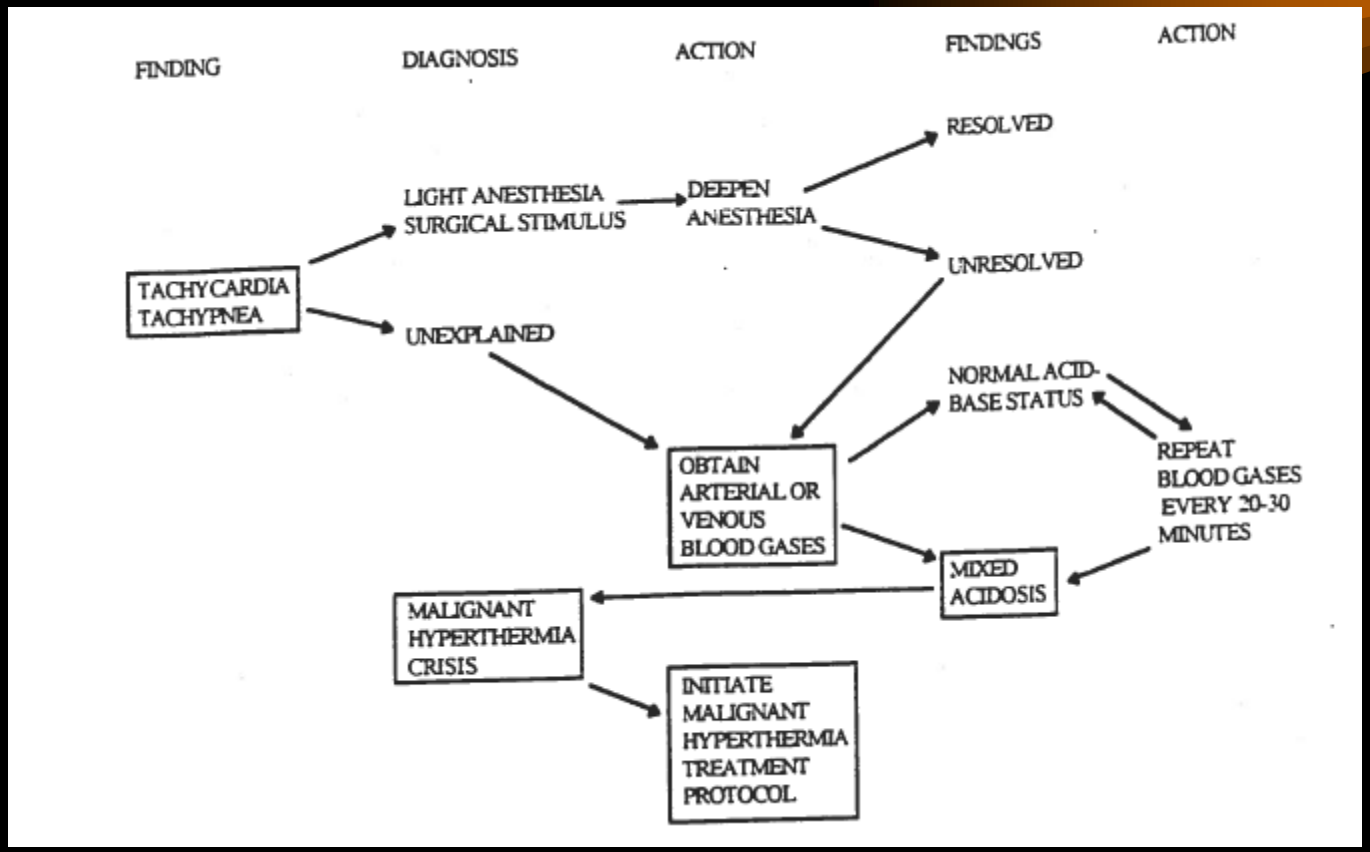
2 year old who come in for an umbilical hernia. He weighs 22 pounds and showing signs of increase end tidal CO_2 and muscle rigidity. What do you do?
Weight 22 lbs/2.2 = 10 kg

Old concentration: .333 mg/ml
New concentration: 50 mg/ml

First initial dose is 2.5 mg/kg
How much do you give? 10 kg x 2.5 = 25 mg

Old concentration: 75 ml (2 vials = 20 mg Vials)
New concentration: 0.5 ml (1 vial = 250 mg Vial)
Very Big Difference in Volume

MH Schematic



Treatment of symptoms of MH

- Hypocalemia- Calcium Chloride
- Decrease Glucose- Dextrose
- Calcium Uptake- Dantrolene
- Decrease HR and BP- Epinephrine
- Tachycysrhythmia- Esmolol
- Fluid Retention- Lasix
- Increase Glucose- Insulin
- Ventricular Dysrhythmia- Lidocaine
- Fluid Retention- Mannitol
- Dysrhythmias- Procainamide
- Acidosis- Sodium Bicarb

ALL DRUGS LISTED CAN BE FOUND IN THE MH CART

Supplies located in MH cart:

DRAWER ONE: Medications

DRAWER TWO: Dantrolene supplies

DRAWER THREE: Artline and lab supplies

DRAWER FOUR: Anesthesia supplies

DRAWER FIVE: Irrigation supplies

Remember to add at time of MH crisis

- Located in Center core 2 refrigerator:
  - 1000cc NS bags
  - 3000cc NS bags
  - Pediatric or adult NG
- Located in Pharmacy refrigerator:
  - Regular insulin
- Located in Pump room (between 1 + 2):
  - ICE

Labs for MH crisis:

Labs for a MH crisis are located in Epic under the OR bundles.

MH CRISIS ORDER SET INCLUDES:

- ABG
- CBC no Differential
- Creatine Kinase
- LDH
- Na, Cl, Ca, Mg
- PT, PTT, Platelet
- Fibrin-split product
- Fibrinogen, D dimer
- Urine (UMAC)
  - myoglobin
  - note specimen source

Laboratory Findings

Table 3: *Laboratory Findings of Acute MH*

	Normal Ranges
ABG	
⇓ pH	7.35–7.45
⇓ PO_2	80–100 mm Hg
⇑ PCO_2	35–45 mm Hg
Electrolytes	
⇑ K	4.0–5.4 mEq/L
⇑ Ca	4.5–5.5 mEq/L
⇑ Mg	1.8–2.4 mg/dL
⇓ Na	138–148 mEq/L
Serum	
⇑ Lactate	0.7–2.1 mmol/L
⇑ Pyruvate	0.03–0.08 mmol/L
⇑ CPK *(creatine phosphokinase)*	40–280 U/L
⇑ LDH *(lactic dehydrogenase)*	3.13–6.18 U/L
⇑ Aldolase	Age specific
⇑ Myoglobin	6–85 ng/mL
⇑ Glucose	80–120 mg/dL
⇑ Creatinine	0.5–1.4 mg/dL
⇓ PT	10–12
⇓ PTT	22–27
⇓ Platelets	50,000

MH Crisis Tasks

- The nurse taking care of the child is responsible for task one and nine:
  - Task One: Call for more help and assign tasks
  - Task Two: Retrieve the MH cart and code cart, open carts and wait for further assignments
  - Task Three: Retrieve supplies listed on top of MH cart and start to fill ice bags

MH Crisis Tasks cont.

- Task Four: Assist with anesthesia art line, cvp line, and lab draws and retrieving labs when results are final
- Task Five: Prepare Dantrolene and hand to anesthesia
- Task Six: Insert Foley and NG
- Task Seven: Assist surgeon with placement of peritoneal catheter is applicable

MH Crisis Tasks cont.

- Task Eight: Temperature regulation: ice head, arm pits, and groin area, lavage bladder, peritoneal cavity, and stomach: stop once temp. reaches 38.5 C
- Task Nine: Assist with transfer of patient to PICU

- Tasks are to be done simultaneously
- Task one and nine should be combined
- Tasks two and six can be combined
- Tasks three and seven can be combined

Can MH occur outside of the Operating Room?

- Yes. While most cases of MH occur during general anesthesia, the one-hour period immediately following surgery (including the recovery room) is also a critical time. In addition, MH can occur if trigger anesthetics and/or succinylcholine are used in any location, such as emergency rooms, dental surgeries, surgeon's offices or intensive care units.

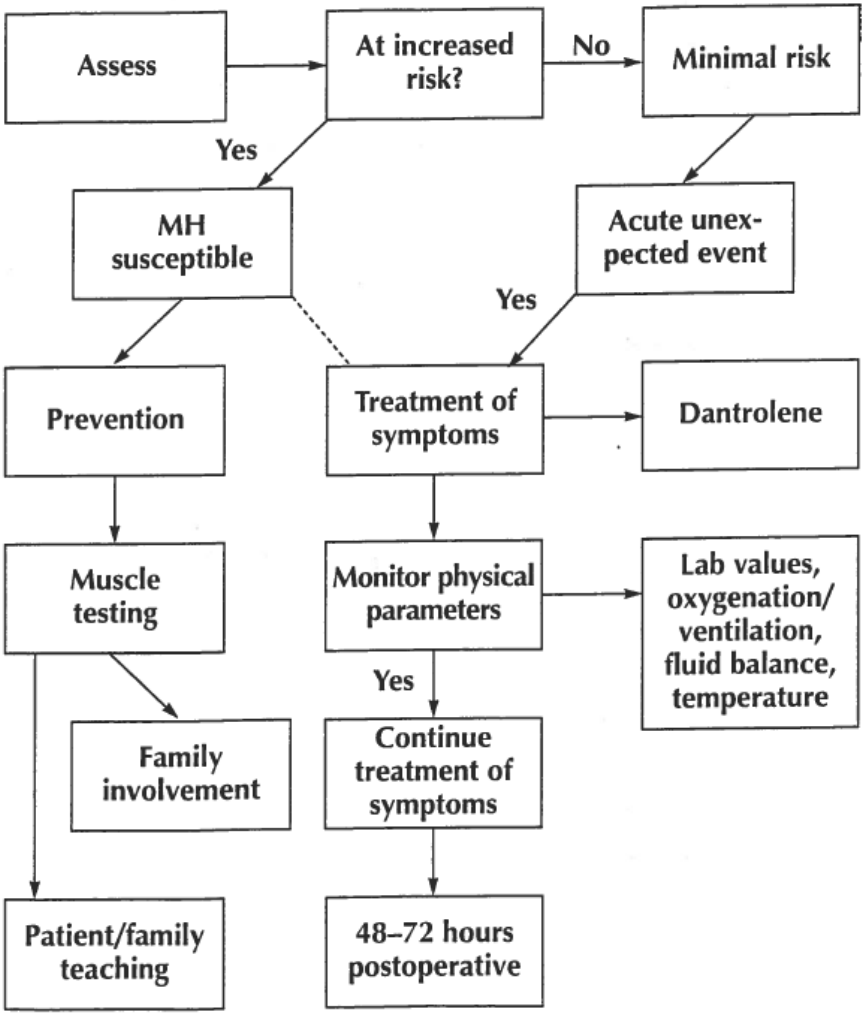
Can Anything other than Anesthetic Drugs Trigger MH?

Studies have shown that a small percent of people who develop muscle breakdown following exercise only, or afterheat stroke, harbor the genetic changes associated with MH susceptibility. It is still unclear if the muscle breakdown and other changes result from these non-anesthetic incidences. In the absence of a personal or family history of heat stroke or exercise-induced muscle breakdown or evidence of muscle disorders, ask your personal physician to consult with an MH expert.

Additional information

- Malignant Hyperthermia Association of the United States (MHAUS)
  - 1-800-98-MHAUSS
- http://www.mhaus.org
- MH Hotline: On-call anesthesiologists available to consult in MH emergencies may be obtained 24 hours a day:
  - 1-800-MH HYPER (1-800-644-9737)

Table 2: *Malignant Hyperthermia Flow Chart*



AORN Standards & Guidelines

SOME WISCONSIN FAMILY NAMES ASSOCIATED WITH MALIGNANT HYPERTHERMIA

Ambrowiak
Auclair
Arbelovski
Beholovek
Berg
Bielke
Black
Blosczynski
Brill
Check
Dreikosen
Ebert
Fahey
Falkowski
Fenske
Fosware
Frieders
Gassner
Graveen
Green
Griesmer
Gross
Hall
Handrick
Hoven
Imhoff
Jakubowski
Kamenick
Kamke
Kelley
Kennedy
Kilian
Knoeck
Komenic
Krautkramer
Kurtzweit
Lyon
Mahalak
Mcguire
Martin
Marschner
Masanz
McHugh
Melder
Mijal
Newman
Nigbur
Nowak
O'Connor
Oppman
Peebles
Olson
Peters
Rasmussen
Robertson
Rogillard
Ross
Sattler
Schara
Schiefelbein
Schill
Schmeckel
Seliger
Sonnentag
Staeck
Stanley
Stone
Stroming
Syring
Tessmer
Ugoretz
Wasser
Webba
Witberler
Wolf
Zahn
Zarda

Family Names

A Case from 2009

MH QUIZ:

1. Malignant Hyperthermia is a complication of:
    a. General anesthesia
    b. Local anesthesia
    c. Regional anesthesia
    d. Spinal anesthesia
2. The etiology of MH is:
    a. A bacteria
    b. A virus
    c. Genetic skeletal muscle receptor abnormality
    d. Unknown

MH QUIZ cont.

3. This is the most consistent early symptom of MH.

    A. Dark blood in the operative field

    b. Increased skin temperature

    c. Muscle flaccidity

    d. Increased of end-tidal CO2

4. Currently this is the most definitive diagnostic test for MH?

    a. A tourniquet test of muscle ischemia

    b. Muscle biopsy

    c. Muscle contraction strength in the hand

    d. The metabolism of blood platelets

MH QUIZ cont.

5. Which of these are likely to trigger MH?

A. Enflurane

B. Halothane

C. Nitrous Oxide

D. Succinylcholine

a. A, B

b. C, D

c. A, B, D

d. All of the above

MH QUIZ cont.

6. A sudden increase in this element within muscle cells initiates the biochemical reactions of MH:

   a. Calcium
   b. Magnesium
   c. Potassium
   d. Sodium

7. This is currently the drug of choice in treating MH?

   a. Calcium chloride
   b. Dantrolene sodium
   c. Lidocaine hydrochloride
   d. Procainamide hydrochloride

MH QUIZ cont.

8. Which of the following are essential if the drug of choice is to be fully effective in treating MH?

A. Body temperature must be lowered

B. Dantrolene must be given as soon as possible

C. Hypertension must be corrected

D. Metabolic Acidosis must be corrected

a. C, D

b. A, B, C

c. A, B, D

d. All of the above

MH QUIZ cont.

9. Treatment of MH may include which of the following?

A. Administering iced intravenous solutions

B. Inserting a Foley catheter

C. Irrigating the wound with cold saline solution

D. Surface cooling with a cooling mattress

a. A, B

b. C, D

c. A, C, D

d. All of the above

MH QUIZ cont.

10. A patient can experience a MH crisis

    a. Prior to surgery

    b. In the recovery room

    c. A month after surgery

    d. None of the above

Congratulations you've completed the MH quiz!

MH Rap