"The Longest 17 Minutes of My Life"
MALIGNANT HYPERTHERMIA in a Pediatric Patient

Terri Passig, RN, BSN, CPAN, CAPA, CCRN

DEFINITION
“Malignant Hyperthermia (MH) is an inherited muscle disorder triggered by certain types of anesthesia that may cause a fast-acting life-threatening crisis.”

(Retrieved from http://www.mhaus.org/)

History of Malignant Hyperthermia
• April 1960-first documented case
• Published findings in 1962

Br J Anaesth 1962; 34:395–6

Causes of MH
• MH susceptible people have a mutation that results in the presence of abnormal proteins in their muscle cells
• Over 80 genetic defects have been linked to MH
• 50-70% involve mutation of RYR1 receptor on the long arm of chromosome 19
• Another causative gene is CACN1S
• Autosomal dominant (child or sibling have 50% chance of inheritance)

Progression of MH
Increase concentration of calcium in the muscle cell causes:
• Hypercalcemia → muscles to contract and become rigid
• Hypermetabolic state
• Accelerated cellular processes increase oxygen consumption
• Carbon dioxide and heat produced
• ATP (Adenosine triphosphate stores are depleted)

Progression of MH
• Lactic acid is produced
• Acidosis, hyperthermia, and ATP depletion cause destruction of the muscle cell
• Increase release of K+, CK, and myoglobin into the extracellular fluid
• End result=tachypnea, tachycardia, cardiac dysrhythmias, hyperkalemia, hypercalcemia, hyperthermia, myoglobinuria, and rhabdomyolysis.
**Who is susceptible to MH?**
- Autosomal dominant inheritance
- Children & siblings of a patient with MH susceptibility have a 50% chance of inheriting the gene and are also susceptible.
- The individual may completely be unaware of their risk until they or a family member have surgery.
- It is important to note that not everyone develops MH upon each exposure to the triggering agents!

**Incidence of MH**
- 1 in 30,000 anesthetics in children
- 1 in 100,000 in adults
- Geographical areas

**MH AND MUSCLE DISEASES**
- Central Core Disease
- King Denborough Syndrome
- Multiminicore
- Muscular Dystrophies
- Myotonias

**WHAT DRUGS TRIGGER MH?**

**Unsafe Drugs**
- Inhalation Agents:
  - Halothane
  - Enflurane
  - Isoflurane
  - Desflurane
  - Sevoflurane
- Depolarizing Muscle Relaxant
  - Succinylcholine

**Safe Drugs**
- N2O
- Barbiturates
- Local anesthetics
- Benzodiazepines
- Non-Depolarizing Relaxants
- Ketamine
- Propofol
- Anticholinergics

**SIGNS OF MH**

**EARLY VS. LATE SIGNS**

**EARLY SIGNS**
- Increased End Tidal CO2
- Muscle Rigidity
- Masseter Muscle Spasm
- Generalized rigidity
- Tachypnea
- Tachycardia/dysrhythmias
- Hyperkalemia

**LATE SIGNS**
- Cutaneous changes: mottled skin - cyanosis
- Pyrexia (1° q 15 min.)
- DIC
- Rhabdomyolysis
- Renal Failure
- Left ventricular failure
How is MH Treated?

- Have a Plan
- Discontinue inhalation agents, succinylcholine
- Hyperventilate with 100% oxygen
- Get additional help
- **Dantrolene 2.5 mg/ kg IV push up to 10 mg/ kg**
- Cool patient: gastric lavage, surface, wound, etc.

Dantrolene Sodium is the **ONLY** Treatment for MH

- Skeletal Muscle Relaxant
- 20 mg bottle (Mannitol-3000 mg) reconstitute with 60 ml. of **sterile water**
- Prevents ongoing release of calcium from the storage sites in the muscle
- Enhances reuptake of calcium

Dantrolene Sodium

**After crisis:**

- Give Dantrolene 1 mg/kg IV every 4-6 hours for up to 48 hours
- Side effects: fatigue, muscle weakness, difficulty walking, dizziness, blurred vision, nausea, thrombophlebitis
- Recrudescence rate is 25%

Possible Complications of MH

- CNS damage: coma, seizures, permanent CNS damage
- Paralysis
- Blindness
- Renal failure
- Recurrence of syndrome
- Muscle edema and weakness
- Compartment syndrome
- Multi System Organ Failure
- Death

Other Interventions

- Sodium Bicarbonate
- Glucose & Insulin (Hyperkalemia)
- Treat arrhythmias
- Arterial blood gases
- Electrolytes, coagulation studies, CK & myoglobin
- Insert Foley Catheter/NG Tube

History of Dantrolene

- Macrodantin developed for treatment of urinary tract infections in early 1970s
- 1979 FDA approves use for MH
# MH Testing

- **Halothane, Caffeine Contracture Test**
- The ‘Gold Standard’
- 30 centers worldwide, only 5 in US and Canada
- Cost: $6,000–$10,000

# CHCT Pros and Cons

- **Pros:**
  - Positive result establishes definitive diagnosis for patient who is tested.
  - Negative result allows patient freedom of choice regarding anesthetic use
- **Cons:**
  - Patient must undergo invasive surgical procedure; 2-7 days relative disability
  - Testing can only be performed in specialized Biopsy Centers
  - Patients must travel to center!
  - Expensive

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# Genetic Testing

- **RYR1 Genetic Test (Ryanodine receptor of skeletal muscles)**
- Released in 2005
- Involves DNA sequencing on the gene where MH mutations reside
- Only two labs in the U.S. perform this test
- Cost $800-$4000

# Genetic Testing-Pros and Cons

- **Pros:**
  - Less expensive
  - Less invasive
  - No need to travel
  - If causative mutation found in family member, other family members can have predictive testing carried out with a high degree of accuracy, without need for CHCT, and at a lower cost than the first person tested.
- **Cons:**
  - Due to discordance and the heterogeneity of MH, absence of a causative mutation does not rule out MH susceptibility; muscle contracture test would be needed to confirm the individual is not susceptible to MH
  - Insurance may not cover

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# MH Case Presentation

- 6 yo girl for BMT & adenoidectomy
- 17.6 kg, NKDA
- Tylenol/Versed PO pre-med
- No family hx of GA complications
- Parents report snoring; no sleep study done

# Past Medical History

- Ex-31 week preemie with NICU stay
- Hospitalized @ 6 mo. with pneumonia
  - Asthma
  - + MRSA (in NICU)
- Extremely anxious parents and patient!
**Medication History**

- Pulmicort
- Singulair
- Nasonex
- Bromfed

**The Saga Begins......**

- 0855-0859: sitting on OR table for induction with Nitrous oxide and slow addition of Sevofluorane.
- OAW placed with some resistance (small mouth?). PIV started
- Propofol given in two doses
- Intubated without difficulty
- Bed turned to 90 degrees

**Smooth Sailing....(so far)**

- 0900: \( \text{ETC02} 66, \text{PIP} 13, \text{HR} 166, \text{O2 sat} 98\% , \text{BP} 100/57 \) — sat probe repositioned, N2O DC'd
- 0905: \( \text{ETC02} 54, \text{PIP} 29, \text{HR} 157, \text{O2 sat} 98\% , \text{BP} 81/40 \) — sevo continued
- 0908: Surgery begins. Precedex 4 mcg given. After first ear tube placed, sx'd for mod. clear secretions. Fentanyl 5 mcg, Zofran 2 mg given. \( \text{ETC02} 60, \text{PIP} 22, \text{HR} 157, \text{O2 sat} 98\% , \text{Temp.} 37^\circ \text{C} (98.6 \text{ F}) \)
- 0912: BMT complete. Pt. repositioned by surgeon and again by CRNA

**Hmmm, Do We Have a Problem?**

- 0915: Surgeon comments that child's mouth is a little small. "I think she's a little light because she's swallowing." CRNA states that she has been running her 'a little light' because sats had not recovered. Fentanyl and Precedex given. \( \text{ETC02} 77, \text{PIP} 18, \text{HR} 162, \text{T} 37^\circ \text{C} (98.6 \text{ F}) \) Discussed possibility that ETT may have been slightly advanced during mouth gag placement; readjusted. Surgeon states pt. had left lung cyst while in NICU (parents did not report this during pre-op eval)
- 0920: Hand-ventilated to decrease CO2 to 65

**Procedure Complete, Are We OK??**

- 0925: Surgeon refers to H & P to confirm "left-sided cyst" per her notes. \( \text{ETC02} 67, \text{PIP} 17, \text{O2 sat} 97\% , \text{T} 37^\circ \text{C} (98.6 \text{ F}) \) ETT lavage and sx; albuterol given

**We Think We Have a Problem....**

- 0932: MDA called to room; scenario explained, \( \text{ETC02} 76, \text{HR} 166, \text{Esophageal temp} 37.5^\circ \text{C}, (99.5 \text{ F}) \) MDA turns hand over to obtain ABG and notes muscle rigidity...
- 0934: Sevo off, 10 L gas flow, MH cart and all available help to room. Room temp decreased. \( \text{ETC02} 84, \text{HR} 167, \text{O2 sat} 97\% , \text{T} 37.5^\circ \text{C} \)
- 0936: \( \text{ETC02} 97, \text{HR} 167, \text{O2 Sat} 96\% , \) surgeons, ANMs, RNs and techs present
The Team at Work

• 0939: ETCO2 80, HR 175, O2 Sat 98%, T 37.5° C (99.5 F)
  - Dantrolene mix started
  - 2nd PIV and AL placed
  - NG placed and lavaged with cold saline
  - Cooled IVF hung
  - Cooling blanket on

• 0945: ETCO2 51, HR 189, O2 sat 98%, T 37.5° C (99.5 F)
  - Dantrolene 40 mg given
  - Ice packs to groin and axilla
  - Foley placed
  - ABGs (ISTAT): 7.16, 61.9, 110, -5
  - Na 139, K 5.5, I Ca++ 1.09

....and More Teamwork!

• 0950: ETCO2 45, HR 169, O2 sat 97%, T 38.1° C (100.6 F)
  - Additional Dantrolene 40 mg given
  - MH Hotline called
  - ISTAT: 7.23, 56.1, 314, -4, 23.7
  - Na 126, K 5.3, I Ca++ 0.87

• 0958: ETCO2 45, HR 169, O2 sat 99%, T 38.3° C (100.9 F)

Progress!

• 1000: ETCO2 38, HR 120, O2 sat 100%, T 38.3° C (100.9 F)
  - Propofol drip started, Zemuron & Versed given
  - CVL inserted
  - CBC, Coags, CK, BMP & UA sent

• 1010: ETCO2 34, HR 122, O2 sat 100%, T 37.4°C (99.3 F)
  - MHAUS recommendations are:
    * remove ice packs once temp < 37.5
    * Coags, CK, UA (already sent)
    * extubate pt. when awake
    * continue Dantrolene x24 hrs.

Whew, Time to Leave the OR!

• ETCO2 continued to ↓ to 28
• Temp ↓ to 36.5 (97.7 F)
• 1045: to PICU; pt. awakening upon arrival and extubated shortly thereafter
• Dantrolene was continued x 24 hrs
• CK levels, electrolytes, coags, lactate, urine dipstick q 6h x24h
• Daily UAs
• Monitored for muscle weakness r/t Dantrolene
• Discharged on POD 4

Creatine Kinase
Follow Up

• Genetic Consult
• Genetic testing revealed RYR1 Gene, Tier One
• Family declined muscle biopsy and testing of other family members at this time

Lessons Learned

• Although staff had received education re: reconstituting Dantrolene, a verbal review at the time of mixing is helpful
• Very helpful to have needless devices for vials
• Know lab profiles that will be indicated
• Communication, communication, communication!!

MH in the Headlines

Strong Had Close Call With Death
The Nba Player Twice Had Reactions To Anesthesia, But Quick Work By The Doctors Saved Him.
June 17, 1999 | By Tim Povtak of The Sentinel Staff

“An operating table nearly became a death bed for Orlando Magic player Derek Strong during routine outpatient surgery to repair a broken nose. Malignant hyperthermia, two words that every anesthesiologist prepares for, but prayers he never hears, touched off a frantic chain of events Friday that left Strong fighting for his life.”

MH Headlines

PREVENTION OF MH?

• Preoperative personal/family history of anesthetic problems, neuromuscular disorders
• Temperature/end tidal CO2 monitoring during general anesthesia
• Recognition of masseter rigidity
• Investigate unexplained tachycardia, hypercarbia, hyperthermia
• Availability of Dantrolene
• Avoid trigger agents in susceptible patients

Possibilities on the Horizon

• “Comparison of Systemic Effects of 3,4-Methylenedioxymethamphetamine, of Ryanodex® Therapy and Uncoupling Protein 3 Expression in Malignant Hyperthermia Susceptible and Normal Swine”

S. Becker1, M.U. Gerbershagen1, S. Burmester1, J.K. Schütte1, A. Starosse1, C. Hötzel1, U. Schäfer2, F. Wappler1
Department of Anesthesiology and Intensive Care Medicine
Institute for Research in Operative Medicine
University Witten/Herdecke, Germany
SUMMARY

• MH is a metabolic myopathy affecting skeletal muscle
• All potent inhalation agents and Succinylcholine are the triggers of MH
• Inheritance of MH in humans is autosomal dominant
• The basic defect in MH is an increase in intracellular calcium of skeletal muscle
• End tidal CO2 increase is the most sensitive and specific clinical sign in the OR
• Prompt treatment with Dantrolene 1-2 mg/kg is the only treatment for MH
• Help and assistance are available from MH hotline 1-800-MH-HYPER.

Come Visit us in FLORIDA!!

Malignant Hyperthermia Association of the United States in conjunction with Orlando Health, Florida Society of PeriAnesthesia Nurses (FLASPAN), and Florida Society of Anesthesiologists (FSA) presents a one day conference on malignant hyperthermia in Orlando, FL. On June 29, 2013.

• Register today and to sit along side healthcare professionals and students, and patients and families learning about Malignant Hyperthermia from experts affiliated with MHAUS.

For more information, go to www.mhaus.org

QUESTIONS?