Malignant Hyperthermia

“Hot Off the Press”
2014 PGA, NYC

Ron Litman
litmanr@email.chop.edu
Relevant Disclosures and Conflicts of Interests
MHAUS
Guidelines Changed:
New Recommendations for Preparation & Treatment

Michael Denborough, 1929-2014
HENRY ROSENBERG
2015 ASA DISTINGUISHED SERVICE AWARD WINNER
MHAUS Hotline: 800-MH-HYPER
MHAUS Hotline Stats 2014

- 31 Hotline consultants
- > 400 calls thus far 2014
- > 200 website queries
MHAUS Hotline Stats 2014
Ages of pts

Bar chart showing the distribution of ages for hotline stats 2014.
MHAUS Hotline Stats 2014
Diagnoses

- Likely MH
- Possibly MH
- Unlikely MH
- Not MH
- Unknown
MHAUS Hotline Stats 2014
Location Episode Began

- Ward (postop)
- PACU (postop)
- No Anesthetic
- N/L
- ICU (postop)
- During or after emergence (pt still in OR)
- During maintenance of GA
- During induction of GA
Important MH Principles
Clinical News

Clinical Presentation, Treatment, and Complications of Malignant Hyperthermia in North America from 1987 to 2006

Table 1. Anesthetic Drug Triggers for 284 Malignant Hyperthermia Events

<table>
<thead>
<tr>
<th>Anesthetic drug</th>
<th>Frequency</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>+Succinylcholine, −Volatile</td>
<td>2</td>
<td>0.7</td>
</tr>
<tr>
<td>+Succinylcholine, +Volatile</td>
<td>153</td>
<td>53.9</td>
</tr>
<tr>
<td>−Succinylcholine, +Volatile</td>
<td>128</td>
<td>45.1</td>
</tr>
<tr>
<td>−Succinylcholine, −Volatile</td>
<td>1</td>
<td>0.4</td>
</tr>
</tbody>
</table>

Larach, Anesth Analg 2010;110:498-507
Clinical Presentation, Treatment, and Complications of Malignant Hyperthermia in North America from 1987 to 2006

Larach, Anesth Analg 2010;110:498-507
# Table 1. Characteristics of Index Adverse Anesthetics in 129 Malignant Hyperthermia-Susceptible Probands

<table>
<thead>
<tr>
<th>Demographics</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Male sex</td>
<td>79 (61.2%)</td>
<td></td>
</tr>
<tr>
<td>Age (y) at onset, median (range) [IQR]</td>
<td>23 (1–70) [10–33]</td>
<td></td>
</tr>
<tr>
<td>Caucasian</td>
<td>123 (95.3%)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Medical history</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prior muscle symptoms</td>
</tr>
<tr>
<td>Prior unremarkable anesthetics</td>
</tr>
<tr>
<td>Prior unremarkable anesthetics (range) [IQR]</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Anesthetic triggers</th>
<th>n (%) [95% CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td>+Succinylcholine, −volatile</td>
<td>20 (15.5%) [10–23]</td>
</tr>
<tr>
<td>+Succinylcholine, +volatile</td>
<td>51 (39.5%) [31–49]</td>
</tr>
<tr>
<td>−Succinylcholine, +volatile</td>
<td>58 (45.0%) [36–54]</td>
</tr>
<tr>
<td>−Succinylcholine, −volatile</td>
<td>0 (0.0%) [0–3]</td>
</tr>
</tbody>
</table>

Marilyn Green Larach, MD, FAAP,∗ Barbara W. Brandom, MD,∗† Gregory C. Allen, MD, FRCPC,‡ Gerald A. Gronert, MD,§ and Erik B. Lehman, MS¶
SHAFER, DEXTER, BRULL DECLARE WAR ON SKIN TEMP

“If you don’t monitor core temperature routinely, start today.”
SHAFAER, DEXTER, BRULL DECLARE WAR ON SKIN TEMP

“Do it right, with a continuous electronic measurement of core temperature.”
“This is better than explaining to patients, parents, or the next of kin, why you chose to save $6.”
Most MH deaths from hyperthermia!
12 year old child has acute MH in OR

CHCT shows MH susceptibility

8 mos later: dies after football practice: T 108 F

Ryr-1 mutation detected in pt and relatives

Tobin et al. JAMA, 286, 2001
Identical de novo Mutation in the Type 1 Ryanodine Receptor Gene Associated with Fatal, Stress-induced Malignant Hyperthermia in Two Unrelated Families

Linda Groom, B.Sc.,* Sheila M. Muldoon, M.D.,† Zhen Zhi Tang, Ph.D.,‡
Barbara W. Brandom, M.D.,§ Munkhuu Bayarsaikhan, Ph.D.,‖ Saiid Bina, Ph.D.,#
Hee-Suk Lee, M.D.,** Xing Qiu, Ph.D.,†† Nyamkhishig Sambuughin, Ph.D.,‡‡
Robert T. Dirksen, Ph.D.§§

Anesthesiology 2011; 115:938

7 reported cases
STOP

To protect private Patient Information

Only (1) family allowed at the desk at a time

Last name appears on monitor when prescription is ready

Thank You.
Anesthesia for Known MH Patients

- Non-triggering technique
- Carefully monitor etCO₂
- Normal discharge criteria
- ASC should be adjacent to hospital
Preparation of Anesthesia Workstations for MH Susceptible Patients

4 alternatives:
ASC Anesthesia for Known MH Patients

Vapor-Clean, Dynasthetics
Immediate Treatment of MH

Important Steps

- Mobilize personnel
- **DANTROLENE**
- Arrange transfer
- Continue active treatment
- **800-MH-HYPER (644-9737)**
RYANODEX

- Eagle Pharmaceuticals
- 250 mg/5 mL
- Decreased time to preparation
- Less volume load
- **1** successfully treated case!
- **More data next year!**
- Contains subclinical amts of mannitol
- **Why is mannitol in older versions of dantrolene?**
- MHAUS changed website guidelines on treatment of myoglobinuria
Why Joan Rivers Matters
Why Joan Rivers Matters
CCBs probably detrimental during dantrolene admin

Never withhold dantrolene in MH pts on maintenance CCBs.

MHAUS has retracted website statement
Malignant Hyperthermia

MHAUS Hotline 1-800-644-9737  Surgery Centers: 911 and transport arrangements

Anesthesiologist
1. CALL FOR HELP!
2. Stop triggering agents and place charcoal filters in circuit
3. Hyperventilate with 100% O₂ @ 10L/min
4. Start TIVA
5. Give Ryanodex 2.5 mg/kg IV
6. Aggressive IV hydration
7. Active cooling if T > 38°C
   • Bair Hugger to cool
   • Cold IVF 0.9% NS
   • Ice packs to head, groin, axillae
   • Cold lavage, cavity irrigation
8. Place lines
   • Arterial line
   • Foley catheter
   • NG tube
9. Obtain Labs
   • ABG, glucose, CK, lactate, electrolytes, CBC, serum myoglobin, coags, D-dimer, fibrinogen
   • Urine myoglobin

Nursing
1. Call Anesthesia techs for MH equipment
2. Obtain:
   • Supplies for wound irrigation and closure
   • Urinary catheter tray
   • Ice packs

Anesthesia Techs
1. Bring:
   • MH cart
   • Defibrillator
   • ISTAT, glucometer
   • Arterial and central line supplies
2. Prepare cold 0.9% NS IVF

IN EVENT OF PVCs, DYSRYTHMIA, OR ARREST ASSUME HYPERKALEMIA

Surgeon
1. Irrigate cavity with cold fluid
2. Stop procedure when appropriate
3. Place urinary catheter
4. Assist with line placement
5. Call ICU to arrange bed

Treatment Goals
1. HD Stability
2. Temp <38°C
3. Prevent Rhabdomyolysis
   • Aggressive IV hydration with 0.9% NS
   • Maintain urine >2ml/kg/hr
4. Correction of Acidosis and Hyperkalemia
   • Hyperventilation
   • NaHCO₃ 1-2 mEq/kg
   • CaCl₂ or Ca Gluconate
   • Insulin 0.1U/kg with D50

RYANODEX
• Each vial contains 250mg
• Dissolve each vial with 5 mL sterile water
• Give 2.5mg/kg IV bolus
• Repeat dose if signs of MH persist (up to 10mg/kg)
  - Ca Channel blockers are contraindicated after administration of Dantrolene!
  - Dantrolene causes potentiation of NMBD

References: www.mhaus.org
MHAUS GUIDELINES

Testing for Malignant Hyperthermia (MH) Susceptibility:

How do I counsel my patients?
Muscle Contracture Testing (CHCT)
CHCT Testing, U.S. and Canada

University of Minnesota
Minneapolis, MN
Paul A. Iaizzo, PhD
(612) 624-7912 or -3959

Uniformed Services University of the Health Sciences
Bethesda, MD
(Military & Civilian)
Sheila M. Muldoon, MD

University of California
Davis, CA
Timothy Tautz, MD

Wake Forest University
Winston-Salem, NC
Joseph R. Tobin, MD

Toronto General Hospital
Toronto, Ontario
Julian Loke, MD, FRCPC
Genetic Testing: RYR1 Gene Sequencing

RYR1: gene structure and mutational spots

NH₂
C35
R614

D2129
R2458

DHP R binding

RH₂
R4214
R4914

Calmodulin binding

Myoplasmic domain

Transmembrane
European MH Group Finds NEW MUTATIONS!
## Malignant Hyperthermia Susceptibility NextGen Sequencing (NGS) Panel

### Test Methods

- **NextGen Sequencing**
- **Deletion/Duplication Testing via Array Comparative Genomic Hybridization**

#### NextGen Sequencing

<table>
<thead>
<tr>
<th>Test Number</th>
<th>Test</th>
<th>Price</th>
<th>CPT Code(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1383</td>
<td>NextGen Sequencing (3 genes)</td>
<td>$1,690</td>
<td>81479 (x2), 81408</td>
</tr>
</tbody>
</table>

In addition, Targeted Familial Mutation testing via Sanger sequencing is available for any gene in the panel:

<table>
<thead>
<tr>
<th>Test Number</th>
<th>Test</th>
<th>Price</th>
<th>CPT Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>100</td>
<td>Targeted Familial Mutations - Single Exon Sequencing</td>
<td>$250</td>
<td>81479</td>
</tr>
<tr>
<td>200</td>
<td>Targeted Familial Mutations - Double Exon Sequencing</td>
<td>$370</td>
<td>81479</td>
</tr>
<tr>
<td>300</td>
<td>Targeted Familial Mutations - Triple Exon Sequencing</td>
<td>$440</td>
<td>81479</td>
</tr>
</tbody>
</table>
Malignant Hyperthermia
“Hot Off the Press”

Ron Litman
litmanr@email.chop.edu