Faces of MH – A Freak Accident Leads to an MH Crisis

Editor’s Note: Each year around this time MHAUS asks for donations to help fund the fight against malignant hyperthermia. Solicitation of charitable donations is just part of the game for non-profits, and for MHAUS in particular, individual donations are an important part of that game plan; for without the generous donations from people like you, MHAUS wouldn’t be able to provide the lifesaving education, products, and services that help protect patients against MH. The following story, as told by Ben’s wife Chelsi Hise, epitomizes the vital importance of the MH Hotline as well as the quick actions of the medical staff. After reading the story, we hope you’ll consider making a year-end charitable donation to MHAUS. And thank you to all of those who have supported the fight against MH.

I heard so many times from everyone who had treated Ben over that week that no one had ever seen an actual case of MH before. This included his nurses, ER doctors, his surgeon, and even his anesthesiologist...the same man whose knowledge of MH and quick diagnosis of the condition saved my husband’s life.

It was Saturday, July 2, 2016, when my husband was trying to repair our roof before a big storm moved in. The rain moved in quicker than expected and he was trapped on our metal roof. He began to slide and somehow ended up cutting his right hand on his pinky and ring fingers.

We rushed to the ER, where he got 20 stitches and was sent home with a follow up at a clinic in Bloomington for Tuesday, July 5.

That Tuesday, we got to Bloomington early that morning and we were turned away from the Orthopedic Clinic we initially went to, as they did not accept our insurance. Through some frantic calls, I was able to get him a consult with an orthopedic doctor.

We met quickly with the doctor, who recommended emergency surgery to repair the hand, as he was losing feeling in his fingers.

He was rushed into what was supposed to be a one to two hour procedure....two hours passed, then three... On nearing the fourth hour, his doctor came out to speak with me.

He explained that the hand surgery had gone extremely well, in fact he is considering it to be one of his most successful surgeries as he was able to repair both severed nerves and both severed tendons and my husband was expected to have a full recovery.

The doctor then went on to explain that about an hour into the surgery, Ben began to have a fever. His anesthesiologist alerted the nurses and requested that they immediately call the Malignant Hyperthermia Hotline when his heart began to race.

The anesthesiologist conferred with the operator on the MH hotline, and quickly began...continued on page 8
In the news ...

Two Exercise-induced Heat-related Deaths Highlight Importance of Recognizing Early Signs of Heatstroke

These unfortunate deaths continue the discussion among MH experts about the relationship between MH and non-anesthetic MH-like illnesses

This past summer brought the news of two unfortunate exercise-induced heat deaths. The first occurred during a Maryland Terrapins college football workout when a 19-year-old offensive lineman collapsed and later died of heatstroke. The second occurred in Ohio when a 50-year-old Cleveland police officer collapsed during a fitness test and later died from multiple system organ failure brought on by rhabdomyolysis.

These two deaths were much discussed by MH hotline consultants, and brought attention to MHAUS’ recommendation related to heat or exercise-induced rhabdomyolysis. (A reading of the full recommendation is found on the MHAUS website under “MHAUS Recommendations”).

The recommendation states, in part, “there is a poorly-defined relationship between MH susceptibility and the development of a non-anesthetic MH-like illness during conditions of heat, exercise, stress, or viral illness. This non-anesthetic-induced MH-like condition may demonstrate many of the same clinical signs as anesthetic-induced MH including hyperthermia, muscle rigidity, rhabdomyolysis, and life-threatening hyperkalemia.”

However, the recommendation continues, “the relationship between MH and non-anesthetic MH-like illnesses has been confirmed by experimental human and animal studies as well as human case reports. Multiple case reports exist of patients with a history of heat- or exercise-induced rhabdomyolysis who subsequently developed MH during exposure to anesthetic triggering agents or tested positive when an MH diagnostic muscle biopsy was performed (CHCT or IVCT) or exhibited a pathogenic mutation in the main gene, the RYR1 gene, that is causal for Malignant Hyperthermia. These non-anesthetic episodes of rhabdomyolysis have ranged from mild symptoms such as persistent cramping during exposure to heat or exercise, to severe muscle breakdown that resulted in clinically significant rhabdomyolysis, or death due to hyperkalemia.”

“Conversely, several case reports exist of patients known to be MH susceptible who subsequently developed a serious or fatal MH-like syndrome during exposure to heat or as a result of intense exercise, or both. It has been estimated that MH-related RYR1 pathogenic variants are found in approximately 20 to 30% of cases of heat- or exercise-induced rhabdomyolysis.”

It is not known if the Maryland college football player or Cleveland police officer were MH-susceptible.

In their conclusion, “the hotline consultants were unable to definitively answer the question of whether the patients who have experienced heat- or exercise-related illnesses should be anesthetized with MH susceptibility precautions. Therefore, the consultants agree that surgical patients with a previous history of a non-anesthesia-related MH-like illness should be considered on a case-by-case basis.”

Further, “the hotline consultants also agreed that there is insufficient evidence to determine the estimated risk of non-anesthetic MH-like illness in patients with suspected or confirmed MH susceptibility and thus requires a confident risk-benefit analysis which is currently not possible. It was agreed that as providers, we must communicate with families, coaches, athletic trainers, and the patient’s physicians to ensure that signs and symptoms of an MH-like event are quickly recognized and treatment is rapidly instituted.”

When it comes to recognizing the signs of heatstroke, interested parties can view a Ted Talk that demonstrates what happens when a person gets heatstroke so that families, coaches, athletic trainers, and the like can take appropriate action to help save a life. Simply visit ed.ted.com and in the search bar type “What happens when you get heat stroke? - Douglas J. Casa”. The video has received over 1 million views.
Meet the New Staff of the North American MH Registry

The North American MH Registry (NAMHR) has a new home at the University of Florida, Department of Anesthesiology, in Gainsville, Florida, and with the new home comes new staff.

**Director – Nikolaus Gravenstein, MD**, currently holds The Jerome H. Modell, MD, Professor of Anesthesiology, and Professor, Department of Neurosurgery, at the University of Florida College of Medicine. Dr. Gravenstein has held numerous other positions at the university since receiving his MD from the University of Florida in 1980.

**Assistant Director – Cameron Smith, MD, PhD**, is Assistant Professor of Anesthesiology, Division of Acute and Perioperative Pain Medicine, Department of Anesthesiology, at the University of Florida. Dr. Smith received his MD from Virginia Commonwealth University School of Medicine, Medical College of Virginia.

**Registry Manager – Amy M. Gunnett, RN, CCRC**, currently holds the positions of Clinical Research Coordinator III, at the University of Florida College of Medicine, Department of Anesthesiology, and Supervised Clinical Provider, Department of Nursing, UF Health Shands Hospital, in Gainsville, Florida. She received her Associate of Science in Nursing from Sante Fe Community College in Gainsville, Florida.

**Data Manager – Patrick Tighe, MD, MS**, is Co-Director, Perioperative Cognitive Anesthesia Network (PeCAN), Department of Anesthesiology, Associate Professor with Tenure, Department of Anesthesiology, and Program Director, Perioperative Analytics Group, Department of Anesthesiology, all at the University of Florida. Dr. Tighe received his MD from the University of Florida, College of Medicine in 2005 and his MS in Clinical and Translational Sciences from the University of Central Florida.

**Data Assistant Manager – Lei Zhang, MS**, currently holds the position of Application Developer Analyst II, Department of Anesthesiology, at the University of Florida. His previous position was Statistical Research Coordinator III. Mr. Zhang received his MS in Statistical Computing, Data Mining Track, from the University of Central Florida.

MHAUS is grateful to this fine staff for maintaining the North American MH Registry of MHAUS. The Registry is essential for continuing research into our understanding of MH. You can contact the Registry by phone at 888-274-7899 or by emailing Registry Manager Amy Gunnett at agunnett@anest.ufl.edu.
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MHAUS President Reports on the Annual European Malignant Hyperthermia Group (EMHG) Meeting

by Henry Rosenberg, MD
President, MHAUS

Each year investigators, clinicians, students and others interested in malignant hyperthermia and related disorders meet to discuss the latest research and clinical advances in the field of MH, usually in a European location. This year the meeting was held in the Northern Italian town of Ferrara, Italy. It was organized and hosted by Drs. Susan Treves, Francesco Zorzato and Vincento Tegazzin, all well-known authorities in the field. Attendees came from many European countries, Canada, Australia, New Zealand, South Africa, Israel and the United States. Dr. Paul Allen, Sheila Riazi, and I represented MHAUS.

There were 29 scientific abstracts, and three plenary sessions covering clinical presentations of MH, the molecular structure of the Ryanodine receptor, genetics of MH, interesting clinical case reports and disorders other than MH associated with genetic changes and pathophysiologic changes that are found in MH. I can only highlight a few of the excellent presentations. In general, many of the presentations focused on the genetics of MH, the relation of MH to heat and exercise and the diagnosis of MH.

Dr. Andrew Marks, Chairman of the Department of Physiology, Center for Molecular Cardiology, Columbia University, NYC, opened the meeting with a detailed description of the molecular structure of the Ryanodine receptor, genetics of MH, interesting clinical case reports and disorders other than MH associated with genetic changes and pathophysiologic changes that are found in MH. I can only highlight a few of the excellent presentations. In general, many of the presentations focused on the genetics of MH, the relation of MH to heat and exercise and the diagnosis of MH.

The list of variants in RYR-1 gene that are causal for MH has been housed on the website of the EMHG. Over 300 variants have been described. A study from New Zealand and Australia described further searches in the literature for changes in the DNA of the gene that has been associated with either MH or other myopathies. There are several efforts under way to catalog all the RYR-1 DNA variants and relate them to clinical findings of MH.

Dr. Carlo Reggiani of the Department of Biomedical Sciences of the University of Padua demonstrated that the intracellular organelle, the mitochondrion, may play a role in the pathogenesis of MH. Inhibition of ROS (reactive oxygen molecules) production by the mitochondria can inhibit and normalize a caffeine-induced uncontrolled rise in intracellular calcium, a key step in the development of hypermetabolism. ROS production has been previously shown to promote calcium release from the sarcoplasmic reticulum by Susan Hamilton’s group.

A study derived from work by Drs. Riazi, Islander, Heytens, Voermans, Treves and Jungbluth showed that of 29 patients (all MH susceptible by contracture test or genetic test) who...
RYANODEX® is formulated for speed and efficiency during the critical challenges presented by malignant hyperthermia (MH).1

- Simple and rapid reconstitution within 10 seconds2
- One-minute administration of a loading dose by 1 provider1,2
- Significantly fewer vials and less IV fluid volume required3,5,6
  - One vial of RYANODEX® provides the same amount of dantrolene sodium as 12.5 vials (13 vials reconstituted) of other formulations

RYANODEX®: Because every minute counts3,4

Choose RYANODEX®:
formulated for rapid reconstitution and administration with fewer vials and less fluid volume.1

Indications
RYANODEX® (dantrolene sodium) for injectable suspension is indicated for the treatment of malignant hyperthermia in conjunction with appropriate supportive measures, and for the prevention of malignant hyperthermia in patients at high risk.

Important Safety Information
RYANODEX® is not a substitute for appropriate supportive measures in the treatment of malignant hyperthermia (MH), including:

- Discontinuing triggering anesthetic agents
- Increasing oxygen
- Managing the metabolic acidosis
- Instituting cooling when necessary
- Administering diuretics to prevent late kidney injury due to myoglobinuria (the amount of mannitol in RYANODEX® is insufficient to maintain diuresis)

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References:

Please see Brief Summary of full Prescribing Information on the adjacent page.

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Woodcliff Lake, NJ
RWA-MH-2016-043 7/2016
RYANODEX® (dantrolene sodium) for injectable suspension, for intravenous use.

Brief Summary of Prescribing Information. See Package Insert. For full Prescribing Information, see Package Insert.

INDICATIONS AND USAGE
RYANODEX® is indicated for the:
• Treatment of malignant hyperthermia in conjunction with appropriate supportive measures (see Warnings and Adverse Reactions).
• Prevention of malignant hyperthermia in patients at high risk.

DOSAGE AND ADMINISTRATION (Selected Information)
In addition to RYANODEX treatment, institute the following supportive measures:
• Discontinue use of malignant hyperthermia (MH) triggering anesthetic agents (i.e., volatile anesthetic gases and suxamethonium).
• Manage the metabolic acidosis.
• Institute cooling when necessary.
• Administer diuretics to prevent left kidney injury due to myoglobinuria (the amount of myoglobin in RYANODEX is insufficient to maintain diuresis).

Administer RYANODEX by intravenous push at a maximum dose of 1 mg/kg. If the physiologic and metabolic abnormalities of MH continue, administer additional boluses up to the maximum cumulative dosage of 10 mg/kg. If the physiologic and metabolic abnormalities require, repeat RYANODEX dosing by intravenous push starting with 1 mg/kg.

DOSAGE for Prevention of Malignant Hyperthermia
The recommended prophylactic dose of RYANODEX is 2.5 mg/kg administered intravenously as a single dose at least 1 minute, starting approximately 75 minutes prior to surgery. Avoid agents that trigger MH.

If surgery is prolonged, administer additional individualized RYANODEX doses during anesthesia and surgery.

DOSAGE for Pediatric Patients
The recommended weight-based dose of RYANODEX for pediatric patients in the treatment and prevention of MH is the same as for adults for these indications (see Dose and Administration).

Reconstitution and Administration Instructions
The suspension must be reconstituted prior to administration:
Reconstitute each vial of RYANODEX lyophilized powder by adding 5 mL of sterile water for injection as indicated agent. (Do not reconstitute with any other solution, e.g., 5% dextrose injection, 0.9% sodium chloride injection).
Shake the vial to ensure an orange-colored uniform suspension. Visually inspect the vial for particulate matter and discoloration prior to administration.

Use the contents of the vial within 6 hours after reconstitution. Store reconstituted suspensions at controlled room temperature (15° to 30°C) or 25°C.

(For complete Dosage and Administration Section, see full Prescribing Information)

CONTRAINDICATIONS
None.

WARNINGS AND PRECAUTIONS
Muscle Weakness
RYANODEX is associated with skeletal muscle weakness. The administration of RYANODEX in human volunteers has been associated with loss of grip strength and weakness in the legs. Patients should not be permitted to ambulate without assistance until they have normal strength and balance.

RYANODEX has been associated with dyspnea, respiratory muscle weakness, and decreased respiratory capacity. Monitor patients for the adequacy of ventilation.

RYANODEX has been associated with dizziness, respiratory muscle weakness, and decreased respiratory capacity. Monitor patients for the adequacy of ventilation.

Table 1: Adverse Events in Healthy Volunteers

<table>
<thead>
<tr>
<th>Number of subjects</th>
<th>RYANODEX</th>
<th>Dantrolene Sodium Comparator</th>
</tr>
</thead>
<tbody>
<tr>
<td>(N=30)</td>
<td>(N=31)</td>
<td>(N=31)</td>
</tr>
<tr>
<td>Headache</td>
<td>1 (3)</td>
<td>4 (13)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>1 (3)</td>
<td>2 (9)</td>
</tr>
<tr>
<td>Diaphoresis</td>
<td>5 (17)</td>
<td>4 (13)</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>4 (13)</td>
<td>4 (13)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>4 (13)</td>
<td>3 (10)</td>
</tr>
</tbody>
</table>

Table 2: Adverse Events in Healthy Volunteers

<table>
<thead>
<tr>
<th>Adverse Events</th>
<th>Number of subjects</th>
<th>RYANODEX</th>
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<tr>
<td>Fatigue</td>
<td>4 (13)</td>
<td>4 (13)</td>
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</tr>
</tbody>
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equal at delivery; neonatal levels then fell approximately 50% per day for 2 days before declining sharply. No fetal respiratory and neuro muscular side effects were observed in this study.

Postmarketing Experience
The following adverse reactions have been identified during postapproval use of another formulation of dantrolene sodium for injection. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Cardiovascular
Adverse reactions associated with RYANODEX include chest pain, palpitations, and hypotension.

Central Nervous System
Adverse reactions associated with RYANODEX include headache, dizziness, tremor, and sedation.

Respiratory
Adverse reactions associated with RYANODEX include respiratory depression and respiratory distress.

OVERDOSAGE
Overdosage Symptoms
Overdosage symptoms include, but are not limited to, muscle weakness and alterations in the state of consciousness (e.g., lethargy, coma), somnolence, dizziness, and hallucinations.

Management of Overdosage
Employ general supportive measures for acute overdosage of RYANODEX.

POTENTIAL COUNSELING INFORMATION
Inform patients, their families, or their caregivers of the following:

Muscle Weakness
Muscle weakness (i.e., decrease in grip strength and weakness of leg muscles, especially walking down stairs) is likely to occur with the use of RYANODEX. Patients should be provided assistance with standing and walking until their strength has returned to normal (see Warnings and Precautions).

Difficult Swallowing
Caution is indicated at meals on the day of administration because difficulty swallowing and choking have occurred with the use of dantrolene sodium products in general. Dysphagia has been reported with the use of RYANODEX (see Warnings and Precautions).

Dizziness and Somnolence
The use of RYANODEX has been associated with dizziness and somnolence. (see Warnings and Precautions).

Driving or Operating Machinery
Symptoms such as “dizziness” may occur. Since some of these symptoms may persist for up to 40 hours, patients must not operate an automobile or engage in other hazardous activities during this time (see Warnings and Precautions).

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treatment for MH with dantrolene.

Ben’s CO2 levels rose, his muscles began to spasm, and his temperature was still high after the treatment and during recovery. His doctor called for emergent transport to the emergency room.

When we arrived, the nurses quickly began to administer dantrolene again, drawing labs, and putting Ben on what we called “the ice man blankie.”

Late on Tuesday evening, Ben was transferred to the ICU because his temperature was still nearly 102°. His nursing staff and doctors were so excellent and optimistic about his condition; I never even had a doubt that he was going to be okay.

Wednesday, July 6, his temperature was down to 99-100°, he was transferred to a step down floor, the Progressive Care Unit. He was monitored closely there for two more days. He had his worst night on July 7th. It was then that his fever spiked again, and he began to develop bronchitis. Again, the hospital reacted quickly and treated him immediately for everything.

The next afternoon, amazingly, he was released!

I heard so many times from everyone who had treated Ben over that week that no one had ever seen an actual case of MH before. This included his nurses, ER doctors, his surgeon, and even his anesthesiologist…the same man whose knowledge of MH and quick diagnosis of the condition saved my husband’s life.

Ben has now begun the healing process from this huge ordeal. He felt very sore and flu like for days after the incident, he said every muscle in his body felt tight and sore. But, he has been able to rest somewhat comfortably and is gaining strength with every passing day.

We have already added MH to all of our children’s medical history as a precaution for any future procedures they may have to have. We’ve warned every member of Ben’s family that it is a possibility that they carry the same genetic precursor. We pray that we, nor anyone else, ever have to go through this. But, if they do, we pray that their doctors are able to diagnose and treat quickly and effectively.
Contribute to an MHAUS fund listed below using quick, easy, and secure credit card transactions. Donations of all sizes and payment plans are welcomed – whether it’s a one-time gift, monthly contribution, part of a matching gifts program, or a planned gift, including appreciated stock or other securities. Visit https://mhaus.site-ym.com/donations/

James Vincent Cox Memorial

General Fund
Your contribution to the General Fund allows MHAUS to direct funds to a broad spectrum of organization support including operations, travel for MHAUS exhibition at professional conferences, and day-to-day office operation that allow for our important mission to be realized.

Honor Your Anesthesia Care Professional
Have you recently gone through surgery and were extremely pleased that your anesthesia professional was there for you? Did their attitude, attention, level of concern for your health and welfare make you feel comfortable during a stressful time? MHAUS offers this program for you to recognize a specific anesthesia professional and express your appreciation!

Ruth (Whitehill) Hrizo Fund

MH Hotline
Support the MH Hotline to dramatically increase the odds of patient survival during an MH crisis. MH Hotline experts provide life-saving advice voluntarily through the MH Hotline, which receives about 1,000 calls worldwide needing medical referral each year, at no cost to the caller.

Geoffrey Warren Keller Fund
Geoffrey Warren Keller, a malignant hyperthermia (MH) susceptible, who passed away on September 9, 2012. Geoff, age 26, will be honored as a loving husband, son, brother, and friend. His family and friends have come together to organize a series of concerts and swim meets to memorialize Geoff, raise awareness about MH, and fundraise to benefit the Malignant Hyperthermia Association of the US (MHAUS) mission to promote the optimum care and scientific understanding of MH and related disorders.

Patricia Belle Sparlin Gronert Memorial Fund

Lila & Jerry Lewis Memorial Fund
Established in 1986 contributions to this fund supports MH research and special projects.

Vincent A. Napolitano Memorial Fund
Contributions to the Napolitano Fund, established in 1990, will support MHAUS efforts for education, reaching a range of healthcare professionals, MH susceptible patients, families, and friends.

Shah Educational Awareness Fund
In honor of Tina Shah, The Shah Educational Awareness Fund was established to alert and educate psychiatric, medical, and nursing professionals who may diagnose and treat patients during Neuroleptic Malignant Syndrome (NMS) episodes, and to increase awareness and ensure patients with NMS are recognized and treated efficiently and effectively.

Solomon and Florence Rosenberg Research Fund
Established in 1995 to support any type of research related to MH or allied syndromes. The research may be laboratory based, clinical or epidemiologic in nature, or may even be research into how to educate people about MH.

Speakman Fund
Mrs. Speakman’s story: “My husband, Cliff, was only 56 years old when he died from Neuroleptic Malignant Syndrome (NMS). An otherwise healthy man, Cliff had never suffered from a major illness, never undergone major surgery nor had he ever been hospitalized. Cliff’s story is a tragic one, but it is helpful for me to share it with others in order to create awareness of this rare condition.”

Smart Strategies for Year-End Charitable Giving
The Tax Cuts and Jobs Act signed into law last year has raised the bar on charitable giving when it comes to tax-deduction benefits. That’s because the standard deduction has increased to $12,000 for single filers and $24,000 for married couples, which essentially limits the financial incentive of charitable deductions; indeed, according to a new congressional report, 60% fewer households will itemize this year. However, there remain smart financial strategies of which donors can still take advantage.

One strategy reported on the CNBC business news website is “bunching,” wherein you give a greater amount every other year; in other words, instead of giving $5,000 every year, you give $10,000 every other year. This way, you could potentially itemize one year and then take the standard deduction the next, yet you’re still giving the same amount to your favorite charity.

Another strategy for retirees, 70-1/2 or older, reported in an article for Morningstar Investment Research, is to transfer money from an IRA to a qualified charity in order to meet required minimum distributions (and you may not need to itemize your deductions to benefit). Of course, you only do this if you don’t need the money.

A third option reported in Forbes magazine is to establish a “donor advised fund,” wherein you make an initial large contribution and then make smaller distributions to your favorite charities.

Each of these strategies is unique to each individual, and so you should discuss your personal financial situation with your investment advisor and tax professional before making any decisions.
Do We Need Dantrolene and MH Carts on Maternity Units?
An MH Hotline Consultant Responds to a Study in Anesthesiology

Dr. Cynthia Wong, an MH Hotline Consultant with the Malignant Hyperthermia Association of the United States, has penned an editorial response to a study appearing in the August 2018 issue of Anesthesiology (vol. 129, no. 2). In the study, the authors conduct a cost-benefit analysis of maintaining a fully stocked MH cart versus an initial dantrolene treatment dose for maternity units.

The authors conclude “it is not of cost benefit to maintain a fully stocked malignant hyperthermia cart with a full supply of dantrolene within 10 minutes of maternity units. We recommend that hospitals institute alternative strategies (e.g., maintain a small supply of dantrolene on the maternity unit for starting treatment).” MHAUS recommends that dantrolene be available for administration within ten minutes.

In her response, Dr. Wong takes issue with some of the assumptions used by the authors. To begin, she suggests the authors “did not consider several factors that may play an important role in the cost-effectiveness analysis, particularly their conclusion that the newer, concentrated formulation of dantrolene is not cost effective.”

Furthermore, she states, “another important aspect of the authors’ calculation is the assumption that dantrolene and the other supplies and drugs necessary to treat an MH crisis can be delivered to the maternity unit in a timely manner when needed in a crisis.”

Dr. Wong continues, “An additional complication of the authors’ proposal (storing 13 vials of the older formulation of dantrolene as a starter dose on the unit) is the storage of sterile water. The Malignant Hyperthermia Association of the United States recommends storing 100-ml vials of water in the MH cart to reconstitute the older formulation. Bags of sterile water are not recommended because they may be mistaken for intravenous fluid bags.”

In her summary, Dr. Wong notes, “The exercise of calculating the cost benefit of specific therapies is critical to wise allocation of our limited resources.” She also agrees “that the strategy of stocking dantrolene and an MH cart in every anesthetizing location in which triggering anesthetic agents are administered, no matter the frequency of use of these drugs, should be reconsidered.”

However, Dr. Wong suggests the issue requires further analysis. In her response, she writes, “The analysis should not only take the rate of general anesthesia into account, but should also consider training costs.”

She continues, “It may indeed make more sense to annually train obstetric team members to obtain the MH cart from a central location. However, the details of how the dantrolene and other MH cart supplies will be transported to the maternity unit are critical to the decision making.”

You will find both the study, “Cost-benefit Analysis of Maintaining a Fully Stocked Malignant Hyperthermia Cart versus an Initial Dantrolene Treatment Dose for Maternity Units” and Dr. Wong’s editorial response “Dantrolene and Malignant Hyperthermia Carts: Do We Need Them on Maternity Units?” in the August 2018 issue of Anesthesiology.

continued from page 5

developed an MH episode, or a history of intense exercise or signs of infection were frequently noted in the 72 hours preceding the surgery. This finding may indicate that environmental factors, particularly exercise, may “prime” the genetically predisposed muscle to the onset of MH. They suggested adding a question about exercise in the 3 days prior to surgery as possible indicator of increased risk of MH.

Another study from Holland, Belgium and the UK drew attention to histologic changes typically found in muscle disorders such as central core disease to similar changes in muscle from MH susceptibles and to those who developed non-anesthetic rhabdomyolysis (muscle breakdown). This points to a connection between clinical alterations (e.g., rhabdomyolysis) in muscle from patients with certain muscle disorders and those with MH susceptibility. The diagnostic test for MH susceptibility commonly used in Japan is the calcium-induced calcium release test in single fibers (CICR). Dissecting single fibers (a single cell) from a block of muscle is technically challenging, but offers the possibility of testing multiple fibers for MH susceptibility from a single patient’s biopsy. The study presented by Dr. Carlos Ibarra Moreno compared the single fiber test with the caffeine-halothane contracture test, but found only slight agreement between the tests. He provided reasons for the discrepancy.

Dr. Feliciano Protasi from Chieti, Italy reviewed the common features on a cellular level, between environmental/exertional heat stroke and MH. He concluded that “the mechanisms underlying hyperthermic episodes triggered by anesthetics and by heat and exertion are virtually identical....,” suggesting that treatment of one condition might be effective in the treatment of the other. Two studies of a mouse model for MH, whereby a gene that predisposes to MH is incorporated into the genetic makeup of a non-MH susceptible mouse, showed that the animals develop signs of MH with exposure to halothane and that the muscle displays an elevated sensitivity to caffeine, halothane and potassium induced depolarization.

The EMHG meeting demonstrates the world-wide interest in MH and related disorders; it highlights many of the unanswered questions and the often novel approaches to diagnose MH and counsel patients and their family. The next EMHG meeting will occur on May 16-18, 2019 in Potsdam, Germany.
NEW MHAUS Recommendation: Masseter Muscle Rigidity (MMR): Definition, Relationship to Malignant Hyperthermia (MH), and Management

Background: MMR can be generally defined as a marked difficulty in manual mouth opening that interferes with and impedes direct laryngoscopy and tracheal intubation without the presence of temporomandibular joint dysfunction. When MMR occurs in response to administration of succinylcholine in the absence of an underlying temporomandibular joint disorder or myotonia, it may be an initial sign of MH [1-4]. As early as 1969, Gibson et al reported two cases where they described the severe nature of the rigidity of masseter muscles when MMR occurs [5, 6].

Discussion: Confusion often arises when diagnosing MMR due to its similarity with the normal but variable degree of increase in masseter muscle tension that may occur after succinylcholine administration in healthy patients [6-8]. This is an inherent characteristic of succinylcholine administration and has also been linked to administration of subclinical doses in children [9-10]. To differentiate between the normal rises in masseter tension versus a case of true MMR, assessing masseter rigidity is helpful. The term 'jaws of steel' (coined by Kaplan et al [11]) aptly emphasizes the severe nature of the rigidity. When MMR occurs, it may be both a harbinger of acute MH and/or associated with clinically significant rhabdomyolysis [11, 12, 13]. Therefore, clinicians should seek other concomitant signs of the presence of acute MH, such as tachycardia or hypercarbia that are inappropriate for the clinical situation, generalized trunk or limb rigidity, hyperthermia, cola-colored urine indicative of myoglobinuria, and/or peaked T waves or other arrhythmias consistent with hyperkalemia. However, in some patients who have subsequently progressed to MH, those signs did not appear immediately after MMR appearance. Sufficient evidence exists in the literature of cases in which MH ensued following MMR that it is prudent to cancel elective surgery when MMR occurs [11-14]. If the surgical procedure is emergent, then a non-MMH triggering anesthetic should be instituted. Whether or not the case is cancelled, several hours of careful observation for additional signs of MH are warranted. This approach of employing non-triggering anesthetic in emergency cases, was first reported in a definitive fashion by Donlon et al in 1978 [14] and later by others [15, 16]. The anesthesia provider should obtain a blood sample to screen for metabolic acidosis, hyperkalemia, and elevated creatine kinase levels. A urine sample should also be obtained to check for heme, which, if positive without microscopic red blood cells, may represent either myoglobinuria or hemoglobinuria. Serum creatine kinase measurements (CK) should follow immediately after and at 6-8 hours. CK may not be elevated immediately following MMR with peak levels not achieved until 12 to 24 hours following succinylcholine administration [17]. If CK is greater than 5 times the upper limit for normal value, then appropriate treatment for rhabdomyolysis, including measures to prevent acute damage to the kidneys from myoglobinuria should be instituted [18]. While cola-colored urine and elevated creatine kinase may occur following MMR, development of any other additional signs of MH should prompt immediate dantrolene administration and other adjunctive therapies [1]. In patients who have myotonia, administration of succinylcholine may result in MMR and rigidity of the total body [19, 20]. Prior history of myotonia is the most helpful factor in differentiating between MMR and myotonic contractures

Conclusions: MMR may be the first sign of an acute MH event. However, no conclusive data exist for clinicians to determine the likelihood of developing MH after an episode of MMR. If no other signs of MH are observed, the patient may still be at risk for developing clinically significant rhabdomyolysis and should be observed and treated as necessary. Patients who develop rhabdomyolysis without other signs of MH should be referred to a neurologist to rule out underlying myopathies. If no myopathies are found, evaluation for MH susceptibility may be indicated (https://www.mhaus.org/testing/introduction-to-mmh-testing/). When an anesthetic is necessary in patients who experienced MMR during a previous anesthetic but have not had a full evaluation for MHS or myopathy, such patients should receive a non-triggering anesthetic for their procedure. Caveat: No MH or neurologic workup is indicated if no postoperative rhabdomyolysis or signs of MH occur and the patient informs the anesthesiologist that he/she has a history of temporomandibular joint disorder and/or his/her post-anesthetic examination reveals an inability to open the mouth well.

References:
MHAUS Happenings, Events and Notices

THANKS! MHAUS thanks the following State Society of Anesthesiology – New Jersey, Ohio, and Wisconsin – for their financial support. Our appreciation also goes out to the Association of Nurse Anesthetists, Illinois. Call the MHAUS office to ask Gloria how your group can join their ranks.

MHAUS Welcomes Five New PAC Members
MHAUS is pleased to announce the addition of four new members to the Professional Advisory Council (PAC). They are Thierry Girard, Department of Anesthesia Intensive Care Medicine, University Hospital, Basel, Switzerland; Harvey Rosenbaum, UCLA Medical Center, Los Angeles, CA; Henrik Rueffert, Helios Klinik Scheuditz, Department of Anesthesiology, Intensive Care Medicine, Pain Therapy, Germany; Charlie Watson, MD, Easton, CT; and Stacey Watt, MD, University of Buffalo. The members of PAC are medical professionals throughout the world who are experts in Malignant Hyperthermia and together approve and generate all content published by MHAUS. There are 18 members on the Professional Advisory Council, and MHAUS is grateful for their exemplary work.

Hotline Consultant Jerome Parness Announces Retirement
Dr. Jerome Parness retired from the University of Pittsburgh School of Medicine effective June 30, 2018. As well, he announced that he will step back from frontline duties related to the MH Hotline. He said that serving on the Hotline, doing research on the mechanism of action of dantrolene, and generally being involved in Malignant Hyperthermia issues have been some of the highlights of his professional and personal life. MHAUS thanks Dr. Parness for his tireless work in combating MH and wishes him well as he embarks on a new phase of his life.

New MHS Patient Discussion Webinar Now Available Online
Watch the discussion with MH susceptible individuals and MH experts. MH susceptible patient, Cheryl Mercer and two MH experts, Drs. Joe Tobin and Stacey Watt address your “burning” MH questions. The webinar was held July 11, 2018. Watch now.

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