As the New Year approaches, MHAUS wants to take this opportunity to recognize a few of the *Faces of MH* while encouraging our members to find ways to make a difference in their community by building awareness of malignant hyperthermia and helping to fund MH research and education.

Throughout these pages you’ll discover the real life stories of MH survivors and their families. Most of these stories have happy endings, such as that of 8-month-old Maverick; tragedy, unfortunately, shades others. But that’s the reality of MH, and for all the accomplishments in fighting MH – and there have been many – there still remains much to do.

This is the time of year when MHAUS reaches out to our members asking for your generous financial donations – and this year is no different. You’ll find on page 5 a long list of charitable funds to which you can direct your dollars to support specific causes, such as educational and research programs, or the MH Hotline.

You’ll also learn how you can donate to MHAUS (at no additional cost to you) when you do your holiday shopping through AmazonSmile.

But MHAUS wants you to know that as much as we appreciate your financial donations, there are other donations – donations of time and energy – that mean just as much, if not more. On page 4 you’ll learn how you can further MH research by submitting your MH test results to the North American MH Registry (NAMHR) of MHAUS, and on page 8 you’ll discover how MHAUS makes it easy for you to host an event in your community – and you’ll find photos of a recent event held in MHAUS’ hometown of Sherburne, NY. From financial donations to donations of time and energy to the simple act of writing a letter (see page 9) – all of these acts can make a difference, for even a single letter could save a life.

On page 10, a 20-year member of the MHAUS Board of Directors reflects on the many successes over the years, successes for which we should be thankful, but his story contrasts with that of another board member whose personal tragedy brought him to MHAUS. It goes to show there remains much to learn (such as the possible relationship of non-surgical awake triggers to MH).

You can begin on page 2 where MHAUS Executive Director Dianne Daugherty outlines how and where money is spent. Then ask yourself how you might make a difference in your community. What passions do you have that might meld with a fundraiser? Contact the NAMHR of MHAUS about submitting your MH test results. Visit the MHAUS web site to learn about forming your own MH Chapter Group. Download sample letters that you can mail to family, medical professionals, educators, and insurance companies. And if you want to make a financial donation, we’ll accept that, too.

**On the inside**

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Malignant Hyperthermia (MH) is an inherited muscle disorder which, when triggered by potent inhalation anesthetics and succinylcholine, may cause a life-threatening crisis. The incidence of MH is low, but, if untreated, the mortality rate is high. Since the advent of the antidote drug, dantrolene sodium, and with greater awareness of the syndrome, the mortality rate has decreased. Great advances in our understanding of MH have been made since it was first recognized in the early 1960s, but the nature of the fundamental defect(s) is still unknown.

MHAUS advocates that all surgical patients undergoing general anesthesia should receive continuous temperature monitoring, that adequate supplies of dantrolene be stock near the OR and that monitoring, that adequate supplies of dantrolene sodium be stocked near the OR and that monitoring, that adequate supplies of dantrolene sodium be stocked near the OR and that monitoring, that adequate supplies of dantrolene sodium be stocked near the OR and that monitoring, that adequate supplies of dantrolene sodium be stocked near the OR and that monitoring, that adequate supplies of dantrolene sodium be stocked near the OR and that monitoring, that adequate supplies of dantrolene sodium be stocked near the OR and that monitoring, that adequate supplies of dantrolene sodium be stocked near the OR and that monitoring, that adequate supplies of dantrolene sodium be stocked near the OR and that monitoring, that adequate supplies of dantrolene sodium be stocked near the OR and that monitoring, that adequate supplies of dantrolene sodium be stocked near the OR and that monitoring, that adequate supplies of dantrolene sodium be stocked near the OR.

MHAUS members help us in our mission to save lives from malignant hyperthermia in many ways: when you purchase our products, your purchase not only equals nearly 26% of the MHAUS revenue needed to function, but also assists in MH preparedness efforts to increase patient safety level; your additional donations equal about 8% of our total revenue – if you could find it in your heart to increase your yearly donation slightly, it would allow us to make an even bigger difference; the income from your membership dollars is about 7.5% of our revenue – if each of you could encourage just one more person of the benefits of being a member of MHAUS, imagine the positive impact on this percentage and the positive ripple effect that will be felt; more members equals more purchases of products (at a 30% discount, of course) and results in another facility successfully prepared to address an unforeseen MH event and bring their patient to a safe and positive outcome.

As members of MHAUS, your ongoing support allows us to provide you this newsletter on a quarterly basis to keep you abreast of recent changes and pertinent information that will assist you, whether you are a healthcare professional or an individual who is MH-susceptible, or a family member of someone who is affected by malignant hyperthermia. In addition, we act as a "watchdog" for you in the MH world, notifying you of new information as we become aware of it so that you have the most up-to-date specific resources available to make informed choices in your personal or work life. Add to that the timesaving products we develop, design and produce for your use so that you don’t have to take your own precious time to do so. The MH Mock Drill Kit, CPK, Operating Room Protocol Poster, MH Procedure Manuals for all types of facilities are all designed to give you the tools you need, and they are reviewed by MH experts so you can be certain of correct content. The MH Prep Check, our newest program, allows you direct access to an MH expert “to visit your facility” in order to assure you have

continued on page 2
the tools and plan of action appropriately designed for an MH event. This accessibility is made available to you through MHAUS’ internal efforts and the willingness of the MH Hotline Consultants to travel to share their MH expertise with their peers. Taking advantage of a Prep Check will assure your MH plan is ready for the next Regulatory visit.

We are focused on our MHAUS web site at www.mhaus.org to provide quick access to answers to your questions and we have enhanced our social media efforts to regularly share MH education broadly. Many of you have probably accessed the site for quick references and found it helpful; we plan to add to its resource value by sharing the newest products or programs we are aware of (or have developed ourselves internally) on the home page via a rolling display. You will soon see products that could prove helpful to your MH readiness efforts or offer alternatives to what you are using now.

Plans are underway to also provide short informative video clips and webinars designed to answer the frequent questions we are asked here in the office and through our online contact forms. As a member of MHAUS, you will have either free or reduced cost access to the webinars that will require payment to view, with the possibility of CME or CEU credits attached to them.

A Knowledge Bank of frequently asked questions and their answers is being added to the site to more quickly respond and offer additional resources when a question is typed in the search box at the top of the page. We want you to find what you need as quickly as possible and still give you other possibilities for further resources in your research efforts.

Though our focus is on providing MH education through a multitude of sources, the oversight of expenses to do so is watched very closely to assure every dollar is spent as wisely as possible. The Board of Directors oversees the financial picture and is highly involved in the decisions made as to which products and/or programs best fit the mission of MHAUS and provide the most relevant resources to our members and all others needing any type of assistance with MH readiness plans.

The result is solid cost containment. For instance, we focus about 11.5% of the budget on programs made available to customers of all types and about 6% for production of products. We allocate a little over 2.5% of the budget to cover the cost of attending meetings where we know our resources for MH preparedness are sought. We do this by carefully monitoring travel costs and/or limiting the number of meetings we attend. Sometimes we exhibit every other year. In this way, we are still sharing the information directly and answering MH questions at the exhibit booth to the best of our ability, but we are very focused in our choices on where to go to meet the largest need.

In the end, the work you are doing must be rewarding in whatever way is important to you. We are there, and will remain, to lend a helping hand wherever possible, so that we can help you save lives from the devastation of MH – THAT IS OUR GOAL FROM OUR WORK WORTH DOING.

I hope you will find membership and support of MHAUS a worthy recipient in the coming year. Best wishes for a wonderful fall season.

Maverick’s Story

On April 6, 2016, my 8-month-old son underwent a urological procedure. The doctors were done with the surgery and were applying the dressings when they noticed that Maverick’s CO2 levels had gone up. My son’s temperature had dramatically increased and he had a heart rate of 200.

The doctors, nurses, and staff caught the MH crisis very early on and acted on it quickly. The hospital was very well prepared and took exceptional care of our baby. During his recovery time, we received a ton of information on MH and were referred to MHAUS. We, along with friends and family, had no prior knowledge of MH and were in total shock when our son had this reaction.

Now we are in the process of working with genetics to get ourselves tested to find out who carried the gene. This was a very scary and unexpected situation. We want to help spread awareness about MH. We are hoping that in the near future that testing for MH becomes more available and easier to conduct.

Today, Maverick Domingo Longoria is full of life and continues to grow, learn, and amaze us! His strength is beyond words. We love him so much!

– Valerie M. Longoria, Maverick’s mother
Cheryl Mercer shows off her MH Research Pig. Visit the MHAUS web site and help feed the MH Research Pig by ordering your MH Research Piggy Bank.

Cheryl’s Story –

In 1986, I underwent emergency surgery for an appendectomy. I was living in Iowa City at the time, finishing up college and my parents and fiancé lived about two hours away in Illinois. I recall telling someone at the hospital that my father had experienced a problem with anesthesia years ago when having a fishbone removed from his throat. I didn’t really know any more details than that.

My parents told me they would head to Iowa City and see me after the surgery. (I appreciated a nun coming to my room and saying a prayer for my safe recovery.) The next thing I knew I was waking up, unable to speak because I had a tube down my throat. I was confused regarding what was happening and wrote on my mom’s hand, “Am I going to die?”

The doctor came in and explained that I had an episode of malignant hyperthermia. I spent the night in ICU and was discharged four days later. At the time, I did not feel any residual effects of what had happened. My medical records indicated that just 10 minutes into the surgery, the surgeon recognized that my skin was cyanotic and becoming rigid. My temperature escalated to over 106 rapidly, and my CK levels were described as “astronomical.” Fortunately, the anesthesiologist recognized the signs of MH and reacted immediately.

My father sought information about MH and came across MHAUS. He and I attended our first conference in Minneapolis many years ago trying to connect with others who might know about this rare disorder. Thinking that my father was the carrier of the MH, my brother had a muscle biopsy with positive results. My father died in 2000 so we were never able to get genetic testing done on him.

Other family members and I were all tested and it turned out that I have two mutations, my sister has one, and my son has one. Just this year, we decided we should test my mother to determine if, in fact, I may have received a gene from both of my parents. It turns out that my mother has one known variant for MH, one of the mutations that I have but not the one my sister and son have. Consequently, we would conclude that my father had the mutation that my sister, son, and I have. My brother has not yet had the genetic testing.

I have experienced “Awake symptoms” over the years but they have become more frequent and severe in recent years. Moderate exercise has resulted in elevated CK levels as high as 10,000. Muscle cramping and twitching are frequent, and I take Dantrolene as needed.

The wonderful people associated with MHAUS, particularly Dr. Barbara Brandom, Dr. Sheila Muldoon, and Dr. Mary Theroux, have been a great resource and support network for my family and me. I encourage support for MHAUS and the work they do!

— As told by Cheryl Mercer

Help Further MH Research by Submitting Your MH Test Results

Take part in MH research by submitting your MH test results to the North American Malignant Hyperthermia Registry, the research arm of MHAUS.

Our NAMHR of MHAUS is a member of the Global Rare Diseases Patient Registry Data Repository (GRDR) program. Our de-identified data integration into GRDR will allow query by investigators to accelerate research across all rare diseases and to develop novel diagnostics and therapeutics for patient benefit.

The Registry’s goal is to acquire, analyze, and disseminate case-specific clinical and laboratory information related to malignant hyperthermia susceptibility. Registry functions are consistent with HIPAA, OHRP, and IRB regulations. Registry data can be used to conduct research into the epidemiology, diagnosis, clinical course, and treatment of MH. Each potential study must have IRB approval from its parent institution, and approval from our Scientific Advisory Committee.

Objectives of the Registry are to:
• Maintain a central database of individuals with MH susceptibility and similar syndromes. (With the person’s consent, specific identifiers are included in the Registry. Otherwise, only de-identified data is entered.)
  • Provide information storage and analysis services to MH diagnostic referral centers for standardization and validation of MH diagnostic testing procedures, including genetic tests.
  • Investigate the epidemiology of MH in order to improve diagnosis, treatment, and prevention of MH episodes.
  • Give a registered person the security of knowing that there is a central repository of information concerning their MH susceptibility status.
Think MHAUS for Year-End Charitable Giving

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
Remembering Ruth Hrizo.

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.”

Do Your Holiday Shopping on AmazonSmile To Support MHAUS

AmazonSmile is a simple and automatic way for you to support MHAUS every time you shop, at no cost to you!

When you shop at smile.amazon.com, you’ll find the exact same low prices, vast selection and convenient shopping experience as Amazon.com, with the added bonus that Amazon will donate 0.5% of the purchase price to MHAUS.

To shop at AmazonSmile simply go to smile.amazon.com from the web browser on your computer or mobile device and set up your Amazon-Smile account. You may also want to add a bookmark to AmazonSmile to make it even easier to return and start your shopping at AmazonSmile.

Tens of millions of products on AmazonSmile are eligible for donations. You will see eligible products marked “Eligible for AmazonSmile donation” on their product detail pages. And yes, you can use the same account on Amazon.com and AmazonSmile. Your shopping cart, Wish List, wedding or baby registry, and other account settings are also the same.
RYANODEX® is formulated for speed and efficiency during the critical challenges presented by malignant hyperthermia (MH)⁴:

- Simple and rapid reconstitution within 10 seconds²
- One-minute administration of a loading dose by 1 provider¹²
- Significantly fewer vials and less IV fluid volume required¹⁵₆
  - 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 counts³⁴**

Learn more at Ryanodex.com or call 855.318.2170

**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)

RYANODEX® (dantrolene sodium) for injectable suspension, for intravenous use.

Brief Summary of Prescribing Information. See Package Insert

For Full Prescribing Information

INDICATIONS AND USAGE
RYANODEX® is indicated for the:

• Treatment of malignant hyperthermia in conjunction with appropriate supportive measures (see Warnings and Precautions)

• Prevention of malignant hyperthermia in patients at high risk.

DOSAGE AND ADMINISTRATION

In addition to RYANODEX treatment, institute the following supportive measures:

• Discontinue use of malignant hyperthermia (MH)-triggering anesthetic agents (i.e., volatile anesthetics and succinylcholine).

• Manage the metabolic acidosis.

• Institute cooling when necessary.

• Administer dextrose to prevent late kidney injury due to myoglobinuria (the amount of myoglobin in RYANODEX is insufficient to maintain diuresis).

Administer RYANODEX by intravenous push at a minimum dose of 1 mg/kg. If the physiologic and metabolic abnormalities of MH continue, administer a maintenance infusion of up to the maximum cumulative dosage of 10 mg/kg. If the physiologic and metabolic abnormalities require it, 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 period of 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 Dosage and Administration).

Reconstitution and Administration Instructions

The suspension is reconstituted with injection water and must be reconstituted prior to administration.

Reconstitute each vial of RYANODEX lyophilized powder by adding 5 mL of sterile water for injection. 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.

Must use the contents of the vial within 6 hours after reconstitution. Store reconstituted suspensions at controlled room temperature (15°-30°C; 59°-86°F).

(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 to 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 dysphoria. Assess patients for difficulty swallowing and drooling.

Somnolence and Dizziness

Somnolence and dizziness can occur following administration of RYANODEX and may persist up to 48-hour post-dose. Patients should not be permitted to ambulate without assistance until they have normal strength and balance. Patients must not operate an automobile or engage in other hazardous activities for 48-hour post-dose.

The concomitant use of sedative agents with RYANODEX may increase the risk of somnolence and dizziness.

Potential for Tissue Necrosis with Extravasation

Care must be taken to prevent extravasation of RYANODEX into the surrounding tissues due to its high pH. Immediate treatment is necessary if extravasation occurs. See Warnings and Precautions for potential for tissue necrosis.

ADVERSE REACTIONS

Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

In a study designed to evaluate the safety and tolerability of RYANODEX, healthy volunteers were randomly assigned to receive treatment with RYANODEX or an active comparator at doses ranging from 1 to 2.5 mg/kg. The RYANODEX dose was infused over the course of 1 minute for each of the doses evaluated.

The active comparator was an ineffectual formulation of dantrolene sodium that differed from RYANODEX in that it contained dantrolene sodium and mannitol instead of dantrolene sodium and mannitol at concentrations of 0.33 mg/mL and 50 mg/mL, respectively. When reconstituted for the patient’s prescribing information. The active comparator was infused at a rate that administered 20 mg of dantrolene per minute for each of the doses evaluated.

Table 1 displays the most common adverse events in this study. These data are not an adequate basis for comparison of the types or frequency of adverse events types between RYANODEX and the dantrolene sodium comparator.

Adverse events increased in frequency with increasing doses in the trial, but did not differ in frequency between the two treatment groups. RYANODEX-treated subjects were more likely to report immediate adverse events of flushing, dizziness, and drowsiness than those receiving the active comparator.

In all dose groups, hand grip strength declined after dosing. In general, the decline in hand grip strength was more pronounced and occurred more rapidly RYANODEX-treated subjects in the 1.0, 1.75, 2.0 and 2.5 mg/kg treatment groups. In the 2.5 mg/kg treatment group, the decline in hand grip strength was in amount and was similar between the two treatment groups.

Table 1: Adverse Events in Healthy Volunteers

<table>
<thead>
<tr>
<th>Event</th>
<th>RYANODEX (n=60)</th>
<th>Dantrolene Sodium Comparator (n=31)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache</td>
<td>1 (3)</td>
<td>4 (13)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>1 (3)</td>
<td>2 (6)</td>
</tr>
<tr>
<td>Vision blurred</td>
<td>1 (3)</td>
<td>1 (3)</td>
</tr>
<tr>
<td>Pain in extremity</td>
<td>1 (3)</td>
<td>1 (3)</td>
</tr>
<tr>
<td>Muscular Weakness/</td>
<td>1 (3)</td>
<td>1 (3)</td>
</tr>
<tr>
<td>Asthenia</td>
<td>Restless</td>
<td>1 (3)</td>
</tr>
<tr>
<td>Black</td>
<td>Tachycardia</td>
<td>1 (3)</td>
</tr>
<tr>
<td>Infusion site pain</td>
<td>1 (3)</td>
<td>0</td>
</tr>
<tr>
<td>Headache</td>
<td>1 (3)</td>
<td></td>
</tr>
</tbody>
</table>

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.

Pulmonary Edema

There have been reports of pulmonary edema developing in randomized patients with malignant hyperthermia crises with another dantrolene sodium form. The contributory effect of the diluent volume and mannitol in these cases is not known.

Thrombocytopenia and Thrombocytosis

There have been reports of thrombocytopenia following administration of intravenous dantrolene sodium. Tissue necrosis following extravasation to have been reported (see Warnings and Precautions).

Dysfunction/Sympathetic Reactivation

There have been reports of urticaria and erythema possibly associated with the administration of dantrolene sodium for injection. Anaphylaxis has been reported.

Injection Site Reactions

Injection site reactions including pain, erythema, and swelling, commonly due to extravasation, have been reported.

DRUG INTERACTIONS

Calcium Channel Blockers

Cardiovascular collapse in association with malignant hyperthermia has been reported in patients receiving dantrolene in combination with calcium channel blockers. The concomitant use of RYANODEX and calcium channel blockers is not recommended during the treatment of malignant hyperthermia.

Muscle Relaxants

The concomitant administration of RYANODEX with muscle relaxants may potentiate the musculonervous block.

Antipsychotics and Antianxiety Agents

The concomitant administration of RYANODEX with antipsychotic and antianxiety agents may potentiate their effects on the central nervous system (see Warnings and Precautions).

USE IN SPECIFIC POPULATIONS

Pregnancy

Category C

Adequate and well controlled studies have not been conducted with RYANODEX in pregnant women. However, animal reproduction studies have been conducted with dantrolene sodium. In these studies, dantrolene sodium administered to rats and rabbits produced embryotoxicity (rabbits) and decreased pup survival (rats) at doses seven times the human oral dose. RYANODEX should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Labor and Delivery

In one uncontrolled study, 100 mg per day of prophylactic oral dantrolene sodium was administered to term pregnant patients. No labor and delivery complications were noted. Dantrolene readily crosses the placenta, with maternal and fetal blood levels approximately equal at delivery; neonatal levels then fell approximately 50% per day for 2 days before declining sharply. No fetal respiratory and neuromuscular side effects were observed in this study.

Nursing Mothers

Dantrolene is present in human milk. In one case report, low dantrolene concentrations (less than 2 micrograms per milliliter) were measured in the breast milk of a lactating woman during repeat intravenous dantrolene administration over 3 days. Because of the potential for serious adverse reactions of respiratory depression and muscle weakness in nursing infants from dantrolene, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Pediatric Use

The safety and efficacy of RYANODEX in the treatment and prevention of malignant hyperthermia in pediatric patients has not been determined. RYANODEX is based on clinical experience with other intravenous dantrolene sodium products, which suggests adult weight-based doses are appropriate for pediatric patients.

Geriatric Use

Clinical studies of RYANODEX did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experiences have not identified differences in responses in these elderly and younger patients. In general, dose selection in an elderly patient should be cautious, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

OVERDOSAGE

Overdosage Symptoms

Overdosage symptoms are limited but are not limited to, muscular weakness and alterations in the state of consciousness (e.g., lethargy, coma), vomiting, diarrhea, and crystalluria.

Management of Overdose

Employ general supportive measures for acute overdose of RYANODEX.

PATIENT 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 returned to normal (see Warnings and Precautions).

• Difficulty Swallowing

Difficulty swallowing 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). Dysphonia and Somnolence

Dysphonia and Somnolence

Dysphonia 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 activity during this time (see Warnings and Precautions).

Revised: 7/2014

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Woodside, La Jolla, CA 92077

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Woodside, La Jolla, CA 92077 7/2016
Ruth Ann’s Story

Twenty-eight years ago in June, my 7-year-old son went in to have surgery for his tonsils – routine surgery that his sister had a few months before. Our small town hospital was going through bankruptcy but the anesthesiologist refused to do the surgery without dantrolene…even though, at the time, we had no knowledge of MH running in our family.

Praise the Lord! Our son was life-flighted out due to an MH crisis during the surgery. After the MH episode, it was suggested that my family be tested for MH. My son’s father also has MH. My son and his family now wear medic alert bracelets. If that anesthesiologist hadn’t made sure he was prepared, who knows what would have happened. Knowledge is power.

– As told by Ruth Ann Bruce

MHAUS Helps Make Hosting Your Own MH Event Easy

MHAUS members have been instrumental in building MH awareness through a variety of community events, including benefit concerts, athletic competitions, such as the annual Geoff Keller Memorial Swim, and other recreational opportunities, such as the recent Memorial Motorcycle Ride held in MHAUS’ hometown of Sherburne, NY. (See photos below). MHAUS is proud to have the support of so many people in local communities who donate their time, talents and resources to help build awareness about MH through events such as those noted, as well as those conferences like the one day MH Mini-Conference and MH Scientific Conferences. These events raise funds to help support the MH Hotline, outreach, and research.

Hosting your own event is easy. If you are interested in planning to co-host an event, MHAUS has staff champions to help you every step of the way. For more information contact Fay at: 607-674-7901 or by email at: Fay@mhaus.org

Do you have an MH Survival Story? Tell us about it. Visit the MHAUS web site at www.mhaus.org and click on “Faces of MH” under the “Get Involved” tab.

Kickstands Up at MH Memorial Motorcycle Ride

The weather was perfect for the MH Memorial Motorcycle Ride held on August 13 in MHAUS’ hometown of Sherburne, NY. With the generous support of sponsors, donors, and all participants, MHAUS raised nearly $900. This money will be directed toward MHAUS’ Education Fund to continue work educating the healthcare community about early recognition of MH to help prevent unnecessary deaths. MHAUS can help you host events of all kinds in your community. See article above for details.
In 2008 my brother, Warren, went in for a back operation in Manchester, UK. The operation was successful but then he had a reaction to the general anesthetic. He started to shake and was very hot. The surgeon had only seen MH once before and he tried to deal with it himself before calling for help. The antidote, dantrolene, wasn't in the operating room, but half way down the hall.

Once they gave Warren dantrolene, he calmed for a short time. However, he started reacting again causing him to get very hot. At this time, we were told that if Warren survived, he would have been brain damaged. Warren passed away.

Of course, this totally devastated our family. At the time, we didn't know much about malignant hyperthermia and Warren did not know that he was MH susceptible. Since then, we have all had a muscle biopsy. My dad and I both have MH susceptibility. Thank goodness my children are alright.

– As told by Natalie Bruce

Build MH Awareness in Your Community with a Letter Writing Campaign

Malignant Hyperthermia Association of the United States (MHAUS) was founded by families who lost their children to Malignant Hyperthermia (MH) or could not find information about MH; in 1981 they found each other - and a doctor performing MH testing – and agreed “to make current information about MH available to all who need it!

Visit the MHAUS website for sample letters to aid discussions about MH with family, healthcare professionals, educators, and insurance companies. Click on the Patient’s link found on the Home Page.

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Important Safety Information

The use of Revonto in the management of malignant hyperthermia crisis is not a substitute for previously known supportive measures. These measures must be individualized, but it will usually be necessary to discontinue the suspect triggering agents, attend to increased oxygen requirements, manage the metabolic acidosis, institute cooling when necessary, monitor urinary output, and monitor for electrolyte imbalance. Patients who receive i.v. dantrolene sodium preoperatively should have vital signs monitored.

If patients judged malignant hyperthermia susceptible are administered dantrolene sodium preoperatively, anesthetic preparation must still follow a standard malignant hyperthermia susceptible regimen, including the avoidance of known triggering agents. Monitoring for early clinical and metabolic signs of malignant hyperthermia is indicated because attenuation of malignant hyperthermia, rather than prevention, is possible.

Despite initial satisfactory response to i.v. dantrolene there have been reports of fatality, which involve patients who could not be weaned from dantrolene after initial treatment. The administration of i.v. dantrolene is associated with loss of grip strength and weakness in the legs, as well as drowsiness and dizziness. There have been reports of thrombophlebitis following administration of intravenous dantrolene. Tissue necrosis secondary to extravasation has been reported. Injection site reactions (pain, erythema, swelling), commonly due to extravasation, have been reported. Fatal and non-fatal liver disorders of an idiosyncratic or hypersensitivity type may occur with dantrolene sodium therapy.

*From the date of manufacture
†For until solution is clear

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Curt’s Story –

Note: Curt & Kathleen Keller are members of the MHAUS Board of Directors.

September 9, 2012 – it’s Sunday morning and I am getting ready to do my ministerial duties at church. I turn on my cell phone and see a message from my daughter-in-law asking me to call her as soon as possible. When I call her back, I learn that our son, Geoffrey Keller, had a malignant hyperthermia episode from an awake trigger and might not survive. My wife Kathy and I got in the car and began a seven-hour drive to Tennessee. However, we received the call that Geoffrey passed away about an hour into the drive.

We knew nothing of awake triggers (non-surgical triggers). Twenty-three years prior to his death, Geoffrey had an MH episode while under anesthesia. We were told by the doctor that we had little to worry about because as long as we knew he had MH anesthesiologists could be ready and use non-triggering agents.

We were able to track MH on my side of the family by identifying a cousin who died in surgery due to complications in the late 60’s. He was having a jaw set that he broke playing sports. I was too young to know much of that at the time and I did not know this cousin. However, a year after Geoffrey’s MH episode in the hospital, my niece was going to have surgery to put tubes in her ears. The doctor did not believe there was MH in the family. I had to have the hospital that treated Geoffrey fax the records to the hospital where my niece was set to have surgery. After they received the records, the doctors didn’t want to do the surgery.

Six years before my son died, my father had to have heart surgery. He had an MH episode during surgery. Evidently, he had neglected to tell the doctor about MH in the family and the anesthesiologist never asked about any history. He survived the surgery, but never left the hospital. He died in the hospital a week later.

Before I go on, I want to say that I cannot say enough good things about the doctors associated with MHAUS. Men and women I had never met took the time to talk with me about Geoffrey and provided me with information and comfort after he died. I will forever be grateful to them.

After Geoffrey’s death, my wife and I decided that we would do what we could to help prevent others from going through the pain we have gone through and continue to go through.

We have designed and completed several fund raisers for MHAUS and hope others will do the same. We have asked that the funds we raise go toward research and information for awake triggers. As I have learned more about awake triggers, I have learned about “awake symptoms” – issues those of us with MH can have, such as muscle cramping and heat sensitivity. (I know that “awake symptoms” is not a technical term, but I am not sure what else to call these issues.)

I have been trying to do what I can to promote further education regarding awake symptoms and awake triggers. I have also tried connecting with others who are MH susceptible. Somehow, I feel we are connected, having similar experiences that others may not understand. I will continue to do what I can, and hope anyone who is MHS will feel free to get in touch with me to share their feedback and concerns.

– As told by Curt Keller
Yes!

I want to support MHAUS in its campaign to prevent MH tragedies through better understanding, information and awareness.

A contribution of: ❑ $35 ❑ $50 ❑ $100 ❑ $250 ❑ $500 ❑ $1000 (President’s Ambassador)

or ❑ $ ____________, will help MHAUS serve the entire MH community.

Please print clearly:

Name: ________________________________________________________________

Address: ______________________________________________________________

City: ____________________ State: _____________ Zip: ____________

Phone: ________________________ E-mail: ____________________

❑ I am MH-Susceptible          ❑ I am a Medical Professional

Please charge my   ❑ Visa   ❑ Mastercard   ❑ Discover   ❑ American Express

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Please clip out this handy coupon, or feel free to photocopy if you prefer to keep your issue intact, then mail to: MHAUS, PO Box 1069, Sherburne, NY 13460-1069
THANKS! MHAUS thanks the following State Societies of Anesthesiology – Alabama, California, and Ohio – for their financial support. Our appreciation also goes out to the following Associations of Nurse Anesthetists: Illinois and Minnesota. Call the MHAUS office to ask Gloria how your group can join their ranks.

Sheila Riazi Wins Research Competition
Congratulations to Sheila Riazi, who won the Richard Knill Research Competition at the Canadian Anesthesiologists Society meeting. Richard Knill was an academic anesthesiologist and pulmonary researcher who died suddenly in 1995, and the competition honors his spirit of inquiry and scholarship. This is a great and well-earned honor for Dr. Riazi and colleagues. Dr. Riazi has been very dedicated to understanding MH and its variants.

MHAUS Seeks Applicants for New Home of Registry
The Malignant Hyperthermia Association of the United States (MHAUS) is searching for a supportive location to house the North American MH Registry of MHAUS. Recent events have compelled MHAUS to relocate the Registry for the present, but MHAUS’ ultimate goal is to assure continuation of a solid location to house important pertinent personal clinical data for MH-susceptibles (and family members) pertaining to their MH susceptibility. In addition, the Registry contains rich, focused clinical MH-related data which is de-identified and, therefore, can be used for research projects and publications. The application period for the RFPs ends promptly on November 1, 2016 at 11:59 pm. If you are interested in this opportunity, please complete the information requested on the MHAUS web site for consideration by the RFP Review Committee.

Eagle Pharmaceuticals Reports Positive Outcome From FDA Meeting for Ryanodex for Exertional Heat Stroke NDA Submission
Eagle Pharmaceuticals announced that the U.S. Food and Drug Administration (“FDA”) has determined that no additional human safety and efficacy data is required for the submission of Eagle’s New Drug Application (“NDA”) for Ryanodex® for the treatment of exertional heat stroke (“EHS”). “Following our positive meeting with the FDA, we have an agreement for an NDA submission for EHS. We anticipate requesting priority review of the application and, if granted by the FDA, being the first to market with a potentially life-saving treatment for EHS as early as next year,” said Scott Tarriff, President and Chief Executive Officer of Eagle Pharmaceuticals. If Ryanodex is approved by the FDA for treatment and management of exertional heat stroke, it would be the first medication to receive such a designation.

MHAUS
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