Medical Professionals Hotline Consultants & Writers Honored By MHAUS

The annual MHAUS Recognition Reception was held in October at the San Diego Marriott Hotel and Marina during the American Society of Anesthesiologists (ASA) meeting in San Diego, CA. Over 50 people attended the reception to honor the accomplishments and dedication of medical professionals, Hotline consultants, and writers.

“The Recognition Reception is always a highlight of the year,” said MHAUS Executive Director Dianne Daugherty. “Not only does it provide the opportunity to honor the work of those who share a common interest in the prevention of MH, but the reception also allows for the chance to meet colleagues and renew old friendships.”

Dr. Thomas Markus Metterlein, Resident Department of Anesthesiology, University Hospital Regensburg, Regensburg, Germany, received the Daniel Massik Award for his scholarly research paper “Magnesium Does Not Influence the Clinical Course of Succinylcholine-induced Malignant Hyperthermia.”

The Hotline Partnership Awards honored the collaborative efforts of Dr. Harvey Rosenbaum, UCLA Medical Center, Los Angeles, CA, who has been an MH Hotline consultant for 19 years, and Dr. Kenneth Lee, Overlake Hospital, Bellevue, WA, who called the Hotline seeking advice and guidance.

The MHAUS Media Award went to *Outpatient Surgery Magazine* for its role in promoting MH awareness. Associate Editor Kent Steinriede, of Malvern, Pennsylvania, accepted the award.

Dr. Donald and Anita Kaufman received the MHAUS Special Recognition Award for their commitment to MH awareness and prevention.

“I want to personally congratulate each award recipient for their hard work in fighting MH,” said MHAUS President Dr. Henry Rosenberg, who handed out the individual awards. “MHAUS appreciates the dedication of professionals such as these. Together, their efforts promote MH awareness and help save lives.”

MHAUS continued this message of awareness and prevention at its exhibit booth during the ASA meeting. Visitors picked up informational literature and could ask questions of MH experts.

“The exhibit booth was constantly busy with people asking about our educational products and general questions,” said Dr. Rosenberg. “Altogether, it was a very productive ASA meeting.”

On the inside ...

Executive's Corner .................................................. 2
MHAUS Recognition Reception ................................. 3
Research Advances Redefining MH .............................. 4
Common Denominators in Complex Diseases ....... 6
Hotline Summary ...................................................... 8
MH Glossary .......................................................... 10
Happenings .............................................................. 12
Happy New Year From MHAUS

As I watch light snowflakes of winter fall outside my window and think about preparing for the upcoming holidays, I am reminded of the message all within the MHAUS office and those affiliated with us focus on all year long - Be Prepared for MH!

The MHAUS Board of Directors and staff just yesterday held our first “GoToMeeting” online meeting. This is another way we are using the technological tools now available to everyone in order to share information in an immediate manner and transmit via a multitude of devices, wherever you are. It is mind-boggling! Board members, Registry and staff simultaneously viewed documents placed on my office computer screen “desktop” from the comfort of their own particular office or home computer. They were able to comment either via the telephone conferencing option or within the “chat box” provided. We discussed many topics, shared insight and feedback, and made important decisions to move MHAUS forward - all without driving on treacherous snowy winter roads – at least those here in Upstate New York. What a time we live in…!

This coming year a lot of changes will continue to improve the MHAUS website. We will encourage exciting growth in various small groups now developing at the “grass roots” level of MHAUS in the United States and all over the world. MHAUS has the MH experts, MH educational materials, and clear direction for all medical professionals’ use to recognize and treat MH before it can do harm. We are blessed with an empowering board and dedicated staff who are always willing to help however they can. We now need your direct assistance to get the word out where you live…we need your head, hands, and hearts to reach out to those who may not be aware of the devastation which can be prevented through MH preparedness! We have information to help you build awareness in your community. Contact us with ideas and requests via email, Facebook, and our website. We are listening…

I have a question for you this New Year: Have those of you who are medical professionals made sure your staff has participated in an MH Mock Drill? Are they comfortable if they must handle an unforeseen MH event? Do you know where your Dantrium® IV / Dantrolene Sodium for Injection is and how many vials you have on hand? If you are in an ambulatory surgery center or emergency room at a hospital, do you have an MH Transfer of Care Guide or emergency room at a hospital, do you have an MH Transfer of Care Guide? Are your medical professionals made sure your particular facility’s MH preparedness contact. Why can’t it be you? We are here to help you and your facility achieve that goal.

We will be having two separate MH Mini-conferences this coming year, starting with the first in Ottawa, Ontario, Canada in early June and another later in June in Florida. Have you signed up if you are near either location? Don’t wait too long! Watch our website for upcoming event information and attend whenever you can to assure you will become your particular facility’s MH preparedness contact. Why can’t it be you? We are here to help you and your facility achieve that goal.

So, when you are setting up your New Year’s Goals for the 2011 Year, please put MH preparedness and training at the top of your list…your patients will thank you and we will thank you. Happy New Year from MHAUS!
(Top-to-bottom) Kent Steinriede, Dr. Harvey Rosenbaum, Dr. Thomas Markus Metterlein, and Dr. Kenneth Lee

(Above) Dr. Joe Tobin speaks with a visitor to the MHAUS booth. (Below) Dr. Henry Rosenberg speaks with Dr. Bill Fritz, one of his former trainees, now in practice in Johnstone, PA., and Dr. David Seitman, a former colleague and anesthesiologist.
Malignant hyperthermia (MH) has long been defined as an inherited disorder of skeletal muscle, triggered in susceptible individuals by potent volatile anesthetic agents and/or succinylcholine. Data presented at the 2010 scientific conference of the Malignant Hyperthermia Association of the United States (MHAUS), however, suggest that it may be time to revisit this definition.

Held in April 2010 at the University of Pittsburgh Medical Center, and funded in part by the National Institutes of Health, the MHAUS conference brought together an interdisciplinary group of experts including clinicians, research scientists studying mechanisms of calcium regulation in skeletal muscle — a key element in the development of MH — and geneticists involved in MH research and counseling to share the latest advances and ideas as they relate to our understanding of MH and other muscle disorders. This was our largest scientific conference ever, with 15 invited speakers and nearly 60 additional attendees including MHAUS MH Hotline consultants, anesthesiologists new to the field, nurses and scientists.

One point agreed upon by all attendees was that MH is a complex disorder, displaying both phenotypic and genetic heterogeneity. The clinical presentation of MH can vary enormously, complicating diagnosis and delaying treatment. More than 200 genetic variants in RYR1 (skeletal muscle ryanodine receptor gene, the primary gene associated with MH susceptibility) alone have been found, although only about 30 of these variants are considered diagnostic for MH susceptibility. Other genes may be involved as well.

So, why revisit our definition of MH?

Working with genetically engineered animal models of MH (with RYR1 mutations causal for MH incorporated into their genome), experts in muscle physiology and biochemistry have shown that MH episodes can be triggered by both anesthetics and heat stress. The biochemical mechanisms behind this heat sensitivity are being elucidated as well, and may explain why individuals who harbor specific genetic mutations may be susceptible not only to anesthetic-induced MH, but also to heat- and exercise-induced MH.

Muscle disorders such as rhabdomyolysis can be confused with MH clinically, and furthermore, may have environmental causes, such as extreme exercise under hot conditions. They also may be caused by a variety of medications, notably statins. Investigations into cases of unexplained exertional rhabdomyolysis (ER) and heat-related illness have identified the presence of RYR1 mutations previously associated with MH in some patients, indicating that MH susceptibility might predispose to these adverse events in some people. Do individuals with these genetic variants have an increased risk for developing an MH episode when exposed to heat or exercise?

Uncovering physiologic pathways leading to the cellular changes that are the hallmark of MH will increase our understanding of the risk factors for the condition as well as our awareness of potential triggers of this potentially fatal event.

A critical part of our ability to prevent MH episodes is the development of reliable diagnostic tests, so that individuals at risk for an MH episode — whether induced by anesthetics, other drugs, heat or exercise — can be identified and preventive measures can be put in place.

What is the status of testing for MH susceptibility?

Although genetic testing for MH susceptibility is a reality and is used regularly, the accuracy of the test is limited. Therefore, at this point, for individuals suspected to be at risk for MH, the caffeine–halothane muscle contracture test is the best available confirmatory assay. Indeed, our European colleagues will not even progress to genetic testing until the phenotype has been confirmed through the contracture test. However, this is not always feasible in the United States for several reasons,
Continued from page 4

including cost, accessibility of biopsy centers and insurance coverage.

Researchers continue to work toward identifying and functionally characterizing novel gene variants, in an effort to increase the sensitivity of genetic testing for MH susceptibility. The effort requires a multidisciplinary collaborative approach, in which clinicians help to identify patients with confirmed MH episodes, geneticists work to identify gene variants, and basic scientists are involved in functional studies of these variants. In the process, researchers often work with clinical investigators and use information from the North American MH Registry and the MHAUS Hotline.

These key collaborations allow for identification of causal mutations in MH-susceptible individuals. However, as noted earlier, there are many gene variants of unknown functional significance as well. The complexities of this process call for the involvement of MH experts and genetic counselors when making decisions regarding clinical testing.

Conferences such as this one provide a critical forum for clinicians and researchers to share new data, discuss confounding cases, and strategize regarding future research efforts. This collaboration between researchers and clinicians is essential for the advancement of science in general, and more specifically, for advances in MH and also the care of the population at risk for MH and related disorders.

Sharon J. Hirshey Dirksen, PhD, is Scientific Officer at the Malignant Hyperthermia Association of the United States (MHAUS). Henry Rosenberg, MD, is President of MHAUS and director of the Department of Medical Education & Clinical Research at Saint Barnabas Medical Center, in Livingston, N.J.

Editor’s Note: This article originally appeared in Anesthesiology News and has been reprinted here with permission.

Acknowledgements: Funding for this conference was made possible (in part) by an R13 Grant (1R13AR05422-01) from the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), including co-funding from the Office of Rare Disease Research (ORDR) and MHAUS. We are also grateful for the generous financial support from UPMC.

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SAVE TIME...WHEN TIME MATTERS MOST!
Common Denominators in Complex Diseases: The role of ryanodine receptors in cardiac and brain function

by Alexander Kushnir
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Malignant hyperthermia (MH), heart failure, and epilepsy are three complex pathologies with diverse signs and symptoms but may share a common underlying mechanism. In MH, a skeletal muscle disorder, patients experience sudden, and potentially fatal, rapid increase in body temperature and intense muscle contraction while undergoing general anesthesia. In heart failure, a syndrome characterized by the inability of the heart to pump enough blood to provide the body with sufficient circulation, patients suffer from decreased exercise tolerance and shortness of breath, and are at risk for fatal ventricular arrhythmias. Clinical manifestations of patients with epilepsy, a condition defined as the recurrence of rapid bursts of electrical activity in the brain, vary from brief loss of consciousness to rapid, uncontrolled jerking movements and serious disability. However, despite these apparent differences, there is a growing body of evidence suggesting that these disorders and others may share a common denominator: hypercalcemia, the elevation of calcium levels in the body.

Calcium, a critical element in multiple cellular functions, is stored inside cells within a storage compartment called the endo/sarcoplasmic reticulum (E/SR). In many cell types, in order for calcium to get out of the E/SR, the calcium must pass through a specialized calcium channel called the ryanodine receptor (RyR). For example, during skeletal and cardiac muscle contraction RyR receives a trigger stimulus causing it to open and release the calcium from the SR. This calcium then binds to various muscle components resulting in shortening of the muscle fibers and muscle contraction. The calcium is subsequently pumped back into the SR where it becomes available for another round of release.

There are two clinically relevant, closely related, forms (technically called isoforms) of RyR: RyR1, found predominantly in skeletal muscle, and RyR2, found predominantly in cardiac muscle. Both RyR1 and RyR2 are also present in the brain. Both are mediators of calcium release in the cell. Mutations in the gene(s) that lead to production of RyR1 are characteristic of MH. These mutations have been found to cause RyR1 calcium leak in some cases even without the exposure to anesthetic agents resulting in the generation of dangerous reactive oxygen and nitrogen species, which damage mitochondria. This creates a vulnerable environment susceptible to the pathologic effects of the volatile anesthetic.

Skeletal muscle fatigue following intense exercise and severe muscle weakness in the inherited muscle disorder Duchenne muscular dystrophy have also been linked to structural and functional abnormalities in RyR1 which result in SR calcium leak. Recent work from our laboratory has shown that this increased calcium leak leads to the production of certain compounds called reactive nitroso intermediates. When they bind to the ryanodine receptor the functional characteristics are altered leading to further calcium leak and muscle weakness and eventually muscle destruction. Within the cell a protein called calstabin-1 ordinarily stabilizes the calcium channel so that it functions normally. However, in the altered state produced by increased calcium, the binding of this protein is inhibited and therefore the calcium channel becomes leaky. Our laboratory has shown that a novel compound, S107, stabilizes the binding of calstabin1 to RyR1 and results in reduced SR calcium leak and improved exercise capacity in normal mice and improved calcium dynamics and muscle function in mice with muscular dystrophy.

Approximately ten years ago mutations in the gene responsible for the production of the cardiac form of the calcium channel, RyR2, were discovered to be associated with a rare cardiac arrhythmia: catecholaminergic polymorphic ventricular tachycardia (CPVT). In this inherited syndrome, there is no gross morphological abnormalities in the heart but the heart is at increased risk for developing exercised induced fatal ventricular arrhythmias. These RyR2 mutations result in reduced affinity of calstabin2 to RyR2. During exercise there is further disruption of the binding of calstabin, causing SR calcium leak and destabilization of the carefully regulated electrical

continued on page 7
Continued from page 6

properties of the cell membrane leading to the induction of the arrhythmia. It was subsequently discovered that S107 stabilized the calstabin2/RyR2 interaction and prevented the SR calcium leak leading to a reduction in the number of fatal arrhythmias in mice with CPVT.

Calcium leak through altered RyR2 in the heart has also been linked to the pathogenesis of heart failure. In patients with heart failure the body attempts to compensate for the reduced cardiac function by increasing circulating levels of catecholamines, the molecules used to make the heart beat stronger during exercise. However, while acute catecholaminergic activation of the heart improves cardiac function, chronic stimulation causes depletion of calstabin2 from RyR2 resulting in calcium leak, and reduced cardiac function. S107, which enhances the binding of calstabin2 to RyR2 eliminates the SR calcium leak and improves cardiac function in heart failure.

Although less well understood, E/SR calcium leak in nerve cells through dysfunctional RyR2 has been linked to the various forms of epilepsy. Mice with mutations in RyR2 gene, destabilize the channel and cause it to leak calcium. The mice develop seizures and exhibit profound bursts of electrical activity in various parts of the brain. Similar to what was observed in the heart and skeletal muscle, treating these mice with S107 reduced the abnormal neuronal calcium leak/electrical burst activity and ameliorated the seizures in these mice.

There are many questions regarding the pathologic role of RyR calcium leak, which remain to be answered. Why does RyR1 calcium leak contribute to MH in some patients but muscle fatigue, or muscle weakness in such syndromes as Central Core Disease or Duchene muscular dystrophy? If RyR2 calcium leak is responsible for heart failure and seizures then why don’t patients who have heart failure develop epilepsy? Multiple experimental approaches spawning from strong interdisciplinary collaborations will be necessary to answer some of the many questions in the exciting field of dysfunctional RyR calcium handling.

Editor’s Note:

Patients with RYR 1 mutations (in MH for example) are not at greater risk to problems described with RyR2. While dantrolene has clearly been shown to reverse the changes found in MH, the drug has not been tested in the other syndromes related to ryanodine receptor abnormalities. In addition, the compound S107 has yet to be tested in animal models of MH.

Selected References:

Role of RyR leak in heart failure: PKA phosphorylation dissociates FKBP12.6 from the calcium release channel (ryanodine receptor): defective regulation in failing hearts.
Marx SO, Reiken S, Hisamatsu Y, Jayaraman T, Burkhoff D, Rosembilt N, Marks AR.

Role of RyR leak in seizures: Leaky Ca2+ release channel/ryanodine receptor 2 causes seizures and sudden cardiac death in mice.

Role of RyR leak in muscular dystrophy: Hypemitosylated ryanodine receptor calcium release channels are leaky in dystrophic muscle.

Challenge yourself with the MH Case of the Month. Visit the MHAUS website at www.mhaus.org
MH Hotline Activity From Sept. - Dec. 2009

by Dr. Margaret Weglinski

During the months of September through December 2009 thirteen volunteer physicians answered 62 calls to the MH Hotline. 54 calls involved patients who were experiencing at least one symptom suggestive of MH and the caller was asking for assistance in determining whether or not the patient actually had MH (case consultations). Eight calls involved only questions about MH. Consultants working on the Hotline included Drs. Allen, Chapin, Gronert, Litman, Melton, Millman, Miller, Rosenbaum, Rosenberg, Shukry, Skoog, Theroux, and Watson. One of the case consultations was deemed definitely MH and four were deemed probably MH by a Hotline Consultant. There was one death. Although it wasn’t always recorded on the report form, at least six of the cases occurred in a non-hospital setting. Twelve of the 62 calls involved children 5 years of age or younger.

The majority of callers were anesthesiologists from the United States (representing 22 states). Calls were also received from Canada and Venezuela. In addition to anesthesiologists, the Hotline was contacted by nurse anesthetists, anesthesiology residents, adult and pediatric intensivists, a cardiothoracic surgeon, an emergency medicine physician, and a physician assistant.

The one case that was definitely MH and resulted in a death involved a 5-year-old girl undergoing dental restoration at a freestanding surgery center located across the street from a hospital. The procedure was performed under general anesthesia and during the first hour the patient’s temperature was noted to gradually increase from 37°C (98.6°F) to 38°C (100.4°F) and her end-tidal carbon dioxide increased from 45 mmHg to 53 mmHg. End-tidal carbon dioxide is continuously measured during general anesthesia via the patient’s breathing tube. Carbon dioxide is a gas that is formed by metabolism in the body and exhaled by the lungs. An increase in end-tidal carbon dioxide can signal an increase in metabolism. The normal range for end-tidal carbon dioxide is roughly 35-45 mmHg. By the end of the second hour of surgery, the patient’s end-tidal carbon dioxide had increased to 59 mmHg, her heart rate had increased from 110 to 140, and both full body and jaw rigidity were noted. Within the next 5 minutes, her end-tidal carbon dioxide rocketed to 99 mmHg and her temperature rose to 40°C (104°F) (using a forehead temperature probe; it was actually 41°C (105.8°F) using a nasal temperature probe). The diagnosis of MH was made, the volatile agent was discontinued, hyperventilation was begun, dantrolene was given, a second intravenous line was inserted, and active cooling started. It was at this point that the MH Hotline was contacted and the anesthesiologist was connected with Dr. Chapin. By this time the patient’s temperature had decreased to 38.5°C (101.3°F) and 2.5 mg/kg of dantrolene had been administered. Shortly after they began discussing the case, the patient suffered a cardiac arrest and cardiopulmonary resuscitation (CPR) was initiated. There were two other anesthesiologists and many others helping to take care of the patient. There was no equipment available at the surgery center to measure an arterial blood gas or potassium level. A venous blood sample was sent to the hospital lab across the street and the results showed the patient to be acidotic (pH 6.87) and have a potassium level of 8.7 mmol/L (upper limit of normal is around 5.3 mmol/L). This was treated with glucose and insulin and decreased to 6.3 mmol/L. The team continued to give dantrolene to the patient, resulting in a total of 6-7 mg/kg administered. CPR was continued throughout this period and although pulses were obtained intermittently, a stable cardiac rhythm and blood pressure couldn’t be maintained. CPR was performed at the surgery center for at least two hours before the patient was transferred to the hospital across the street. She was pronounced dead shortly thereafter. Dr. Chapin stayed on the phone for the entire two hours helping with the case. A request was made to the family for tissue and blood samples from the patient to test for genetic mutations for MH as well as a referral to a nearby MH testing center for muscle biopsy and contracture testing for family members. Unfortunately, the family was hostile and angry and refused any further testing for the patient or themselves. It was a sad and frustrating day for all involved. It emphasized once again how quickly MH can progress and that even with prompt recognition and treatment it can be extremely

continued on page 9
difficult to conquer. It also highlighted some of the challenges of treating an MH crisis in an ambulatory surgery center where laboratory support is often not available and the optimal timing of transfer of a critically ill patient to a hospital must be considered.

A trend that seems to show no sign of abating is that of calls (5 of them) involving patients undergoing laparoscopic surgery who developed elevated end-tidal carbon dioxide levels after insufflation of carbon dioxide into the abdomen. Laparoscopic surgery is a minimally invasive type of surgery in which an instrument called a laparoscope is inserted through a small incision in the abdominal wall in order to view structures within the abdomen and pelvis. The abdominal cavity is distended and made visible by instillation of absorbable gas, most commonly carbon dioxide. All of the cases involved increases in end-tidal carbon dioxide with a corresponding respiratory acidosis on arterial blood gas measurement. Two of the 5 cases had extensive subcutaneous emphysema (condition where excess gas, in this case carbon dioxide, spreads under the skin). The respiratory acidosis resolved in all the cases after the abdomen was deflated. None of the patients were suspected to have MH.

Two calls were received regarding pregnant patients whose baby’s father had either a personal or family history of MH. Both callers wanted to know what to do in case the pregnant woman needed a general anesthetic. They wondered if the fetus was at risk of developing MH if the mother was administered a triggering anesthetic. Although there are no case reports of a fetus developing an MH crisis at the time of delivery, a non-triggering anesthetic is recommended for the mother if general anesthesia is required. All known triggering agents cross the placenta to varying degrees. However, succinylcholine (used to cause temporary paralysis) crosses the placenta to such a small degree that it can be used for an airway emergency if absolutely necessary. Optimal management for these patients, as for all parturients, is a regional anesthetic (epidural or spinal) for labor and delivery.

Even if hotline consultants do not know all the answers to all MH-related problems, because we have so much more to learn about MH, having an expert available to provide on-the-spot advice is extremely valuable and when moments count, lives are saved.

In the U.S. and Canada, the MH Hotline is

1-800-MH-HYPER (1-800-644-9737)

Outside the U.S., call 1-315-464-7079

Meet This Issue’s Hotline Consultant

Dr. Margaret Weglinski, Assistant Professor of Anesthesiology at the Mayo Clinic in Rochester, Minnesota, has been a Hotline Consultant since 1997.

“What I like best about my work with the Hotline is the chance to speak with health care providers from around the country,” she says. “Whether it’s answering a straightforward question about MH or trying to determine whether or not a patient is experiencing an MH episode, I find it rewarding to (hopefully) be of assistance.

In her spare time, Dr. Weglinski likes to travel, bike and hike, and says she tries to combine the three as often as possible.
Glossary of MH-related Terms

Contracture test – This is the test that is used to determine a patient’s susceptibility to MH. Muscle is taken from the thigh (about the size of a fingernail) and cut into strips of about half inch long and mounted in a chamber and made to contract by electrical stimulation. When the anesthetic halothane is introduced in the chamber the muscle not only contracts but develops a contracture (a sustained contraction). This contracture is typical for MH susceptibles. The drug caffeine may also lead to an abnormal contracture, as may a variety of other anesthetics. Although the test is highly accurate, the inconvenience of the biopsy and the requirement for special technical expertise limits its use.

Creatine kinase – An enzyme found in cells, especially muscle cells. Normal levels are up to about 200 iu/L. In cases of muscle membrane breakdown, the enzyme leaks out of the cell. This may occur from any type of muscle trauma, including malignant hyperthermia. After surgery CK levels may normally rise to 1,000 to 2,000 iu/L. When there is severe muscle damage the level may rise to 10,000 or more. At these levels, the muscle pigment, myoglobin, can be expected to be elevated in the blood as a result of muscle damage. In other words, elevated CK is a marker for leakage of myoglobin from the cell. Elevated levels of myoglobin can lead to temporary or permanent kidney damage. After an episode of MH the CK levels may be mildly or dramatically elevated depending in part on the promptness of treatment. In general, peak levels of CK occur about 24 hours after injury and may be elevated for days. Hence, in suspected cases of MH it is important to determine CK levels. In case of heart muscle damage, CK may be elevated, but this represents a slightly different form of CK. CK from regular muscle is termed CK MM, from heart muscle, CK-MB.

Dexmedetomidine – A selective agonist used as the hydrochloride salt as a sedative for patients in intensive care units.

General anesthetics – Compounds that produce loss of consciousness, pain relief and amnesia. General anesthetics are either gaseous agents such as halothane, sevoflurane, and desflurane (all triggers of MH), Nitrous oxide – an agent that also may produce a MH trigger. There are a variety of agents that are given intravenously that also may produce anesthesia such as the narcotics, benzodiazepines (e.g. Valium and Versed) which produce pain relief and sedation. Hypercapnia – Excessive carbon dioxide in the blood.

Iatrogenic – Induced inadvertently by a physician or surgeon or by medical treatment or diagnostic procedures.

Local anesthetics – These compounds block transmission of nerve impulses involved in pain sensation. These are the “caine” drugs - novocaine, bupivacaine, lidocaine, mepivicaine. None trigger MH and are safe to use in the MH susceptibles. These drugs are commonly used by dentists, anesthesiologists, pain physicians and surgeons among others.

LMA – laryngeal mask airway – This device was introduced into practice only a few years ago. The device is often used when tracheal intubation is not needed, but control of the airway is desirable. It is a tube that is so constructed that it does not enter the tracheal but forms a seal around the entrance to the trachea (the glottis). Insertion of the LMA is not as traumatic as insertion of an endotracheal tube and does not require deep levels of anesthesia or muscle paralysis.

Molecular genetics – Genetics is the study of inheritance. Molecular genetics is the study of how changes in DNA structure, such as mutations, affect the function of the genes. Molecular, because the study of DNA entails understanding of molecular or submicroscopic changes.

Muscle relaxants – These are drugs that are more properly termed paralyzing agents. There are two classes of muscle relaxants, non-depolarizing and depolarizing agents based on their mode of action. Typical non-depolarizing agents are vecuronium, pancuronium and rocuronium. None are triggers of MH. However, one depolarizing agent, succinylcholine is a potent trigger of MH. These agents are administered intravenously and are therefore given by anesthesiologists, ER physicians and intensive care physicians.

Neuroleptic malignant syndrome – (NMS) This is a constellation of signs and symptoms marked by high fever, muscle breakdown, acidosis, muscle rigidity and other signs similar to MH. However, the syndrome is induced by drugs used in the treatment of major psychiatric disorders. These drugs include thorazine, haloperidol (Haldol), olanzapine and other potent antipsychotic agents. The syndrome is not inherited and does not predispose to MH. That is, there is no greater frequency of MH in those experiencing NMS or vice versa. Interestingly, dantrolene is effective in treating NMS. There is no diagnostic test specific for NMS susceptibility.

Opiate – A medication or illegal drug that is either derived from the opium poppy, or that mimics the effect of an opiate

Oxygen saturation – The main purpose of the blood is to carry Oxygen to the various parts of the body along with nutrients and to remove carbon dioxide and other byproducts of metabolism. The amount of Oxygen in a given quantity of blood is not easy to measure, however the saturation level of the hemoglobin in the blood that carries the Oxygen can easily be measured with an external probe attached to a pulse oximeter. Normal Oxygen saturation is above 98%. At levels below about 90% insufficient oxygen is delivered to the blood, which may lead to many problems.

Pseudocholinesterase – An enzyme that degrades the drug succinylcholine. In about one in 2500 patients this enzyme is deficient. Therefore succinylcholine which usually causes muscle paralysis for about 5 minutes leads to paralysis that may last several hours. It is not life-threatening so long as the patient is connected to a ventilator. Susceptibility to this problem is not related to MH.

Reversal agents – There are several drugs that can antagonize or “reverse” the effects of other drugs. The drug, Narcan, or naloxone reversed the effect of narcotics (including the analgesia from these agents). Some drugs, neostigmine and pyridostigmine and edrophonium, reverse the effects of the non-depolarizing muscle paralyzing drugs.

Rhabdomyolysis – When muscle is damaged and cells are disrupted, the intracellular constituents begin to leak into the blood stream. This includes creatine kinase, myoglobin and the electrolyte potassium. This is termed rhabdomyolysis. This breakdown may be manifested by muscle pain and in extreme cases dark or cola colored urine.

Subcutaneous emphysema – Gases that are introduced into a body cavity, for example as part of laparoscopic surgery may, in some cases migrate from the body cavity to the tissues under the skin. This is called subcutaneous emphysema. It is recognized because a cracking sensation is felt on touching the skin. The gases eventually are absorbed into the blood stream.

Tachycardia – A rapid heart rate, usually defined as greater than 100 beats per minute.

Tracheal intubation and mainstem intubation – In order to control gas exchange during anesthesia a plastic tube is often placed in the trachea (windpipe). This is done usually when the patient is first anesthetized. One end of the tube is connected to a ventilator or respirator to control ventilation. Since the windpipe bifurcates just below the neck line, if the tube is inserted too deeply, the end may go into one of the branches of the trachea (usually the right side) and therefore only one lung will be ventilated. This may lead to a decrease in oxygen in the blood, and rarely an increase in carbon dioxide as well.

Trendelenberg
Steep head down position.
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The Sandi Ida Glickstein Fund was established for the purpose of providing free ID tags for MH-susceptible patients who qualify.

To take advantage of this program, please send us a letter indicating why you would like MHAUS to provide you with a complimentary ID tag.

The goal of the free ID tag program is to ensure the safety of MH-susceptibles during an emergency situation and to prevent a tragic outcome from MH.

For further information, please contact MHAUS at P.O. Box 1069, Sherburne, N.Y. 13460-1069; call 607-674-7901, or visit www.mhaus.org.

Have you visited us lately? Log on to www.mhaus.org to get the latest information on MH, order materials, post a message to the bulletin board or learn about the “Hotline Case of the Month.”
THANKS! MHAUS is grateful for the financial support of the following State Societies of Anesthesiology: Alabama, California, Maryland, and Michigan. Call the MHAUS office to ask how your group can join their ranks!

Transfer Of Care Guidelines Now Available
MHAUS joined forces with the Ambulatory Surgery Foundation (ASF) in developing Transfer of Care Guidelines for MH Patients. Together, the two organizations worked to identify a panel of experts representing key medical specialties at critical points along the transfer continuum, including clinicians and administrators specializing in patient care at ASCs, anesthesia care providers, an emergency medicine physician, emergency medical technician, and of course, experts in MH. The Transfer of Care Guideline is available for $55.00 each, including shipping. To order please contact MHAUS at P.O. Box 1069, Sherburne, N.Y. 13460-1069; call 607-674-7901, or visit www.mhaus.org.

Have You Seen The New MHAUS Video Online?
Visitors to the MHAUS home page are now greeted with a new video “Understanding Malignant Hyperthermia.” The 8-minute video also contains a brief synopsis of MHAUS’ almost 30-year history.

We Want To Hear From You
Let us know how you think MHAUS can better serve you. Call 607-674-7901 or email info@mhaus.org. Your comments and suggestions are important.

EMHG Annual Meeting
The 2011 European Malignant Hyperthermia Group (EMHG) Annual Meeting will be held in Nijmegen, Netherlands from June 8th until June 10th. The dates are just before the Euroanaesthesia 2011 meeting in Amsterdam (June 11-14). For more information visit the EMHG website at www.emhg.org.

Upcoming Meetings Where MHAUS Staff Will Be
NTEN, March 17-19, Washington D.C.; AORN, March 19-24, Philadelphia, PA; AACN-NTI, April 30 - May 5, Chicago, IL; ORNAC, May 8-13, Regina, Saskatchewan, Canada; ASCA, May 11-14, Orlando, FL; AANA, August 6-10, Boston, MA.