



# The Communicator

## Blood Test For MH Opens New Era

After years of investigation, a new era has opened for those affected by a life-threatening inherited disorder, malignant hyperthermia (MH). This new hope for MH families comes in the form of a long-awaited molecular genetic diagnostic test. It means patients and their families who have been uncertain about whether they are susceptible to this potentially fatal disorder of anesthesia may now have a chance of discovering if they are at risk by means of DNA analysis obtained from a blood sample.

MH is an inherited metabolic disorder of muscle. Ordinarily there are no outward signs of any problem. When MH-susceptible individuals are administered certain general (gas) anesthetics and a paralyzing drug, they may develop changes in metabolism that, if not recognized, could turn deadly. Since it runs in families, children, parents and siblings of an MH susceptible have a 50% chance of inheriting MH. Aunts, uncles and grandchildren have a 25% chance. MH affects as many as one in ten thousand people.

Until now, the only test for MH susceptibility has been based on testing a muscle sample at a specialized MH diagnostic center (see [www.mhaus.org](http://www.mhaus.org) for a listing). Now there is another option, at least for some of those suspected of being at risk for MH. Based on many years of research at laboratories and in hospitals in many different countries, and with the assistance of a grant from the Malignant Hyperthermia Association of the United States to PreventionGenetics ([www.preventiongenetics.com](http://www.preventiongenetics.com)), a Marshfield, Wisconsin biotechnology company concentrating on molecular genetic diagnosis and

DNA analysis, a genetic test to determine susceptibility is now available.

"Since MH was first described in 1961, investigators have been searching for a test to identify those at risk that is not invasive, expensive and cumbersome," says Henry Rosenberg, MD, the President of MHAUS. "The genetics test does not take the place of the current muscle biopsy, but it could identify the 50% of those at risk in an MH-susceptible family. It is not a screening test. However, it is a first step. Further work will increase the sensitivity of the test for those without a family history of MH. Those with the DNA change, as identified by the blood test, are virtually assured of being at risk for MH. However, those who do not have a known mutation may also be at risk because not all mutations are identified."

James Weber, Ph.D., President of PreventionGenetics, states "We are pleased to be the first lab in North America to offer a DNA test for MH. This test fits perfectly with our mission of preventing disease and disability through genetic testing. With this new test and working together with MHAUS and researchers, we should be able to make a major reduction in the rate of MH."

*See page 2-3 for genetic testing FAQs.*

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The Communicator is published four times each year by the Malignant Hyperthermia Association of the United States (MHAUS) and is made possible by a generous grant from Proctor & Gamble Pharmaceuticals, manufacturers of Dantrium. The Communicator is intended to serve the information needs of MH-susceptible families, health care professionals, and others with an interest in MH.

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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 stocked near the OR and that thorough family histories be obtained.

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# FAQs: MH Molecular Genetic Testing

*MHAUS is developing an information brochure concerning molecular genetic testing for MH. In the interim, here is some basic information concerning genetic testing for Malignant Hyperthermia.*

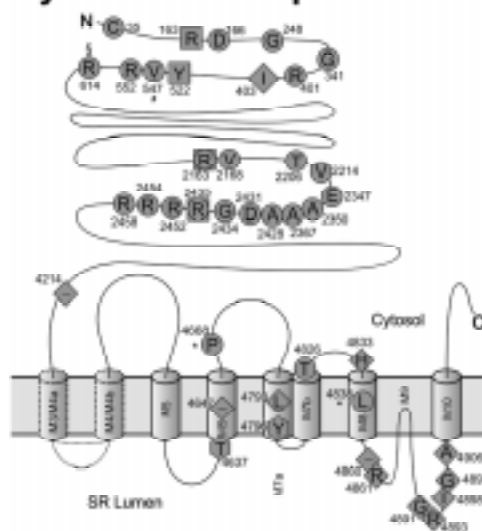
## Will molecular genetic testing replace the caffeine halothane contracture test (CHCT) using biopsied muscle?

A: No. Not all MH susceptibles will, at present, have evidence of a DNA change. The CHCT by contrast is a very sensitive test, meaning that virtually all those with risk and susceptibility for MH will be detected by the contracture test. The genetic test will detect only about 30% of those at risk. However, the genetic test is very specific -- that is, those with a positive test are virtually assured of being at risk for MH.

## Why should someone have a genetic test?

A: If a person is known to be MH susceptible and has a DNA change (mutation) known to be causative for MH, then his or her relatives may be diagnosed as MH susceptible through the DNA test. Those in the family with this mutation are therefore MH susceptible and do not need to undergo the muscle biopsy test for

## Ryanodine Receptor RYR1



- malignant hyperthermia (MH)
- malignant hyperthermia/central cores (MH/CC)
- ◆ central core disease (CCD)
- central core disease with nemaline rods (CCD/rods)
- deletion    \* CIGR-Test    \* Caffeine MH    § swine MH as well

confirmation. However, the absence of the mutation does not mean that the patient is not at risk for MH.

## Do I need a referral for genetic testing? Who should refer me for testing?

A: Yes, a referral is needed. If you have had a biopsy test, the biopsy center director should refer you. However, any licensed physician or genetic counselor may make the

*continued on next page*

**The Malignant Hyperthermia Association of the United States is a not-for-profit organization dedicated to reducing the morbidity and mortality of malignant hyperthermia and other heat-related disorders by: improving medical care related to MH; providing support information for patients; and improving the scientific understanding and research related to MH and other kinds of heat-related syndromes.**

**For more information or for materials on malignant hyperthermia or MHAUS' programs, call 607-674-7901; write MHAUS, 11 East State St., PO Box 1069, Sherburne, NY 13460; or visit us on the Internet at [www.mhaus.org](http://www.mhaus.org).**

referral.

**Does a patient need to have a biopsy or special procedure to enable a genetic test?**

A: No. This is the virtue of the genetic test. All that is required is a blood sample that is sent to the diagnostic laboratory.

**Who should have the genetic test?**

A: People who should consider having the genetic test are:

- a.) those who have been tested positive by the muscle biopsy
- b.) those who have been found to have a mutation causative for MH under a research protocol
- c.) relatives of those with a known mutation for MH
- d.) relatives of those who have been tested positive by the muscle biopsy
- e.) those with a very high likelihood of having experienced an MH episode in the judgement of a physician with experience in MH diagnosis

**How do I determine if I or a relative has a high likelihood of having experienced an MH episode?**

A: This is a complex question that depends on the evaluation of medical records and events that transpired during or following anesthesia. If you are registered in the North American MH Registry of MHAUS database, a likelihood figure may be calculated. Please contact the Registry at 888-274-7899. If not, you may need to release your medical information to your physician or to one of the MHAUS designated consultants to review the records (at no charge if you are a member of MHAUS). Please contact MHAUS via the Web site at [www.mhaus.org](http://www.mhaus.org) or call

the administrative office at 607-674-7901 for further details.

**What is the inheritance pattern of MH? Who should be tested if I am found to have a mutation?**

A: MH is inherited in an autosomal dominant pattern. This means that children, parents and siblings of an MH susceptible have a 50% chance of inheriting MH susceptibility. Aunts and uncles of the MH susceptible and grandchildren have a 25% chance. More distant relatives have a lesser chance. The decision to spend money to determine susceptibility is complex and individual and requires guidance by an expert in genetics and MH.

**How much will genetic testing cost?**

If the search involves looking for one specific mutation, such as when a family member has already been identified with a specific mutation, the cost will be about \$200. For full details, contact PreventionGenetics.

**Will insurance cover the cost of the test?**

A: That depends on the insurance company. Many companies will have to be educated as to the nature of the MH syndrome and the validity of the test. This has not yet been done and is a major task that MHAUS will begin in the

**For more, contact  
PreventionGenetics LLC:**  
3700 Downwind Drive  
Marshfield, Wisconsin  
54449 USA  
Phone: 715-387-0484  
Fax: 715-384-3661  
[www.preventiongenetics.com](http://www.preventiongenetics.com)

near future. Meanwhile, contact your own insurance company for details. MHAUS can provide the insurance company with references as to validity of the test.

**Should I have genetic counseling done prior to or following genetic testing?**

A: We strongly advise such counseling to help interpret the results of the test and evaluate family members for testing.

**If I have a test, what result will my doctor receive?**

A: The result will indicate one of the following:

- a.) No DNA variation found
- b.) Mutation associated with MH and or Central Core Disease found
- c.) DNA variation found of uncertain significance.

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# Report From The Annual Meeting Of The EMHG

By Barbara Brandom, M.D.

The 24th Annual Meeting of the European Malignant Hyperthermia Group (EMHG) took place May 19-21, 2005 in Mainz, Germany. This was an international meeting. Work performed in Japan, New Zealand, Canada, the United States, Bulgaria, England, France, Germany, Hungary, Italy, Latvia, Poland and Switzerland, was presented. For more details see [www.emhg.org](http://www.emhg.org). There were guest lectures on the history of research in Malignant Hyperthermia (MH), on Fibromyalgia (a chronic pain syndrome associated with skeletal muscle and its connective tissues), and on MH and its relationship with other hyperthermic syndromes. There were short reports on several clinical aspects of MH, on Central Core Disease (CCD), on the invitro contracture test (IVCT) and alternative diagnostic approaches

## NEW! MH Case Of The Month

Have you challenged yourself with the new MH Case of the Month? Visit [www.mhaus.org](http://www.mhaus.org) and go to the *Home or Professionals' Info Center* pages and submit what you think is the correct way to proceed with these actual MH cases. Answers with narratives are provided for the previous month's cases. **You could be a winner, too!**

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***Discussion of the genetics of MH susceptibility was particularly noteworthy because of the rapid introduction of new information in this area. Evidently, the genetic picture is not a simple case of having one gene variation in the areas previously reported.***

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for MH susceptibility, and on the evolving understanding of MH genetics.

Discussion of the genetics of MH susceptibility was particularly noteworthy because of the rapid introduction of new information in this area. Evidently, the genetic picture is not a simple case of having one gene variation in the areas previously reported. A more complete genetic survey not infrequently identifies ryanodine receptor type 1 gene (RYR1) mutations in several areas that may contribute to the MH phenotype (the clinical syndrome).

As was noted in a previous study of 30 patients from the United States<sup>1</sup>, many novel sequence variants were identified outside the three most studied ryanodine "hot spots." Other RYR1 mutations lie outside these areas.

Discordance, the genetic term used to describe the situation when a mutation is found in the RYR1 gene in an MH Negative

individual or when a family is known to have an MH mutation, but no mutation is found in the actual MHS (MH Susceptible) individual, remains a problem (6.8%). Sessions emphasized that results of genetic screening alone cannot be equated with a MH Negative diagnosis.

The suggestion was relayed that some individuals have more than one genetic variant that may play a role in their MH susceptibility.

A multi-center study from Grenoble, Marseille, Lille and Paris, France; Toronto, Canada; and Padua, Italy, reported molecular, pharmacologic, histologic and functional data from 179 families. In those diagnosed as MHS by IVCT testing, 60% had mutations in one of the 32 known RYR1 exons studied.

Rachel Robinson of Leeds, UK, noted that 392 sequence variants have been reported in RYR1. Of these, 67 are associated with MH, 18 with both MH and CCD, and 30 with CCD alone. However, only 23, perhaps 29 now, have been definitely demonstrated to be causative of MH.

Vincenzo Tegazzin of Padova, Italy, reported a novel deletion, which produces a truncated, dysfunctional RYR1. He also noted that in 43 of the 50 MHS individuals in whom his group found mutations, 10 were located in exons 47 to 89, within the second RYR1 "hot spot." He argued that CCD and RYR1 mutations causative of MH in hot spots

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## LCDR Alan Lovejoy Honored For Saving “Son’s Life”

LCDR Alan Lovejoy is Chief Nurse Anesthetist aboard the USS Vinson (CVN 70) in the Gulf war zone. Our son, Petty Officer Jonathan Pasquinelli, is assigned to this ship as part of the “air wing” and required an emergency appendectomy while on board.

He had an MH episode and Lcdr Lovejoy “just happened” to know what it was, recognized it, and reversed it in time to save our son’s life. Thank you, Lcdr Lovejoy.

*J. Jeffrey Pasquinelli  
M.A. Pasquinelli  
Carson City, Nevada*

### ***How You Can Honor Your Anesthesia Care Professional***

MHAUS has developed a way you can recognize a particular anesthesia professional in print!

Through our program call “Honor Your Anesthesia Professional,” we offer the following: For a \$50 donation or more, your personal thank you message can be directed to your “special” anesthesia professional in our quarterly newsletter, The Communicator. We will print your personal message (25 words or less) as well as highlight the names of those professionals in a prominent location in The Communicator for a full year.

Additionally, recognition will be highlighted on the MHAUS website reserved for this elite group. If an address is available, MHAUS will send a congratulatory letter to the anesthesia professional passing along the appreciation of one of his/her patients.

If you feel your anesthesia professional deserves your special thanks, please call or email the MHAUS administrative offices to express your appreciation of their outstanding care!

## EMHG Report

*continued from page 4*

one and two are frequently found in the same person, but that when RYR1 mutations are in hot spot three, CCD and MHS may not coexist. He also stated that only 50% of MmD patients have been found to be MHS. He reports 6% discordance between MHS status by IVCT and genetic analysis.

Sheila Muldoon, from the Uniformed Services University of the Health Sciences in Bethesda, Maryland, reported on 14 patients who were studied after clinical MH episodes. Her group looked for 17 RYR1 mutations in 11 exons. Only ten of these patients had positive IVCTs. Four were not tested by contracture testing for clinical reasons. Mutations were

found in 12 of the 14. Persistent myopathic symptoms were present in four cases, including the two patients in whom no RYR1 mutation was found.

Jane Halsall of Leeds reported a review of 75 cases of MH occurring during or within one hour of the end of general anesthesia. All cases had MHS or MH equivocal results on subsequent contracture testing. No cases in which anesthesia was aborted due to succinylcholine induced muscle spasm were included. MH occurred earlier during halothane anesthesia, but there were cases of MH recognized after five to 210 minutes of exposure to isoflurane and 10 to 210

minutes of sevoflurane.

Albert Urwyler of Basel presented the results of invitro testing of calcium release of the B-lymphocytes from a child who died of propofol infusion syndrome following head trauma. Propofol did not increase intracellular calcium in this model.

The tour of Mainz on the path to a dinner cruise on the Rhine was enjoyable as was the interaction with many old friends.

<sup>1</sup>Sambuughin N, et al., *Anesthesiology* 2005;102(3):515-21

*For a more detailed account of the Annual Meeting of the European Malignant Hyperthermia Group, please visit the Malignant Hyperthermia Association of the United States web site at [www.mhaus.org](http://www.mhaus.org).*

## Bogota, Colombia, Hosts MH Symposium

In the U.S. the availability of the MH treatment drug dantrolene is taken for granted as is the awareness of the syndrome. This is not necessarily the case in other countries, however.

Drs. J. Ernesto Rojas and Victor M. Neira have worked tirelessly to heighten the awareness of MH in South America as well as worked at setting up a biopsy center testing lab. A symposium this past spring on MH at the Colombia Society of Anesthesiologists in Bogota, Colombia, brought the condition of MH and its treatment to the forefront. The anesthesiologists in that country are very interested in providing optimum care to their patients and getting the treatment

*Pictured (left-right) Dr. J. Ernesto Rojas, Dr. Henry Rosenberg, Dr. Victor M. Neira, Dr. Manuel Antonio Galindo, president of the Latin-American Confederation of Societies of Anesthesiology, and Dr. Rafael Maria Sarmiento, one of the most active anesthesiologists in Colombia.*



drug available throughout this country of 40 million people.

Speakers and topics included: Clinical Spectre of MH, Dra. Dora Komar; Molecular Biology in the Postgenomic Era, Dr. J. Eduardo Caminos; Molecular Biology and MH, Dr. Henry

Rosenberg; Hospital Procedure Manual, Dr. J. Ernesto Rojas; Legal Aspects of MH in Argentina, Dra. Dora Komar; Diagnostic Tests in MH, Victor M. Neira; Future of Diagnostic Tests, Dr. Henry Rosenberg; What is MHAUS, Dr. Henry Rosenberg.

## MHAUS Loses Beloved Founder, Owen R. Davison

Owen R. Davison, 90, a resident of Country Meadows in Hershey, died on April 11, 2005.

He was the husband of Viola Short Davison, and of Jean C. Davison, who died in 1998.

Born in Bethel, Ohio, he was the son of Owen C. and Marie R. Davison. He graduated from DePauw University in 1937 and received his master's degree from the University of Cincinnati a year later. His interest in social work dictated his career path as he worked for the juvenile court system in Cincinnati, the Community Chests of Kansas City, MO, Evanston, IL, and Montclair, NJ, and then served as the executive director of the United Fund and later the Health and Welfare Council of Philadelphia. He

ended his career in social work as an Associate Executive Director of the United Way of Pennsylvania.

After retiring, Mr. Davison served as a volunteer international management consultant under the auspices of the International Retired Executive Service Corps on economic development projects in Brazil, Indonesia, Ecuador, Costa Rica, and Jamaica.

He was a founder and officer of the **Malignant Hyperthermia Association of the United States**. This came about after the death of his eldest son, Richard Davison, in 1978, from this heretofore unknown condition.

Mr. Davison was active in his local church and was a founder and former board chairman of St. Matthew's Methodist Church of

Valley Forge. More recently he was an elder of the Derry Presbyterian Church in Hershey.

In addition to his wife, he is survived by his son Douglas Davison and his wife, Barbara of Elverson; his daughter, Rev. Susan Archer of Silver Spring, MD; and his seven grandchildren and eight great-grandchildren.

A celebration of his life and memorial service was held at the Derry Presbyterian Church of Hershey on Sunday, April 17th with a reception following.

In lieu of flowers, memorial contributions were requested to be made to the Memorial Fund or the Outreach Programs of the Derry Presbyterian Church, 243 East Derry Road, Hershey, PA 17033 or to a charity of choice.

# MHAUS To Offer Two Writing Awards

The Malignant Hyperthermia Association of the United States (MHAUS) is pleased to announce the availability of awards in the amount of \$2000 and \$1500 to the first place and second place authors, respectively, of manuscripts related to malignant hyperthermia (MH).

In order to promote awareness of MH and its various manifestations and to encourage continued study of the syndrome, Mr. George Massik, a founding member of MHAUS, has graciously offered to support two writers' awards. **The Daniel Massik Fund** at The Foundation for

Jewish Philanthropies in Buffalo, NY was established by Mr. Massik in memory of his son who died from MH. These awards will provide a stipend of \$2000 for First Place and \$1500 for Second Place to an anesthesia resident/fellow or an anesthesiologist who is within five years of ending his/her training to attend the annual meeting of the American Society of Anesthesiologists Meeting or another meeting of similar merit.

The Awards will be given to the primary author of the best manuscript concerning malignant hyperthermia. The format may be a case report, literature review or

original study. The document should address a significant issue related to the problem of malignant hyperthermia. Those participating must currently be a resident/fellow in anesthesiology or an anesthesiologist who is within five years of ending his/her training. The paper must be a minimum of three double-spaced typed pages and a maximum of 10 pages. Include author's CV.

Deadline for receipt of the manuscript in the MHAUS office is **August 2, 2005**. The award will be presented at the annual MHAUS Recognition Reception at the annual meeting of the American Society of Anesthesiologists meeting in New Orleans in October 2005. Winners will be notified by August 31, 2005 to allow time for travel plans.

For further information regarding the application process for this award, please contact MHAUS, attention Gloria Artist, either via regular mail at P.O. Box 1069, Sherburne, NY 13460, fax at 607-674-7910 or email [gloria@mhaus.org](mailto:gloria@mhaus.org).

## Looking for a way to make your gift last?

Lifetime Memberships in MHAUS are now available for a one-time cost of \$500 or more. MHAUS Lifetime Members receive a special membership card, no renewal notices, an uninterrupted subscription to *The Communicator*, as well as special acknowledgement in the MHAUS Contributor List each year.

## The Lila and Jerry Lewis Memorial Fund

There are many special people who take the time each year to remember their loved ones in a way that helps MHAUS. The people below have made gifts during FY 04-05 in memory of Lila and Jerry Lewis. We are most grateful for their support and special tribute gifts.

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Marilyn Glassman's Birthday  
By James & Sharon Felder

### Memorials

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By Alan J. Levine  
Steve & Mickey Lewis  
Marilyn Lewis Glassman

# MH Hotline Activity For October-December 2004



In this three-month period, 73 calls requesting help with management of a patient and 17 other elective calls were made to 16 volunteer physician anesthesiologists through the MH Hotline. Calls came from 52 physician anesthesiologists and from nine nurse anesthetists working in operating rooms, on rounds and in a pain clinic. Calls also came from nine physicians caring for patients in the intensive care unit and from six physicians seeing patients in the emergency room, hospital ward or office. This diverse group of callers, also including a family practitioner, an internist, pharmacists, several surgeons, as well as specialists in intensive care and emergency medicine, shows that the Hotline serves a wide spectrum of health care providers. Calls were received from 36 of the United States in this quarter.

There were no deaths in this series of cases. Although most of the cases were judged by the consultants *not* to be episodes of malignant hyperthermia (MH), there were eight cases in which MH was either definite or very likely and the patient was treated for acute MH. There were five more cases in which MH was seriously considered as a diagnosis while more information was gathered. The average age of all the cases discussed was 31 years, but the oldest was 74 years old

and the youngest was less than a week old. Eighteen patients were ten years old or younger. As expected, fever and biochemical evidence of muscle injury were common findings. The median temperature of the entire group was 39°C and seven patients had a temperature greater than 41°C, a potentially dangerous temperature no matter what the cause. Three patients had serum potassium levels greater than 5 meq/l. The highest creatine kinase (CK) — muscle enzyme released into the blood when muscle is injured — levels measured were 12,000 iu, 92,000 iu and 100,000 iu in three different patients. Median CK was 4,000 iu, in the 23 patients with whom this data was available.

Several themes recurred in these cases. Complications from the succinylcholine occurred in five cases. Perhaps the most bothersome case was the call that was received weeks after surgery, asking if the patient who had mild renal failure after shoulder arthroscopy should be evaluated for occult myopathy. The young man had received succinylcholine and desflurane without problems during anesthesia. No other information is available so it is unknown if myoglobinuria could have been detected in this patient in the recovery room. Perhaps mild dehydration and non-steroidal analgesics were the only causes of this dangerous post-operative complication. But there are other patients in whom significant rhabdomyolysis was documented after administration of succinyl-

choline. A child received two doses of succinylcholine in an attempt to facilitate endotracheal intubation for tonsillectomy during sevoflurane anesthesia. Masseter muscle rigidity occurred. CK was 5,000 iu that afternoon and 12,000 iu the next day. Surgery was cancelled and there was no evidence of increased metabolism. An older patient weighing more than 120 kg also received two doses of succinylcholine during attempted tracheal intubation. Apparently, uncomplicated sevoflurane anesthesia followed for two hours. Due to surgical considerations, this patient went to the ICU three hours after the end of anesthesia. There serum potassium of 6.3 meqv/l and CK 12,000 of iu was noted. The next day CK was 92,000 iu. These and other calls prompt review of a reasonable evaluation and treatment strategy after succinylcholine induced rigidity or isolated post-op rhabdomyolysis. The consultants suggest:

- 1.) **Document heart rate, respiratory rate (minute ventilation if possible) blood pressure and temperature.** This will document that life threatening hyperthermia is not present and allow evaluation of more subtle evidence of increased metabolism.
- 2.) **If vital signs are grossly abnormal, obtain blood gases and treat for MH.** Please fill out an AMRA case report. See [www.mhreg.org](http://www.mhreg.org) and call 412-692-5464 for instructions.

*continued on next page*

# In the U.S. and Canada, the MH Hotline is 1-800-MH-HYPER.

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

**3.) Document CK, potassium and urine output.** Dipstick of the urine will screen for the presence of myoglobin in the urine. If there is no myoglobin in the urine post-op, then the patient did not suffer significant muscle injury during anesthesia. If dehydration and exposure to other nephrotoxic drugs later induces renal injury, data obtained in the recovery room can show that myoglobin was not present at that time to add to this risk.

**4.) If CK is elevated but there is no evidence of increased metabolism, continue to check CK every 12 to 24 hours until it begins to decline.** CK usually is greater the second and third day after injury to muscle than it was initially. CK can be checked at intervals of one to two weeks after discharge to see if it returns to normal. A neurologist should be consulted to follow the patient and pursue the diagnosis of occult myopathy. However, very often no muscle disease that could be responsible for increased CK is found.

**5.) If CK is normal (there is no myoglobin in the urine and all abnormalities of vital signs resolved over eight hours) then the patient can be discharged.**

Questions about the safety of inhalation anesthetics in pediatric patients with possible myopathy arose in three cases. The most

dramatic of these was a two-month-old baby with arthrogryposis who at the end of abdominal surgery had tachycardia, end-tidal carbon dioxide of 70 torr, pH 6.9, K<sup>+</sup> 9 meq/l and severe metabolic acidosis. This patient received sevoflurane. Other details are not available. One wonders if this child may eventually be found to have a congenital myopathy or King-Denborough syndrome. Pre-op calls about children known to have nemaline rod myopathy or Walker Warburg syndrome asked if inhalation anesthetics are safe in such cases. The caller and the consultant preferred intravenous anesthetics when practical, but it was later found that the child with nemaline rods had experienced

many inhalation anesthetics with no complications. This myopathy is one of several in which the histologic finding that has led to diagnosis in the past is associated with several genetic and protein abnormalities. There is little evidence to support the claim that all myopathic patients are MH susceptible, but all wish to avoid the course of the baby with arthrogryposis.

We sincerely thank Drs. Herlich, Watson, Wong, Allen, Chapin, Gronert, Litman, Melton, Millman, Parness, Rosenbaum, Rosenberg, Theroux, Wedel, Weglinski and Brandom for their service to those health care providers who called the MH Hotline. We all hope we have helped some patients.

## *Meet This Issue's Hotline Consultant*

The Hotline Activity was summarized this issue by Dr. Barbara Brandom, a clinical pediatric anesthesiologist at the Children's Hospital of Pittsburgh, Department of Anesthesiology, Pittsburgh, PA., and the Presbyterian-University Hospital, Department of Anesthesiology, Pittsburgh, PA. Dr. Brandom is also a Professor of Anesthesiology at the University of Pittsburgh, School of Medicine, Department of Anesthesiology, Pittsburgh, PA.

Dr. Brandom is actively involved in supporting studies of the genetics of MH, publishing case reports and review articles about clinical aspects of the syndrome of MH, and in organizing the NAMHR to provide a repository for information regarding both the clinical syndrome and its diagnostic tests including genetic data.



# Some Helpful Malignant Hyperthermia Terms

## **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.

## **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 is often used as an adjunct to these agents. It is not a complete anesthetic, and also not an MH trigger. There are a variety of agents that are given intravenously that also may produce anesthesia such as the barbiturates (e.g. thiopental), propofol, and ketamine. None are MH triggers. A variety of other agents are often used during anesthesia such as the narcotics, benzodiazepines (e.g. Valium and Versed) which produce pain relief and sedation.

## **Local anesthetics**

These compounds block transmission of nerve impulses involved in pain sensation. These are the "caine" drugs - novocaine, bupivacaine, lidocaine, mepivacaine. 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.

## **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, the one depolarizing agent, succinylcholine is a potent trigger of MH. These agents are administered intravenously and are therefore given by anesthesiologists, emergency room physicians and intensive care physicians.

## **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.

## **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.

## **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.

## **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 one

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.

## **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 thiorazine, 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.

## **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.

## **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.

## **Triggering agents for MH**

These are drugs that will lead to the onset of MH. These include all the potent gas anesthetics and succinylcholine.

## Slide Show Presentation For MH Risk Available

MHAUS offers a slide show kit (CD-ROM and/or slides format) with lecture notes on "Managing Malignant Hyperthermia Risk in Today's Surgical Environment." This presentation reviews the risk of MH and assesses current trends in the management of MH in the inpatient and outpatient settings. Two CMEs are available.

This is a valuable tool to assist in developing standard of care practice guidelines and algorithms to ensure patients at risk will have access to appropriate interventions for treating MH. This program is arranged so that it can also be used as a self-study program to enhance individual knowledge of MH and the risks involved.

Cost is \$125 plus shipping and handling for either the slides or the CD. For both formats, the cost is \$135 plus shipping and handling. Call 607-674-7901 or visit [www.mhaus.org](http://www.mhaus.org) to order.

## Every MH-Susceptible Should Wear A Medical ID Tag

MHAUS now has help available for the MH-susceptibles who have no insurance or cannot afford to purchase a medical ID tag.

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 for 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](http://www.mhaus.org).

***Have you visited us lately? Log on to [www.mhaus.org](http://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."***

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

A contribution of:  \$35 (Basic)  \$50  \$100  \$250  \$500  \$1000 (President's Ambassador) or  (other amount) \$ \_\_\_\_\_, will help MHAUS serve the entire MH community.

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# MHAUS Happenings, Events and Notices

□ **Congratulations to Dr. Steve Karan**, staff anesthesiologist with FirstHealth Moore Regional Hospital of Pinehurst, NC, who was name *Physician of the Year* by the hospital's clinical staff. Dr. Karan was honored for his teamwork with the hospital's six patient care units as well as his compassion and professionalism with all his patients.

Dr. Karan studied chemistry at West Point before entering medical school at Philadelphia's Temple University on an Army scholarship. He completed his internship and residency at the Walter Reed Army Medical Center in Washington, D.C., and spent 12 years on active military duty. After his residency, he was assigned to the Armed Forces Medical School in Bethesda, MD., where he was the physician in charge of medical

student anesthesiology training. He later became involved in research, concentrating on malignant hyperthermia. Dr. Karan has worked with the Malignant Hyperthermia Hotline to help anesthesiologists across the country manage active MH cases. Dr. Karan has been a staff anesthesiologist with FirstHealth Moore Regional Hospital since 1997.

*Editor's Note: parts of this article were contributed by FirstHealth of the Carolinas and first published in "The Pilot" of Southern Pines, NC.*

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**"Malignant Hyperthermia Update on Susceptibility Testing,"** has been published in the June 15, 2005, issue of the *Journal of the American Medical Association* by Ronald S. Litman, D.O. and Henry Rosenberg, M.D., C.P.E.

also goes to the following state components of the American Society of PeriAnesthesia Nurses: **Arkansas, Texas and Wisconsin.** Call the MHAUS office today to ask how your group can help.

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