David O. Warner, M.D., Editor

XXIVth Annual Meeting of the European Malignant Hyperthermia Group. Mainz, Germany. May 19–21, 2005.

The XXIVth Annual Meeting of the European Malignant Hyperthermia Group took place May 19–21, 2005, in Mainz, Germany.* Research was presented from nine European countries, including Bulgaria and the new European Union members, Hungary, Latvia, and Poland, as well as from Japan, New Zealand, Canada, and the United States. There were three guest lectures by professors Richard Ellis, M.D. (President of the European Malignant Hyperthermia Group), Wilfred Nix, M.D. (Department of Neurology, University of Mainz, Germany), and Philip M. Hopkins, M.D. (Department of Anesthesia, University of Leeds, United Kingdom), and several short reports on clinical aspects of malignant hyperthermia (MH), central core disease (CCD), the *in vitro* contracture test and alternative diagnostic approaches for MH susceptibility, and the genetics of MH. Most interesting were the reports of ryanodine receptor genetics.

Analysis of the entire ryanodine receptor gene type 1 (*RYR1*) coding region in Switzerland and Japan confirmed a previous study of 30 patients from the United States[1] in that many novel sequence variants were found outside the three much-studied "hot spots." *RYR1* mutations were found in only 40% of Swiss MH-susceptible families when the genetic examination was restricted to the three hot spots. However, *RYR1* sequence variants were found in 27 of 36 MH-susceptible patients when the entire coding region of *RYR1* was examined. Six of these were previously described mutations, and 21 were new findings of unknown significance (novel mutations). Similarly, 6 known and 22 novel sequence variants were found in a sample of 34 Japanese MH-susceptible individuals when the entire coding region was examined. The functional effects of all of these novel variants have not been determined. Of the 392 sequence variants reported in *RYR1* to date, 67 are associated with MH susceptibility, 18 are associated with both MH and CCD, and 30 are associated with CCD only. However, only 23 have been shown to decrease the threshold for calcium release in a biologic system and meet the other criteria† necessary to designate the genetic change causative of MH.

The sensitivity of a genetic test of MH susceptibility is difficult to define without consideration of patient characteristics. A multicenter study from Grenoble, Marseille, Lille, and Paris, France; Toronto, Canada; and Padua, Italy, reported clinical, molecular, pharmacologic, histologic, and functional data from 179 families. In those with a diagnosis of MH susceptibility by contracture testing, 60% had mutations in 1 of the 32 *RYR1* exons examined by denaturing high-performance liquid chromatography and sequencing. In only 20% of the 50 individuals who did not have contracture testing but were studied after a clinical MH event were *RYR1* mutations identified. In contrast, causative mutations were identified in 12 of 14 patients in a series from North America that looked for 17 *RYR1* mutations in 11 exons. Ten of these 14 patients also had positive contracture tests. Four were not tested by contracture test for clinical reasons. Persistent myopathic symptoms were present in 4 cases, including the 2 patients in whom *RYR1* mutation was not found.

Examination of a limited number of exons can produce misleading results. Two *RYR1* mutations were found in 6 of 179 families. In a different study, 8 families had two and 2 families had three *RYR1* variants. Two very common *RYR1* mutations in Europe and North America, Gly341Arg and Arg614Cys, are rare in Japan. A discordance of 6% between MH-susceptible status by contracture testing and mutation analysis was reported again. Therefore, both positive and negative results of a genetic test of MH susceptibility must be interpreted carefully.

Genetic confirmation of CCD was reported by the clinical diagnostic laboratory in Leeds, England. Before performing such a test, the clinical and histologic evidence supporting the diagnosis of CCD is evaluated. In 30 such cases, *RYR1* exons 95 and 100–104 contained sequence variants in 30%. Of these, 70% were novel. A sequence variant in these exons does not automatically indicate that the patient is susceptible to MH. MH susceptibility should be evaluated by contracture testing in such cases. The absence of mutations in exons 95 or 100–104 of *RYR1* does not rule out CCD, because there are six other known loci for the histologic and clinical diagnosis of CCD.

A new mutation, Ile4138Thr, was found in a woman who had masseter spasm followed by several days of muscle pain after succinylcholine administration for cesarian delivery without exposure to inhalation anesthetics. Contracture test results in this proband and two other relatives were positive. Histologic findings of CCD were present in these MH-susceptible individuals, and there was a reduction in the EC_{50} for 4 chloro-m-cresol and halothane on calcium flux in their myotubes. MH-negative relatives, by contracture testing, had normal histology and normal *RYR1*. More cases of suspected MH should be evaluated by all of these methods.

Data supporting revised recommendation for postoperative treatment of MH-susceptible patients from New Zealand was presented. Presumed MH-susceptible patients had nontriggering anesthetics as day surgery patients. In the total of 72 patients, 39 were diagnosed with MH susceptibility with positive contracture tests, and 3 were diagnosed by DNA analysis. Propofol, narcotics, antiemetics, and nonsteroidal antiinflammatory drugs were given. Capnography and other noninvasive monitoring were used. The average anesthetic duration was 45 min. After 60 min in the postanesthesia care unit, patients went to a second-stage recovery area for 90 min before discharge home. Some children went home sooner after tympanostomy tube placement. The next day, 68% of cases were contacted. There were no reports of postoperative fever or muscle pain. Pain at the incision and nausea were commonly reported.

Also noteworthy is the demonstration from Wurzburg, Germany, that sevoflurane cannot be substituted for halothane in *in vitro* contracture testing. This group continues to work on the microdialysis measurement of intramuscular metabolism after local injection of RYR1 agonists halothane and caffeine as a less invasive test to diagnose MH.

The next meeting of this group will be in Riga, Latvia.‡

Barbara W. Brandom, M.D.,§ Sheila M. Muldoon, M.D. §University of Pittsburgh Medical Center, Pittsburgh, Pennsylvania. bwb@pitt.edu

Reference

1. Sambuughin N, Holley H, Muldoon S, Brandom BW, deBantel AM, Tobin JR, Nelson TE, Goldfarb LG: Screening of the entire ryanodine receptor type 1 coding region for sequence variants associated with malignant hyperthermia susceptibility in the North American population. ANESTHESIOLOGY 2005; 102:515–21

* More information available at: www.emhg.org. Accessed July 22, 2005.

† Listing of these criteria available at: www.emhg.org. Accessed July 22, 2005.

‡ Further details available at: www.emhg.org. Accessed July 22, 2005.

(Accepted for publication July 19, 2005.)

43rd Western Anesthesia Residents Conference. University of California at Irvine, Orange, California. April 29–May 1, 2005.

The 43rd Western Anesthesia Residents Conference (WARC) was hosted by the Anesthesiology Department of the University of California, Irvine, California. WARC was held from April 29 to May 1, 2005, at the Hyatt Regency Hotel (Garden Grove, California). The conference started with registration and a welcome reception on Friday evening followed by a Chief Residents and Chairs dinner. An overview of the conference was given by Peter Breen, M.D. (Chair, UCI Medical Center, Orange, California), in the Chairs dinner.

One hundred eighty-five residents, researchers, and faculty members preregistered for the conference. In all, more than 220 people participated in various parts of the conference. The conference attracted a record number of participants, which was evident by the 33% increase in the number of abstracts that were presented during the conference. For the first time at WARC, we had to divide abstracts into two groups for awards because of an overwhelming number of abstracts (a record 120 submissions this year). The abstracts were separated into research and case report (including computer model and retrospective analysis) categories. Incidentally, we had an equal number of abstracts in both categories. Research abstracts were presented in four oral sessions and a poster discussion encompassing three concurrent sessions. Case reports were presented two different times, using three concurrent sessions at each time. The abstracts were categorized based on the subspecialty of anesthesiology. Studies from almost all subspecialties were presented during the conference, which gave every participant something to look forward to in relation to his or her subspecialty of interest. An attempt was made to have a faculty moderator with experience in a subspecialty moderate that session throughout the conference to offer each investigator an opportunity to present his or her work to a moderator experienced in that particular field of research.

Saturday morning's program started with a brief welcome address by Dr. Breen. He welcomed all of the attendees and wished the presenters all the best. He also acknowledged overwhelming support from various exhibitors. The conference is sponsored by all the academic institutions in the Western region. The presence of exhibitors made the conference more lively and offered the attendees an opportunity to learn about new products. Nitin Shah, M.D. (Director, WARC 2005, UCI Medical Center), gave detailed information about abstract presentations and awards. The scientific program followed, with two oral sessions of research abstracts and a break to view the posters and to visit the exhibits. This was followed by lunch. The whole afternoon was dedicated to the poster discussion sessions. Between 1:00 and 5:30 PM, three poster discussion sessions were arranged to cover a large number of abstracts, with a break after each session to visit with the exhibitors. A total of approximately 110 abstracts were presented during the day.

Saturday evening included an entertaining and informative presentation on "Wine, Health, and History" by Philip J. DiSaia, M.D. (Dorothy J. Marsh Chair in Reproductive Biology, UCI Medical Center). Participants thoroughly enjoyed the history of wine and the relation of wine and health while sipping wine before dinner. A sumptuous dinner marked the end of Saturday.

Sunday morning included two oral sessions, with a break in between to visit with the exhibitors. The remaining research abstracts were presented during these oral sessions. The conference ended with lunch, during which three awards in each category were presented.

Research Awards

1. Mohab M. Ibrahim, Ph.D., University of Arizona, Tucson, Arizona. "CB_2 Cannabinoid Receptor Activation Produces Antinociception by Stimulating Peripheral Release of Endogenous Opioids."

- This rat study suggests that CB_2 receptor activation stimulates release from keratinocytes of B-endorphin, which acts at local neuronal μ-opioid receptors to inhibit nociception. This mechanism allows for the local release of B-endorphin where CB_2 receptors are present, leading to anatomical specificity of opioid effects.

2. Jason Miller, M.D., UCI Medical Center, Orange, California. "Subanesthetic Sevoflurane Preferentially Inhibits Human Emotional Memory."

- This volunteer study suggests that sevoflurane at 0.25% end-tidal concentration may help to prevent cases of awareness by preferentially blocking recall of emotionally laden information.

3. Edward Lee, M.D., Harbor-UCLA Medical Center, Los Angeles, California. "Pelvic Colocalization within Dorsal Root Ganglion."

- This rat study demonstrates that neural input from two different pelvic organs (uterus and colon) projected to the same cell body within the same dorsal root ganglion. It is plausible that this population of dichotomizing (branching) neurons plays a vital role in the mechanism of nociceptive transduction at the level of primary afferent neurons.

Case Report Awards

1. Nathan Kudrick, M.D., UCI Medical Center, Orange, California. "Inadvertent Breathing Bag Obstruction Causes Decreased Tidal Volume during Mechanical Ventilation with the Draeger Narkomed 6000 Anesthesia Machine."

- This case report identified that the Narkomed system uses the reservoir bag as a component of the compensation mechanism, and an obstruction of the bag may impair proper ventilator function.

2. Brian Pitts, M.S., M.D., UC Davis Medical Center, Sacramento, California. "Development of an Interactive Multimedia Software Program that Models the Cardiac Pressure-Volume Relationship."

- The author has developed a computer-aided instruction model that teaches the hemodynamic variations throughout the cardiac cycle by correlating intracardiac pressure with volume and time.

3. Judi Cain, M.D., Loma Linda University Medical Center and Children's Hospital, Loma Linda, California. "Airway Management of Newborns with Pierre Robin Sequence: The Use of Disposable vs. Multiple Use Laryngeal Mask Airways (LMA) for Fiberoptic Intubations."

- Two cases revealed that a 3.0-mm endotracheal tube can pass through a No. 1 multiuse LMA, whereas only a 2.5-mm endotracheal tube could pass through a No. 1 disposable LMA.

The annual meeting concluded after the awards ceremony. The 2006 WARC will be hosted by the University of Utah, Salt Lake City, Utah.

The author thanks the faculty, staff, and residents of the Department of Anesthesiology, University of California at Irvine Medical Center, Orange, California.

Nitin Shah, M.D., University of California at Irvine Medical Center, Orange, California, and Long Beach Veterans Affairs Healthcare System, Long Beach, California. nitin.shah@med.va.gov

(Accepted for publication August 19, 2005.)