REQUEST FOR PROPOSALS

MALIGNANT HYPERTHERMIA ASSOCIATION OF THE UNITED STATES

Clinical Incidence of Malignant Hyperthermia (MH)

December, 2019

MHAUS (mhaus.org) is a not for profit patient advocacy organization established in 1981 to "promote optimum care and scientific understanding of MH and related disorders" through education and information promote scientific advances related to MH and related disorders.

Malignant Hyperthermia, first described in the 1960s, is a potentially fatal pharmacogenetic disorder inherited in an autosomal dominant pattern. It often presents in a dramatic manner during, or shortly after, anesthesia. Prompt treatment requires following the protocol which must include administration of the drug dantrolene in order to reduce the reported mortality rate without treatment of approximately 70%.

A network of scientists and physicians and others have been studying the disorder for many years. As a result, the scientific understanding of MH has advanced dramatically while the mortality rate has declined significantly. In up to 70% of individuals the disorder is linked to pathogenic variants in one of three genes: The Ryanodine Receptor type one (*RYR1*), the CACNA1S and the STAC3 genes. Remarkably, one in about 1,000 individuals in the general population carry one of the pathogenic variants.

Definitive diagnosis in the laboratory is based on a muscle biopsy testing protocol only available in a limited number of labs. However, more recently, in appropriate patients, assessment of the presence of one of at least 50 pathogenic variants has begun to replace the muscle biopsy test.

The *American College of Medical Genetics* lists variants in the *RYR1* gene as "actionable".

Because the syndrome presents in a variety of often subtle ways, MH is sometimes misdiagnosed or not identified. Data on the clinical incidence of MH, mortality and morbidity from the syndrome is mostly based on anecdotes and small series of cases as the penetrance of the gene is not well understood. As many individuals with MH are misclassified by ICD 9/10 codes, the diagnosis needs to be verified by an MH expert. Some studies have shown that examination of anesthesia electronic medical records may be helpful in defining the clinical incidence and morbidity of MH. Because MH is uncommon, MHAUS is seeking to define the clinical incidence of MH using data gathered by electronic anesthesia recording systems from sites with at least 500,000 records.

The cases should encompass both outpatient as well as inpatient surgeries and endoscopies.

The data should include the following deidentified data:

- Total number of anesthetics administered
- Duration of study (beginning and end dates)
- Type of facility(ies)
- Type of anesthetics including the name of the inhalation agents and/or succinylcholine
- Age and sex of patients
- Height and weight of patient
- Associated morbidities, preop diagnoses
- Number of previous anesthetics for a given individual
- Pre-surgery body temperature
- Surgical procedure (emergency vs elective) and duration
- Time of onset of MH after initiation of anesthesia
- Relevant laboratory data during and after the episode
- Dantrolene administration
- If yes, dose(s) and time(s) and the preparation of dantrolene used
- Presence of postoperative rhabdomyolysis
- Post procedure morbidity and mortality
- Any tests for susceptibility to MH that were carried out
- Family history of MH or syndromes resembling MH

Optional: genetic characterization of the patients who are classified as MH susceptible.

Funding of up to $50,000 is available for the study.

The proposal will be reviewed by our Professional Advisory Council consisting of experts in MH, genetics, and related disorders.

The response should enumerate and describe the qualifications of the participants and any limitations on such a study by the Institution as well as budgetary requirements for personnel and equipment and approximate duration of data gathering.

All responses should be submitted to:

Henry Rosenberg, MD, President of MHAUS ((henry@mhaus.org)

or Dianne Daugherty, MHAUS Executive Director (dianne@mhaus.org)

by February 14, 2020