

## **Malignant Hyperthermia Testing in 2010**

**Terasa Bulger<sup>1</sup>**

<sup>1</sup>*Palmerston North Hospital, Palmerston North, New Zealand*

Malignant Hyperthermia (MH) is a rare pharmacogenetic condition inherited in an autosomal dominant fashion. It is caused by abnormal calcium homeostasis in skeletal muscle triggered by suxamethonium and volatile anaesthetic agents.

### History of MH testing

Although In Vitro Contracture testing (IVCT) is the gold standard of MH testing, since its discovery in 1960 by Denborough there have been many other ways of testing for MH. Serum Creatine Kinase (CK) is raised in 60% of MHS patients, but also in 10% of normal patients. There have been tests of platelets for ATP depletion, metabolites of glycolysis and myophosphorylase ratios, as well as nuclear MRI studies, the tourniquet twitch test and tests of muscle relaxation. None of these tests approach the specificity and sensitivity of IVCT .

### IVCT

Performed Palmerston North NZ, and Westmead, Royal Perth and Royal Melbourne in Australia. Using a TIVA GA or regional anaesthetic, a strip of Vastus lateralis is removed . The muscle is attached to a strain gauge and then suspended in a carboxygenated Krebs solution. After ensuring muscle viability, Caffeine and Halothane are added and contractures measured. There are three potential outcomes. Abnormal contracture to both caffeine and halothane is MHS (susceptible). MHE (equivocal) is response to either caffeine or halothane but not both. MHN (normal) is no abnormal response.

### Genetic testing

Developed in 1990. The RYR1 gene encodes the skeletal muscle isoform ryanodine receptor (Calcium channel release receptor). It is fundamental to excitation contraction coupling and skeletal muscle homeostasis. It is mapped to Chromosome 19q13.2. Mutations in this gene are thought to be associated with MHS in more than 50% of cases and nearly all cases of Central Core disease(CCD) The mutation has to be associated with abnormal calcium release, and if other criteria are fulfilled it is called a causative mutation. 30 causative mutations have been identified worldwide and a positive test for a causative mutation indicates MH susceptibility.

### Discordance

The major problem with genetic testing for MH is discordance. This is when the patient has a negative DNA test and a positive muscle biopsy. Hence all patients with a negative DNA test have to be confirmed by a negative muscle biopsy.

### New Testing methods

These include less invasive muscle biopsy testing, direct injection of a triggering agent into the muscle and a new gene test for calsequestrin. The utility and ethics of these tests will be discussed.