

## Screening

### Testing for MH

In the UK all patients who have a suspected reaction should be referred to the Leeds unit. This is normally done by the anaesthetist, although geneticists, GPs, dentists, other doctors often refer cases if there is a family history or suspect past event. The MH Unit will assess each case and advise about testing. It is stressed that an MH negative diagnosis is very important and patients will be refused testing only if there is clear evidence that MH is not involved.

Testing (screening) of a new case is by a muscle biopsy called an in-vitro contracture test (IVCT). This involves exposing muscle tissue samples while still living to halothane and caffeine following a standard protocol devised by the European MH Group. Normal muscle will relax when exposed to halothane whereas MH muscle will contract and this can be measured. MH muscle is more sensitive to caffeine and will contract at much lower concentrations than normal muscle. Because the tests are done on living tissue the patient has to come to Leeds for a 2 night hospital stay due to the travel involved. The muscle samples are taken from the inner thigh just above the knee through a 2-3 inch incision. This is usually done under a local anaesthetic nerve block. The results of the test are known that day so their implication both to the patient and the family can be discussed before leaving hospital. If the tests are positive, ie MH susceptible, further testing of the family will be organised. This is done on the basis of the mode of inheritance. First degree relatives will be offered testing first ie parents, siblings and children. It is important that MH susceptible individuals ensure that all family members are informed about MH and instructed to tell any anaesthetist treating them until such time that they are shown to be MH negative (normal). Please see the example letter you can use to inform the family. If the tests are negative then the reaction was not due to MH and patients can be treated as normal with regards to future anaesthesia. Occasionally the tests are borderline and for safety reasons these are classified as positive.

Not all patients can have a biopsy, these include children less than 10-12yrs (30kgs), pregnant women, and patients on prolonged steroid therapy. If the proband cannot be tested, eg a young child or deceased, then the nearest most appropriate relative is tested. In the case of a young child this would be the parents.

Once the proband has been confirmed as MH susceptible, a blood sample taken at the time of the biopsy will be screened to see if they carry one of the genetic mutations that can be used to test for MH. At present only around 60% of families carry one of these mutations of which there are currently 27. BMHA has obtained a lottery grant to help the Leeds Unit identify more mutations and so increase the number of families that can be offered a genetic blood test for MH. If a mutation is identified then relatives can be offered a preliminary DNA genetic blood test to see if they carry the same familial mutation. If they do then they can be considered MH susceptible without needing to have a muscle biopsy. However if they don't carry the familial mutation then a confirmatory biopsy is required before an MH negative (normal) diagnosis can be made. This is for reasons of safety as the genetics of MH is complex and not completely understood. This follows the protocol set up by the European MH Group.

### Anaesthesia for MH susceptible patients

Safe anaesthesia can be provided but should not be done without due consideration. Members of MH families should be treated as though they are susceptible until they have been formally tested for safety reasons. If you are having a planned operation you will probably be seen by a preassessment nurse. Make sure you tell them about MH, (if

necessary show your red card), its importance and ensure that they inform the anaesthetist if they know who it will be or the anaesthetic department if not. It is then the anaesthetist's job to ensure that you are given safe anaesthesia. In an emergency remember to ask to see the anaesthetist who will very pleased to be forewarned. Again use your warning card to help get the message across to non- anaesthetic staff, and your warning disc is there if you are unconscious when taken to hospital.

If you have a family history of MH it is not always necessary to be tested before any surgery. Clearly in an emergency there would be no time to do this but even in elective surgery provided the anaesthetist is happy that an "MH safe" technique poses no extra risk or difficulty it would be OK to go ahead – but that is the decision of the anaesthetist involved.

Pregnant patients, whether or not it is the mother or father who is MH susceptible, should ask the midwife to arrange for them to see the obstetric anaesthetist during the pregnancy. He/she is responsible for all the anaesthetic services in the maternity unit so can discuss all the possible scenarios and make plans. There is a leaflet available for pregnant patients.

### **Conditions associated with MH**

The only truly associated condition is central core disease (CCD) which is also inherited and located close to the RYR1 gene. It should be emphasised that the vast majority of MH patients do not have CCD and not all CCD patients have MH. CCD is usually a mild non-progressive or slowly progressive muscle disease causing weakness in the arms and legs and sometimes a curved spine and heart problems. Patients who are known to have CCD should regard themselves as potentially at risk from MH if anaesthesia is required and inform the anaesthetist. Patients known to have CCD (because they have had a different kind of muscle biopsy) will be offered screening for MH even if they have not had an anaesthetic problem. Sometimes CCD is discovered by chance when the muscle taken at the biopsy of someone who has had an MH reaction is examined under the microscope by the pathologist.

Some other conditions that may be related to MH are heat stroke which occurs when exercising in hot, humid conditions with heavy loads such as in Army exercise training and exertional rhabdomyolysis which is severe exercise causing muscle breakdown and release of myoglobin. MH patients are not advised to alter their normal activities but, as with all individuals, care must be taken when doing heavy work/exercise in hot, humid environments. The Armed Services are sometimes reluctant to take on a new recruit with MH as it may be difficult to provide safe anaesthesia "in the field" as well as the possible association with heat stroke.

### **Family responsibilities**

MH patients have a responsibility to their family, to ensure they are warned about MH and being prepared to undergo screening for the benefit of the family not just themselves. After a positive biopsy or DNA result a family tree of the whole family not just immediate relatives should be drawn up and everyone warned. In this way another MH reaction, maybe this time fatal, can be prevented. Sometimes there are difficulties in family relationships and in these circumstances the Leeds Unit may be able to help with communication. There is an example letter available for you to use to help explain to the family as well as the information booklet.